HSB
Health and Science Bulletin
VOLUME 12 • NUMBER 4 • DECEMBER 2014
ISSN 1729-343X

Inside

Building capacity for minimally invasive autopsies in Bangladesh

Information on cause of death is essential for designing public health interventions to prevent premature death. The invasive nature of an autopsy procedure is perceived by many to be against the teachings of Islam. However, formative research in Bangladesh suggests that collecting diagnostic specimens after death through minimally invasive procedures, such as postmortem needle biopsies, may be acceptable. Our objective was to build capacity to conduct minimally invasive autopsies, pilot informed consent and specimen collection procedures, and evaluate the feasibility and acceptability of the procedure at one hospital in Bangladesh. After receiving an opinion from Islamic scholars, training staff on the procedure, and designing a room in the hospital to conduct the procedure safely, we approached family members of 15 patients who died from acute meningo-encephalitis or acute respiratory illness to request their consent for a minimally invasive autopsy. Five families (33%) agreed to the collection of brain and/or lung tissue specimens, indicating that postmortem needle biopsy may be feasible as a tool to help determine cause of death in hospitals in Bangladesh.

icddr,b

Understanding causes of deaths is crucial for preventing premature deaths. Verbal autopsy is an approach that uses structured questionnaires to interview family members of deceased patients to report in lay language the signs and symptoms that preceded death in order to assign a probable cause of death. However, the non-specific nature of diagnoses using verbal autopsy (1) limits the development of effective public health interventions, such as pathogen-specific therapeutics or vaccines, to prevent deaths. Detecting pathogens in biological specimens can help diagnose infectious causes of death, though collecting these specimens before patients die is not always possible, especially when patients die shortly after arrival at the hospital, mostly due to delayed care-seeking. Diseases, such as rabies, that might not be detectable in blood, and cerebrospinal fluid specimens in the early stages of illness (2), could be detected in brain biopsy specimens. Though brain specimens are used to determine etiologies of infection, they are often impractical to collect while the patient is alive, particularly in low- and middle-income countries. Lung biopsies may also detect infections that may not be easily detected from blood and sputum. Therefore, postmortem autopsy could be a potential procedure for specimen collection that might lead to pathogen discovery in Bangladesh.

Although, full autopsies are used to determine cause of death, including deaths in fatal outbreaks (3-5) in many countries, they may not be feasible for determining cause of death in Bangladesh. In Bangladesh, autopsies are performed only as part of the legal system, to determine unnatural causes of death like accidents, homicides, or suicides. In a recent qualitative study, civil surgeons, physicians, and community members reported that families of deceased persons often used bribes and the influence of local political leaders to avoid autopsies because they involve removing organs from bodies and result in obvious cutting and stitching of bodies, which families find objectionable (6). Although Islam does not expressly prohibit postmortem examinations, a commonly known hadith, or tradition based on reports of sayings by the Prophet Hazrat Muhammad (Sallallahu Alayhi Wassallam), states, "The breaking of the bone of a dead person is like breaking the bone of a live person" (7,8). One interpretation is that the dead feel pain just as the living do; hence any examination of a corpse should be gentle, respectful and as minimally invasive as possible (9).

In 2009, a qualitative study explored the acceptability of minimally invasive postmortem needle biopsies among families of case-patients who died during four Nipah infection outbreaks from 2004 to 2007 in Bangladesh. Most family members and religious and community leaders agreed that postmortem needle biopsies would be acceptable under certain circumstances, including when they benefit the community and society and when the family trusts the research team (6). The objective of this study was to pilot informed consent and specimen collection processes for minimally

invasive autopsies, evaluate the feasibility and acceptability of the procedure in a surveillance hospital, and build capacity to conduct the procedure in Bangladesh.

The Bangladesh Medical and Research Council (BMRC) institutional review board and icddr,b's Research Review Committee and Ethical Review Committee reviewed and approved the protocol.

In March 2012, we invited Islamic scholars from Faridpur District to the Institute of Epidemiology, Disease Control and Research (IEDCR) in Dhaka to participate in a group discussion to learn their opinions about postmortem needle biopsies. Eight religious scholars participated, including muftis, mawlanas, Islamic shari'ah researchers and imams from different mosques. Two of the participants were from the villages where an outbreak of Nipah encephalitis occurred in 2004. All of the scholars agreed that it is permissible in Islam to conduct postmortem needle biopsies for the benefit of humans, including determining cause of death. We summarized their discussion in Bengali language and asked them to review the summary. They signed a summary statement and expressed their willingness to discuss the subject when necessary with families of deceased patients approached for the pilot study.

Because we planned to target deaths suspected to be from infections which could pose a risk to healthcare workers or increase the chance of environmental contamination and nosocomial transmission, we consulted with biosafety experts and made several modifications to a designated procedure room. These modifications included creating a laminar airflow system and applying epoxy coating to the floor and plastic paint on the walls to enable decontamination with hypochlorite swabs.

A team of physicians from Faridpur Medical College Hospital (FMCH) and icddr,b travelled to Chulalongkorn University in Bangkok, Thailand, to receive practical hands-on training on trans-orbital and trans-nasal brain biopsies and percutaneous lung biopsies. In addition, the trainers demonstrated appropriate procedures for storage of tissues. Since community members believed it was important that postmortem needle biopsies be performed on deceased adults by physicians of the same sex (6) and all of the physicians who were trained in Bangkok were male, adult deceased patients were only enrolled from the male medicine ward. Male physicians performed the biopsies on children of both sexes from the paediatric ward.

A team of sociologists, physicians, and epidemiologists conducted the pilot study at FMCH, where surveillance for acute meningo-encephalitis and acute respiratory illness has been ongoing in collaboration with IEDCR and icddr,b. In mid-January 2014, the team met the FMCH hospital superintendent, professors of medicine and paediatrics, the principal of the medical college, assistant registrars, medical officers, intern doctors, and senior nurses in

the hospital. We discussed the study objectives and procedures, as well as previous postmortem formative activities and findings and the opinions and perspectives of the religious scholars from Faridpur regarding minimally invasive procedures for determining cause of death.

We asked healthcare workers to inform us of any deaths among patients with fever and acute respiratory illness or features of acute brain dysfunction, including altered mental status, convulsions, unconsciousness or focal neurological deficits. The study team's cell phone number was posted in the hospital ward and the healthcare workers' room and hospital staff were asked to call the team as soon as possible after the death of patients meeting these criteria.

