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Surveillance updates

A controlled trial to prevent Nipah virus transmission in Bangladesh

Nipah virus is a fatal zoonotic disease transmitted from *Pteropus* bats to humans, typically through consumption of raw date palm sap contaminated by bat excretions. Date palm harvesters sometimes use a skirt-like barrier called a *bana* to protect the date palm sap from bats. The Government of Bangladesh discourages people from drinking raw date palm sap as a way to reduce risk of Nipah virus. In 2012-2014, we developed, implemented and evaluated two behaviour change interventions: one that discouraged drinking raw sap and one promoting drinking only *bana*-protected sap. Over two consecutive sap collection seasons we interviewed and observed 6,220 community members and 665 date palm sap harvesters to compare practices after exposure to the interventions. At the end of the evaluation, less people reported consuming raw date palm sap, the consumption of *bana*-protected sap increased and the reported use of *banas* increased. We found that promoting the use of *banas* could provide an effective, complementary intervention for people who want to continue drinking raw sap.

Nipah virus is a fatal zoonotic disease transmitted from *Pteropus* bats to humans, typically through consumption of raw date palm sap contaminated by virus in bat urine or saliva (1-2,7). Outbreaks have occurred almost every year in Bangladesh since 2001. Infected humans sometimes transmit the virus to other people, posing a risk of regional outbreaks or a pandemic (3-5).

Date palm sap harvesting and raw consumption is common in Bengali culture (7). Date palm sap harvesters (*gachhis*) consider bats a nuisance, because they can spoil the sap, and some report that they occasionally use skirt-like barriers (*bana*) to interrupt bat access by covering the shaved part of the tree, to protect the sap flow and collection pot (6). *Banas* can successfully interrupt bats' access to the sap and have been well accepted by *gachhis* (7-10). The Government of Bangladesh also discourages drinking raw date palm sap in an effort to reduce the risk from Nipah virus.

We developed and implemented two behaviour change interventions: one that discouraged drinking raw sap and one promoting drinking only *bana*-protected sap to reduce the risk of NiV transmission. We assessed the impact of two different intervention approaches, in terms of how they changed the date palm sap consumption habits of local residents.

We conducted a community based intervention trial where we compared the two behaviour change interventions implemented in two separate endemic districts and had control communities in a third Nipah endemic district. In two sub-districts of Rajbari district, we recommended “no raw sap” consumption for two consecutive sap collection seasons (2012-13 and 2013-2014). In two sub-districts of Faridpur district during the 2013-2014 season, we recommended to abstain or only drink *bana*-protected sap- “only safe sap”. Two local NGOs delivered the intervention using community mobilization, opinion leaders, community meetings and posters in addition to awards as incentives for *gachhis* to use *banas* in the “only safe sap” intervention area. We broadcasted public service announcements (PSAs) through closed circuit television.

We conducted quantitative surveys and observed behaviours in the intervention and control areas before and after the intervention to collect data on respondents' raw sap consumption practices and exposure to the intervention messages. The evaluation team conducted baseline surveys using two pre-tested standardized questionnaires and face-to-face-interviews. In 2012, they collected data from community residents in the “no raw sap” intervention and control areas. In 2013, they collected data from community residents and *gachhis* in the “only safe sap” intervention and control areas. In 2014, two months after the intervention,

we collected endline data among community residents and *gachhis* from the intervention and control areas.

For two months in 2012-2013 the evaluation team observed sap selling points in the “no raw sap” intervention and control areas. The following season (2013-2014) they observed selling points in all three study areas. Every two weeks they conducted observations in at least five different points per area and recorded the number of trees harvested and covered by *banas* and the number of persons who consumed and bought raw sap to take home. The team estimated the amount of sap sold by observing the size of the pots and consulting with the *gachhis*.

We assessed the statistical significance of the impact of the interventions using a regression model, adjusted for clustering at the village-level. We used difference in differences analysis of the proportions among the control and intervention groups between baseline and endline. To measure the association of exposure to the intervention with consumption of raw date palm sap, we calculated the odds ratio (OR) with 95% confidence interval. From the observation data, we calculated the number of trees harvested and covered with *banas*, the proportion of people who drank raw sap, and the amount of raw sap people drank and bought from *gachhis*.

