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Clinical Spectrum of H1N1 2009 Pandemic Influenza-A

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Abstract

Background: *The first case of 2009 pandemic Influenza A (H1N1) virus infection in India (Hyderabad) was reported in May, 2009. We describe the clinico-epidemiological and radiological characteristics of patients who were hospitalized with influenza A (H1N1) infection.*

Material & methods: *From June 2009 to June 2010, we observed 110 H1N1 Influenza A viruspositive patients who were admitted in our institute i.e., Osmania Medical College, Hyderabad and they were taken into the study. Demographic, clinical, radiological, laboratory and management data were collected and analyzed statistically. Real time reverse transcriptase-polymerase chain reaction (RT-PCR) testing was used to confirm infection.*

Results: *Of 110patients Commonest age group was 20-40 years (65.9%),70.8%were males and >90% are from urban background. 25.4% had recent travel history [international history-18.2%, domestic-7.2%]. Obesity is one of the most important co-morbid ill-ness adversely influencing the progress of disease. Mean duration of hospital stay was 5days in72.2%. The most common symptoms were fever (94.5%), followed by cough, rhinitis, sore throat and myalgia. Commonest associated symptoms were vomitings, diarrhoea and headache. Radiologically pneumonia was reported in 23.6% patients. Mortality was 8.1%. Oseltamivir well tolerated by all patients.*

Conclusions: *H1N1Influenza A is unpredictable, whose presentation varies in both extent and severity. The progression of the disease is more aggressive & catastrophic when associated with co-morbidities. Treatment with Oseltamivir (75 milligrams twice a day for 5 days) within 48 hours of the onset of symptoms of Influenza proved to be beneficial*

Keywords: *H1N1 influenza A, Real time reverse transcriptase-polymerase chain reaction, Oseltamivir.*

I. Introduction

Influenza A (H1N1) is a new virus causing illness in human beings. It was first detected in Mexico in April 2009.[1] It was originally referred as "swine flu" because many of the genes in this new virus were found in pigs in United States (US). Furtheron, it has been found that this new virus strain is an apparent re-assortment of four strains of influenza A virus subtype H1N1. Analysis at the United States Centers for Disease Control and Prevention (CDC) identified the four component strains as one endemic in humans, one endemic in birds, and two endemic in pigs (swine).[2] The World Health Organization (WHO) raised the pandemic level 5 to 6, the highest level after the documentation of human to human transmission of the virus in atleast three countries in two of the six world regions defined by the WHO.[3]

The first confirmed case of H1N1 virus infection in Hyderabad (A.P., India) was documented in May 2009. After that many positive cases were reported throughout the India. All Influenza A (H1N1) positive patients were quarantined in isolation ward to prevent contamination. This report summarizes the clinical, radiological and epidemiological characteristics of 110 confirmed cases of 2009 pandemic influenza A (H1N1) infection in Government general and chest hospital (GGCH), Osmania medical college (OMC), Hyderabad from June 2009 to June 2010.

II. Materials And Methods

A total of 110 patients found to be positive and admitted in GGCH, OMC,Hyderabad from June 2009 to June 2010 were included for analysis. Categorization of influenza A (H1N1) cases was done according to guidelines issued by Ministry of Health and Family Welfare, Government of India(Table1).[4]In this study 110 patients belonged to category C were included.

Variables: Several types of data were collected from the patients including demographic parameters, co-morbid illness, onset of illness and treatment. Data regarding hospitalization, whether intensive care needed, relation with obesity, duration of antiviral drug and disease outcome were collected prospectively from GGCH, OMC, Hyderabad

Laboratory confirmation of infection

The 2009 H1N1 virus detected with the use of areal time RT-PCR assay in accordance with the protocol from the US Centers for Disease Control and Prevention, as recommended by the WHO.[5] Two swabs from nasopharynx and pharynx were collected from suspected patients and their contacts for detection of influenza A (H1N1) virus by real time RT-PCR assay.

III. Results

From June 2009 to June 2010, a total 110 human cases of infection with H1N1 influenza A were included in this study.

The analysis ofthe present studyshowed that the disease is more common in the age group 20-40 years with male to female ratio of approximately 3:1. The median duration of diagnosis was less than 1week after the onset of illness in > 80% of cases. Most of the patients (72.7%) improved with treatment and were discharged in a stable condition on day 5 (from the time of admission) and only 7.2% remained in hospitalfor > 10 days (table 2). Most of the confirmed cases were from urban background (>90%) than rural.

H1N1 influenza A cases in the present study were classified into 3 grades based on severity of illness. Most of the patients (71.8%) were mildly ill. Symptom wise analysis showed that majority (94.5%) had fever (table 4). Among the co-morbid conditions, pregnancy, diabetes mellitus and obesity (table3) were associated with high morbidity (table 5).Also the mortality was high with, pregnancy (75%), diabetes mellitus (30%) and Obesity (25%).

