

Spectrum of Influenza B Viral Infection in Indian Children: A Tertiary Centre Experience

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Abstract

Introduction: Influenza viral infection in children can range from subclinical illness to multi system involvement. The morbidity associated with influenza B viral infection is often overlooked. India being the second most populous country, accounts for 20% of global childhood deaths from respiratory infections. There is paucity of data on the clinical features and complications of influenza B viral infections in children from the Indian subcontinent. Our objective was to study the clinical profile, seasonality, complications and outcome associated with Influenza B viral infection in children < 18 years of age.

Material and Methods: We conducted a retrospective observational study at a tertiary care hospital in South India. Children less than 18 years of age admitted to our paediatric unit were included in the study. We reviewed the case sheets of 56 patients who tested positive for influenza B virus during the study period and recorded their clinical and laboratory data. Throat swab obtained from cases were tested by RT-PCR. The illness was classified as upper respiratory tract infection, pneumonia and severe pneumonia. Outcome measures analysed were- mortality, need for oxygen supplementation or assisted ventilation, duration of oxygen support, duration of ICU/ hospital stay and time for defervescence following initiation of oseltamivir therapy.

Results: The mean age of the study population was 6.98 years. Majority of the affected children were > 5 years of age in the school going category with a male to female ratio of 3:2. The diagnosis based on clinical and radiological findings included upper respiratory tract infection (URTI) in 44 (78.5%) cases followed by pneumonia in 11(19.6%) and severe pneumonia in one (1.7%) child. The peak incidence was in the month of March. Malnutrition was the most common risk factor affecting 22 (39.3%) cases followed by history of asthma in eight (14.3%). Three children required oxygen supplementation at admission. The median duration of hospital stay was seven days. The median duration for defervescence following initiation of oseltamivir therapy was 24 hours. Mortality was recorded in one infant who died of acute respiratory distress syndrome.

Conclusions: Influenza B virus should be screened in all children having underlying high risk medical condition, presenting with pneumonia or upper respiratory tract infection. Oseltamivir therapy should be initiated early in the management of influenza B viral infections to prevent complications.

Key words: children; Influenza B virus; pneumonia; RT-PCR; oseltamivir

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Introduction

Influenza B virus (IBV) infection is generally considered as a mild disease and is given less importance compared to influenza A virus (IAV) infection. However 20-50% of the overall influenza viral infections have been attributed to IBV by various studies across the globe.¹⁻²

During the 2010-2011 season in USA, 38% of deaths in children due to influenza viral infections were due to IBV.³ Among those children who died, 49% had no underlying high risk medical condition and only 50% of the children were treated with anti viral medications indicating missed opportunity in treatment and prevention of complications.³ Influenza related complications such as pneumonia, myocarditis and encephalitis has been well known among children with Influenza A virus infection.¹ However Influenza B associated pneumonia have rarely been reported. Research on the seasonality of influenza within India has been crucial in determining the peak season and proper timing of influenza vaccination.

Studies have shown peak influenza activity from January to April in Srinagar, June to October in Delhi, Kolkata and September to December in Chennai.⁴ Hence in this study we evaluated the clinical characteristics, seasonality, laboratory data, chest X-ray findings, treatment response to oseltamivir therapy and outcomes of infection due to IBV in children.

Material and Methods

After obtaining approval from the institutional ethics committee (IEC:690/2018), children less than 18 years of age who were admitted in our paediatric unit at a tertiary care level hospital in Southern India and diagnosed with influenza B virus infection between October 1st 2017 to September 31st 2018, were consecutively enrolled into this retrospective observational study. The medical records of study subjects were reviewed and data regarding age, gender, anthropometry, clinical symptoms and signs, history of contact with a known case of influenza, vaccination status, pre existing illness like asthma, prematurity (born at < 37 weeks gestation), course of current illness were recorded. Anthropometry was plotted on WHO growth charts and malnutrition was considered in children < 5 years with weight for age < 3rd percentile or BMI < 3rd percentile in those > 5 years of age. Laboratory data at admission including complete blood counts, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), liver transaminases, creatinine, creatinine phosphokinase (CPK) were collected. Throat swab was collected from suspected cases at admission and sample was tested using Taq

Man real time polymerase chain reaction (RT-PCR) for three viruses namely H1N1, H3N2 and IBV. The results were obtained within 24 hours of sample collection.