Between mid-January and mid-March 2014, upon being informed of deaths of patients who might meet enrollment criteria, the study team went to the patient ward, verified the clinical criteria with attending physicians and nurses, and introduced themselves to the families of the deceased patients. Guardians of the deceased patients were identified. For children, parents were the guardians. For adults, spouses or accompanying adults were considered to be the guardians. We described the purpose of the study to the guardians and explained that while the findings might not benefit their families, they might help prevent deaths in the future by identifying treatable causes of death. Before written informed consent was obtained, details of the procedure and its minimally invasive nature were described and families had the opportunity to ask questions. After this, all available family members were asked for their consent to perform the procedure. Decision-making involved multiple family members, and the procedure was only conducted if all persons named as guardians of the deceased provided written informed consent and other family members present in the hospital gave verbal consent.

The study team transferred enrolled deceased patients to the procedure room and, based on recommendations from the formative study, offered family members the opportunity to observe the procedure from a separate room through a glass window. Team members wore N95 face masks and goggles, disposable surgical gowns, and sterile gloves. Oral and rectal swabs were collected using swab sticks. Two sterile disposable biopsy guns with 14 gauge biopsy needles and 15mm long cores (Temno system, CareFusion, San Diego, CA), one for brain and one for lung tissue, were used to obtain biopsies from each patient. Brain tissue was collected from four deceased patients via both trans-orbital and trans-nasal biopsies. Lung tissue was collected percutaneously at the intercostal space at the mid-axillary line from the deceased patients. Standard biosafety measures to dispose of medical waste were followed. After specimen collection, the bodies were wrapped in plastic sheets and returned to the families. Specimens were then transported to the icddr,b laboratory.

Between January 16 and March 20, 2014, 21 deceased patients met the clinical criteria for meningo-encephalitis or acute respiratory illness in paediatric medicine and adult male medicine wards. Families of six patients could not be approached because the patients died during the night and the study team was not notified until the morning, by which time the families had already taken the bodies away. We approached the families of the 15 remaining deceased patients. One family asked about Islamic teaching on postmortem needle biopsy but was not interested in discussing it with the Islamic scholars. Among the families of the 15 deceased patients, five (33%) family guardians consented to postmortem biopsies. The ages of deceased patients who underwent the procedure ranged from 4-60 years. Guardians of a sixth patient consented to only collection of rectal and oral swabs. In two other families, guardians of the patients consented but other family members did not and so specimens were not collected from these patients.

Specimens collected in this pilot study will be tested for known etiologic agents and examined by a pathologist to help determine cause of death. In addition, a team of experienced sociologists visited the families of all 15 deceased patients approached in this study, including those who did and did not give consent, to learn about their perspectives on the consent process and experiences with the study. Findings from these study components are not yet available.

Reported by: Faridpur Medical College Hospital; Institute of Epidemiology, Disease Control and Research, Ministry of Health and Family Welfare, Government of Bangladesh, Centre for Communicable Diseases, icddr,b

Supported by: Institute of Epidemiology, Disease Control and Research, Ministry of Health and Family Welfare, Government of Bangladesh; and Centers for Disease Control and Prevention, Atlanta, USA

Comment

One-third of the families approached in this pilot study agreed to collection of brain and lung specimens by minimally invasive procedures, suggesting that postmortem needle biopsies are acceptable at FMCH. We built the capacity to conduct postmortem needle biopsies at FMCH by discussing the acceptability of the procedure with religious leaders and healthcare workers and obtaining their support, training physicians to perform biopsies, renovating a procedure room to maintain biosafety, and giving the physicians an opportunity to perform biopsies. Follow-up qualitative research with families about the procedure will help to improve communication between families and physicians and researchers during the consent process for the procedure. The next step will be to continue piloting the procedure at FMCH and to begin to pilot the procedure at two additional hospitals in other geographic locations in Bangladesh.

References

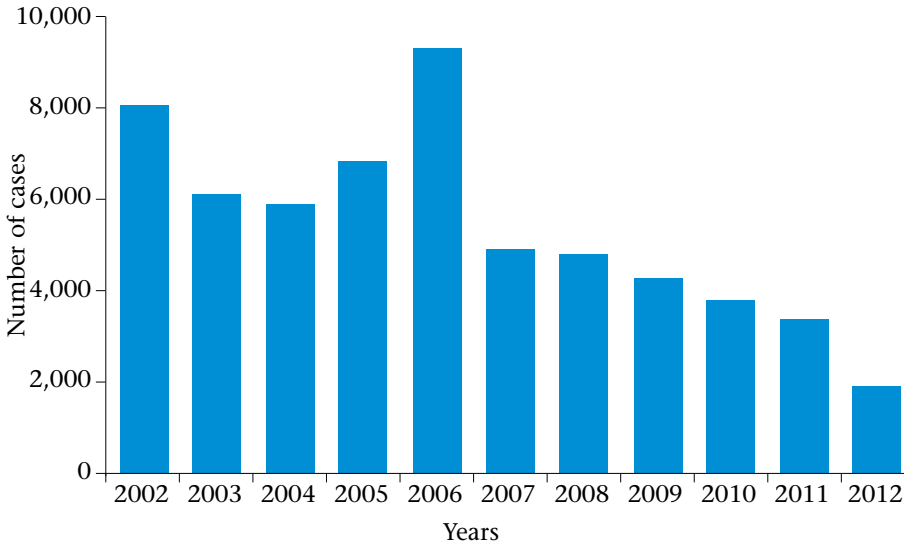
1. Fottrell E, Byass P. Verbal autopsy: methods in transition. *Epidemiol rev* 2010;32(1):38-55.
2. Tong TR, Leung KM, Lee K, Lam AW. Trucut needle biopsy through superior orbital fissure for diagnosis of rabies. *Lancet* 1999;354(9196):2137-8.
3. Iwasenko JM, Howard J, Arbuckle S, Graf N, Hall B, Craig ME *et al*. Human cytomegalovirus infection is detected frequently in stillbirths and is associated with fetal thrombotic vasculopathy. *J Infect Dis* 2011;203(11):1526-33.
4. Shieh W, Zaki SR. Advanced Pathology Techniques for Detecting Emerging Infectious Disease Pathogens. In: Tang, Yi-Wei, Stratton, Charles W. (Eds.) Advanced Techniques in Diagnostic Microbiology. Springer; 2013. p. 873-90.
5. Zhang YC, Jiang SW, Gu WZ, Hu AR, Lu CT, Liang XY *et al*. Clinicopathologic features and molecular analysis of enterovirus 71 infection: Report of an autopsy case from the epidemic of hand, foot and mouth disease in China. *Pathol Int* 2012;62(8):565-70.
6. Gurley ES, Parveen S, Islam MS, Hossain MJ, Nahar N, Homaira N *et al*. Family and community concerns about post-mortem needle biopsies in a Muslim society. *BMC medical ethics* 2011;12(1):10.
7. Ibn Majah. Book 6, Hadith 1685.
8. Sunan Abu Dawud, Book 20, Hadith 3201.
9. Rispler-Chaim V. The ethics of postmortem examinations in contemporary Islam. *J Med Ethics* 1993;19(3):164-8.

