

**A COMPARATIVE STUDY ON NUTRITIONAL STATUS AND
PREGNANCY OUTCOMES OF PRE-GESTATIONAL DIABETIC AND
NON-DIABETIC PREGNANT MOTHERS**

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**Thesis submitted to the University of Dhaka
for the degree of Doctor of Philosophy**

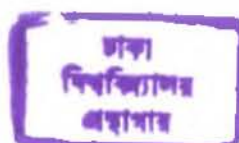
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**Institute of Nutrition and Food Science,
University of Dhaka, Bangladesh
February 2004**

Dedicated
To
The loving memory of my father (late) A K M Shahidul Haque
Mother Nurun Nahar Begum
and
The diabetic and non-diabetic pregnant women
Of Bangladesh

401612



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Shireen Begum

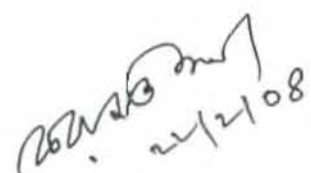
Certificate

This is to certify that the thesis submitted by Shireen Begum bearing the title **“A comparative study on nutritional status and pregnancy outcomes of pre-gestational diabetic and non-diabetic pregnant mothers”** for the award of Ph.D. degree in Nutrition, an independent and original work done by her as a research scholar in the Institute of Nutrition and Food Science, University of Dhaka and that this thesis has not been used as the basis for the award of any degree, or fellowship.

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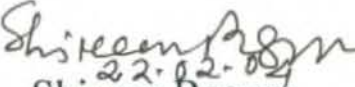
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Declaration

I hereby declare that this thesis entitled “**A comparative study on nutritional status and pregnancy outcomes of pre-gestational diabetic and non-diabetic pregnant mothers**” has been composed by my self and all the works presented here in are my own. I further declare that this work has not been submitted any where for my academic degree.


22.02.2024
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Abstract

Background and objectives:

The diabetic pregnancy is beset with many problems but the pregnancy outcome is largely unknown in Bangladesh. The present study was conducted at Bangladesh Institute of Research and Rehabilitation in Diabetes, Endocrine and Metabolic Disorders (BIRDEM), Dhaka, a specialized tertiary care center for the diabetic pregnant women and their infants. The objectives of this study were to compare the nutritional status, pregnancy outcome and perinatal outcomes of a cohort of diabetic pregnant mothers and their singleton newborns with their non-diabetic counterpart.

Methodology:

This prospective study was conducted on a cohort of two hundred pre-gestational diabetic pregnant women (DM) and their matched control of non-diabetic (NDM) pregnant women. The sample was drawn from the women who attended at the outpatient department of the (BIRDEM) Hospital for antenatal checkup. The total period of study spanned over a period of 19 month (15th May 2000 to 15th December 2001). Pregnant women during their first trimesters (<12th week) were screened and selected for the study. The group was matched for gestational age, parity and occupation of the husband. They were followed up at each trimester of the pregnancy, during labor, postpartum period and the newborns were followed up prospectively by home visits till perinatal period.

The relationships between maternal nutritional status (detected by early pregnancy weight, weight gain, MAC, hemoglobin concentration) and glycemic status (glycosylated hemoglobin percentage and blood glucose levels) in each trimester with the maternal, fetal and perinatal outcomes were examined. Anthropometric measurements of mothers and newborns were taken following standard techniques. Gestational age was detected by last menstrual period (LMP) and subsequently confirmed by ultra-sonography (USG).

Result:

The groups were not different on matching characteristics. They were significantly different ($p<0.001$) in monthly income and education with lower values for DM mothers. The DM mothers were significantly older ($p<0.001$) than their counterparts. Nutritional status at enrollment was significantly different between the groups in all measurements ($p<0.001$) with higher values for DM mothers. The DM mothers were more obese (31.5% vs. 18.0%; $p<0.001$) than the non-diabetic mothers who were underweight (5.5.0% vs. 17.5%) during early pregnancy ($p<0.001$). In all 3 trimesters, the rate of anemia was found more in the DM group and mean hemoglobin concentrations were also lower in this group ($p<0.001$).

Mean values for fasting blood glucose, postprandial blood glucose and glycosylated hemoglobin percentage were higher than normal range for diabetic mothers in the first trimester and gradually declined to normal in the third trimester. Maternal morbidity was more in DM group in all three trimesters ($p<0.001$).

Total weight gain was significantly higher ($p<0.02$) in the DM group (8.6 ± 3.2 vs. 7.9 ± 2.5 kg) than that of the NDM group. Total weight gain between 1st and 2nd trimester was not different between the groups but differed significantly ($p<0.02$) between 2nd & 3rd trimester in favor of the diabetic group. Both the group gained MAC in 1st trimester to 2nd trimester but losses in 2nd to 3rd trimester, but the group difference was not significant.

Live birth rate in the DM group was found 98.0%, which was 100.0% in the NDM group. Breech presentation and cesarean section was more in DM group. The rate of low birth weight was found 21.6% in the DM group and 24.1% in the NDM group in this study. A greater proportion of infants of DM mothers were 'large for gestational age' (LGA) and the difference was significant between the groups at the level of $p<0.001$.

Overall rate of preterm (<37week) in DM was more than the NDM group 41.5% vs 6.2% and baby born <34 week of gestational age was 16.2% in DM group and none in the NDM group. Nutritional status of the newborns was significantly different between the groups with higher values for the DM group by all anthropometric measurements.

Mean birth weight was found significantly ($p<0.001$) greater in the infants of diabetic mothers (IDMs) ($2850.6\pm577.1\text{g}$) than that of the infants of NDM mothers ($2651.1\pm344.4\text{g}$). All macrosomy babies were found among diabetic mothers and IDMs suffered significantly ($p<0.001$) more from perinatal morbidity. Most important perinatal morbidities were jaundice, and respiratory distress syndrome.

Only the infants of diabetic mother experienced perinatal mortality and the rate was observed 55/1000 total births. Diabetic mothers experienced nine (9) fetal losses constituting a rate of 45/1000 total live births compared to no loss in the NDM group. There were 2 abortions, 5 stillbirths and 2 late fetal deaths (IUD) in the DM group. The rate of congenital anomaly was 10/1000 total births in the DM group who were neither under regular antenatal check up or had a euglycemic state throughout the pregnancy.

In DM group strong relationship was found between the maternal nutritional status and fasting blood glucose level with the maternal morbidity. Mothers with glycosylated hemoglobin percentages more than 6.0 % at 3rd trimester was found 3.2 times at risk for developing maternal morbidity.

Relationship was found between the maternal nutritional status and neonatal nutritional status (birth weight & MAC and head circumference) in both the groups. Maternal risk factors identified for developing perinatal morbidity was found monthly income <10,000/- (2.5 fold), total weight gain <7.0 kg (2 fold), 3rd trimester HbA_{1c}% >6.0 (12.5 fold) and for 3rd trimester maternal morbidity (8 fold).

The neonatal factors having risk of developing perinatal morbidity were found, LBW (8 fold), IUGR (18 fold) and apgars score <8 at birth (12 fold). Maternal glycemic status was found significantly associated with large for gestational age (LGA), macrosomy and perinatal morbidity in the DM group.

On multiple regression analyses, newborns of diabetic mothers found to have higher weight, head, chest and mid arm circumferences after controlling possible confounding factors. After controlling all the confounders, family income and total weight gain had shown significant effects on birth weight in both the group.

Conclusion:

Maternal family income, education, nutritional status in early pregnancy, and weight gain during pregnancy, are highly correlated with maternal morbidity and neonatal nutritional status. Maternal glycemic status, maternal morbidity, low weight gain, low family income, low birth weight, low MAC, IUGR and low apgar score were important risk factors for perinatal morbidity. Though adversity in the maternal fetal and perinatal outcomes are more in DM pregnant but the complications can be averted by regular antenatal care and monitoring of blood glucose.

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Abbreviations and Acronyms

DM	Diabetic pregnant women (pre-gestational)
NDM	Nondiabetic pregnant women
GDM	Gestational diabetic pregnant women
IDMs	Infants of diabetic mother
FBG	Fasting blood glucose
GTT	Oral glucose tolerance test
ANC	Antenatal Care
BBS	Bangladesh Bureau of Statistics
BMI	Body Mass Index
BP	Blood Pressure
BWt	Birth Weight
CED	Chronic Energy Deficiency
CHL	Crown Heel Length
CHO	Carbohydrate
CC	Chest Circumference
DCCT	Diabetes Control Complications Trial
DIEP	Diabetes In Early Pregnancy Study
HA	Height for Age
HAZ	Height for Age Z-score
Hb	Hemoglobin
HC	Head Circumference
HBA ₁ C	Glycosylated hemoglobin

HSC	Higher Secondary Certificate
INFS	Institute of Nutrition and Food Science
IUD	Intra-uterine fetal death
LBW	Low Birth Weight
LMP	Last Menstrual Period
MAC	Mid Arm Circumference
MCH	Maternal and Child Health
MAC	Mid Arm Circumference
NPNL	Non-pregnant non-Lactating.
RR	Relative risk
OR	Odds Ratio
PHC	Primary Health Care
PNSS	Pregnancy Nutrition Surveillance System
PPH	Postpartum Hemorrhage
PAHO	Pan American Health Organization
RDA	Recommended Daily Allowance
SSC	Secondary School Certificate
UNICEF	United Nations Children's Fund
Vita	Vitamin
WA	Weight for Age
WAZ	Weight for Age Z-score
WH	Weight for Height
WHZ	Weight for Height Z- score.

Chapter 1

INTRODUCTION

1.1 Introduction

Diabetes is one of the life threatening public health problems in the world. The prevalence of diabetes was 143 million in 1997 and is projected to be 300 million in 2025 (1). Increasing trend was observed due to change in dietary and life style (2). Type-1 diabetes mellitus complicates less than 0.5% of all pregnancies, yet it is one of the greatest challenges in the obstetric medicine (3).

West and Kalbfleisch were the first to report the prevalence of diabetes in Bangladesh in 1966 and found a rate of 1.5% (male: 1.2%; female 2.5%). Their diagnostic criteria were different from the one recommended by the WHO. In 1983, Mahtab and Ibrahim observed a prevalence rate of 0.7% in semi-urban and rural areas (4) and Ali et al in 1987 found a rate of 1.07% in a rural sample (5). Recent studies showed increasing trends in the prevalence of diabetes in Bangladesh, it was 2.1% in 1995 and 4.1% in 1997 (6). This trend is also reflected by a ten-fold increase of registered diabetic cases from 26,349 to 254,656 between 1980 to 2001 at the outpatient department of the Bangladesh Institute of Research and Rehabilitation in Diabetes, Endocrine and Metabolic Disorders (BIRDEM) Hospital. A total of 42631 women was attended among them 1084 was diabetic pregnant women and delivered in this hospital in the year 2000–2001 (7). The rates of pre-gestational (DM) and gestational diabetic pregnant (GDM) were found 2.3% (8) and 4.8% in 2002 in a rural study in Bangladesh (9).

After the discovery of insulin in 1921 there is a considerable improvement of diabetic pregnancy outcomes in well controlled diabetic women (10) but even 12 year's after the Saint Vincent's declaration in 1989, a study in 2002, showed that the infants of women with pre-gestational diabetes mellitus had 6.4 times more at risk of congenital malformation and 5.1 times at risk of perinatal mortality than the infants of general population (11).

In order to identify and quantify the risks of adverse pregnancy outcome in diabetic pregnancies a number of studies have been undertaken spanning different parts of the world including, England, America, Australia, Africa, Caribbean countries, Pakistan, India Srilanka and other Asian countries. It is observed that diabetic gravida are till now at higher risks for increased obstetrical complications including cesarean section, maternal morbidity like, pre-eclampsia, eclampsia, polyhydromnios, ante-partum and post-partum infection, hemorrhage, and pregnancy induced hypertension (12-15).

Though a substantial decrease of the rate of fetal loss and congenital anomalies were documented from the early 19th century (16) but still the adverse effects on fetus and neonates are higher than the general population and nondiabetic pregnant women as observed in a number of studies. Higher rates of fetal loss, congenital malformations, pre-term, large for gestational age, macrosomy, low birth weight, intra uterine growth retardation, intrauterine death, birth injury, birth asphyxia, perinatal morbidity and mortality, neonatal morbidity and mortality were observed very high among the infants of diabetic pregnant women (17,18). Maternal morbidities were also found very high among the of diabetic pregnant women. No ethnic difference was observed for adversity of diabetic pregnancy outcomes (19). The other recent studies also observed similar results of adverse pregnancy outcome of pre-gestational diabetes (20,21).

A few small-scale hospital based studies on diabetic pregnancy in Bangladesh have provided similar results of adverse pregnancy outcomes of diabetic pregnancy (22,23), but these studies had methodological shortcomings, all of these studies were cross-sectional, and retrospective only.

Most of the pregnancy complications especially abortion, malformation, birth defects, and retarded fetal growth take place in early pregnancy and most of these complications occurred in those who had poor diabetic control at conception (24).

Researchers suggested for pre conception care and planning and regular blood glucose monitoring during pregnancy to reduce the adverse pregnancy outcomes for diabetic pregnant women (25,26). Identification and quantification of risk determination of adverse pregnancy outcome are limited due to the fact that most of the studies did not differentiate between the gestational and pre-gestational diabetes in their studies.

We are not aware of any study in Bangladesh where early-pregnancy weight or serial measurements of the weight and blood glucose level in each trimester were examined to see their relationship with maternal, fetal or perinatal outcomes in diabetic pregnant women. The effect and timing of nutritional deficiency and glycemic status at different trimesters on pregnancy outcomes and perinatal outcomes need to be explored and compared in diabetic and non-diabetic mother-infant pair.

The limitation of available literature and to get a clear picture of anthropometric changes in different trimesters, the present study is designed to compare the nutritional status, pregnancy outcome and perinatal outcome of a cohort of diabetic gravida with their non-diabetic counter parts throughout the pregnancy period starting from the 1st trimester. And to explore the relationship between the maternal nutritional status, and glycemic status with that of the maternal, fetal and perinatal outcome.

1.2 Background information

1.2.1 Diabetes: Definition, history and classification

The term diabetes mellitus describes a metabolic disorder of multiple etiologies characterized by chronic hyperglycemia with disturbances of carbohydrate, fat and protein metabolism resulting from defects in insulin secretion or insulin action or both (27)

History of diabetes:

Diabetes Mellitus was recognized in antiquity but its history has been characterized by numerous cycles of discovery, negligence and rediscovery. The term 'diabetes' is Ionian Greek word, which means to 'run through', or a siphon; was first used by *Aretaeus of Cappadocia* in the 2nd century AD. Subsequently, the Roman physician, *Galen (AD 131-201)*, made further improvement in describing the disease. During 5-6th centuries AD, *Susruta* and *Charuka*, two notable Indian physicians and few other *Chinese and Japanese physicians* also described about diabetes and the sweetness of diabetic urine. Later, this was emphasized in the Arabic medical texts. During 9th –11th centuries, *Avicenna (AD 960-1037)* described accurately the clinical feature of diabetes. Blood fluid contains sweet sugar was first reported by *Dobson (1735-84)*.

Insulin was discovered first at 2 *am* on the 31st October 1921 at the University of Toronto through collaboration between *Banting, Best, James and Macleod*. First, they applied insulin to lower blood glucose level in a pancreatectomized dog. In human diabetic patient (*Thompson*) insulin was tested in January 1922 by the Toronto research team and the introduction of regular insulin treatment for diabetes was started in 1923 (28).

Classification and diagnostic criteria:

In 1979, National Diabetes Data group (*NDDG*) proposed for the first time the definition, classification and diagnostic criteria of diabetes. WHO modified this *NDDG* classification in 1980 and later in 1985, which is now widely accepted. These classifications are described below in brief.

A. National Diabetes data group (*NDDG*): Diabetic patients are classified based on the severity and prognosis of the patient:

Type 1 (IDDM): Insulin dependent diabetes mellitus: characterized by more severe and acute presentation, usually involves a significant weight loss and liable to spontaneous ketosis, usually accompanied by subnormal blood c-peptide levels following B-cell destruction.

Type11 (NIDDM): Non Insulin dependent diabetes mellitus: characterized by slow onset, mostly the patients are overweight with less intense hyperglycemia, ketosis is less and usually occurs after prolonged starvation, with strong familial history and involving children & young adult & boys are more affected.

Type-111 (GCI): Gestational carbohydrate intolerance: obese and non obese.

MRDM (Malnutrition related diabetes mellitus): characterized by an onset at younger age, emaciation, heavy glycosuria accompanied by little or no ketonuria (29).

Diagnostic criteria:

For early detection, the proposed blood glucose values are given below in tabulated form as recommended by the WHO Expert Committee Diagnostic value of oral glucose tolerance test:

Diagnostic value of oral glucose tolerance test: (30)

	Glucose concentration, mmol/l (mg/dl)			
	Whole blood		Plasma	
	Venous	Capillary	Venous	Capillary
Diabetes mellitus (DM):				
Fasting value	6.7(120)	6.7(120)	7.8(140)	7.8(140)
2-hrs after glucose load	10.0(180)	11.1(200)	11.1(200)	12.2(200)
Impaired glucose tolerance (IGT):				
Fasting value	<6.7(<120)	<6.7(<120)	<7.8(<140)	<7.8(<140)
2-hrs after glucose load	6.7-10.0 (120-180)	7.8-11.1 (140-200)	7.8-11.1 (140-200)	<12.2 (160-200)

For epidemiological and population screening: the 2-hr value after 75 g oral glucose may be used alone or with fasting value

B. WHO classification: Classification of diabetes mellitus and allied categories of glucose tolerance (30).

1. Clinical classes:

a. Diabetes mellitus (DM):

1. Insulin dependent diabetes mellitus (IDDM)

2. Non-insulin dependent diabetes mellitus (NIDDM):

a. Non-obese

b. Obese

3. Malnutrition-related diabetes mellitus (MRDM)

4. Other type of diabetes associated with certain conditions and syndromes

Impaired glucose tolerance (IGT):

- a. Obese
- b. Non-obese
- c. Associated with certain conditions and syndromes.

II. Gestational diabetes mellitus (GDM)

2. Statistical risk class:

1. Subjects with normal glucose tolerance but having substantial increased risk of developing diabetes:
 - a. Previous abnormality of glucose tolerance.
 - b. Potential abnormality of glucose tolerance (30).

C. New classification of diabetes: (31)

The new classification based on etiological process rather than treatment modality. The new classification proposes that hyperglycemia regardless of the underlying cause, can be subcategorized as follows: (latest ADA /WHO classification)

1. Established Diabetes:

1. Insulin requiring for survival
2. Insulin requiring for control (i.e. for metabolic control, not for survival)
3. Non-insulin requiring (i.e. with treatment by non-pharmacological methods or drugs other than insulin)

Majority of the type-1 diabetics requiring insulin for survival fall in class 1, and majority of the type-2 diabetics fall into the other 2 & 3 classes. This classification will hopefully remove the confusion between insulin dependent and insulin treated.

2. IGT and fasting hyperglycemia:

IGT is not in a separate class like before, but is now categorized as a stage in the natural history of disordered carbohydrate metabolism. IGT is coupled with impaired fasting glucose (IFG: 6.1-6.9 mmol/l; 110-125 mg /dl).

Recent changes of Diagnostic criteria

The diagnostic criteria have been changed on many occasions over recent decades. In 1985, the WHO recommended diagnostic thresholds based on the 75 g oral glucose tolerance test (OGTT), which became the “gold standard” for subsequent years. The epidemiological data collected over the last decade lead both the WHO and the ADA recently to review the diagnostic criteria. The new information related to the fasting plasma glucose (FPG) threshold previously 7.8 mmol/L (140 mg /dl) rather than to the 2 hr plasma glucose (PG) threshold. As a result of these findings the ADA and WHO (in 1997 and 1998 respectively) recommended the following changes.

1. The (fasting plasma glucose) FPG threshold is lowered from 7.8 mmol/l to 7.0 mmol/l (140mg to 126 mg/dl).
2. The (Impaired fasting glycemia) IFG: (FPG 6.1-6.9 mmol/l (110 –125 mg /dl) (31).

1.2.2 Epidemiology of diabetes:

Socio-economic status:

A number of publications documented that poor social class is more prone to develop diabetes and its complication (32). This is also supported by *Barkers hypothesis of fetal origin of diseases*, which states that low birth weight, and under nutrition in pregnant mothers, intrauterine growth retardation and under nutrition in early childhood predispose to adult chronic diseases like diabetes and cardiovascular disease. Malnutrition and infectious diseases in early life predispose to impaired insulin secretion and / or store that might lead to diabetes in adults (33).

Age and parity:

Age was found as a risk factor for diabetes (34). Maternal age is an important determinant of pregnancy outcome. The importance of age is that the adverse pregnancy outcomes were experienced by increment of maternal age (35). A recent study by Seoud in 2002, in Lebanon, found that multiparous older women have a higher rate of antepartum complications like, preterm delivery, cesarean section pre-eclampsia, gestational diabetes, chronic hypertension, labor-induction and also intrauterine fetal deaths compared to younger counterpart. In older primipara, only preterm-delivery, cesarean section rate and uterine fibroid were found higher (36).

Physical activity:

Regarding risk of diabetes and physical activity, study by Berkowitz found that diabetes is more common in the sedentary population (37). But in Bangladesh, a cross sectional survey in village population near Dhaka city, Bari in 1995 found that prevalence of diabetes was equal in both sedentary or active physical workers (38).

Rural urban settings:

Controversial results exist regarding rural urban difference for the prevalence of diabetes. However, rural urban difference was observed in case of female in a study, where the crude prevalence of diabetes was found 11.1% for men & 10.6% for women in urban setting, whereas in rural setting this was 10.3% in men & 4.8% in women (39). On the other hand, in a recent study in 2001 in East Poland, the prevalence of diabetes (Type-2) was detected more in rural than in urban setting (17.6% vs 14.1%) (40).

Nutrient risk for DM:

In a review article, it was suggested that the exposure to nitrosamines in women in Iceland at the time of conception increased the risk of IDDM in their children, particularly for males. To find out a causal association between IDDM and duration of breast-feeding, extensive studies were undertaken and it was found that a short duration of breast-feeding during infancy was associated with an increased risk of developing IDDM. The possible association may point to an etiological role of cow's milk protein. Early introduction to cows milk protein triggers the autoimmune destruction of the beta cells (41).

Epidemiology of insulin dependent diabetes (Type-I)

Insulin dependent diabetes mellitus (Type-I) is a chronic irreversible disease of any age characterized by severe insulinopenia and dependence on exogenous insulin to sustain life. The incidence of the disease shows a wide variation in geographical and ethnic distribution, which has been interpreted as evidence of both environmental and genetic factors in the etiology of (Type-I). The incidence in adult varies from population to population. About 25 to 50% of the patients are diagnosed by the age of 15 yrs, whereas only 10-15 % after the age of 40yrs. In Bangladesh, a marked increase in incidence was observed in recent years (42).

Epidemiology of non-insulin dependent diabetes (Type –2):

It is established that other than genetic predisposition, obesity, increasing age and sedentary habits are the most important risk factors for type-2 diabetes. Central obesity i.e., high waist-hip ratio (WHR) is an important risk factor for type-2 diabetes than the general obesity (43). Most studies observed that subjects with increased waist-hip ratio (WHR) had excess risk for insulin resistance syndrome or syndrome-'X'. This syndrome encompasses central obesity, hyperglycemia, hyperinsulinemia, hypertension and dyslipidemia (44,45).

Aetiopathogenesis of diabetes:

Autoimmune and non-autoimmune causes: In the aetiopathogenesis of diabetes, both autoimmune and non-autoimmune causes are suggested.

Genetic cause: There is an increased risk of developing Type-I, in the family members of those with the disease, which reflects genetic cause.

Environmental factors and autoimmune causes: Certain viral infections like Coxsackie's B virus (especially B-4), rubella, mumps, cytomegalovirus, mycoplasma pneumoniae may be responsible. These infections may damage beta cell directly or by triggering autoimmune responses. Certain vectors, cow's milk albumin, nitrosamine, smoked food and nitrates all are thought to be involved in the genesis of Type-I (46).

High-risk individuals should be screened for:

Type-2: Obesity specially truncal obesity with BMI 30-40 and subjects having one or more parents or siblings with Type-2 and those who are over 70 year of age.

Type-I: One or more siblings with Type-I pregnancy, pancreatic disease and alcohol abuses. Some endocrinopathies including Cushing's disease and use of potentially diabetogenic drugs are also high-risk conditions (46).

Prevalence and epidemiology of pre-gestational and gestational diabetes:

Diabetes is the second commonest medical disorder complicating pregnancy with an annual incidence of about 5%. Pre-gestational diabetes (DM) has an incidence of about 2-4/1000 live births (47). Incidence of gestational diabetes (GDM) varies widely. In Caucasian, it was 1-2 percent, among Asian 4-5% and in the USA it was 3-5%. In the USA study the risk was found more among the non-white women. Increasing maternal age and family history of DM were detected as risk factors for GDM (48).

1.3 Diabetic pregnancy: Basic information

Diabetes mellitus and pregnancy may be presented in two patterns: ^(ADA, 1984)

1. Pregnancy in diabetes (pre-gestational DM): abnormal glucose tolerance either in the form of diabetes or glucose intolerance before gestation.
3. Diabetes in pregnancy (GDM)-defined as carbohydrate intolerance of variable severity with onset or first recognition during present pregnancy (49).

1.3.1 Evolution of classification for diabetes in pregnancy

Priscilla White of the Joslin clinic from Boston, USA, published the best-known classification of diabetes in pregnancy in 1949. Subsequently, she modified this in 1965 and 1971. This classification of diabetes proposed more than a half century ago was accepted worldwide. The white classification is particularly slanted toward women with Type-I except the class-A, which includes women with Type-II. This classification is attempted to predict the outcome of pregnancy, according to various metabolic, obstetric and other risk factors, and graded the prognosis from class-A (best) to class-F (worst). Placement of women into a class depends upon her age, time of onset of diabetes and /or duration of diabetes. Moreover, the emergence of micro vascular or macro vascular (coronary artery disease) complication places her in another class. The most recent revision of this classification was in 1980.

Brown and Hare did a subsequent attempt to update the classification and incorporated two other conditions, ischaemic heart disease and renal transplantation. Another system the “prognostically bad signs in pregnancy” classification is based on the risk factors encountered during the pregnancy itself.

A combination of these two classifications predicts fetal outcomes more accurately, but their complexity has made them obsolete. A uniform classification is still needed for both epidemiological and clinical purposes.

Both the WHO and National Diabetic Data Group (NDDG) of the National Institute of Health have endorsed the classification based on etiology. The WHO classification differs only by recognizing IGT before pregnancy. The WHO classification is simple but has no prognostic value (50).

The White classification (Revised): This classification considers the age of onset, duration of pregnancy and prognosis of diabetes mellitus.

Gestational diabetes: Abnormal OGTT (oral glucose tolerance test) discovered during pregnancy; euglycemia may or may not be maintained by diet alone and insulin may be required.

Class A: Discovered before pregnancy; controlled with diet alone, any duration or age of onset.

Class B: Onset age ≥ 20 y or duration less than 10y.

Class C: Onset age 10-19 y or duration 10-19 y.

Class D: onset age <10 y, duration >20 y, background retinopathy or hypertension (not pre-eclampsia).

Class E: Calcification of pelvic vessels.

Class G: Poor obstetric history.

Class R: Proliferate retinopathy or vitreous hemorrhage.

Class F: Nephropathy with over 500mg /day proteinuria.

Class RF: Criteria for both classes R and F co-exist.

Class H: Atherosclerotic heart disease, heart disease clinically evident.

Class T: Prior renal transplantation.

All classes below A require insulin therapy. Class R, F, RF, H and T have no onset or duration criteria but usually occur in long-term diabetes.

White's classification system is not ideal due to failure to recognize the metabolic instability, which is the principal prognostic factor in the insulin dependent diabetic pregnant patients.

Subsequently, WHO modified and made a simplified classification as follows:

The WHO classification:

Pre-gestational diabetes:

- Insulin dependent diabetes.
- Non-insulin dependent diabetes.
- Secondary diabetes.

Gestational diabetes:

- Impaired glucose tolerance of pregnancy.
- Undiagnosed pre-existing diabetes.
- Undiagnosed pre-existing 'impaired glucose tolerance'.

The most recent classification: by Hare (1994)

1. Uncomplicated DM.
2. Complicated DM +

1. 3. 2 Pathogenesis in diabetic pregnancy

Role of insulin in normal non-pregnant mothers

Insulin is the preeminent controller of fuel storage, release and consumption in mammalian systems. Its levels are low during the fasted state and high in the feed state. These levels affect the availability of fuel endogenously and the storage of fuel when calories are supplied exogenously. In prolonged starvation or fasting state, glucose is supplied by de novo synthesis from stored protein, a process termed '*gluconeogenesis*'. Muscle preferentially releases *alanine* and *glutamine* for gluconeogenesis. When small amount of glucose is taken, in a quantity sufficient to meet the obligatory needs, sufficient insulin is secreted to limit the glycemia and limit gluconeogenesis, thus sparing protein. Large amount of glucose results in greater amount of insulin secretion, and there is not only a suppression of hepatic output of glucose, but also a promotion of peripheral glucose uptake at higher insulin concentrations (51).

Insulin secretion

Insulin secretion by the β -cells is in the central scheme to role of insulin. The beta cells rapidly assess the glucose load and in less than one minute, secrete insulin for prompt disposal of glucose when glucose level rises, and the peripheral uptake of glucose occurs within 10 minutes. At the time of ingestion of full meal, insulin secretion is at its highest level. The fat is stored by several mechanisms. Glucose is conserved as fat, storage of dietary fat is obtained from meal and there is a slowing of lypolysis by higher insulin level. Protein is degraded as amino acid and insulin is stimulated by some of these amino acids. Only protein intake cannot maintain blood glucose level because amino acids derived from dietary protein also stimulates *glucagon*, another hormone secreted by alpha cells of islets of langerhans in pancreas, which stimulates *gluconeogenesis* and *glycogenolysis*. After a carbohydrate rich meal, the rising glucose level diminishes glucagon release. Moreover, glucose and amino acid synergistically tend to increase insulin secretion thus diminishing the liver's need to produce glucose (51).

Protein conservation

Insulin has a ubiquitous effect on protein metabolism. It controls the rate of synthesis and release of protein in the muscle as well as it tends to reshuffle the amino acids that are released by the muscle during fasting. This is why the muscle cells preferentially release *alanine* and *glutamine* during fasting state. Therefore, this mechanism is very finely tuned and insulin is the prepotent hormone for protein synthesis during lactation. The catabolic thresholds are altered by ketoacidosis, trauma and pregnancy. Thus pregnancy, which is associated with higher insulin levels than in the non-pregnant state, also exhibits alterations in tissue sensitivity to insulin and hence, intermediary metabolism. Diabetes is the equivalent of a super fasted state.

The lack of insulin permits the metabolic machinery to run at a faster rate and catabolism (tissue breakdown) to predominate over anabolism (tissue synthesis). All these mechanisms occur in non-pregnant state (51).

Insulin and pro-insulin in normal pregnancy

In normal pregnancy, which is associated with higher insulin levels than in the non-pregnant state, there is alterations in tissue sensitivity to insulin and hence, intermediary metabolism. Insulin secretion increases approximately twofold by the third trimester, but there is a diminished effectiveness at the peripheral levels. This insulin resistance is due to increasing levels of estrogen, progesterone and especially human placental lactogen (hPL), also known as human chorionic somatomammotropic hormone produced by the placenta.

As the placenta increases in size, hPL increases linearly, reaching its maximum concentration in the maternal circulation at approximately 38 weeks of gestation and then decrease just prior to delivery. In the pregnant women, these increasing levels of hPL are responsible for peripheral insulin resistance, hyperinsulinemia, and carbohydrate intolerance (51).

The Insulinogenic Index (the insulin response per unit glycemic stimulus) is significantly greater in normal pregnancy than in the GDM. The insulin secreting capacity of a normal weight gestational diabetic subject is generally less than that of the normal pregnant women. Glucagon secretion is often abnormal in diabetic patients. Fasting plasma glucose is slightly but significantly increased in late normal pregnancy but remains unchanged in gestational diabetes (52).

1. 3. 3 Maternal fetal nutrition

Maternal metabolism in normal and diabetic pregnancy

In the pregnant state, the teleological emphasis changes. The mother must reorder her priorities so that not only the need of the pregnant mother met but also those of the growing fetuses. Therefore, alterations are made in normal metabolic mechanisms to protect both the mother and fetus

Freinkle in 1980 emphasized three important events that occur when the conceptus (placenta and fetus) is grafted onto the maternal uterus, they are as follows:

1. The conceptus becomes an additional site for the metabolism of maternal hormones.
2. The conceptus becomes a new site for hormone biosynthesis.
3. By its own growth, the conceptus alters maternal fuel economy (53).

Intergeneration cycle of poor nutrition

The intergeneration cycle of poor nutrition of girls (as reflected by short stature) and high parity resulting in maternal depletion make a vicious cycle of fetal undernutrition in developing countries (54). It is established that one important component of maternal nutritional status having effect on pregnancy outcome is energy balance, which is reflected in the size of the body stores.

From 1979, the *Pregnancy Nutrition Surveillance System (PNSS)* of the Center for Disease Control (CDC) in the USA showed that pre-pregnancy under weight and inadequate gestational weight gain were both associated with greater risks for low birth weight (LBW) (55).

There have been many changes during the last half-century in the reproductive habits of the people, the technology and management of childbirth and the care of the newborn infants. Throughout this period, birth weight and infant survival has been, and continues to be, a central focus of professional and social interest.

Effect of maternal nutritional status on fetus and Nutrients supply to the fetus

Researchers initially concentrated upon the effects of lack, or excessive intake of individual nutrients on fetal health and then progressed to the attempted definition of minimal and '*optimal dietary intake*' of mothers (56). Now, they have progressed from crude observations to the study of intracellular functions. The logical starting point seems to be with the fetus in utero and with maternal fetal nutritional relationship.

For many years, animal investigations demonstrated that intrauterine nutrition is an important regulator of fetal growth. Recent studies have established that the same is true for human fetuses (57). It is possible that intrauterine nutrition also conditions brain growth and future development. Giard in 1980 summarized the multi-species evidence of ten year from 1970 to 1980 to see the uptake and utilization of carbohydrates and amino acids by the fetus. Roux in 1981 has summarized the evidence of the relation of the maternal-fetal nutrient exchange with respect to fatty acids, neutral fats, phospholipids, sphingolipids, steroids and lipoproteins.

Effect of maternal diet on fetal lipid metabolism indicates that maternal diet can influence synthesis, storage and transport of nutrients to the fetus. The characteristic features of nutrition during pregnancy, maternal-fetal relationships and some effects of nutrition interventions on fetal growth are reviewed by different researchers and found that maternal nutritional status had immense effects on the well being of the fetus, and the fetus makes contact with the maternal organism via the placenta.

Nutrients and oxygen are supplied to the placenta via the uterine artery and are transported to the fetus via the umbilical vein. Carbon dioxide and urea derived from the catabolism of various nutrients in fetal tissues are transported to the placenta via the umbilical artery and excreted in the uterine vein.

Glucose: Glucose crosses the placental barrier by a process of diffusion and the total blood glucose level follows closely to the maternal level.

Amino acid: Amino acid crosses the placenta by active transport. Sometimes it may be influenced by transport competition as well as substrate interaction.

Free Fatty acid (FFA): Free Fatty acid (FFA) transfer is controversial and may be by simple diffusion.

Ketone bodies: Ketone bodies pass freely through the placenta. Some fuels e.g., lactic acid may originate directly in the placenta.

Placental metabolism

The placenta can no longer be considered as an inert membrane across which the nutrients are transferred to the fetus. The placenta through its own metabolism may influence the composition of the nutrient supply from the maternal circulation. In vitro analyses, it has been shown that the placenta has the capacity for amino acid metabolism and its conversion, for lactate production and for lipid synthesis.

The birth weight is dependent upon the growth rate of the fetus and the total length of the gestational period. Human for example, produces small fetal mass (5%) and does so over a long gestational period of 270 days. Though the human fetus has a higher body fat contents (16% body weight) than the other mammals (58).

Factors affecting feto-maternal nutrition

These are as follows:

1. Absolute concentration of individual metabolites in the maternal circulation
2. Placental blood flow:
 - a. Trans-placental transfer mechanism is the main factor for transfer of fuel.

- b. Availability of one fuel may modify another fuel (substrate interaction) e.g., ketone bodies in excess spare glucose and lactic acid as placental oxidative fuel. Maternal glucose crosses the placenta freely by facilitated diffusion and is abstracted continuously in direct proportion to maternal glucose level.
- c. Placenta is not wholly passive in these exchanges but auto regulates its metabolism by influencing trans-placental transfer and also forming new fuel from stored fetal precursors. The transport of maternal fuels to the fetus requires normal placental intermediary metabolism and maternal dietary intake.

Uterine and umbilical blood flows

There is a logarithmic increase in absolute blood flow to the uterus as gestation advances and an increase in blood flow parallel with the increase in fetal body weight. The rise in uterine blood flow results from the increase in maternal cardiac output and a decrease in uterine vascular resistance due to vasodilatation effects produced by estrogens and mediated locally by progesterone. Similarly, the umbilical blood flow increases with fetal age and is related to the gradual rise in the arterial blood pressure and cardiac output of the fetus. However, the relationship between uterine blood flow and placental transport of nutrients is not linear. The changes in uterine blood flow will not therefore necessarily be associated with proportional changes in placental transport of nutrients to the fetus (59).

According to *Pederson theory* (60), during a normal pregnancy, following changes occur in maternal carbohydrate metabolism:

1. Decreased fasting plasma glucose.
2. Increased postprandial plasma glucose level.
3. Beta-cells hypertrophy and hyperplasia.
4. Decreased insulin sensitivity.
5. Enhanced lipolysis .

Metabolic effects of normal pregnancy on carbohydrate metabolism

Physiological changes occur throughout pregnancy, which provide metabolic environment that initially favors maternal fat deposition and latter optimizes fetal growth. By the eighth week of pregnancy, fasting plasma glucose concentrations start to fall and reach its extreme level by the 12 wks of gestation. In contrast, postprandial glucose level rises throughout the pregnancy. Pederson hypothesis states that the fetus responds to increased supply of nutrients by making more insulin and adding fat to organs and thus gains in weight. By the third trimester, increasing *insulin resistance* triggers the cessation of fat accretion, the lypolysis of stored fat, and the release of free fatty acids from fat stores (60).

Catalano and co-workers in 1991 studied insulin response longitudinally in normal and pregnant women and found a 60% decrease in insulin sensitivity by 36 weeks of gestation. Insulin release to glucose load is increased up to 23 times over that in non-pregnant women (61). Mirghani in 2000 concluded that *increasing insulin resistance* in skeletal muscle and liver, which reduces the glucose uptake and increases hepatic glucose production, is a maternal adaptation to the fuel needs of the rapidly growing fetus (62).

Metabolic effects of normal pregnancy on lipid

Though most of the metabolic effects are mediated through carbohydrate metabolism, but understanding of the lipid metabolism is equally important due to the fact that alterations in lipid metabolism have profound effects on carbohydrate metabolism. Particularly, the free fatty acids (FFA), triglycerides, phospholipid and cholesterol are affected by pregnancy related hormonal changes. The plasma level of FFA and glycerol falls from early to mid-pregnancy and then rise significantly. Thus accumulation of body fat occurs in first and second trimester of pregnancy (anabolic phase). In the last trimester of pregnancy, the reverse change takes place with a rise of the plasma level of FFA and glycerol (catabolic phase). Free fatty acids are the alternative

metabolic fuel for the mother and are thought to diminish her glucose utilization and help preserve glucose from the maternal diet for use by the growing fetus. In the fasting state, when insulin levels are low, hPL enhances lipolysis and hence there is an increased production of FFA .

Metabolic effects of normal pregnancy on protein

Plasma protein is decreased in pregnancy. Most amino acid concentrations in fetal compartment are higher than the maternal compartment till term. At term, fetal and maternal plasma ratio of amino acid is similar. Young suggests that the fetal gluconeogenesis is relatively poor and fetal liver conjugating mechanisms are also poor, thus amino acid transport to the maternal circulation is relatively slow. Trophoblastic cell contains metabolically labile amino acids in higher concentration (which is synthesized de-novo by the placenta) than the neutral branched chain and basic amino acids. These metabolic activities have important roles in the delivery of amino acids to the fetus (63).

1. 3. 4 Hormonal changes in normal and diabetic pregnancy

Pregnancy is a great stressful physiological condition in woman during her reproductive period. For nourishment of the fetus, pregnancy brings about important changes in structures, metabolic and endocrine functions of the mother, that tends to become more marked with the advancement of pregnancy. Adjusted maternal fetal-hormonal physiology favors the fetus to get an uninterrupted supply of its fuel according to its needs (64). Extensive hormonal changes occur in pregnancy in order to maintain constant supply of fuel to increasing demands of mother and fetus. The ovaries, fetal adrenal cortex and pancreases all involved in bringing these hormonal changes.

