Spectrum of H1N1 influenza infection in Indian children: A tertiary centre experience

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Abstract

Objective: To study the clinical profile, severity, outcome and risk factors for H1N1 influenza infection in children <18 years.

Method: Children <18 years admitted to the Paediatric Department of our hospital and confirmed to have H1N1pdm2009 influenza infection from December 2016 to November 2017 were included. We reviewed the case sheets of the study population and captured the required data. Illness was classified as mild, progressive or severe illness and treated as per CDC guidelines. Outcome measures analysed included – mortality, duration of ICU / hospital stay, need for oxygen supplementation or assistive ventilation.

Results: Our study involved analysis of 31 children. We found clustering of cases from 1-5 years accounting for 56% with no sex predilection. We observed a bimodal seasonal peak in incidence of infection from December to February (32%) and June to August (42%). Malnutrition was most common risk factor affecting 15/31 (48.4%) children followed by pre-existing medical illness 10/31 (30%). Risk stratification done as per CDC recommended guidelines showed the majority of the children (64.5%) manifesting as mild illness. Chest x-ray showed bilateral non-homogeneous peri-hilar opacities with air bronchogram in 19 (61%) children. Seven (22%) children required admission to ICU, 6 (20%) required oxygen therapy and 1 required noninvasive ventilation. Two children had developed hypotension requiring inotropes. No mortality was observed in the current study.

Conclusions: H1N1 Influenza is still causing significant morbidity among children, especially in those with malnutrition and preexisting medical illness.

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Introduction

In March 2009, Mexico reported the first case of a new strain of H1N1 influenza[1]. Soon after that in April 2009, India reported its first case. The same year there were 27,236 laboratory confirmed cases with 981 deaths in India due to H1N1 Influenza. During post-pandemic period, again there was resurgence of disease with 30,000 laboratory confirmed cases and 1700 deaths in 2015. Thus, H1N1 continued to cause significant morbidity and mortality[2-5]. By the end of 2017, as per WHO report influenza activity remained low in South Asia including the Indian subcontinent. Though globally Influenza A (H3N2), Influenza B were prevalent, India reported maximum cases of H1N1pdm2009 strain[6]. Severity of Influenza is known to change with strain, season and susceptibility of host. However, after 2009-10 epidemic there is paucity of data regarding the pattern of disease in Indian children with H1N1 influenza. This hospital-based retrospective study was done to analyse the trend of H1N1 influenza disease and severity in children.

Objectives

To study the clinical profile, severity, outcome and risk factors for influenza infection in children <18 years.

Method

We conducted a retrospective observational study in a tertiary care centre of Karnataka, South India. Study population included children less than 18 years of age admitted to the Paediatric Department of our hospital and confirmed to have H1N1pdm2009 influenza. Real time polymerase chain reaction (PCR) of the throat swab performed at our virology laboratory (CDC accredited) was used to confirm the diagnosis. The study period involved cases from December 2016 to November

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2017. All the children were admitted to isolation ward or intensive care unit (ICU) and managed with oseltamivir and other appropriate measures as per the hospital protocol and CDC guidelines[3]. Institutional ethics committee clearance was obtained. Children who were discharged against medical advice were excluded.

We reviewed the case sheets of the study population and the following data were captured viz. age, anthropometry, history of contact, vaccination status, risk factors, clinical features, course of illness, complications, investigations and management details. Malnutrition status was assessed based on WHO weight for height charts (in children less than 5 years) or body mass index (BMI) charts (in children more than 5 years). Illness was classified as mild, progressive or severe illness as per Centre for Disease Control (CDC) guidelines[3]. Outcome measures which could be extracted from case sheet were chosen, which included mortality, duration of ICU / hospital stay, need for oxygen supplementation or assistive ventilation.

Data were analysed using software SPSS version20. Mean and standard deviation were used to describe data following normal distribution. Median and interquartile range were used to describe skewed data.

Results

A total of 31 children satisfied the inclusion criteria and were selected for the study. Baseline characteristics and symptomatology at presentation are depicted in table 1.