Update on the kala-azar elimination programme in Bangladesh

Visceral leishmaniasis, or kala-azar (KA), is a vector-borne disease caused by *Leishmania* species, protozoan parasites. KA is endemic in Bangladesh. Data suggest that more than 60% of KA cases reported worldwide during 2004-2008 occurred in Bangladesh, Nepal and India. In 2005, these three countries signed a memorandum of understanding with the aim of reducing the KA burden in each country to less than one case per 10,000 per year by 2015. In 2008, the Government of Bangladesh initiated a National KA Elimination Program (NKEP). This report provides an update on the program and identifies challenges to reducing the KA burden in Bangladesh. The program focuses on three elements: early case detection, effective treatment, and vector control. The number of KA cases identified in Bangladesh decreased from 6,892 to 1,902 during 2005-2012 and the number of sub-districts classified as hyper-endemic for KA decreased from seven in 2008 to three in 2012. NKEP has made substantial progress since its inception but has not yet met its goal.

Visceral leishmaniasis, or kala-azar (KA), is a vector-borne disease, caused by the *Leishmania* species protozoan parasites that are transmitted by infected female phlebotomine sandflies. *L. donovani* is the *Leishmania* species commonly found in South Asia. KA is characterized by prolonged fever, wasting and enlargement of the spleen. If left untreated, KA is generally fatal. KA primarily affects the poor (1). It is estimated that 200 million people are at risk of infection and 200,000-400,000 new cases of KA occur worldwide each year (2). Data collected between 2004 and 2008 showed that sixty percent of estimated cases worldwide occurred in Bangladesh, Nepal and India (2,3). Post-kala-azar dermal leishmaniasis (PKDL) is a complication of KA. After successful treatment of KA, 10% of patients may develop some dermal spots (Figure 3). These patients are the reservoir of KA. In 2008, the Government of Bangladesh initiated the National KA Elimination Programme (NKEP), with the goal of reducing the incidence of KA to less than one case per 10,000 population by 2015. NKEP focuses on hyper-endemic areas in the country (Figure 1) and on three elements: 1) early case detection, 2) effective treatment, and 3) vector control (5). From 2008 to 2012, the number of cases decreased steadily from 4,824 to 1,902 (Figure 1). In the same time period, the number of hyper-endemic sub-districts (incidence rate more than 2.5 per 10,000 population) decreased from seven to three and the incidence in Mymensingh District, the district with the highest incidence, fell from 8.7 to 2.6 per 10,000 population (5). This report provides an update on the programme and identifies challenges to reducing the KA burden in Bangladesh.

Figure 1: Annual number of kala-azar cases detected in Bangladesh, 2002-2012 (5)

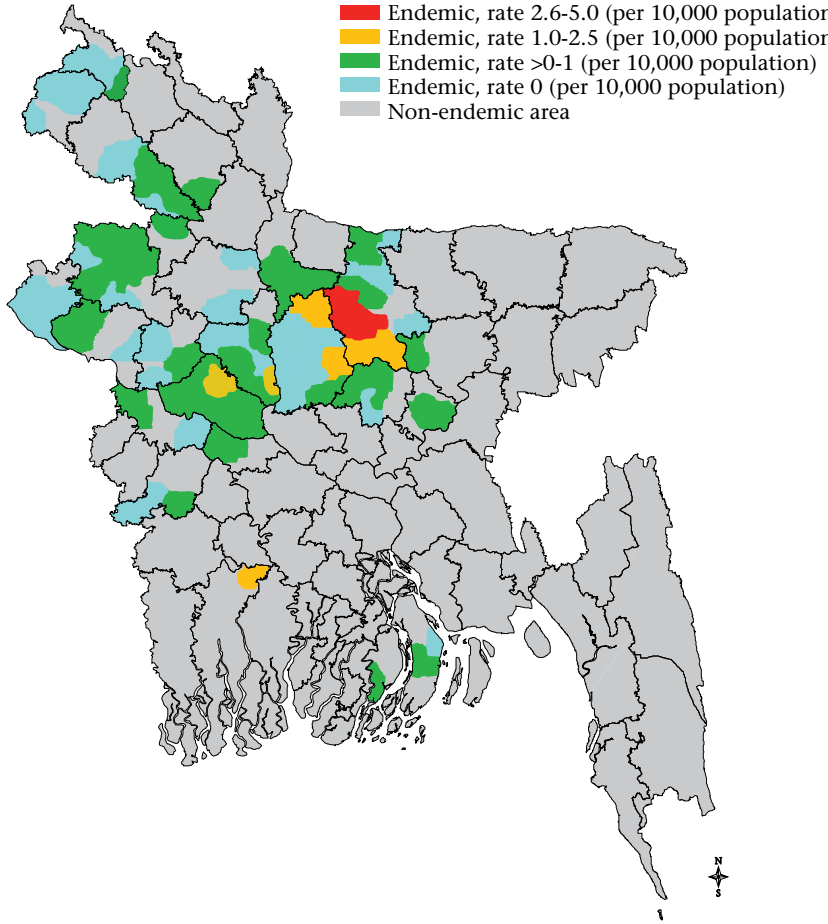


One of the first steps that NKEP took was to introduce the rK39 rapid diagnostic test (RDT) to Bangladesh. This is a sensitive, specific, commercially available, and inexpensive (less than one USD/test) diagnostic test that is easy to perform. It requires only one drop of blood and detects antibodies for rK39, *Leishmania* antigen. This test obviates the need for using the conventional microscopic method for diagnosing KA, which consists of obtaining an aspirate from the spleen, a procedure which requires trained professionals and poses risks to patients (6). NKEP defined a KA case as an illness with fever for more than two weeks, an enlarged spleen and a positive rK39 test result. NKEP defined PKDL as an illness in a person with past history of KA that consists of maculo-papular or nodular skin lesions and a positive rK39 test result (7). The sensitivity and specificity of the rK39 RDT can vary, but in an analysis of studies from different countries, the World Health Organization (WHO) reported 94% sensitivity and 91% specificity compared with microscopic examination of splenic aspirates, which is considered the gold standard for diagnosis (6). In 2008, NKEP distributed rK39 test kits to all upazilla health complexes (UHCs) in Bangladesh.