Conceptus as a whole acts as an endocrine structure. Special placental hormones like HCG, hPL, estrogen and progesterone along with maternal other steroid and protein hormones are increased in many folds in an adaptive fashion (65).

Maternal-fetal metabolism in diabetic pregnancy

In diabetes, the normal maternal-fetal nutrient transfer mechanism is amplified and higher concentrations of maternal glucose and other metabolic fuels (tryglycerides, amino acids, free fatty acids & ketone bodies) are transported to the fetus.

It has been hypothesized that the pregnancy related decrease in maternal insulin sensitivity is beneficial for fetal growth, as a rise in postprandial glucose concentration aids in transfer of glucose to the fetus, a process termed "*facilitated anabolism*". Glucose is spared for trans-placental flux and lipogenesis is enhanced for energy reserve. Free fatty acids are used as an alternate fuel source for the mother, while glucose and amino acids are spared for the obligatory needs of the conceptus.

Altered metabolic changes result in maternal hypoglycemia, hypoalaninemia, and hyperketonemia. *This triad of alterations during the fasting state in pregnancy has been called "accelerated starvation" by Freinkel and is apparent after 12-16 hours of fasting.* The enhanced lypolysis has been likened to the "*accelerated starvation*" and it is probably due to placental hormones. The metabolic actions of hPL in the second half of pregnancy include decrease in insulin sensitivity and glucose tolerance, and an increase in lipolysis and proteolysis. In combination, these changes facilitate the transfer of glucose and amino acids to the fetus. Pregnancy therefore exerts true physiological challenge to insulinogenic reserve. Thus impacts on metabolism will be greater when pregnancy and diabetes mellitus co-exist. Pregnancy in established diabetes will worsen the condition. Increased nutritional demands and increasing insulin resistance together accelerate the risk of adverse maternal and fetal outcomes. The fetus responds to increased supply of nutrients by making more insulin and adding fat to organs and gaining weight (66).

1. 3. 5 Effect of pregnancy on diabetes and insulin need in diabetic pregnancy

There are three levels of insulin deficit in diabetic pregnancies. There is a wide range of variation of insulin requirement in Type-1 diabetic pregnancy. The degree of increase is related only to maternal weight gain during 20-29 week of pregnancy and maternal weight at booking. The mildest of these is the woman with gestational diabetes whose only manifestation is an abnormal glucose tolerance test. The fasting glucose level is normal, but after a glucose load or mixed meal, glucose level is higher, indicating underutilization of glucose.

The mother with Type-2 also has to increase her insulin production to counteract pregnancy related insulin resistance. Before pregnancy, these women already have decreased insulin sensitivity. Further demand in pregnancy put stresses on β -cell function causing most 'diet-treated' women to require insulin (or oral agents where the insulin is not available) obligatory in early pregnancy. If the insulin deficit is a bit more severe, the fasting plasma glucose will rise, signifying overproduction of glucose and this elevation occurs in the absence of a meal. Both of these conditions occur in gestational diabetes, which is a relatively mild disturbance of maternal metabolism.

Carbohydrate tolerance deteriorates early in pregnancy in pregestational diabetic women, in parallel with the physiological decrease in insulin sensitivity. Women with Type-I diabetes are dependent on increased insulin dosages to maintain glycemic control. Pregnancy induced lipolysis makes women with Type-I diabetes more susceptible to diabetic ketoacidosis. This can develop quickly and with relatively mild hyperglycemia; if untreated, *may cause fetal death*. Early pregnancy is characterized by enhanced insulin sensitivity. There is a good evidence to support theories of disordered insulin secretion as a primary defect in GDM (66).

1. 3. 6 Effect of diabetes on pregnancy

In diabetes, there are maternal and fetal consequences as a result of abnormal carbohydrate metabolism and derangement of other nutrient metabolism during pregnancy. The birth defect, fetal loss and perinatal loss in diabetic pregnancy are still a major concern throughout the world despite high technology and modern management and remain even today a great challenge for diabetologist, obstetrician and nutritionist. In order to understand adverse effects in fetus, the embryopathic effect of diabetes needs detailed discussion.

1. 3. 6. 1 Effects of diabetes on embryogenesis

Joslin's initial publication concerning diabetes and pregnancy appeared in 1915, seven years before the discovery of insulin. Priscilla in 1949 found that perinatal loss was reduced by insulin but congenital anomalies remained unchanged in infants of diabetic mothers (IDMs).

The teratogenic effect of insulin during embryonic period had first shown in chick embryo by Zwilling in the late 1940s. In 1942, Lawrence and Oakley published their research results and reviewed the existing literature. The authors summarized that by treatment with insulin, maternal morbidity was reduced but fetal death remained very high (49%). The attention of researchers was then to find out the underlying mechanism of this adversity of diabetic pregnancy. The earlier researchers commented that, uncontrolled diabetes could cause major fetal malformation as well as fetal losses through early spontaneous abortions in both humans and animals (67).

Later several reports from different countries spanning 1980 to 1995, confirmed that the rate of congenital anomalies were very high in diabetic pregnancy and poor glycemic control in early pregnancy was responsible for fetal losses and birth defects in diabetic pregnancies (68-70).

Patho-physiology of embryogenesis

The mechanism of the diabetic embryopathy is still incompletely understood. Observation in humans were confused by the inability to separate glucose and other metabolite levels from insulin levels. The intrauterine metabolic environment in early pregnancy also influences embryogenesis and the causes of diabetic malformations are likely to involve both genetic and environmental factors. In early post implantation embryogenesis, even before the development of the chorio-allantoic placenta, the embryo is critically dependent upon glycolysis for its energy supply. Interruption of this energy supply can result in embryonic defects in fetuses of diabetic mothers. Poor glycemic control tends to have both very high and very low blood sugar levels, and there is a possibility that transient episodes of hypoglycemia could be etiological factor (71).

In rodents Gurnot in 2000, showed that maternal hyperglycemia adversely affected the pre-implantation embryo, both by reducing the total number of blastocysts formed and by decreasing the total cell-mass of those that survived and implicated glucose as the major teratogen in diabetic pregnancies. But the precise biochemical mechanisms involved are unknown. Blastocyst cell mass was found reduced predominantly in the inner cell layer and this could be prevented by treating diabetic mothers with insulin from the day of conception (72).

1. 3. 6. 2 Potentially teratogenic processes in diabetic pregnancies

It has recently been implicated that super physiological concentrations of metabolic substrates including glucose, pyruvate and hydroxy butyrate might cause teratogenesis in diabetic pregnancies

1. *Increased production of oxygen derived free radicals.*
2. *Abnormalities of basement membrane components:* Haillwell in 1994- documented enhanced production of oxygen-derived free radicals by immature embryonic mitochondria.

3. *Abnormalities of myoinositol and arachidonic acid metabolism* (73)

4. *Abnormalities of zinc metabolism*: Animal study suggests that maternal diabetes amplifies the embryopathic effects of mild zinc deficiencies. Transfer of zinc from mother to fetus may be impaired. It was documented that abnormal Zn metabolism, particularly hyperzincuria is known to occur in human diabetic subjects and it has been postulated that the excessive Zn excretion in diabetes may lead to marginal Zn deficiency (74).

1. 3. 6. 3 Effect of diabetes on fetal pancreatic development

Insulin is detectable in the fetal pancreas as early as 9 weeks after conception. The growth and replication of β -cells are regulated by the nutritional insulin secretagogues such as D-glucose, D mannose and various essential amino acids. Animal experiments observed that fetal islets depletion is particularly responsive to essential amino acid in early pregnancy and to glucose in late pregnancy. Human studies have shown an increase in pancreatic β -cell mass and also an increase in insulin secretion in fetuses of poorly controlled diabetic women by 16 weeks of gestation. Both conditions increased through the second trimester until 26 weeks of gestation. This priming of fetal cells in mid-gestation may account for the persistent *fetal hyperinsulinemia* throughout pregnancy, even when the expectant mother enjoys good metabolic control and this might be a cause of accelerated growth of the fetus in diabetic mothers.

1. 3. 6. 4 Effect of fetal hyperinsulinemia in diabetic pregnancy

1. Increased growth of insulin-sensitive tissue.
2. Increased deposition of adipose tissue.
3. Accelerated skeletal maturation.
4. Increased hepatic glycogen content.
5. Delayed pulmonary maturation (impaired surfactant production).
6. Delay in switch from fetal hemoglobin to adult hemoglobin.
7. Polycythemia (increased erythropoietin production) (75).

1.3.6.5 Effects of diabetes on fetal growth

Recent work suggested that there might be ethnic differences in the influence of maternal hyperglycemia on infant birth weight, with a significantly greater influence in Asian than in Caucasians. Insulin like growth factor may play a major role in fetal growth. There is evidence that problems of growth retardation may be initiated prior to the 12th gestational week. Mills in 1994 found that the period of greatest fetal wastage and organogenesis occur prior to the 12th week of gestation. It is documented that fetal growth depends on nutrient transfer from mother to fetus, which is ultimately determined by placental size. Uterine blood flow and nutrient supply all these factors can be influenced by maternal diabetes (76).

1.3.7 Diabetic pregnancies: Immunity and infection

A number of studies examined the magnitude of infection and its relationship with diabetes in pregnancy. High rates of maternal infections were observed in diabetic pregnancies and significant association with maternal blood glucose level was also documented. Severe deficiencies in the immune mechanisms involving defective production of leukocytes and lymphocytic activities explained the proneness of infection in diabetic patients (77).

1.4 Nutritional status of diabetic pregnant women

Peterson in 1998 documented the relationship of maternal nutritional status with congenital anomalies (78). A study by Clark in 1997 found that the GDM patients had significantly higher pre-pregnancy weight and higher pregnancy BMI compared to non-GDM patients. Risk for GDM increased with greater weight gain in early adulthood (79). In Bangladesh, in a cross-sectional comparative study at the BIRDEM found that the maternal weight and mid arm circumference (MAC) at term were higher among the pre-gestational diabetic group than that of the non-diabetic group. Similarly, GDM mothers also found to have higher weight and MAC compared to pre-gestational diabetic group in another study at the BIRDEM by the same research group (80).

1. 5 Diabetic pregnancy outcome and complications

Pregnancy in pre-existing insulin dependent diabetic case is a great challenge in obstetric medicine. Prior to the introduction of insulin in 1921, the rate of fetal loss was in excess of 50% due to miscarriage, premature labour, late intra-uterine death and neonatal death. But with improved obstetrical care and medical management, perinatal mortality rates are now comparable with those of the general population. The large-scale study at the Joslin clinic on diabetic pregnant women found the following important pregnancy complications: maternal morbidity, fetal loss, preterm, large for date, macrosomy, and intrauterine late fetal death. Subsequently, the discovery of Insulin has reduced this mortality rate (46). Very few studies were conducted in our country and all of them observed adverse pregnancy outcomes in both gestational and pre-gestational diabetic pregnancies in Bangladeshi women (81,82).

1. 5. 1 Maternal morbidity in diabetic pregnant women

The diabetic gravida is at greater risk for increased obstetrical complications. Major risks for GDM and diabetic pregnancies are high maternal morbidity and mortality. Association between pregnancy induced hypertension and pre-gestational diabetes is clearly documented. Urinary tract infection, a common complication of pregnancy is found significantly associated with mean maternal fasting blood glucose level in DM pregnant women. Different morbid conditions was pregnancy-induced hypertension, pre-eclampsia, pyelonephritis, postoperative endometritis, monilial vulvo-vaginitis, clinical chorioamnionitis, and necrotizing fascitis in poorly controlled diabetic pregnant women. The other common morbidities are postpartum bleeding, and polyhydramnios (83-85).

Past obstetrical history

Compared with the non-diabetics, it was observed in different studies in country and abroad that the diabetic pregnant women suffered significantly more from bad obstetrical histories (86).

Infections

Pregnancy constitutes a state of relative immune deficiency, specially impaired cell-mediated immunity. Patients with insulin dependent diabetes are more prone to develop infection, possibly related to poor metabolic control and also due to deficiencies in immune mechanism. About 80% of Type-I pregnancies were complicated by at least one episode of infection, compared with 26% in non-diabetic women. Most common infections were uro-genital, respiratory, wound, endometrial and post cesarean section infections.

Diabetic gravida were at an increased risk for post cesarean-section infection, compared to non-diabetic women. Monilial vulvo-vaginitis, although benign, may cause significant maternal discomfort and were found more frequent and sever in poorly controlled diabetic pregnant mothers (86). More incidences of postoperative endometritis and wound infections in diabetic mothers were observed. Necrotizing Fascitis, a rare condition involving the vulva is a potentially fatal complication of vulval infection was also found in diabetic pregnancy (87).

Hypertension and related complications

Pregnancy induced hypertension and pre-eclampsia are two important morbidities in DM pregnant women and diabetic pregnancy complicated by pre-eclampsia is of much concern because of poor perinatal outcomes (88). At the Joslin clinic, Green reviewed all diabetic pregnancy outcomes from 1983-1987 and observed that in the White class B, 14.4% mothers suffered from hypertensive complications. In other groups, C, D, F and R rates were 22.4%, 24.8%, 31.2% and 7.2% respectively. Urinary albumin with hypertension or edema is suggestive of risk for pre-eclampsia and eclampsia and complicates diabetic pregnancy (89).

Polyhydromnios

The rate of Polyhydromnios in diabetic mothers was found 12.7% by Nahar in 1992 in Bangladesh (82). Diabetes mellitus may be associated with polyhydromnios and has been reported for approximately 14.0% of all cases of poly hydromnios. There is a wide variation (1.5% to 66%) in the reported cases of polyhydromnios in case of diabetic pregnancies. And the mechanisms are due to macrosomia or due to an imbalance in water movement between the fetal and maternal compartments. Severe polyhydromnios may lead to premature rupture of the membrane (PROM), premature labor, and cord prolapse or abruptio placenta. The mechanism for the increase in amniotic fluid volume has not been clearly understood, but possibly it happens due to fetal osmotic diuresis induced by maternal-fetal hyperglycemia in poorly controlled diabetes (90).

1. 5. 2 Cesarean section in diabetic pregnancy

Diabetic women are more at risk for cesarean section compared to non-diabetic mothers. Though reductions in other adverse pregnancy outcomes were achieved, but the rate of cesarean section is still very high in diabetic mothers. Studies in abroad and Bangladesh (81, 82) also observed that the GDM and DM pregnancies are at greater risk for cesarean sections (91). The importance of early cesarean section is that, it saves the late fetal death; but is also accompanied by increased rate of preterm, which in turn is associated with more perinatal morbidity and mortality.

1. 5. 3 Pregnancy Weight gain

It is believed that low-income non-pregnant women in developing countries subsist at a marginally adequate level of energy balance, which usually determines their body weight for height in the lower limit of reference values. However, when they become pregnant, their energy intakes become limited for both maternal physiological adjustments and for sustaining normal

fetal growth. This is reflected in a low maternal weight for height near term. Thus, higher percentages of these women suffer from both “chronic” and “gestational under nutrition” combined. This has a strong negative effect on fetal growth in non-diabetic pregnant women (92). Different studies in abroad found a strong relationship between weight gain and different obstetrical complications like macrosomia and other fetal outcomes in diabetic pregnant women (93, 94).

1. 5. 4 Birth outcomes of diabetic pregnancy

1. 5. 4. 1 Fetal losses

The most adverse birth outcomes that are increased in a poorly controlled diabetic pregnancy include fetal loss, abortion stillbirth and neonatal death. Though the total incidence of fetal losses has declined dramatically since the introduction of insulin at the beginning of the 20th century, different authors still reported comparative higher losses than the normal population. (95). Mills in 1998 observed 462 pregnancies in 355 women with pregestational diabetes and found 5% termination of pregnancy. Diabetic pregnant women with tight glycemic control from as early as 12th week of pregnancy observed no fetal wastage Relationship between maternal glycemic status and fetal loss was well documented (96). Though controversial results emerged from different research results, but most of the authors suggested for tight metabolic control and pre-conception counseling to reduce the rate of fetal losses in the DM pregnant women. Optimal maternal metabolic control, improved fetal surveillance and intensive neonatal care have together reduced fetal and neonatal losses in the IDDM pregnancies.

1. 5. 4. 2 Spontaneous abortion

In Bangladesh, abortion rate was found 4.8% & 15% by Nahar in 1992 (82) and Karim in 1993 (23) respectively. Forty percent (40%) or more of abortions are due to fetal abnormalities as a consequence of structural, chromosomal or genetic defects. The rate was found higher among the diabetic pregnant women than that of the nondiabetic pregnant women in the diabetic early pregnancy study (DIEP) the DIEP study also observed that maternal blood glucose and glycated hemoglobin percentages prior to and early pregnancy are related with spontaneous abortions in the type-I pregnant women (97). In the Scotland, Penney in 2003 in a prospective population based cohort study with DM mothers found 7.3% abortion and 14.7% miscarriages.

Different threshold values for blood glucose are proposed to be associated with different fetal complications, like spontaneous abortion, stillbirth, and congenital anomalies (98).

1. 5. 4. 3 Stillbirth in diabetic pregnancy

Historically, diabetic pregnancies often were terminated in late, unexpected *intrauterine deaths*. Consequently, obstetric teachings during 1960s and 1970s were dominated by a pro-active approach for early delivery of the diabetic pregnant women, which inevitably resulted in increased neonatal morbidity and mortality from prematurity. Improved obstetric and medical care have since then reduced the frequency of stillbirth, but remained approximately four times higher than that of the non-diabetic population in a study in 1982 (99). It is not clear why well-controlled diabetic women with reassuring antepartum surveillance have an increased risk of intrauterine demise. Different researchers observed increased risk of late fetal deaths in diabetic pregnancies in variable ranges (100-103).

The exact cause of unexplained late stillbirth in diabetic pregnancies is not clear. Animal studies showed that chronic hyperglycemia caused increased aerobic and anaerobic glucose metabolism leading to increased oxygen consumption, increased lactate production, fall in the pH and oxygen tension, ketoacidosis, maternal vascular disease and pre-eclampsia. These changes are thought to be responsible for sudden fetal deaths that may occur late in diabetic pregnancy. Placental dysfunction and competition for essential nutrients may cause hypoxia, acidosis and hypocalcemia in fetus. These may lead to dysrhythmias and severe fetal hypertrophic cardiomyopathy resulting in sudden fetal death. There is also a possibility that greater oxygen affinity of glycated hemoglobin over the non-glycated hemoglobin impairs oxygen delivery to the fetus. Normally, fetal hemoglobin HbF, (high oxygen affinity) is replaced by the adult HbA (lower oxygen affinity) in late pregnancy. Diabetes can alter this by affecting the switch from HbF to HbA (104).

1. 5. 4. 4 Congenital malformation in diabetic pregnancy

Numerous reports from around the world spanning several decades documented higher rates of congenital anomalies in infants of DM pregnant women. Cordero in 1993 showed rates ranged from 6.0%-9.0% for major and minor anomalies in IDMs (105). Following the DIEP study, further study at the Joslin clinic on 451 diabetic pregnant women with known HbA1c% found that, among the women with first trimesteric HbA1c: $\leq 9.3\%$, the rate of major malformation was 3.1% compared to mothers having HbA1c: 12.8-14.4% who had a rate of 33.3%.

Common anomalies were malformations involving the CNS, cardiovascular and skeletal systems (96). Combs in 1991 reviewed and pointed out the fact that all of these malformations arose before the seventh week of gestation (106).

Pathogenesis

Diabetes during pregnancy can amplify the teratogenic effects of a mild maternal zinc deficiency. The possible explanation is that an inhibition of glycolysis could result from some other metabolic disturbances in diabetes, such as elevated butyrate levels. Specific investigation of this possibility however has shown that butyrate reduces ribose availability from the pentose phosphate pathway and thus DNA synthesis is hampered, but does not alter glycolysis.

The other theory is nutrient teratogenesis, which leads to congenital malformation (106). In the event of contradictory or conflicting findings about the pathophysiology of malformation in diabetic pregnancy, there is a need to investigate other factors besides blood glucose level like genetic or other teratogenic nutrients or environmental factors in the development of congenital anomalies.

1. 5. 4. 5 Pre-term in diabetic pregnancy

Premature births were found more among the infants born to DM pregnant women. Coombs and Kitzmiller in 1991 found a 56.0% incidence of pre-term births prior to 37 gestational weeks and a 23.0% incidence before 34 gestational weeks. Longstanding diabetes, especially when associated with peripheral vascular disease and hypertensive complications are more associated with prematurity (106).

Catalano in 1998 explored the relationship between maternal glycemic status and the incidence of preterm and found a strong inverse association between maternal glucose and gestational age. Gestational age was found significantly shortened with higher glucose concentration. Even after controlling the potential confounders, gestation was significantly shortened by 1.8 days for gravidas with glucose concentrations of 100-130 mg/dl and by 4.8 days for glucose concentrations of >130mg/dl (61). Greene and co-workers evaluated complications of prematurity in insulin-requiring diabetic pregnant mothers at the Joslin Clinic between 1983 and 1987. Four hundred and thirteen singleton gestations were reviewed and 110 (26.6%) babies were delivered prior to the 37th gestational week. Causes of preterm were, pre-eclampsia (32.7%), spontaneous rupture of membrane (25.0%), fetal distress (12.5%), idiopathic premature labor (13.5%), hemorrhage (3.8%), Hydromnios (3.8%) and others (4.8%). Greene in 1989 found no relationship between prematurity and maternal age and number of living children, previous term births, history of previous perinatal mortality, or previous spontaneous or induced abortions (107).

Theresa and co-workers in 2001 found a 12 fold increased risk of very preterm in diabetic mothers with high glucose concentration accompanied by chorioamnionitis (108). Regarding the timing of maternal glycemic status, Mello and co workers in a recent observation in 2001, concluded that HbA_{1c} concentration at 28th week of pregnancy was the best predictor for preterm (109).

1. 6 Fetal size in diabetic pregnancy

1. 6. 1 Birth weight

The distribution curve of birth weights of IDMs is shifted to the right of infants of non-diabetic population, so that the former neonates tend to be relatively heavier than the latter, after adjustment for gestational age. This finding suggests that, irrespective of the actual birth weight, all infants of diabetic mothers exceed their genetic potential for growth. Because the immediate risk of gestational diabetes appears to be overgrowth of the fetus (macrosomia) and the control of fetal growth is complex and multifactorial, the exact relationship between glycemic control and fetal size is unclear (110).

Ray et al in 2001 in their Diabetes Endocrine and Pregnancy Outcome Study in Toronto (DEPOSIT) found higher mean birth weight for IDMs compared to non-diabetic women ($3791.0\text{g} \pm 523.0\text{g}$ vs $3593.0 \pm 426.0\text{g}$) and also found a higher rate of LGA babies among those who were not treated properly (111).

1. 6. 2 Birth weight- relation with maternal variables

Fetal macrosomia can occur independently of maternal glycemic control. Recent research results published from 1980 to till date revealed linear relationships of maternal blood glucose level with birth weight of the offspring both in pre-gestational and gestational diabetic women.

A large-scale study (n=1157) on non-diabetic pregnant women in the USA showed a dose response increase in birth weight by 50 g and 200 g paralleled with maternal glucose concentrations of 99-130 mg /dl and >130mg/dl respectively. After controlling the potential confounding variables (age, parity, ethnicity, clinic payment status, smoking, pre-gravid BMI, gestational weight gain, prior low birth weight baby and duration of gestation), higher glucose concentrations were found to be associated with decreased risk of 'fetal growth restriction' ($P<0.05$) and increased risk of 'large for gestational age' ($p<0.001$) (112).

The other factors most consistently predictive of fetal weight are maternal weight followed by total weight gain. However, as maternal obesity increases, particularly greater than 135% of ideal body weight, the influence of maternal weight gain on birth weight decreases. Mothers having Type-I DM over a period of 5 years showed a moderate significant correlation ($r= 0.43$ $p<0.001$) between maternal glycosylated hemoglobin concentration at delivery and birth weight and indicated that 18% of variance in the birth weight could be ascribed due to glycemic control in the third trimester. When compared with the same number of non-macrosomic pregnancies in diabetic women, it was found that the mothers of the macrosomic infants were more obese, had a history of previous macrosomic birth, higher concentrations of serum human placental lactogen and urinary estriols in their third trimesters (113).

Patho-physiology of fetal growth of infants of diabetic mother

Fetal and infant growths are characterized by “critical periods” during which all essential nutrients must be available, otherwise growth and development will not proceed normally (114).

The description of insulin like growth factor-I and growth factor-II by Rinderknecht and Humbel in 1976 and subsequent isolation by Samaan et al made a great advance in the field of infant growth. Later, these factors were termed as ‘*suppressible*’ and ‘*non-suppressible*’ insulin by Froesch et al. But the mechanism of action is still not clear. Naguib and co-workers in 1990 studied insulin like growth factor I and factor II levels in premature, average weight for gestational age, large for gestational age and small for gestational age newborns and found significant differences among the groups ($p<0.01$). ‘Insulin like growth factor-II’ was found lower in SGA and higher in LGA suggesting an important role of ‘insulin like growth factor-II’ in fetal growth (115).

1. 6. 3 Large for gestational age (LGA)

Pre-gestational diabetic mothers were more likely to have babies at either extremes of birth weight while mothers with gestational diabetes mellitus were more likely to have large babies. Women not treated had still higher rates of newborns with LGA.

Different researchers elucidated relationship between maternal glycemic status and LGA. Raychaudhury in 2000, in his study in the UK found that excessive growth of the fetus, which started before the 24 weeks of gestation due to poor glycemic control, continued despite subsequent satisfactory glucose control. So, the author suggested that strict glycemic control during first and second trimester might reduce LGA infants (116).

1. 6. 4 Macrosomia

Macrosomia is a birth weight in excess of 90th percentile when corrected for gestational age and alternatively, a birth weight over 4000g is also described as macrosomia. Clothery in 1995 from his study at Brigham and women's hospital during 1983–1984, concluded that incidence of macrosomia was more in IDMs born to mothers without vascular or renal diseases. This is associated with increased perinatal morbidity and mortality. Maternal risk for macrosomy includes operative delivery (117). So for every pregnant diabetic woman who is obese and periodic fundal measurements are not normal, should have ultrasound examination of the fetus every 4 weeks, starting from 20 weeks of gestation, to monitor fetal growth (118).

Variable rates of macrosomy were observed in different studies conducted in country and abroad. In all Bangladeshi studies, rates were found higher among the IDMs (23, 80). Raised prevalence of macrosomia was observed in DM pregnant women by Langer et al in 1991 (119).

In these studies, the researchers didn't use a standard definition for macrosomy, instead some used a definition of birth weight greater than 90th percentile for gestational age, others used an absolute birth weight greater or equal to 4000.0 g and still others used a cut-off of 4500.0 g.

Percentile rank takes gestational age into account, whereas a static limit does not, so chance of over or under estimation remains in calculating the rate of macrosomy babies in these studies of diabetic pregnant women. There is a need for using a universal standard definition of macrosomy baby by gestational age for research purposes.

Type of macrosomy babies

Recently attention has been focused by researchers for clinical significance of macrosomic babies and grouped the IDMs with macrosomia into *proportionate* (weight proportional to length) and *disproportionate* (weight disproportionately high relative to the length) macrosomy babies. Acker in 1985 observed that the rate of proportionate and disproportionate macrosomy were 26.0% and 19.0% respectively in diabetic pregnant women vs. 7.0% and 1.0% in babies born to non-diabetic women. The disproportionate macrosomic were characterized by *high ponderal index (wt/ht^3)* and the mean body length was significantly less than the proportionate ones. Significance of typing of macrosomy baby is that the disproportionate macrosomy suffers more from different type of morbidities than that of the proportionate macrosomy babies (120).

Complications of Macrosomic babies

Neiger in 1992 found that the macrosomy babies were not only over weight but had increased 'shoulder to head circumference' ratios than their non-diabetic weight matched counterparts. Complications of macrosomia are birth injuries especially brachial plexus injury, asphyxia, and perinatal death. There was a two-fold increase in neonatal mortality rate in those babies who weighted greater than 4500.0 g and had shoulder dystocia. The disproportionate macrosomy babies were more morbid than their proportionate counter part and they suffered more from hyperbilirubinemia, polycythemia and hypoxia. '*Fuel-mediated teratogenesis*' used to describe the long-term effect of macrosomia. The hypothesis is that, these children had altered

response to insulin secretion and childhood obesity with defective neuro-regulation of insulin secretion (121).

Patho-physiology of Macrosomic babies

Patho-physiology of fetal macrosomia is complex. Several factors have been implicated in the fetal macrosomia, including gender, parity, race, pre-pregnancy weight and weight gain during pregnancy (122). Freinkel in 1980 modified this hypothesis to include abnormal fetal metabolism of other metabolic fuels including protein and lipids. Different other animal studies support these findings. The degree to which the level of maternal glycemic control contributes to macrosomia has been subject to much debate. Several studies have found a positive correlation between macrosomia and glucose levels. The argument relating macrosomia to glycemia control ignores the contribution of abnormal levels of other metabolic fuels that stimulate fetal insulin secretion. An elevated serum glucose concentration in diabetic pregnancy is also associated with elevated levels of serum fatty acids and amino acids (123). Further research is needed for elucidation of the role of other nutrients in the causation of macrosomy.

1. 6. 5 Low birth weight (LBW) and intrauterine growth retardation (IUGR) in diabetic pregnancy

Low birth weight (LBW) and intra uterine growth retardation (IUGR) have been reported to be associated with impaired insulin secretion and insulin resistance in the first trimester, which presumably inhibit mitochondrial activity and proliferation of trophoblastic cells of the placenta (124).

Recent experimental studies in 2000 concluded that in the first trimester, stable levels of ambient glucose supply are necessary for normal human trophoblastic growth. Poorly controlled diabetes is often associated with *early fetal and placental growth delay*. Under maternal hyperglycemia, the total number of trophoblastic cells was found lower starting from 7th weeks

to 12th weeks. The data demonstrated that hyperglycemia affects *proliferation and mitochondrial activity of trophoblast* with distinct changes at various stages of embryonic growth in first trimester of pregnancy. The mechanisms underlying the effects on mitochondria and proliferation are different, only the former are sensitive to the intracellular redox-status whereas the latter is an osmotic effect. In diabetic mothers, *hypoglycemia* has been associated with increased risk of *fetal growth restriction*. A relationship between maternal glucose level and fetal growth was also observed in mothers who do not have diabetes (125).

1. 7 Perinatal outcomes in diabetic pregnancy

1.7. 1 Perinatal morbidity

Higher rate of perinatal morbidities in IDMs was observed in different studies. Perinatal morbidity was found 32.0% and the common perinatal morbidities were macrosomia related with birth trauma, RDS, hypoxia, neonatal hypoglycemia, hypocalcemia, hyperbilirubinemia and polycythemia. The occurrence of RDS in infants in diabetic mothers is thought to be the result of fetal hyperinsulinemia suppressing surfactant production (126). Kuo in 1992 observed that hyperbilirubinemia was present in 27.0% of infants in diabetic mothers with glycosylated hemoglobin concentration greater than 7.0% in early gestation (127). Perinatal growth failure in long term causes obesity in adult life in IDMs (128).

A strong positive association was observed between perinatal morbidity and maternal glycemic status. Diabetic patients with tight glycemic control from 12th week of gestation observed no perinatal morbidity. It was observed that disproportionate macrosomic babies were more morbid from hyperbilirubinemia and hypoglycemia in both perinatal and neonatal periods in a case control study between macrosomic and non-macrosomic babies. It is evident that preconception blood glucose control and planned pregnancy with a close monitoring for maintaining euglycemic state throughout the pregnancy can improve the pregnancy outcomes including perinatal morbidity (129).

1.7. 2 Perinatal mortality

Now a day, it is well recognized that the perinatal survival is encouragingly good and there is a 95.0% chance of having a healthy baby as a result of advanced medical, obstetrical and neonatal treatment and management of diabetic pregnancies. One of the major causes of perinatal mortality is congenital anomaly and Kizmiller found 50.0% of the perinatal mortality was due to congenital anomalies (130).

Alam in 1995 and Rowsan in 1998 observed a rate of perinatal death 171.8/1000 live births and 128.0/ 1000 live birth respectively in infants of diabetic mother in Bangladesh (131,132).

A racial difference was noted and the risk was found more in the black population than in the white DM pregnant women (133). For Northeast England Hawthorne in 1997 found four fold risk of perinatal mortality for IDMs (134). There is also a difference between countries. Comparative prospective studies between Norway and North East England between 1994-1997 observed 1.5 fold risk of perinatal mortality for IDMs in Norway, which was higher than North East England (135).

Risk estimation was calculated in a study in abroad. Dunne et al in 1999 in their study found a five-fold risk for perinatal mortality in Type-I DM pregnant mothers complicated by nephropathy than the background population (136).

A secular trend was also observed, the perinatal mortality rate in Tokyo decreased from 10.8% during 1971-75 to 1.1% in 1986-1990 (137). Most of the other authors found higher rates of perinatal mortality in diabetic mothers in England and Wales, Africa and India (138-140).

1. 8 Management of diabetic pregnancy

The pregnancy outcome had started to improve even before the start of the large-scale prospective trial "Diabetes Control and Complication Trial (DCCT)", which reported major reduction in congenital malformation rate with tight glucose control. A matched comparative study demonstrated that early institution of tight metabolic control could prevent adverse pregnancy outcomes observed in gestational diabetic mothers (141).

For pre-gestational diabetic pregnant women, the most important aspect is to have a good glycemic control in pre conception period to lessen the risk of congenital malformations. Careful assessment of diabetic complications is essential before planning for pregnancy. In the absence of major complications, good glycemic control gives the pregnant diabetic mothers the same chance for having a healthy baby as the rest of the population (142).

Numerous studies all over the world were conducted to find out the proper way to improve the adverse pregnancy outcomes of diabetic pregnancies and most of them evidenced that good metabolic control is absolutely necessary for reduction in adverse pregnancy outcomes. Jaff in 1994 also recommended that detection and strict glycemic control are the keys for successful outcomes (143).

It is well documented, that regular blood glucose monitoring among the women who are pregnant or planning to be so should be ensured. But with unplanned pregnancies and pregnancies among women who have not received preconception care are still common.

The services for non-pregnant women need to be as effective as for those attending preconception or ante-natal clinics." This means that diabetes services in general need to be reconfigured to optimize glycaemia over the whole population. A prospective population based study conducted by Langer in 2002 also observed that the mean blood glucose level was a good predictor of perinatal outcomes and intensified management approach was significantly associated with improvement in perinatal outcomes (144).

Hawthorne in 2000 makes a cautious conclusion that major difficulties in all studies conducted on diabetic pregnant women were the lack of a standardized measure of diabetic control in pregnancy. Many different ranges of HbA1C% are in use and it poses a serious problem for all audits in pregnancy including diabetic pregnancy (145)

This review of literature reflects that though some of the studies showed improvement in the pregnancy outcome near to normal but most of the studies till date reported adversity of varying ranges in maternal, fetal and perinatal outcomes associated with diabetic pregnancies. However, all of them agreed that maternal glycemic control prior to pregnancy and pre-conception counseling are essential to substantiate the efforts directed towards the maintenance of euglycemic condition throughout the pregnancy period.

Like the other developing countries Bangladesh needs much more attention in this regard where most of the diabetic pregnant women come for one or two antenatal checkups during the whole pregnancy period.

Only a few come to deliver in modern medical facilities in Bangladesh. So diabetic pregnancy is not timely diagnosed in most centers. To find out the contribution of diabetes and maternal nutritional status in IMR and MMR this study is designed and carried out.

1.9 Rationale

Diabetes is increasing in Bangladesh. Substantial number of diabetes-complicating pregnancy is attending in BIRDEM, total of 1084 pregnant women was attended and delivered in this hospital in the year 2000–2001(7)

Infant mortality rate (IMR) is a sensitive indicator of health status of a country contributes substantially by diabetes and maternal undernutrition.

Also IMR and child morbidity is influenced to a great extent by the rate of perinatal and neonatal mortality and morbidity. Improvement of adverse pregnancy outcome is an important area for work essential to reduce the MMR, IMR and under 5-mortality rate. Maternal nutritional status in normal pregnancy had immense influence on birth outcome and IMR (54). The diabetes itself is a metabolic disorder and brings a number of changes, to diabetic women. Becoming pregnant she is more vulnerable to expose in metabolic alteration, which again influences adversely birth weight, and neonatal health status. On the other hand the mother become more morbid and chance of increased MMR.

We are not aware of any study in Bangladesh where nutritional status by early-pregnancy weight or serial measurements of the weight and blood glucose level of diabetic pregnant women in each trimester were examined to see their relationship with maternal, fetal and perinatal outcomes.

Considering all these lapses the present study was designed to study the nutritional status, pregnancy outcome and perinatal outcome of a cohort of diabetic gravida with their non-diabetic counter parts. And thereby to find out the factors affecting IMR and MMR in relation with maternal undernutrition and diabetes during pregnancy. And to recommend for the diabetic pregnant and malnourished normal pregnant for reduction of IMR and MMR.

1.10 Objectives

General objective:

This study aimed at comparing the maternal nutritional status, pregnancy outcome and perinatal outcome between the diabetic and non-diabetic pregnant women attended at BIRDEM hospital. And to explore the relationship between the maternal nutritional status, and glycemic status with that of the maternal, fetal and perinatal outcome.

Specific objectives:

1. To determine the nutritional status of diabetic and non-diabetic pregnant women by pre-pregnancy weight, height, mid arm circumference (MAC), hemoglobin concentration and blood glucose level at 1st trimester (<12th wk of gestation), 2nd trimester (24-28th wk of gestation) and 3rd trimester (32-34th wk of gestation) of pregnancy.
2. To measure the changes in glycosylated hemoglobin (HbA1C) levels of the diabetic pregnant by different trimesters.
3. To list and compare the outcomes of pregnancy in terms of maternal morbidity, mortality, live birth, stillbirth, pre-term, LBW, healthy newborn, perinatal morbidity and mortality of both groups.
4. To find out the relationship of maternal nutritional status and glycemic status with maternal, fetal, and perinatal outcomes and to recommend appropriate ways and measures to correct them.

Chapter 2

MATERIALS AND METHODS

2. MATERIALS AND METHODS

2.1 Research Design

The study was a prospective matched cohort study comprising 200 pre-gestational diabetic (DM) pregnant women and 200 non-diabetic pregnant (NDM) women as a comparison group. The women were selected following the inclusion and exclusion criteria. Data was collected prospectively starting from the first trimester (<12 week) until the perinatal period. The maternal anthropometry and neo-natal anthropometry was measured following standard techniques. Outcomes of pregnancy in terms of maternal, fetal and perinatal morbidity were listed. Finally, the nutritional status and outcomes was compared between the two groups.

2.2 Study Area and the study subject

Bangladesh is the densely populated country in the world with high infant mortality, low nutritional status, low literacy, high morbidity and low per-capita income. On the other hand because of change of life style factors and food habit the number of chronic diseases like diabetes is increasing.

The Bangladesh Institute of Research and Rehabilitation for Diabetes Endocrine and Metabolic Disorders (BIRDEM) is a tertiary care hospital for diabetic patients. This hospital especially serves the urban semi urban and rural population of the Dhaka city and the refereed cases from other areas of the country. The obstetric and gynecology department of BIRDEM are providing the antenatal, natal and postnatal services to the diabetic and non-diabetic pregnant women and their newborn. The neonatal intensive care unit (NICU) is especially equipped and resourceful to care and serve specially the sick newborn of the diabetic pregnant women. For convenience, this study was confined to BIRDEM hospital for diabetic mother and for non-diabetic pregnant the Rajdhani clinic Magbazar and Central hospital of Dhanmandi

^
mother

(Private clinic/hospital, was also included as they provide standard service to the pregnant of BIRDEM standard).

2.3 Study period

A total period of 19 month from 15th May 2000 to 15th December 2001 the data collection was ended in December 2001.

2.4 Ethical aspects

Ethical clearance was obtained before data collection from Bangladesh Medical Research Council (BMRC). Strict confidentiality was maintained about information obtained and privacy was maintained throughout the study.

2.5 Enrollment of sample

The screening of pregnant women attending BIRDEM hospital for antenatal check-up started at first trimester (before 12 week of gestational age). During screening for enrollment a questionnaire were designed (Appendix 1) which contained several related events and probing questions for correctly assessing maternal age, gestational age and duration of diabetes. At initial enrollment, the subject was informed about the nature, duration and possible utilization of the study and a consent letter in Bengali was signed by them. It was ensured that the participation in the study is entirely voluntary and they could withdraw at any stage of the study.

2.6 Questionnaire

Eight questionnaires and recording formats were designed and used for collecting information. The first questionnaire (*Appendix 1*) was used for screening of the women for enrollment, contained identification information, gestational age, duration of diabetes, number of children, and family history of diseases.

The second part of the questionnaire (*Appendix II*) was used for collecting details information on socio-demographic, past obstetrical information and past medical information.