Table 1: ***Baseline characteristics and symptomatology of the study population at presentation (n=31)***

Characteristic	Result
Sex, male - n (%)	17 (54.8)
Age in months	
-Median (IQR 25-75)	46 (22-71)
-Range	03-188
Age (in years) distribution - n (%)	
<1year	06 (19)
1-5 years	17 (56)
5-10 years	07 (22)
>15 years	01 (03)
Malnourished – n (%)	15 (48.4)
Pre-existing illness – n (%)	10 (32.3)
-Hyperactive airway disease	05
-Immunosuppression*	03
-Known cardiac disease	02
Contact history with a diagnosed case of H1N1 – n (%)	03 (09.6)
Previous influenza vaccination status	None were immunised
Symptomatology at the presentation – n (%)	
-fever	30 (96.8)
-rhinitis	29 (93.5)
-cough	25 (80.6)
-vomiting	09 (29.0)
-hurried breathing	08 (25.8)
-poor feeding	08 (25.8)
-lethargy	08 (25.8)
-myalgia$	08
-headache$	06

**- 1 child had ALL and was on chemotherapy (BMF-95 protocol), 2 children had nephrotic syndrome on alternate day oral steroid therapy at 1mg/kg/day*

$- children greater than 4 years were only analysed as younger children cannot appropriately report headache or myalgia

Males constituted 54.8% of the study population indicating that there was no sex predilection. Mean age of presentation was 46 months, ranging from 3 to 188 months. Most of the cases were clustered between 1 and 5 years of age. Out of 31 children, 15 (48.4%) were found to be malnourished. Pre-existing illness acting as a risk factor was present in 10 (30%) children and hyperactive airway disease was the most common among them in 5 children. Immunosuppression was a risk factor in 3 children, 1 child had leukaemia and was on chemotherapy, 2 children had nephrotic syndrome on alternate day oral steroid therapy at 1mg/kg/day. History of contact with a diagnosed case of influenza A was present in 3 children. None of the study population received an influenza vaccine in the past. Fever was

most common symptom observed in 96.8% of children in our study.

Analysis of investigations (Table 2) showed a mean haemoglobin of 10.8 g/dl. Median leucocyte count was 6900/µL with a median lymphocyte percentage of 53% indicating relative lymphocytosis in the study population. Median C-reactive protein level was normal. Chest x-ray showed bilateral non-homogeneous peri-hilar opacities with air bronchogram in 19 children and right lower zone consolidation changes in 3 children. No child had an effusion, pneumothorax or other complications. Risk stratification done as per CDC recommended guidelines showed the majority of the children (64.5%) manifested as mild illness.

Outcomes measured are presented in Table 3.

Table 2: ***Investigation parameters trend and risk stratification of the study population (n=31)***

Parameter	Result
Hb, g/dl (Mean ± SD)	10.8 ± 1.15
Leucocyte count - (Median, IQR 25-75) - Total count, /µL - neutrophil % - lymphocyte %	 6900 (5000-9200) 56 (44 – 72) 53 (43 – 66)
C- reactive protein, mg/L Median (IQR 25-75) Range	 03 (01.3 – 07.1) 0.8-22.4
Chest x-ray findings - n (%) - Bilateral non-homogenous peri-hilar infiltrates with air bronchogram - Lobar consolidation - Others (effusion, pneumothorax etc.)	 19 (61.29) 03 (09.6) 0
CDC grading – n (%) -Mild or Uncomplicated illness -Progressive illness -Severe or complicated illness	 20 (64.5) 05 (16.1) 06 (19.4)

Table 3: ***Outcomes measured***

Outcome measured	
Duration of hospitalization in days (Median, IQR 25-75)	 07 (05-08)
Intensive care unit admission -Requirement –n (%) -Duration, days (Median, IQR 25-75)	 07 (22.6) 04 (02.5-06.25)
Oxygen requirement – n (%)	06 (19.3)
Intravenous fluids - Requirement – n (%) - Duration, days (Median, IQR 25-75)	 07 (22.6) 03 (02-05)
Assisted ventilation requirement[*] - n	01
Inotropes requirement[$] - n	02
Mortality	0

**- 1 child with a lung consolidation required non-invasive ventilation (HHFNC) for 36 hours*
$ - 2 children had developed hypotension (one child had culture negative sepsis and another coexisting dengue illness) during hospital stay and required inotropic support.

The median duration of hospital stay was 7 days. Seven children required admission to ICU with a median ICU duration of 4 days. Oxygen supplementation was used for 6 out of 8 children with tachypnoea. One child required non-invasive ventilation in the form of humidified high flow nasal cannula (HHFNC) for 36 hours. Intravenous fluids were required in 7 children at admission due to associated tachypnoea and poor oral intake. If poor oral intake alone without tachypnoea was present, nasogastric feeding was preferred. Two children had developed hypotension (one child had culture negative sepsis and the other coexisting dengue illness) during the hospital stay and required inotropic support. No mortality was observed in the current study.

