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Inside

Management of sick children with severe pneumonia at first-level facilities is safe and effective in Bangladesh

Guidelines on Integrated Management of Childhood Illness (IMCI) for severe pneumonia recommend referral of children to hospitals for treatment. However, frequently children who are referred do not actually attend a hospital. We conducted an observational study to assess the safety and effectiveness of treating children in ten first-level health facilities in Matlab upazila of Bangladesh using modified IMCI guidelines. According to the modified guidelines, most children aged 2–59 months with severe pneumonia were treated locally in first-level facilities, with referral only when children had danger signs or other severe classifications/illnesses. We collected information during two time periods: before implementation of the modified guidelines (May 2003 to April 2004) and after full implementation (September 2004 to August

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2005). Children were more likely to receive appropriate management for severe pneumonia after the guidelines were modified (90% versus 36%, p<0.0001). Simple local adaptations of the IMCI guidelines, with appropriate training and supervision, could allow safe and effective management of severe pneumonia at first level health facilities, especially if compliance with referral is difficult because of geographic, financial, or cultural barriers.

The Government of Bangladesh incorporated Integrated Management of Childhood Illness (IMCI) into its child-health policies in 1998 to reduce child deaths and improve child health and development. The IMCI strategy was designed to improve health workers' skills, community practices related to child health and development, and to strengthen the health system supports for child health activities (1). The IMCI guidelines assist workers at first-level health facilities to systematically assess each sick child who presents for care, and assign a classification that can be used to establish correct treatment and need for referral to a higher level facility or hospital (2). However, reports from countries that have implemented IMCI show that difficulty with referral, such as failure to attend the referral facility during a specific episode of illness, which undermines the potential effectiveness of this strategy for reduction of child mortality. The lower rates of compliance with referral, generally due to geographic inaccessibility, financial and social constraints of the caregivers involved, or a caregiver's failure to recognize the severity of the child's illness (3,4). Low rates of compliance with referral have been a particular issue with pneumonia, which causes more than 2 million child deaths worldwide every year – more than any other disease. Case management is the primary intervention for pneumonia-related mortality in most developing countries. IMCI guidelines recommend that patients who have non-severe pneumonia should be treated at first-level facilities with first-line antibiotics, and those who have severe pneumonia should be referred to higher level facilities (5).

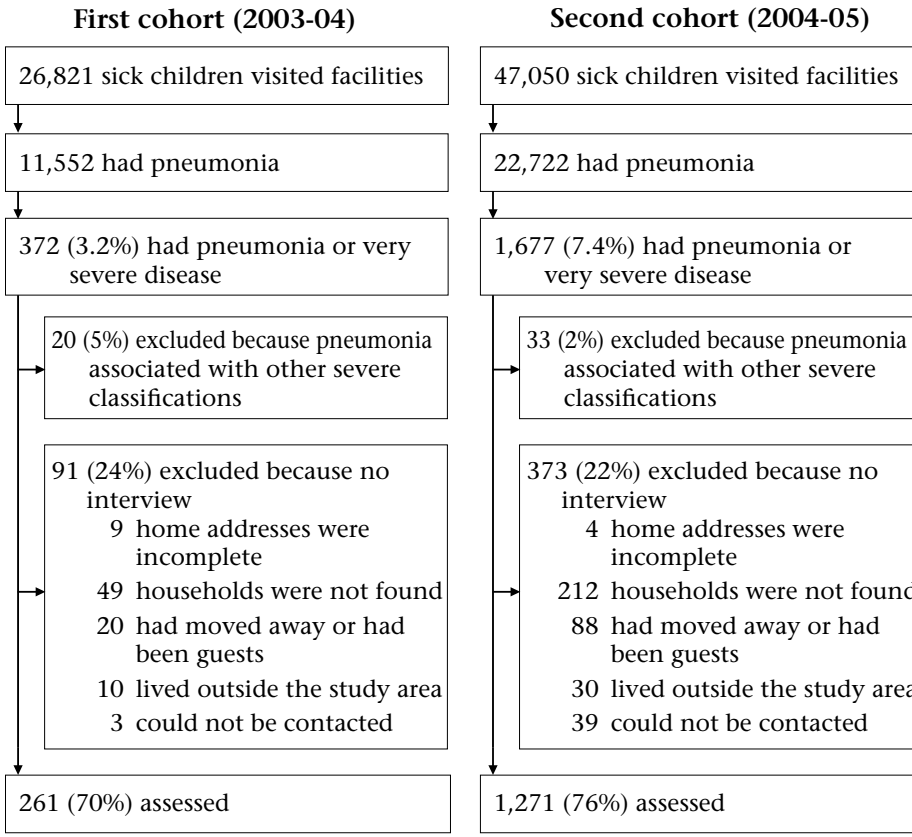
An IMCI multi-country evaluation study was carried out in Matlab upazila (subdistrict) of Bangladesh through active collaboration between the Government of Bangladesh (GoB), the International Centre for Diarrhoeal Disease Research, Bangladesh (ICDDR,B), and the World Health Organization (WHO) during 2002-2003 (6). After implementation of IMCI, the quality of care in IMCI facilities improved and use of the facilities for any childhood illness and pneumonia increased gradually (7). However, rates of compliance with referral in 2002-03 were less than 37% and had decreased to 17% by the end of 2003 (El Arifeen S, unpublished data).

