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THE STUDY OF CLINICAL PRESENTATION, MORBIDITY PROFILE AND OUTCOME WITH H1N1 INFLUENZA A IN ADMITTED CHILDREN

Yudhavir S. Shekhawat[1]*, Anurag Singh[2] and Pramod Sharma[3]

[1]Senior Resident, AIIMS, Jodhpur (Rajasthan).
[2]Professor, Dr. S.N. Medical College, Jodhpur.
[3]H.O.D Dr S.N.Medical College Jodhpur.

***Corresponding Author: Dr. Yudhavir S. Shekhawat**
Senior Resident, AIIMS, Jodhpur (Rajasthan).

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ABSTRACT

Background- Influenza virus is a common human pathogen that has caused serious respiratory illness and death. In April 2009 a new strain of Influenza virus A H1N1 began to spread in several countries around the world and India confirmed its first case on 16 May 2009. The 2013-2014 influenza season was marked by the resurgence of pandemic A/H1N1virus causing substantial morbidity and mortality around the world. **Objective-** The study of clinical presentation, morbidity profile and outcome of H1N1 influenza A in admitted children of a Tertiary health centre. **Methods-**130 patients satisfying the WHO criteria of CAP were enrolled. Nasopharyngeal Aspirates of these patients were tested for H1N1 virus by using the Real Time Reverse Transcriptase Polymerase Chain Reaction assay. Clinico-epidemiological profile and outcome of positive patients were analysed. **Results**- Twenty-three (17.7%) patients were confirmed (positive) for H1N1influenza A. Maximum 13(56.5 %) patients were in the age group 1-5 years. Male (73.9%) were affected more than Females (26.1%). The common symptoms were rapid breathing (100%), fever (82.6%) and cough (95.7%). Malnutrition was present in 10 (43.5%) cases. Total 3 (13.0%) patients were taken on mechanical ventilator, out of them no one survived. **Conclusion**- Clinician should consider H1N1 influenza A in the differential diagnosis of patients who presented with acute onset of fever, cough and breathlessness. The routine laboratory investigations in children with H1N1 influenza A were non-specific. There was no specific laboratory characteristic shown to have a significant association with the severity of illness or poor outcome. Poor prognostic factors as derived in the current study were the development of ARDS, need of mechanical ventilation and associated co-morbid illness.

KEYWORDS: H1N1 influenza A, Community Acquired Pneumonia (CAP), (RT-PCR) Real Time Reverse-Transcriptase Polymerase Chain Reaction.

INTRODUCTION

Influenza A is a viral respiratory infection often indistinguishable from common cold or other respiratory diseases. Transmission is air borne and through direct contact with infected droplet.[1] It causes significant morbidity and mortality in childhood.[2] Infants, young children and people 65 years of age and older account for the highest rates of influenza-related hospital admission.[3]

In April 2009, two cases of human infection with novel influenza with swine origin were confirmed by the Centre for Disease Control (CDC) for the first time.[4] The 2009 H1N1 virus contained a unique combination of gene segments which had not previously been identified in humans or animals.[5]

The symptoms of 2009 H1N1 influenza are expected to be similar to the symptoms of regular human seasonal influenza and include fever, cough, sore throat and myalgia. A feature seen more frequently with 2009 H1N1 influenza is gastrointestinal upset with almost a quarter of patients presenting with vomiting and diarrhea.[6,7]

The 2013-2014 influenza season was marked by the resurgence of pandemic A/H1N1virus causing substantial morbidity and mortality around the world. Collecting information about the clinical and epidemiological aspects of pandemic H1N1 virus infection is still going on since these characters may be variable in different geographical regions, therefore, regional studies on this subject can provide a better vision of the infection profile. This will help in the case management or infection prevention in latter waves of this pandemic.

AIMS AND OBJECTIVES

To study the clinical presentation, morbidity profile and outcome of H1N1 influenza A in admitted children of a Tertiary health centre.