Laboratory data showed thrombocytopenia in 8.1%, altered liver function tests in 3.6%. Radiologically lobar consolidation was noted in 23.6%, diffuse multifocal pattern in 6.3% and pleural effusion 0.9% (table 6). Mortality was 100% with bilateral extensive consolidation. The adverse effects of oseltamivirobserved were elevation of serum bilirubin (7.2%), diarrhea (3.6%), vomiting (0.9%) and itching(0.9%). These adverse effects started within 48 hours of thetreatment and resolved spontaneously or with symptomatic treatment.

IV. Discussion

Thoughseasonal influenza outbreaks occur every year, healthy adults usually are not at risk for serious complications.[6]The recent H1N1 A influenza pandemic created panicin the general population globally and posed a serious challenge to the medical profession.

A systematic study of clinical and laboratory data of these patients would enable us to understand the presentation and clinical features of the disease betterand also guide us to take measures to prevent as well as control such outbreaks effectively. The treatment as per CDC guidelineswould also enlighten on the clinical efficacy and adverse effects of anti-viral drugs.

The analysis ofthe present studyshowed thatthe disease is more common in the age group (20-40 yrs). In this majority (65.9%) were relatively young, who were otherwise normal without any co-morbidities. Males were (70.8%) commonly effected than females (29.2%) and the male to female ratio is approximately 3:1.In the present study, the duration of symptoms was less than 1week in > 80% of cases. Most of the patients i.e., 72.7% improved with treatment and were discharged in a stable condition on day 5 (from the time of admission) and only 7.2% remained in hospital for > 10 days. In a similar study, by Rajesh K Chudasama et al,[7]the median age was 27 years, and 51.5% were males and medium time for discharge was 6 days.

The study showed most of the confirmed cases are from urban background (>90%) than rural. 25.4% had travel history [International (18.2%) and domestic (7.2%)] from high prevalent areas. And13.6 % of cases wereclose contacts of H1N1 A positive patients. 3.6% showed nosocomial transmission, and in 57.4% of cases, there was no history of travel and exposure to H1N1 A influenza cases. Cases were classified into 3 grades. Out of 110 patients, majority (79) had mild illness. [8]

Other important observations of the study was that, among the 8 (7.2%) obese (BMI 30-40) patients, 6 presented with bilateral fluffy shadows on chest X-ray consistent with severe multilobar involvement and all those 6 patients were given withoseltamivirbeyond 5-day course and higher-dose (150 mg orally twice a day). In a similar studyby LM Napolitano et al,[9]of the 10 patients who developed ARDS, 9 were obese and they were received oseltamivir and amantadine beyond the standard 5-day course, including higher-dose oseltamivir (up to 150 mg orally twice a day). Obesity is one of the most important co-morbid illness, adversely influences the progress of disease. Extremely obese ICU patients had higher rates of mortality, nursing home admission, and ICU complications compared with moderately obese patients. [9]

Other important observation noted is that the pregnancy is associated with severe disease and higher risk for influenza associated mortality. Out of 4 pregnant women, only one survived and the other 3 patients died due to respiratory failure. The patient who survived was in 1st trimester whereas others who succumbed were in 3rd trimester. Similar results were reported by Rajesh K Chudasama et al. [7]In the United States during the 2009 H1N1 influenza Apandemic, increased rates of hospitalization have been observed among pregnant

women compared with the general population,[10]particularly during the second and third trimesters. Most deaths have been related to respiratory failure resulting from severe pneumonia with multifocal infiltrates and acute respiratory distress syndrome.[10] Symptom wise analysis showed that majority (94.5%) had fever [high grade &mostly subsided within 2 days of Oseltamivir , paracetamol] followed by cough67.2 % as opposed to a study by Rajesh K Chudasama et al [7] and BinCao et al, [11]where in, the most common symptom was cough followed by fever and sore throat.But the study conducted by Dawood FS et al,[2] most coomon symptom was fever followed by cough. Among complications, type I respiratory failure was noted in 12.7% of patients . Respiratory failure was the reason for intensive care unit admission for all four patients with pandemic A (H1N1) in the study by Kelvin KTo W et al.[12]Mortality was observed in 9 patients (8.1%).3 of them were pregnant (third trimester), 2 had Diabetes Mellitus, 2 were obese. One patient had systemic hypertension, diabetes mellitus type2, CAD, bronchial asthma, old TB and one patient had no co-morbidities.

Laboratory data showed thrombocytopenia in 8.1%, altered liver function tests in 3.6% (In these casesserum bilirubin was <2.5mg/dl). Radiologically lobar consolidation was noted in 23.6%, diffuse multifocal pattern in 6.3% and pleural effusion 0.9%. Mortality was 100% with bilateral extensive consolidation. Lobar consolidation resolved with early treatment of oseltamivir, but in these patients hospital stay was increased and also 150 mg of oseltamivir twice a day, was given instead of 75mg.In the studyby Seema Jain et al, [13]40% had findings consistent with pneumonia.

Oseltamivir was given to all the patients and most of the patients tolerated well. The adverse effects observed were elevation of serum bilirubin (7.2%) (serumbilirubin was <2mg/dl). diarrhoea (3.6%) , vomitings(0.9%) , itching(0.9%). These adverse effects started within 48 hours with oseltamivirtreatment and resolved spontaneously or with symptomatic treatment.