Therefore the investigators, with GoB approval, modified the IMCI guidelines for management of children with severe pneumonia aged 2-59

months who represented the majority of all referrals. Under the modified guidelines children aged 2-59 months with severe pneumonia were to be referred to the hospital only if the health worker assessed that the child had one or more danger signs (i.e. inability to drink or breastfeed, vomiting everything, convulsions, and lethargy or unconsciousness), stridor, or signs and symptoms of other severe classifications requiring advanced skills or equipment not available at the first level facility. All other children with severe pneumonia were to be treated at the first-level facilities with oral amoxicillin. Caretakers were asked to make a follow-up visit two days later, and to contact the local community-based health worker. On follow-up on the basis of reassessment, treatment for the child was either continued or changed to oral cefradine as a second-line antibiotic, if there was no sign of improvement. If the child did not return for follow-up, the community-based health worker was asked to visit the child at home to assess the child as a safety measure of the new intervention. The government upazila health complex and ICDDR,B hospital located in the Matlab upazila township served as the referral facility for the study area, the distance between referral and first-level facilities was 5-27 km by road (calculated from GIS data).

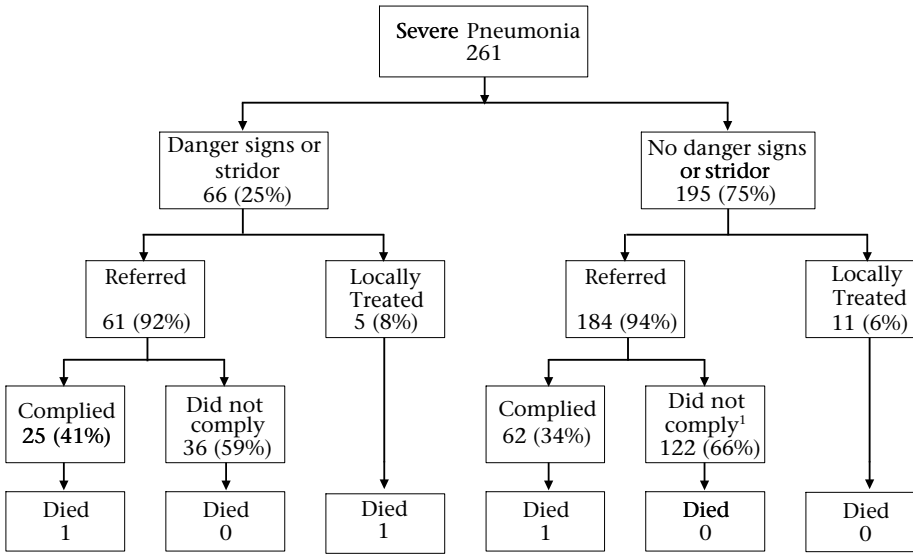
We conducted an observational study to assess the safety and effectiveness of the modified IMCI guidelines in ten IMCI intervention facilities in Matlab. Detailed information on this study has been published in the Lancet (8). In this study we compared outcomes between two time-periods: all children with severe pneumonia seen at the first-level facilities during the 12 months before introduction of the modified management guidelines (May 2003 to April 2004), and during 12 months after complete implementation (September 2004 to August 2005). We reviewed facility records to identify and collect information on the characteristics and management of illness, including referrals and admissions to hospital for all children aged younger than 5 years with severe pneumonia. Trained interviewers who were unaware of the study objectives visited the homes of enrolled children and interviewed their caretakers using a standard survey protocol to obtain details of care-seeking about the episode of severe illness and their final outcome, including mortality data. The outcome of the episode of pneumonia was classified as 'death' if the child had died within 3 months of the first presentation at the local facility. If a child with severe pneumonia without danger signs or stridor received the recommended antibiotic (cotrimoxazole, oral amoxicillin, or oral cefradine) at the first-level facility, or if a child with severe pneumonia (irrespective of danger signs or stridor) was referred to and reached referral facility, the child was considered as appropriately managed. Children who had classifications of severe disease other than pneumonia and those who had incomplete information from household follow-up interviews were excluded from analysis (Figure 1).

Figure 1: Children, aged 2–59 months, assessed for appropriateness of management of severe pneumonia



Children with severe pneumonia did not differ in sex, age or maternal education between the two cohorts/time-periods. There was an increase in overall visits by sick children aged 2–59 months by 75% in the second time-period compared with the first, and visits for pneumonia increased by 97%. In the first time-period/cohort 25% of children (66/261) with severe pneumonia had danger signs or stridor compared to 2% (31/1271) during second cohort/time-period (Figure 2). After introduction of the modified guidelines (second time period), the proportion of severe pneumonia cases with or without danger signs or stridor who were referred to higher level facilities was reduced from 245 (94%) of 261 children to 107 (8%) of 1,271 children ($p<0.0001$).

