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Burden and outcome of human influenza in a tertiary care hospital of Bangladesh

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ABSTRACT

Objective: To determine the magnitude and outcome of influenza in southern part of Bangladesh and also to identify intrusion of novel influenza virus. **Methods:** This study was conducted for two years (2008–2009) in outpatient and inpatient department of both paediatrics and medicine discipline of Khulna Medical College Hospital. Nasal and throat swab specimens were collected from each influenza like illness (ILI) case and kept together in a virus transport media and transported to international centre for diarrhoeal disease and research, Bangladesh laboratory. Influenza virus was detected by rRT-PCR including types and subtypes. **Results:** A total of 526 patients were enrolled during the study period with the mean (SD) age of 19 (17) years. Identification of influenza virus was 14% and positive cases were mostly found in under-five children (24%). The vast majority (88%) of influenza cases were found during April to September. Virus detection rate was higher in inpatient department (IPD) (21%) than in outpatient department (12%). The dominant virus type and subtype was influenza A (87%) and H3 (49%), respectively. Type A was significantly higher than type B in causing severe illness compared to ILI (*OR*=7.04, 95% *CI*: 2.76–18.7, *P*<0.01). Headache and chest indrawing was found in significantly higher proportion (*P*<0.05) in influenza positive IPD cases. Among 31 hospitalized cases majority (77%) recovered completely except two cases that needed referral for additional support. **Conclusions:** Influenza mostly affected under-five children and young adult. The peak season here was late summer and rainy season.

1. Introduction

The world has witnessed three major influenza pandemics in the last century and Spanish flu (1918–1919) was the most devastating among those, killing over 40 million people worldwide[1,2]. Till now, influenza remains as the most common viral infections affecting 5%–15% of global population resulting in an estimated deaths of 250 000 to 500 000 each year[3,4]. In the United states, influenza causes infections of 5%–20% population resulting in an average mortality of 36 000 annually[5]. In temperate countries, young children and the elderly are the most vulnerable group and seasonal peaks occur during winter[6]. Epidemiology report on influenza from Asia and Africa is not adequate. However a recent surveillance report from India showed that 5%–12% of Influenza like illness (ILI) was due to influenza virus and it was particularly more prevalent in rainy season[7].

The new strain of highly pathogenic avian influenza (H5N1) has been circulating among domestic poultry and wild bird in Eastern Asia since 1996[4]. Although the virus is highly fatal, it does not easily spread from birds to human but it may develop such capacity at any moment. Bangladesh, having the high population density and abundant domestic poultry, is at higher risk of developing new influenza than the neighbouring countries[8,9]. International centre for diarrhoeal disease and research, Bangladesh (ICDDRB) in 1994–1995 conducted a population based surveillance for influenza in under-five children in Kamalapur, a densely populated low income community of capital city and found influenza virus among 14% children with acute respiratory illness and also identified the first human case of avian influenza in Bangladesh[10,11].

Acute respiratory infection is a dominant public health hazard particularly in developing countries and influenza has important contribution in it[12,13]. The majority of influenza cases manifests mild illness except a few requiring hospitalization[14,15]. The understanding of magnitude and clinical course of influenza could be

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extremely helpful to develop appropriate policy for its prevention and management. This study was done to explore the burden and outcome of influenza patients and to identify the novel influenza cases in a tertiary hospital of southern part of Bangladesh.

2. Materials and methods

The study was conducted from January 2008 to December 2009 in Khulna Medical College Hospital (KMCH) which is located in the southern part of Bangladesh and remains as a vulnerable area for intrusion of any novel virus infections due to its location in the coastal belt, harboring the sea port, close proximity with land borders and also raising the poultry in the locality. The paediatrics and medicine department of this hospital deals with 200 to 300 patients daily in outpatient department (OPD) and 800 to 1 000 patients monthly in inpatient department (IPD). Ethical permission for this study was taken from the ethical review committee of ICDDRB and KMCH. Two physicians were recruited as Research Assistant for two department and trained for case selection, data entry and sample collection. Signed consent was taken from each patient or parents of patients (<18 years) before enrollment.