MATERIALS AND METHODS

This was a prospective, single-centre study designed to identify the clinic-epidimiological profile of children with diagnosis of community acquired pneumonia admitted in the hospital and were positive for H1N1 influenza A virus The study was duration based study conducted over 12 consecutive months from 2013-2014.

An informed consent was taken from patient's attendant before enrolling the patient in the study. The study protocol was approved by the Ethical committee of Umaid Hospital, Dr S.N. Medical College, Jodhpur, Rajasthan, India.

Eligible patients were infants and children under the age of 18 years who were admitted to pediatric wards and intensive care unit (ICU), fulfilling the WHO IMCI case definition of CAP or acute respiratory infection; all such eligible children were tested for influenza viruses. Children with duration of illness >7 days; those with previous hospitalization within the preceding 30 days, evidence of immunodeficiency were excluded.

Each child underwent a detailed history and clinical examination. The co-morbid conditions associated and immunization status were also noted. The diagnosis of H1N1 influenza A was confirmed by testing of combined nasal and throat swabs with the use of a real-time reverse transcriptase polymerase chain reaction (RT-PCR) assay. Children were treated with oseltamivir as per the available guidelines issued by the Ministry of Health, Government of India, which were periodically revised.[8]

Statistical methods

Data was managed on Microsoft (r) Excel spread sheet, all the entries were double checked and analysis was performed using SPSS version 16.

RESULTS

In a period of 1 year a total of 130 throat swabs were taken for RT-PCR from diagnosed community acquired pneumonia patients, out of them 23(17.7%) swabs were found positive and labelled as confirmed case of swine flu.

Table 1: Baseline characteristic of children enrolled in the study.

	Number (n)	Percentage (%)
I. Gender		
Male	17	73.9
Female	6	26.1
II. Age group		
<12 months	7	30.4
12 -59 month	13	56.5
>_60 months	3	13.1
III. Co-morbidity		
Malnutrition	10	43.5
Asthma	2	8.6
Others	1	4.3
IV. Associated illness	4	17.3
(malaria and septicemia)		
V. Immunization status		
Immunized	9	39.1
Not immunized	14	60.9

Table 1 shows that majority of the children 17 (73.9%) were male and 13(56.5%) were in the age group of 1 to 5 year. The median age of presentation in swine flu positive cases was 24 months. The common associated co-morbidities were malnutrition (43.5%) followed by asthma (8.6%).

Table 2: Presenting symptoms, clinical examination findings at admission.

	Number (n)	Percentage (%)
I. Symptoms		
Fever	19	82.6
Cough	22	95.7
Rapid breathing	23	100
Pain abdomen	2	8.7
Convulsion	1	4.3
Vomiting	4	17.4
Loose motion	2	8.7
II. Signs		
Crepitations	20	87
Chest retractions	19	82.6
Wheeze	6	26.1
Abnormal breath sounds	5	21.7

Table 2 shows the clinical characteristics of the admitted patients. The common symptoms were fever(82.6%), cough(95.7%) and rapid breathing(100%). The other symptoms were pain abdomen, vomiting, loose motions and seizures. The signs in the decreasing order of frequency were chest retractions(82.6%), crepitations(87.0%), wheeze (26.15), and abnormal breath sounds (21.7%).

Table 3: Distribution of patients according to mode of oxygenation.

Mode of oxygenation	Number (n)	Percentage (%)
1.oxygen by prongs/mask	15	65.2
2.CPAP	1	4.3
3.Invasive ventilation	3	13.1
4.No oxygen	4	17.4

Table 3 shows patient distribution according to the mode of oxygenation. In the study 69.5% were oxygenated with prongs and CPAP. Oxygen was not required in 17.4% of patient. Mechanical ventilation was required in 13.0% of cases. All the patients on mechanical ventilator expired.

Table 4: Outcome of the patients according to risk factors.