Figure 2a: Management and outcome of children with severe pneumonia seeking care at the first-level facilities: Before the introduction of the modified management guidelines (May 2003-April 2004)



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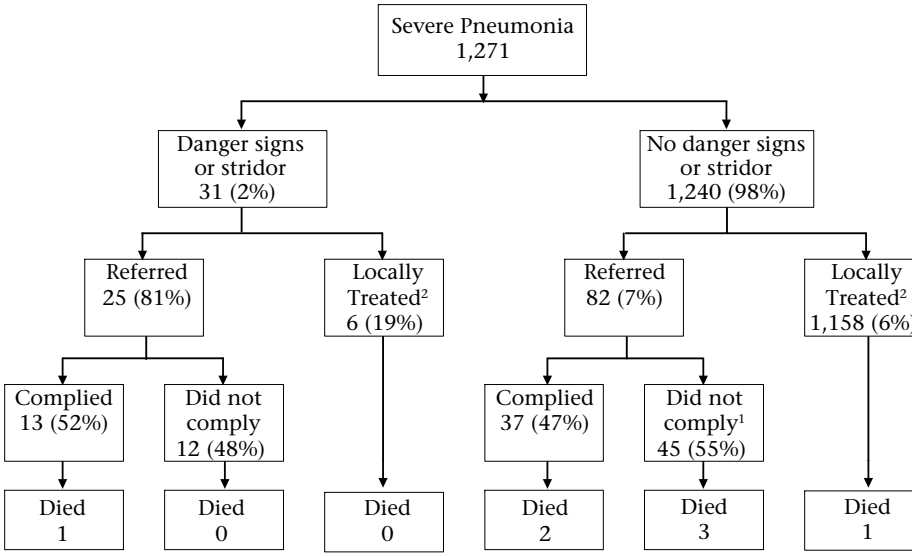
Almost all cases of severe pneumonia without danger signs or stridor were referred before modification of the guidelines, whereas less than a tenth were referred after modification. The rest of the children were treated locally at the first-level facility. Although both the original and modified guidelines recommended referral for children with severe pneumonia with danger signs or stridor, six children who had severe pneumonia with danger signs or stridor were treated by the first-level facility staff after modification of the guidelines. Facility records do not show why these children were not referred.

For children with severe pneumonia who were aged 2-59 months and initially sought care at first-level facilities, the overall rate of compliance with referral was 36% before modification of the guidelines, compared with 47% after modification (p=0.047). Figure 2 shows that the proportion of children with danger signs or stridor who complied with referral increased from 41% before modification to 52% afterwards. Before modification of the guidelines, only 94 of 261 (36%) children with severe pneumonia were appropriately managed. This proportion increased to 1,145 of 1,271 (90%) children after modification, mainly because of the local treatment of most

children with antibiotics (p<0.0001; crude OR [odds ratio] 16.1, 95% CI 11.8 –22.1; OR adjusted for maternal age and household wealth 15.7, 11.3–21.8).

Figure 2b: Management and outcome of children with severe pneumonia seeking care at the first-level facilities: After the introduction of the modified management guidelines (September 2004-August 2005)



[1]unknown 2 [2]unknown 6

We looked at any evidence of excess mortality due to severe pneumonia after modification of the guideline. Before introduction of the modified guidelines, three children died as a result of the original illness, with an overall case-fatality rate of 1.1% (95% CI 0.2-3.3%). Two of these children had been referred by first-level providers and one was locally treated (this child had convulsions and should have been referred). After the guidelines were modified seven children died, with a case-fatality rate of 0.6% (0.2-1.1%). Six were referred and one was locally treated (and had no danger signs). The case-fatality rates in the two cohorts did not differ (p=0.39).

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Comment

Our findings show that modifications to the IMCI guidelines for severe pneumonia increased the appropriate management of cases of severe pneumonia in children who presented at first-level facilities in a rural Bangladesh setting. Before introduction of the modified guidelines, only about a third of such cases were treated according to the existing guidelines, because many of the recommended referrals to hospital were not complied with. After modification, almost all were treated appropriately. Our results also showed that the revised guidelines were safe without an increase in risk of death as the case-fatality rate for severe pneumonia did not change between the two cohorts.

Although our data did not allow us to assess the effectiveness of treatment, findings from this study suggest that local modification of international guidelines was desirable and can improve their effectiveness. The modified IMCI guidelines enabled health workers to treat most cases of severe pneumonia in children seen at first-level facilities appropriately, without an increase in risk of death. This change transferred the care of severe illness closer to home, which allowed a larger proportion of the severe pneumonia cases to receive appropriate treatment at the community level. Modification of guidelines was accepted by health workers, produced good outcomes, and is likely to have reduced health-care costs to families and referral hospitals. We recommend that these modifications be adopted by the Government of Bangladesh as part of their national implementation of IMCI, and that WHO and other national programmes assess whether similar changes should be introduced in other contexts. Results from an equivalence trial of oral amoxicillin and injectable penicillin in the treatment of severe pneumonia support this recommendation. We also recommend that once the modified guidelines have been scaled up, safety and adherence to the guidelines by health workers should be monitored, especially in hard to reach areas. This is also crucially important to help guide the development of effective, efficient and locally relevant health systems.

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Invasive pneumococcal disease among children in rural Bangladesh: Results from a population-based surveillance

We conducted population-based surveillance for invasive pneumococcal disease in Mirzapur, Bangladesh. Village healh workers assessed children 1-59 months of age with reported fever, cough or difficult breathing during weekly home visits using a clinical algorithm and referred ill children to the study hospital. From July 2004 to June 2007, we isolated 26 *Streptococcus pneumoniae* strains (86 episodes of invasive pneumococcal disease per 100,000 child-years). Invasive pneumococcal diseases were more common during infancy. The most prevalent pneumococcal serotypes were 1, 5, 14, 18C, 19A, and 38. Nearly 80% of the isolates were resistant or exhibited reduced susceptibility to cotrimoxazole. New vaccines could prevent substantial pneumoccal disease among rural residents of Bangaldesh.