The third part of the questionnaire (*Appendix III*) provide information of first trimester (Within 12th week of pregnancy) on the nutritional status of mother detected by anthropometric measurements, obstetrical examination of pregnancy (confirmed by obstetrician), clinical examination of mother for maternal health and nutritional deficiency, dietary and drug compliance history, biochemical measurements for hemoglobin, blood glucose and HbA_{1c} for blood glucose control of the diabetic mother and pregnancy outcome of first trimester. The fourth part of the questionnaire (*Appendix IV*) provides same information of second trimester (26th to 28th of pregnancy). The fifth part of the questionnaire (*Appendix V*) provides information of third trimester (32-34th week).

The sixth part of the questionnaire (*Appendix VI*) contains information of delivery & pregnancy outcomes. Record details of delivery, outcome of pregnancy, birth complication, blood glucose level at birth of Infants of diabetic mother (IDMs) and clinical examination of the newborn including Apgar score.

The seventh part (*Appendix VII*) was used to collect data on nutritional status of the newborn by details anthropometry, blood glucose level of IDMs and maternal postpartum nutritional status by anthropometry (3-5days of delivery).

The eighth part recorded (*Appendix VIII*) perinatal morbidity (Confirmed by clinical examination and biochemical test) and details of perinatal mortality.

2. 7 Selection of Subject

The study was a prospective matched cohort study (diabetic pregnant women as cohort and non-diabetic pregnant women as control), comprising 400 pregnant women (200 non-diabetic and 200 diabetic).

A preliminary report (7) showed that out of 25 mothers attending daily at the OPD (out patient department) of the BIRDEM hospital for their antenatal care, on an average 5 to 10 mothers attended for their 1st antenatal visit (within 12th of conception). Among the 10 mothers finally on an average 1 to 2 subjects could be studied daily thus completing 200 DM mothers conveniently by 6 months.

2. 7.1 Diabetic pregnant women as cohort

Inclusion criteria:

Age 20-40 y.

Gestational age <12th weeks.

Women having pre-gestational diabetes
(between 1 and 5 yr.)

Exclusion criteria:

Multiparity (Birth order >5)

Any other medical problem could adversely affected on
pregnancy and delivery.

2. 7. 2 Non-diabetic pregnant women as Control group:

For the control groups the same number of non-diabetic pregnant women attending for antenatal checkup in the Rajdhani clinic, Magbazar and Central hospital of Dhanmandi was enrolled with same inclusion and exclusion criteria. The two groups were matched by:

Gestational age (<12th weeks)

Parity and Husband's occupation

2. 7. 3 Calculation of sample size:

Statistical basis of the sampling:

Two- sample situations.

Hypothesis tests for two population proportions.

Level of significance 5%, Power of the test 90%

P1 (proportion of diabetic pregnant women)

P2 (proportion of non diabetic women)

X (1-p1), p2-p1 (risk difference of the occurrence)

Alternative hypothesis (two-sided test) Risk difference: $\neq 0$

Variable	p1	p2	X=1-p1	p2-p1	S	%In preliminary study(diabetic)	% in prelimin (non diabetic)
Overweight	.26	0	.74	.26	77	26%	0
MUAC>23.5cm	.87	.76	.13	.11	161	87%	76%
Anemia	.54	.23	.46	.31	54	54%	23%
Largefor gestational age(LGA) baby	.35	0	.65	.35	36	35%	0%
Health status >8A/S	.28	.47	.72	.19	125	28%	47%
H/OAbortion	.50	.25	.50	.25	77	50%	25%
Perinatal morbidity	.57	.11	.43	.46	21	57%	11%
Perinatal mortality	.06	0	.94	.88	14	6%	0

Maximum calculated sample size is 161 to get the expected difference between the two groups; by considering 25% non-response or dropout rate the final sample size is 200.

Calculated sample size: 400 (200 DM and as control 200 NDM)

2. 8 Details procedure of selection of sample

2. 8 .1 Diagnosis of the pregnancy and confirmation (88)

Gynecologist did clinical diagnosis and pregnancy test was done as needed. Pregnancy test:

Principle: pregnancy test depends on agglutination reaction of the antigen (HCG) present in urine with antibody either polyclonal or monoclonal available commercially.

Test used:

The standard Immunological techniques used.

1. Direct agglutination test (Betatex direct- Omega diagnostic LTD)

Latex particle coated with HCG antibodies are mixed with urine containing HCG. An agglutination reaction indicates a positive and absence of agglutination reaction indicates a negative one. The sensitivity is 0.5 IU HCG / ml.

2. 8. 2 Duration of pregnancy: Calculation of Expected Date of Delivery (EDD)

The duration of pregnancy has traditionally been calculated clinically in terms of 280 days or 40 weeks calculated from the first day of the last menstrual period and is termed as gestational period.

But fertilization usually occurs 14 days prior to the expected missed period and in a previous normal cycle of 28 days duration, it is about 14 days after the first day of the period. Thus, the true gestation period may be calculated by subtracting 14 days from 280 days i.e. 266 days. This fertilization or ovulatory age is widely used by embryologist (90).

Excellent reliability of Expected date of delivery was done:

First the EDD was calculated by LMP and then confirmed by USG at 16-24 week of pregnancy (88).

Clinical examination for detection of gestational age:

The height of the uterus is:

At second trimester:

Mid way between the symphysis pubis and umbilicus at 16th week.

At the level of umbilicus at 24th week.

At the junction of the lower third and upper two third of the distance between the umbilicus and ensiform cartilage at 28th week.

At third trimester:

The distance between the umbilicus and the ensiform cartilage was divided into three equal parts. The fundal height corresponds to the junction of the upper and middle third at 32 week

Up to the level of the level of ensiform cartilage at 36th week.

At term:

Its come down to 32 weeks level at 40th week because of enlargement of the presenting part. To determine whether the height of the uterus corresponds to 32 weeks or 40 weeks, enlargement of the head should be tested (88).

2. 8. 3 Diagnosis and selection criteria of control

The nondiabetic pregnant having no history of diabetes and hypertension were enrolled. Screening for diabetes was done following O Sullivan's criteria for selection of control by excluding gestational diabetes at first contact or during 24 and 30 week of gestation (31). High risk patient with a history of GDM and bad obstetrical history or large baby in previous childbirth and obese was screened earlier (18-22 week) (88).

Procedure:

For detection of GDM: 2hr after glucose: 75g glucose load if more 7.8 mmol/ l then GDM (with BOH routinely done at first checkup and if any risk factor present then at 28 week of pregnancy and at term).

2 hr postprandiol: after breakfast 7.8 mmol/ l: if no BOH or no risk factor Patient with higher value then advised for *fasting glucose measurement* and if more than 6.0 mmol/l she is diagnosed as GDM. And exclude from the sample. (88).

2. 8. 4 Monitoring of blood glucose of pre-gestational diabetic pregnant women:

Uncontrolled case monitored at hospital at least after 3 days with home monitoring.

Normally 2 weekly in well controlled and routinely 10-14 days at hospital with home monitoring.

At delivery close monitoring and readjustment of blood glucose level was done accordingly.

2. 9 Socio-demographic and other related information

Women's socio-demographic information, past obstetrical history, clinical examination, anthropometry, and biochemical findings were recorded at enrollment. We examined the relationship of maternal nutritional status and other variables at early pregnancy and pregnancy outcome, birth weight and perinatal outcome.

The mother were followed up for 10 months and examined the relationship of maternal anthropometry, maternal glycemic status and other variables in second and third trimester with pregnancy outcome and birth outcome of the two groups.

Finally 187 diabetic mother-infant pair and 199 non-diabetic mother infant pairs provide full information over the 12-month period.

Age, educational status, occupational and smoking status of the mother were recorded. Duration of diabetes, method of diagnosis of diabetes, number of living or dead children delivered (Parity), age of last child, number of conception (gravida), past obstetrical history, past medical history, total

monthly income, previous month expenditure of food, history of consumption of rice, protein, vegetables and oil of both groups were also collected. Husbands' educational and occupational status, monthly income and total monthly family income were recorded along with compliance history of insulin and diet and exercise in case of diabetic mother.

2. 10 Quality control

Observations whether made by human or machine, involve some degree of error. Errors affect two important aspects of data quality—validity and reliability. Anthropometric evaluation like other technique is subject to error in both data collection and interpretation. Therefore there is a need to assess whether the degree of reliability of a given measurement is large or small.

Considering the above-mentioned point the present study computed '**tem**' and '**R**' coefficient of reliability.

The error was computed at three different times of the study, before the starting of data collection, at the eighth month of data collection and at the end of the data collection. Equipment error was checked by calibration of the equipment. Intra-observer error was calculated. Ten subjects not from the study group were used in obtaining the technical error of measurement (**tem**) and reliability (**R**). The TEM was obtained by carrying out two repeated measurements of the same anthropometric variables on the same subject by the same observer.

Technical error of measurement (tem): Defined as the squared root of the sum of the squared differences (Σd^2) of replicates (the same measurement taken on the same subject i.e. standard deviations of replicate measures) divided by twice the number of pairs (2N). The mathematical expression is as follows:

$tem = \sqrt{(\sum d^2) / 2N}$ (where d is the difference between measurements, and N is the number of individuals measured) (147).

One way of assessing the accuracy of a given measurement is to compare the values of 'tem' with values obtained by a well-trained anthropometrist. If the examiners 'tem' comes close to the reference value in a series of repeated measurements can be considered accurate (147).

The present study, the Reliability coefficient was done by using the following formula used for reliability assessment for continually distributed health status variables.

R was calculated using the following equation (147).

$R = 1 - \{(TEM)^2 / (SD)^2\}$ (Where SD is the inter-subject variance) and R denotes reliability coefficient. R ranges from 0-1. The coefficient indicates the degree to which a given measurement is error free. For example, a measurement reliability $R = 0.80$ indicates that the measurement is 80% error free (147).

The intra-observer tem's was calculated along with the co-efficient of reliability (R) based on two repeated measures for each anthropometric variable. The respective TEM and Rs for maternal and neonatal anthropometry is tabulated and compared with reference values cited by several reputable authors (Table a & b) and hence TEMs were not incorporated in statistical analysis.

2. 11 Mothers' Anthropometric Variables

2. 11.1 First trimester at enrollment: (<12 wk)

Height, Weight, Mid Arm circumference (MAC), Body Mass Index (BMI).

2. 11. 2 Second trimester: (26-28 wk) Weight, Mid Arm circumference (MAC), Weight gain, Changes of MAC.

2. 11. 3 Third trimester at enrollment: (29 –36 wk)

Weight, Mid Arm circumference (MAC), Weight gain, Changes of MAC.

2. 11. 4 Postpartum : (3-5 days)

Weight, Mid Arm circumference (MAC), Weight gain, Changes of MAC.

2. 12 Mothers' Bio-chemical Variables : (Each trimester)

Hemoglobin level, Fasting blood glucose level : Corresponding urine sugar, Blood glucose level - 2 hr after glucose/ food: Corresponding urine sugar. Glycosylated hemoglobin percentage (HbA_{1C}), Routine examination of urine. Changes in hemoglobin concentration, Changes in blood glucose level
Changes in glycosylated hemoglobin percentages

2. 13 Mothers' other Variables

A detailed clinical examination of all mothers was done at enrollment, in each trimester and at postpartum.

2. 14 Infant's anthropometric variables

Newborn: (at birth or within 12 hr to 24hr of delivery)

Birth weight, Recumbent length, Head circumference, Chest circumference

Mid Arm Circumference (MAC), Abdominal circumference

2. 15 Infant's bio-chemical variables

Blood glucose level at birth (Only for infants of diabetic mother).

2. 16 Infant's other variables

Gestational age: Determined by LMP of mothers at the time of enrollment and subsequent USG was done for confirmation of gestational age.

2. 17 Infant's Health status

Clinical examination: A detailed clinical examination was done at the time of birth, Apgar score, perinatal morbidity, perinatal mortality

2. 18 Variable (Outcome)

2. 18. 1 Pregnancy outcomes (Maternal)

Complication during pregnancy:

Maternal morbidity and mortality, Type of delivery,
Complication during the process of labor.

2. 18. 2 Pregnancy outcomes (Infant)

Fetal complication:

Fetal loss, abortion, Intra-uterine death (IUD), Stillbirths.

Birth outcomes:

Live birth, stillbirth, Term, pre-term, post-term,
Large for date (LFD), Intrauterine growth retardation (IUGR),
Low birth weight (LBW).

Nutritional status of the newborn: Anthropometric measurements

Health status of the newborn: Clinical examination

Health status of the perinate: Perinatal morbidity, Perinatal mortality

2. 19 Data Collection

The screening and selection of sample was done over a period of 6 months. The socio-demographic and obstetrical information was collected by face-to-face interview. All anthropometric measurements were done at each trimester and postpartum. Neonatal anthropometry was done immediately after birth and /or 12 to 24 hr of birth.

Each household of enrolled sample was visited for collection of perinatal information, which was planned and cross- checked.

Strict confidentiality was maintained about information obtained and privacy was maintained during examination.

2. 20 Anthropometry (Measurement)

2. 20. 1 Maternal Anthropometric Measurements

All anthropometric measurements were taken using the methods described by Jelliffe & Jelliffe (146) and Frisancho (147).

Maternal weight

Maternal weight was measured by using modified DETECTO scale (health scale, automated for weight measurement. The adult automated weighing machine (Health scale) was used to avoid inaccuracy of measurement and parallax error. Checking and calibration before each weighing session was done. Subjects had minimum clothing's, empty stomach and bladder, and without shoes. The balance was placed on a hard flat surface and check from zero balance before each measurement. The subject was stand unassisted, in the center of the platform and asked to look straight a head, standing relaxed. Body weight was recorded to the nearest 0.1 kg (146).

Maternal Height

Heights were taken by the same DETECTO scale (health scale), having a fixed metallic vertical beam bar scale marked in centimeter and millimeter with a movable headpiece to touch the vertex during height measurement. The mother was asked to wear minimum clothing and to maintain an upright position with her feet together and the back of the heels touching the pole of the anthropometer. Then the horizontal arm was lowered onto the subject's head. After ensuring that the subject's heels did not leave the platform the measurement was taken. Height was recorded to the nearest millimeter (0.1

cm). If the reading falls between two values, the lower reading was recorded. Successive measurements were taken within five millimeters. In cases where large amounts of adipose tissue prevent the heels, buttocks, and shoulders from simultaneously touching the wall, subjects asked simply to stand erect.

Mid Arm Circumference

Non-stretchable plastic tapes were used for the measurement of circumferences. By international agreement, the left arm, while hanging freely, was measured to the nearest 0.1 cm at its midpoint (146).

After flexing the elbow to 90 degree, the mid point of the left arm was measured by locating the lateral tip of the acromion at the shoulder and a small mark was made at the identified point. The most distal point on the olecranon process of the ulna (at the point of the elbow) was located and marked. The measuring tape was placed over these two marks on the back of the elbow joint and used to find the midpoint between them, which was marked with a marker pen. Then the arm was allowed to hang freely by the side of the trunk with the palm facing the thighs. The tape was placed around the arm and positioned perpendicular to the long axis of the arm at the marked midpoint. With the tape snug to the skin but not compressing soft tissues, the circumference will be recorded to the nearest 0.1 cm.

2. 20. 2 Newborn's Anthropometry

Pediatric scale was used for measuring newborn's weight and standard wooden anthropometric board was constructed according to UNICEF guideline for measuring recumbent length. In recording measurements three measurements were taken and the average of these three measurements were recorded.

Birth Weight

Pediatric scale with a pan was used to measure the weight of the baby. Scale was calibrated to zero after each measurement. The scale was calibrated

every month using objects with known weight. The infant with a diaper was placed on the scale making sure the weight is distributed equally on each side of the pan (about the center of the pan). Once the infant lying quietly, weight was recorded to the nearest 10g. To obtain a nude weight, weight of diaper was subtracted from the observed weight of infant. Caution was taken to wait for the needle to stop moving and edema was also noted.

Recumbent Length

Recumbent length was obtained using the modified infanto-meter locally made by UNICEF guideline made of plywood. Measuring board was placed on a hard surface or steady table. With the mother's help, the child was laid on the board. The assistant stand on the opposite side of the board facing the measurer to help the child calm and cup his hands over the child's ear with her arms comfortably straight. The child was placed, as such that the head was against the base of the board so that the child looked straight up. The child's line of sight should be perpendicular to the ground. Assistant's head was straight over the child's head and he looked directly into the child's eyes. Then it is ensured that the child is lying flat and in the center of the board. Anthropometrist's left hand was placed on the child's shins (above the ankles) or knees. He pressed them firmly against the board with his right hand, place on the foot piece firmly against the child's heels. The child's positions was checked and repetition of any steps if necessary.

When the child's position was correct, anthropometrist read and recorded the measurement to the nearest 0.1 cm. The foot piece was removed, and the left hand released from the child's shins or knees and supported the child during the recording.

Head Circumference

A narrow, flexible, and non-stretch plastic tape was used and measurements were done to the nearest millimeter (0.1cm).

The infant was with the left side facing the anthropometrist, looking straight ahead so that the line of vision is perpendicular to the body and the Frankfurt plane is in horizontal position. The tape was placed anteriorly just above the supra-orbital ridges covering the most prominent part of the frontal bulge, and posteriorly just over the part of the occipital protuberance, which gives the maximum circumference.

Care was taken to ensure that the tape is at the same level on each side of the head and is pulled tightly to compress the hair. The child's head should be steadied, passing it round the head at the same level on each side, and laying it over the maximum occipital prominence at the back (Parietal eminence laterally and occipital protuberance behind).

Chest Circumference

A narrow, flexile, and non-stretch plastic tape was used and measurements were done to the nearest millimeter (0.1cm). Measurement was done at the level of nipple with no cloth in the body. When the baby was calm and quite lying flat on bed.

2. 20. 3 Maternal biochemical variables

5 ml blood was collected aseptically from each patient.

In BIRDEM, a standard protocol is maintained for sample collection and biochemical investigation. Quality control and time-to-time standardization was also ensured by the hospital.

1. Hemoglobin level:

At each trimester maternal hemoglobin level was estimated by cyanmethemoglobin method.

2. Blood glucose level: Glucose is determined after enzymatic oxidation in the presence of glucose oxidase.

3. Glycosylated hemoglobin percentage (HbA_{1C}):

By Gel electrophoresis was estimated at each trimester.

4. *Examination of urine for glucose:* By Benedicts qualitative method
5. *Urine for albumin :*By Sulpho-salicyalic acid test
6. *Urinary tract infection:* Confirmed by culture sensitivity test

2. 20. 4 Neonatal biochemical variables

Cord blood glucose level of the newborn babies born of diabetic pregnant women was estimated by Glucometer at birth.

2. 21 Data entry and Data analysis plans

Data was entered and analyzed by using (SPSS version -11) software. Distribution of each variable was examined.

The differences in anthropometric and outcome variables between the groups was compared using t-test for quantitative data and normally distributed variables. Non-parametric tests were being done for non-normally distributed variables and chi-square test for categorical data to calculate the differences in anthropometric and outcome variables between the groups. Finally, in order to control the confounding factors, multiple regression analysis was done.

Chapter 3

RESULTS

RESULTS

QUALITY CONTROL

Table a & b shows the results of the reliability analyses of the data. Quality of the data was maintained in this study by reliability analyses before the start of data collection, at the sixth month and at the end of data collection.

Table c shows matching criteria for the two groups, and there was no significant difference between the DM and NDM group on any matching variable.

Basic information

Table 1 presents the basic socio-demographic characteristics of the family. The diabetic mothers were significantly older (28.8 ± 3.6 vs. 27.2 ± 3.4 ; $p < 0.001$) than their non-diabetic counterpart. About 28.0 % mothers from the diabetic group were above 30 years of age compared to only half of them (15.5%) in the diabetic group. It is observed that, diabetic mothers were less educated than mothers without diabetes. Significantly fewer mothers from the DM group were graduates (15.5% vs. 42.5%; $p < 0.001$) and 11.0% of them had education below grade 5 (primary) compared to none from the NDM group. Similarly, the husbands of respondents in DM group were less educated. In the DM group 59.0% were graduates compared to 85.0% in the NDM group.

Significantly more mothers (90.0% vs. 68.0%; $p < 0.001$) in the diabetic group were housewives and only 6.0% of them were employed in some sorts of professional activities compared to $\approx 30\%$ in the non-diabetic group.

The mean $\pm$ SD of total family income was also significantly different between the groups and mean monthly income was less for DM group (Taka: 12821.0 ± 7712.2 vs. 16362.5 ± 7669.8 ; $p < 0.001$). As the distribution was not normal, percentile values were calculated and it was also found that median monthly income was significantly less for the diabetic group (50th percentile value: Taka: 10,000.0 vs. 15,000.0 $p < 0.001$).

Table 2 shows that the total expenditure on food in the diabetic group was less compared to the non-diabetic group but the difference was not significant (Taka: 6311.1 ± 2973.4 vs. 6928.2 ± 3320.5). As the distribution was not normal, percentile distribution was calculated and median values were found, Taka 5000/- and Taka 6000/- respectively for DM and NDM group and this difference was significant ($p < 0.01$). The monthly consumption of rice was significantly higher among the DM group (median consumption in kg: 40.0 vs. 35.0), whereas daily consumption of meat and fish (median consumption in gm: 500 vs. 1000; $p < 0.001$) and monthly oil consumption (median consumption in liter: 4.9 ± 1.6 vs. 5.6 ± 1.8 ; $p < 0.001$) were significantly less in the DM group.

Percentage distribution of family history of diabetes, duration of diabetes and how the diabetes was diagnosed are shown in **Tables: 3 & 4**. Most of the DM pregnant women have got positive family history of diabetes (80.5%) whereas only 14.5% in the NDM group had a positive family history. Between the DM group, about 74.0% was found having this problem for less than 3 years. Although majority in the DM group had a positive family history, only 38.0% was diagnosed to have diabetes on routine medical check up, and 41.0% after general symptoms. Most importantly, 22.0% were diagnosed following severe pregnancy complications like spontaneous abortion, stillbirth and intra-uterine death IUD.

Table 5 presents the past obstetrical history of the pregnant women by groups. Although the groups were matched by parity, there was a significant difference when number of conceptions was considered. The percentage of 4th gravida was significantly more in the DM group (40.0% vs. 16.5%).

Birth spacing was more for the diabetic mothers. The mean age (month) of the last child in the DM group was significantly greater than that of the NDM group (55.6 ± 31.2 vs. 45.3 ± 24.0 ; $p < 0.001$) and about half (51.7%) of them had age of last child more than 48 months compared to only 25.0% in the NDM group.

Table 6 describes the past obstetrical history in their immediate previous pregnancy, the groups were significantly different on a number of variables (Table 6). In the DM group, 61.0% was delivered in the hospital or private clinics whereas this rate was 83.1% in the NDM group. More DM mothers (31.4%) experienced caesarian sections compared to only 5.2% in the NDM group. Significantly less delivery in the DM group were conducted by qualified doctors or nurse (63.4% vs 84.3%; $p < 0.01$). About 44.0% mothers in the DM group had medical complications in their past delivery compared to only 2.4% in the NDM group. The important complications were, gestational diabetes ($n=30$ vs. 1), edema ($n=25$ vs. 1), and hypertension ($n=5$ vs.0).

Table 7 presents the history of the previous delivery in terms of fetal complications, birth complications and specific obstetrical complications. The total abortion rate was 8 times higher among the DM mothers. The rates of IUD and stillbirth were 8.5% and 1% respectively in the DM group as compared to none in the NDM group. Birth complications were also significantly higher in the DM group (14.5% vs.1.9%) and the important complication was asphyxia. History of previous complication was 5 times higher in the DM group. Fetal distress, pre-eclampsia, and prolonged labor were important obstetrical complications.

Comparison of maternal nutritional status (detected by anthropometry), maternal biochemical variables and maternal outcome of the two groups:

Table 8 describes the maternal nutritional status as detected by anthropometry at enrollment (<12 week of gestational age). Although the groups were not different on heights, mean weight in kg (57.5 ± 10.1 vs. 54.3 ± 8.2 ; $p < 0.001$), mean MAC in cm (27.2 ± 2.5 vs. 26.0 ± 2.4 ; $p < 0.0001$) and mean BMI (24.6 ± 3.7 vs. 23.2 ± 3.1 ; $p < 0.0001$) were significantly higher for the diabetic group. Skin fold thickness at 3 places were also measured for a sub-sample and on triceps and biceps skin-fold thickness, the diabetic group showed significantly higher values compared to non-diabetic group.

Table 9 presents pregnancy under nutrition detected by early pregnancy BMI. The diabetic group was more overweight & obese (31.5% vs. 18.0%; $p<0.01$) whereas, the NDM group was more underweight (5.5% vs. 17.5%; $p<0.001$) than their counterpart.

Table 10 shows that, diabetic mothers had significantly higher values compared to non-diabetic mothers for mean weight, MAC and BMI in all 3 trimesters and also at postpartum

Table 11 describes the groups by weight and MAC changes between trimesters. The mean weight gains of mothers between 1st and 2nd trimester were 5.5 ± 2.8 kg and 5.3 ± 2.3 kg respectively for DM and NDM groups. When the total weight gain (between 3rd and 1st trimester) was calculated, the difference still remained significant (8.6 ± 3.2 vs. 7.9 ± 2.5 ; $p<0.02$) between the groups. Weekly weight gain was calculated by dividing the weight changes between 1st and 2nd or 2nd and 3rd or 1st and 3rd trimester by gestational age detected by ultrasonography. Weight gain velocity between 1st and 2nd trimester was greater for DM group (0.328 ± 0.17 vs. 0.302 ± 0.014) and the difference approached significance level ($p=0.08$). Between 2nd and 3rd trimester, the rate declined in both groups (not significant on *paired t tests* in either group) and there was no group difference. But when velocity was calculated between 1st and 3rd trimester, there was a clear group difference with greater values for DM group (0.328 ± 0.13 vs. 0.299 ± 0.10 ; $p<0.01$). Both the groups gained MAC between 1st and 2nd trimester and there was no significant group difference. There was a loss in MAC in both groups over the period of 2nd and 3rd trimester and the difference still remained insignificant between the groups. When the total MAC change was calculated between 1st and 3rd trimester, diabetic group showed a loss of 0.03 cm whereas the NDM group gained 0.18 cm, and the difference was insignificant.

Table 12 presents the distribution in MAC changes over different periods, which was not normal, then the percentile distribution was calculated and nonparametric test (Mann-Whitney U test) was done. There was a loss in

both groups between 2nd and 3rd trimester and the median values were -0.65 vs. -0.40 respectively for DM and NDM group, which were significantly different ($p < 0.01$).

Table 13 & 14 shows the weight gain patterns of the two groups by different nutritional status. Although the sample size was very small in some of the groups, there was a significant group difference (DM and NDM) in the total weight gain between 1st to 2nd and 1st to 3rd trimester in case of underweight mothers. In case of overweight mothers, the weight gain was significantly different between the groups only during 1st to 2nd trimester. There was no significant group difference in case of normal or obese mothers in the total weight gain in any period. Similar pattern was observed when weekly weight gain was considered for different nutritional status of mothers (Table 14).

Table 15 presents the fasting and after breakfast blood glucose levels in all three trimesters by groups. As expected, the NDM group had normal levels (fasting 4.0 – 5.5 mmol/l and 2 hours after food: <7.8 mmol /L) in all 3 trimesters. In case of the DM group, both fasting and postprandial blood glucose levels were slightly higher though these values goes down as the pregnancy progressed.

Table 16 shows the percentages of DM pregnant mothers in different trimesters that were under good control by using two cut-off values for fasting blood glucose level. Taking a higher cutoff value as used by NDDG (National diabetes data group) group, 86.6% of mothers were under good control.

Table 17 presents that in the DM group, mean HbA_{1c} % was 6.4 ± 2.1 at the first trimester and values went down to normal in subsequent trimesters. The percentages of mothers with good control (HbA_{1c}%: <6.0) increased progressively over the trimesters

Table 18 Percentile distributions of the glycosylated hemoglobin (HbA_{1c}) percentages in DM pregnant women showed a gradual increase of good control of blood glucose from first trimester to third trimester.

Table 19 presents the percentages of anemic mothers by different trimesters. In case of the DM group, there was a steady increase of rate of anemia with the progress of the pregnancy. But NDM group did not follow this pattern, rather the rate increased from first (10.6 %) to second trimester (13.0 %) and then decreased at the third trimester (11.6%). In all 3 trimesters, percentages of anemic mothers were more in the DM group compared to the NDM group, especially in 2nd and 3rd trimesters (2nd Trimester: 31.6% vs. 13% and 3rd Trimester: 36% vs. 11.6%).

Table 20 describes that although mean hemoglobin concentrations were within normal range in all 3 trimesters, there were significant differences between the groups in favor of NDM group. There was a fall in the mean hemoglobin concentrations in both groups, from 1st to 2nd trimester and from 2nd to 3rd trimester there was a slight rise in the mean concentration. The decrease in hemoglobin concentrations from 1st to 2nd trimester was significantly greater for the DM group.

Table 21 shows that the more DM pregnant mothers had sugar and albumin in urine compared to very few in the NDM group. Four mothers in the NDM group were found to have urinary tract infection in the 1st trimester and very few mothers in the DM group had so in the 2nd and 3rd trimester.

Table 22 presents that the mean systolic and diastolic blood pressures and pulse rate were within normal range, however the DM group showed significantly higher values compared to the NDM group in all trimesters.

Table 23 shows that the DM pregnant women suffered significantly ($p < 0.001$) more from different types of morbidities throughout the pregnancy than that of the NDM group.

Table 24 describes about the specific morbid conditions of the pregnant mothers in the first, second and the third trimester by groups. In the 1st trimester, 11 cases of threatened abortions were found in the DM group compared to none in the NDM group. Six cases of APH (ante-partum hemorrhage), 9 cases of pregnancy-induced hypertension and 7 cases of pre-eclampsia were found in the DM group in the 2nd trimester. Two cases of

Polyhydramnios were found in the DM group compared to none in the NDM group in the 3rd trimester.

Fig 1 shows that in the third trimester (29th week to term), 85.7 from the DM group and 80.0% from the NDM group did not miss any antenatal visit. About ninety one percent (91.4%) mothers from the DM group and 81.5% from the NDM group attended their regular antenatal visits from 1st contact to 28th week of pregnancy. During this period, only 3.5% in the DM group and 2.0% in the NDM group did not visit at all after their first contact.

Fig 2 presents that, diabetic mothers were delivered mostly by cesarean section (69.3%) and the rest undergoes normal delivery (30.7%). On the other hand only (6.5%) mothers without diabetes were delivered by cesarean section.

Fig 3 shows fetal presentation by groups. It was observed that in the DM group the breech presentation was more among the diabetic pregnancy (11.1% vs. 1.0%), and one case of 'transverse lie' was found only in the DM group (table not shown).

Fig 4 presents the birth complication of the newborns by group. The infants of diabetic mothers suffered more birth complications than their non-diabetic counterpart (25.7% vs. 8.5%) and the group difference was significant.

Fig 5 shows neonatal hypoglycemia (defined as blood glucose level <35 mg/dl or <2.0 mmol/dl) was found only 12.0%.

Fig 6 presents the preterm between the two groups, preterm babies were found more among the IDMs 41.5% than that of the NDM group (6.2 %).

Pregnancy outcomes

Table 25 & 26 shows that there were 9 fetal losses from the first trimester to till delivery and all losses occurred in the DM group. In the first trimester, there were 2 complete abortions. Among 5 losses in the 2nd trimester, there were 2 congenital anomalies and 3 termination of pregnancy due to APH and other causes. In the 3rd trimester there were 2 cases of intrauterine death (IUD) in the DM group compared to none in the NDM group.

Table 27 shows overall rate of preterm (<37week) in DM was more than the NDM group 41.5% vs 6.2 %. No post maturity was found in both the group. The infant of DM born at <32 week and 34 week of gestational age was 1.5 % & 14.7%. From 35 week of pregnancy till 39 week of pregnancy the number of infant from DM group is as follows. The rate was for DM and NDM respectively, 7.4% vs 3.5% at 35 wk, and 17.9% vs 2.7% at 36 wk, 55.8% vs 60.8 at 37 wk, 6.8% vs 14.1% at 38 wk and 1.9% vs 14.6% at 39 wk of pregnancy.

Neonatal nutritional status at birth

Table 28 describes the newborns' nutritional status by anthropometric measurements. In all measurements infants of DM group had significantly greater values compared to infants of NDM group. On average, mean weight in the DM group was about 200g higher than that of the NDM group.

Table 29 shows that a greater proportion of infants of DM mothers were 'large for gestational age' (LGA) and the difference was significant between the groups at the level of $p < 0.001$. The rate of very low birth weight (3.8% vs. 3.5%) and low birth weight (21.6% vs. 24.1%) were not significantly different between the groups.

Table 30 & 31 presents the anthropometric variables and placental weight by gender separately for diabetic and non-diabetic group. The placental weight was found significantly higher for male and except for abdominal circumference in all measurements, male babies had significantly

higher values compared to female babies in DM group and the association was found strong (<0.001) (Table 30). Table 31 shown that the trend of IDMs was absent in the non-diabetic group where there was no sex difference in placental weight. But in the NDM group the birth weight, MAC and head circumference was significantly different by sex but with weak association (<0.05).

Table 32 shows the distribution of intrauterine growth pattern by groups. Intrauterine growth retardation is defined into different groups taking into account of birth weight and gestational age. The number of term-IUGR was significantly less in the DM group ($n= 3.8\%$ vs. 26.4%) and on the other hand, the preterm IUGR were more (about 7 times) in the DM group.

Health status of the neonates detected by Apgar score at birth is shown in the **Table 33**, the present study apgar score below 7 is considered as low apgar score, which needs mild resuscitation. Significantly more babies from DM group were found severely asphyxiated (3.2) and mild asphyxiated (23.7%) compared to only 8.0% from NDM group at 1 minute of birth.

Perinatal outcomes

Table 34: Distribution of health status of perinates by groups is shown in Table 34 Significantly more infants (53.8%) from DM group were morbid during their perinatal period compared to that of the NDM group (13.0%). Most important morbid conditions were respiratory distress syndrome, jaundice and umbilical cord sepsis and more infants from DM group suffered from these conditions.

Table 35 presents perinatal mortality. Perinatal death was found only among the IDMs. Only four (4) early neonatal deaths were observed within 7 days of birth. A total perinatal death was observed 11(5.5%) in IDMs. According to new WHO definition, the perinatal mortality rate includes both the stillbirth rate and the death within 1st week of life, thus constituting a perinatal death rate of $55.0 / 1000$ total live birth in this sample.

Relationship of perinatal morbidity with maternal characteristics

As perinatal morbidity is related to different socioeconomic factors as well as maternal and newborns nutritional factors, we pulled both groups and analyzed risk estimation. The perinatal morbidity of infant from both group had significant relationship with selected socio-economic, and maternal nutritional status in early pregnancy and throughout the pregnancy.

Table 36 shows the relationship of perinatal morbidity with monthly income, maternal education and maternal morbidity in different trimesters. Significantly more risk ($RR=2.5$) was involved when family income fell below Taka 10,000. Similarly, infants whose mothers had education less than SSC were 1.5 times more at risk of developing perinatal morbidity. It was also found that, infants of mothers who were morbid in the third trimester were more at risk for perinatal morbidity ($RR: 7.9$).

Table 37 shows the relationship of maternal nutritional status (early pregnancy weight, total weight gain and height) and risk of developing perinatal morbidity. The infants of those mothers who weighed less than 50.0 kg at early pregnancy (less than 12 week) were 1.4 times more at risk for developing perinatal morbidity. When total weight gain was considered on a cutoff of 7.0 kg, mothers who gained less than that, the babies were more (2.1 times) at risk of developing perinatal morbidity. Maternal height is an important anthropometric indicator for past nutritional status. In our sample, infants of mothers who had a height of less than 150.0 cm were 1.7 times more at risk of developing perinatal morbidity.

Relationship of perinatal morbidity with newborn's nutritional and health status

Table 38 shows the relationship of newborn's nutritional and health status and risk of developing perinatal morbidity. The LBW babies were more at risk of developing perinatal morbidity ($RR=7.7$). If we consider, intrauterine growth retardation, preterm IUGR babies were 18 times more at risk of developing perinatal morbidity. Infants who had Apgar score at 1

minute below 8 were 12 times more at risk of developing perinatal morbidity. Newborns who had MAC below 9.0 cm were 5 times more at risk and those who were overweight or obese ($PI > 2.1$) were 1.6 times more at risk.

Relationship of perinatal morbidity with maternal glycemic status

In a separate calculation, we also estimated risk involved in perinatal morbidity with maternal glycemic status as reflected by $HbA_{1c}\%$ and fasting and postprandial blood sugar in case of diabetic mothers only. **Table 39** shows only those variables, which were significantly related. Maternal HbA_{1c} at 3rd and also at 2nd trimester were good predictor of risk ($RR: 12.46$ and $RR = 3.3$ respectively) for perinatal morbidity. Only fasting blood glucose at 3rd trimester (above 5.0 mmol/l) was detected as a significant risk factor for perinatal morbidity ($RR = 2.1$) than fasting or postprandial blood glucose at any other trimester.

Relationship of LGA with maternal glycemic status

Table 40 Shows relationship of maternal glycemic status at 3rd trimester with macrosomy. Maternal $HbA_{1c}\%$ and postprandial blood glucose at 3rd trimester both were good predictors for macrosomy. The risk of developing macrosomy is six fold when the pregnant women were not under good control of blood glucose as detected by glycosylated hemoglobin percentages 6.0% and above.

Table 41 shows relationship of maternal glycemic status throughout pregnancy with LGA. Maternal $HbA_{1c}\%$ at all 3 trimesters was a good predictor for LGA. Postprandial blood glucose at 3rd trimester (above 6.5 mmol/l) was a significant risk factor for LGA ($RR = 2.8$) than postprandial blood glucose at any other trimester.

Relationship of maternal morbidity at three trimesters with the selected maternal variables

Table 42 Maternal morbidity at third trimester was found to be associated significantly with third trimester ($p<0.002$) and second trimester ($p<0.03$) hemoglobin concentration. In both the trimester the risk of morbidity was increased by two to three folds. The anemia was detected by WHO cutoff value <11.0 gm%.

Table 43 describes the relationship of maternal morbidity at three trimesters with the selected maternal variables having significant association. Maternal morbidity at first trimester, second trimester and third trimester was related with maternal glycemic status at all three trimester, but only the third trimester glycemic status was found to be associated significantly ($p<0.002$) with third trimester maternal morbidity. When the maternal third trimester HbA_{1c} % was above 6.0% the risk of morbidity was increased three fold. The early nutritional status as reflected by maternal MAC <25.5 cm and early pregnancy weight <50.0 kg was significantly related with the maternal morbidity at third trimester. The maternal MAC <25.5 cm reflects more (RR=3.0) the risk of developing morbidity than that of the early pregnancy weight <50.0 kg (RR=1.9).

(BOTH GROUP)

Correlations between newborn's nutritional status (by anthropometric measurements) and selected maternal variable

Socioeconomic:

Table 44 shows the bivariate correlations between newborn's anthropometric measurements and some socioeconomic and biological characteristics of mothers for both groups. Maternal age and education were not significantly associated with any of the newborn's anthropometric measurement whereas monthly family income was significantly associated with all measurements except chest circumference. Birth order (1=first; 2=else) was significantly correlated with birth weight (0.21), baby MAC (0.17), head circumference (0.12) and length (0.15).

Maternal nutritional status:

Birth weight was significantly correlated with early pregnancy weight (0.32), early MAC (0.25) maternal height (0.23) and BMI (0.29). Baby MAC was significantly correlated with early pregnancy weight (0.34), early MAC (0.28) maternal height (0.24) and BMI (0.30). Baby's head circumference was significantly correlated with early pregnancy weight (0.30), early MAC (0.27) maternal height (0.18) and BMI (0.29). Baby's recumbent length was significantly correlated with early pregnancy weight (0.38), early MAC (0.27) maternal height (0.52) and BMI (0.18). Baby's chest circumference was significantly correlated with early pregnancy weight (0.20), early MAC (0.18), maternal height (0.12) and BMI (0.20). Placental weight showed significant correlations with all the newborn's anthropometric measurements especially with birth weight (0.67) and MAC (0.58) where correlations were high. Total weight gain was significantly correlated with all newborn's anthropometric measurements and explained more for birth weight (0.40) and head circumference (0.33) (**Table 44**).

Maternal glycaemic status and hemoglobin status.

Table 45 Maternal Hb% at 2nd trimester showed significant correlation with only chest circumference whereas at 3rd trimester with baby MAC (0.16) and head circumference (0.16) only. Birth weight was significantly correlated with 1st and 2nd trimester fasting blood glucose level whereas baby MAC was significantly correlated with 2nd and 3rd trimester fasting blood glucose level. Chest circumference became significantly related with only 1st trimester fasting blood glucose level. Postprandial blood glucose levels at 2nd and 3rd trimester were significantly correlated with birth weight and baby MAC. Chest circumference was significantly correlated with 2nd trimester postprandial blood glucose level.

(DM GROUP)**Correlations between newborn's nutritional status (by anthropometric measurements) and selected maternal variable***Socioeconomic:*

Table 46 shows the bivariate correlations between newborn's anthropometric measurements and some socioeconomic and biological characteristics of mothers for DM group. Family income was significantly associated with newborn's all anthropometric measurements including chest circumference. Maternal age and education were not significantly associated with any of the newborn's anthropometric measurement whereas monthly family income was significantly associated with all measurements except chest circumference. Birth order (1=first; 2=else) was significantly correlated with only baby MAC (0.17), and length (0.18).