In the OPD, the study cases were enrolled both in the paediatrics and medicine department for consecutive two days each month to determine the influenza virus. Twenty cases were selected in each month from patients suffering from ILI, defined as fever and cough or sore throat. In addition to this, specimen was collected from IPD as well to detect influenza virus who met the criteria for severe acute respiratory illness (SARI) *eg*. fever (>38 ℃), cough or sore throat and difficult breathing. The criteria for SARI were homologous to severe pneumonia in children according to WHO case definition[12,13]. Patients suffering from more than a week were excluded because of poor detection rate of virus after acute stage[7]. There was no limitation in number for selection of SARI cases. The research assistants collected information on demographics, work exposure, travel history, provisional diagnosis, treatment and outcome of the disease in a pre-designed structured form.

After collection from each case, nasal and throat swab were put together in a single container of viral transport media and stored in liquid nitrogen dewar. The field assistant transported them to the virology laboratory of ICDDRB every two weeks. Influenza virus was detected by real time reverse transcriptase polymerase chain reaction (rRT-PCR) and influenza A virus was further subtyped into H1, H3 and H5 in the laboratory.

The patients in the OPD could not be followed but the patients in IPD were monitored for the progress of diseases in respect to the dominant clinical features. Routine investigations including X-ray chest were done in the admitted cases. All the SARI cases were managed with oxygen, nebulizations, fluids and antibiotics according to necessity.

The data at the end were verified, cleaned and analyzed using SPSS-12 software. Descriptive statistics were followed in most part. However two-way contingency table, *Chi* square test and Fisher's exact test were applied to compare the association of laboratory confirmed cases and the non-confirmed cases with different variables. *P* value less than 0.05 was considered as significant.

3. Results

Samples were collected from 526 patients during the study period. The mean (SD) age of the patients was 19 (17) years with the age ranging from 1 month to 90 years. The male female ratio was 1:1.3. Among all, 243 (46%) patients were from paediatrics department and 283 (54%) from medicine department. On the other way, the cases from OPD of both department were 377 (72%) and the IPD were 149 (28%) in total. In terms of year, 217 (41%) patients were enrolled in 2008 and 309 (59%) in 2009.

Influenza virus was detected in 75 (14.3%) cases and the mean±SD age of the positive cases were 24 ± 19 years with the age range from 5 months to 75 years and the male female ratio of 1:1.6. Children under five years constituted 24% of the total and next (15%) in frequency was young adult of 21-25 years (Figure 1). All the positive cases round the two years were sorted in months serially and a distinct variation was noticed (Figure 2). The proportion of influenza cases were 88% during six months from April to September. This peak incidence coincided with late summer and rainy season in Bangladesh.

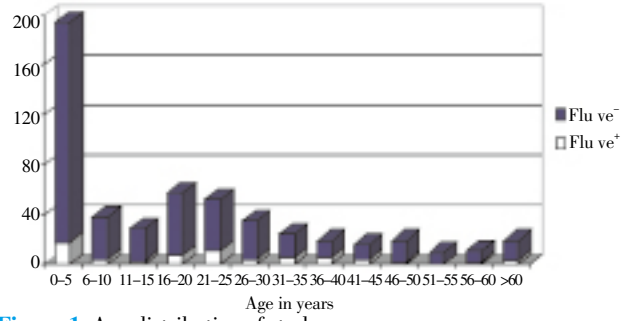

Figure 1. Age distribution of study cases.