Based on clinical signs and symptoms along with radiological findings the illness was classified as URTI, pneumonia and severe pneumonia. URTI was defined as illness caused by acute infection involving the upper respiratory tract including the nose, sinuses, pharynx or larynx. Pneumonia was defined as acute respiratory infection with evidence of fast breathing with age specific respiratory rates as per WHO classification with or without chest retractions.⁵ Severe pneumonia is defined as acute respiratory infection with severe respiratory distress including chest retractions, nasal flaring, grunting, poor feeding, lethargy with or without additional symptoms like vomiting convulsions and impaired sensorium.⁵ Chest X-ray was done at admission in children diagnosed with pneumonia and severe pneumonia or in those children not responding to first line of treatment. All children diagnosed with IBV infection were admitted in the isolation ward or Paediatric Intensive Care Unit (PICU) and treated with oseltamivir and other appropriate measures as per the hospital protocol and CDC guidelines⁶. Outcome measures including mortality, duration of hospital/PICU stay, need for oxygen supplementation or assisted ventilation and time for defervescence following initiation of oseltamivir therapy were recorded. Data was analysed using SPSS version 20. Mean and standard deviation were used to describe data following normal distribution. Median and interquartile range was used to describe skewed data.

Results

About 56 children < 18 years of age were diagnosed and admitted with IBV infection in our paediatric unit during the study period. The baseline characteristics and clinical features at presentation are depicted in table 1.

Fever and cough were the predominant symptoms at presentation in 100% and 91% of the cases respectively with a median duration of five days. Majority of these children were greater than five years of age in the school going category and about 40% were malnourished. The peak incidence was seen in the month of march with 24 (42.9%) cases (figure 1).

None of these children had a history of contact with a known case of influenza and none had received an influenza vaccine in the past. Majority of the children had URTI (44, 78.5%) and recovered well without any complications. Pneumonia was observed in eight (14.2%) children aged greater than five years and three (5.3%) children between one to five years. The median age of presentation with pneumonia/severe pneumonia

was 5.54 years. One child aged 11 months who presented with severe pneumonia requiring assisted ventilation and inotropic support, died within three days of hospital admission with ARDS and septic shock. This child had elevated creatine kinase-muscle/brain (CK-MB=32.6 ng/ml) suggestive of myocardial involvement. However blood culture was sterile and gastric aspirate did not show the presence of acid fast bacilli.

Apart from respiratory symptoms, 10 (17.9%) children diagnosed with pneumonia had vomiting at presentation requiring IV fluids. Immunodeficiency predisposing to IBV infection was considered in one child aged seven years with pneumonia, who had acute lymphoblastic leukaemia and was on maintenance phase chemotherapy as per BFM-95 protocol. Co-infection with hepatitis A and IBV was observed in one child aged 5.58 years with pneumonia who presented with fever and jaundice. The laboratory parameters at admission are depicted in table 2. Band forms were seen in seven cases with a median of 12.5%.

Chest x-ray was obtained in 23 cases of which 12 had abnormal findings. All children with pneumonia and severe pneumonia had abnormal chest x-ray findings. Prominent perihilar opacities with air bronchograms were seen in nine out of 12 (75%), right lobar consolidation with perihilar opacities in two out of 12 (16.6%), extensive reticulo granular opacities in one out of 12 (8.3%), and normal chest x-ray findings in 11 cases with URTI (Figure 2). Adenoid hypertrophy was detected on x-ray neck lateral view in five children who had symptoms of mouth breathing and snoring at night.

The outcome measures are depicted in table 3. Only three children required oxygen supplementation via nasal cannula to maintain oxygen saturation > 90% whereas invasive ventilation at admission was required in only one child who died of severe pneumonia. Oseltamivir therapy was initiated in all children except the one with severe pneumonia who died before we could initiate therapy. Defervescence was achieved within a median duration of 24 hours following initiation of oseltamivir therapy.

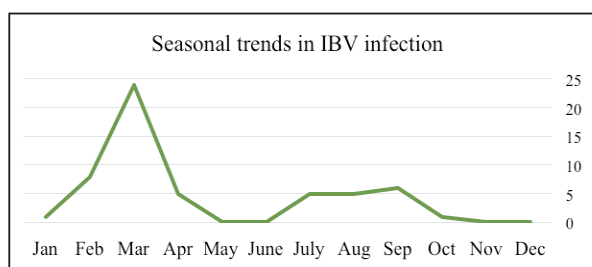


Fig. 1: Shows the number of cases of IBV infection throughout the year

Table 1: Baseline characteristics and symptomatology of the study population at presentation

