ORIGINAL ARTICLE

CLINICAL CHARACTERISTICS AND OUTCOME OF THE INFLUENZA (H1N1) PATIENTS ADMITTED TO THE TERTIARY CARE HOSPITAL, PESHAWAR

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ABSTRACT

Objective: To evaluate the clinical characteristics and outcome of H1N1 patients admitted to a tertiary care hospital in Khyber Pakhtunkhwa.

Material and Methods: A prospective observational study was carried out from December 2015 to February 2016 in Northwest General Hospital & Research Centre Peshawar. Data was collected using a structured format and statistical analysis was done using SPSS version 16. P-value less than 0.05 was considered statistically significant.

Results: The mean age of patients was (45.23±15.037) years. Average length of hospital stay was 7.85± 11.7 days, and 50% of them were females. Clinical manifestations included fever, shortness of breath, and dry cough. Hypertension 9 (34.61%), asthma 4 (15.38%) and pregnancy 3(11.53%) were the most common co-morbidities. Real time PCR was positive in 11(42.31%) patients. Among 26 patients 17(65.4%) survived and 9(34.6%) died. The clinical parameters between the deaths and survivors were compared, among these parameters: length of hospital stay (p=0.006), oxygen saturation (p=0.009) and respiratory support in terms of non-invasive ventilation and invasive mechanical ventilation (p=0.02) were statistically significant.

Conclusion: The present study revealed the serious nature of H1N1 infection with high mortality. This emphasizes the need for early institution of the antiviral therapy and close monitoring in these patients irrespective of PCR positivity.

Key Words: H1N1, Influenza, Mortality, infection.

This article may be cited as: Ijaz M, Samad A, Ali I, Khalil A. Clinical characteristics and outcome of the H1N1 patients admitted to the tertiary care hospital, Peshawar. J Med Sci 2017; 25: (1) 27-32.

INTRODUCTION

In recent years, a novel influenza A virus was found in Mexico in 2009[1] named as Swine flu (H1N1). This finding was followed by a global outbreak of pandemic flu, influenza H1N1 (Swine Flu) that spread swiftly across the continents and claimed around 18000 lives from 209 countries around the globe[2-4]. Genetically H1N1 (swine flu) virus is a 'reassortant' virus" a product of human, swine and avian flu virus genes[5].Humans lacks both innate and acquired immunity against this super virus thus spreads with ease among humans[6]. In 2015, around 31000 people suffered this illness, in Indian swine flu outbreak, of which around 1700 deaths were reported[7].

Recently, as of February 2016, more than 250 laboratory confirmed H1N1 pdm/09 cases have been reported from Caribbean islands and South America. Out of more than 155 thousand specimens collected from 98 countries by World Health Organization in the month of February 2016, approximately 30% tested positive for influenza viruses, of which 80% were influenza A, mainly (H1N1)pdm/09.[8]

Since the detection of first laboratory confirmed case of swine flu in Pakistan on August 10th 2009, sporadic cases are reported annually[9]. Pakistan was plagued with an epidemic of H1N1 during the winter of 2015/2016 (lasting uptil February 2016), in which more than 240 cases were confirmed[10]. In our part of the country, clinical specimens obtained from patients with suspicion of H1N1 are usually reported after 4-5 days for logistic reasons and lack of facilities for quantitative

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Date Received: June 21, 2016
Date Revised: November 20, 2016
Date Accepted: January 5, 2017

determination of Influenza virus in the city. On the other hand, the infectivity period of patient presenting with these symptoms is from one day before and until 3 days after the onset of symptoms[6]. Hence, isolation and definitive treatment of patient after qPCR confirmation would significantly increase the morbidity, mortality and cross-infection. In this scenario, clinical judgment and suspicion is critical for the better primary and secondary prevention of this disease. The present study was undertaken to evaluate the clinical characteristics and outcome of H1N1 patients admitted to a tertiary care hospital in Peshawar and to appraise the health related personnel regarding the burden of the problem and need for continuous vigilance to be carried out.