Acute respiratory infections are among the leading causes of childhood mortality in developing countries, including Bangladesh(1,2). *Streptococcus pneumoniae* (pneumococcus) is identified consistently as the leading cause of bacterial pneumonia in these populations (3,4). The data presented here is from the first three years of a population-based surveillance for invasive pneumococcal diseases in a rural community of Bangladesh.

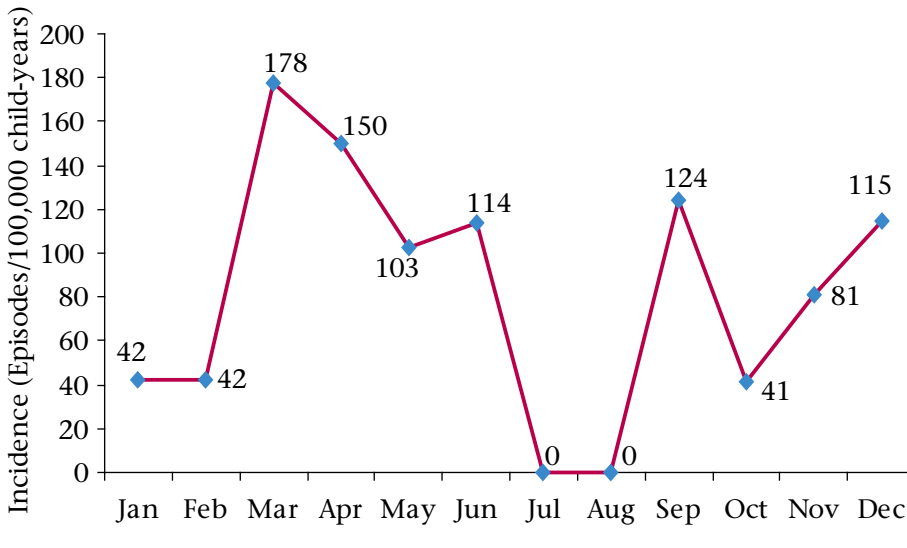
The surveillance was set-up in Mirzapur, a rural sub-district of Bangladesh, located 60 km north of the capital, Dhaka. Mirzapur has an estimated population of 400,000, distributed in 13 unions and 219 villages. The estimated annual birth cohort is 11,000. The area is served by a 750-bed non-profit private hospital (Kumudini Hospital), and a 31-bed government Upazilla (sub-district) Health Complex, each with laboratory and X-ray facilities. Six of the 13 unions of Mirzapur formed the population for this surveillance. All children aged 1-59 months residing in study area during the study period were enrolled in the surveillance. Informed consent from the mothers or caretakers of the children was obtained before enrollment. Trained village health workers visited every enrolled household weekly and asked the mother (or caretaker) of the child whether the child was experiencing any illness at the time of the visit. If the mother or caretaker reported that the child had fever or cough or difficult breathing then the village health worker assessed the child. The health workers used a predefined algorithm to classify the childrens' illnesses. Children classified as having possible severe pneumonia, suspected meningitis, very severe disease or high fever/possible bacteraemia were referred to Kumudini Hospital (the study referral hospital). There, children 1-59 months of age coming from the study area, including those referred by the village health workers, were examined by the study physicians. Study nurses collected blood cultures from sick children admitted in the hospital with suspected pneumonia, severe pneumonia, very severe disease or high fever (>38°C), or meningitis. Study physicians recommended collecting a cerebrospinal fluid (CSF) sample in cases of suspect meningitis. However, on-duty clinicians exercised their judgment and had the final decision on whether or not a blood and/or CSF sample would be collected. Study physicians obtained and recorded clinical information from the children who met standardized surveillance case definitions. Invasive pneumococcal disease was confirmed based on isolation of the organism from blood and/or cerebrospinal fluid. Isolates were identified, tested for susceptibility to antibiotics, and serotyped following standard procedures (Cheesbrough, CLSI)(5,6).

From July 2004 to June 2007 a total of 22,378 children were enrolled in the surveillance contributing to an estimated 30,392 person-years of observation. At the hospital, there were 17,353 sick-child visits at the outpatient and emergency departments of the hospital from among the children enrolled in the surveillance. Among them, 15,860 were referred by village health workers and 1,493 children came to the hospital by themselves without any referral. Among the children seen at the hospital, 2,596 were admitted. A total of 6,925 blood samples and 41 CSF samples were obtained from these children at outpatient, emergency and inpatient departments.

From these blood and CSF samples 93 organisms were isolated (isolation rate: 1%). *Salmonella typhi* (39%), *Streptococcus pneumoniae* (28%) and *Haemophilus influenzae* type b (12%) were the three most common isolates. Among the 52 isolates from children aged below two years 23 (44 %) were *S. pneumoniae*. Hib was found among 8 of the 35 children below one year of age who yielded any isolate. On the other hand, *Salmonella typhi* was found entirely among children aged 1-4 years, particularly those >24 months.

Twenty-five positive *S. pneumoniae* isolates from blood cultures and one from CSF translate into an invasive pneumococcal disease rate of 86 cases/100,000 child-years observed. Half of these cases were hospitalized. The incidence varied by month (Figure 1), but this may reflect random variation among a small number of isolates.