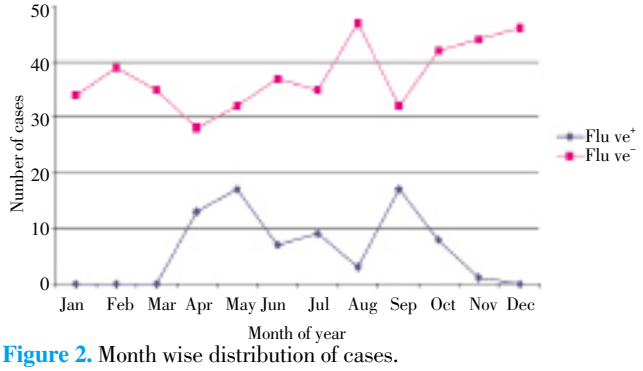

Figure 2. Month wise distribution of cases.

Among 149 cases 31(20.8%) were tested positive for influenza which is much higher than positivity (11.7%) in OPD (Table 1). Predominant virus type was influenza A and it was significantly higher than influenza B in SARI cases in comparison to ILI cases (*OR*= 7.04; 95% *CI*: 2.76-18.7; *P*<0.01). On subtyping of influenza A virus, 37 (49.3%) of all the viruses (75) was detected as H3 and 9 (12.1%) as H1. Although no cases of influenza A/H5 was found but 19 (25.3%) pandemic influenza A (H1N1) cases was detected in 2009 (Table 2).

During observation of SARI cases in IPD, clinical features like stridor (10.0%) and altered mental state (54.8%) was found proportionately higher in virus positive cases than their negative counterpart but those were not significant.

Table 1
Virus detection rate in different clinical situation in two departments[*n* (%)].

Clinical Condition	Sample collection	Virus detection	Flu virus A			Flu virus B		
			Paediatrics	Medicine	Total (%)	Paediatrics	Medicine	Total (%)
SARI	149	31 (20.8)	3 (2.0)	27 (18.1)	30 (20.1)	0 (0.0)	1 (0.7)	1 (0.7)
ILI	377	44 (11.7)	15 (4.0)	20 (5.3)	35 (9.3)	5 (1.3)	4 (1.0)	9 (2.4)
Total	526	75 (14.3)	18 (3.4)	47 (9.0)	65 (12.4)	5 (1.3)	5 (1.0)	10 (1.9)

Table 2
Virus type and subtype in different year [*n* (%)].

Year	Sample collection	Virus isolation	Flu virus A				Flu virus B
			H1	H3	Pan flu*	Total	
2008	217	20 (9.1)	9 (4.1)	2 (0.9)	0 (0.0)	11 (5.0)	9 (4.1)
2009	309	55 (17.8)	0 (0.0)	35 (11.3)	19 (6.2)	54 (17.5)	1 (0.3)
Total (%)	526	75 (14.3)	9 (1.7)	37 (7.0)	19 (3.6)	65 (12.4)	10 (1.9)

*Pan flu– Pandemic flu 2009 (H1N1).

But headache (64.5%) and chest indrawing (61.3%) was significantly higher ($P<0.05$) in the virus positive cases (Table 3). Among the 31 hospitalized flu positive cases majority (77.4%) recovered completely (Table 4). Few cases left the hospital in a hurry with partial recovery except only two cases that required referral to national chest disease hospital for further supportive care. Comparing the recovery status between seasonal influenza and pandemic influenza 2009, no significant difference in outcome was observed.

Table 3
Clinical features of hospitalized cases in relation to flu virus [*n* (%)].

Feature	Presence	Flu ve$^+$	Flu ve$^-$
Headache	Yes	20 (64.5)*	41 (34.7)
	No	11 (35.5)	77 (65.3)
Respiratory distress	Yes	16 (51.6)	55 (46.6)
	No	15 (48.4)	63 (53.4)
Stridor	Yes	3 (9.7)	6 (5.1)
	No	28 (90.3)	112 (94.9)
Altered mental state	Yes	17 (54.8)	53 (44.9)
	No	14 (45.2)	65 (55.1)
Tachypnea	Yes	18 (58.1)	60 (50.8)
	No	13 (41.9)	58 (49.2)
Chest indrawing	Yes	19 (61.3)*	46 (39.0)
	No	12 (38.7)	72 (61.0)

*$P<0.05$, *vs.* Flu ve$^+$.