Characteristic	Results
Male / female [n (%)]	34(60.7%)/ 22 (39.3%)
Age in years – median (range)	5.85 (0.95-17.53)
< 1 year- n (%)	1(1.7%)
1 to 5 years- n (%)	19(33.9%)
> 5 to 18 years- n (%)	36(64.3%)
Symptoms at presentation: n (%)	
Fever	56 (100)
Cough	51 (91.1)
Tachypnea	12 (21.4)
Wheeze	4 (7.1)
Myalgia ^π	9 (16.1)
Vomiting	10 (17.9)
Abdominal pain ^π	5(8.9%)
Joint pain ^π	2(3.6%)
Febrile seizure	3 (5.3%)
Clinical signs at presentation: n (%)	
Crepitations	8 (14.3)
Ronchi	7 (12.5)
Hepatosplenomegaly	3 (5.3%)
Pre existing illness: n (%)	
Malnutrition	22 (39.3)
History of asthma ^α	8 (14.3)
Known cardiac disease	1 (1.7%)
Immunodeficiency	1 (1.7%)
Gastro-esophageal reflux disease	1 (1.7%)
Prematurity	3 (5.3%)
Diagnosis category: n (%)	
URTI	44 (78.5%)
Pneumonia	11 (19.6%)
Severe pneumonia	1 (1.7%)

^π- children greater than 4 years were only analysed as younger children cannot appropriately report, abdominal pain, joint pain or myalgia

^α- Children > 5 years of age were only considered.

Table 2: Laboratory parameters of the study population at presentation

Laboratory parameters	Median (Range)
Haemoglobin (g/dL)	12.5 (7.4-16.7)
Total WBC count (per μ L)	6400 (2100-27700)
Neutrophils %	46.5 (7.7-84.7)
Lymphocyte %	38.0 (5.0-80.4)
Monocyte %	9.4 (0-19.0)
Eosinophils %	0.2 (0-7.0)
Platelet count (per μ L)	218000 (14000-551000)
Creatinine (mg/dL)	0.41 (0.2-1.0)
CRP (mg/L)	2.05 (0-98.89)
ESR (mm/hr)	15.5 (2-51)
AST (IU/L)	34.0 (11-182)
ALT (IU/L)	18.5 (9-428)
CPK (U/L)	77.0(33-2850)

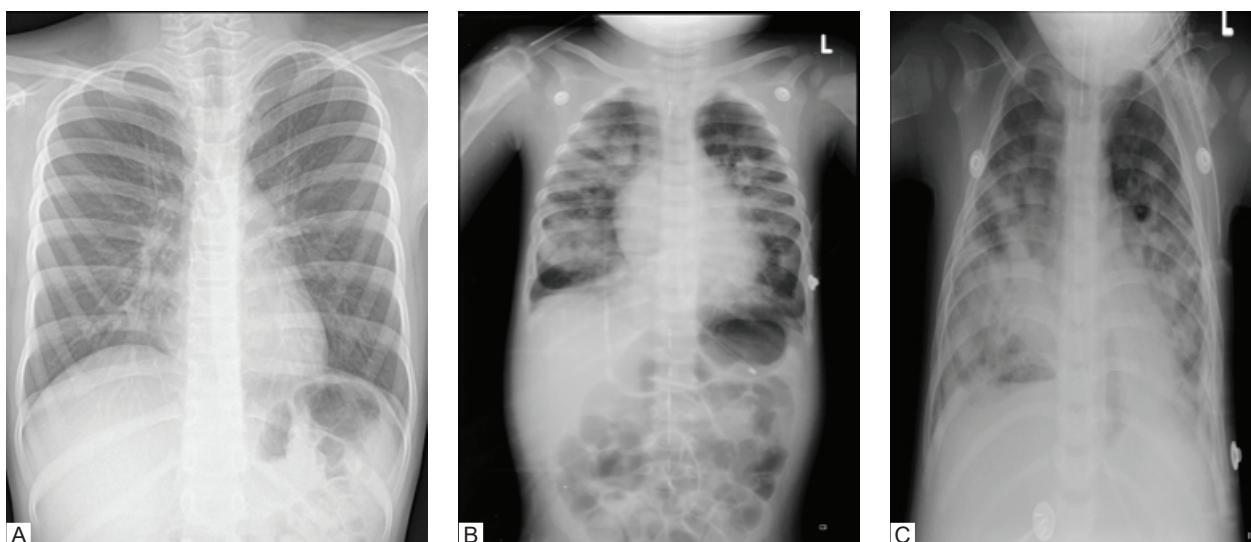


Figure 2. Representative chest x-rays of patients with IBV infection.