MATERIAL AND METHODS

A prospective observational study was carried out from December 2015 to February 2016 at the Department of Medicine & Allied, Northwest General Hospital & Research Centre (NWGH&RC), Peshawar, Pakistan; Northwest General Hospital is a project of Alliance Healthcare (Pvt.) limited, and it is a 220 bedded state of the art hospital and research facility based in the Hayatabad, Peshawar.

All participants admitted to Medical Ward were screened for eligibility. Confirmed and suspected cases were included in the study based on the initial respiratory symptoms and clinical suspicion. The data was recorded using a predesigned structured format. Demographic data, co-morbid diseases, and clinical laboratory data, hospital stay and outcomes were collected prospectively. Patients were followed up until death or hospital discharge, whichever occurred earlier. Ethical approval for the study was obtained from hospital ethics committee.

Patients were admitted in concordance with hospital admission policy and treated in isolation rooms specified for H1N1 suspected/confirm cases. All patients were treated with antipyretics, fluids, anti-viral, supplemental oxygen for those requiring it and Non invasive ventilation and invasive mechanical ventilation for suitable candidates.

Data are expressed as mean±standard deviation SD), median, percentage, or frequency. Continuous variables in normal and non-normal distribution were compared using unpaired Student's t-test and rank-sum test, respectively; Categorical variables were compared using chi-square test or Fisher's exact tests as appropriate; the remaining were summarized with informal descriptive analysis. A two-sided P value less than 0.05 was considered to indicate statistical significance. All analyses were carried out with SPSS software for Windows (release 16.0).

RESULTS

The mean age of the patients was 45.23±15.03 years and 50% of them were male. 23(88.5%) were married, 6(23.1%) were Afghan nationals while rest of the 20 patients were local, 2(7.7%) were smokers, 5(23.1%) gave history of exposure to birds and animals with in the week before onset of the symptoms, 6(23.1%) had travel history in recent days and none of the 26(100%) patients had ever been vaccinated against flu.

Table 1: Demographic and clinical characteristics of the patients

Variables	No. of patients & %ages
Age (years) Median 41 years	45.23±15.037
Gender	
Male	13(50%)
Female	13(50%)
Marital status	
Married	23(88.5%)
Unmarried	3(11.5%)
Nationality	
Pakistani	20(76.9%)
Afghani	6(23.1%)
Symptoms duration before seeking medical consultation (days)	5.9±3.42
Smoking	
Current smoker	2(7.7%)
Non smoker	24(92.3%)
History of travel	
Yes	6(23.1%)
No	20(76.9%)
Exposure to animal and birds	
Yes	5(23.1%)
No	21(80.8%)
Previous flu vaccination	
Yes	00(00%)
No	26(100%)
Symptoms	
Fever	24(92.30%)
Temperature	37.45±0.44C°
Shortness of breath	22(84.61%)
Dry cough	24(92.30%)
Productive cough	1(3.84%)
Sore throat	4(15.38%)
Diarrhea	2(7.69%)
Body aches	2(7.69%)
Chest pain	4(15.38%)
Loss of appetite	1(3.84%)
Haemoptysis	2(7.69%)

Table: 2 Underlying illness and outcomes of the patients with influenza A (H1N1) virus

Variables	Value
Co-morbidites	N%
Hypertension	9 (34.61%)
Diabetes mellitus	2(07.69%)
Asthma	4(15.38%)
Pregnancy	3(11.53%)
Others*	7(26.92%)
None	7(26.92%)
Length of hospital stay (days)	7.85± 11.7
Mortality	34.6%

*Immune thrombocytopenic purpara, Psoriasis,dyslipidemia,Ishcemic heart disease, Pulmonary tuberculosis

Table 3: Laboratory profile /Investigation

Variables	Value*
C-Reactive Protein mg/dl	8.2870±7.98 (0.60-35)
Platelets per/liter	221.9±93.15(69.0-471)
Spo2 (percentage)	81.73± 12.1 (60-99)
Leukocyte count ($\times 10^9$ L−1)	8.5± 4.9 (2.60-22.10)
ALT/SGPT iu/L	47.28± 42.25(10-192)
Serum Albumin g/dl	3.5±0.5(2.60-4.60)
RT-PCR	
Positive	11(42.31%)
Negative	15(57.69%)