Table 4
Outcome of flu positive hospitalized cases [*n*(%)].

	n	Full recovery	Partial recovery	Referred
Flu A & B	17	13(76.5)	3(17.6)	1(5.9)
Pandemic flu	14	11(78.6)	2(14.3)	1(7.1)
Total	31	24(77.4)	5(16.1)	2(6.5)

4. Discussion

Peoples leaving in and around Khulna suffered from Influenza regardless of age. The mean age of sufferer in this series was 19 years. The study emphasized the circulation of influenza virus in the southern part of Bangladesh and the overall detection rate was 14%. This detection rate is consistent with findings from other parts of the world such as Thailand (6%–9%) and India (5%–12%) [7,16]. However much higher virus isolation rate was found in a hospital based study from Kenya (48%) which might be due to inclusion of admitted cases only.17 In contrast to this only 2% influenza virus was detected in another hospital based study on acute lower respiratory infections in children of Bangladesh[18].

Both ILI and influenza positive cases were seen more commonly in children and young adult. Although young people seeks hospital care more commonly, this particular age group vulnerability corroborates with finding from other parts from Asia[7,16]. Acute respiratory infections (ARI) is responsible for 21% death of under-five children in developing countries[12,13]. Influenza is an important contributor of ARI and many cases require hospitalizations[14,15]. Here, 41% of confirmed influenza cases were obtained from admitted patients in paediatrics and medicine ward.

The seasonality of influenza was mid six months of the calendar year which is late summer and monsoon in Bangladesh. This observation is consistent with findings from other parts of this country and our neighbouring country as well but quite different from that of temperate zone where it occurs in winter season[3,4,7,10]. The seasonality of human influenza was again different from avian influenza in birds that runs in parallel with arrival of migratory birds in winter (November–February)[19,20]. This difference in seasonality might be a blessing for mankind because of less opportunity for reassortment of avian flu with human flu[21,22].

Infection with influenza A was 87% which outweighed the infection with influenza B. The virus subtyping revealed A/H3 was predominant than other subtype. The proportion of influenza virus subtype was similar to that in other parts of the world[4,6]. However the isolation rate of influenza A was much higher in medicine IPD than paediatrics IPD which is possibly due to severity of disease manifestation in adult requiring hospitalization.

The ILI and SARI, both were increased in 2009 in comparison to 2008 because of the visit of pandemic influenza A (H1N1). Since the detection of first case of pandemic flu in Mexico in April 2009, the pandemic wave hit Bangladesh on June 2009[23,24]. Eight hundred and twelve cases of pandemic flu was identified in the country up to December 2009 along with 6 fatality[24,25]. In this study 19 cases of H1N1 were detected having the majority (74%)

from medicine IPD which again supports the severity of the disease in adult. None of the pandemic influenza A cases was detected in paediatrics IPD.

The clinical course of admitted patients revealed that headache and chest indrawing was more prevalent in virus positive cases. Influenza, like other respiratory virus causes predominantly an upper respiratory illness except a few causing pneumonitis which supports present finding[15,26]. The outcome of OPD cases remains obscure as they could not be followed. However, the outcome of the IPD cases was largely satisfactory (77%) and only two cases were referred for additional support. Although the overall mortality of pandemic flu was 1%-2%, it caused a panic across the globe[8,27]. However, it is difficult to understand the fatality with such a small number (19) of study cases.

The principal limitation of this study depends on its hospital based nature which may not reflect the true picture in the community. Secondly, the case number is small for reporting epidemiology, which could have been increased by increasing the days of sample collection. Lastly, the follow-up of OPD cases could have yielded a better picture of the real outcome of the disease.

In conclusion, Influenza virus was an important cause of childhood and adult respiratory diseases in Khulna. The peak season for influenza in this region was late summer and rainy season. Pandemic influenza was identified in later half of 2009 but without any fatality. Further large scale study is required in order to formulate appropriate health intervention.

Conflict of interest

None of the author has any conflict of interest to declare.

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