The second element of NKEP is effective treatment. In 2009, a new drug, miltefosine, was introduced as an alternative to sodium stiobogluconate (SSG), the drug that had been previously used but requires inpatient treatment for 28 days to receive intramuscular injections. Miltefosine can be administered orally for 28 days on an outpatient basis. Several months after the introduction of miltefosine in Bangladesh, another drug, liposomal

amphotericin, which can be administered as a single dose for the treatment of KA, was introduced in Bangladesh (8,9). Single-dose liposomal amphotericin B (sLAB) is very effective and has fewer side effects than miltefosine and SSG (8,9). However, sLAB requires equipment to maintain a cold chain and more clinical monitoring than is needed for treatment with miltefosine or SSG (9). The WHO, in collaboration with the Government of Bangladesh, trained 96 doctors and 96 nurses in hyper-endemic areas (Figure 2) to administer sLAB for the treatment of KA (9).

Figure 2: Kala-azar (KA)-endemic areas of Bangladesh according to the number of KA cases (stratification of areas by rates of infection of the year 2012)



The third element of the NKEP is vector control. Two things are important for transmission of leishmaniasis. One is the vector, sandflies, and the other is the reservoir, persons with leishmaniasis, and particularly those with the chronic form, or PKDL (if a sandfly bites a person with PKDL and then bites someone else, there is a risk of KA transmission)(10). Beginning in 2011, NKEP focused on vector control to reduce the transmission of the parasite to humans. Trials of indoor residual spraying in two areas in Mymensingh District (11) and long-lasting insecticide treated bed nets in Rajshahi and Mymensingh District (12) were conducted. These trials were successful and NKEP began to use these vector control methods in hyper-endemic sub-districts of Bangladesh (Figure 2).

Figure 3: A person with post-kala-azar dermal leishmaniasis

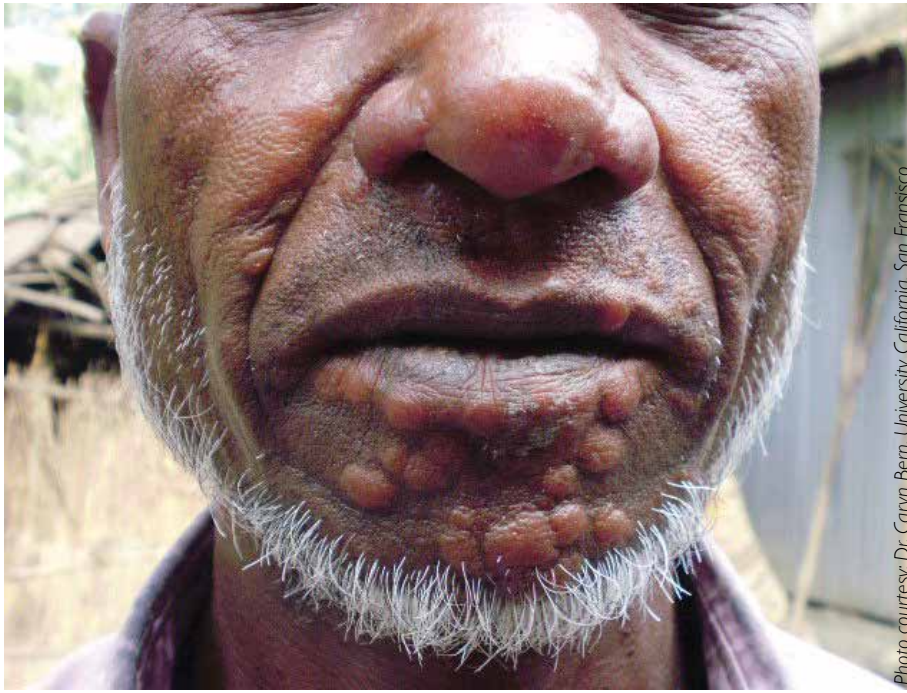


Photo courtesy: Dr. Caryn Bern, University California, San Fransisco

Reported by: Parasitology Laboratory, icddr,b

Supported by: Communicable Disease Control Unit, Directorate General of Health Services, Ministry of Health and Family Welfare, Government of Bangladesh and Emerging Vaccine Sciences, Centre for Vaccine Sciences, icddr,b

Comments

Since NKEP was initiated in 2008, the number of KA cases has declined steadily. Although NKEP has been a successful programme, which can be attributed in large part to the introduction of a new diagnostic test and treatment and vector control, there are still several challenges.

First, the programme uses passive case detection, in which the government relies on the patient's attendance at government hospitals. KA patients who go to private doctors or private facilities may be missed in addition to those who do not access healthcare. A study conducted in sub-districts of Mymensingh and Rajshahi districts found that 75% of deaths due to KA occurred at home and that none of these deaths were reported in Bangladesh's KA surveillance system (13). Implementation of active surveillance in areas endemic for KA, would capture more cases, enhance monitoring of the burden and mortality from KA and would likely increase access to effective treatment.

Second, though the rK39 RDT is a sensitive and specific test that is easy to perform and inexpensive, it has some limitations. For example, the test cannot distinguish between current and past KA infections because it detects antibodies against *Leishmania* spp., which can persist for years after infection with KA (6). Current KA infections need to be treated, whereas past infections do not, so physicians need to use judgment to determine the clinical implications of a positive RDT test result. A rapid test that specifically identifies a current infection, perhaps by detecting antigen to *Leishmania*, would be beneficial for appropriate clinical management of KA.

Third, although sLAB is an effective treatment regimen, it requires the maintenance of a cold chain until it is administered and it requires that patients' temperature, blood pressure, and fluid status are closely monitored. However, the necessary resources and training are lacking in some UHC hospitals, particularly those in rural settings. A study conducted in Mymensingh District before mid 2013 reported that of five UHC hospitals, most lacked the necessary resources such as 5% Dextrose, distilled water, disposable infusion sets, disposable syringes, and gloves (9), needed to administer sLAB. Ensuring that there are adequate supplies and trained personnel to administer sLAB in UHCs will be necessary to further reduce KA.

Finally, vector control requires more attention. NKEP's use of indoor residual spray and long-lasting insecticide treated bed nets, has some limitations. Excessive use of insecticides can result in insecticide resistance in sandflies (14). Use of insecticides also has a negative impact on the environment. However, integrated vector control management is necessary to reach the NKEP goal of reducing KA incidence. It will be important to develop and pilot insecticides with limited deleterious environmental effects.

Treatment of persons with PKDL is also important for controlling transmission. Persons with PKDL are the reservoir for infection and might

play a role in the re-emergence of KA several years later. Persons with PKDL are thought to have contributed to the resurgence of KA in South Asia in the 1990s (9). In the 1960s, government officials in South Asia initiated a programme to eradicate malaria by using insecticides to reduce the number of mosquitoes and interrupt transmission. This was successful in reducing the number of mosquitoes and it also reduced the number of sandflies. Subsequently, both malaria and KA cases declined markedly (10). In the 1990s, KA again resurged, likely from transmission of the *Leishmania* parasite from persons with PKDL to sandflies and then onward to previously uninfected persons (10,15). As of 2012, 325 persons with PKDL had been treated (5). Campaigns should be conducted to raise awareness about the role that persons with PKDL play in KA transmission and the individual and societal benefits that treatment will bring. Diagnosis of KA and PKDL can also be complex. KA can be mistaken for a variety of febrile illnesses and PKDL can be confused with leprosy. Training providers to be able to detect and appropriately treat KA and PKDL will be very important.