Figure 1: Seasonality in incidence of invasive pneumococcal disease (mean incidence/month)



Serotypes 1, 5, 14, 18C, 19A and 38 comprised more than three-fourths of the *S. pneumoniae* isolates, with 5, 14 and 19A being most common (Table 1). The *S. pneumoniae* isolates were completely sensitive to chloramphenicol, ampicillin and ceftriaxone (Table 2). Sensitivity to ciprofloxacin was also high (96%). In contrast, only 23% of the *S. pneumoniae* isolates were sensitive to cotrimoxazole with 38% resistant and 38% with reduced susceptibility.

Table 1: Pneumococcal serotype distribution of invasive isolates by age

Serotype	Age group (in months)					
	1-11	12-23	24-35	36-47	48-59	Overall
1	0 (0)	1 (11)	1 (100)	0 (0)	0 (0)	2 (8)
5	4 (29)	1 (11)	0 (0)	0 (0)	0 (0)	5 (19)
10F	0 (0)	1 (11)	0 (0)	0 (0)	0 (0)	1 (4)
12A	0 (0)	0 (0)	0 (0)	0 (0)	1 (100)	1 (4)
14	2 (14)	3 (33)	0 (0)	1 (100)	0 (0)	6 (23)
18B	0 (0)	1 (11)	0 (0)	0 (0)	0 (0)	1 (4)
18C	1 (7)	1 (11)	0 (0)	0 (0)	0 (0)	2 (8)
19A	2 (14)	1 (11)	0 (0)	0 (0)	0 (0)	3 (11)
35B	1 (7)	0 (0)	0 (0)	0 (0)	0 (0)	1 (4)
38	2 (14)	0 (0)	0 (0)	0 (0)	0 (0)	2 (8)
45	1 (7)	0 (0)	0 (0)	0 (0)	0 (0)	1 (4)
Untyped	1 (7)	0 (0)	0 (0)	0 (0)	0 (0)	1 (4)

() Numbers in parentheses: percent distribution within each age group

Table 2: Antimicrobial susceptibility pattern of S. pneumoniae *isolated from blood or CSF*

Antimicrobial agent	Total tested	Number susceptible	Reduced susceptibility	Resistant
Chloramphenicol	26	26 (100)	0 (0)	0 (0)
Cotrimoxazole	26	6 (23)	10 (38)	10 (38)
Ampicillin	26	26 (100)	0 (0)	0 (0)
Ceftriaxone	26	26 (100)	0 (0)	0 (0)
Ciprofloxacin	26	25 (96)	0 (0)	1 (4)
Penicillin	26	22 (85)	4 (15)	0 (0)

Reported by: ICDDR,B, Dhaka Shishu Hospital, Kumudini Hospital, Johns Hopkins Bloomberg School of Public Health, and Centers for Disease Control and Prevention, UAS

Supported by: The Pneumococcal Vaccines Accelerated Development and Introduction Plan; ICDDR,B

Comments

The age distribution of *S. pneumoniae* and Hib isolates are consistent with reports from other countries with *H. influenzae* b found almost entirely in the first year of life and *S. pneumoniae* being most common in the first two years of life. This suggests that Hib and *S. pneumoniae* vaccines given in early infancy should be effective in reducing much of the disease caused by Hib and *S. pneumoniae*.

The incidence of invasive pneumococcal disease of 86 per 100,000 child-years in Mirzapur is consistent with findings from other populations in Africa and Latin America where rates ranged from $15/10^5$ in Mali (3), $34/10^5$ in Chile (8), $152/10^5$ in the Gambia (4), $436/10^5$ in Kenya (9), to $447/10^5$ in Kamalapur, Bangladesh (10) have been reported. However, the reasons for the large variation in reported pneumococcal incidence by region remains unclear. There are differences in case detection procedures, eligibility criteria, case definitions and laboratory techniques in these studies. However, there are also likely to be true differences in disease incidence.

The most common serotypes identified were 1, 5, 14, 18C, 19A, and 38. Only two of these serotypes, (14 and 18C) which accounted for 31% of the isolates are covered in the 7-valent pneumococcal conjugate vaccine available in the market(7). The newer, but not yet available 10-valent (PCV7 antigens plus serotypes 1, 5, and 7F) vaccine covers 58% of the isolates and the new 13-valent (PCV10 antigens plus serotypes 3, 6A and 19A) vaccine covers 69%.

In the Mirzapur rural community, nearly 80% of the *S. pneumoniae* isolates were resistant or exhibited reduced susceptibility to cotrimoxazole. Previous reports, from urban Dhaka and largely from meningitis cases, indicated that almost two-thirds of the strains were resistant to cotrimoxazole(5). The Government of Bangladesh should reconsider its recommendation of cotrimoxazole as the first choice antibiotic for the presumptive treatment of pneumonia.

A number of limitations of the study likely contributed to an under-estimation of the true magnitude of invasive pneumococcal disease in Mirzapur. The once a week home visits may have missed cases whose parents sought care from other providers. Besides, as the village health workers were not offering any treatment, but only referral, there was little incentive for the community to actively seek their help in case of childhood illnesses. Moreover, blood cultures were not collected in all eligible cases and would have contributed to some cases of invasive pneumococcal diseases being missed. Finally, current blood culture techniques remain of low sensitivity and do not identify all invasive pneumococcal disease cases.

This study adds further evidence that invasive pneumococcal disease contributes substantially to childhood illness in Bangladesh. One-half of the invasive pneumococcal disease cases were in children seen in the outpatient department, particularly with symptoms of upper respiratory infections or fever. Prevention through appropriate vaccines in the public health system and high coverage of treatment of possible cases with appropriate antibiotics can reduce the burden of disease.