(A) shows perihilar opacities with right lower lobe involvement

(B) shows bilateral extensive reticulo-granular opacities on day 1 in the infant with severe pneumonia

(C) shows progression to ground glass opacities with cystic areas in between, on day 3 in the infant with severe pneumonia

Table 3: Outcomes measured

Outcome measured	Results
Duration of hospitalisation in days- (median/range)	7 (3-16)
PICU admission:	
Requirement- n (%)	3 (5.4%)
Duration of stay in days- median(range)	4 (2-7)
Oxygen supplementation:	
Requirement- n (%)	3 (5.4%)
Duration in days- median (range)	4 (1-7)
Assisted ventilation:	
Requirement – n (%)	1 (1.7%) [£]
Duration in days- median	3
Intra venous fluids:	
Requirement – n (%)	18 (32.1%)
Duration in days- median (range)	2 (1-3)
Inotropes administration:	
Requirement – n (%)	1 (1.7%) [¥]
Duration in days- median	3
Oseltamivir therapy:	
Number of children who received- n (%)	55 (98.2%)
Duration of therapy in days- median (range)	10 (5-10)
Time to defervescence following initiation of therapy in hours- median (range)	24 (0-120)
Antibiotic usage:	
Requirement – n (%)	42 (75%)
Duration in days- median (range)	7 (5-10)
Type of antibiotic: n (%)	
Amoxicillin-clavulanic acid	15 (35.7%)
Azithromycin	2 (4.7%)
Ceftriaxone	25 (59.5%)
Mortality- n (%)	1 (1.7%)

£: one child who died of severe pneumonia required synchronised intermittent mandatory ventilation for 3 days.

¥: one child with severe pneumonia required inotropic support with dopamine(10 µg/kg/min) for 3 days.

Discussion

In our study we described IBV associated illness in children ranging from mild upper respiratory infection to multi organ dysfunction including death. Our study has also described the seasonal trend in IBV infection in southern part of India. The importance of Influenza B virus infection in causing significant morbidity and mortality has been highlighted recently by few studies whereas in the past IBV was considered less virulent than IAV.⁷ The data on clinical spectrum of IBV infection from India is limited. Influenza virus B should be tested in high risk category including immunocompromised patients, chronic medical conditions like asthma and heart failure.⁸ In the present study, 11 (19.6%) children have presented with pneumonia and one child with severe pneumonia which is comparable with the reported incidence of IBV pneumonia ranging from two to 20%.⁶ Similar results were observed in a study from Taiwan where the incidence of IBV associated pneumonia was 18.4%.⁷ The median age of IBV infection in our study was 5.85 years which is consistent with other studies across the globe where the reported incidence is highest among pre school and school going children.⁹

Apart from respiratory symptoms, IBV is also known to cause gastro intestinal symptoms,⁷ encephalitis,¹⁰ seizures,¹⁰ myocarditis,¹¹ musculo-skeletal involvement including arthritis and myalgia.¹² In our study we observed that 10/11 (90%) children with pneumonia had vomiting. All these children were administered IV fluids at admission to prevent dehydration. Studies have shown that the odds of mortality is significantly greater with IBV than IAV.¹³

Malnutrition and asthma have been identified as risk factors for hospitalisation among children with influenza viral infections.¹⁴ Nearly 40% of the children in our study were malnourished and 14% had underlying asthma. In our study the peak incidence of IBV infection was immediately following the winter season during the month of March, whereas a study from Mumbai has reported highest incidence during monsoon season.¹⁵

With regards to laboratory parameters in our study, the median WBC count and CRP was in the normal range supporting the diagnosis of viral infection. Chest x-ray findings among children with pneumonia in our study showed predominantly perihilar involvement whereas a study from Taiwan has reported varied findings of alveolar consolidation, interstitial infiltration and ground glass opacities.⁷ Only three children in our study required PICU admission and oxygen supplementation. All children with confirmed IBV infection were treated with oseltamivir and defervescence was seen within a median duration of 24 hours. Oseltamivir therapy is recommended within 48 hours of the onset of flu-like symptoms in children at high risk of developing complications due to influenza viral infections and empirical anti viral prophylaxis should be administered

to close contacts.⁷ None of our children in the high risk category were vaccinated against influenza indicating low awareness among the general population and low coverage of the vaccine. Our study was limited due to the small sample size and we focussed mainly on viral aetiology since it is understudied in our region. This prevented the possibility of analysing the role of bacterial pathogens and mixed viral/bacterial co-infections. Further more different strains of IBV may circulate in different flu seasons and thus the clinical spectrum may vary from year to year. However our study observations are important as they address the varied clinical spectrum of IBV infection and its outcome in children from South India.

Conclusion

Pneumonia should be considered in children with IBV infection, especially in those with pre-existing illness such as asthma and malnutrition. Early detection of IBV infection among high risk group of children is extremely important in order to initiate oseltamivir therapy early in the course of illness to prevent complications and reduce morbidity and mortality.

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