The findings presented in this report indicate that progress is being made in reducing the number of KA cases in Bangladesh. However, efforts will be needed to improve case detection, treatment, and control of vectors and reservoirs. Continued technical and financial assistance from national and international agencies will be essential for NKEP to achieve its goal to reduce the incidence of KA to less than one case per 10,000 population in every endemic sub-district by 2015.

References

1. Alvar J, Yactayo S, Bern C. Leishmaniasis and poverty. *Trends Parasitol* 2006;22(12):552-7.
2. Alvar J, Vélez ID, Bern C, Herrero M, Desjeux P, Cano J *et al.* Leishmaniasis worldwide and global estimates of its incidence. *PLoS One* 2012;7(5):e35671.
3. Joshi A, Narain JP, Prasittisuk C, Bhatia R, Hashim G, Jorge A *et al*. Can visceral leishmaniasis be eliminated from Asia? *J Vector Borne Dis* 2008;45(2):105-11.
4. Rahman KM, Islam S, Rahman MW, Kenah E, Ghalib CM, Galive CM, *et al*. Increasing incidence of post-kala-azar dermal leishmaniasis in a population-based study in Bangladesh. *Clin Infect Dis* 2010;50(1):73-6.
5. Directorate General of Health Services, Ministry of Health and family planning, Bangladesh. Data from 2008 to 2013. (Personal communication)
6. World Health Organisation. The use of Visceral leishmaniasis rapid diagnostic test. The Philippines: UNICEF/UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases, 2008. 20 p. (http://www.who.int/tdr/publications/documents/vl-rdts.pdf, accessed on 02 July 2014).

7. Huda MM, Hirve S, Siddiqui NA, Malaviya P, Banjara MR, Das P *et al*. Active case detection in national visceral leishmaniasis elimination programs in Bangladesh, India, and Nepal: feasibility, performance and costs. *BMC Public Health* 2012;12:1001.
8. Mondal D, Alvar J, Hasnain MG, Hossain MS, Ghosh D, Huda MM *et al*. Efficacy and safety of single-dose liposomal amphotericin B for visceral leishmaniasis in a rural public hospital in Bangladesh: a feasibility study. *Lancet Glob Health* 2014;2(1):e51-7.
9. Maintz EM, Hassan M, Huda MM, Ghosh D, Hossain MS, Alim A *et al*. Introducing single dose liposomal amphotericin B for the treatment of visceral leishmaniasis in rural bangladesh: feasibility and acceptance to patients and health staff. *J Trop Med* 2014;2014:676817.
10. Addy M, Nandy A. Ten years of kala-azar in west Bengal, Part I. Did post-kala-azar dermal leishmaniasis initiate the outbreak in 24-Parganas? *Bull World Health Organ* 1992;70(3):341-6.
11. Huda MM, Mondal D, Kumar V, Das P, Sharma SN, Das ML *et al*. Toolkit for monitoring and evaluation of indoor residual spraying for visceral leishmaniasis control in the Indian subcontinent: application and results. *J Trop Med* 2011;2011:876742.
12. Mondal D, Huda MM, Karmoker MK, Ghosh D, Matlashewski G, Nabi SG *et al*. Reducing visceral leishmaniasis by insecticide impregnation of bed-nets, Bangladesh. *Emerg Infect Dis* 2013;19(7):1131-4.
13. Huda MM, Chowdhury R, Ghosh D, Dash AP, Bhattacharya SK, Mondal D. Visceral leishmaniasis-associated mortality in Bangladesh: a retrospective cross-sectional study. *BMJ Open* 2014;4(7):e005408.
14. Stauch A, Duerr HP, P icado A, Ostyn B, Sundar S, Rijal S *et al*. Model-based investigations of different vector-related intervention strategies to eliminate visceral leishmaniasis on the Indian subcontinent. *PLoS Negl Trop Dis* 2014;8(4):e2810.
15. Bern C, Courtenay O, Alvar J. Of cattle, sand flies and men: a systematic review of risk factor analyses for South Asian visceral leishmaniasis and implications for elimination. *PLoS Negl Trop Dis* 2010;4(2):e599.

Preparedness for preventing emergence of Ebola virus disease in Bangladesh

The current outbreak of Ebola virus disease (EVD) in West Africa and the subsequent spread to other countries demonstrates the risk of extension to unaffected countries, including Bangladesh. While the chances of introduction of EVD into Bangladesh may be low, the extremely high population density in the country coupled with inadequate healthcare services and limited infection control practices in most hospitals make Bangladesh highly vulnerable to sustained transmission in the event of importation. To enhance the country's capacity to detect, respond to, and prevent emerging epidemics of international concern, Bangladesh needs to develop a comprehensive preparedness plan that builds on existing strengths of outbreak response procedures and core capacities of the 2005 International Health Regulations and focus on reducing identified gaps in healthcare delivery.

On March 21, 2014, the Ministry of Health in Guinea reported an outbreak of Ebola virus disease (EVD) to the World Health Organization (WHO) (1). The outbreak began in December 2013 and was initially localized in the forest region of Guinea, bordering Liberia and Sierra Leone (1-3). However, the outbreak escalated because of poor health infrastructure, deficits in healthcare capacity, stigma, public fear and inadequate international response early in the outbreak (4). The outbreak extended to neighbouring Liberia and Sierra Leone and a case was also identified in Nigeria in late July 2014 (5-7). As of August 6, 2014, Guinea, Liberia, Sierra Leone, and Nigeria had officially reported 1,779 cases and 961 deaths (8). Recognizing the potential for the virus to spread throughout and beyond Africa, the WHO Director-General declared EVD to be a Public Health Emergency of International Concern (PHEIC) on August 8, 2014 (9-11).

Ebola is a single-stranded, negative-sense RNA virus that causes a severe, often fatal, acute viral illness. While the natural reservoir host of the Ebola virus has not yet been identified, once an infection occurs in humans, EVD can spread from person to person through physical contact with the infected body fluids (e.g., blood, saliva, vomit, urine, and stool) from living patients or corpses. Unsafe burial is one of the main routes for transmission of the disease (7).