The evaluation team interviewed 6,220 community members and 665 *gachhis* during the baseline and endline surveys (Table 1). Participants reporting that they drank raw sap at least once a month markedly declined from baseline to endline in all communities, but more so in the intervention than control areas. Consumption of *bana*-protected sap significantly increased in the “only safe sap” area (3% vs. 43%) while it remained similar in the control area (26% vs. 27%) from baseline to endline. Respondents among the “only safe sap” group reported an increase in asking *gachhis* about *bana* use before consumption but this decreased in the control group from baseline to endline.

The evaluation team observed that raw sap consumption at the selling points declined in the “no raw sap” area between the two seasons. In the control area, observed sap consumption also slightly declined (Table 2).

In the “only safe sap” area, *gachhi*-reported *bana*-usage increased from 11% to 90% from baseline to endline (Table 1). We also found a high level of reported *bana*-use in the control area and observed just a slight decrease from baseline to endline (66% to 57%). In the “only safe sap” area, although the reported use of *banas* increased, the total number of harvested trees declined from baseline to endline and *gachhis* reported an unavailability of sap. In the control area, the number of harvested trees was noticeably fewer than the intervention areas, but remained fairly constant throughout the study (Table 1). During the 2013-14

season, we observed 7% of trees with *banas* and 31% of *gachhis* using *banas* in the “only safe sap” area compared to 26% of trees with *banas* and 55% of *gachhis* using *banas* in the control area. During the community meetings respondents from the “only safe sap” area were more likely to report consuming raw sap (54% vs. 43%, OR 1.5, 95% CI 1.0-2.3, $p=0.02$). However, they were less likely to consume sap from an unprotected source (16% vs 28%, OR 0.5 CI 0.3-0.9, $p=0.01$).

Table 1: Gachhis’ report about the trees they harvested and bana use during baseline and endline data collection from the “no raw sap,” “only safe sap” and control areas, Bangladesh 2013 to 2014

Trees harvested for raw sap consumption, raw sap selling, and <i>bana</i> use	Control area <i>gachhi</i>		“Only safe sap” intervention area <i>gachhi</i>		“No raw sap” intervention area <i>gachhi</i>	Difference of (“Only safe sap” Difference 2014-2013) - (Control Difference 2014-2013)	Comparing control endline and “only safe sap” endline	Comparing control endline and “no raw sap” endline
	Baseline 2013 N=105 n (%)	Endline 2014 N=150 n (%)	Baseline 2013 N=110 n (%)	Endline 2014 N=150 n (%)	Endline 2014 N=150 n (%)			
Harvested trees harvested for raw consumption last season								
Median (IQR)	6 (3,10)	5 (2,10)	60 (25, 100)	19 (5,40) ^{†††}	10 (2,40)	(-40) ^{†††}	^{†††}	^{†††}
Frequency of selling raw sap								
At least a few times	64 (61)	81 (54)	90 (82)	109 (73)	102 (68)	(-2)	^{††}	[†]
Proportion of sap sold for raw consumption per week during the peak of the last sap collection season (in liters)								
Median (IQR)	10 (6,30)	20 (10,40)	30 (15,80)	37.5 (15,70)	13.5 (8,30)	(-2.5)	[†]	
Used banas last season								
Used banas on trees harvested for raw sap consumption	69 (66)	85 (57)	12 (11)	135 (90) ^{†††}	47 (31)	(88) ^{†††}	^{††}	^{†††}

*Cluster adjusted
[†]Open-ended responses with multiple answers allowed
[†]P value < 0.05
^{††}P value < 0.01
^{†††}P Value < 0.001

Table 2: Observation of date palm sap harvesting, consumption and selling at gachhis’ households during 2012-13 and 2013-14 sap collection seasons*

Observation findings	2012-13 sap season		2013-14 sap season		
	“No raw sap” intervention area N=46	Control area N=36	“No raw sap” intervention area N=46	“Only safe sap” intervention area N=48	Control area N=38
Number of trees harvested “observed”, median (IQR) [§]	-	-	16 (12, 27) ^{†††}	16 (11, 24) ^{†††}	7 (3, 13)
Mean number of persons who consumed raw sap [†] (SD) “protected or unprotected”	3.14 (2.22)	5.45 (3.78) [†]	3.20 (2.20)	3.00 (2.83)	2.95 (1.85)
Mean number of persons who purchased raw sap and took it home to use ^{††} (SD)	1.85 (1.21)	3.77 (2.98) [†]	1.56 (1.33)	1.65 (0.93)	2.25 (2.00)