*Mean ±SD and range

On average patients had their first medical consultation 6 days after the onset of symptoms, among 26 patients 24(92.30%) developed fever with a mean value of 37.45±0.44 C. Other most common symptoms were Shortness of Breath (SOB) 22(84.61%), dry cough 24 (92.30%), chest pain and sore throat 4(15.38%). The less common symptoms were Productive cough, Diarrhea, Body aches, Loss of appetite and Haemoptysis) are given in Table 1. Hypertension 9(34.61%) and asthma 4(15.38%) were reported as the most common co-morbidities, whilst three of the patients were pregnant. The median durations of symptoms before admission 5.9±3.42 and average length of hospital stay was 7.85± 11.7 days. In this study 17(65.4%) survived and 9(34.6%) patients died. As shown in Table 2. Detailed laboratory values collected on the day of admission included are given in Table 3.

There were no significant differences between the deaths and survivors regarding gender, age, smoking, history of travel and exposure to animals and birds, symptoms duration before seeking the medical consultation, and laboratory values.

We also compared the length of hospital stay which was significantly associated with outcome p=0.006, Oxygen saturation on arrival was statistically significant among survivors p=0.009. The use of inva-

Table 4: Comparison of clinical features between survivors and death

Variables	Value		P-value
	Survivors N=17	Death N=9	
Age	44.18±16.24	47.22±13.12	0.63
Gender			0.21
Male	7(26.9%)	6(23.1%)	
Female	10(38.5%)	3(15.5%)	
Smoking			0.63
Smoker	1(3.8%)	1(3.8%)	
Non-smoker	16(61.5%)	8(30.8%)	
History of travel			0.42
Yes	6(23.07%)	0	
No	11(42.30%)	9(34.61%)	
Exposure to animal and birds			0.77
Yes	3(11.5%)	2(7.7%)	
No	14(53.8%)	7(26.9%)	
Length of hospital stay (days)	10.24±13.84	3.3±2.69	0.006*
Symptoms duration before seeking the medical consultation	6.41±3.75	4.89±2.57	0.28
Number of underlying diseases	0.88±0.86	1.11±0.60	0.48
C-reactive protein	7.89±8.33	14.13±8.92	0.09
Platelets	236.50±103.41	194.22±66.52	0.28
Leukocyte count (×109 L−1)	8.71±4.99	7.98±5.10	0.51
ALT/SGPT iu/L	48.14±46.80	45.57±30.33	0.89
Albumin	3.54±0.48	3.30±0.62	0.35
Oxygen saturation (%)	86.11±11.61	73±8.71	0.009*
Support			0.02*
Non invasive ventilation	3(11.5%)	5(11.2%)	
Invasive Mechanical ventilation	1(3.8%)	2(7.7%)	
None	13(50.0%)	2(7.7%)	

sive mechanical ventilation was significantly higher in the deaths than the survivors (18.9% vs15.3%, $p<0.02$). Comparison of other clinical features between the survivors and the deaths are summarized in Table 4.

Radiological pattern of all the patients were analyzed in detail for various abnormalities. Ground glass opacities were presents in 13(50%) of our patients. Patchy opacities were noted in 8(30.76%) of the subjects, while 3(11.53%) showed consolidation. 21 patients had both central and peripheral distributions and all of them had multi-zonal involvement, not a single patient had single zone involvement. Majority of the 20(76.22%) had bilateral involvement as their initial presentation .Pleural effusion was found in 2(7.6%) patients and in 3(11.53%) patients initial chest x-rays were normal.

DISCUSSION

Most of the patients in this study were middle aged. Age group of population involved with H1N1 worldwide is variable in different studies done in other parts of the world. This varied presentation may be due to the ubiquitous involvement of the H1N1 virus in any age group person without any predisposing factor[11].