Infected patients have travelled to Mali, Nigeria, Senegal, Spain and the United States where they developed the disease and also transmitted infections to other people within these countries, highlighting the need for all countries to prepare for the introduction of cases (12,13). Increasing case numbers in West Africa may increase the risk of infection from people who travel

from affected countries, including those traveling back to their countries of residence. Persons at highest risk of infection in West Africa, including those engaged in healthcare, pose the greatest risk of transmission of EVD. EVD may also be transmitted by people involved in humanitarian work and United Nations Peacekeeping operations. The extremely high population density in Bangladesh coupled with inadequate healthcare services and limited infection control practices in most of the healthcare facilities in the country, put Bangladesh at risk for sustained transmission of EVD should importation of cases occur. Conditions in the country make it imperative that Bangladesh develop capacity for a comprehensive response to EVD. This report describes activities undertaken to date to prevent introduction of Ebola into Bangladesh, to control its spread in the event of importation, and lessons learned from these activities.

Following the declaration of Ebola as a PHEIC, Bangladesh's Minister of Health immediately established three high-level committees that operate at the inter-ministerial, intra-ministerial, and directorate levels of Bangladesh's Ministry of Health and Family Welfare (MOHFW) and defined the roles and responsibilities of each committee to coordinate overall EVD preparedness and response activities. The committees established collaboration with government, national, and international agencies including the Institute of Epidemiology, Disease Control and Research (IEDCR), the Communicable Disease Control program of Bangladesh's Directorate General of Health Services, icddr,b, WHO, the US Centers for Disease Control and Prevention (CDC), and the United States Agency for International Development (USAID) to assess the risk of introduction of EVD into Bangladesh and assist with EVD preparedness and response activities.

The International Health Regulations 2005 (IHR) is a legally binding global framework to support national and international programs and activities aimed at preventing, protecting against, controlling, and providing a public health response to the international spread of disease (14). As an initial step, MOHFW officials enhanced ongoing activities to increase core capacities under IHR to detect, prevent, and control EVD cases at points of entry including airports, seaports, and land crossings. Screening desks were established at immigration checkpoints at these points of entry. These desks were staffed by trained healthcare workers and equipped with personal protective equipment (PPE), screening questionnaires, and flow charts for further medical evaluations and/or referral. Thermal scanners were installed at the country's three international airports, two major land ports and one seaport for screening international passengers for fever. Medical evaluation rooms were designated at the major points of entry to isolate persons with possible infection; these are equipped with PPE, emergency medical supplies, and medicines. Two ambulances were provided by MOHFW's Communicable Disease Control programme and based at Hazrat Shahjalal

International Airport in Dhaka. These ambulances have been designated for transfer of possible EVD cases to a dedicated Ebola treatment centre for further evaluation and management. An Ebola treatment centre was established at the emergency ward in Kurmitola General Hospital near Hazrat Shahjalal International Airport and three hospitals were identified in the districts of Sylhet, Chittagong, and Khulna to house Ebola treatment centres, should the need arise.

In Bangladesh, IEDCR leads a collaborative team of multi-disciplinary professionals at the national level to investigate and support response to any disease outbreak or public health event of national or international concern within 72 hours. Teams of health professionals have also been trained and deployed at the district and sub-district levels for rapid response. IEDCR has conducted nationwide orientations on EVD and emerging infections for rapid response team members and other personnel at national points of entry. To date, approximately two thousand healthcare providers have been trained to enhance EVD surveillance and outbreak response. IEDCR staff are currently developing guidelines and standard operating procedures for Ebola response and case management, with assistance from WHO, CDC, icddr,b and USAID. To increase public awareness, several orientation sessions with media have been organized by government officials. In November 2014, researchers from IEDCR and icddr,b reviewed existing documents and interviewed key informants from government and selected national and international agencies. Interview questions were based on a checklist adapted from WHO's criteria to assess the critical elements for Ebola preparedness and response in unaffected countries (Table) (15).

Table: Description of critical elements for assessing preparedness status for preventing Ebola virus disease in Bangladesh, November 30, 2014

Critical components	Description
Overall coordination	Roles and responsibilities of national authorities and international partners in preparedness activities under a shared set of objectives clarified to minimize duplication of efforts and ensure maximum impact from limited resources that are currently available.
Rapid response teams (RRT)	Round the clock availability of a group of experienced experts who can reach any part of the country within 24 hours to contain/stop an outbreak early on, survey the first case(s), provide health care in a central facility, engage with the community and carry out infection, prevention and control measures.

Continued from previous page

Critical components	Description
Laboratory	Equipped to ensure that samples are safely collected and transported to laboratories which are ready to swiftly analyze them.
Capacities at points of entry	Points of entry are ready to deal with an Ebola virus disease case including the preparation of facilities as well as increasing staff capacity for effective targeted screening to prevent cross-border transportation of infections.
Case management:	
a) Ebola treatment centre (ETC)	Developing or repurposing facility with fully operational physical infrastructure as well as the capacity of staff to manage upto 15 patients with EVD.
b) Safe burials	Ensuring safe burial with due regard to local custom and religion while ensuring safe handling of deceased.
Epidemiological surveillance	Availability of a cross-country effective alerting/ notification system to immediately investigate a person for potential EVD.
Contact tracing	Availability of systems in place to rapidly identify and track the chain of transmission within the first 72 hours of reporting a confirmed/suspected case to stop/limit the transmission to other people.
Infection prevention and control (IPC)	Develop capacity for optimum IPC and support facilities to ensure safe working conditions within healthcare facilities.
Public awareness and community engagement	Promote the understanding of Ebola among at-risk communities and address any stigma hampering EVD emergency healthcare and effective surveillance.

In November 2014, a Bangladeshi national returning from the Republic of Côte d'Ivoire, arrived with fever and was suspected to have EVD. The 57-year-old businessman was admitted to a private hospital in Dhaka with fever, headache, vomiting, drowsiness, foot ulcers, low platelet count, and hyperglycemia. He was referred to the Ebola treatment centre after physicians suspected EVD. The ambulance team that transported the patient to the Ebola treatment centre went to the hospital emergency unit instead

of the triage area designated for Ebola patients and the patient was neither examined nor treated until the arrival of the outbreak investigation team two hours after admission. Strict infection control procedures could not be followed given the absence of PPE donning or doffing areas, hand washing stations, adequately trained cleaning staff and waste management facilities at the centre. The patient, who was later diagnosed with cerebral malaria and uncontrolled diabetes mellitus, provided an instructive test case on preparedness and management capacity at the Ebola treatment centre. WHO has recommended conducting simulation exercises to test preparedness, readiness, and functionality of all elements of the EVD preparedness plan to identify gaps and needs for improving readiness. MOHFW plans to conduct these exercises in the near future.