Maternal nutritional status:

A strong positive association was observed between the newborns nutritional status and maternal nutritional status. Birth weight was significantly correlated with early pregnancy weight (0.28), early MAC (0.21) maternal height (0.18) and BMI (0.31). Baby MAC was significantly correlated with early pregnancy weight (0.30), early MAC (0.24) maternal height (0.18) and BMI (0.30). Baby's head circumference was significantly correlated with early pregnancy weight (0.27), early MAC (0.26) maternal height (0.18) and BMI (0.28). Baby's recumbent length was significantly correlated with early pregnancy weight (0.35), early MAC (0.28) and BMI (0.22). Maternal height was observed having very strong correlation with newborns length (0.54). Baby's chest circumference was significantly correlated only with early pregnancy BMI (0.19). Placental weight showed significant correlations with all the newborn's anthropometric measurements specially birth weight (0.67). Total weight gain was found significantly correlated with all newborn's anthropometric measurements and explained more for birth weight (0.35), MAC (0.30) and head circumference (0.30).

Maternal glycemic status and hemoglobin status:

Table 47 Maternal hemoglobin concentration at 3rd trimester showed a significant correlation with length of the baby also positively correlated with (0.17) and head circumference (0.15) only. Glycemic status at 2nd trimester was significantly correlated with birth weight (0.24) baby MAC (0.25) and chest circumference (0.28). Postprandial blood glucose levels at 1st and 3rd trimesters were not significantly correlated with any of the newborn's anthropometric measurement. But fasting blood glucose at 1st trimester(0.22) and postprandial blood glucose at 2nd trimester(0.30) showed strong positive correlation with birth weight of the newborn.

(NDM GROUP)**Correlations between newborn's nutritional status (by anthropometric measurements) and selected maternal variable***Socioeconomic:*

Table 48 shows the bivariate correlations between newborn's anthropometric measurements and some socioeconomic and biological characteristics of mothers for NDM groups. Maternal age was not significantly associated with any of the newborn's anthropometric measurement whereas maternal education showed strong association but explains less (0.14) than that of the monthly family income (0.16). Monthly family income was significantly associated with all measurements except recumbent length.

Maternal nutritional status:

Birth weight was significantly correlated with early pregnancy weight (0.33), early MAC (0.28) maternal height (0.32) and BMI (0.34). Baby MAC was significantly correlated with early pregnancy weight (0.37), early MAC (0.26) maternal height (0.35) and BMI (0.31). Baby's head circumference was significantly correlated with early pregnancy weight (0.33), early MAC (0.24) maternal height (0.20) and BMI (0.30). Interestingly Baby's recumbent length was highly significantly correlated with maternal height (0.52) and then early

pregnancy weight (0.35), early MAC (0.20) and BMI (0.28). Baby's chest circumference was significantly correlated with early pregnancy weight (0.20), early MAC (0.19), and BMI (0.15). Total weight gain was significantly correlated with all newborn's anthropometric measurements and explained more than the IDMs for birth weight (0.48) and MAC (0.46). Placental weight showed significant correlations with all the newborn's anthropometric measurements especially with birth weight (0.79), baby MAC (0.63) and length (0.55) where correlations were high.

Table 49 presents the comparison of macrosomy babies born to diabetic mother with that of the non-macrosomy babies by selected maternal variables. *Mann-Whitney U test* was done and found significant relationship. Maternal weight gain per week was found significantly different between the two groups. The mean $\pm$ SD of weight gain was found higher among the mother of the macrosomy babies. Third trimester fasting blood glucose and postprandial blood glucose and glycosylated hemoglobin percentages was found highly significantly different between the groups with a greater value for macrosomy babies.

Multiple regression analysis to see the independent effect of diabetes on newborn's anthropometry.

As newborn's weight, height MAC and other anthropometric measurements were related to income, maternal education, maternal anthropometry and other factors, we calculated a series of multiple regression analyses to control the effects of these confounders in order to see the independent effect of diabetes on newborn's anthropometry.

Table 50 shows the multiple regression model where each of the newborns anthropometric measurement was predicted in separate analysis. Only those variables, which we found significantly and highly correlated with the newborn's anthropometric measurement in bivariate analyses were either offered or entered as independent variables in block 1 and 2. In the 1st block

for all measurements except chest circumference we entered sex and monthly income. In the 2nd block, we offered early pregnancy weight; early pregnancy MAC and total weight gain for all measurements. Birth order was additionally offered in case of baby MAC, head circumference and recumbent length. As maternal height was highly significant in bivariate analyses, we offered maternal height as extra variable in case of recumbent length. Finally, in the 3rd block we forced to enter the group.

Table 50.a shows that total income; early pregnancy weight and total weight gain predicted birth weight significantly. After controlling all these, diabetes had independent effect on birth weight.

Table 50.b shows that total income, early pregnancy weight and total weight gain and birth order significantly predicted baby MAC. After controlling all these, the group did not show any effect on baby MAC.

Table 50.c shows that early pregnancy weight and total weight gain significantly predicted baby head circumference and group did not show any effect on baby head circumference.

Table 50.d shows that maternal height, maternal MAC and total weight gain significantly predicted recumbent length. After controlling all these, the group did not show any effect on recumbent length.

Table 50.e shows that early pregnancy weight and total weight gain significantly predicted chest circumference of the newborn. After controlling all these, diabetes had independent effect on chest circumference.

Tables:*Table: a*

Reliability coefficient(R) & Intra class correlation coefficient (r)
of the researcher in comparison to supervisor
(Maternal anthropometry)

<i>Maternal anthropometric Variable</i>	<i>Intra-class correlation coefficient(r)</i>	<i>Reliability coefficient (R)</i>
Weight (kg)	0.98	0.97
Height (cm)	0.96	0.96
Mid arm circumference (cm)	0.97	0.97

Table: b

Reliability coefficient(R) & Intra class correlation coefficient (r)
(Neonatal anthropometry)

<i>Neonatal anthropometric Variable</i>	<i>Intra-class correlation coefficient(r)</i>	<i>Reliability coefficient (R)</i>
Weight (gm)	0.97	0.98
Recumbent length (cm)	0.94	0.92
Mid Arm Circumference (cm)	0.92	0.93
Head circumference (cm)	0.91	0.91
Chest circumference (cm)	0.95	0.95
Abdominal circumference (cm)	0.92	0.93

Table: c

Matching characteristics of the two groups at enrollment

Matching variables	DM (n=200)	NDM (n=200)	p value
Gestational age:			
By LMP ¹	9.3±2.0	9.5±2.0	NS
By USG ¹	8.6±2.0	8.9±1.9	NS
<10 wk ²	46.5	46.5	
10-12 wk ²	53.5	53.5	
Parity:			
Primi ²	14.0	14.0	NS
Multi-Para ²	86.0	86.0	
Husband's occupation:			
Office Work ²	43.0	43.0	
Business ²	40.5	41.0	NS
Other ²	16.5	16.0	

DM: Diabetic; NDM: Non-diabetic

¹ Independent sample t-test done² values Percentages and χ^2 test performed

Table: 1

Socio-demographic characteristics of the family by groups

Variables	DM (n=200) n (%)	NDM (n=200) n (%)	p value ^a
Age of mother (y):			
Mean±SD ¹	28.8±3.6	27.2±3.4	<0.001
<25	35 (17.5)	71(35.5)	
25-30	109 (54.5)	98 (49.0)	<0.001
31-35	56 (28.0)	31(15.5)	
Mother's education:			
<5y schooling	22 (11.0)	nil	
6-10 y schooling	41 (20.5)	20 (10.0)	<0.001
SSC to HSC ²	106 (53.0)	95 (47.5)	
Graduate & above	31 (15.5)	85 (42.5)	
Husband's education:			
<5y schooling	5(2.5)	nil	
6-10 y schooling	17(8.5)	2(1.0)	<0.001
SSC to HSC ²	60(30.0)	28(14.0)	
Graduate & above	118(59.0)	170(85.0)	
Respondent's occupation:			
Housewife	180(90.0)	136(68.0)	
Service	12(6.0)	59(29.5)	<0.001
Others	8(4.0)	5(2.5)	
Family income per month (Taka): Mean±SD ¹	12821.0±7712.2	16362.5±7669.8	<0.001
Percentile 25	7000.0	10000.0	
Percentile 50	10000.0	15000.0	<0.001 ^b
Percentile 75	15000.0	20000.0	

¹ independent sample t test performed²SSC: Secondary School Certificate, HSC: Higher Secondary Certificate^a p value for χ^2 test^b p value for Man Whitney test;

Percentages in the parenthesis

Table: 2

Percentile distribution of last month's expenditure and consumption of food by groups

<i>Variables</i>	<i>DM (n=200)</i>	<i>NDM (n=200)</i>	<i>p value</i> ²
Monthly total expenditure on food (Taka):			
<i>Mean±SD</i> ¹	6311.1±2973.4	6928.2±3320.5	NS
25 th percentile	4000.0	5000.0	
50 th percentile	5000.0	6000.0	<0.01
75 th percentile	8000.0	8000.0	
Monthly consumption of rice per family per month (kg):			
<i>Mean±SD</i> ¹	41.0±16.4	35.6±14.1	<0.001
25 th percentile	30.0	30.0	
50 th percentile	40.0	35.0	<0.002
75 th percentile	45.0	40.0	
Daily consumption of fish & meat (gm):			
<i>Mean±SD</i> ¹	628.3±416.1	835.3±815.9	<0.002
25 th percentile	250.0	500.0	
50 th percentile	500.0	1000.0	<0.001
75 th percentile	1000.0	1000.0	
Monthly consumption of oil (liter):			
<i>Mean±SD</i> ¹	4.9±1.6	5.6±1.8	<0.001
25 th percentile	4.0	5.0	
50 th percentile	5.0	6.0	<0.0001
75 th percentile	6.0	7.0	

² *p value for Man Whitney test*

¹ *p value Independent sample t-test*

Table: 3

Family history of diabetes by groups

<i>Variables</i>	<i>DM (n=200) Percentages</i>	<i>NDM (n=200) Percentages</i>
Nothing contributory	19.5	85.5
Father	29.5	6.0
Mother	16.5	5.0
More than one member of the family	23.5	2.0
Other close relative	11.0	1.5

Table: 4

Duration and diagnosis of diabetes in the DM group

<i>Variables</i>	<i>DM (n=200) Percentages</i>	<i>Percentages</i>
Duration of diabetes:		
Mean±SD	27.9±15.9	
<12 month	46	23.0
13-24 month	49	24.5
25-36 month	52	26.0
37-48 month	28	14.0
49-60 month	25	12.5
How diabetes was diagnosed:		
Routine medical checkup	75	37.5
Following symptoms	82	41.0
Following spontaneous abortion	25	12.5
Following IUD	17	8.5
Following still birth	01	0.5

Table: 5

Past obstetrical history by groups

<i>Variables</i>	<i>DM (n=200) n (%)</i>	<i>NDM (n=200) n (%)</i>	<i>p value^a</i>
Number of conception (gravida)			
1 st gravida (primi)	16 (8.0)	28(14.0)	<0.001
2 nd gravida	51 (25.5)	76(38.0)	
3 rd gravida	53 (26.5)	63(31.5)	
4 th gravida	80 (40.0)	33(16.5)	
Age of last child (mo)			
<i>Mean±SD¹</i>	<i>55.6±31.2</i>	<i>45.3±24.0</i>	<0.001
11-24	19(11.0)	8(4.7)	<0.001
25-36	36(21.0)	70(40.7)	
37-48	28(16.3)	51(29.6)	
49 & above	89(51.7)	43(25.0)	

Percentages in the parenthesis;

^a *p value for χ^2 test*¹ *p value by independent sample t-test*

Table: 6

Past obstetrical history by groups (continued)

<i>Variables</i>	<i>DM (n=172)* n (%)</i>	<i>NDM (n=172)* n (%)</i>	<i>p value^a</i>
Place of past delivery:			
Hospital or private clinic	105(61.0)	143(83.1)	<0.01
Home delivery	67(39.0)	29(16.9)	
Method of past delivery:			
Normal delivery	114(66.3)	160 (93.0)	<0.001
Cesarean section	54(31.4)	9(5.2)	
Therapeutic delivery	4(2.3)	3(1.8)	
Delivery conducted:			
Doctor /nurse	109(63.4)	145(84.3)	<0.01
Traditional birth attendant	32(18.6)	21(12.2)	
Untrained Dai	23(13.4)	6(3.5)	
Relative/untrained personnel	8(4.6)	nil	
Past medical complications:			
Yes	75(43.6)	4(2.4)	<0.001
No	97(56.4)	168(97.6)	
Specific medical complications:			
Hypertension	6	nil	<0.001
Edema	25	1	
Hypertension and edema	12	1	
Gestational diabetes	30	1	
Other	2	1	

Percentages in the parenthesis^a *p value for χ^2 test** *excluding 28 primi cases*

Table: 7

Past obstetrical history by groups (continued)

<i>Variables</i>	<i>DM (n=172) n (%)</i>	<i>NDM (n=172) n (%)</i>	<i>p value^a</i>
Fetal complications			
Yes	99(57.6)	7(4.0)	<0.001
No	73(42.4)	165(96.0)	
Specific Fetal complications			
One abortion	54(31.4)	7(4.0)	<0.001
Two & above abortion	27(15.7)	nil	
Late fetal death (IUD)	16(9.3)	nil	
Still birth	2(1.2)	nil	
Past birth complication			
Yes	25(14.5)	3(1.9)	<0.001
No	147(85.5)	169(98.3)	
Specific birth complications			
Asphyxia	16	1	<0.001
Umbilical cord sepsis	3	nil	
Jaundice	3	nil	
Other	2	2	
Past obstetrical complication			
Yes	65 (37.8)	12 (7.0)	NS
No	107(62.2)	160(93.0)	
Specific obstetrical complications			
Fetal loss	3	1	
Prolonged labor	17	2	
Induction failure	6	4	
Ruptured membrane	1	nil	
Pre-eclampsia	9	2	
Maternal distress	5	nil	
Fetal distress	14	1	
Other	10	2	

^a *p value for X² test*

Table: 8

Maternal biological characteristics at enrollment (<12wks of gestation).

<i>Variables</i>	<i>DM (n=200) Mean±SD</i>	<i>NDM (n=200) Mean±SD</i>	<i>p value¹</i>
Weight (kg)	57.5±10.1	54.3±8.2	<0.001
Height (cm)	152.5±4.6	152.7±4.6	NS
BMI	24.6±3.7	23.3±3.1	<0.0001
MAC (cm)	27.2±2.5	25.2 ±2.4	<0.0001
Triceps SKF in (mm) ²	15.3±4.5	14.0±5.0	<0.03
Biceps SKF In (mm) ³	10.0±2.9	9.1±3.7	<0.05
Sub Scapular SKF in (mm) ⁴	24.2±6.3	22.7±6.6	NS

²: DM (n=123), NDM (n=109), ³: DM (n=123), NDM (n=109), ⁴: DM (n=106), NDM (n=86)¹ p value by independent sample t-test ,SKF: Skin fold thickness

Table: 9

Percentages of pregnant mothers by different categories of early pregnancy body mass index(BMI) by groups

<i>Early pregnancy BMI</i>	<i>DM (n=200) Percentages</i>	<i>NDM (n=200) Percentages</i>	<i>p value^a</i>
Underweight (<19.8)	5.5	17.5	<0.0001
Normal (19.8-26.0)	63.0	64.5	
Over weight & Obese (26.1 & above)	31.5	18.0	

^a p value for χ^2 test

Reference: 250

Table: 10

Maternal anthropometric measurements
at three trimesters compared by groups

Variables	DM		NDM		p value ¹
	n	mean±SD	n	mean±SD	
Weight (kg)					
1 st trimester	200	57.3±10.0	200	54.3±8.2	<0.001
2 nd trimester	197	63.0±10.2	199	59.6±8.5	<0.001
3 rd trimester	190	66.2±10.7	199	62.2±9.0	<0.001
Postpartum (2-5 days)	184	58.5±10.5	199	54.8±8.8	<0.001
Mid arm circumference (cm)					
1 st trimester	200	27.2±2.6	200	25.2±2.4	<0.001
2 nd trimester	197	27.7±2.7	199	26.6±2.3	<0.001
3 rd trimester	190	27.2±2.8	199	26.2±2.4	<0.001
Postpartum (2- 5 days)	184	26.4±2.6	199	25.3±2.3	<0.001
Body mass index (BMI)					
1 st trimester	200	24.6±3.7	200	23.3±3.1	<0.001
2 nd trimester	197	26.2±3.7	199	25.5±3.3	<0.001
3 rd trimester	190	28.4±4.0	199	26.6±3.5	<0.001
Postpartum (2- 5 days)	185	25.1±3.6	189	23.5±3.4	<0.001

¹ p value by independent sample t-test

401612



Table: 11

Change in maternal weight, MAC and BMI in three trimesters
Compared by group

<i>Variables</i>	<i>DM Mean± SD</i>	<i>NDM Mean±SD</i>	<i>p value^b</i>
Total weight gain (kg)			
1 st trimester to 2 nd trimester ¹	5.5±2.8	5.3±2.3	0.48
2 nd trimester to 3 rd trimester ²	3.1±2.5	2.6±1.8	0.02
1 st trimester to 3 rd trimester ³	8.6±3.2	7.9±2.5	0.02
Weight gain (kg)/week			
1 st trimester to 2 nd trimester ¹	0.328±0.17	0.302±0.14	0.08
2 nd trimester to 3 rd trimester ²	0.324±0.25	0.296±0.19	0.26
1 st trimester to 3 rd trimester ³	0.329±0.13	0.299±0.10	0.01
Change in MAC (cm)			
1 st trimester to 2 nd trimester ¹	0.51±1.2	0.63±1.0	0.39
2 nd trimester to 3 rd trimester ²	-0.52±1.1	-0.45±0.5	0.14
1 st trimester to 3 rd trimester ³	-0.03±1.6	0.18±1.1	0.30

^b p value by independent sample t-test

1: DM: n=197, NDM: n=199. 2: DM: n=190, NDM: n=199, 3: DM: n=184, NDM: n=199,

Table: 12

Change of mid arm circumference (MAC) between
different trimesters compared by groups

<i>Variables</i>	<i>DM</i>	<i>NDM</i>	<i>p value</i> ^{<i>b</i>}
1 st trimester to 2 nd trimester ¹			
25 th percentile	0.00	0.00	0.579
50 th percentile	0.70	0.80	
75 th percentile	1.30	1.30	
2 nd trimester to 3 rd trimester ²			
25 th percentile	-1.10	-0.70	0.002
50 th percentile	-0.65	-0.40	
75 th percentile	-0.17	-0.20	
1 st trimester to 3 rd trimester ³			
25 th percentile	-1.00	-0.70	0.088
50 th percentile	0.00	0.30	
75 th percentile	1.00	1.00	
1 st trimester to postpartum ⁴			
25 th percentile	-0.18	-0.20	NS
50 th percentile	-0.70	-0.40	
75 th percentile	1.8	-1.5	

^b: *p* value for Man Whitney- U test was done

¹: DM: *n*=197, NDM: *n*=199. ²: DM: *n*=190, NDM: *n*=199,

³: DM: *n*=184, NDM: *n*=199, ⁴: DM: *n*=184, NDM: *n*=199,

Table: 13

Total weight gain (kg) by different categories of nutritional status at three trimesters compared by groups

Nutritional status by BMI	1-2Tm total gain		2-3Tm total gain		1-3Tm total gain	
	DM	NDM	DM	NDM	DM	NDM
Underweight ¹ (<19.8)	7.0 $\pm$ 3.9	5.0 $\pm$ 2.0*	3.0 $\pm$ 2.0	2.0 $\pm$ 1.5	10.1 $\pm$ 3.6	7.0 $\pm$ 2.3**
Normal ² (19.8-26.0)	5.5 $\pm$ 2.5	5.7 $\pm$ 2.2	3.0 $\pm$ 2.2	2.5 $\pm$ 1.6	08.4 $\pm$ 3.1	8.2 $\pm$ 2.4
Overweight ³ (26.1-30)	5.5 $\pm$ 3.3	3.5 $\pm$ 2.7*	3.2 $\pm$ 3.1	4.1 $\pm$ 2.7	08.7 $\pm$ 3.5	7.6 $\pm$ 3.2
Obese ⁴ (30 & above)	5.2 $\pm$ 2.6	6.1 $\pm$ 1.2	4.0 $\pm$ 2.7	2.7 $\pm$ 0.8	09.1 $\pm$ 3.4	8.8 $\pm$ 1.3

1. Underweight: DM: 11; NDM: 35

2. Normal: DM: 123; NDM: 128

3. Overweight: DM: 36; NDM: 25

4. Obese: DM: 27; NDM: 11

* $p < 0.01$; ** $p < 0.001$ by independent sample t-test

Table: 14

Weekly weight gain (kg) by different categories of nutritional status at three trimesters compared by groups

	1-2Tm gain/wk		2-3Tm gain/wk		1-3Tm gain/wk	
	DM	NDM	DM	NDM	DM	NDM
Underwt ¹	0.44 $\pm$ 2.6	0.28 $\pm$ 1.3*	0.29 $\pm$ 0.19	0.23 $\pm$ 0.17	0.38 $\pm$ 0.15	.26 $\pm$ 0.09*
Normal ²	0.32 $\pm$ 0.14	0.32 $\pm$ 0.13	0.32 $\pm$ 0.24	0.29 $\pm$ 0.18	0.32 $\pm$ 0.13	0.31 $\pm$ 0.09
Overwt ³	0.33 $\pm$ 0.21	0.20 $\pm$ 0.15*	0.32 $\pm$ 0.30	0.42 $\pm$ 0.30	0.33 $\pm$ 0.13	0.28 $\pm$ 0.12
Obese ⁴	0.30 $\pm$ 0.14	0.34 $\pm$ 0.09	0.38 $\pm$ 0.20	0.31 $\pm$ 0.10	0.33 $\pm$ 0.14	0.33 $\pm$ 0.05

1. Underweight: DM: 11; NDM: 35

2. Normal: DM: 123; NDM: 128

3. Overweight: DM: 36; NDM: 25

4. Obese: DM: 27; NDM: 11

* $p < 0.01$; ** $p < 0.001$ by independent sample t-test

Table: 15

Fasting and after breakfast blood glucose level at 3 trimesters by groups

Variable	DM mean±SD	NDM Mean±SD	p value ^b
Fasting blood glucose (mmol/L):			
1 st trimester (≤12 wk) ¹	6.8±2.6	4.6±0.7	<0.01
2 nd trimester (26 th -28 th wk) ²	5.8±1.7	4.7±1.1	<0.01
3 rd trimester (32 nd -34 th wk) ³	5.0±1.2	4.7±0.5	<0.05
After breakfast glucose (mmol/L):			
1 st trimester (≤12 wk)	9.2±3.2	5.8±1.2	<0.01
2 nd trimester (26 th -28 th wk)	7.3±2.2	5.5±1.2	<0.01
3 rd trimester (32 nd -34 th wk)	6.3±1.7	5.3±0.5	<0.01

^bp value by independent sample t-test ¹ DM = 199, NDM = 199 ² DM = 193, NDM = 199, ³ DM = 187, NDM = 199

Table: 16

Percentages of diabetic mothers who are under good control by different cut-off values for fasting blood glucose.

Variables	n	<5.6mmol/l ¹ Percentage	<5.0mmol/l ² Percentage
1 st trimester (≤12 wk)	199	38.7	22.9
2 nd trimester (26 th - 28 th wk)	193	52.3	28.5
3 rd trimester ((32 nd -34 th wk)	187	86.6	52.4

¹ Target to achieve fasting blood glucose 5.6 mmol/L (NDDG group) ¹⁰

² Target to achieve fasting blood glucose 5.0 mmol/L (BIRDEM Research group),

Table: 17

Distribution of diabetic mothers by Glycosylated hemoglobin status (HbA₁C)

HbA ₁ C%	n	Cut-off value (<6%) Percentage	Mean±SD
1 st trimester (≤12 wk) ¹	199	42.2%	6.4±2.1
2 nd trimester (26 th - 28 th wk) ²	193	73.7%	5.1±1.6
3 rd trimester (32 nd -34 th wk) ³	187	81.0%	5.1±1.1

HbA₁C: Glycosylated hemoglobin percentages

*Cutoff value for good control by NDDG¹⁰

Table: 18

Percentile Distribution of diabetic pregnant women by level of glycosylated hemoglobin percentages (HbA₁C%)

Glycosylated Hemoglobin%	n	25 th percentile	50 th percentile	75 th percentile
1 st trimester (≤12 wk)	199	5.0	6.0	6.0
2 nd trimester (26 th - 28 th wk)	193	4.5	5.0	5.0
3 rd trimester (32 nd -34 th wk)	187	4.5	5.0	5.0

Table: 19

Distribution of pregnant mothers by anemia (Hb%: <11.0 g/dl) by group

Variable	DM		NDM		p value ^a
	n	(%)	n	(%)	
1 st trimester (≤12 wk)	33	(16.8)	21	(10.6)	0.08
2 nd trimester (26 th - 28 th wk)	61	(31.6)	25	(13.0)	<0.01
3 rd trimester (32 nd -34 th wk)	68	(36.0)	23	(11.6)	<0.01

^a p value for χ^2 test ¹ DM =196, NDM =198; ² DM =193, NDM= 192; ³ DM =189, NDM =199

Table: 20

Mean ±SD of Hb% (gm/dl) and changes in Hb% over three trimesters by groups

<i>Variables</i>	<i>DM</i>		<i>NDM</i>		<i>p value</i> ^{<i>b</i>}
	<i>n</i>	<i>Mean±(SD)</i>	<i>n</i>	<i>Mean±(SD)</i>	
Hemoglobin concentration					
1 st trimester (≤12 wk)	196	11.8±1.2	198	12.2±0.97	<0.01
2 nd trimester (26 th - 28 th wk)	193	11.1±0.9	192	11.6±0.9	<0.001
3 rd trimester (32 nd -34 th wk)	189	11.2±1.0	199	11.8±0.9	<0.01
Change in Hb%					
1 st trimester to 2 nd trimester	190	-0.74±1.0	190	-0.56±0.8	<0.05
2 nd trimester to 3 rd trimester	186	0.10±0.9	192	0.18±0.5	NS

^b p value by independent sample t-test

Table: 21

Percent distribution of pregnant mothers by urine glucose
urine albumin and urinary tract infection by groups

Variables	DM Percentage	NDM Percentage
Urinary glucose:		
1 st trimester (≤ 12 wk) ¹	14.0	nil
2 nd trimester (26 th - 28 th wk) ²	18.0	3.0
3 rd trimester (32 nd -34 th wk) ³	13.0	1.0
Urinary albumin:		
1 st trimester (≤ 12 wk) ¹	6.5	Nil
2 nd trimester (26 th - 28 th wk) ²	15.0	2.0
3 rd trimester (32 nd -34 th wk) ³	8.0	Nil
Urinary tract infection:		
1 st trimester (≤ 12 wk) ¹	Nil	2.0
2 nd trimester (26 th - 28 th wk) ²	1.5	0.5
3 rd trimester (32 nd -34 th wk) ³	1.5	Nil

1: DM = 199, NDM = 199; 2: DM = 193, NDM = 199; 3: DM = 187, NDM = 199

Table: 22

Percent distribution of pregnant mothers by
blood pressure and pulse rate by groups

Variables	DM (n=200) Mean $\pm$ SD	NDM (n=200) Mean $\pm$ SD	p value ^b
Maternal systolic blood pressure:			
1 st trimester (≤ 12 wk) ¹	115.6 $\pm$ 11.0	110.2 $\pm$ 8.5	<0.001
2 nd trimester (26 th - 28 th wk) ²	122.8 $\pm$ 9.7	116.7 $\pm$ 8.6	<0.001
3 rd trimester (32 nd -34 th wk) ³	123.4 $\pm$ 7.6	121.8 $\pm$ 4.5	<0.001
Maternal diastolic blood pressure:			
1 st trimester (≤ 12 wk) ¹	76.0 $\pm$ 8.4	67.9 $\pm$ 5.4	<0.001
2 nd trimester (26 th - 28 th wk) ²	80.4 $\pm$ 9.0	68.9 $\pm$ 5.5	<0.001
3 rd trimester (32 nd -34 th wk) ³	76.0 $\pm$ 7.3	70.2 $\pm$ 5.3	<0.001
Maternal pulse rate per minute:			
1 st trimester (≤ 12 wk) ¹	72.7 $\pm$ 4.9	71.3 $\pm$ 4.4	<0.001
2 nd trimester (26 th - 28 th wk) ²	72.6 $\pm$ 3.6	70.8 $\pm$ 2.8	<0.001
3 rd trimester (32 nd -34 th wk) ³	71.6 $\pm$ 2.4	72.3 $\pm$ 2.0	<0.001

^b p value by independent sample t-test

¹ DM = 199, NDM = 199; ² DM = 193, NDM = 199; ³ DM = 187, NDM = 199

Table: 23

Last month's maternal morbidities in different trimesters by groups

Trimesters	n (%)	p value ^a
1 st trimester (≤12 wk)		
DM (n=200)	78 (39.0)	<0.001
NDM (n=200)	41 (20.5)	
2 nd trimester (26 th - 28 th week)		
DM (n=197)	101 (51.3)	<0.001
NDM (n=199)	43 (21.6)	
3 rd trimester (32 nd -34 th week)		
DM (n=189)	78 (41.3)	<0.001
NDM (n=199)	07 (03.5)	

^a p value for X² test

Table: 24

Last month's specific maternal morbidities in different trimesters by groups

Morbid conditions	DM	NDM
1 st trimester (≤ 12 wk):		
Vomiting	36	25
Temperature	12	3
Threatened abortion	11	2
UTI	3	nil
Uncontrolled blood sugar	3	nil
Others	13	11
2 nd trimester (13- 28 th wk):		
Ante-partum hemorrhage (APH)	6	Nil
Edema	41	22
Pre-eclampsia (PET)	7	1
Pregnancy induced hypertension	9	nil
Temperature	12	1
Spotted bleeding	2	nil
UTI (Urinary tract infection)	3	nil
Uncontrolled blood sugar	3	3
Other	18	16
3 rd trimester (29 th wk & above):		
Ante-partum hemorrhage (APH)	6	nil
Edema	13	1
Pre-eclampsia (PET)	2	nil
Pregnancy induced hypertension	10	2
Polyhydromnios	2	nil
Uncontrolled blood sugar	14	1
Others	31	3

Table: 25

Comparison of pregnancy outcomes in
Different trimesters by groups

<i>Fetal outcome</i>	<i>DM n (%)</i>	<i>NDM n (%)</i>
1 st trimester (≤ 12 wk): ¹		
Abortion	2(1.0)	Nil
Healthy pregnancy	198(99.0)	200(100.0)
2 nd trimester (13- 28 th wk) ² :		
Fetal loss	5 (2.5)	Nil
Healthy singleton pregnancy	191 (96.5)	200(100.0)
Twin	2(1.0)	Nil
3 rd trimester (29 th wk & above) ³ :		
IUD	2(1.0)	Nil
Not available	2(1.0)	Nil
Healthy singleton newborn	187(97.9)	199 (100.0)

¹ DM: n=200, NDM:n =200; ² DM:n =198, NDM::n= 199; ³ DM:n =191, NDM:n =199

Table: 26

Causes of fetal loss in diabetic group

<i>Cause of termination of pregnancy</i>	<i>n (%)</i>	<i>Per thousand total birth</i>
1 st trimester (≤ 12 wk) ¹ : Complete abortion	2(1.0)	10/1000 total birth
2 nd trimester (13- 28 th wk) ² : Stillbirth	5 (2.5)	25.0/1000 total birth
3 rd trimester (29 th wk & above) ³ : IUD	2(1.0)	10.0/1000 total birth
Total loss	9(4.5)	45.0/1000 total birth

¹ DM =200, ² DM =198, ³ DM =191

Table: 27

Comparison of newborn by Gestational age categories (at birth)

<i>Gestational age</i>	<i>DM (n=185) Percentage</i>	<i>NDM (n=199) Percentage</i>
<32 week	1.5	nil
32-34 week	14.7	nil
35 week	7.4	3.5
36 week	17.9	2.7
37 week	55.8	60.8
38 week	6.8	14.1
39 week	1.9	10.6
40 week	nil	4.5

Table: 28

Mean and SD of newborns anthropometric measurements at birth by groups (both sex combined)

<i>Variables</i>	<i>n</i>	<i>DM Mean±SD</i>	<i>NDM n</i>	<i>Mean±SD</i>	<i>p value</i>
Birth weight (g)	185	2850.6±577.1	199	2651.1±344.4	<0.001
Crown heel length (cm)	181	45.8 ±2.1	197	45.7±1.5	NS
Mid arm circumference (cm)	181	9.6±1.2	198	9.3±0.9	<0.002
Head circumference (cm)	181	34.0±0.8	197	33.9±0.6	<0.03
Chest circumference (cm)	180	33.1±0.8	194	32.7±0.7	<0.001
Ponderal Index (PI)*	181	2.99±0.6	197	2.78±0.3	<0.001

*PI: wt/ht³ (146)

Tabl:29

Comparison of newborn by birth weight categories

<i>Birth weight</i>	<i>DM (n=185)</i>	<i>NDM (n=199)</i>	<i>p value</i>
Very low birth weight: <2000g	7(3.8)	7(3.5)	
Low birth weight: 2000-2499g	40(21.6)	48(24.1)	
Appropriate for gestational age (AGA): 2500-3300g	101(54.6)	138(69.3)	<0.001
Large for gestational age (LGA): 3301g & above	37(20.0)	6(3.1)	

Table:30

Mean and SD of newborns anthropometric measurements at birth by sex (DM)

<i>Variables</i>	<i>n</i>	<i>Male Mean±SD</i>	<i>Female n Mean±SD</i>	<i>p value</i>
Placental weight (gm) ¹	82	637.6±141.8	81 565.3±124.0	<0.001
Birth weight (g) ²	90	2997.1±606.7	95 2711.8±513.1	<0.001
Crown heel length (cm) ³	87	46.2±2.0	94 45.4±1.3	<0.001
Mid arm circumference (cm) ⁴	87	9.9±1.2	94 9.3±1.1	<0.001
Head circumference (cm) ⁵	88	34.0±0.8	93 33.9±0.6	<0.03
Chest circumference (cm) ⁶	88	33.2±0.6	92 32.9±0.8	NS
Abdominal circumference (cm) ⁷	87	32.4±1.2	92 32.1±1.0	NS

¹:n=163 ; ²:n=185; ³:n=181, ⁴: n=181; ⁵: n=181; ⁶: n=180; ⁷: n=179;

Table:31

Mean and SD of newborns anthropometric measurements at birth by sex (NDM)

Variables	Male		Female		p value
	n	Mean±SD	n	Mean±SD	
Placental weight (gm) ¹	110	510.0±58.1	82	519.5±83.0	NS
Birth weight (gm) ²	116	2787.1±374.6	83	2659.5±374.6	<0.05
Crown heel length (cm) ³	116	45.7±1.5	81	45.5±1.4	NS
Mid arm circumference (cm) ⁴	114	9.3±1.0	84	9.8±1.6	<0.05
Head circumference (cm) ⁵	116	34.2±0.5	81	33.6±0.2	<0.05
Chest circumference (cm) ⁶	114	32.8±1.3	80	32.9±0.8	NS
Abdominal circumference (cm) ⁷	112	30.9±1.0	80	32.0±1.2	NS

¹:n=192 ; ²:n=199; ³:n=197⁴: n=198; ⁵: n=197; ⁶: n=194; ⁷: n=192

Table:32

Distribution of intrauterine growth retardation (IUGR) babies by groups

IUGR	DM (n=184) n(%)	NDM n=198) n(%)
Group -1: (Term but <2.5 kg)	7(3.8)	52(26.4)
Group -2: (Preterm and <10 th percentile for gestational age)	6(3.3)	1(0.5)
Group -3: (Term but <10 th percentile for gestational age)	8(4.3)	33(16.2)
Group -4: (Term and preterm but weight >10 th percentile for gestational age)	163(88.6)	112(56.9)

p<0.001

Table:33

Health status of the neonates detected by Apgar score at birth (1 minute) and 5 minutes after birth by group

Variables	DM (n=186)	NDM (n=199)	p value
Apgar score at 1 minute			
Severe depression (0-3)	6(3.2)	Nil	<0.001
Mild depression (4-6)	44(23.7)	16(8.0)	
Normal (7-10)	136(73.1)	183(92.0)	
Apgar score at 5 minute			
Severe depression (0-3)	2(1.1)	Nil	<0.001
Mild depression (4-6)	37(19.9)	10(5.0)	
Normal (7-10)	147(79.0)	189(95.0)	

Table:34

Distribution of health status of the perinates by group

Perinatal morbidity	DM (n=186)	NDM (n=178)	p value
Perinatal morbidity			
Yes	100(53.8)	23(13.0)	<0.001
No	86 (46.2)	155(87.0)	
Specific morbid conditions:			
Respiratory distress syndrome (RDS)	20	8	
Jaundice	38	13	
Temperature	7	2	
Umbilical cord sepsis	6	Nil	
Ophthalmia neonatarum	12	Nil	
Convulsion of the newborn	2	Nil	
Skin infection	8	Nil	
Oral thrush	7	Nil	
Admission to neonatal ICU	53	13	
Cause of admission:			
Jaundice	28	11	
Temperature	9	1	
RDS	16	1	

ICU: Intensive care unit; Percentage in parentheses

Table:35

Distribution of perinatal mortality in DM group*

<i>Perinatal mortality</i>	<i>DM (n=198)</i>	<i>Per thousand total birth</i>
Perinatal mortality		
Death within 1 st week of birth	4(2.0)	55 /1000 total birth
Stillbirth	7(3.5)	
Time of death from birth		
12-24hr	1	
24-36hr	1	
37-48hr	1	
72-84hr	1	
Causes of Death within 1 st week of birth		
Respiratory distress syndrome (RDS)	3	
Jaundice	1	
Causes of stillbirth (From 24wk of pregnancy)		
Congenital anomaly	1	35/1000 total birth
Antepartum hemorrhage (APH)	2	
Other	2	
Intra uterine death (IUD)	2	

*NDM (n=199): No perinatal mortality was found

Total birth: Live birth and still- birth

Table: 36

Relationship of perinatal morbidity with monthly income
Maternal education and morbidity (both group)

Socio-economic & other	Perinatal morbidity			χ^2	RR (CI)
	Yes	No	Total		
Monthly income					
<10,000/	56 (37%)	96(63%)	152	15.4 p<0.001	2.5 (1.6-4.0)
10,0000/ &above	44 (19%)	189(81%)	233		
Total	100	285	385		
Respondents education					
<SSC	25 (32%)	52(68%)	77	NS	1.5 (0.9-2.6)
SSC & above	75 (24%)	233(76%)	308		
Total	100	285	385		
3 TM maternal morbidity					
Yes	50(61%)	32(39%)	82	66.4 p<0.001	7.9 (4.6-13.5)
No	50(17%)	253(83%)	303		
Total	100	285	385		
2 TM maternal morbidity					
Yes	46 (34%)	89(66%)	135	7.1 p<0.01	1.9 (1.2-2.3)
No	54(22%)	196(78%)	250		
Total	100	285	385		

Table: 37

Relationship of perinatal morbidity
With maternal nutritional status (both group)

Maternal anthropometry	Perinatal morbidity			χ^2	RR (CI)
	Yes	No	Total		
Early pregnancy weight					
<50.0 kg	34(38%)	56(56%)	90	NS	1.4 (0.9-2.2)
50.0 kg & above	66(22%)	229(78%)	295		
Total	100	285	385		
Height					
<152.0 cm	54(32%)	117(68%)	171	5.03 p<0.02	1.7 (1.1-2.7)
152.0 cm & above	46(21%)	168(78%)	214		
Total	100	285	385		
Weight gain					
<7.0 kg	52(35%)	98(65%)	150	9.7 p<0.002	2.1 (1.3-3.3)
7.0 kg & above	48(20%)	187(79%)	235		
Total	100	285	385		

Table: 38

Relationship of perinatal morbidity with
Newborn's biological characteristics (both group)

Neonatal characteristics	Perinatal morbidity			χ^2	RR (CI)
	Yes	No	Total		
Low birth weight					
<2500g	58 (57%)	44(43%)	102	p<0.0001	7.7 (4.6-12.9)
2500 g & above	42 (15%)	241(85%)	283		
Total	100	285	385		
IUGR					
Preterm IUGR	6(86%)	1(14%)	7	<0.0001	18.12 (2.2-152.5)
Other	94(25%)	284(75%)	378		
Total	100	285	385		
PI (>2.1)					
Obese & overweight	34(16%)	137(64%)	214	<0.01	1.6 (1.1-2.2)
Other	66(39%)	148(86%)	171		
Total	100	285	385		
Baby MAC					
<9.0 cm	47(49%)	49(51%)	96	<0.0001	4.8 (2.9-8.0)
9.0 cm & above	53(18%)	236(82%)	289		
Total	100	285	385		
²A/S: (1 minute)					
<8	43(72%)	17(28%)	60	<0.0001	11.9 (6.3-22.3)
8 & above	57(17%)	268(82%)	325		
Total	100	285	385		