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Molecular typing of HIV-1 strains in Bangladesh

Viral isolates from 272 HIV-1 positive patients were subtyped by sequencing part of the gag gene. Overall, subtype C (41%) was the most predominant type. Phylogenetic analysis of the commonest subtype C strains suggests that they were introduced in Bangladesh from different parts of the world. Although most of the subtype C strains obtained from injecting drug users were closely related, the strains obtain from other patients were heterogeneous. These data suggest that injecting drug users were not frequently transmitting HIV to other at risk populations. As Bangladesh is at the early phase of the HIV epidemic, intervention programmes for those most-at-risk of infection should be further strengthened to prevent a major epidemic.

National HIV surveillance in Bangladesh indicates that the HIV prevalence among most-at-risk-population groups (sex workers, injecting drug users, males having sex with males) is less than 1% (1-4). However, the data regarding genomic diversity of HIV strains and patterns of transmission in Bangladesh are limited. Numerous subtypes, sub-subtypes and circulating recombinant forms of HIV have emerged during the last 50 years worldwide. At least 9 different genetic HIV-1 subtypes and over 34 circulating recombinant forms have been defined, which account for the majority of cases in the AIDS pandemic. Subtype data have been important because the major challenge in controlling AIDS lies in the diversity of HIV and its enormous evolutionary potential. Moreover, gene sequence data can be used to identify the geographical origin of local HIV strains and their relationships with each other and with global HIV strains (5). In this article, we report a summary of our work characterizing Bangladeshi HIV strains by sequencing their gag genes (6).

During 1999–2005, blood samples positive for HIV were collected through three different sources:

1. HIV surveillance which obtains samples from injecting drug users, female sex workers, transgenders, men who have sex with men, heroin smokers, and patients with sexually transmitted infections from different parts of the country.
2. Surveys which obtains samples from TB patients attending two TB clinics or hospitalized in a TB hospital in Dhaka.
3. Samples collected from clients attending the voluntary counseling and testing unit in ICDDR,B, Dhaka.

A total of 286 blood samples were positive for HIV by ELISA. Of these, 272 (95%) were confirmed as positive by Line Immune Assay and 14 (5%) were indeterminate. Sufficient amplified DNA for subtyping was available for 198 of 272 samples (73%). The subtype distribution of Bangladeshi isolates is shown in Table 1. Subtype C (41%) was the most predominant followed by CRF07_BC (24%) and CRF01_AE (9%). Other subtypes such as A1 (7%), B (3%), D (2%) and several recombinant forms were also detected.

Table 1. HIV-1 subtypes circulating in Bangladesh: 1999-2005

Population group	Subtypes (numbers)*							
	A1	B	C	D	G	CRF Others	CRF BC	Total
Injecting drug users	0	1	49	0	0	1	10	61
Heroin smokers	0	0	2	0	0	0	0	2
Female sex workers	1	0	4	0	0	4	14	23
Transgenders	1	0	1	0	0	1	2	5
Males who have sex with males	1	0	2	0	0	1	2	5
Patients with sexually transmitted infection	0	0	3	0	0	1	1	5
Patients attended Voluntary Counseling and Testing Unit	10	4	21	4	9	29	19	96
Tuberculosis patients	0	0	1	0	0	0	0	1
Total	13	5	82	4	9	37	48	198

*subtyping was determined based on partial gag gene sequence using genotyping tools in HIV database (modified from Sarker et al., 2008).

We further analyzed the partial gag gene sequences of subtype C to determine their transmission and genetic relationship with global HIV strains because subtype C was the most common HIV strain in Bangladesh. We estimated similarity of these strains' sequence using Kimura 2-parameter model (7). A high similarity (more than 98% identity at the nucleotide level) was detected among 26 (84%) of 31 Bangladeshi samples obtained from injecting drug users, which were similar to strains described in the GenBank database from female sex workers in India. The remaining 5 isolates obtained from injecting drug users were better matched with Ethiopian and South African strains (91–93% nucleotide identity). The strains among patients seen in the voluntary counseling and testing unit were diverse (<93% nucleotide identity), and were similar (>96% nucleotide identity) to HIV strains circulating in India, Zimbabwe and Ethiopia. Five strains from female sex workers were closely related to each other with more than 95% identity but not to the other 2 strains from female sex workers (92% nucleotide identity). Among 7 strains isolated from female sex workers included in the phylogenetic analysis, only 1 was similar to a strain from an injecting drug user (95% nucleotide identity). Two of the

heroin smokers had identical strains (100%), which best matched strains from injecting drug users (99%). The strain from 1 patient with a sexually transmitted infection was 100% identical to a strain from female sex worker.

We constructed a phylogenetic tree which included gag regions of Bangladeshi subtype C isolates and reference strains from different geographical regions available in GenBank database (data not shown). Most of the isolates from injecting drug users (n=26) clustered very closely together with Indian strains with the exception of 4 strains clustering with Ethiopian and South African strains. Isolates from other most-at- risk-populations did not show the same degree of homogeneity. For example, the isolates from sex workers were mapped to different branches with Chinese, Zimbabwean and South African isolates. Transgender isolates clustered with either Chinese or Indian strains. The single isolate from a Bangladeshi tuberculosis patient clustered most closely to an isolate from the United States. Strains from the voluntary counseling and testing unit were scattered throughout the phylogenetic tree and shared common origin with strains from different countries like India, Myanmar, Zimbabwe and Ethiopia. The clustering pattern of the HIV strains suggests that there was very little overlap in the strains obtained from injecting drug users and those from other Bangladeshi most-at-risk-populations. Phylogenetic analysis also indicated that some isolates from families clustered suggesting that clients transferred the viruses to their wives and children (data not shown).