*Usual observation period was 5:30 am to 7:30 am
§Items were not observed in 2012-13 season
†P-value was calculated by comparing the “no raw sap” intervention area with the control area;
‡P-value was calculated by comparing the “only safe sap” intervention area with the control area
†P value < 0.05, ‡P value < 0.01, ††P Value< 0.001
†Denominator was the gachhis household where raw sap consumption occurred
††Denominator was the gachhis household where persons purchased raw sap and took away

* Cluster adjusted

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Comments

Reported raw sap consumption significantly declined in all areas. Consumption of *bana*-protected sap increased in the “only safe sap” area. These reported changes in behaviour were supported by observation. The team also observed a decline in the amount of raw sap selling in the “no raw sap” and control areas.

Our intervention consisted of both interpersonal and mass media dissemination of the same messages within a particular period of time. Studies suggest that exposure to more than one type of communication can contribute to behaviour

change (11, 12). For example, in our study, seeing the poster and the PSA alone was not associated with changes in behaviour, but participants in the “only safe sap” area who were exposed to the poster, PSA, and the community meetings reported a decrease in risk behaviour.

Although raw sap consumption declined, participants continued to report raw sap consumption in both intervention groups after the intervention, suggesting that abstaining from sap consumption might be difficult. Asking people to drink “only safe sap” is less demanding than asking people to stop drinking sap altogether, given the long tradition of drinking raw sap (13), and therefore, might be useful in reducing Nipah risk. Health-related studies show that modest changes to behaviours are easier to achieve than more substantive changes (14-16).

The primary outcome of our study was measured through respondent report, and since community residents knew about the intervention in their community, they may have reported that they followed the recommended behaviour even if they did not in reality change their practices. Social desirability or courtesy bias may have induced respondents to under-report their sap consumption practice and over-report *bana* use (19, 20).

The emerging nature of NiV warrants longer term interventions to continue to raise awareness among villagers and stimulate behaviour change to reduce the risk of this bat borne zoonosis. Promoting the use of *banas* could provide an effective, complementary intervention for those who may not be willing to end their raw sap consumption, that is both low-cost and culturally acceptable (17,18).

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Zika virus infection in pregnancy: a systematic review of disease course and complications

Chibueze EC, Tirado V, da Silva Lopes K, Balogun OO, Takemoto Y, Swa T *et al.* Zika virus infection in pregnancy: a systematic review of disease course and complications. *Bull World Health Organ.* E-pub: 9 June 2016. doi: <http://dx.doi.org/10.2471/BLT.16.178426>.

Abstract

Objectives: To characterize maternal Zika virus (ZIKV) infection, including its natural history, risk of adverse pregnancy and birth outcomes, and describe the range of associated clinical manifestations and abnormalities with the aim of complementing evidence base for WHO interim guidance on pregnancy management in the context of ZIKV infection.

Methods: We searched MEDLINE, EMBASE, CINAHL, World Health Organization Global Health Library, Cochrane Central Trials Register, and Cochrane Database of Systematic Reviews from inception until March 2016. Two review authors independently screened and assessed full texts of eligible reports and extracted data from relevant studies. The quality of studies was assessed using the Newcastle-Ottawa Scale (NOS) and the National Institute of Health (NIH) tool for observational studies and case series/reports, respectively.

Results: Among 142 eligible full-text articles, 18 met the inclusion criteria (13 case series/reports and five cohort studies). No study suggested a higher risk of ZIKV infection in pregnant women after *Aedes* mosquito exposure compared to the non-pregnant population. Common symptoms among pregnant women with suspected/confirmed ZIKV infection were fever, rash and arthralgia. Apart from one case of Guillain-Barré syndrome among ZIKV-infected mothers, no other case of severe maternal morbidity or mortality reported. Complications reported in association with maternal ZIKV infection included a wide range of fetal and newborn neurological and ocular abnormalities; fetal growth restriction, stillbirth and perinatal death. Microcephaly was the main neurological complication

reported in eight studies, with an incidence of about 1% in one study. Seven studies reported no symptoms in some ZIKV-infected pregnant women. Normal birth outcomes were also reported. No study reported on clinical features or complications following ZIKV co-infection with other flaviviruses in pregnant women.