¹PI: ponderal Index, ²A/S: Apgar Score,

Table: 39

Relationship of perinatal morbidity with maternal glycemic status in (DM) group (n=186)

<i>HbA₁C%</i>	<i>Perinatal morbidity</i>			<i>X²</i>	<i>RR (CI)</i>
	Yes	No	Total		
3rd trimester					
6.0 & above	48(91%)	5(4%)	53	p<0.001	12.46 (4.5-34.2)
<6.0	52(39%)	81(61%)	133		
Total	100	86	186		
2nd trimester					
6.0 & above	55(85%)	10(15%)	65	p<0.001	4.2 (4.5-34.2)
<6.0	45(37%)	76(63%)	121		
Total	100	86	186		
3rd trimester-fasting blood glucose level					
5.0 mmol/l & above	57(58%)	41(42%)	98	p<0.01	2.1 (1.1-3.8)
<5.0 mmol/l	43(49%)	45(51%)	88		
Total	100	86	186		

Table: 40

Relationship of macrosomy with maternal glycemic status in (DM) group (n=185)

<i>Glycemic status</i>	<i>Macrosomy</i>			<i>X²</i>	<i>RR (CI)</i>
	Yes	No	Total		
3rd trimester HbA₁C%					
6.0 & above	5(15%)	28(85%)	33	p<0.003	6.4 (1.6-25.3)
<6.0	4(3%)	148(97%)	152		
Total	9	176	185		
3rd trimester-Postprandiol blood glucose mmol/l					
6.5 & above	5(11%)	40(89%)	45	p<0.02	4.2 (1.1-16.3)
<6.5	4(3%)	136(97%)	140		
Total	9	176	185		

Table: 41

Relationship of LGA with maternal
glycemic status in (DM) group (n=185)

<i>HbA_{1c}%</i>	<i>Large for gestational age (LGA)</i> Yes No Total			<i>X²</i>	<i>RR</i> <i>(CI)</i>
3rd trimester					
6.0 & above	14(42%)	19(58%)	33	p<0.001	3.8 (1.7-8.5)
<6.0	23(15%)	129(85%)	152		
Total	37	148	185		
2nd trimester					
6.0 & above	17(39%)	27(61%)	44	p<0.001	3.3 (1.5-7.1)
<6.0	20(14%)	121(86%)	141		
Total	37	148	185		
1st trimester					
6.0 & above	29(30%)	67(70%)	96	p<0.001	3.7 (1.6-8.7)
<6.0	8(9%)	81(91%)	89		
Total	37	148	185		
3rd trimester- Postprandiol blood glucose mmol/l					
6.5 mmol/l & above	16(36%)	29(64%)	45	p<0.007	2.8 (1.3-5.9)
<6.5 mmol/l	21(15)	119(85%)	140		
Total	37	148	185		

Table 42

Relationship of maternal morbidity with
Maternal characteristics (DM) group (n=189)

<i>Maternal hemoglobin concentrations (g%)</i>	<i>Maternal morbidity (3 TM)</i> Yes No Total			<i>X²</i>	<i>RR</i> <i>(CI)</i>
3rd trimester					
<11.0	38(57%)	29(43%)	67	p<0.002	2.6 (1.4-4.7)
11.0 & above	40(33%)	82(67%)	122		
Total	78	111	189		
2nd trimester					
<11.0	32(53%)	28(47%)	60	p<0.03	2.0 (1.1-3.6)
11.0 & above	46(36%)	83(64.5%)	129		
Total	78	111	189		

Table 43

Relationship of maternal morbidity with
Maternal characteristics (DM) group (contd.) (n=189)

Variables	Maternal morbidity (3 TM)			X^2	RR (CI)
	Yes	No	Total		
3rd trimester HbA₁C%					
6.0 & above	26(67%)	13(33%)	39	p<0.002	3.2 (1.5-6.8)
<6.0	52(35%)	98(65%)	150		
Total	78	111	189		
Early pregnancy MAC					
<25.5 cm	28(64%)	16(36%)	44	p<0.01	3.0 (1.5-6.0)
25.5 cm & above	50(34%)	95(66%)	145		
Total	78	111	189		
Early pregnancy weight					
<50.0 kg	23 (55%)	19(45%)	42	p<0.06	1.9 (1.0-3.8)
50.0 kg & above	55(38%)	92(62%)	147		
Total	78	111	189		

Perinatal morbidity: 1 TM HbA₁C% NS

3 TM morbidity: 1 TM & 2 TM HbA₁C% NS,

2 TM & 1 TM morbidity: HbA₁C%, hb% and MAC: NS

LGA vs duration of DM <35 month: NS

Macrosomy: 1 TM & 2 TM HbA₁C%: NS

Table: 44

Bivariate correlation analysis of neonatal anthropometry
with maternal variables (both group)

<i>Variable</i>	<i>Birth weight</i>	<i>Baby MAC</i>	<i>Head circumference</i>	<i>Recumbent length</i>	<i>Chest circumference</i>
Maternal SES and other:					
Monthly income	0.17**	0.24**	0.20**	0.14**	0.08
Education	ns	ns	ns	ns	ns
Birth order	0.21**	0.17**	0.12*	0.15**	ns
Placental weight	0.67**	0.58**	0.40**	0.26**	0.39**
Maternal age	ns	ns	ns	ns	ns
Age of last child in month	ns	ns	ns	ns	ns
Maternal anthropometric variables:					
Early pregnancy weight	0.32**	0.34**	0.30*	0.38*	0.20
Maternal height	0.23**	0.24**	0.18***	0.52***	0.12*
Early pregnancy MAC	0.25**	0.28**	0.27**	0.27**	0.18**
Early pregnancy BMI	0.29**	0.30**	0.29**	0.18**	0.20**
Total weight gain	0.40**	0.23**	0.33**	0.28**	0.26**

Table: 45

Bivariate correlation analysis of neonatal anthropometry
With maternal variables (**both group**)

<i>Maternal biochemical variables:</i>	<i>Birth Weight</i>	<i>Baby MAC</i>	<i>Head circumference</i>	<i>Recumbent length</i>	<i>Chest circumference</i>
Maternal hb% (1TM)	ns	ns	ns	ns	ns
Maternal hb% (2TM)	ns	ns	ns	ns	0.15*
Maternal hb% (3TM)	ns	0.16*	0.16*	ns	ns
Fasting blood glucose (1TM)	0.12*	ns	ns	ns	0.13*
Fasting blood glucose (2TM)	0.19***	0.12*	ns	ns	ns
Fasting blood glucose (3TM)	ns	0.11*	ns	ns	ns
Postprandiol blood glucose (1TM)	ns	ns	ns	ns	ns
Postprandiol blood glucose (2TM)	0.20***	0.10*	ns	ns	0.13*
Postprandiol blood glucose (3TM)	0.12*	0.13**	ns	ns	ns

Table: 46

Bivariate correlation analysis of neonatal anthropometry
with maternal variables (DM)

Variable	Birth weight	Baby MAC	Head circumference	Recumbent length	Chest circumference
Maternal SES and other:					
Monthly income	0.32**	0.40**	0.26**	0.21**	0.21**
Education	ns	ns	ns	ns	ns
Birth order	ns	0.17**	ns	0.18**	ns
Placental weight	0.67**	0.58**	0.40**	0.26**	0.36**
Maternal age	ns	ns	ns	ns	ns
Age of last child in month	ns	-0.16	ns	ns	ns
Maternal anthropometric variables:					
Early pregnancy weight	0.28**	0.30**	0.27**	0.35**	ns
Maternal height	0.18**	0.18**	0.18**	0.54***	ns
Early pregnancy MAC	0.21**	0.24**	0.26**	28**	ns
Early pregnancy BMI	0.31**	0.30**	0.28**	0.22**	0.19*
Total weight gain	0.35**	0.35**	0.32**	0.23**	0.30**

Table: 47

Bivariate correlation analysis of neonatal anthropometry
with maternal variables (DM)

<i>Maternal biochemical variables:</i>	<i>Birth weight</i>	<i>Baby MAC</i>	<i>Head circumference</i>	<i>Recumbent length</i>	<i>Chest cir</i>
Maternal hb%(2TM)	ns	ns	ns	ns	ns
Maternal hb%(3TM)	0.17*	0.15*	0.24*	ns	ns
Fasting blood glucose (1TM)	ns	ns	ns	ns	ns
Fasting blood glucose (2TM)	0.22***	ns	ns	ns	ns
Fasting blood glucose (3TM)	ns	ns	ns	ns	ns
Postprandiol blood glucose (1TM)	ns	ns	ns	ns	ns
Postprandiol blood glucose (2TM)	0.30**	ns	ns	ns	ns
Post prandiol blood glucose (3TM)	ns	ns	ns	ns	ns
Maternal hbA1C% (1TM)	ns	ns	ns	ns	ns
Maternal hbA1C% (2TM)	0.24**	0.25**	0.19*	ns	0.28**
Maternal hbA1C% (3TM)	ns	ns	ns	ns	ns

Table: 48

Bivariate correlation analysis of neonatal anthropometry
with maternal variables (NDM)

<i>Variable</i>	<i>Birth weight</i>	<i>Baby MAC</i>	<i>Head circumference</i>	<i>Recumbent length</i>	<i>Chest circumference</i>
Maternal SES and other:					
Monthly income	0.16**	0.18**	0.20**	ns	ns**
Education	0.14**	ns	ns	ns	ns
Birth order	ns	ns	ns	0.18**	ns
Placental weight	0.79**	0.63**	0.48**	0.55**	0.36**
Maternal age	ns	ns	ns	ns	ns
Age of last child in month	ns	-0.16	ns	ns	ns
Maternal anthropometric variables:					
Early pregnancy weight	0.33**	0.37**	0.33**	0.35**	ns
Maternal height	0.32**	0.35**	0.20**	0.52***	0.20**
Early pregnancy MAC	0.28**	0.26**	0.24**	0.20**	ns
Early pregnancy BMI	0.34**	0.31**	0.30**	0.28**	0.15*
Total weight gain	0.48**	0.46**	0.32**	0.34**	0.18*

Table:49

Comparison between the macrosomy and Non-macrosomy
Babies by maternal variables (n=187)

<i>Variables</i>	<i>Macrosomy Mean±SD (n=11)</i>	<i>Non-macrosomy Mean±SD (n=176)</i>	<i>p value</i>
Early pregnancy BMI	25.0±4.0	24.7±3.7	NS
Weight gain/wk			
1 st trimester	7.0±2.8	5.4±2.8	NS
2 nd trimester*	5.3±4.3	3.1±2.9	0.02
3 rd trimester*	11.1±3.8	8.6±3.6	0.01
Fasting blood glucose (mmol/l):			
1 st trimester	7.5±3.1	6.7±2.6	NS
2 nd trimester*	6.7±3.0	5.6±1.4	0.02
3 rd trimester**	6.4±2.6	5.0±1.0	0.0001
After breakfast blood glucose (mmol/l):			
1 st trimester	9.9±2.9	9.1±3.3	NS
2 nd trimester*	8.3±3.9	7.0±1.9	0.04
3 rd trimester*	8.3±3.4	6.2±1.4	0.0001
Glycosylated hemoglobin %:			
1 st trimester	7.3±1.9	6.2±2.0	0.9
2 nd trimester	5.8±1.5	5.0±1.4	0.6
3 rd trimester**	6.0±1.1	5.0±1.1	0.004

Table: 50.a

Significant regression co-efficient, SE and CI of independent factors from
multiple regression analysis predicting birth weight

<i>Variables</i>	<i>B (Regression coefficient)</i>	<i>SE</i>	<i>p value</i>	<i>95% CI</i>
$(R^2 = 0.25)$				
Sex	81.8	43.5	0.06	-3.7 to 167.4
Total income (log)	210.1	102.8	0.04	7.9 to 412.3
Early pregnancy weight (kg)	11.5	2.5	0.001	6.5 to 16.5
Total weight gain (kg)	49.7	7.6	0.001	35.8 to 63.6
Group	-155.4	46.7	0.001	-247.3 to -63.6

Table: 50.b

Significant regression co-efficient, SE and CI of independent factors from
multiple regression analysis predicting baby MAC

<i>Variables</i>	<i>B (Regression coefficient)</i>	<i>SE</i>	<i>p value</i>	<i>95% CI</i>
$R^2 = 0.27$				
Sex	0.13	0.1	0.20	-0.07 to 0.3
Total income (log)	0.61	0.2	0.01	0.07 to 1.1
Early pregnancy weight (kg)	0.03	0.01	0.001	0.01 to 0.2
Total weight gain (kg)	0.11	0.02	0.001	0.8 to 0.1
Birth order	0.37	0.14	0.012	0.8 to 0.6
Group	-0.23	0.11	0.350	-0.4 to -0.01

Table: 50.c

Significant regression co-efficient, SE and CI of independent factors from multiple regression analysis-predicting baby head circumference

Variables	B (Regression coefficient)	SE	p value	95% CI
$R^2 = 0.20$				
Sex	0.02	0.06	0.71	-0.10-0.15
Total income (log)	0.22	0.15	0.16	-0.08-0.52
Early pregnancy weight (kg)	0.17	0.003	0.001	0.01-0.25
Total weight gain (kg)	0.07	0.01	0.001	0.05-0.09
Group	-0.06	0.07	0.414	-0.19-0.08

Table: 50.d

Significant regression co-efficient, SE and CI of independent factors from multiple regression analysis-predicting baby crown-heel length

Variables	B (Regression coefficient)	SE	p value	95% CI
$(R^2 = 0.35)$				
Sex	0.14	0.16	0.38	-0.17-0.44
Total income (log)	-0.22	0.37	0.55	-0.95-0.51
Maternal height	0.18	0.02	0.001	0.15-0.22
Maternal MAC	0.09	0.03	0.012	0.02-0.15
Total weight gain (kg)	0.14	0.02	0.001	0.1-0.2
Medical problem	0.09	0.17	0.60	-0.2-0.4

Table: 50.e

Significant regression co-efficient, SE and CI of independent factors from
multiple regression analysis-predicting chest circumferences

<i>Variables</i>	<i>B (Regression coefficient)</i>	<i>SE</i>	<i>p value</i>	<i>95% CI</i>
$(R^2 = 0.13)$				
Sex	0.02	0.07	0.7906	-0.16-0.13
Early pregnancy weight (kg)	0.01	0.004	0.0031	0.004-0.20
Total weight gain (kg)	0.06	0.01	0.0001	0.04-0.08
Group	-0.25	0.07	0.0012	-0.39-0.09

FIG-1. Percent of pregnant women with ANC till 2nd trimester by group

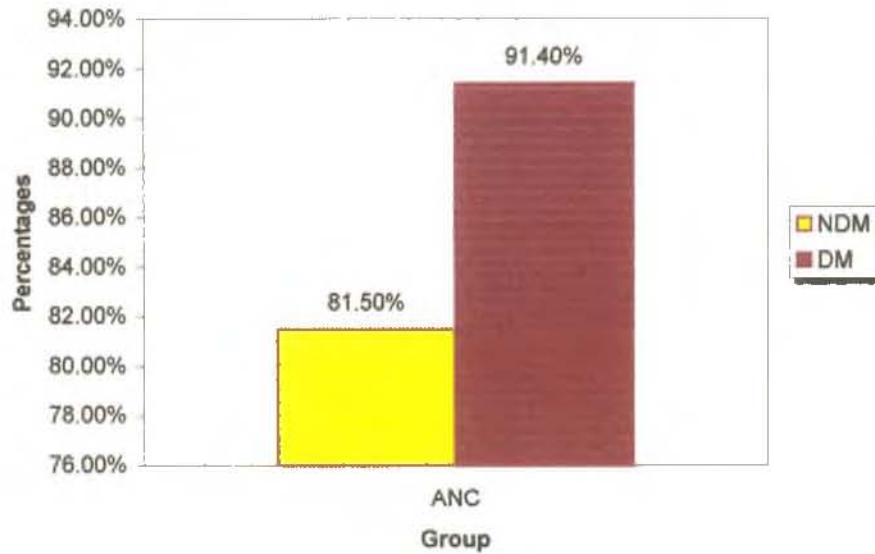


FIG-2. Bar diagram showing the percentages of cesarean section by group

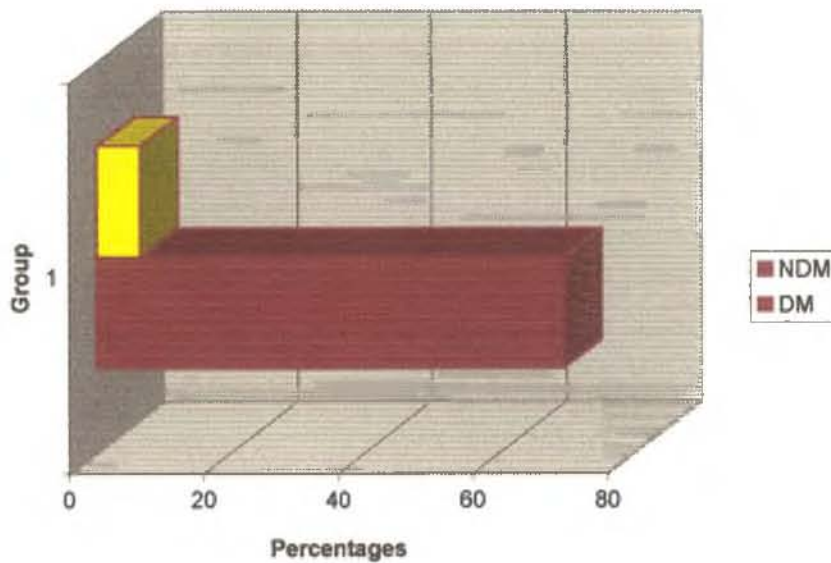


FIG-3. Infants of DM group by fetal presentation(n=187)

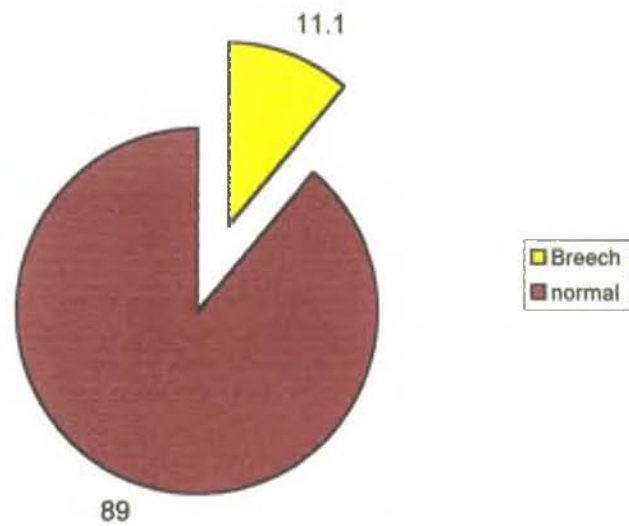


FIG-4. Birth complications by group

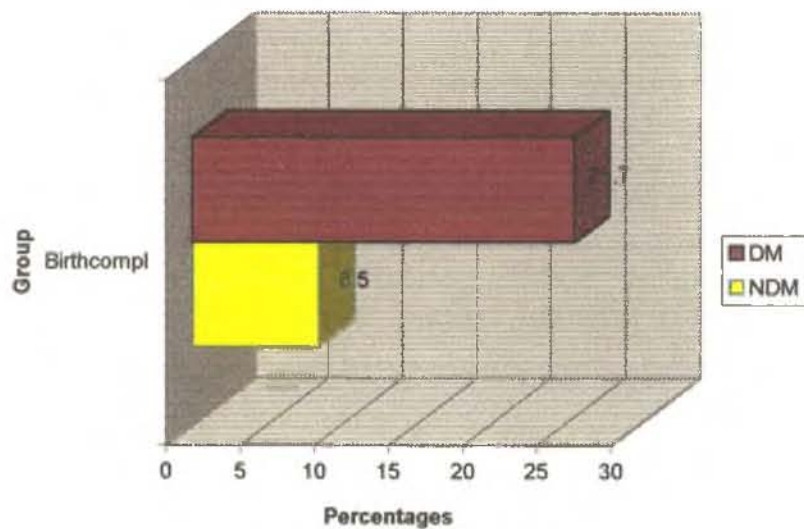


FIG-5. Pie chart showing percentages of neonatal hypoglycemia in IDMs (n=187)

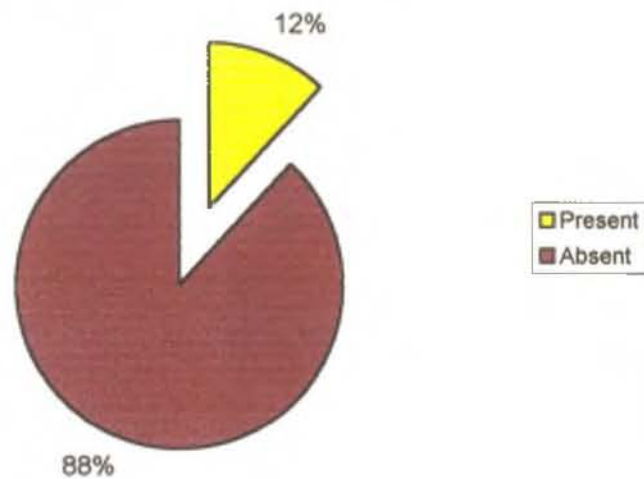


FIG-6. Bar diagram showing the preterm deliveries by group

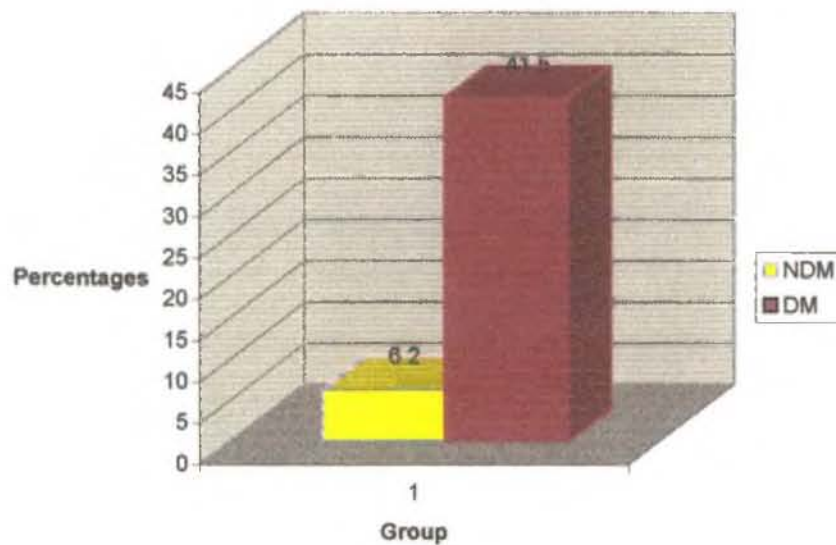


Fig. 7.a Measurement of triceps skinfold thickness with a Lange skinfold caliper. The triceps skinfold is measured with the subject's arms hanging loosely and comfortably at his/her side. The triceps skinfold is picked up with the left thumb and index finger of the examiner, approximately 1 cm proximal to the midpoint marked in figure II.10a.

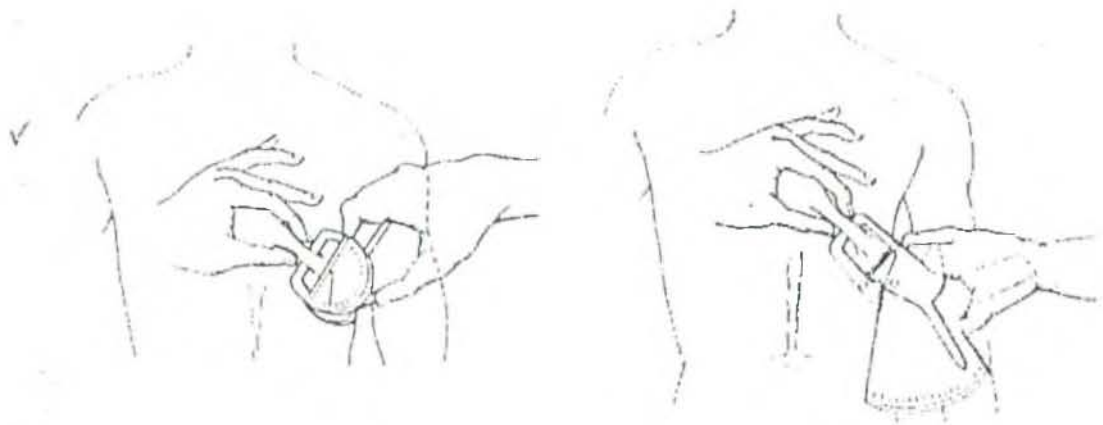
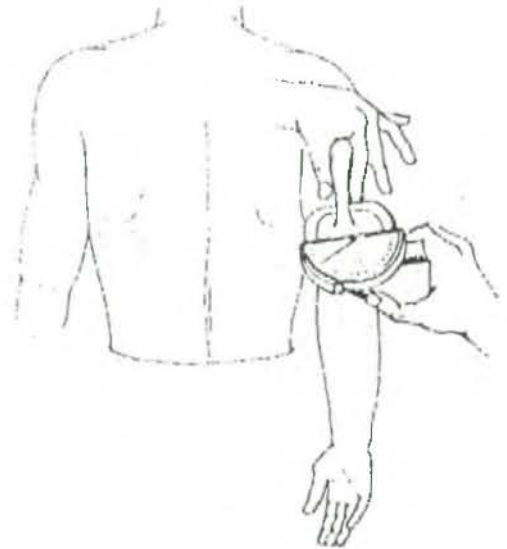


Fig. 7.b Measurement of subscapular skinfold thickness with (a) a Lange skinfold caliper and (b) a Slim Guide caliper. Subscapular skinfold thickness is measured with the subject standing with arm and shoulder relaxed. The examiner should grasp a horizontal pinch of skinfold at about 1 cm below the tip of the right scapula (shoulder blade). The jaws of the caliper are applied 1 cm infero-lateral to the thumb and finger raising the fold, and three readings are taken rapidly.

TABLE 4 RECOMMENDED WEIGHT GAINS FOR PREGNANT WOMEN BASED ON BODY MASS INDEX (BMI)

WEIGHT CATEGORY BASED ON BMI*	TOTAL WEIGHT GAIN†		1ST TRIMESTER GAIN		2ND AND 3RD TRIMESTER WEEKLY GAIN	
	lb	kg	lb	kg	lb	kg
Underweight (BMI < 19.8)	28–40	12.5–18	5	2.3	1.07	0.49
Normal weight (BMI = 19.8–26)	25–35	11.5–16	3.5	1.6	0.97	0.44
Overweight (BMI > 26–29)	15–25	7–11.5	2	0.9	0.67	0.3
Obese (BMI > 29)	at least 15	6				

[Data from Subcommittee on Nutritional Status and Weight Gain During Pregnancy and Subcommittee on Dietary Intake and Nutrient Supplements During Pregnancy, Food and Nutrition Board, National Academy of Sciences. Nutrition During Pregnancy, Parts I and II, Washington, DC: National Academy Press, 1990.]

*Metric BMI = weight (kg)/height (m)². See Appendix 20.

†Young adolescents and black women should strive for gains at the upper end of the recommended range. Short women (< 62 in. or < 157 cm) should strive for gains at the lower end of the range.

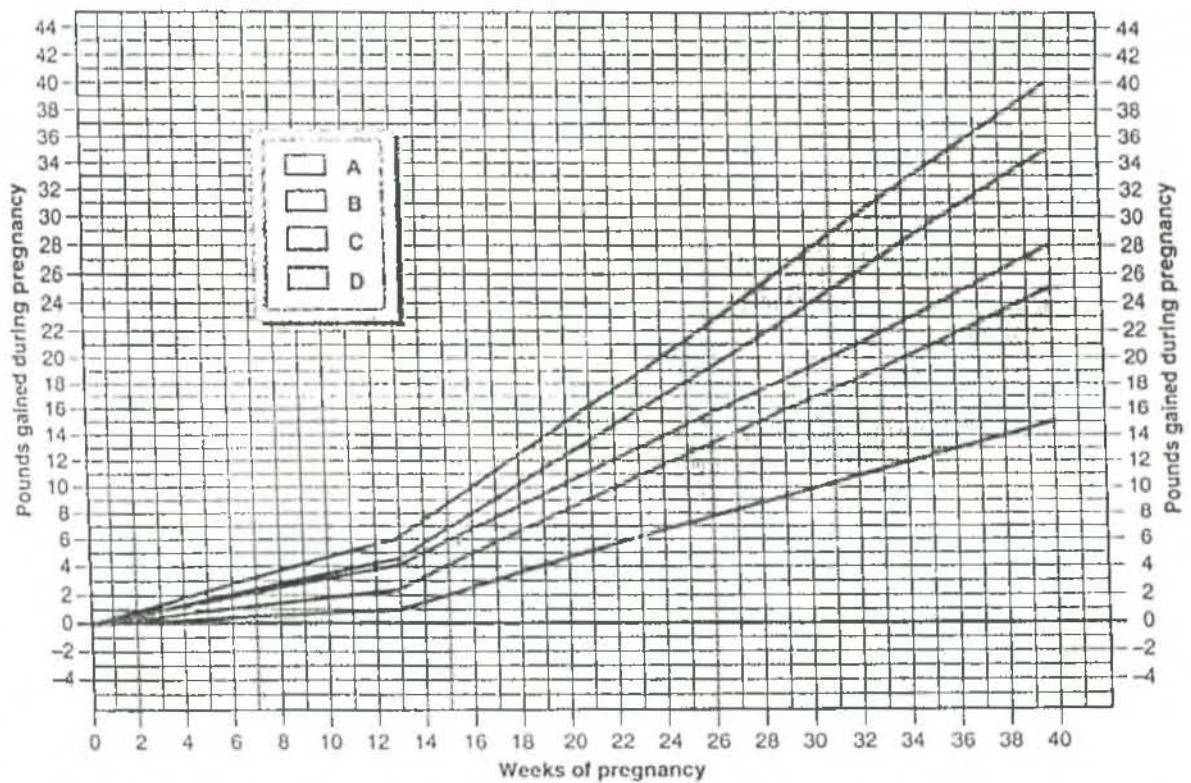
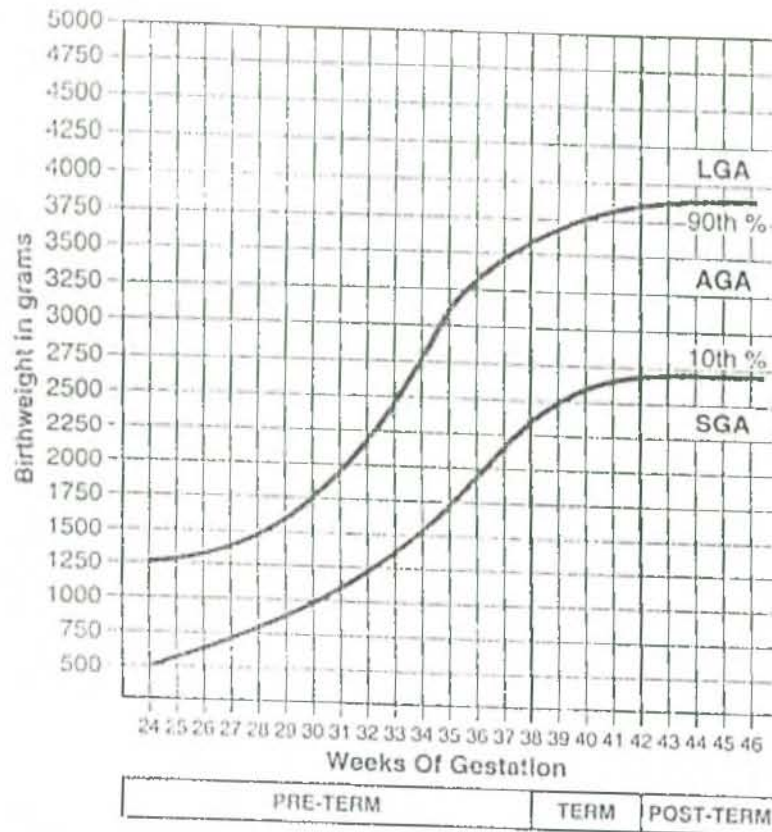
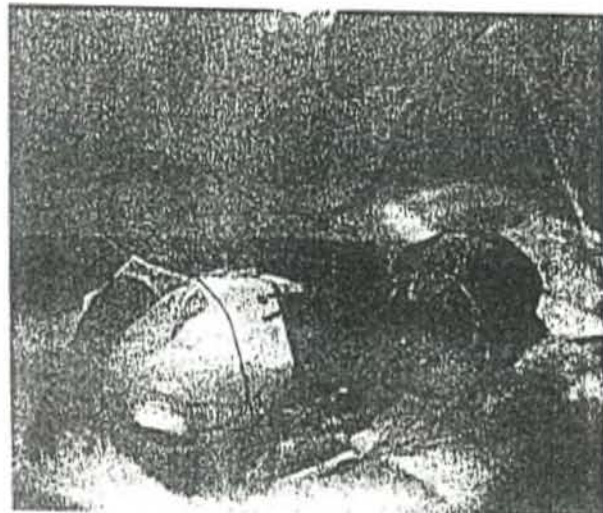


FIGURE 6 Women who are of normal weight prior to pregnancy should aim for a weight gain in the B–C range (25 to 35 lb) during the pregnancy. Underweight women should gain in the A–B range (28 to 40 lb). Women who are overweight prior to pregnancy should gain in the D range (15 to 25 lb).

Fig. - 8



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FIGURE 5-2 Classification of neonates based on maturity and intrauterine growth. *SGA*, small for gestational age; *AGA*, appropriate for gestational age; *LGA*, large for gestational age. (From Battaglia FC, Lubchenco LO. A practical classification of newborn infants by weight and gestational age. *J Pediatr* 71:159, 1967.)



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FIGURE 5-6 A R., born at 27 weeks' gestation, had a birth weight of 870 g (1 lb 14 oz).

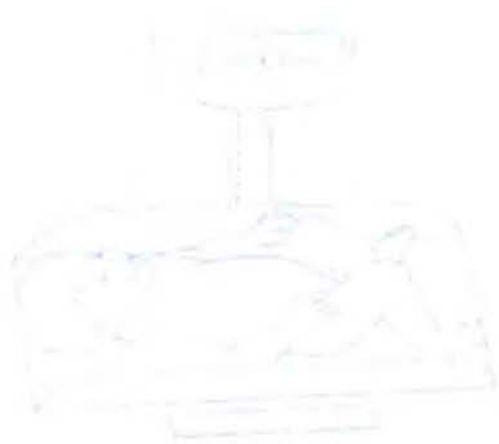


Fig-10



Fig. 31.3: Postmaturity pregnancy complicated with chronic hypertension delivered by C.S at 36 weeks. The baby weighed 4.9 kg with features of dysmaturity.

Fig-11



Fig-12



Fig-13

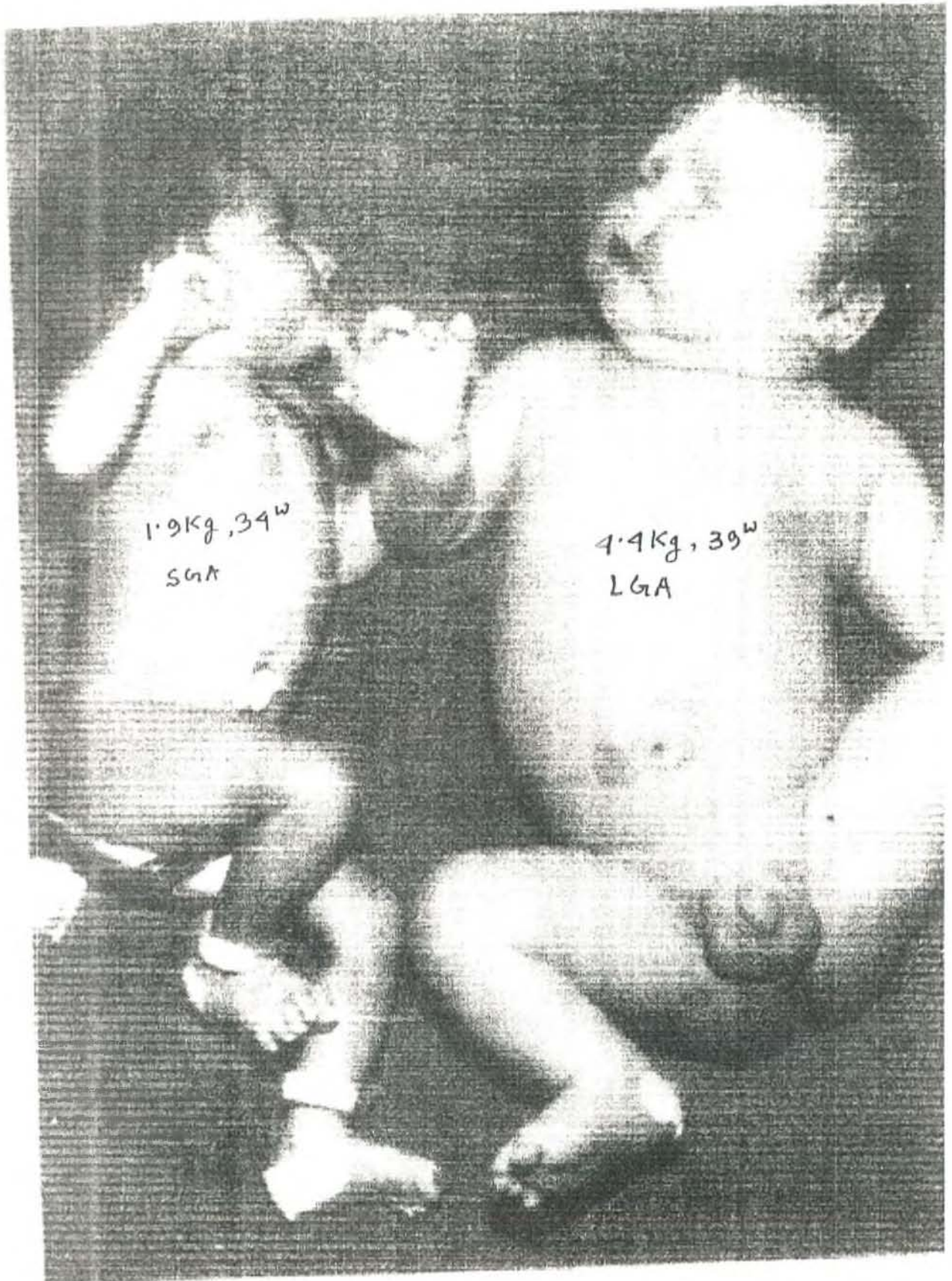


Fig-1A

Chapter 4

DISCUSSION

Discussion

Maternal characteristics

In this study, the diabetic mothers were found comparatively older and less educated compared to non-diabetic mothers (NDM). The total monthly family income was less in them. This is also reflected in their expenditure on food and dietary consumption pattern. The diabetic group was found to consume more rice and less meat or fish and less oil compared to their control. There are a few studies where detailed socio-demographic information or dietary history was sought for diabetic pregnant mothers in Bangladesh. Similarly in one study in Pakistan Shera et al in 1999 found the diabetic pregnant women were older than the non-diabetic counterpart (148). Jhon in 1997 also found similar result that age as a major risk factor for pregnancy outcome in diabetic pregnant women (149). Socio-economic status especially income of the family and maternal education are important factors for pregnancy outcomes (150). A group difference was found for education and monthly income between the groups in the present study. Similar with the present study findings, Ali et al in 1999 in Bangladesh found that, the diabetic pregnant were from less educated and lower income group than that of the non-diabetic pregnant women (22). Though the study by Ali et al did not matched the two groups. However, the present study findings are similar with the Brazilian study by Brazillian Gestational Diabetes study group in 2000 where they found the highest rate of diabetes in the 'urban low-income group' compared to other groups (151).

Very few of the DM pregnant women were found working rather most of them were housewives. Like the findings of the present study, Nahar (82) in Bangladesh, Engelgan et al 1995 and Camacho et al in 2000 also found that the diabetic pregnant mothers were mostly housewives (152, 153).