Of the 70 clients from the voluntary counseling and testing unit, 54 (77%) reported that they worked abroad. The other 16 were presumed infected from individuals who had worked abroad (12 were wives and four were children of HIV positive migrants) (Table 2). The majority of the migrants had traveled to Saudi Arabia and UAE while others worked in India, Nepal,

Table 2: Migration history of HIV patients attending Voluntary Counseling and Testing Unit at ICDDR,B

Country of migration	Migrants (n)	Spouse of migrant (n)	Child of migrant (n)	Total (n)
Saudi Arabia	22	7	1	30
UAE	9	2	1	12
Malaysia	8	1	0	9
India	5	1	0	6
Singapore	4	1	1	6
USA	1	0	0	1
Nepal	1	0	1	2
Multiple	4	0	0	4
Total	54	12	4	70

Malaysia and Singapore. All migrant workers reported buying sex from women while abroad. Genetic analysis confirms that the HIV-1 strains from some of these migrant workers were most similar to HIV-1 strains from the countries where they worked. These findings suggest that the HIV-1 infections in migrant workers were acquired while working abroad.

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Comments

Similar to reports from Asia and African countries, we found that subtype C was the predominant HIV-1 subtype circulating in Bangladesh (8, 9). The clustering of subtype C strains recovered from injecting drug users supports the findings from behavioral surveillance which suggest that transmission of HIV is occurring within this group, presumably through sharing of needles and syringes (4). Unlike the strains from injecting drug users, the majority of HIV-1 strains from the clients of the voluntary counseling and testing unit were not subtype C, and those that were subtype C did not cluster together, suggesting a diverse geographical origin of infection. The diverse genotypes recovered from clients of voluntary counseling and testing unit were demonstrated by the phylogenetic analysis, where strains shared multiple branches with global strains. Most of the clients from voluntary counseling and testing unit acquired their infection through heterosexual sex while on travel to other countries. Some of them seem to have transferred the virus to their wives and children. None of the strains from clients of the voluntary counseling and testing unit clustered with isolates from injecting drug users, sex workers, or transgenders, suggesting that once infected migrants return home, they mainly transmit HIV to their families, a view supported by a behavioral study on married couples separated because of migration (10).

In summary, our results suggest that there have been few HIV introductions into the injecting drug users where transmission seems driven by the sharing of needles and syringes. Moreover there is evidence to suggest that migrant workers regularly introduce HIV in the country but they appear to spread the virus primarily to family members. The data also suggests there is limited spread between different most-at-risk-populations (e.g. between injection drug users and sex workers). As strains from two female sex workers were almost identical with that recovered from one injecting drug

user and a sexually transmitted infection patient, however, it is apparent that some limited spread is taking place between most-at-risk-populations. Therefore, in Bangladesh, ongoing intervention programmes that target specific at risk populations (e.g. injection drug users, female sex workers) should be further strengthened to limit progression of the epidemic. Considering that returned migrants constitute the largest group of persons living with HIV in Bangladesh, efforts to prevant infections to migrants and their families are urgently needed. Future interventions should also address the limited but important interaction between at-risk populations (11, 12).

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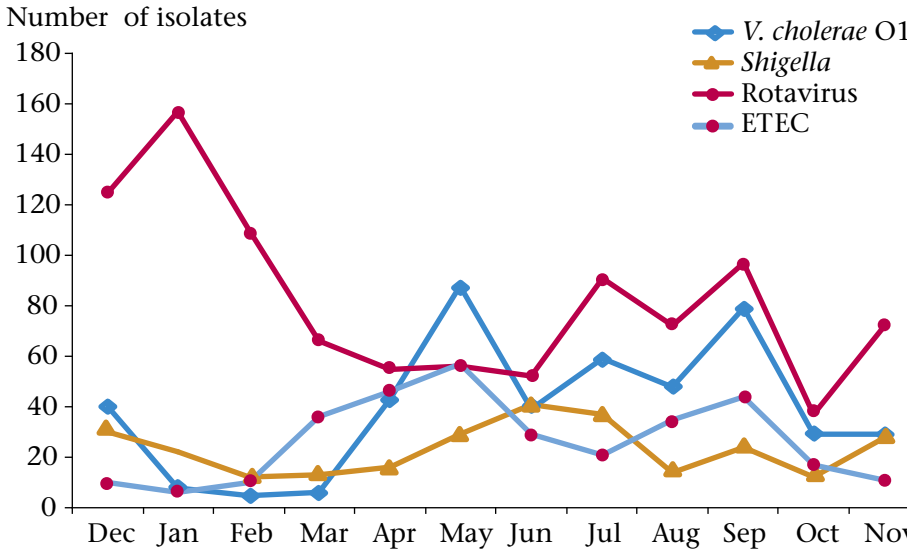
Surveillance Updates

With each issue of the 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.