Conclusion: Given the wide and variable fetal and newborn presentations/complications associated with prenatal ZIKV infection, identifying effective strategies to reduce the impact of ZIKV infection on families and health systems in resource-constrained settings remains a challenge. This review highlights key evidence gaps that should be urgently addressed in the global response to the current ZIKV outbreaks.

Significant effects of oral phenylbutyrate and vitamin D3 adjunctive therapy in pulmonary tuberculosis: a randomized controlled trial

Mily A, Rekha RS, Kamal SM, Arifuzzaman AS, Rahim Z, Khan L *et al.* Significant effects of oral phenylbutyrate and vitamin D3 adjunctive therapy in pulmonary tuberculosis: a randomized controlled trial. *PLoS One* 2015 Sep 22;10(9):e0138340. doi: 10.1371/journal.pone.0138340.

Abstract

Background: Development of new tuberculosis (TB) drugs and alternative treatment strategies are urgently required to control the global spread of TB. Previous results have shown that vitamin D3 (vitD3) and 4-phenyl butyrate (PBA) are potent inducers of the host defense peptide LL-37 that possess antimicrobial effects.

Objective: To examine if oral adjunctive therapy with 5,000IU vitD3 or 2x500 mg PBA or PBA+vitD3 to standard chemotherapy would lead to enhanced recovery in sputum smear-positive pulmonary TB patients.

Methods: Adult TB patients (n = 288) were enrolled in a randomized, double-blind, placebo-controlled trial conducted in Bangladesh. Primary endpoints included proportions of patients with a negative sputum culture at week 4 and reduction in clinical symptoms at week 8. Clinical assessments and sputum smear microscopy were performed weekly up to week 4, fortnightly up to week 12 and at week 24; TB culture was performed at week 0, 4 and 8; concentrations of LL-37 in cells, 25-hydroxyvitamin D3 (25(OH)D3) in plasma and ex vivo bactericidal function of

monocyte-derived macrophages (MDM) were determined at week 0, 4, 8, 12 and additionally at week 24 for plasma 25(OH)D3.

Results: At week 4, 71% (46/65) of the patients in the PBA+vitD3-group ($p = 0.001$) and 61.3% (38/62) in the vitD3-group ($p = 0.032$) were culture negative compared to 42.2% (27/64) in the placebo-group. The odds of sputum culture being negative at week 4 was 3.42 times higher in the PBA+vitD3-group ($p = 0.001$) and 2.2 times higher in vitD3-group ($p = 0.032$) compared to placebo. The concentration of LL-37 in MDM was significantly higher in the PBA-group compared to placebo at week 12 ($p = 0.034$). Decline in intracellular Mtb growth in MDM was earlier in the PBA-group compared to placebo (log rank 11.38, $p = 0.01$).

Conclusion: Adjunct therapy with PBA+vitD3 or vitD3 or PBA to standard short-course therapy demonstrated beneficial effects towards clinical recovery and holds potential for host-directed-therapy in the treatment of TB.

Incidence of and risk factors for hospital-acquired diarrhoea in three tertiary care public hospitals in Bangladesh

Bhuiyan MU, Luby SP, Zaman RU, Rahman MW, Sharker MA, Hossain MJ *et al.* Incidence of and risk factors for hospital-acquired diarrhea in three tertiary care public hospitals in Bangladesh. *Am J Trop Med Hyg* 2014 Jul;91(1):165-72.

Abstract

During April 2007-April 2010, surveillance physicians in adult and paediatric medicine wards of three tertiary public hospitals in Bangladesh identified patients who developed hospital-acquired diarrhoea. We calculated incidence of hospital-acquired diarrhoea. To identify risk factors, we compared these patients to randomly selected patients from the same wards who were admitted >72 hours without having diarrhoea. The incidence of hospital-acquired diarrhoea was 4.8 cases per 1,000 patient-days. Children <1 year of age were more likely to develop hospital-acquired diarrhoea than older children. The risk of developing hospital-acquired diarrhoea increased for each additional day of hospitalization beyond 72 hours, whereas exposure to antibiotics within 72 hours of admission decreased the risk. There were three deaths among case-patients; all were infants. Patients, particularly young children, are at risk for hospital-acquired diarrhoea and associated deaths in Bangladeshi hospitals. Further research to identify the responsible organisms and transmission routes could inform prevention strategies.