Family history and past obstetrical history

Diabetes runs through the family. Most of the DM pregnant women of this study had a positive family history for diabetes. Either father or mother or any other close relatives were diabetic in the family. Similarly higher rate of positive family history was found in diabetic pregnant women in a study conducted in

Bangladesh by Karim et al in 1993 (23). McNeil et al in 2001 in their recent studies also found a high rate of positive family history in both pre-gestational diabetic and gestational diabetic pregnant women (154) and the finding was in accordance with the present study findings. The present study observed that, though 81.0% of the pregnant women had a positive family history for diabetes, but only 37.0% of the cases were diagnosed by routine medical checkup and the rest were diagnosed following any sort's of problem. Among them, a sizeable number (21.5%) were diagnosed following severe pregnancy complications like fetal losses. A greater birth interval for diabetic mothers was also observed. Similar findings were observed by different other studies. Jahangir in Bangladesh found a greater interval between marriage and first pregnancy in diabetic mothers compared to non-diabetic group. About 79.0% of the diabetic mothers in his study were diagnosed first during pregnancy (131). Similarly Hussein et al in Palestine also found that most of the diabetic pregnant women were diagnosed following any sort's of problem and the birth interval was higher in diabetic pregnant women (155). This has got importance for routine checkup of all reproductive aged women with a positive family history of diabetes for early diagnosis of diabetes and preconception counseling and planning for pregnancy. In the DM group, history of cesarean sections were more in the previous childbirths and a good number of mother suffered from different medical complications and obstetrical complications, like abortions and late fetal death during their previous pregnancies. Similar findings are observed by Nahar in Bangladesh and the history of pregnancy-induced hypertension, pre-eclampsia, infection and cesarean section were found higher in the diabetic mothers (82). Another study of a ten-year outcome analysis in Northern Ireland by Hadden et al in 2001 observed adverse fetal, maternal and infant outcome in diabetic pregnancy and the findings was in accordance with the present study findings (156).

Comparison of pregnancy outcome and birth outcome

Poor glycemic control in early pregnancy in both type-1 and type-2 diabetic mothers were found to be associated with an increased risk of spontaneous abortion, congenital malformations & other adverse pregnancy outcomes. It is reflected though the pregnancy outcomes are improving, the diabetic pregnancies need much more attention. For convenience we will discuss the pregnancy outcomes separately as fetal outcome, birth outcome and perinatal outcome.

Birth outcome

Live birth

Live birth rate in the DM group was found 98.0% in our study, which was cent percent in the NDM group. Ivy in Bangladesh found live-birth rate of 95.5% in the diabetic mothers (132), which was lower than the present study. The rate was observed to be comparatively better than the rate found (80.3%) by Halwagy et al in 2001 with 547 diabetic mothers (157). The live birth rate was higher in the present study, possibly due to the fact that, almost all of the pregnant women were under close supervision, regular monitoring and were delivered in the hospital.

Preterm

In the present study, mean $\pm$ SD of gestational age was found lower (36.4 ± 1.7) in the DM group in comparison to the NDM group (38.1 ± 0.6). Nahar in Bangladesh found a mean gestational age of 36.8 ± 2.1 weeks, which was near to similar to the present study (82). Dolberg in 2000 found higher mean gestational age of the IDMs than the present study (37.0 ± 0.20 wk) (158).

Delivery of a baby before 37 weeks of pregnancy by normal vaginal delivery without any effort is considered as spontaneous preterm in this study. In the present study, preterm (less than 37 weeks) rate was higher (41.5%) in the DM group but on NDM group it was only 6.2%. This includes elective cesarean sections and also spontaneous preterm. Spontaneous preterm was only 10.2%. The spontaneous pre term rate was found higher (16.3%) than the present study in DM pregnant women in another study conducted at BIRDEM hospital in Bangladesh (159).

A number of research articles throughout the world documented variable number of preterm deliveries in the DM pregnant women. Reduction of rate of preterm babies born to diabetic mother takes place till date with time. Kaim in 1995 in his longitudinal studies of 2 cohorts of diabetic pregnant women also found a decline from 53.5% to 12.0% over the periods from 1980-86 to 1987-92. The rate observed by Kaim in 1995 was near to our present study (160). Similarly in a 14-year study in Poland by Mironiuk in 2001, from 1987 to 2000 on pregestational diabetes of 'White class B-RF', observed a decrease in the percentages of prematurity from 51.6% to 20.0%. Preterm rate observed in this study was higher than the present study (161). Lao & Ho in 2003 studied 2168 Chinese women with singleton pregnancies and found that gestational glucose intolerance affect gestational length (162).

Possible cause of variation of the rate of preterm in different study in country and abroad with this study is due to variation of the rate of cesarean section earlier to prevent the late fetal death. Also, in most of the reports, spontaneous preterm labor and iatrogenic or therapeutic preterm delivery are not separately described thus complicating quantification of incidence of preterm delivery.

Fetal loss

The present study found a reduction in adverse pregnancy outcomes by good glycemic control and regular antenatal checkup of the DM pregnant women. The rate of fetal loss was only 45/1000 total births in the DM pregnant women compared to no loss in the NDM group. There were 2 abortions, 2 congenital malformations, 3 stillbirths and 2 late fetal deaths (IUD) in the DM group who were neither under regular antenatal check up nor had a euglycemic state throughout the pregnancy. Another study observed a lower rate of fetal losses 20-40/1000 total birth than the present study by optimum maternal metabolic control in the DM pregnancies (163). Though different other studies observed fetal losses in varying number in the DM pregnant women, but similar with the present study findings, they also observed that the rate of fetal loss is higher in DM pregnant women than the non-diabetic pregnant women and the general population (164,165).

It is reflecting from the present study that regular blood glucose monitoring and good glycemic control during pregnancy resulted in reduction of fetal losses in the DM pregnant mothers.

Spontaneous abortion

In the present study spontaneous abortions in the DM group were found only 10/1000 total birth. A higher rate of abortion was found in 1998 by Ivy in Bangladesh (48/1000 total birth)(132). Karim in a hospital based cross-sectional study in Bangladesh also found higher rate of abortion among the DM pregnant women (15/1000 total birth)(23). The rate of abortion was higher in these two country studies possibly due to the fact that, both of the studies were small scale cross sectional hospital based studies, instead the present study was a matched cohort study. Moreover, Karim and Ivy didn't differentiate the GDM and pre-gestational diabetes in their study but the present study includes only pre-gestational diabetic women. In contrast to the present study findings, Dorman also observed higher rate of abortion (18/1000 total birth) among the DM pregnant women in 1999 (166). Kabadi in 2002 in a population cohort study in the UK also observed a higher rate of abortion 22/1000 total birth, than the present study (167).

The possible cause of variation and higher rate of abortion was may be due to the fact that, the UK study was a population-based study but present study was a tertiary care hospital based study. Whereas the majority of the pregnant women of the present study were well motivated to attend the antenatal visits for follow-up and were under cover of one antenatal care umbrella comprising the obstetrician, diabetologist and nutritionist at the BIRDEM from early week of pregnancy.

Intrauterine death (IUD)

The present study, found that the late fetal death rate, was 10/1000 total births, which occurred between 32 and 36 weeks of gestational age. In contrary with the present study findings, Akhter in Pakistan found a higher rate of late fetal death, 53/1000 total births in their study (168). Similar with the present study findings, a recent large-scale study on singleton pregnancy (n=10,614,679) in the

United States by Smulian in 2002 found diabetes as a potential risk factor for fetal death particularly in third trimester and detected a 3-fold risk for fetal death for diabetic mothers delivering at or beyond 24 weeks' of gestational age (169). The lower rate of the late fetal death in present study is possibly due to a high rate of cesarean section in this sample, which prevent late fetal death of high risk DM mother in this cohort.

Congenital malformation

The pregnant women in the present study experienced 2 (10/1000 total birth) congenital anomalies only in the DM group. One with cleft palate, one with anencephaly. These babies with congenital anomalies were born to mothers who were not under regular antenatal care and didn't had a regular monitoring of blood glucose level at home. Though all of them attended for their first visits at the BIRDEM hospital, only one of them came to the hospital for delivery and delivered a baby with cleft palate. Pregnancy was terminated for one at a private clinic for anencephaly at 26 week of pregnancy. Our finding is close to the findings of Reece in 1998 where they found congenital anomalies 13/1000 total births in well-controlled DM pregnant women (170). Different researcher found higher rate of congenital anomalies among the IDMs but with a wide variation. Higher rate (43/1000 total birth) of congenital anomalies was observed by Ivy in 1998 in Bangladesh, than the present study (132), whereas Karim et al in their study in Bangladesh observed no congenital anomaly (23) among the infants of DM pregnant women. Similarly diabetes control and complication trial study (DCCT) found a higher rate (four fold) of congenital anomalies than the present study and the rate was 47/1000 total births (171). Reduction of the rate of congenital anomalies was observed with time, Jay and Sullivan in 1980 found a very high rate of congenital anomalies, 220/1000 total births (172) on the other hand Rosmery et al in their population based study in 2002 has brought down the rate of major malformation as low as nearly 20/1000 total births with a good glycemic control in pre or early pregnancy period, though the rate was higher than the present study findings (173). Another recent study found higher rate (40/1000 total birth) of congenital anomalies in a cohort of infant of diabetic mother (174).

Possible cause of lower rate of congenital anomalies in the present study than the other study may be due to variability of maternal glycemic status in early pregnancy and throughout the pregnancy. It is reflecting that the present study sample was under such a level of good glycemic status that lowers the rate. It is not still clear whether good glycemic control in the 1st trimester is the only factor that protects diabetic mothers from having congenital anomalies in their fetuses, rather other factors like genetic or teratogenic nutrients or environmental factors may be working in conjunction with poor glycemic control in the development of congenital anomalies. So there is a need for further in depth study to explore the underlying factors associated with or responsible for congenital anomalies in infants of diabetic pregnant women.

Fetal size: live born singletons

Birth weight

In this study, mean birth weight was found significantly greater (2850.6 ± 577.1 g) in the IDMs than that of the infants of NDM mothers (2651.1 ± 344.4 g). The rate of low birth weight was lower in IDMs 21.6% vs 24.1% in NDM groups. A significantly greater mean birth weight (about 285 g higher) was observed for male babies compared to females in the present study. In a study in Bangladesh, the mean birth weight of the infants of DM was found higher than the present study $3040 \text{g} \pm 500 \text{g}$ and they also found similarly that the IDMs birth weight was higher than the NDM groups ($2750 \text{g} \pm 360 \text{g}$). Low birth weight babies were found 13.3% among the infants of DM and 17.3 % among the NDM groups respectively in that study conducted at BIRDEM hospital (175). Variable range of birth weight was observed in different studies abroad. Two other studies by Casson et al (164) in 1997 in North East England, and Schaefer et al in 2003 (176) found higher mean birth weight of IDMs than the present study, which ranges between 3509.0g and 3100.0g respectively. In contrast to the present findings, Casson et al found girls heavier than boys in their population cohort study with 462 unselected pregestational diabetic pregnant women although the difference was not significant.

The difference is due to the fact that the study by Begum et al (159) did not differentiate the GDM and pregestational DM. And the other study sample were taken at any time during pregnancy so the lower range of mean birth weight of IDMs in the present study may be due to the early entry at <12th gestational week and close monitoring of blood glucose.

Large for gestational age (LGA)

The present study defined LGA as birth weight above 3300g (46). Twenty percent (20.0%) of IDMs in this study were 'large for gestational age' (LGA) compared to only 3.0% in the NDM group. Two studies in Bangladesh observed a higher rate of LGA than the present study among the infants of DM pregnant women. Karim et al (23) observed, 30.0 % and Kundu in 2000 (177) observed 35.0% LGA in their studies on diabetic pregnant women attended at BIRDEM hospital. The different studies observed higher rate than the present study. Morris et al in their study found 36.0% LGA infants in women who had HbA_{1c}% more than 7.0% (178). Gold in 1998 found an increase number (25.5%) of large for gestational age infants born to diabetic mother than that of the non-diabetic counter part (179). Other researchers concluded that maternal blood glucose level influences the fetal growth and large for gestational age infant born more from mother with uncontrolled blood glucose level at any time during pregnancy. Samasima et al in their recent studies in 2000, in 250 Japanese diabetic pregnant women observed a lower rate of LGA than the present study in well controlled diabetic pregnant group (15.0%), in contrary the rate was found higher than the present study among the poor controlled group (27.0%) (180). Wolf et al also found similar result as Samesima, and the rate of LGA was only 22.0 % in their study. The rate observed by Wolf was close to the present study (181).

Regarding the timing of fetal growth spurts, a retrospective study was conducted by Wong et al in a tertiary care hospital of Australia between 1st January 1994 and 31st December which included all pregnant women with pregestational diabetes type-1. An analysis was done to find out the relationship between the maternal diabetic control and fetal growth. This study concluded that fetal growth acceleration of LGA babies take place in the second trimester from as early as

18th week of pregnancy. This study did not show any relationship of maternal glycemic status with LGA and disputing the finding of relationship of LGA with maternal glycemic status (182).

The possible cause of lower rate of LGA in this study is possibly due to the fact that the pregnant women were mostly under good glycemic control throughout the pregnancy. Also the present study sample was only the pre-gestational diabetic pregnant women.

Macrosomia

IDMs born to mothers without vascular or renal disease have an increased incidence of macrosomia. Diabetic mothers with vascular or renal disease usually showed lower incidence of macrosomia. The present study defined macrosomy as infants with birth weight over 4000g (46). The present study, found only 9 (4.9%) macrosomic babies in the DM group and on the other hand only 2(1.0%) LGA in the NDM group. Like the present study similar findings (5.8%) also observed in a study at BIRDEM in pregestational diabetic women (22). Higher rate (12.0%) of macrosomia than the present study was observed in infants of DM pregnant women by Jardim in 1997 (183).

Bergmann in 2003 evaluated secular trends of macrosomia and its determinants in Berlin from 1993 to 1999. Lower trends were observed from 1993 (35.0%) to 1999 (21.0%)(184). But the rate was much higher than the present study. Possible cause of variation of macrosomic babies born to DM pregnant between these studies and the present study may be due to variation of standard used to define macrosomy and severity of diabetes of the pregnant women i.e. whether complicated or uncomplicated.

Apgar score

Apgar score detects health status of the neonate at birth, at 5 minutes and at 10 minutes after birth. Significantly more (26.9%) babies from the DM groups were found Apgar score <7 at 1 minute compared to NDM group (8.0%). At 5 minutes, about 95.0% neonates of the NDM mothers had an A/S score of 7-10, whereas the rate was still lower in the neonates of DM mothers (79.0%).

Similarly, other studies in Bangladesh also observed more babies with low Apgar scores at birth (<7) among the DM group, 25.0% found by Kundu and 30.0% by Ivy (177,132). The rate of low A/S observed by Kundu was close to the present study. On the other hand rate was higher in study conducted by Ivy. Similar with the present study findings lower A/S was found in IDMs than the infants of NDM in different other studies (185-187). Vaarasmaki in 2000 observed 25.0% of IDMs having apgar score <7 and the rate was found higher than that of the general population. The result was close to the present study findings (188).

The higher rate of IDMs with low A/S warned that the DM pregnant women needed to be delivering under expert Obstetrician and in a well-equipped delivery room with modern facilities.

Birth complication

The infants of diabetic mothers of this cohort suffered significantly more from different birth complications compared to non-diabetic counterpart (25.7% vs. 8.5%). Similar with the present study findings, the Hyperglycemia and Adverse Pregnancy Outcome study (HAPO) Corporative Research group in their 5-year prospective observational study in 2002 found more babies with birth asphyxia and neonatal morbidity in IDMs than the general population (189).

No shoulder dystocia was observed in our sample. In contrast to the present study findings, Nieger found that infants of diabetic gravida experienced shoulder dystocia five times more frequently than infants of non-diabetic mothers (190). Modanlou in 1990 (191) and Jeanne in 1993(192) stated shoulder dystocia as an important complication of macrosomia in IDMs. Lindsly in 1997 also found more shoulder dystocia (four times more than the general population) and birth injury among the IDMs in their studies in abroad (193). The present study found no shoulder dystocia, because the pregnant women were under close supervision and cesarean sections were performed where indicated. Shoulder dystocia due to big baby also causes maternal distress in addition to fetal distress, which need to be addressed (194).

Perinatal morbidity

In the present study the rate of perinatal morbidity was found higher (53.8%) in the infants born to diabetic mothers than that of the non-diabetic (13.0%). Ivy in 1998 in a hospital based study in Bangladesh found lower rate of 31.9% than the present study (132). Earlier study before 1980s by Solar et al found very high rate of perinatal morbidity 52.0% (195), which was similar with the present study findings. Though it is encouraging that a lower trend was observed with advancement of time. Rudge et al in their 10 years retrospective analysis from 1990s to 1999s found lower rate of perinatal morbidity among the IDMs (46.0% to 22.0%) than the present study (196).

Another recent study by Szilagyi in 2001 found much lower rate (19.0%) than the present study (197). Tasnim et al in 1998 observed a rate of perinatal morbidity 32.7% in Bangladeshi infant born from normal pregnancy (198), which is also lower than the present study.

The rate of perinatal morbidity was found higher in the present study than that of the Ivy's study on DM pregnant women in Bangladesh and most of the other study abroad. Also the rate is higher than the rate among the infants born to normal pregnant women in Bangladesh.

This reflects that though the attempt to deliver the IDMs by cesarean section save the life of the fetus in DM pregnancy but, possibly these infants were suffered more due to high rate of preterm delivery, lower immune level of DM mothers and staying in home at perinatal period, which needs further consideration.

Type of perinatal morbidities

Regarding the type of morbidities, the important morbidities were found respiratory distress syndrome (RDS), jaundice, umbilical cord sepsis and ophthalmia neonatorum among the infants of IDMs in the present study.

Hyperbillirubinemia:

In this study, we found 38 cases of jaundice diagnosed clinically and among them only 12.0% were diagnosed as hyperbilirubinemia by biochemical test. Different other studies in country and abroad also observed jaundice and RDS in IDMs as the important morbidities (82,23). Similarly the Mexican study by Sandoval in 1995 observed lower rate of perinatal morbidities (47.3%) than the present study and but the type of morbidities observed were similar with the present study findings, hyperbilirubinemia (11.0%), hypoglycemia (8.0%) and hypocalcaemia (4.0%) (126). Hyperbilirubinemia was defined as over 15 mg /dl in this study like Kitzmiller study. Kitzmiller study found 19.0% Hyperbilirubinemia in IDMs at Brigham and Women's Hospital (199). The rate of hyperbillirubinemia observed in this study is very close to the findings of Sandoval study but lower than the Kitzmiller study. The difference may be due to different sample.

Respiratory distress syndrome (RDS):

Only 20 cases of clinically diagnosed cases of RDS were found in the present study. Similarly Pearson in 1998 found respiratory distress as one of the important perinatal and neonatal morbidities among the IDMs (200). A study among the South Indians by Ramachandran in 1998 also found jaundice and RDS as the most important morbidities of IDMs (201). Similarly higher rate of RDS were found among the IDMs in other studies and the relationship of hyperinsulinemia and respiratory distress syndrome among the IDMs were studied in these studies. Stubbs et al studied the relationship of hyperinsulinemia and respiratory distress syndrome among the IDMs and found strong positive relationship between the RDS and hyperinsulinemia (202). Subsequently Kjos and coworkers in 1990 (203) and Robert in 1997 analyzed the association between the maternal glycemic status and occurrence of RDS among the IDMs and found strong and significant (<0.001) association (204). Later studies by Lao in 2001 further established the findings of the prior study and concluded, that good glycemic control could reduce the RDS to a large extent (205). The present study findings of higher rate of RDS were similar with the other studies

mentioned where they also found higher rate of RDS among the IDMs. Respiratory distress syndrome needs special mention and further consideration as 75% of total perinatal mortality in this study sample was due to RDS.

Neonatal hypoglycemia:

Neonatal hypoglycemia (defined as blood glucose level <35 mg/dl or <2.0 mmol/dl) was found only 12.0%, which was symptomatic and needs resuscitations. In Bangladesh the rate was found higher (19.0%) in Nahar's study in 1992 (82) and Ivy's study in 1998 (21.0%) than the present study (132). The rate observed in present study was found very close to other two recent studies where the pregnant women were under good glycemic control throughout the pregnancy. Pal et al in 2000 in Nepal, found the rate of neonatal hypoglycemic at birth 11.3% (206). Similarly Agarwai in 2001 found a rate of 13.0% hypoglycemia at birth among the IDMs in India and the rate was higher than the present study (207). Possible cause of lower rate of hypoglycemia in the present study than the other studies is that the mother of this sample was under good glycemic control in third trimester and at delivery.

Perinatal mortality

Only 4 early neonatal deaths (perinatal deaths), 2 IUD and 5 stillbirths were found in the IDMs but no perinatal death and stillbirth were observed in control group. This constitutes a perinatal mortality rate of 55/1000 total births. The present study used the definition according to recent WHO definition, referred by Nelson in 1998 (208), which include stillbirth and early neonatal death within 7 days of birth in perinatal death. No one died due to congenital anomaly during perinatal period. Respiratory Distress Syndrome (RDS) was found the major cause (75.0%) of early neonatal death in the present study. a higher rate of perinatal mortality was observed by Ivy in 1998 in her cross-sectional study in Bangladesh (128.0/1000 live birth)(132). Similarly Jahnagir in 1995 found a rate of 171.8/1000 live births, which is much higher than the present study (131).

Variability of perinatal mortality was observed by different studies. Most of the other authors found higher rates of perinatal mortality among the IDMs than the

general population. The variation of the rate of perinatal mortality was observed among the IDMs in different region. In a multi-center survey of diabetic pregnancy in France, perinatal mortality was found slightly higher in diabetic women than the general population (18/1000 live birth vs. 12/1000 live birth) but the overall rate was lower than the present study (209).

Huddle et al in Africa found higher perinatal mortality rate of 66/1000 live birth (210). Sobondi et al in 2000 in Saudi found the rate, which was similar (54/1000 total live birth) with the present study (211) but one very recent study conducted abroad by Cundy in 2000 found lower rate (32/1000 live birth) than the present study (212). Greater risk (2.5 fold) of perinatal mortality was observed by Dunny et al in a twelve-year outcome analysis from 1990-2002 of pregnancy with type-2 diabetes (213).

This variability of perinatal mortality rate of different studies with the present study findings is possibly due to different time period and also most of the study didn't differentiated the complicated from uncomplicated diabetes mellitus for analysis. The definition of perinatal mortality used variably in different studies. Some of the earlier author didn't include the late stillbirth rate in their analysis but most of the author recently use the WHO definition of perinatal mortality, which includes late fetal death, early stillbirth rate and use total live birth as the denominator (208). Instead of high perinatal morbidity rate the rate of early neonatal death is low, which reflects better management of perinates who were morbid and admitted to neonatal intensive care unit of BIRDEM.

Glycemic status

The mean values for glycosylated hemoglobin percentages in all 3 trimesters in this study were found lower ($5.1\% \pm 1.6$) than the mean values found in study by Langer et al (6.5%) in a group of diabetic pregnant women (214). The possible reason is that the Langer study was cross-sectional in nature and the pregnant women of the present study were under regular antenatal visits and under regular monitoring for blood glucose from the first trimester. Choudhury et al in 1988 compared the fasting blood glucose level of a group of Bangladeshi pregnant women with that of the non-pregnant control group and observed no

significant difference between the groups. Mean value of the fasting blood glucose level of the non-diabetic women of the present study was very close to that of the normal pregnant women of that study (215).

In this study, mean values for fasting blood glucose, postprandial blood glucose and glycosylated hemoglobin percentage of diabetic mothers were higher in the first trimester and gradually declined to normal in the third trimester. And a large proportion of (around 60.0%) diabetic mothers were not under good glycemic control by all indicators at their first trimester. The finding of diabetes control and complication trial is similar with the present study findings. The DCCT study reported that, only 44.0% of all patients had an HbA_{1c} % within the reference range at least once during the study period (171). Other researchers from different countries over a period of time from 1998 to 2001 also shared similar experience and suggest improving the early glycemic status of the diabetic pregnant women (216-218). This reflects a poor pre-conception care & counseling of diabetic mothers. It is also difficult to do such type of care in a setting in a developing country like Bangladesh.

Maternal morbidity

Infection:

In the present study, only 3 mothers (1.5%) in their last trimester from the DM group suffered from urinary tract infection. This figure is quite low compared to the finding of Nahar study in Bangladesh (8.5%) (132). Possible cause of a very low rate of infection in this study population is that, they were uncomplicated cases and were under good control after enrollment at first trimester, also the duration of diabetes was not so long but only 1-5 years.

The other infections (respiratory tract infection and skin infection) were found higher among the DM pregnant women in the present study compared with their counterpart. No cases of post-wound infection was found in this sample. Higher rate of infection among the DM pregnant women was observed by different other studies. The infection rate was found higher (17.0%) than the present study in the prospective study conducted by Eric in Ohio (219). Higher rate of maternal

morbidity especially infection (10.0%) was also found in another 5 year retrospective population based study on pregnancy outcome of pregestational diabetic women in Germany (220). But the recent study by Rosmery et al in 2002 in a population-based study observed lower rate of wound infection (3.0%) and urinary tract infection (4.0%) and the rate was close to the rate of present study (221). The possible cause of higher infection rate is that the other studies was not a matched cohort study rather they included at any time of pregnancy, on the other hand it is reflecting that in the present study sample proper antenatal care from the very beginning of the pregnancy may lower the infection rate close to the nondiabetic pregnant women.

Hypertension & other related morbidity

Though the mean values of both systolic and diastolic pressure were within normal limits in all three trimesters, 9 mothers developed hypertension by the 2nd trimester in the DM group compared to none in the NDM group. These 9 mothers who developed 'pregnancy induced hypertension' in the 2nd trimester, were no longer hypertensive in the 3rd trimester, rather 10 new cases developed hypertension during that time.

There were only 7 cases of pre-eclampsia (3.5%) in the 2nd trimester and they were under control by the 3rd trimester but 2 new cases of pre-eclampsia developed in that time.

A hospital based cross-sectional study in Bangladesh found a rate of pre-eclampsia of 21.0%, which was much higher than the present study (23).

In a study in the UK higher rates than the present study was observed, where pre-eclampsia complicated 13.6% of diabetic pregnancy, and in that study, individually in 'White class B', the rate was found 10.9% (222). Similarly Rosen et al observed higher rate 15.0% in 2001 than the present study (223).

The occurrence of low pregnancy-induced hypertension and pre-eclampsia in the DM group in this study is possibly due to regular antenatal care from the first trimester.

Anemia

The rate of anemia was found more in the DM group than their counterpart in all 3 trimesters but higher in the 3rd trimester (36.0% vs 11.6%). The rate was increased in the DM group from 1st trimester to last trimester. In a cross-sectional comparative study at the BIRDEM hospital, Ali et al in 1999 found higher rate of anemia in diabetic mothers compared to non-diabetic mothers (22). In another study of DM and GDM pregnant mothers at the BIRDEM by the same research group, 38.0% of pregestational diabetic mothers were found anemic which is close to the present study findings (224).

Why diabetic mothers are more anemic than that of the non-diabetic group is not clear. But there is a possible theoretical explanation, it is established that the diabetic patient has disturbed metabolism of many nutrients especially zinc and the diabetic patient was observed deficient in zinc and suffered from zincuria and zincanemia (225). That alteration of zinc metabolism reduces vitamin A absorption, which is again linked in the causation of anemia. The possible mechanism is that vitamin A deficiency reduces the non-heme iron absorption in blood and there is a strong relationship between vitamin A deficiency and occurrence of anemia (226-228). There is a need to explore the causal relationship of developing anemia in diabetic pregnant mothers. Because the anemia it self complicates pregnancy outcomes.

Polyhydromnios

Only 2 (1.0%) cases of Polyhydromnios were found in the DM pregnant women in this study. This rate was lower than the other studies in Bangladesh, Ivy in 1998, found 12.7% (132) and Begum et al in 2000 found 4.8% (224). The diabetes care and research group in Europe conducted study on DM pregnant women and found higher rate of polyhydromnios (15.0%) than the present study in women with uncontrolled blood glucose level (229). A ten-year outcome analysis of diabetic pregnant women in Northern Ireland found decreasing trends of polyhydromnios in well-controlled diabetic pregnant women (230). Possible cause of higher rate in those studies than that of the present study was due to the

cross sectional design and inclusion of all classes of diabetes i.e. pregestational and gestational diabetic cases.

Fetal presentation and cesarean section

It was observed that in the DM group the breech presentation was more compared to the NDM group (11.1% vs. 1.0%), and only one case of 'transverse lie' was found in the DM group in the present study. In this sample, cesarean section was more (69.3%) among the DM pregnant women than the non-diabetic pregnant women (6.5%). At BIRDEM hospital of Bangladesh Banu in a large-scale retrospective study on outcome of diabetic pregnancy found lower rate (52.8%) of cesarean section in comparison to the present study. But the rate was higher than the non-diabetic pregnant women of that sample (81). A lower rate of cesarean section (48.0%) were found than the present study in diabetic pregnant women in a study conducted by Robert et al in 2001(231). Possibly due to the fact that the present study didn't differ the number of cesarean section due to cause directly or indirectly related with maternal diabetes from the number of cesarean section due to other cause.

The comparison of maternal nutritional status of the diabetic and non diabetic pregnant women

The enrollment weight was taken before 12 wks of gestation, which was considered as the early pregnancy weight. In this study almost all anthropometric measurements including early pregnancy weight, early pregnancy BMI, MAC, biceps and triceps skin fold thickness and total weight gain were found significantly greater in diabetic pregnant women than that of the non-diabetic pregnant women. The present study tried to find out nutritionally at risk mothers on the basis of accepted cut-offs points for MAC and BMI for different outcomes. On these cut-offs, no group difference was observed. A cross-sectional study in Bangladesh also observed similar results (224).

Percentage of overweight and obese detected by BMI was significantly more in the DM group whereas percentage of underweight women was more in

the NDM group in the present study. Similar with the present study it was observed that the incidence of diabetes was twice among the women, who were 20.0% or more over ideal weight than that of non-obese (232). Similar with the present study findings, Sullivan also found that the women with greater weight are subsequently developed diabetes (233). Findings of Hanson in 1995 substantiated the findings of Sullivan's study and commented that weight gain and weight fluctuations developed latter diabetes (234). Similar like the present study findings of higher weight in DM pregnant the studies by Anastosion in 1998 and Branchte in 2000 found greater weight and short height in gestational diabetic pregnant women in abroad (235,236).

Weight gain

In both DM and NDM groups, near half of the mothers suffered from “chronic maternal undernutrition” as detected by WHO cut-off value of weight gain of <350g / week. When we considered underweight and gestational undernutrition, DM mothers were found comparatively better than their non-diabetic counterpart. This apparent better state may not be a reflection of better nutritional status for diabetic women rather increased lipogenesis in diabetes may be a causative factor (237). Fetal and infant growths are characterized by “critical periods” during which all essential nutrients must be available, otherwise growth and development will not proceed normally (238). We will refer 'total weight' gain as weight gain.

In the present study, the difference became significant between the groups for total weight gain and total weight gain per week. Although the total weight gain was significantly greater in DM (8.6 ± 3.2) group than that of the NDM (7.9 ± 2.5) group, this gain is much lower compared to a group of diabetic mothers in New York Hospital (14.5 kg) observed by Jovanovic 1980 (239).

MAC changes

The use of arm circumference for nutritional status monitoring for prediction of pregnancy outcome has been recommended by various researchers due to its ability to predict various pregnancy outcomes and its practical

advantages compared to other anthropometric measurement (240). In our study, both the groups gained MAC till 28th wk of pregnancy & lost between 29th to till delivery, though the group differences were not significant. The percentile distribution observed a significant difference between the groups and median loss for diabetic mothers was found significantly more.

As we did not find any study on MAC changes in diabetic mothers, the discussion will be concentrated on non-diabetic pregnant women only. Similar with the present study, in Kenya, Jansen et al found an increase of MAC in first two trimesters and then a decrease between the second and third trimesters (240). In India, Agarwal et al reported that mean arm circumference was similar in all three trimester (241). Similar with the present study the above described study also found a loss of MAC throughout the pregnancy.

Weight changes by early pregnancy weight categories

It is established that undernutrition affects birth weight and other pregnancy outcomes. Similarly, excessive weight gain is also detrimental to neonatal and maternal health (242).

In the present study, an attempt was made to analyze the weight gain according to different nutritional status as recommended by WHO consultative group on pregnancy outcome. The variation of weight gain by different weight status in early pregnancy is overt in this study. In the DM group, underweight pregnant mothers gained maximum while normal mothers gained least, whereas in case of NDM group obese mothers gained maximum and underweight mothers gained least. Compared to the recommended weight gain pattern for different nutritional categories (243), the underweight, normal and overweight mothers of both groups gained, whereas the obese mothers gained more than the recommended values in the present study.

Relationship between maternal characteristics with perinatal morbidity

Relationship between maternal characteristics with perinatal morbidity was elucidated in the present study and found increased risk of developing

perinatal morbidities when maternal monthly income <10,000/-, height <152 cm, total weight gain <7.0 kg. A number of studies in Bangladesh found strong relationship of maternal monthly family income, maternal height and total weight gain with perinatal morbidity and neonatal death (244-246).

Many fold-increased risk of developing perinatal morbidity was observed in the present study in IDMs of mother with uncontrolled blood glucose level at any time during the pregnancy. Risk found 12.5 fold when maternal third trimester glycosylated hemoglobin percentages was >6.0% and 4.2 fold when maternal second trimester glycosylated hemoglobin percentages >6.0%. Cousine in 1991 also found similar results in both pre-gestational and gestational diabetes, there is an increased rate of perinatal morbidity in infants born to mothers with uncontrolled blood glucose level (247). Similarly Hosamane in 1990 showed positive association between maternal blood glucose level and perinatal morbidity and mortality (248).

Relationship between maternal nutritional status and glycemic status with neonatal nutritional status at birth of DM group

It is well recognized that there are multiple factors, which contribute to fetal nutritional status in utero. The effect of intrauterine fetal nutrition is reflected by nutritional statuses of the newborn at birth and detected by birth weight and other anthropometric measurement. However the study of these factors is complex, because of the inter-relationship between the various variables and the difficulties in determining an independent effect of any particular variable on birth weight.

This study examined selected socio-demographic and maternal anthropometric variables, which are known and established by most of the authors (249-251).

Relationship between neonatal anthropometric measurement and associated variables were examined in two ways, birth weight, length, head circumference and mid arm circumference was treated as continuous variables and also as categorical variables using 2.5 kg as low birth weight, >3300.0 g as large for date

and >4000.0 kg as macrosomy. Relationship between perinatal health status and neonatal anthropometric measurement and maternal glycemic status was treated as categorical variables using <7.0 kg as low weight gain, <MAC <9.0cm as low nutritional status of the newborn and glycated hemoglobin percentages <6.0 as good glycemic status.

Relationship between maternal socio-demographic status and birth weight

There is a large volume of data where marked socio-economical differentials in birth weights have been repeatedly reported in different studies. In this study relationship was found between the total monthly family income with nutritional status at birth, as reflected by birth weight and mid arm circumference of the newborn in both the group. And explains 32% of variation of birth weight due to one unit change of monthly income of the family in case of IDMs. Similar result was observed by different studies. A gradient of birth weight was observed by different studies in different socio-economic status (252,253). Similar Positive association was observed between family income and birth weight in some other recent studies. Even within low-income group the difference (100-150g) existed between the poorest and the less poor (254-256).

Relationship between mother's educational status and mean birth weights was found when both group combined together but individual analysis for the DM group found no relationship. However the NDM group existed strong positive relationship. WHO multi-centric study also found similar findings like the present study, that there is a strong positive relationship between mother's educational status and mean birth weight. A trend for increasing mean birth weights with more education was apparent in the Bangladesh, India, and Srilanka in (257). Kramer in 1991 in his Meta analysis also found strong relationship between mother's educational status and birth weight (258).

Unlike the study by Fekeri in 1994 and by Shamema in 2000, the present study found no relationship between birth spacing and birth weight (259,260). Possible cause is due to the matching of the two groups by parity in the present study.

Maternal nutritional status and relationship of neonatal nutritional status

The present study observed strong significant positive association of maternal nutritional status (early pregnancy weight, early MAC, maternal height, early pregnancy BMI and weight gain) during pregnancy and newborn nutritional status at birth as reflected by birth weight, baby mid arm circumference, baby's head circumference and recumbent length. But baby's chest circumference was significantly correlated only with early pregnancy BMI.

After controlling the other factor the family income, maternal weight and weight gain shows independent effect on birth weight of both the group in the present study. Similar result was found by most of the studies, where they examined the relationship between maternal pre-pregnancy weight and weight gain on birth weight. A similar finding was observed in Bangladesh by Ahmed et al in 1994 and Shamema in 2000 where they found significant correlation between maternal weight gain and birth weight (260, 261). Fung et al in Singaporean women reported significant relationship between birth weight and maternal weight (262) and the results was similar with the present study. Richard in 1999 (263) and Olson in a very recent study in 2003 (264) found significant relationship of maternal weight gain with neonatal birth weight. And the present study finding is very similar with the findings of the above-mentioned studies in this respect. In Tanzania, Eastman and Jackson in 1998 found 10% of the variation in birth weight could be explained by maternal pre-pregnancy weight and pregnancy weight gain (265). Whereas in the present study 25% of the variation of birth weight is explained by maternal early pregnancy weight and weight gain during pregnancy. In accordance with the present study findings the CDC Pregnancy Nutrition Surveillance System (PNSS) in USA showed that pre-pregnancy under weight and inadequate gestational weight gain were associated with greater risk for low birth weight (LBW) (266).

We were limited in our discussion to compare only the study conducted on normal pregnant women because extensive research on relationship of maternal

weight, BMI, weight gain and MAC with pregnancy outcome, neonatal outcome and perinatal outcome on diabetic women are not available.

Neonatal nutritional status relationship of glycemic status and:(IDMs)

In this study birth weight was found significantly correlated with 1st and 3rd trimester fasting blood glucose level whereas, baby MAC was significantly correlated with 3rd trimester fasting blood glucose level. A Postprandiol blood glucose level at 2nd trimesters was significantly correlated with birth weight. The finding is in accordance with study by Jovanovic in USA (267), where they also found strong positive relationship between maternal blood glucose level and birth weight.

Finally in Logistic regression analysis diabetes showed significant ($p<0.001$) independent effect on birth weight MAC, chest circumference and ponderal index of infants of diabetic mother in this study and explains 25%, 27%, 20% and 13% of variation of the birth weight, MAC, head circumference, chest circumference and ponderal index respectively.

There are a number of studies showing the relationship of maternal glycemic status with birth weight of the infant of diabetic mother. Birth weight was found commonly related to maternal glycemic status. Fujimoto in 2000 found 36% LGA infants in women who had HbA₁C% more than 7.0% (268).

Maternal morbidity relationship with maternal glycemic status

Maternal morbidity at first trimester, second trimester and third trimester was related with maternal glycemic status for all three indicators (Fasting blood glucose, postprandiol blood glucose and glycosylated hemoglobin percentages) at all three trimesters. When the maternal third trimester HbA₁C% was above 6.0% the risk of morbidity was increased three fold in this study. Similarly, Sibai in 2000 and Partidas in 2000 found strong positive relationship between HbA₁C% $>6.0\%$ ($p<0.001$) with maternal morbidity in pre-gestational diabetic pregnant women (269,270).

Preterm relationship with maternal glycemic status

We did not find any relationship of 3rd TM HbA_{1c}% with preterm delivery. This finding is different from the recent study where the timing of blood glucose control was evaluated in depth and concluded that HbA_{1c}% in the third trimester is related to preterm delivery in DM pregnant women. Lepereq et al found that HbA_{1c}% at 28th week of pregnancy is the best predictor of preterm in 2002 (271). Another study by Kovilam in 2002 in Type-1 DM pregnant women in Ohio also found similar association of poor glycemic control with an increased risk of spontaneous preterm delivery, where for one percent increase of glycosylated hemoglobin the risk of spontaneous preterm delivery was increased by 37% (272). Possible reasons of difference of findings are that most (81.0 %) of the mothers in the DM group in this study were under good control at third trimester.

Limitation of the study: This study examined selected biochemical findings for perinatal morbidity and mortality instead of details bio-chemical examination. In addition this study didn't examined autopsy of the infants.

The maternal nutritional status was detected only by anthropometrical measurement and hemoglobin status but details bio-chemical parameters were not included due to resource constraints. Also we were limited to do this study in multicentric trial. This research may be triad in a multi-centric trial.

Chapter 5

SUMMARY AND CONCLUSION

Summary

Backgrounds:

Diabetes is an emerging health problem in Bangladesh. The infants of diabetic mother suffered more from perinatal morbidity and mortality thus contributing a significant proportion of infant mortality in Bangladesh. The diabetic pregnancy is beset with many problems but the pregnancy outcome and perinatal outcome of IDMs is largely unknown in Bangladesh. With this end in view, the present study was designed and conducted. This study aimed at comparing the maternal nutritional status, pregnancy outcome and perinatal outcome between the diabetic and non-diabetic pregnant women attended at BIRDEM hospital. And to explore the relationship between the maternal nutritional status, and glycemic status with that of the maternal, fetal and perinatal outcome.

Methodology:

This prospective study was conducted on a cohort of two hundred pre-gestational diabetic pregnant women (DM) and their matched control of non-diabetic (NDM) pregnant women. The sample was drawn from the women who attended at the outpatient department of the (BIRDEM) Hospital for antenatal checkup. The total period of study spanned over a period of 19 months (15th May 2000 to 15th December 2001). Pregnant women during their first trimesters (<12th week) were screened and selected by inclusion criteria for the study. The group was matched for gestational age, parity and occupation of the husband. They were followed at each trimester of the pregnancy, during labor, postpartum period and their newborns at clinic and in their homes till perinatal period.