Reported by: Institute of Epidemiology, Disease Control and Research (IEDCR) and Centre for Communicable Diseases, icddr,b

Supported by: Government of the People's Republic of Bangladesh, World Health Organization and Centers for Disease Control and Prevention, Atlanta, USA

Comments

The ongoing EVD epidemic has resulted in 18,603 cases and 6,915 deaths as of December 17, 2014 (8). This epidemic has been devastating in Guinea, Liberia, and Sierra Leone. The exportation of EVD cases greatly concerns Bangladesh and other countries, but it has also served as an opportunity to build public health and clinical services capacity to respond to EVD and other emerging infections. The multi-disciplinary, collaborative outbreak investigation and response capacity of IEDCR and icddr,b, that have been developed through experience handling outbreaks with the collaboration of CDC, WHO and other agencies has increased Bangladesh's capacity to detect, respond to, and prevent epidemics. The EVD preparedness activities have allowed Bangladesh to build on existing strengths of the IHR core capacities.

There is a need to systematically assess national, district and sub-district health system capacities and gaps in preparedness to respond to highly infectious epidemics. The response to the patient from the Republic of Côte d'Ivoire revealed several deficiencies in preparedness, including issues with logistics, infection control, human resources, and waste management. Lessons from this case helped guide the efforts to modify procedures and protocols at the Ebola treatment centre in Bangladesh, a centre that can be used for managing other highly infectious diseases, such as the Middle East Respiratory Syndrome-Coronavirus (MERS-CoV).

Development of a comprehensive preparedness plan and procedures for early detection and safe management of cases, management of travelers coming to Bangladesh from Ebola-affected countries while avoiding unnecessary

restrictions to travel and trade, and ensuring that public health authorities can effectively implement the plan are critical for controlling and preventing an EVD outbreak in Bangladesh. To further prepare Bangladesh for introduction of cases of EVD or other highly infectious diseases, traditions, religious customs and beliefs regarding disease, death and funeral practices should be explored to guide public health measures to control and prevent their transmission.

References

1. World Health Organization. Ebola virus disease outbreak response plan in West Africa - A call for action. Geneva: World Health Organization, 2014.
2. Chippaux JP. Outbreaks of Ebola virus disease in Africa: the beginnings of a tragic saga. *J Venom Anim Toxins Incl Trop Dis* 2014;20(1):44.
3. Del Rio C, Mehta AK, Lyon GM, 3rd, Guarner J. Ebola hemorrhagic Fever in 2014: the tale of an evolving epidemic. *Ann Intern Med* 2014;161(10):746-8.
4. Frieden TR, Damon I, Bell BP, Kenyon T, Nichol S. Ebola 2014--new challenges, new global response and responsibility. *N Engl J Med* 2014;371(13):1177-80.
5. Bausch DG, Schwarz L. Outbreak of ebola virus disease in Guinea: where ecology meets economy. *PLoS Negl Trop Dis* 2014;8(7):e3056.
6. Forrester JD, Hunter JC, Pillai SK, Arwady MA, Ayscue P, Matanock A, *et al*. Cluster of ebola cases among liberian and U.S. Health care workers in an ebola treatment unit and adjacent hospital - liberia, 2014. *MMWR* 2014;63(41):925-9.
7. Goeijenbier M, van Kampen JJ, Reusken CB, Koopmans MP, van Gorp EC. Ebola virus disease: a review on epidemiology, symptoms, treatment and pathogenesis. Neth J Med 2014;72(9):442-8.
8. World Health Organization. Ebola response roadmap - Situation report. Geneva: World Health Organization; 2014 (http://www.who.int/csr/disease/ebola/situation-reports/en/; accessed on 18 December 2014).
9. System Ebola Epidemiology Team IM. Update: Ebola virus disease epidemic - West Africa, November 2014. *MMWR* 2014;63(46):1064-6.
10. WHO Ebola response team. Ebola virus disease in West Africa--the first 9 months of the epidemic and forward projections. *N Engl J Med* 2014;371(16):1481-95.
11. Hawkes N. Ebola outbreak is a public health emergency of international concern, WHO warns. *BMJ* 2014;349:g5089.
12. Incident Management System Ebola Epidemiology Team CDC, Guinea Interministerial Committee for Response Against the Ebola V, Team CDCGR, Liberia Ministry of H, Social W, Team CDCLR *et al*. Update: Ebola virus disease outbreak - West Africa, October 2014. *MMWR* 2014;63(43):978-81.

13. Lyon GM, Mehta AK, Varkey JB, Brantly K, Plyler L, McElroy AK *et al*. Clinical Care of Two Patients with Ebola Virus Disease in the United States. *N Engl J Med* 2014;371(25):2402-9.
14. World Health Organization. International health regulations (2005). 2nd ed. Geneva: World Health Organization; 2008.
15. World Health Organization. Guide to preparedness and readiness for potential outbreak of Ebola virus disease in non-affected countries. Geneva: World Health Organization; 2014.

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: December 2003-November 2004

Antimicrobial agents	*Shigella* N=64	*V. cholerae* O1 N=273
Mecillinam	85.0	Not tested
Ampicillin	57.1	Not tested
TMP-SMX	36.5	0.0
Ciprofloxacin	35.9	100.0
Tetracycline	Not tested	0.4
Azithromycin	100.0	100.0
Ceftrioxone	100.0	Not tested