Category		Expired	Survived	Inference
I. Age	<1	0	7	X2= 1.50 df=1 P=0.52
	>1	3	13	
II. Sex	M	1	16	X2= 2.94 df=1 P=0.15
	F	2	4	
III. Immunizati-on	Immunised	0	9	X2=2.21 df=1 P=0.25
	Nonimmuni-sed	3	11	
IV. Associated illness	(+)	3	1	X2=16.38 df=1 P<0.001
	(-)	0	19	
V. Anaemia	(+)	3	16	X2=0.72 df=1 P=1.00
	(-)	0	4	
VI. Co-morbid illness	(+)	3	10	X2=2.65 df=1 P=0.22
	(-)	0	10	
VII. Duration of starting oseltamivir	<48 hours	0	9	X2 = 9.77, df= 2, p value=0.01
	48-72 hour	0	8	
	>72hour	3	3	

Table 4 assess the outcome of patient according to risk factors**.** Various factors like age, sex, immunization status, co-morbid conditions (malnutrition, asthma, CHD, Down's syndrome) and time duration of starting oseltamivir after onset of symptoms were analysed regarding their relation to the outcome in H1N1influenza A patients. Statistically significant relationship was found between associated illnesses and outcome of the patients (P<0.0001). These associated illnesses were sepsis and malaria. The patients who were started on Oseltamivir within 72 hour 17(73.9%) of onset of symptoms had better outcome than those who were started late after 72 hours of onset of symptoms. In this study overall cases fatality was 13.0%

DISCUSSION

A novel swine-origin influenza A virus was identified as the cause of outbreaks of febrile respiratory infection ranging from self-limited to severe illness.[9] The most commonly reported symptoms of influenza A [H1N1] virus in different studies include cough, fever, sore throat, malaise and headache.[10-13]

The signs and symptoms of influenza caused by pandemic H1N1 influenza A virus are similar to those of seasonal influenza, although gastrointestinal manifestations appear to be more common with pandemic H1N1 influenza.

Similarly the most frequent symptoms in our patients were fever, cough and rapid breathing. The other symptoms were vomiting, loose motion, pain abdomen and convulsion.

Critical illness due to 2009 influenza A [H1N1] in Canada occurred rapidly after hospital admission, often in young adults, and was associated with severe hypoxemia, multisystem organ failure, a requirement for prolonged mechanical ventilation, and the frequent use of rescue therapies.[14] In the same way, our critical ill patients were intubated and because of respiratory failure required mechanical ventilation. It was required in 13.0% of cases. All the patients on mechanical ventilator expired. Ventilator requirement was an independent risk factor correlating with higher mortality rate and poor prognosis in H1N1 influenza A patients (P value<0.0001).

Jain et al reported that seventy five percent of their patients received antiviral treatment with Oseltamivir. Data suggest that the use of antiviral drugs was beneficial in hospitalized patients especially when this therapy was initiated early.[5] Similarly in our study we found that the patients who were started on Oseltamivir within 72 hour 17(73.9%) of onset of symptoms had better outcome than those who were started late after 72 hours of onset of symptoms. The patients who were referred from the far peripheral centres with delay in diagnosis and treatment with oseltamivir had poor outcome.

CONCLUSION

The current H1N1 pandemic had witnessed more number of cases in the age group of 1 to 5 year. Clinician should consider influenza A in the differential diagnosis of patients who present with fever, cough, breathlessness. There is no specific laboratory characteristic shown to have a significant association with the severity of illness or poor outcome. The malnutrition was the most common co-morbid condition associated with H1N1 influenza A. Poor prognostic factors as derived in the current study were the development of ARDS, use of mechanical ventilation and delay in starting antiviral therapy.

Drawback of the study

The numbers of positive cases tested for H1N1 were limited as it was a single centre study. This analysis may not reflect the actual distribution of the cases and associated co-morbidities at the general population level.

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