Maternal nutritional status (detected by early pregnancy weight, weight gain, MAC, hemoglobin concentration) and glycemic status (glycosylated hemoglobin percentage and blood glucose levels) were measured in each trimester. Anthropometric measurements of mothers and newborns were taken following standard techniques. Gestational age was detected by last menstrual period (LMP) and subsequently confirmed by ultra-

sonography (USG). Maternal, fetal and perinatal morbidity and mortality was also recorded.

Result:

The groups were not different on matching characteristics. They were significantly different ($p < 0.001$) in monthly income and education with lower values for DM mothers. The DM mothers were significantly older ($p < 0.001$) than their counterparts. Nutritional status at enrollment was significantly different between the groups in all measurements ($p < 0.001$) with higher values for DM mothers. The DM mothers were more obese (31.5% vs. 18.0%; $p < 0.001$) than the non-diabetic mothers who were underweight (5.5.0% vs. 17.5%) during early pregnancy ($p < 0.001$). In all 3 trimesters, the rate of anemia was found more in the DM group and mean hemoglobin concentrations were also lower in this group ($p < 0.001$).

Mean values for fasting blood glucose, postprandial blood glucose and glycosylated hemoglobin percentage were higher than normal range for diabetic mothers in the first trimester and gradually declined to normal in the third trimester. Maternal morbidity was more in DM group in all three trimesters ($p < 0.001$).

Total weight gain was significantly higher ($p < 0.02$) in the DM group (8.6 ± 3.2 vs. 7.9 ± 2.5 kg) than that of the NDM group. Total weight gain between 1st and 2nd trimester was not different between the groups but differed significantly ($p < 0.02$) between 2nd & 3rd trimester in favor of the diabetic group. Both the group gained MAC in 1st trimester to 2nd trimester but losses in 2nd to 3rd trimester, but the group difference was not significant. DM pregnant women suffered significantly ($p < 0.001$) more from different types of morbidities throughout the pregnancy than that of the NDM group. Live birth rate in the DM group was found 98.0%, which was 100.0% in the NDM group. Breech presentation and cesarean section was more in DM group. The rate of low birth weight was found 21.6% in the DM group and 24.1% in the NDM group in this study. A greater proportion of infants of DM mothers were

'large for gestational age' (LGA) and the difference was significant between the groups at the level of $p < 0.001$.

Overall rate of preterm (< 37 week) in DM was more than the NDM group 41.5% vs 6.2% and baby born < 34 week of gestational age was 16.2% in DM group and none in the NDM group. Nutritional status of the newborns was significantly different between the groups with higher values for the DM group by all anthropometric measurements.

Mean birth weight was found significantly ($p < 0.001$) greater in the infants of diabetic mothers (IDMs) (2850.6 ± 577.1 g) than that of the infants of NDM mothers (2651.1 ± 344.4 g). All macrosomy babies were found among diabetic mothers and IDMs suffered significantly ($p < 0.001$) more from perinatal morbidity. Most important perinatal morbidities were jaundice, and respiratory distress syndrome.

Only the infants of diabetic mother experienced perinatal mortality and the rate was observed 55/1000 total births. Diabetic mothers experienced nine (9) fetal losses constituting a rate of 45/1000 total live births compared to no loss in the NDM group. There were 2 abortions, 5 stillbirths and 2 late fetal deaths (IUD) in the DM group. The rate of congenital anomaly was 10/1000 total births in the DM group who were neither under regular antenatal check up or had a euglycemic state throughout the pregnancy.

In DM group strong relationship was found between the maternal nutritional status and fasting blood glucose level with the maternal morbidity. Mothers with glycosylated hemoglobin percentages more than 6.0 % at 3rd trimester was found 3.2 times at risk for developing maternal morbidity.

Relationship was found between the maternal nutritional status and neonatal nutritional status (birth weight & MAC and head circumference) in both the groups. Maternal risk factors identified for developing perinatal morbidity was found monthly income $< 10,000/-$ (2.5 fold), total weight gain < 7.0 kg (2 fold), 3rd trimester HbA_{1c}% > 6.0 (12.5 fold) and for 3rd trimester maternal morbidity (8 fold).

The neonatal factors having risk of developing perinatal morbidity was found, LBW (8 fold), IUGR (18 fold) and apgars score <8 at birth (12 fold). Maternal glycemic status was found significantly associated with large for gestational age (LGA), macrosomy and perinatal morbidity in the DM group.

On multiple regression analyses, newborns of diabetic mothers were found to have higher weight, head, chest and mid arm circumferences after controlling possible confounding factors. After controlling all the confounders, family income and total weight gain showed significant effects on birth weight in both the group.

Maternal family income, education, nutritional status in early pregnancy, and weight gain during pregnancy, is highly correlated with maternal morbidity and neonatal nutritional status. Maternal glycemic status, maternal morbidity, low weight gain, low family income, low birth weight, low MAC, IUGR and low apgar score was found as important risk factor for perinatal morbidity. Though adversity in the maternal fetal and perinatal outcome is more in DM pregnant but close monitoring of blood glucose and adequate treatment may control all adverse effects.

Conclusion:

The DM mothers were older than their non-diabetic counterparts. The diabetic pregnant women were significantly different in monthly income & education with lower values for DM mothers.

Nutritional status at enrollment detected by weight and MAC was significantly different between the groups in all measurements and continued to be till to the postpartum. Total weight gain was more in DM group and differed significantly between 2nd & 3rd trimester. In all 3 trimesters, rate of anemia was more in DM group.

Maternal morbidities i.e pregnancy induced hypertension and pre-eclampsia was more in DM group in all 3 trimesters and was found strongly related with maternal glycemic status, family income and nutritional status.

Diabetic mothers experienced fetal losses whereas NDM mothers experienced none. Most of the preterm, LGA and macrosomy babies were found among the diabetic mothers. Infants of diabetic mother suffered significantly more from perinatal morbidity. Perinatal mortality was observed only in infants of diabetic mothers. Maternal glycemic level had strong and significant effect on maternal morbidity, LGA, and perinatal morbidity.

Diabetic group showed independent significant effects on anthropometric measurements like weight, head circumference, chest circumference and mid arm circumference after controlling possible confounding factors.

Nutritional status of the newborns was significantly different between the groups. Low weight gain during pregnancy, and low family income had independent significant effect on birth weight. Lower family income, low maternal education, low maternal nutritional status in early pregnancy, low weight gain during pregnancy, maternal morbidity, low birth weight, IUGR and low apgar score at birth was found significantly associated with perinatal morbidity in both the group.

Lessons from the study:

1. A large number of mothers were not under good glycemic control in first trimester. So this study emphasizes for strengthening of preconception care of already diagnosed diabetic women and the high-risk group from the date of marriage. May be education on diabetes and diabetic pregnancy was too inadequate. Overall risk of DM pregnancy may also be included in the education program.
2. Weight gain pattern was not optimum according to different nutritional status categories by early pregnancy weight. So instead of inadequate diet or knowledge yet they showed that the overall average total weight gain was not bad. This study revealed that the nutrition care and follow-up need strengthening for both the diabetic and non-diabetic pregnant women.
3. Maternal morbidity, pregnancy loss and perinatal morbidity was more in DM group so it needs further consideration to explore the preventive measure. Especially the home care at perinatal period of the newborn may be extended up to perinatal period to reduce perinatal morbidity rate.
4. Due to higher rate of cesarean section late fetal death was reduced but preterm delivery was high and might caused higher rate of perinatal morbidity which needs further emphasis to reduce infant morbidity.
5. Team approach in managing DM with proper blood glucose monitoring, medical care and nutritional care from early pregnancy is needed. The team member consisting of gynecologist, nutritionist, clinical psychologist, and diabetologist will prevent the adverse pregnancy outcome of infant of diabetic mother to a great extent.

Chapter 6

REFERENCES

REFERENCES

1. Amos AF, McCarty DJ, Zimmet P. The rising global burden of diabetes and its complications: estimates and projections to the year 2010. *Diabet Med* 1997; 14 (Suppl.5): S7-S85.
2. Lycka P, Urbonaite B, Ostrausks R, Zalinkevicius R, Dahquist GG. Incidence of type-1 diabetes in Lithuanians aged 0-39 years by the urban-rural setting and the time change differs for man and women during 1991-2000. *Diabetes Care* 2003; 26(3): 671-6.
3. Garner P. Type-1 diabetes mellitus and pregnancy. *Lancet* 1995; 346:157-161.
4. Mahtab H, Ibrahim M, Banik NG, Gulshan-e-Jahan and Ali SMK. Diabetes detection survey in a rural and semi-urban community in Bangladesh. *Tohoku J Exp Med* 1983; 141: 211-217.
5. Ali SMK, Mahtab H, Ibrahim M, Azad Khan AK. Screening for diabetes in two textile mills in Bangladesh. *J Diab Assoc Bangladesh* 1985; 16:13-16.
6. Sayeed MA, Hussain MZ, Banu A, Rumi MAK, Azad Khan AK. Effect of socioeconomic risk factor on difference between rural and urban in the prevalence of diabetes in Bangladesh. *Diabetes Care* 1997; 20:551-5.
7. Annual Reports, BIRDEM. *Diabetic Association Bangladesh* 2000-2001:6-11.
8. Chowdhury T A. Screening of diabetes mellitus in Bangladesh. *Jour of Diabetic Assoc Bangladesh* 1997; 25 (1): 7.
9. Syed M A, Mahtab H, Khanam PA, Amin STE, Khan A, Prevalence of diabetes in a rural community of Bangladesh. *Diabetologia* 2001; 44: (suppl-1): A 106-8.
10. Bliss M. Discovery of Insulin. In: Pickup JC, Williams G eds. *Textbook of Diabetes*. First ed. American Public Health, publishers 1991; 10-16.
11. Garner P. Diabetes and pregnancy outcome. *BMJ* 1997; 315:263-264 (Editorial.).

12. Platt MJ, Stanistreet M, Casson IF et al. Saint Vincent's Declaration 10 years on: outcome of diabetic pregnancies. *Diabet-Med* 2002; 19(3): 216-220.
13. Sibai B M, Caritis S, Hauth J et al. Risk of pre-eclampsia and adverse neonatal outcomes among women with pregestational diabetes mellitus. *AMJ Obste Gynecol* 2000; 182(2): 364-369.
14. Chia YT, Chua S, Thai AC et al. Obstetric outcome of pregestational diabetic pregnancies. *Singapore Med J* 1995; 36:498-500.
15. Cundy T, Slee F, Gamble G, Neale L. Hypertensive disorders of pregnancy in women with type 1 and type 2 diabetes. *Diabet Med* 2002; 19(6): 482-489.
16. Hanson U, Persson B, Thunell S. Relationship between hemoglobin A_{1c} in early type 1(insulin dependent) diabetic pregnancy and the occurrence of spontaneous abortion and fetal malformation in Sweden. *Diabetologia* 1990; 33(2): 100-104.
17. Jovanovic L, Metzger BE, Knopp RH et al. The Diabetes in early Pregnancy Study: beta-hydroxybutyrate levels in type -1 Diabetic Pregnancy compared with normal pregnancy. NICHD-Diabetes in Early Pregnancy Study Group (DIEP) 1978-1984. *Diabetes-Care* 1998; 21(11):
18. Wylie BR, Kong J, Kozak SE, Marshall CJ, Tong SO, Thompson DM. Normal Perinatal mortality in type 1 diabetes mellitus in a series of 300 consecutive pregnancy outcomes. *Am J Perinatol* 2002; 19(4): 169-171.
19. Jensen DM, Sorensen B, Feilberg, Jorgensen N, Westergaard JG, Beck-Nielsen H. Maternal and prenatal outcomes in 143 Danish women with gestational diabetes mellitus and 143 controls with a similar risk profile. *Diabet Med* 2000; 17(4): 281-286.
20. Lao TT, Wong KY. Perinatal outcome in large for gestational age infants. Is it influenced by gestational impaired glucose tolerance *Reprod Med* 2002; 47(6): 497-502.

21. Taylor R, Lee C, Kyne Grzebalski D, Marshall SM, Davison JM. Clinical outcomes of pregnancy in women with type-1 diabetes. *Obstet Gynecol* 2002; 99(4): 537-541.
22. Ali SMK, Begum S. Nutritional status of diabetic and non-diabetic pregnant and their outcome of pregnancy. Proceedings of Diabetic and endocrine society, 3rd December 1999. Held in Dhaka Bangladesh. Diabetic and Endocrine Association Bangladesh 1999: 36-37.
23. Karim E, S Choudhury, F Begum, Z A Latif. Pregnancy outcomes in glucose intolerance: A precondition of good glycemic control. *J Inst Postgrad Med Res* 1993; 8(1): 1-6.
24. Daponte A, Guidozi F, Moisuc D, Marineanu A. Management of diabetic patient in a tertiary center in the developing world. *Int J Gynaecol Obstet* 1999; 64(2): 141-146.
25. Mirghani OA, Saeed OK. A simplified management of diabetic pregnant women. *Saudi Med J* 2000; 21(4): 335-339.
26. Gunton JE, Morris J, Boyce S, Kelso I, Mcelduff A. Outcome of pregnancy complicated by pre-gestational diabetes, improvement in outcomes. *Aust N Z Obstet Gynaecol* 2002; 42(5): 478-481.
27. The Expert committee on the diagnosis and classification of diabetes Mellitus. Report of the expert committee on the diagnosis and classification of Diabetes Mellitus. *Diabetes Care* 1997; 20: 1183-1197.
28. Macfarlane IA, The millennia before insulin. In: Pickup JC, Williams G eds. Textbook of Diabetes. First ed. Am Public Health, publishers 1991; 81:1423-1428.
29. National Diabetes Data Group (NDDG). Classification and diagnosis of diabetes mellitus and other categories of intolerance. *Diabetes* 1979; 29:1039.
30. WHO Expert committee on Diabetes mellitus (1985), WHO. *Technical Reports Series no. 727*. WHO, Geneva.

31. Alberti KGMM, Zimmet PZ, for the WHO Consultation Group: Definition, diagnosis and classification of diabetes mellitus and its complications. Diagnosis and classification of diabetes mellitus: provisional report of a WHO consultation. *Diabet Med* 1998; 15:539-553.
32. Marmot MG, Shipley MJ, Rose G. Inequalities in death-specific explanation of general pattern. *Lancet* 1984; 1003-1081.
33. Barker DJP, Osmond C, Bull AR, Simmons SJ, The fetal origins of adult disease. *BMJ* 2001; 375-376.
34. Quibrera Infante R, Hernandez Rodriguez HG, Aradillas Garcia C, Gonzalez Rodriguez S, Calles Escandon J. Prevalence of diabetes, glucose intolerance, hyperlipemia and risk factors as a function of socioeconomic level. *Rev Invest Clin* 1994; 46(1): 25-36.
35. Katherine & Krasovec. Introduction. In: Katherine Krasovec, Marry Anderson eds. Maternal Nutrition and pregnancy outcome, PAHO, *Technical Series No. 625*; 1991:5-10.
36. Seoud MA, Nasar AH, Usta IM, Melhem Z, Kazma A, Khalil AM. Impact of advanced maternal age on pregnancy outcome. *Am J Perinatol* 2002; 19(1): 1-8.
37. Berkowitz GS, Roman SH, Lapinski RH, Alvarez M, Maternal characteristics, Neonatal outcome and the time of diagnosis of gestational diabetes. *Am J Obstet Gynecol* 1992; 167:976-982.
38. Fazlul Bari. Prevalence of diabetes. MPH Dissertation, National Institute of Preventive and Social Science (NIPSOM), Mohakhali, Dhaka (1995) (unpublished documents).
39. Solomon CG, Willett WC, Carey VJ et al. A prospective study of diabetes and pre-gravid determinations of gestational diabetes mellitus. *JAMA* 1997; 278(13) 1078-1083.
40. Lopatynski J, Mardarowicz G, Nicer T et al. The prevalence of type II diabetes mellitus in rural urban population over 35 years of age in Lublin region (East Poland). *Arch Med* 2001; 106(3): 781-786.

41. T. Tashev. Nutritional aspects of obesity and diabetes and their relation to cardiovascular disease and mortality. *Food and Nutrition Bulletin* 2000; 8 (3): 13-14.
42. Mahtab FU, Mahtab H, Sayeed MA and Azad Khan AK. Server hyperglycemia and macro-albuminuria is more prevalent in the rural and among the poor diabetes. Workshop proceedings, P0829; 161 DF Jul 20-25, 1997; held in Helsinki. (Abstract).
43. Gillium R F. The association body fat distribution with hypertension, hypertensive heart disease, coronary heart disease, diabetes and cardiovascular risk factors in men and women aged 18 to 79 years. *J Chronic Dis* 1987; 40: 421-428.
44. DeFronzo R A, Ferrannini E, Insulin Resistance. A Multifaceted syndrome responsible for NIDDM, Obesity, Hypertension, Dyslipidemia and Atherosclerotic Cardiovascular Disease. *Diabetes Care* 1991; 14:173-194.
45. Ostund RE, Staten M, Kohrt WM et al. The ratio of wais-to-hip circumference, plasma insulin level and glucose intolerance as independent predictors of the HDL₂ cholesterol level in order adults. *N Engl J Med* 1990; 322:229 -234.
46. David B. Acker and Vanessa A. Introduction .In: Florence M Brown & John W. Hare eds. Diabetes complicating pregnancy. Second edition. Willey-Liss, Publishers, Inc, 605 Third avenue, New York, NY 10158-0012: 1995: 1-5.
47. Brudenella M. Diabetic pregnancy. In: Brudenell and Wilds PL eds. Medical and surgical problems in obstetrics. Bristol: Wright 1994: 120-140.
48. Beard R, Maresh M Diabetes In: Swet MD. eds. Pregnancy complication. Delhi: Oxford university press, 1990; 584-632.
49. Workshop Report. Diabetes care and research in Europe: The Saint Vincent declaration. *Diabet Med* 1990; 7:360.

50. John W. Hare and Priscilla White. Gestational Diabetes and the white classification. *Diabetes Care* 1980; 3 (1-6): 394-395.
51. Jhon W Hare and Florence M Brown. Pathophysiology. In: Florence M Brown & John W. Hare eds. *Diabetes complicating pregnancy* Second edition. Willey -Liss, Publishers, Inc, 605 Third avenue, New York, NY 10158-0012: 1995: 1-10.
52. Nafisa Adeeb and N Nagari. Current trends in the management of diabetic pregnancy In: Ratnam SS, Rao KB, Arul KS eds. *Obstetrics and gynecology for postgraduates Vol-1, 1st edition* Madras: Orient Longman limited.1992: 67-76.
53. Freinkel N, Banting Lecture: of pregnancy and progeny. *Diabetes* 1980; 29: 1023-1035.
54. ACC/SCN Fourth Report on the world Nutrition situation. Geneva: *ACC/SCN in collaboration with IFPRI*, 2000: 25-28.
55. Frankle Owen. Nutrition in the community: In: Frankle Owen eds. *The art of delivering services*. 1993. Mosby, Publishers: 100-106.
56. M.G.Olson & Sheills Pregnancy and nutrition. In: M.G. Olson & Maurice Sheills eds. *Textbook of Modern Nutrition in Health and Disease*, 8th edition, 1995 Wiley Liss public. Part-2 1995:817.
57. R. L. Naeye, Maternal nutrition and pregnancy outcomes In: Jhon Dobbing eds. *Maternal nutrition in pregnancy -Eating for two?* 1981. Academic Press: 89-92.
58. Jean Giard. Carbohydrate and amino acid metabolism in the fetus. Gravin C, Arneil and Jack Metcoff. eds. *Pediatric Nutrition*. 1st edition, London Butter Worth & Co. Ltd. 1985: 3-15.
59. Meschia G. The function of the placenta as it relates to the transport of metabolic substrates to the fetus. In: CT Jones eds. *Biochemical development of the fetus and Neonate*. Amsterdam: Elsevier: 495-513.
60. Pederson J, The pregnant diabetic and her newborn. Problem and Management, 2nd ed. Baltimore: Williams and Wilkins, 1977: 46.

61. Catalano PM, Tyzbit ED, Roman NM, Amini SB, Sims EA: Longitudinal changes in insulin release and insulin resistance in non-obese pregnant women. *Am J Obstet Gynecol* 1991; 165:1667-1672.
62. Mirghani OA, Saeed OK. A simplified management of diabetic pregnant women. *Saudi Med J* 2000; 21(4): 335-339.
63. Dorothy R, Hollingsd W. Maternal metabolism in normal pregnancy and pregnancy complicated by diabetes mellitus. *Clin Obstet Gynaecol* 1985; 28 (3): 457-471.
64. Lewis TLT, Chamberlain GVP. eds. In: Obstetrics by Ten Teachers. 5th edition. London: Edward Arnold. 1990: 1-24.
65. Ronald A. Chez. Nutritional factors in pregnancy affecting fetal growth and subsequent infant development. In: Robert M. Suskind and Leslie L. Suskind eds. *Textbook of Pediatric nutrition*, Second edition. Raven press, New York: 22-26.
66. Phelps RL, Metzger BE, Freinkel N, Carbohydrate metabolism in pregnancy. XVII, Diurnal profiles of plasma Glucose, insulin, free fatty acid, triglycerides, Cholesterol and individual amino acids in late normal pregnancy. *Am J Obstet Gynecol* 1981; 167:730-736.
67. Michael F. Congenital malformations In: Florence M Brown and Jhon W Hare eds. Diabetes complicating pregnancy. Second edition. Publishers, Willey-Liss, Inc, 605 Third avenue, New York, NY 10158-0012: 1995: 181-196.
68. Guivarc'h L A, Poulain P, Leveque J, Allannic H, Giraud JR, Grall JY. Pregnancy in the diabetic women. Incidence of malformations, and macrosomia, update on obstetrical management. *J Gynecol Obstet* 1992; 21(6): 697-700.
69. Chung CS, Myrlandopoulos NC. Effect of maternal diabetes in congenital malformations. *Birth Defects* 1975; 11(10): 23.
70. Lowy C, Beard RW, Glodschmidt J. Congenital malformations in babies of diabetic mothers. *Diabet Med* 1986; 3:458-462.

71. Lucas MJ, Leveno KJ, Williams ML, Raskin P, Whalley PJ. Early pregnancy Glycosylated hemoglobin severity of diabetes and fetal malformations. *Am J Obstet Gynecol* 1989; 161(2): 426-431.
72. Gernot Desoye, Distinct effects of hyperglycemia in vitro proliferation and mitochondrial activity of placental trophoblasts at various stages of first trimester human pregnancy. *Magazine of American diabetes association*. Issue: May 2000; 15-20.
73. Hailliwel B. Free radicals and antioxidants: a personal view. *Nutr Rev* 1994; 213-30.
74. Failla ML, Kiser RA. Hepatic and renal metabolism of copper and zinc in the diabetic rat. *Am J Physiol* 1983; 5: 475-87.
75. Salvesen DR, Brudenell M, Proudler AJ, Crook D, Nicolides KH, Fetal pancreatic B-cell function in pregnancies complicated by maternal diabetes mellitus: Relationship to fetal acidemia and macrosomia. *Am J Obstet Gynecol* 1990; 168:898-903.
76. Pederson B, Hanson A. Fetal size at birth in relation to quality of blood glucose control in pregnancies complicated by pre-gestational diabetes mellitus. *Br J Obstet Gynaecol* 1996; 103:427-433.
77. Weinberg ED. Pregnancy associated depression of cell-mediated immunity. *Rev Infect Dis* 1984; 6:814-31.
78. Peterson B, Hanson. Fetal size at birth in relation to quality of blood glucose control in pregnancies complicated by pre-gestational diabetes mellitus. *Br J Obstet Gynaecol* 1998; 103:427-433.
79. Clark CM Jr, Quinn C, Amerman B, Porter B, Fineberg N, Aldasouqui S. Gestational diabetes: should it be added to the syndrome of insulin resistance? *Diabetes Care* 1997; 20(5): 867-71.
80. Begum S, Huda S N, Banu LA, Ali S M K. Comparative study of pregnancy and birth outcomes of diabetic and non diabetic pregnant women in terms of relation of maternal anthropometry and neonatal anthropometry. *Journal of Diabetes and Endocrine* 2001; *VXII*: 24-26

81. Banu L A. Pregnancy outcome of diabetic pregnancy in a developing country. Proceedings of second conference, Diabetes in Middle East, Eastern Mediterranean & South East Asia (DIMEMSA) 02-04 March 2000: 47.
82. Nahar S. An analysis of diabetic pregnancy: A 2-yr study. *BMJ* 1992; 21(3&4): 1660-1664).
83. Palmer SM. Diabetes mellitus. In: Decherney A. H, Pernoll ML. Eds. *Current obstetric and gynecologic diagnosis and treatment*. 8th edition, New Jersey; U.S.A.: Hall International Inc.1994; 368-378.
84. Sidibe EH, Sow AM, Sarr A, Ciss B, Diop SN, Ka Cisse M, Bah MD. Diabetic pregnancy in Senegal (years 1980to 1989). *Ann Endocrine* 1994; 55(5): 191-196.
85. Addison WA, Livengood CH, and Hill GB et al: Necrotizing fascitis of vulvar origin in diabetic patients. *Obstet Gynecol* 1984; 63:473.
86. Goldman M, Kitzmiller JL, Abrams B, Lowan RM. Larose RK, Obstetric Complications with GDM. *Diabetes* 1991; 40 (Suppl 2): 79-82.
87. Sachon C, Grimaldi A, Bosquet F et al. Diabetic pregnancy. Evaluation and prospects from the study of 212 diabetic pregnancy followed-up between1985 and1992. *Ann Med Intern* 1994; 145(6): 391-397.
88. Arias F. Practical guide to high-risk pregnancy and delivery. 2nd edition. St. Louis, Missouri: Mosby-year book inc. 1993; 280-301.
89. Greene MF. Prevention and diagnosis of congenital anomalies in diabetic pregnancies. *Clin Perinatol* 1993; 20(3): 533-547.
90. MDG Gilmer and PA Hurley, Diabetes and endocrine disorder in pregnancy. In: D Keith Edmonds. eds. *Dewhart's Text Book of Obstetric and Gynecology for post graduates*, Sixth edition 2000, Publishers, Blackwell Science division: 197-205.
91. Naylor CD, Serneer M, Chen E, S Kora K. Cesarean delivery in relation to birth weight and gestational glucose tolerance: Patho-physiology or practice style? *JAMA* 1996; 275-: 1165-1170.

92. Women and nutrition, ACC/SCN symposium report, Nutrition policy discussion paper no. 6, Papers from ACC/SCN session, October, 1990.
93. P Rosso, MD. A new chart to monitor weight gain during pregnancy. *Am Jour Clin Nutr* 1985; 41: 644-652.
94. Lepercq J, Hauguel-De, Mouzon S, Timsit J, Catalano PM. Fetal macrosomia and maternal weight gain during pregnancy. *Diabetes Metab* 2002; 28(1): 323-328.
95. Rey E, Monier D, Lemonier MC. Carbohydrate in pregnancy: incidence and neonatal outcomes. *Clin-Invest-Med* 1996; 19(6): 406-415.
96. Mills JL, Simpson JL, Driscoll SD. Incidence of spontaneous abortion and malformations among normal women and insulin dependent diabetic in insulin dependent diabetes mellitus. *Obstet Gynecol* 1998; 84:515-520.
97. Mills JL. Diabetes in early pregnancy study (DIEP): Incidence of spontaneous abortion among normal women and insulin dependent diabetic women whose pregnancies were identified within 21 days of conception. *N Engl J Med*, 1988; 319:1617-1623.
98. Penny GC. Spontaneous abortion and fetal loss in diabetic pregnant women. *Br Jour Obstet Gynecol* 2003; 110(3): 315-8.
99. Wheeler FC, Gollmar CW, Deep LC. Diabetes and pregnancy in South Carolina: prevalence, perinatal morality and neonatal morbidity in 1978. *Diabetes Care* 1982; 5:561-565.

100. Calfee EF, Rust OA, Bofill JA, Ross EL, Morrison JC. Maternal hypoglycemia is it associated with adverse perinatal outcome? *J Perinatol* 1999; 19(5): 379-382.
101. Johnston FD, Nasrat AA, Prescott RJ. The effects of established and gestational diabetic on pregnancy outcome. *Br J Obstet Gynaecol* 1990; 97(11): 1009-1015.
102. Mital S. The diabetics' pregnancy: Review of management and results over seven years period. *Asia Oceania Journ of Obstet and Gynaecol* 1987; 13(3): 277-282.
103. Reece EA, Homko CJ. Diabetes-related complications of pregnancy. *J Nat Med Assoc* 1993; 85(7): 537-545.
104. Salwfa CM. The fetal placental and neonatal pathology associated with maternal diabetes. In: Reece EA Coustau DR, eds. *Diabetes mellitus in pregnancy: Principals and practice*. New York, Churchill Livingstone, 1988: 148-811.
105. Cordero L, Landon MB. Infant of diabetic mother. *Clin Perinatol* 1993; 20:635-648.
106. Combs CA, Kitzmiller JL. Spontaneous abortion and congenital malformations in diabetic. *Clin Obstet Gynecol* 1991; 5(2): 315-18.
107. Greene MF, Hare JW and Krache M et al. Prematurity among insulin requiring diabetic gravida. *Am J Obstet Gynecol* 1989; 161:106-111.
108. Theresa O Scholl, Mary FS, Xinhua C, Carine Lenders. Maternal glucose concentration influences fetal growth, gestation and pregnancy complications. *Am J Epidemiol* 2001; 154:514-20.
109. Mello G, Parretti E, Mecacci F, Lucchetti R, Cianciulli D, Lagazio C. Anthropometric characteristics of full-term infants: effects of varying degrees of "normal" glucose metabolism. *J-Perinat-Med* 1997; 25(2): 197-204.

110. Godfrey K, Robinson S, Osmond C, Cox V. Maternal nutrition in early and late pregnancy in relation to placental and fetal growth. *BMJ* 1996; 312:410-4.
111. Ray JG, Vermeulen MJ, Shapiro JL, Kenshole AB. Maternal and Neonatal outcomes in pregestational and gestational diabetes mellitus and the influence of maternal obesity and weight gain: the DEPOSIT study. Diabetes Endocrine Pregnancy Outcome Study in Toronto. *QJM* 2001; 94(7): 347-356.
112. Madsen H, Ditzel J. The influence of maternal weight, smoking vascular complications and glucose regulation on the birth weight of infants type 1 diabetic woman. *Euro J Obstet Gynecol* 1991; 10(39): 175-179.
113. Moore TR. Fetal growth in diabetic pregnancy. *Clin Obstet Gynecol* 1997 Dec; 40(4): 771-786.
114. Judith E. Brown, Patrica T. Schloesser. Pre-pregnancy weight status, prenatal weight gain and the outcomes of term twin gestations. *Am J Obstet Gynaecol* 1990; 162: 182-6.
115. JS Sussenbach, PH Steenbergh, P Holthuizen. Structure and expression of the Human Insulin like growth factor genes. Mini Review. *Growth Regulation* 1992; 2:1-2.
116. Raychaudhuri K, Maresh MJ. Glycemic control throughout pregnancy and fetal growth insulin-dependent diabetes. *Obstet-Gynecol* 2000; 95(2): 190-194.
117. Jhon P Clothrt. Neonatal management In: Florence M Brown & John W. Hare eds. Diabetes complicating pregnancy second edition. Willey -Liss, Inc, 605 Third avenue, New York, NY 10158-0012: 1995: 177.
118. Ballard JL, Rosen B, Khoury J G, Miodovnik M: diabetic fetal macrosomia: significance of disproportionate growth. *J Pediatr* 1993; 122:115-119.

119. Langer O, Mazze R, The relationship between large-for-gestational-age infants and glycemic control in women with gestational diabetes. *Am J Obstet Gynecol* 1991; 164:103-111.
120. Acker DB, Sachs BP, Freidman EA. Risk factor for shoulder dystocia. *Obstet Gynecol* 1985; (66): 762.
121. Neiger R. Fetal macrosomia in diabetic patient. *Clin Obstet Gynecol* 1992; 35: 138-150.
122. Jays S, Skyler Mary Jo O' Sullivan, and Kathleen K. Holsinger. The relationship between Maternal Glycemia and macrosomia *Diabetes Care* 1980; 3(1-6): 433-434.
123. Freinkel N, Metzger BE, Potter JM. Pregnancy in diabetes. In: Ellen Berg M, Rifkin H eds. *Diabetes mellitus—theory and practice*, third edition. New York, Medical Examination Publishing Company, inc., 1983:689-714.
124. Luke B. Intra uterine growth retardation in diabetes pregnant. *Am J Clin Nutr* 1996; 33:2311-2317.
125. Teranchi Y, Kubota N, Tamemoto H. Insulin effect during embryogenesis determines fetal growth: a possible molecular link between birth weight and susceptibility to type-2 diabetes. *Diabetes* 2000; 49:82-86.
126. Sandoval T, Jimenez G, Uribe S, Partida-Hernandez G, Gonzalez S, Arreola F. Perinatal morbidity and mortality in pregnant women with diabetes mellitus. *Gynecol Obstet* 1995; 63: 181-185.
127. Kuo PL, Lin CK, Lin CR, Chen YP, Chen HY. The effect of third-trimester glycemic control on maternal morbidities in pregestational diabetes mellitus. *J Med Assoc* 1992; 91(2): 237-240.
128. Ong Ken K, Dunger David B. Perinatal growth failure: the road to obesity, insulin resistance and cardiovascular disease in adults. *Res-Clin-Endocrinol-Metab* 2002; 16(2): 191-207.

129. Mello G, ParrettinE, MecacciF, Pratesi M, Lucch etti R, Scarselli G, Excursion of daily glucose profiles in pregnant women with IDDM: relationship with Perinatal outcome. *J Perinat Med* 1997; 25:488-497.
130. Kitzmiller JL, Gavin LA, Gin GD, Javanovic Peterson L, Main EK, Zigrand WD. Preconception care of diabetes: Glycemic Control prevents congenital anomalies. *JAMA* 1991; 265:731.
131. Jahangir A, Diabetic pregnancy study. *MPH dissertation NIPSOM*, Dhaka, Bangladesh. 1995:(35) (Unpublished document).
132. Roksana Ivy. Management and outcome of pregnancy with diabetes mellitus. *FCPS dissertation*, Institute of Post Graduate Medicine and Research, Dhaka 1995(Unpublished document).
133. Bryce FC, Bonansky H J, Remonds S, Buchan PC. A survey of UK diabetic pregnancy management. *Diabet Med* 1991; 8(4): 382-384.
134. Hawthorne G, Robson S, Rayall E A, Sen D, Roberts SH, Ward Platt ME. Prospective population based survey of outcome of pregnancy in diabetic women: results of Northern Diabetic Pregnancy Audit, 1994; *BMJ* 1997; 325:279-81.
135. Heckbert SR, Stephens CR, and Daling JR. Diabetes in pregnancy: maternal and infant outcome. *Paediatr Perinat Epidemiol* 1998; 2(4): 14-26.
136. Dunne FP, Chowdhury TA, Hartland A, Smith T, Brydon PA, McConkey C, Nicholson HO. Pregnancy outcome in women with insulin -dependent diabetes mellitus complicated by nephropathy. *Q J M* 1999; 92(8): 451-454. (Abstract).
137. Omori Y, Minei S, Testou T, Nemoto K, Shimizu M, Sanaka M. Current Status of pregnancy in diabetic women. A comparison of pregnancy in IDDM mothers. *Diabetes Res Clin Pract* 1994; 24 (supl-1): S273-S278.
138. Huddle K, England M, Nagor A, Outcome of pregnancy in diabetic women in Soweto, *Diabet Med* 1993; 10(3): 290-294.

139. Mavalankar DV, Trivedi CR, Gray RH. Levels and Risk factors for perinatal morality in Ahmedabad, India. *Bull WHO* 1991; 69:435-442.
140. McDermott J, Steketee R, Wirima J. Perinatal morality in Malawi. *Bull WHO* 1996; 74:165-171.
141. Sack DA, Chen W, Greenspoon JS, Wolde Tsadik G. Should the same glucose values be targeted for type 1 as for type 2 diabetes in pregnancy. *Am J Obstet Gynecol* 1997; 177:1113-1119.
142. McElvy SS, Miodovik M, Rosenn B, Khoury JC, Siddiqi T, Dignan PS, Tsang RC. A focused pre-conceptional and early pregnancy program in women with type 1 diabetes reduces perinatal mortality and malformation rates to general levels. *J Matern Fetal Med* 2000; 9(1): 14-20.
143. Jaff-MR Medical aspect of pregnancy. *Clin-J-Med* 1994; 61(4): 263-271.
144. Langer O. A Spectrum of glucose thresholds may effectively prevent complications in the pregnant diabetic patient. *Semin Perinatol* 2002; 26(3): 196-205.
145. G Hawthorne Outcome of pregnancy in diabetic women in Northeast England and in Norway, 1994-1997. *BMJ* 2000; 321:730-731.
146. Derrick B Jellife. Direct assessment of community nutritional status. In: E F Patrick Jellife, Alfred Zefras eds. Community nutritional assessment. Oxford Medical publications, 1991: 12-25.
147. Frisanco AR, Klayman JE, Matos J. Influence of maternal nutritional status on pre-natal growth in a Peruvian urban population. *Am J Phys Anthropol* 1977; 46: 265-74.
148. Shera AS, Rafique G, Khawaja IA, Baqai S, King H. Pakistan National Diabetes Survey: Prevalence of glucose intolerance and associated factors in Baluchistan province. *Diabetes Res Clin Pract* 1999; 44(1): 49-58.

149. Jhon R. Barton. Does advanced maternal age affect pregnancy outcome in women with mild hypertension remote from term. *Am Jour Obst Gynaecol* 1997; 176 (6): 1236-1243.
150. Arifeen SE. Birth weight, intrauterine growth retardation and prematurity: a prospective study of infant growth and survival in the slums of Dhaka, Bangladesh. *Doctor of Public Health dissertation*. Johns Hopkins University School of Hygiene and Public Health, Baltimore, 1997.
151. Branchte L, Schmidt ML, Matos MCG, Yamashita. T. Pousada JMDC, Duncan BB. For the Brazilians Gestational Diabetes study group. Short stature and gestational diabetes in Brazil. *Diabetologia* 2000;143(7): 848-851.
152. Engelgan M. The epidemiology of diabetic pregnancy in the US, 1988. *Diabetes care* 1995; 18(7): 1029-33
153. Camacho F, Anderson RT, Bell RA, Goff DC Jr, Duren-Winfield V, Doss DD, Blakrishnan R. Investigation correlates of health related quality of life in a low-income sample of patients with diabetes. *Qual Life Res* 2002; 11(8): 783-796.
154. MacNeil S, Dodds L, Hamilton DC, Armson BA, Vanden Hof-M. Rates and risk factor for recurrence of gestational diabetes. *Diabetes-Care* 2001; 24(4): 659-662.
155. Hussein A, Abdul Rahim H, Awartani F, Giacaman R, Jervell J, Bjertness E. Type 2 diabetes mellitus, impaired glucose tolerance and associated factors in a rural Palestinian village. *Diabet Med* 2000; 17(10): 746-748.
156. Hadden DR, Alexander A, McCane DR, Traub AI. Northern Ireland diabetes Group. Ulster Obstetrical Society. Obstetric and diabetic care for pregnancy in diabetic women: 10 years outcome analysis, 1985-1995. *Diabet Med* 2001; 18(7): 546-553.

157. El Halwagy HE, Gelbaya TA, El Wahab MF, El Din S, Shebl AE, Makhoul G. The mean third trimester postprandial blood glucose of diabetic pregnant patient and infant birth weight in the Kuwaiti population. *Women's Health* 2001; 6(5): 2.
158. Dolberg B K, Lenhard M J. Successful outcome of pregnancy in a patient with generalized lipoatrophic diabetes mellitus. *Endocr-Prac.* 2000; 6(1): 34-36.
159. Begum S, Huda S N, Ali S M K Nutritional status and birth outcomes of the diabetic and non-diabetic pregnant women. *BMRC Bulletin*, 2002; 28 (3): 97-103.
160. Kaim-I. Effect of insulin therapy on duration of pregnancy in women with diabetes. *Gynecol* 1995; 66(6): 318-323.
161. Mironiuk M, Kietlinsk Z, Osuch B, Jezierska K, Kot A, Reinholz JM, Razna I. Effect of intensive prenatal and diabetic mothers-14 years of observation. *J Obstet Gynecol* 2001; 72(12A): 1260-1266.
162. Lao TT and Ho LF. Does maternal glucose intolerance affect the length of gestation in singleton pregnancies? *J Soc Gynecol Investig* 2003; 10(6): 366-71.
163. Garner PR. Glucose metabolism assessment in pregnancy. *Clin-Biochem* 1995; 28(5): 499-502.
164. Casson IF, Clarke CA, Howard CV, Mckendrick O, Pennycook S, Pharoah POD. Outcomes of pregnancy in insulin dependent diabetic women: Results of a five-year cohort study. *BMJ* 1997; 315:275-8.
165. Esther L, Melissa H, Tara I, Chang, Gary F, Mary R. Evidence that elevated glucose causes altered gene expression, apoptosis and neural tube defects in a mouse model of diabetic pregnancy. *Diabetes* 1999; 32(2): 458-465.
166. Dorman JS, Burke JP, McCarthy et al. Temporal trends in spontaneous abortion associated with type 1 diabetes. *Diabetes Res Clin Pract* 1999; 43(1): 41-47.