Surveillance updates

With each issue of HSB, updates of surveillance data described in earlier issues are provided. These updated tables and figures represent the most recent observation period available at the time of publication. We hope these updates will be helpful to health professionals who are interested in current patterns of disease and drug resistance in Bangladesh.

Proportion of diarrhoeal pathogens susceptible to antimicrobial drugs: June 2015-May 2016

Antimicrobial agents	Shigella N=58	V. cholerae O1 N=164
Mecillinam	87.9	3.0
Ampicillin	62.0	11.6
TMP-SMX	46.7	1.8
Ciprofloxacin	44.8	100
Tetracycline	12.0	11.6
Azithromycin	70.7	99.4
Ceftriaxone	91.3	4.3

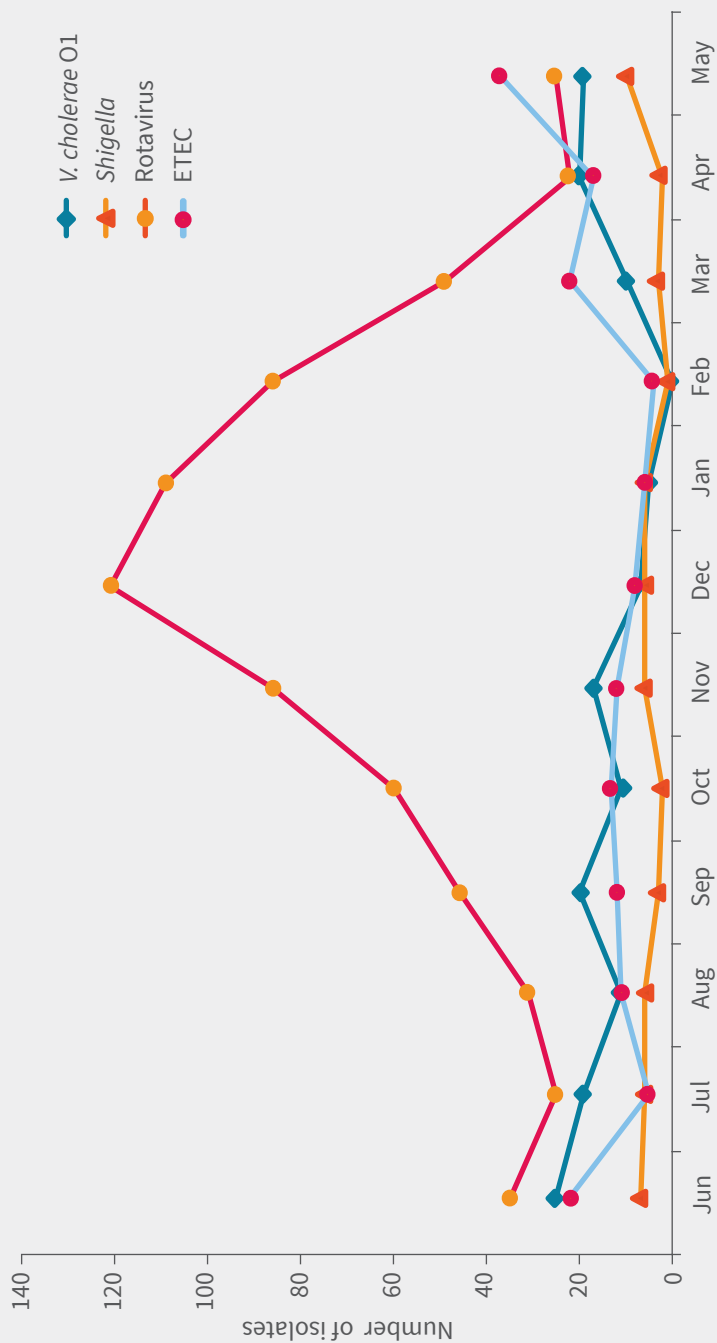
Source: Hospital Surveillance, Dhaka Hospital, icddr,b

Antimicrobial susceptibility pattern of S. typhi among children <5 years during January-June 2016