Discussion

We retrospectively studied the medical records of those hospitalized children with H1N1 infection during the study period. Though infants are thought to be more susceptible to H1N1 infection, we

observed clustering of cases between 1 to 5 years, with 17 (56%) children being affected, whereas six <1-year children accounted for 16% of all cases. Same has been observed in an earlier Indian study[2]. Males constituted 54.8% of the study population indicating there was no sex predilection. We observed a bimodal peak in incidence of infection, one peak from December to February (32%) and the other from June to August (42%). Malnutrition, pre-existing medical illness and immunosuppression are known predisposing factor for acquisition of illness and severity of manifestation. In our series, malnutrition was the most common risk factor, seen in 15 children, followed by pre-existing medical illness. Asthma was the most common medical illness, followed by immunosuppression, congenital heart disease, dengue infection and sepsis. None had neurological/ chronic kidney disease as a risk fctor. These findings are similar to other earlier studies[2,8,9]. This reinforces the need for special care and early prompt treatment of influenza in these special categories of children. In contrast to reports from the developed world, we did not find obesity as a risk factor[10-11].

Fever was the most common symptom seen in our study followed by rhinorrhoea and cough, as observed in similar studies[2,12-13]. Eight children had poor feeding, lethargy and hurried breathing warranting immediate medical attention. Nine children developed gastritis, 8 of them had myalgia, two had shock, of whom one had co-existing dengue fever other had culture negative sepsis. No children had central nervous system involvement or myocarditis. Thus respiratory system was most commonly affected organ system in our study group comparable to similar studies[7].

Predominately normal leucocyte count with relative lymphocytosis and normal acute phase reactants in our series supports the underlying viral illness. Abnormal chest x-ray findings were present in 22 (70%) children, of which bilateral perihilar infiltrates with air bronchogram was seen in 19 (61%) indicating underlying bronchopneumonia. Three children had right side lower zone consolidation. Bronchopneumonia is a characteristic finding expected in H1N1 infection, as observed in our study as well as by others. However lobar consolidation affecting right lower zone seen in 3 children is probably due to straight and wider right bronchus compared to left[2,14].

Risk stratification of all admitted children was done as per CDC guidelines into mild/progressive/ severe illness and treated with Oseltamivir[3]. Other supportive treatment was given based on unit protocol. We observed that the majority 20 (64%) belonged to mild illness category, 5 (16%) had a progressive illness and 6 (19%) had severe illness. Of these, 7 (22%) children required ICU admission and management. Among ICU admitted children all had malnutrition and /or pre-existing medical illness, indicating a trend towards increased susceptibility and severity of illness necessitating close monitoring and care of this special group of children, though this finding is statistically not significant. None of these high-risk children were vaccinated against influenza indicating low awareness and coverage of vaccine. Six children required oxygen therapy and 2 required inotropic support, all of whom belonged to the severe illness group. One child with severe distress was managed with humidified high flow nasal cannula (HHFNC) for the first 36 hours, but none required invasive ventilation. We observed no mortality in our cohort. However, earlier literature, including those from India during the 2009-10 epidemic, observed high ICU admission rate (18-88%), mechanical ventilation (17-39%) and mortality (5-!6%) in contrast to what was observed in our study[7-8,14-15]. In the post-pandemic period H1N1 is known to occur sporadically or in clusters causing significant morbidity and mortality, as evidenced by the 2015 resurgence. However, our study clearly shows a change in the trend of pandemic H1N1 influenza, with less severe infection. It is also noteworthy that all children were promptly treated with oseltamivir as per existing guidelines along with good supportive care and close monitoring of disease progression that would have definitely added to the good outcome of the study population.

The present study has a few limitations. The study being hospital-based, there would be selection bias of recruiting sick cases, and may not reflect the exact incidence of the disease in the community. Because of the small sample size, it is difficult to draw conclusions regarding the statistical significance of risk factors associated with the disease.

The study observations are important as they attempt to fill the knowledge gap about influenza in children from the Indian subcontinent after 2009–10 pandemic. The fact that malnutrition is very much prevalent among young Indian children, one may expect increased susceptibility and severity of influenza in this group of children. It also necessitates early treatment and prompt referral of such high-risk cases. After nine years from the first reported case of H1N1 Influenza in India, there is probably a trend of decreasing virulence of organism during the study period, as noted by the predominately milder degree of illness with no mortality. However, significant disease burden reinforces the need for strengthened surveillance, early treatment, and preventive measures to curtail the spread of H1N1 infection particularly in children.

Conclusions

In the post pandemic era, H1N1 Influenza is still a cause for significant morbidity in children especially in the malnourished and those with significant medical comorbidities.

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