167. Kabadi Udaya M. United Kingdom prospective diabetes study: a different perspective. *Endocr Prac* 2002; 8(1); 61-64.
168. Ahkter J, Qureshi R, Rahim F, Moosvi S, Rehman A, Jabbar A, Islam N. Diabetes of pregnancy in Pakistani women: prevalence and complications in an indigenous South Asian community. *Diabet Med* 1996; 13(2): 189-191.
169. Summulian JC, Ananth CV, Vinzileous AM, Seroza WE, Knuppel RA. Fetal death in United States. Influence of high-risk condition and implications for management. *Obstet Gynecol* 2002; 100(6): 1183-9.
170. Reece EA, Sivan E, Francis G, Homoko CJ. Pregnancy outcomes among women with and without diabetic micro-vascular disease (white's classes B to FR) versus non-diabetic controls. *Am-J-Perinatol* 1998; 15(9): 549-555.
171. Diabetes Control and Complications Trial (DCCT) Research Group. Pregnancy outcomes in the diabetes control and complications trial. *Am J Obstet Gynecol* 1996; 174:1343-1353.
172. Jay S. Skyler, Mary J, O' Sullivan et. al. Blood glucose control during pregnancy. *Diabetes* 1980; 3(1-6): 69-76.
173. Rosemary Temple, Vivien Aldridge, Richard Greenwood, Philip Heyburn, Michael Sampson, Katharine Stanley. Association between outcome of pregnancy and glycemic control in early pregnancy in type 1 diabetes: population based study. *BMJ* 2002; 325:1275-1276.
174. Suhonen L, Hiilesmaa V, Teramo K. Glycemic control during early pregnancy and fetal malformations in women with type 1 diabetes mellitus. *Diabetologia* 2000; 43(1): 79-82.
175. Begum S, Huda S N, Banu LA & Ali S M K. Comparative study of morbidity and birth outcomes of diabetic and non diabetic pregnant women in terms maternal nutritional status. *Proceedings of World Congress of Epidemiology-2001*, June 16-23, 2002, Held in Toronto.

176. Schaefer G UM, Kjos SL, Kilavuz O, Plageman A, Braurer M, Dudenhausen JW. Determinants of fetal growth at different periods of pregnancies complicated by gestational diabetes mellitus or impaired glucose tolerance. *Diabetes Care* 2003; 26 (1): 193-8.
177. Kundo A, Birth outcome in diabetic pregnancy. M Sc Dissertation, INFS, 2001(159).
178. Morris MA, Grandis AS, Litton JC. Glycosylated hemoglobin concentration in early gestation associated with neonatal outcome. *Am J Obstet Gynecol* 1985; 153(6): 651-654.
179. Gold AE, Reilly R, Little J, Walker JD. The effect of glycemic control in the pre-conception period and early pregnancy on birth weight in women with IDDM. *Diabetes Care* 1998; 21(4): 535-538.
180. Sameshima H, Kamitomo M, Kajiya S, Kai M, Furukawa S, Ikenoue S. Early glycemic control reduces large for gestational age infants in 250 Japanese gestational diabetes pregnancies. *Am J Perinatol* 2000; 17(7): 371-376.
181. Wolf HJ, Ebenbichler CF, Huter O, Bonder J, Lechleitner M, Foger B. Fetal leptin and insulin levels only correlate in large for gestational age infants. *Eur J Endocrinol* 2000; 142(6): 623-629.
182. Wong SF, Chan FY, Oats JJ, McIntyre DH. Fetal growth spurt and pre-gestational diabetic pregnancy. *Diabetes Care* 2002; 25(10): 1681-4.
183. Jardim O, Sobral E, Branco EC, Marta E, Carvalheiro M, Fagulha I. Delivery in diabetic pregnancy. *Ann Ist super Sanita* 1997; 33(3): 329-332 (Abstract).
184. Bergman RL, Richter R, Bergman KE, Plaemann A, Brauer M, Dudenhausen JW. Secular trends in neonatal macrosomia in Berlin; Influences of potential determinants. *Pediatr Perinat Epidemiol* 2003 17(3): 244-9.
185. Lutale JK. Outcome pregnancy in diabetic patients in Der-es-Salam. *Diabet Med* 1991; 7(9); 881-889.

186. El Mallah KO, Narchi H, Kulaylat NA, Shaban MS. Gestational and pre-gestational diabetes: comparison of maternal and fetal characteristics and outcome. *Int J Gynaecol Obstet* 1997; 58(2): 203-209.
187. Hadden D, Traub, A, Lowy C et al. Outcome of pregnancy in women with insulin dependent diabetes. *BMJ* 1998; 316:550-550.
188. Vaarasmaki M, Hartikainen A, Anttila M, Pramila S, Koivisto M. Factors predicting perinatal and neonatal outcome in diabetic pregnancy. *Early Hum Dev* 2000; 59(1): 61-70.
189. The Hyperglycemia and Adverse Pregnancy Outcome Study Corporative Research Group. HAPO Study. *Int J Gynecol Obstet* 2002; 78 (1): 69-77.
190. Nieger R. Neonatal morbidity. In: Diabetes complicating pregnancy. Florence M Brown & John W. Hare eds. *Diabetes complicating pregnancy* Second edition. Publishers, Willey –Liss, Inc, 605 Third avenue, New York, NY 10158-0012: 1995:160.
191. Modanlou HD, Dorchester WL, Throsian A, Freeman RK. Macrosomia: Maternal, fetal and neonatal implications. *Obstet Gynecol* 1990; 55: 420-424.
192. Jeanne L. Ballard, Barak Rosen, Jane C, Khoury, Menachem Miodovnik. Diabetic fetal macrosomia: significance of disproportionate growth. *J Pediatr* 1993; 122:115-9.
193. Lindsay B. Incidence of persistent birth injury in macrosomic infants, Association with mode of delivery. *Am Jour Obst & Gynaecol* 1997; 177 (1): 37:139-149.
194. What is so bad about a big baby? *Diabetes Care* 2001; 24(8): 1317. (Editorial).
195. Soler NG, Soler SM, Mallins JM. Neonatal morbidity among infants of diabetic mothers. *Diabetic Care* 1978; 1:340.

196. Rudge MV, Calderon IM, ramos MD, Abbade JF, Rugolo LM. Perinatal outcome of Pregnancies complicated by diabetes and by maternal daily hyperglycemia not related to diabetes. A retrospective 10-year analysis. *Gynecol Obstet Invest* 2000;(50): 108-112.
197. Szilagyi A, Szabo I. Improvement of Perinatal outcome in diabetic pregnant women. *Early Pregnancy* 2001; 5(1): 55-56.
198. Suryea Tasnim, A B Bhuiyan. Out comes of premature rupture of membranes a clinical study. *Bang Journal of Obst and Gynaecol* 1998; 13 (1): 16-20.
199. Kitzmiller JL, Cloherty JP, Younger MD, et al. Diabetic pregnancy and perinatal morbidity. *Am J Obstet Gynecol* 1978; 131:560.
200. Persson B, Hanson U. Neonatal morbidities in gestational diabetes mellitus. *Diabetics Care* 1998; 21 (Suppl 2): B79-84.
201. Ramchandran A, Snehalatha C, Clementina M, Sasikala R, Vijay V. Fetal outcome in gestational diabetes in south Indians. *Diabetes-Res-Clin-Prac* 1998; 41(3) 185-190.
202. Stubbs WA, Stubbs SM. Hyperinsulinism, Diabetes mellitus and respiratory distress of the newborn: A common Link? *Lancet* 1978; 1(8059): 308-309.
203. Kjos SL, Walther FJ, Montoro M, Paul RH, Diaz F, Stabler M. Prevalence and etiology of respiratory distress in infants of diabetic mothers. *Am J Obstet Gynecol* 1990; 163:898-903.
204. Robert MF, Neff RK, Hubbell JP, Taeusch HW, Avery ME. Association between maternal diabetes and the respiratory distress syndrome in newborn. *N Eng J Med* 1997; 294:357-360.
205. Lao TT, Ho LF. Prenatal morbidity and fetal size in gestational impaired glucose tolerance. *J Soc Gynecol Investig* 2001; 8(6): 347-350.
206. Pal DK. Neonatal hypoglycemia in Nepal –I prevalence and risk factors. *Arch Dis Child* 2000; 82:46-51.

207. Agrawai RK, Lui K, Gupta JM. Neonatal hypoglycemia in infants of diabetic mothers. *J Paediatr Child Health* 2000; 36(4): 354-356.
208. N McIntosh. The newborn. In: A G M Campbel, Neil McIntosh eds. *Forfars and Arnei'ls Textbook of Pediatrics*. Fourth edition 1994 Churchill Livingstone, Longman Group UK Ltd.: 112-115.
209. France study group. Multi-center survey of diabetic pregnancy in France. Gestational and diabetes in. *Diabetes Care* 1991; 14(11): 994-1000.
210. Huddle K, England M, Nagor a, Outcome of pregnancy in diabetic women in Soweto. *Diabet Med* 1993; 10(3): 290-294.
211. Sobande AA, Al Bar H, Archibong EI. Diabetes and prenatal loss. A continuing problem. *Saudi Med J* 2000; 21(2): 161-163.
212. Cundy T, Gamble G, Townend K, Henley PG, McPherson P, Roberts AB. Perinatal mortality in type 2 diabetes mellitus. *Diabet Med* 2000; 17(1): 33-39.
213. Dunne F Brydon P Smith K, Gee H. Pregnancy in women with type-2 diabetes: 12 years outcome data 190-2002. *Diabet Med* 2003 20(9): 734-8.
214. O Langer, Rodriguez DA, Xenzkis EM, McFarland-MB, Berkus MD, Arrendondo F. Intensified versus conventional management of gestational diabetes. *Am J Obstst Gynecol* 1994; 170(4): 1036-1046;
215. Chowdhury TA, Rijal BP, Akhter S. Determination of some commonly biochemical parameters in different trimesters of pregnancy. *BMRC Bull* 1988; 14 (1): 29-35.
216. Hod M, Bar J, Peled Y, Fried S, Katz L, Itzhak M. Antepartum mgt protocol: timing and mode of delivery in gestational diabetes. *Diabetes Care* 1998; 21(Suppl2): B113-B117.
217. Fontaine P. Postprandial glycemic variations of pregnancy in diabetes. *Diabetes Metab* 2000; 26 (Suppl 2): 16-19.

218. Delgado Del, Rey M, Herranz L, et al. Effect of pre-conceptional metabolic control in the course of pregnancy in diabetic patient. *Med Clin* 2001; 117(2): 45-48.
219. Eric F Stamler, Maria L. High infectious morbidity in pregnant women with insulin- dependent diabetes: An understated complication. *Am J Obstet Gynecol* 1990; 163; 1217-21.
220. Von Kries R, Kimmerle R, Schmidt JE, Hachmeister A, Bohm O, Wolf HG. Pregnancy outcomes in mothers with pregestational diabetes: a population-based study in North Rhine (Germany) from 1988 to 1993. *Eur J Ped* 1997; 156(12): 963-67.
221. Rosemary Temple, Vivien Aldridge, Richard Greenwood, Philip Heyburn, Michael Sampson, Katharine Stanley. Association between outcome of pregnancy and glycaemic control in early pregnancy in type 1 diabetes: population based study. *BMJ* 2002; 325:1275-1276.
222. Simmons D. Persistently poor pregnancy outcomes in women with insulin dependent diabetes. *BMJ* 1997; 315(7103): 263-264.
223. Rosenn B M, Miodovnik M. Medical Complications of Diabetes mellitus in Pregnancy. *Clin Obstet Gynecol* 2000; 43(1): 17-31.
224. Begum S, Huda SN, Banu LA, Ali SMK. Comparative study of nutritional status and pregnancy outcome of pre-gestational and gestational diabetic pregnant women. *Report submitted to Bangladesh Medical Research Council* 2000. (Unpublished Report)
225. Janet Y. Uriu-Hare, Judith S. Stern and Carl L Keen, Influences of maternal dietary Zinc intake on expression of diabetes-induced teratogenicity in rats. *Diabetes* 1989; 38:1282-90.
226. Basu TK, Basualdo C. Vitamin A hemostasis and diabetes mellitus. *Nutrition* 1997; 13:804-806.

227. Garcia Casal MN, Layrisse M, Solano L, Baron MA. Vitamin A and β -Carotene can improve non-heme iron absorption from rice, wheat and corn by humans. *The Journal of Nutrition* 1998; 128 (3): 646-650.
228. Kolsteren P, Rahman SR, Hilderbrand K, Diniz A. Treatment for iron deficiency anemia with a combined supplementation of iron, vitamin A and zinc in women of Dinajpur, Bangladesh. *Eur J Clin Nutr* 1999; 53(2): 102-106.
229. Diabetes Care and Research in Europe: The Saint Vincent Declaration WHO/IDF Europe. *Diabetic Med* 1990; (7): 360.
230. Haden DR, McCann D, Traub AI. Ten years outcome of diabetes pregnancy in Northern Ireland: the case for centralization. *Diabetic Med* 1998 (Suppl 1); 15:S16.
231. Robert G. Moses, Fracp Sallyanne J, Knight s, Elizabeth M. Lucus, Michelle Moses, Kenneth. Is a higher cesarean section rate inevitable in diabetic pregnancy? *Diabetes care*, 2001; 23(1): 15-17.
232. McMahon MJ, Ananth CV, Liston RM. Gestational diabetes mellitus. Risk factors, obstetric complications and infant outcomes. *J Reprod Med* 1998; 44(7): 656.
233. O'Sullivan J B. Body weight and subsequent diabetes mellitus. *JMA* 1982; 248: 949-52.
234. Hanson AK, Robert L. Narayan K MV, McCane, David R. Pettitt C et al. Role of weight gain, weight fluctuation and incidence of NIDDM. *Diabetes* 1995; 144(3): 261(6)
235. Anastosion E, Alevizaki M, Grigorakis SJ, Phillippon G, Kyprianon M, Souvatzoglou A. Decreased stature in gestational diabetes mellitus. *Diabetologia* 1998; 41: 997-1001.
236. Branchette L, Schmidt ML, Matos MCG, Yamashita T, Pousada JMDC, Duncan BB. Brazilian Gestational Diabetes study group. Short stature and gestational diabetes in Brazil. *Diabetologia* 2000; 43(7): 848-851.

237. Nieger R. Maternal weight. In: Diabetes complicating pregnancy. Florence M Brown & John W. Hare eds. *Diabetes complicating pregnancy* Second edition. Publishers, Willey-Liss, Inc, NY 10158-0012: 1995:145.
238. Judith E Brown, Patrica T Schloesser. Pre-pregnancy weight status, prenatal weight gain and the outcomes of term twin gestations. *Am J Obstet Gynaecol* 1990; 162: 182-6.
239. Jovanovic L, Druzin M, Peterson MC. Effect of euglycemia on the outcome of pregnancy in insulin-dependent diabetic women as compared with normal control subjects. *American J Med* 1981; 71:921-26.
240. Jansen A A J, Kusin J A, Thiuri B, Lakhani SA, Mannet je W (1984): Mackakos project studies No. XXIVG: Anthropometric changes during pregnancy in rural African women. *Tropical Med*, 1984; 36:91-97.
241. Agarwal D K. Nutritional status in rural pregnant women in Bihar and Uttar Pradesh. *Indian pediatric* 24:119-125,1987.
242. Michelen B. Obesity in pregnancy. *Br Jour Nutr* 1996; 75: 659-668.
243. Olson CM. Pregnancy and nutrition. In: Maurice Shell and CM Olson eds. *Textbook of Modern Nutrition in Health and Diseases*. Wyllie liss Publications 1998:417-427.
244. DS Alam, M Yunus, KMA Aziz, et al. Birth weight and its Association with maternal nutrition and Socioeconomic Variable in Rural Bangladesh. *J Diarrh Dis Res* 1998; 16 (1): 21-57.
245. N Nahar, S Afroza, M Hossain. Incidence of Low Birth Weight in three Selected Communities of Bangladesh, *BMRC Bull.* 1998; 24(2): 49-54.

246. Karim E, Mascie Taylor CG. The association of weight, socio-demographic variables and maternal anthropometry in an urban middle class sample from Dhaka, Bangladesh. *Ann Hum Biol* 1997; 24(5): 387-401.
247. Cousins L, Kitzmiller J, Schneider J et al. The California Diabetes and pregnancy Program: implementation of a multi-center with diabetic pregnancies. *J Perinatol* 1992; 12(2): 173-180.
248. Hosamane US, Malhotra S, Narang A, Dhall K. Prenatal outcome in relation to maternal glycemic control in diabetic mothers. *Indian J Med Res* 1990; 92: 216-219.
249. Naeye R. Maternal nutrition and pregnancy outcomes In: Jhon Dobbing eds. Maternal nutrition in pregnancy -Eating for two? 1981. Academic press: 89
250. Katherin Krasovec. Introduction. In: Maternal Nutrition and pregnancy outcomes: Anrhropometric assessment. Ed. Katherine Krasovec & Marry Ann Anderson. *PAHO*, 1991; scientific publication no. 519: 14-25.
251. Gueri M., Jutsum P, and Sorhaindo, B. Anthropometric assessment of nutritional status in pregnant women. *Am J Clin Nutr* 1982; 35:609-616.
252. Kramer MS. Determinants of low birth weight: methodological assessment and meta-analysis. *WHO Bull* 1987; 43:461-6.
253. Ali S M K, Pramanic MA, Yunus H. Maternal nutritional status and Birth out come in rural pregnant women in Bangladesh. *Annual Report, BRAC* 1998: 55-58.
254. J C Das, S T Khanam. Maternal determinants of Birth Weight. *TAS-Journal of Teachers' Association, SBMCH* 1996; 7 (15): 12-15.
255. Arif MA. Maternal socio-cultural status: a novel assessment of risk for the birth of small for gestational age, LBW infants. *J Obst Gynaecol Res* 1998; 24 (3): 215- 222.

256. Tabib B S. Maternal factors contributing low birth weight babies. *Northern Medical Journal* 1994; 111(1): 13-15.
257. World Health Organization. Multicenter study on low birth weight and infant mortality in India, Nepal and Srilanka. *Regional Health Paper* 1994; SEARO, No. 25. New Delhi: SEARO, WHO.
258. Kramer MS, Mc Lean FH, Euson EL, Usher RH. Maternal Nutrition and spontaneous preterm birth. *Am J Epidemiol* 1992; 136(5): 574-83.
259. F.F. Fikree, H. W. Brendes. Risk factor for term intrauterine growth retard, a community based study in Karachi. *WHO Bull* 1994; 72 (4-6): 139-180.
260. Ahmed FU. Association of Maternal Biological factors with birth weights in Bangladesh. *JOPSOM* 1994; 13 (2-3): 52- 57.
261. Sameema Chowdhury, Maternal Nutrition and its Effect on Pregnancy Outcome. *J Obstet Gynaecol* 2000; 15(2): 73-81.
262. Fung KP, Nagan HY, Woo JSK, Wong TW. Maternal determinants of birth weight in normal pregnancy. *Aust Pediatr J* 1988; 24 (3): 184-185.
263. Richard S. Strauss and William H. Dietz. Low maternal weight gain in the second or third trimester increases the risk for intrauterine growth retardation. *J Nutr* 1999; 129:988-99.
264. Olson CM, Strawderman MS, Hinton PS, Pearson TA. Gestational Weight gain and postpartum behaviors associated with weight change from early pregnancy to 1 y postpartum. *Int J Obstet Metab Disord* 2003; 27(1): 117-127.
265. Eastman NJ, Jackson EC. The bearing of maternal weight gain and pre-pregnancy weight on birth weight in full term pregnancy. *Obstet Gynecol Surv* 1998; 23:1003-25.
266. Kim I, Hungerford DW Yip R, Kuester SA, Zyrkowski C, Towerbridge FL. Food intake and anthropometry during pregnancy. *Nutrition* 1997; 13(9): 807-13.

267. Jovanovic-Peterson L, Peterson CM, Reed GF, Metzger BE, Mills JL, Knopp RH. Maternal postprandial glucose levels and infant birth weight: the diabetes in early pregnancy study (DIEP). *Am J Obstet Gynecol* 1991; 164(1 pt 1): 103-111.
268. Fujimoto WY. Back ground and recruitment data for US diabetes prevention program. *Diabetes Care* 2000; 23: B 11-B 13.
269. Sibai BM. Risk Factors, pregnancy complications, and preventions of hypertensive disorders in women with pre-gravid diabetes mellitus. *J Matern Fetal Med* 2000; 9(1): 62-65.
270. Partida Hernandez G, Gomez Garcia A, Arreola Ortiz JF. Glycosylated hemoglobin (HBA1c) in pregnancy. *Ginecol Obstet* 2000; 68:420-424.
271. Lepercq J. obstetrical management of pregestational diabetes mellitus. *Gynecol Obstet Biol Reprod* 2002; 31(6 Suppl): 4S11-4S7.
272. Kovilam O, Khoury J, Miodovnik M, Chames M, Spinnato J, sibai B. spontaneous preterm delivery in the type I diabetic pregnancy :the role of glycemic control. *Matern Fetal Neotal Med* 2002; 11(4): 245-248.

Informed consent form

I hereby consent to participate in the study entitled "A comparative study on nutritional status and pregnancy outcomes of pre-gestational diabetic and non-diabetic pregnant mothers."

I will participate in the following:

- a) Responding to the interviewer regarding my demographic and other study related questions.
- b) Permitting collection of body measurement.
- c) Permitting the examination of the newborn at birth and after 7 days.

I understand that all information will be kept strictly confidential, and I have got the right to ask any question explaining any point. I can withdraw from the study at any time. I am giving consent willingly to take part in the above-mentioned study.

-----date:-----

Participant's signature

Women's verbal consent

The women named below has read the information / has been informed by the interviewer the nature and extent of her participation in this study. She is willing to take part in this study.

Investigator's signature

IDENTIFICATION NUMBER:-----

NAME OF THE WOMEN:-----

ADDRESS OF THE WOMEN:-----

Appendix -I

INSTITUTE OF NUTRITION AND FOOD SCIENCE, UNIVERSITY OF DHAKA

A comparative study on nutritional status and pregnancy outcomes of pre-gestational diabetic and non-diabetic pregnant mothers.

Screening form

(Criteria for exclusion)

ID NO

Date of interview

dd

mm

yy

A.1. Are you from Dhaka City ? Yes ☐ No ☐

A 2. How many living children do you have?

A3. How old are you ?

(If approximation please write about -----)

PROBING to find out the age the following event related questions.

3.a What is your birth year according to English / Bangla year?

How many years after liberation you were born?

(If the age is <20 year or > 35 years stop interview)

A 4. How many years you are suffering from diabetes?

PROBING to find out the time of diagnosing of diabetes and confirmed by observing the notebook.

(If the duration of diabetes is <1 year or > 5 years stop interview)

Part -I Appendix -I

INSTITUTE OF NUTRITION AND FOOD SCIENCE, UNIVERSITY OF DHAKA
A comparative study on nutritional status and pregnancy outcomes of
pre-gestational diabetic and non-diabetic pregnant mothers.

Identification form

IDENTIFICATION: **CODE NO.** _____ **REG. NO.** _____

NAME: _____ **AGE :** _____
DOB: _____

PRESENT ADDRESS: _____

PERMANENT COMMUNICATING ADDRESS OF ANY RELATIVES:

CONTACTING TELEPHONE NO:

_____(O)_____(RES)_____(OR)

DATE OF EXAMINATION_____

BED NO /ADMISSION NO:_____ **Date of admission:**_____

WEEK OF PREGNANCY: _____ **TRIMESTER:** 1ST ☐ 2ND ☐ 3RD ☐

DIABETIC ☐ **NONDIABETIC** ☐

If diabetes-----Duration-----yr ----- months

PART 2

Appendix -2

Basic information

ID. NO. _____

1. SOCIO-DEMOGRAPHIC HISTORY.

Q. 1. Can you please tell me how far you have read?

- 1-10. Exact class ☐ 11. SSC passed ☐ 12. Intermediate ☐ 13. HSC passed ☐
 14. On graduation ☐ 15. Graduated ☐ 16. On MA ☐ 17. Masters passed ☐

Q.2. How far your husband has read ?

- 1-10. Exact class ☐ 11. SSC passed ☐ 12. Intermediate ☐ 13. HSC passed ☐
 14. On graduation ☐ 15. Graduated ☐ 16. On MA ☐ 17. Masters passed ☐

Income:

Q.1. Husband's occupation: (Exact designation) _____

Monthly income: _____tk/-

Q.2. Respondent's occupation: (Exact designation) _____

Monthly income: _____tk/-

Q. 3. Other earning members: _____

Monthly contribution: _____

Q. 4. Added source of income _____/-tk.

Monthly income: _____

Q 5. Total income of the family: _____/-tk

Q.6. Total expenditure on food in last month: _____

a. Rice: _____

b. Vegetables: _____

c. Fish & Meat: _____

d. Snacks and breakfast: _____

e. Oil : _____

f. Others: _____

Q. 7. No of bed room in your house? _____

Q. 8. Total no. of family members in your house ? _____

Q. 9. No. of possession. 1. Car---Yes ☐ 2.No ☐Q. 9. Are you an owner of the house ? 1. Yes ☐ 2.No ☐

Q.10.If in rented house: Rent is :_____tk/- per month.

PART 2 (Contd.)

2. PAST OBSTETRICAL HISTORY.

- Q.1. Para ☐ Gravida ☐ Birth order ☐ ALC: yr -----month-----
- Q.2. Complicated Previous Obst. history : 1. Yes ☐ 2. No ☐ 6. N/A ☐
- Q.3. If yes, what was? Pl. specify:-----
- Q.4. Method of past delivery: 1. Spontaneous vaginal ☐ 2. Other (Forceps, episiotomy, ventouse) ☐ 3. Cesarean ☐ 4. Therapeutic delivery ☐ 6. N/A ☐
- Q.5. Place of delivery:-----
- Q.6. Delivery was conducted by -----
- Q.8. Cause of cesarean delivery-----, therapeutic delivery-----,
Other type of delivery-----
- Q.9. No. of abortion ☐ No. of IUD ☐ No of still birth ☐
- Q.10. Is there any previous medical complication to mother during pregnancy?
1. Yes ☐ 2. No ☐ 6. N/A ☐
- Q.11. If yes what type of complication? 1. Hypertension ☐ 2. Edema ☐
3. Diabetes ☐ 4. Hyper/ edema both ☐ 5. Other ☐ 6. NK ☐
- Q. 12. Is there any medical /birth complication to the previous Baby? .
1. Yes ☐ 2. No ☐ 3. NK ☐ 6. N/A ☐
- Q.13. If yes, What type of complication?
1. Asphyxia ☐ 2. Umbilical cord sepsis ☐ 3. Birth injury ☐
4. Moulding of head ☐
5. Ophthalmia neonatarum ☐ 6. Other, please specify-----7. NK ☐
- Q.14. Birth weight of the previous child: -----

3. PAST MEDICAL HISTORY: (mothers)

- Q: 1. Is there any known medical problem?
1. Yes ☐ 2. No ☐ 3. Not known ☐
- Q. 2. If yes, which of the followings? 1. Hypertension ☐ 2. Diabetes ☐ 3. CHD ☐
4. Anemia ☐ 5. Others ☐

PART 3

Appendix -3

At <12th.

ID.NO. _____

1. NUTRITIONAL STATUS OF PREGNANT MOTHER:

Anthropometry : Height -----cm. Body Weight-----kg.
 MUAC-----cm BMI-----
 Skinfold thickness: 1. Triceps-----mm 2. Biceps-----mm
 3.Subscapular-----mm

2. OBSTETRICAL FINDINGS:

Q: Last menstrual period (LMP) -----

Q: Expected date of delivery (EDD)-----

Q: Is the uterus per abdomen palpable? 1. Yes ☐ 2. No ☐

Q: If yes, Fundal height (SFH):-----cm.

USG : ----- week.

3. GENERAL EXAMINATION:*Build:* Thin /Normal / Overweight /Obese*Jaundice:* (The sites to be noted bulbar conjunctiva, under surface of the tongue, hard palate and skin). 1. Present ☐ 2. Absent ☐*Pulse:*----- *Blood pressure* (mean of the 3 readings) in mm.Hg.:

1.Standing----- 2. Lying-----

Heart: 1. NAD ☐ 2. Any problem, please specify-----*Lungs:* 1. NAD ☐ 2. Any problem, please specify -----*Edema:* 1. Present ☐ 2. Absent ☐**Evidence of malnutrition:**Glossitis : 1. Yes ☐ 2. No ☐ Angular stomatitis: 1. Present ☐ 2. Absent ☐Visible thyroid gland: 1. Present ☐ 2. Absent ☐**Treatment history:** 1. Diet 2. Insulin: Type -----, Dose----- 3.
Other: -----**Gestational diabetes:**During previous pregnancy: 1. Yes ☐ 2. No ☐

If yes: Duration ----- year-----month.

PART 3 (Contd.)

4. MORBIDITY HISTORY:

Q: Any other medical problem in the last 3-month? 1. Yes ☐ 2. No ☐

3. If yes, please specify: -----

Q: Whether treated: 1. Yes ☐ 2. No ☐

Q: Any other medical problem in the last 1-month? 1. Yes ☐ 2. No ☐

3. If yes, please specify: -----

5. BIOCHEMICAL / LABORATORY INVESTIGATION:

Blood Test:

1. Hemoglobin concentration -----gm/ dl (Date of examination-----)

2. If diabetic: HbA_{1c}%-----%

3. Blood sugar level: (Date of examination-----)

a. Fasting-----mmol/l

b. 2 hrs after breakfast (AFB)----- mmol/l

4. Urine Test: a. Sugar:

b. Albumin :

1. Present--++ 2. Present +++ 3. Nil

1. Present ++ 2. Present +++ 3. Nil

c. Urine for Acetone: 1. Present ++ 2. Present +++ 4. >+++ 3. Nil

6. ANY ABNORMAL FINDINGS: (Found in routine examination)

a.

b.

c.

d.

e.

7. OUTCOMES OF PREGNANCY:

Date of next antenatal visit: -----

Date of blood examination:-----

Cause of exclusion or drop out from the study: -----

Date of exclusion: -----

PART 4

Appendix -4

At 26-28th wk.

ID.NO. _____

1. NUTRITIONAL STATUS OF PREGNANT MOTHER:

Anthropometry : Height -----cm. Body Weight-----kg.
 MUAC-----cm BMI-----
 Skinfold thickness: 1. Triceps-----mm 2. Biceps-----mm
 3.Subscapular-----mm

2. OBSTETRICAL FINDINGS:

Q: Last menstrual period (LMP) -----

Q: Expected date of delivery (EDD)-----

Q: Is the uterus per abdomen palpable? 1. Yes ☐ 2. No ☐

Q: If yes, Fundal height (SFH):-----cm.

USG : ----- week.

3. GENERAL EXAMINATION:*Build:* Thin /Normal / Overweight /Obese*Jaundice:* (The sites to be noted bulbar conjunctiva, under surface of the tongue, hard palate and skin). 1. Present ☐ 2. Absent ☐*Pulse:*----- *Blood pressure* (mean of the 3 readings) in mm.Hg.:

1.Standing----- 2. Lying-----

Heart: 1. NAD ☐ 2. Any problem, please specify-----*Lungs:* 1. NAD ☐ 2. Any problem, please specify -----*Edema:* 1. Present ☐ 2. Absent ☐**Evidence of malnutrition:**Glossitis : 1. Yes ☐ 2. No ☐ Angular stomatitis: 1. Present ☐ 2. Absent ☐Visible thyroid gland: 1. Present ☐ 2. Absent ☐**Treatment history:** 1. Diet 2. Insulin: Type -----, Dose----- 3.

Other: ----

Gestational diabetes:During previous pregnancy: 1. Yes ☐ 2. No ☐

If yes: Duration ----- year-----month.

PART 4 (Contd.)

4. MORBIDITY HISTORY:

Q: Any other medical problem in the last 3-month? 1. Yes ☐ 2. No ☐

3. If yes, please specify: -----

Q: Whether treated: 1. Yes ☐ 2. No ☐

Q: Any other medical problem in the last 1-month? 1. Yes ☐ 2. No ☐

3. If yes, please specify: -----

5. BIOCHEMICAL / LABORATORY INVESTIGATION:

Blood Test:

1. Hemoglobin concentration -----gm/ dl (Date of examination-----)

2. If diabetic: HbA_{1c}%-----%

3. Blood sugar level: (Date of examination-----)

a. Fasting-----mmol/l

b. 2 hrs after breakfast (AFB)----- mmol/l

4. Urine Test: a. Sugar:

b. Albumin :

1.Present--++ 2.Present +++ 3. Nil

1.Present ++ 2. Present +++ 3. Nil

c. Urine for Acetone: 1.Present ++ 2. Present +++ 4. >+++ 3. Nil

6. ANY ABNORMAL FINDINGS: (Found in routine examination)

a.

b.

c.

d.

e.

7. OUTCOMES OF PREGNANCY:

Date of next antenatal visit: -----

Date of blood examination:-----

Cause of exclusion or drop out from the study: -----

Date of exclusion: -----

PART 5

Appendix -5

At 32-34th wk.

ID. NO. _____

1. NUTRITIONAL STATUS OF PREGNANT MOTHER:

Anthropometry : Height -----cm. Body Weight-----kg.
 MUAC-----cm BMI-----

2. OBSTETRICAL FINDINGS:Q: Expected date of delivery (EDD)----- ☐Q: Fundal height (SFH):-----cm. ☐

USG : ----- week.

3. GENERAL EXAMINATION:*Build:* Thin /Normal / Overweight /Obese

Jaundice: (The sites to be noted bulbar conjunctiva, under surface of the tongue, hard palate and skin). 1. Present ☐ 2. Absent ☐

Pulse:----- *Blood pressure* (mean of the 3 readings) in mm.Hg.:

1. Standing----- 2. Lying-----

Heart: 1. NAD ☐ 2. Any problem, please specify-----

Lungs: 1. NAD ☐ 2. Any problem, please specify -----

Edema: 1. Present ☐ 2. Absent ☐

Evidence of malnutrition:

Glossitis : 1. Yes ☐ 2. No ☐ Angular stomatitis: 1. Present ☐ 2. Absent ☐

Visible thyroid gland: 1. Present ☐ 2. Absent ☐

Treatment history: 1. Diet 2. Insulin: Type -----, Dose----- 3.

Other: -----

Gestational diabetes:

1. Yes ☐ 2. No ☐

PART 5 (Contd.)

4. MORBIDITY HISTORY:

Q: Any other medical problem in the last 3-month? 1. Yes ☐ 2. No ☐

3. If yes, please specify: -----

Q: Whether treated: 1. Yes ☐ 2. No ☐

Q: Any other medical problem in the last 1-month? 1. Yes ☐ 2. No ☐

3. If yes, please specify: -----

5. BIOCHEMICAL / LABORATORY INVESTIGATION:

Blood Test:

1. Hemoglobin concentration -----gm/ dl (Date of examination-----)

2. If diabetic: HbA_{1c}%-----%

3. Blood sugar level: (Date of examination-----)

a. Fasting-----mmol/l

b. 2 hrs after breakfast (AFB)----- mmol/l

4. Urine Test: a. Sugar:

b. Albumin :

1. Present--++ 2. Present +++ 3. Nil

1. Present ++ 2. Present +++ 3. Nil

c. Urine for Acetone: 1. Present ++ 2. Present +++ 4. >+++ 3. Nil

6. ANY ABNORMAL FINDINGS: (Found in routine examination)

a.

b.

c.

d.

e.

7. OUTCOMES OF PREGNANCY:

Date of next antenatal visit: -----

Date of blood examination:-----

Cause of exclusion or drop out from the study: -----

Date of exclusion: -----

PART 6

Appendix -6

At >34th wk.

ID. NO. _____

1. NUTRITIONAL STATUS OF PREGNANT MOTHER:

Anthropometry : Height -----cm. Body Weight-----kg.
 MUAC-----cm BMI-----

2. OBSTETRICAL FINDINGS:Q: Expected date of delivery (EDD)----- ☐Q: Fundal height (SFH);-----cm. ☐

USG : ----- week.

3. GENERAL EXAMINATION:*Build:* Thin /Normal / Overweight /Obese

Jaundice: (The sites to be noted bulbar conjunctiva, under surface of the tongue, hard palate and skin). 1. Present ☐ 2. Absent ☐

Pulse:----- *Blood pressure* (mean of the 3 readings) in mm.Hg.:

1. Standing----- 2. Lying-----

Heart: 1. NAD ☐ 2. Any problem, please specify-----*Lungs:* 1. NAD ☐ 2. Any problem, please specify -----*Edema:* 1. Present ☐ 2. Absent ☐**Evidence of malnutrition:**Glossitis : 1. Yes ☐ 2. No ☐ Angular stomatitis: 1. Present ☐ 2. Absent ☐Visible thyroid gland: 1. Present ☐ 2. Absent ☐**Treatment history:** 1. Diet 2. Insulin: Type -----, Dose----- 3.

Other: -----

Gestational diabetes:1. Yes ☐ 2. No ☐

PART 6 (Contd.)

4. MORBIDITY HISTORY:

Q: Any other medical problem in the last 3-month? 1. Yes ☐ 2. No ☐

3. If yes, please specify: -----

Q: Whether treated: 1. Yes ☐ 2. No ☐

Q: Any other medical problem in the last 1-month? 1. Yes ☐ 2. No ☐

3. If yes, please specify: -----

5. BIOCHEMICAL / LABORATORY INVESTIGATION:

Blood Test:

1. Hemoglobin concentration -----gm/ dl (Date of examination-----)

2. If diabetic: HbA_{1c}%-----%

3. Blood sugar level: (Date of examination-----)

a. Fasting-----mmol/l

b. 2 hrs after breakfast (AFB)----- mmol/l

4. Urine Test: a. Sugar:

b. Albumin :

1.Present--++ 2.Present +++ 3. Nil

1.Present ++ 2. Present +++ 3. Nil

c. Urine for Acetone: 1.Present ++ 2. Present +++ 4. >+++ 3. Nil

6. ANY ABNORMAL FINDINGS: (Found in routine examination)

a.

b.

c.

d.

e.

7. OUTCOMES OF PREGNANCY:

Date of next antenatal visit: -----

Date of blood examination:-----

Cause of exclusion or drop out from the study: -----

Date of exclusion: -----

PART 7

Appendix -7

At delivery.

ID. NO. _____

Date of delivery: _____ Time of delivery: _____

Q.1. Type of delivery: 1. Normal ☐ 2. Assisted ☐ 3. Cesarean ☐Q.2. Is there any complication? 1. Yes ☐ 2. No ☐

Q.3. If yes, pl. specify: _____

Q.4. Cause of assisted delivery: _____

OUTCOMES OF PREGNANCY:**Fetal:**Live birth: 1. Yes ☐ 2. No ☐ Stillbirth: 1. Yes ☐ 2. No ☐Term: 1. Yes ☐ 2. No ☐ Preterm: 1. Yes ☐ 2. No ☐Small for date: 1. Yes ☐ 2. No ☐ Premature: 1. Yes ☐ 2. No ☐Post term: 1. Yes ☐ 2. No ☐**Gestational age:** By LMP----- By USG-----**Clinical examination: Newborn**Any birth complication: 1. Present ☐ 2. Absent ☐

If present, Pl specify: _____

Baby shifted to neonatal care unit? 1. Yes ☐ 2. No ☐

If yes, cause: _____

Health status: Apgar score: 1. At 1 minute----- 2. At 5 minute----- 3. At 10 minute-----

Nutritional status of the newborn:

Birth weight in kg ----- Recumbent length in cm -----

Mid arm circumference in cm (MAC)-----

Head circumference in cm (OFC)----- Chest circumference in cm (CC)-----

Abdominal circumference in cm-----

Blood glucose level at birth -----

PART 8

Appendix -8

Perinatal findings

ID. NO. _____

Clinical examination:Any medical complication: 1. Yes ☐ 2. No ☐

If yes: what type of complication?

1. Respiratory distress syndrome ☐ 2. Umbilical cord sepsis ☐
 3. Jaundice ☐ 4. Temperature ☐ 5. Diarrhea ☐
 6. Vomiting ☐ 7. Ophthalmia neonatorum ☐
 8. Hemorrhagic disease of the newborn ☐
 9. Convulsion of the newborn ☐ 10. Skin infection ☐
 11. Oral thrush ☐ 12 other ☐

Is the baby admitted in any hospital? 1. Yes ☐ 2. No ☐**Findings:**

1. Clinical: a. _____ b. _____ c. _____ d. _____
 2. Biochemical: a. _____ b. _____ c. _____ d. _____

Treatment outcome:

Perinatal mortality 1. Yes 2. No

The baby died on: Date _____ at age of _____ days

The cause of death:

1. Direct cause _____ 2. Associated cause _____
 3. Factors influencing: a. _____ b. _____ c. _____