As per the observation in this study, those who presented early and received oseltamivir early improved quickly and also got discharged on day5.Treatment with antiviral drugs was associated with a significant reduction in mortality.[14]On the other hand, those who had late diagnosis and received oseltamivirlate, had pneumonia more frequently. Late diagnosis had severe disease and required prolonged hospitalization.

Limitations of the study: The present study is only observational study. The number of children presenting with H1N1 Influenza –A is too small to study the data. The present study did not take history of annual vaccination with Influenza vaccine into consideration and also those with short term follow-up.

V. Conclusions

Influenza is unpredictable, whose presentation varies in both extent and severity. The progression of the disease is more aggressive & catastrophic when associated with co-morbidities. The virus was far less virulent than expected. Oseltamivir within 48 hours of the onset of symptoms of Influenza proved to be beneficial.

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Table 1: Categorization of influenza A (H1N1) patients as per clinical features

Category and clinical features	**Antiviral treatment**	**RT-PCR testing and hospitalization**
Category A Mild fever, cough/sore throat, body ache, headache, diarrhea, vomiting. Patient should be monitored and reassessed after 24 to 48 h	Not needed	Not needed
Category B (1) Signs of category A, and/or high grade fever, severe sore throat. Home isolation is advisable.	May be given	Not needed
Category B (2) Signs of category A, and/or any of the high risk conditions like, children with mild illness but with predisposing risk factors; pregnant women; persons aged 65 years or more; patients with lung, liver, hear, kidney diseases, blood disorders, diabetes, neurological disorders, cancer, HIV/AIDS; long term steroid therapy	Given	No testing required but hospitalization may be needed
Category C In addition to signs and symptoms of category A and B, any of the following: breathlessness, chest pain, drowsiness, fall in blood pressure, sputum mixed with blood, bluish discoloration of nails; children with red flag signs like somnolence, high and persistent fever, inability to feed well, convulsions, shortness of breath, difficulty in breathing; worsening of underlying chronic conditions.	Start immediately	Immediate testing and hospitalization

Table 2: Demographic characteristics, disease history, and outcomes of patients infected with 2009 pandemic influenza A (H1N1) virus

Characteristics	no. of patients (%)
Age	
< 12 years	5(4.5%)
12-20 yrs	7 (6.36%)
20-40 yrs	73 (65.9%)
40-60 yrs	25 (22.6)
Sex	
Male	74 (70.8%)
Female	36 (29.2%)
Duration of symptoms	
<1 week	90 (81.8%)
>1 week	20 (18.2%)
Mode of infection	
Close contact	15 (13.6%)
Travel history	28 (25.4%)
Nosocomial infection	4 (3.6%)
No specific history	63 (57.4%)
Hospital stays in days	
<5 days	80 (72.7%)
5-10 days	22 (20%)
>10 days	8 (7.2%)
Severity of illness	
Mild	79 (71.8%)
Moderate	19 (17%)
Severe	12 (10.9%)
BMI	
Normal	58 (52.7%)
Over weight	44 (40.1%)
Obese	8 (7.2%)
Outcome of patients	
Survived	101(91.8%)
Expired	9 (8.2%)
Addictions	
No addictions	72 (65.4%)
Smoking only	19 (17.1%)
Alcohol only	1 (0.9%)
Both	18 (16.3%)

Table3: Obesity Vs complications influenza A (H1N1) infected patients

BMI	Total no. of patients	No. of patients with complications	% of complications
Normal	58	11	18.9%
Over weight	44	11	25%
Obese	8	6	75%

Table4: Clinical features of influenza A (H1N1) infected patients

Clinical features	no. of patients	Percentage
Common symptoms		
Fever(Commonest)	104	94.5%
Cough(2nd Common)	74	67.2%
Cold	58	52.7%
Sore throat	25	22.7%
Expectoration	32	29%
Dyspnoea	32	29%
Arthralgia	23	20.9%
Myalgia	44	40%
Other Symtoms		
Vomitings	13	11.8%
Headache	6	5.4%
Diarrhoea	4	3.6%
Gastritis	2	1.8%
Mild Hemoptysis	3	2.7%
Pain Abdomen	1	0.9%

Table5: Co-Morbidities of influenza A (H1N1) infected patients

Co-morbidities	no. of patients	Percentage
Diabetes Mellitus	10	9%
Hypertension	5	4.5%
Pregnancy	4	3.6%
Allergy	3	2.7%
Hypothyroidism	3	2.7%
MVP	1	0.9%
Asthma	4	3.6%
CAD	1	0.9%
OSAS	2	1.8%
Tuberculosis	1	0.9%

(MVP- mitral valve prolapse. CAD- coronary artery disease. OSAS- obstructive sleep apnoea syndrome)

Table 6: Laboratory and radiographic findings in influenza a (h1n1) infected patients

Investigation	No. Of Patients	Percentage
Laboratory Findings		
Thrombocytopenia	9	8.1%
Elevated ESR	3	2.7%
Elevated Sr. Bilirubin	4	3.6%
Radiological Findings		
Lobar Consolidation	26	23.6%
Bronchopneumonia	7	6.3%
Pleural Effusion	1	0.9%