Antimicrobial agent	Total tested (N)	Susceptible n (%)	Reduced susceptibility n (%)	Resistant n (%)
Ampicillin	6	5 (83)	0	1 (17)
Cotrimoxazole	6	5 (83)	0	1 (17)
Chloramphenicol	6	5 (83)	0	1 (17)
Ceftriaxone	6	6 (100)	0	0
Ciprofloxacin	6	1 (17)	5 (83)	0
Nalidixic Acid	6	1 (17)	0	5 (83)

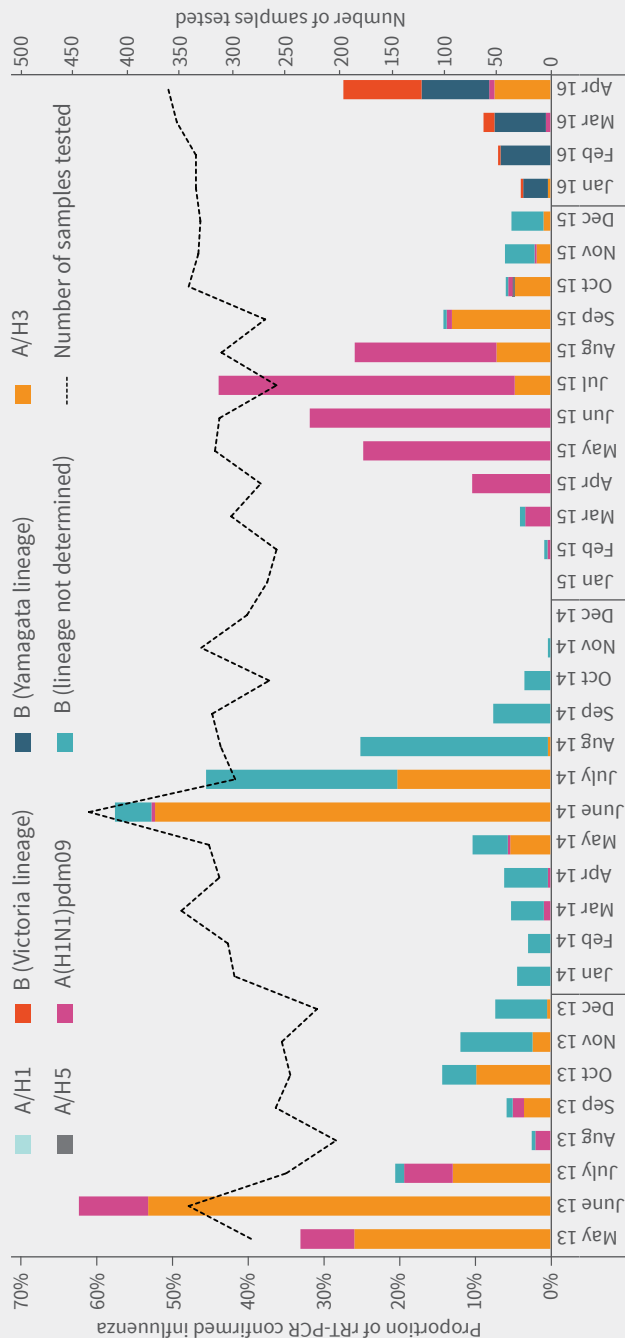
Source: Kamalapur Urban Surveillance, icddr,b

Monthly isolation of *V. cholerae* O1, *Shigella*, Rotavirus and ETEC: June 2015-May 2016



Source: Hospital Surveillance, Dhaka Hospital, icddr,b

Proportion of laboratory-confirmed influenza among hospitalized severe acute respiratory illness (SARI) and outpatient influenza like illness (ILI) cases between May 2013 and April 2016



* Influenza B typing initiated in January 2016

Source: Patients participating in hospital-based influenza surveillance in Dhaka National Medical College Hospital, Community-based Medical College Hospital (Mymensingh), Jahurul Islam Medical College Hospital (Kishoregonj), Rajshahi Medical College Hospital, Shaheed Ziaur Rahman Medical College Hospital (Bogra), LAMB Hospital (Dinajpur), Bangabandhu Memorial Hospital (Chittagong), Comilla Medical College Hospital, Khulna Medical College Hospital, Jessore General Hospital, Jalalabad Ragib-Rabeya Medical College Hospital (Sylhet), Sher-e-Bangla Medical College Hospital (Barisal), Chittaganga Medical College Hospital*, and Dinajpur Medical College Hospital* (*since April 2014)



A skirt-like barrier called *bana* used to protect the date palm sap from bats

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