Proportion of diarrhoeal pathogens susceptible to antimicrobial drugs: December 2007- November 2008

Antimicrobial agents	*Shigella* (n=281)	*V. Cholerae* O1 (n=473)
Nalidixic acid	24.9	Not tested
Mecillinam	82.2	Not tested
Ampicillin	47.7	Not tested
TMP-SMX	37.7	1.3
Ciprofloxacin	85.1	100.0
Tetracycline	Not tested	30.0
Erythromycin	Not tested	3.8
Furazolidine	Not tested	0.2

Monthly isolation of* V. cholerae *O1,* Shigella*, Rotavirus and ETEC December 2007-November 2008



Antimicrobial resistance patterns of 43 M. tuberculosis *isolates: January 2008-August 2008*

Drugs	Resistance type		Total (n=43)
	Primary (n=36)	Acquired* (n=7)	
Streptomycin	4 (11.1)	2 (28.6)	6 (14.0)
Isoniazid (INH)	2 (5.6)	0 (0.0)	2 (4.7)
Ethambutal	0 (0.0)	0 (0.0)	0 (0.0)
Rifampicin	0 (0.0)	0 (0.0)	0 (0.0)
MDR (INH+Rifampicin)	0 (0.0)	0 (0.0)	0 (0.0)
Any drugs	5 (13.9)	2 (28.6)	7 (16.3)

() column percentage *Antituberculous drugs received for 1 month or more

Antimicrobial susceptibility pattern of S. pneumoniae *among children <5 years during July-September 2008*

Antimicrobial agents	Total tested (n)	Susceptible n (%)	Reduced susceptibility n (%)	Resistant n (%)
Ampicilin	12	11 (92.0)	0 (0.0)	1 (8.0)
Cotrimoxazole	12	1 (8.0)	1 (8.0)	10 (84.0)
Chloramphenicol	12	11 (92.0)	0 (0.0)	1 (8.0)
Ceftriaxone	12	12 (100.0)	0 (0.0)	0 (0.0)
Ciprofloxacin	12	12 (100.0)	0 (0.0)	0 (0.0)
Gentamicin	12	1 (8.0)	0 (0.0)	11 (92.0)
Oxacillin	12	10 (84.0)	1 (8.0)	1 (8.0)

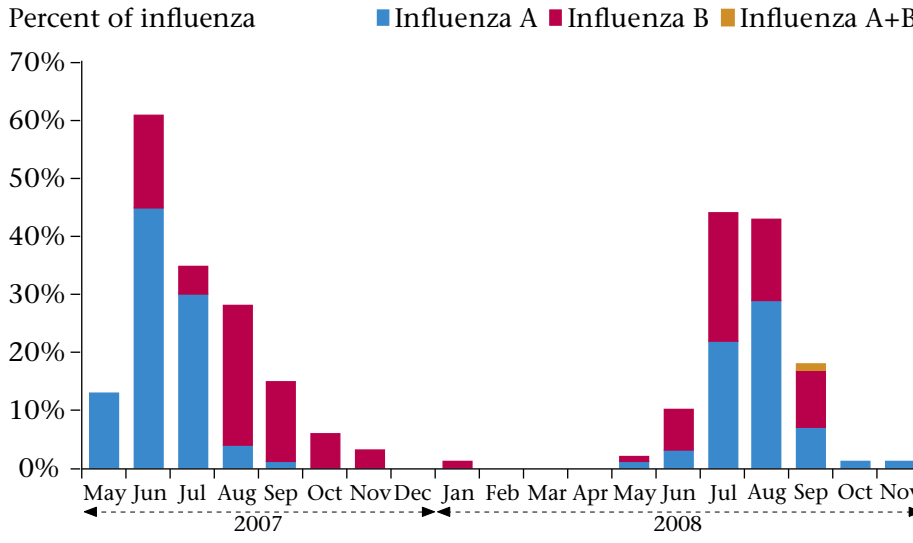
Source: Children participating in PneumoADIP surveillance in Dhaka Medical College Hospital; Chittagong Medical College Hospital; Sir Salimullah Medical College and Mitfort Hospital; ICH-Shishu Sasthya Foundation; Chittagong Maa Shishu O General Hospital; Dhaka Shishu Hospital; Kumudini Hospital, Mirzapur; and ICDDR,B's urban surveillance in Kamalapur (Dhaka) and rural surveillance in Mirzapur (Tangail).

Antimicrobial susceptibility pattern of S. typhi *among children <5 years during July-September 2008*

Antimicrobial agents	Total tested (n)	Susceptible n (%)	Reduced susceptibility n (%)	Resistant n (%)
Ampicilin	87	36 (41.0)	0 (0.0)	51 (59.0)
Cotrimoxazole	87	36 (41.0)	0 (0.0)	51 (59.0)
Chloramphenicol	87	36 (41.0)	0 (0.0)	51 (59.0)
Ceftriaxone	87	87 (100.0)	0 (0.0)	0 (0.0)
Ciprofloxacin	87	41 (47.0)	46 (53.0)	0 (0.0)
Nalidixic Acid	87	6 (7.0)	0 (0.0)	81 (93.0)

Source: Children participating in PneumoADIP surveillance in Dhaka Medical College Hospital; Chittagong Medical College Hospital; Sir Salimullah Medical College and Mitfort Hospital; ICH-Shishu Sasthya Foundation; Chittagong Maa Shishu O General Hospital; Dhaka Shishu Hospital; Kumudini Hospital, Mirzapur; and ICDDR,B's urban surveillance in Kamalapur (Dhaka) and rural surveillance in Mirzapur (Tangail).

Percent of influenza positive specimens by month during May 2007-November 2008



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) and Sher-e-Bangla Medical College Hospital (Barisal)

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