There was no predilection for gender in this study. The clinical presentation remained similar to those from other countries worldwide, with fever, dry cough and shortness of breath being the major symptoms. Other symptoms that were present included chest pain, sore throat and body aches. In this study, 73.07% had co-morbidities like Hypertension, Asthma, and Diabetes Mellitus and pregnancy. One study[12], has found that individuals with co-morbid conditions like, bronchial asthma, COPD, diabetes mellitus, and cardiac disease were more susceptible to H1N1 viral infection. Pregnant women are at greater risk for both influenza and its complications which can particularly increase the mortality[13] in this study there were three pregnant patients. Since the sample size in this case is small; it is difficult to correlate the association of co-morbidities with influenza infection.

In our study none of the patient was previously vaccinated against flu, therefore mass public education and easy availability of the flu vaccine is another potential aspect to be addressed by the health authorities. The mortality in this study was 34.6% is lower than that of Mexico 41.4%, but higher than that of California 11.0%[14,15]. Thompson et al described that influenza related deaths occurs in older patients but the deaths in our patients had a median age 41 years[16]. The radiological presentations in H1N1 patients varied, ranging from ground-glass appearance to confluent or patchy opacities, reticular pattern, multi-zonal involvement and bilateral distribution. These findings are consistent with those observed by other authors[11,17].

Aviram et al[17] studied in detail the radiological presentation in H1N1 pneumonia and, they observed the radiological opacity to be ground-glass in nature in majority of patients (69%), predominantly of central location and less frequently observed in peripheral locations. Consolidation was also frequent in manifestation, and was either patchy in distribution or presented as rounded nodular opacities. In one third of patients air bronchogram could be detected and mid lung zones were most frequently involved sites compared to lower lung zones. Rapidly progressive respiratory failure is relatively common and about 10-30% of hospitalized patients required ICU admission[18]. Intermittent mandatory ventilation, with a lung-protective ventilation strategy, is recommended as the initial approach for managing patients with pandemic A (H1N1) infection complicated by Acute Respiratory Distress Syndrome.

Current CDC guidelines for pandemic and seasonal influenza recommend the use of either Oseltamivir or Zanamivir for hospitalized patients with suspected or confirmed influenza and for outpatients who are at risk for complications[19]. Early initiation of antiviral therapy (within 48 hrs) has been observed to be favorable and is associated with fewer complications[20]. Oseltamivir was given to 16(76.2%) patients as soon as possible in this study and its application is strongly recommended by WHO as well. Oseltamivir is especially important for patients for underlying risk factors[21]. Although Oseltamivir was shown to hasten recovery and reduce viral load, its long-term effectiveness for pandemic H1N1 influenza A remains uncertain[22]. Despite the apparent efficacy of Oseltamivir in mild cases, its efficacy in halting further disease progression of late cases remains uncertain[23]. A study has reported that patients admitted to ICU or those who died were less likely to have received antiviral therapy within 48 hrs after onset of symptoms[24]. Chudasama et al[25] has reported mortality up to 90% in severe disease patients even after complete course of Oseltamivir therapy, possibly because of delayed referral and initiation of antiviral drugs. Though 16(76.2%)of

the patients received Oseltamivir therapy on the first day of admission, the effect could not be assessed as most of the cases were referred and had variable duration, from onset of symptoms to presentation to our centre. Thus, the mortality in this study is also attributed to the delay in presentation. Moreover, the RT-PCR report in this part of the world is obtained by the time patients has progressed from the window period of theraputic oseltamivir treatment. This inconvenience in report availability consequently affects severity of disease and subsequently results in ICU admission or death.

CONCLUSION

Widespread involvement of both lungs as articulated by the presence of multi-zonal involvement and bilateral peripheral opacities on chest radiograph was associated with poor prognosis.

RECOMMENDATIONS

The need for early initiation of the antiviral therapy and close monitoring in these patients irrespective of PCR positivity will reduced the mortality.

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CONFLICT OF INTEREST: Authors declare no conflict of interest

GRANT SUPPORT AND FINANCIAL DISCLOSURE NIL

AUTHOR'S CONTRIBUTION

Following authors have made substantial contributions to the manuscript as under:

Ijaz M: Concept, idea, data collection.
Samad A: Concept and idea.
Ali I: Data collection, statistical analysis & manuscript typing.
Khalil A: Bibliography.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.