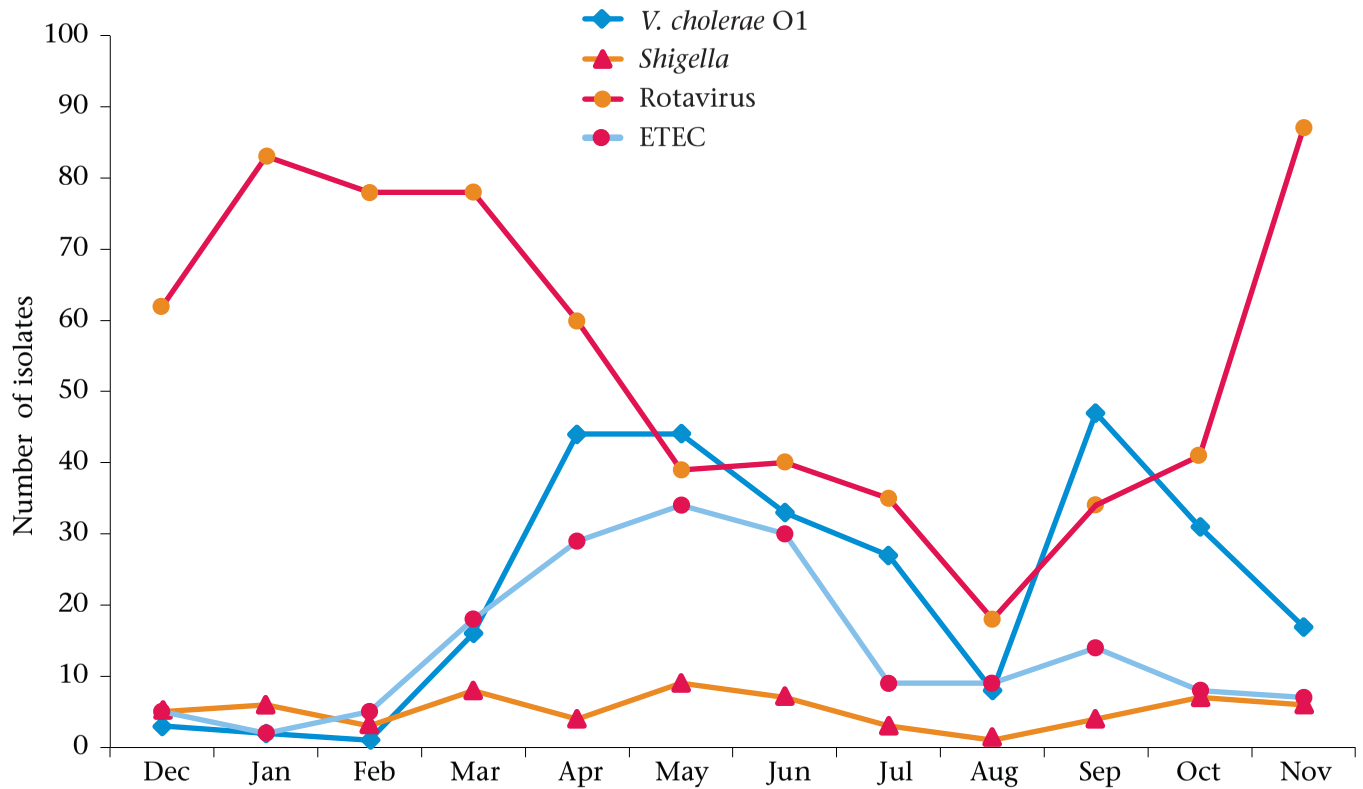
Source: Hospital Surveillance, Dhaka Hospital, icddr,b

Antimicrobial susceptibility pattern of* S. typhi *among children <5 years during October-December 2014

Antimicrobial agent	Total tested (N)	Susceptible n (%)	Reduced susceptibility n (%)	Resistant n (%)
Ampicillin	30	23 (76.8)	0 (0.0)	7 (23.3)
Cotrimoxazole	30	24 (80.0)	0 (0.0)	6 (20.0)
Chloramphenicol	30	24 (80.0)	0 (0.0)	6 (20.0)
Ceftriaxone	30	30 (100)	0 (0.0)	0 (0.0)
Ciprofloxacin	30	1 (3.3)	29 (96.7)	0 (0.0)
Nalidixic Acid	30	3 (10.0)	1 (3.3)	26 (86.7)

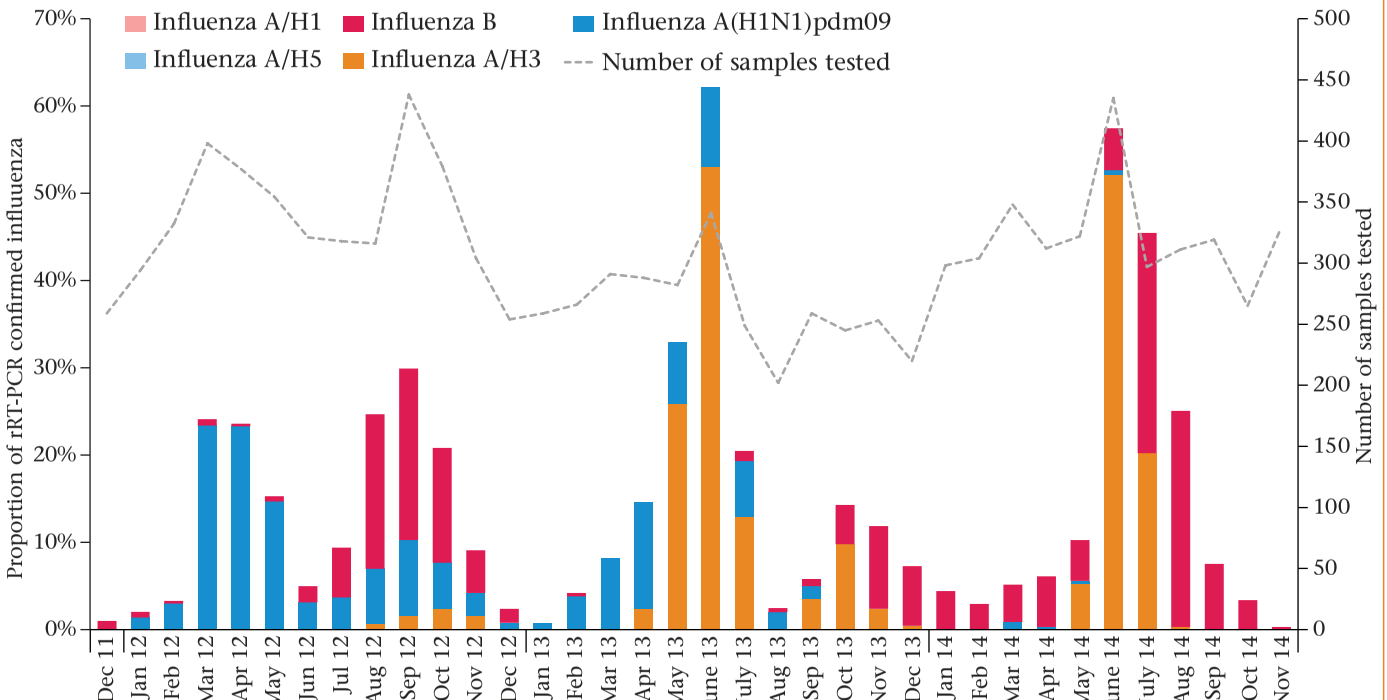
Source: Kamalapur Urban Surveillance, icddr,b

Monthly isolation of V. cholerae *O1,* Shigella*, Rotavirus and ETEC: December 2013-August 2014*



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 September 2011 and August 2014



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), Chittagong Medical College Hospital* and Dinajpur Medical College Hospital* (*since April 2014)

Postmortem needle biopsy in Faridpur Medical College Hospital, 2014

This publication of HSB is funded by icddr,b and its donors who provide unrestricted support for its operations and research. Currently donors providing unrestricted support include: Government of the People's Republic of Bangladesh; Australian Agency for International Development (AusAID); Department of Foreign Affairs, Trade and Development (DFATD), Canada; Swedish International Development Cooperation Agency (Sida) and Department for International Development (UK aid). We gratefully acknowledge these donors for their support and commitment to icddr,b's research efforts.

icddr,b
GPO Box 128
Dhaka 1000, Bangladesh
www.icddrb.org/hsb