

Characteristics and outcomes of hospitalized patients with influenza (H1N1) during 2018–19 at a tertiary care hospital, Peshawar, Pakistan

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Abstract

Swine-origin influenza (H1N1) virus appeared in 2009 which spread worldwide, and it still circulates in the population. This study aimed at exploring the clinical manifestations and results in admitted patients having H1N1 influenza. All patients with confirmed or suspected influenza (H1N1) who reported to NWGH & RC, Peshawar, Pakistan from January 2018 till December 2019 were included in the study. Data was collected on demographics, preexisting medical conditions, duration of hospital stay, clinical laboratory data, outcome, and clinical features. Distribution of variables was assessed using histograms, comparison of continuous variables was done via independent Student's t-test and of categorical variables using Chi Square test. A p value of $[?]0.05$ was set as cut-off for significance. A total of 39 patients presented to the hospital during the study period. Mean age was 52 (15.8) years and the proportion of male and female participants was 43.6% and 56.4% respectively. Clinical features included fever, shortness of breath, cough, chest pain, body aches and sore throat. The most commonly occurring comorbidities were hypertension [21 (53.8%)], diabetes [11 (28.2%)], and chronic kidney disease [3 (7.7%)]. Real time PCR positivity was present in 36 (92.3%) patients. Overall, 30 (76.9%) survived while 09 (23.1%) died. Comparison of the clinical parameters of survivors and non-survivors showed that non-survivors had significantly higher risk of renal failure ($p=0.01$), ionotropic disturbances ($p=0.001$), secondary infection ($p=0.03$), septic shock ($p=0.001$), and respiratory problems, requiring non-invasive ventilation and invasive mechanical ventilation ($p=0.001$).

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Abstract

Swine-origin influenza (H1N1) virus appeared in 2009 which spread worldwide, and it still circulates in the population. This study aimed at exploring the clinical manifestations and results in admitted patients having H1N1 influenza. All patients with confirmed or suspected influenza (H1N1) who reported to NWGH & RC, Peshawar, Pakistan from January 2018 till December 2019 were included in the study. Data was collected on demographics, preexisting medical conditions, duration of hospital stay, clinical laboratory data, outcome, and clinical features. Distribution of variables was assessed using histograms, comparison of continuous variables was done via independent Student's *t*-test and of categorical variables using Chi Square test. A *p* value of $[?]0.05$ was set as cut-off for significance. A total of 39 patients presented to the hospital during the study period. Mean age was 52 (15.8) years and the proportion of male and female participants was 43.6% and 56.4% respectively. Clinical features included fever, shortness of breath, cough, chest pain, body aches and sore throat. The most commonly occurring comorbidities were hypertension [21 (53.8%)], diabetes [11 (28.2%)], and chronic kidney disease [3 (7.7%)]. Real time PCR positivity was present in 36 (92.3%) patients. Overall, 30 (76.9%) survived while 09 (23.1%) died. Comparison of the clinical parameters of survivors and non-survivors showed that non-survivors had significantly higher risk of renal failure ($p=0.01$), ionotropic disturbances ($p=0.001$), secondary infection ($p=0.03$), septic shock ($p=0.001$), and respiratory problems, requiring non-invasive ventilation and invasive mechanical ventilation ($p=0.001$).

Keywords: Infectious disease, H1N1, Influenza, Mortality, morbidity, Pakistan, South Asia

Introduction

Influenza is an acute respiratory illness⁽²⁾ caused by the influenza viruses. These viruses have led to a number of outbreaks and epidemics, causing significant morbidity and mortality globally. Type A and B are the main human pathogens, with the former being very common and associated with most large-scale and serious outbreaks.⁽³⁾ Type A virus possesses the ability to periodically change the structure of its antigen (antigenic shifts and antigenic drifts). . These antigenic shifts and antigenic drifts are linked to annual pandemics. The incubation period of Type A influenza virus is ~24-48 hours, after which symptoms such as rapid onset of fever, headache, fatigue, and muscle pain, start to appear .⁽⁴⁾ These symptoms are associated with manifestations of disease of the respiratory tract, including cough, sore throat and rhinitis.⁽⁵⁾ In these patients, a common and dangerous complication is bacterial pneumonia. The mortality rate is high and mainly attributed to refractory hypoxia.⁽⁶⁾

The widespread H1N1, subtype influenza A virus, appeared first during spring 2009 in Mexico from where it spread swiftly across the globe.⁽⁷⁾ On June 11, 2009, a phase 6 pandemic alarm was declared by the World Health Organization (WHO), suggesting that the 21st century's initial influenza pandemic had started. The height of the local influenza outbreak had gone by in the majority of the countries by the close of 2009.⁽⁸⁾ The novel H1N1pdm09 virus still circulates (with antigenic evolution and variability) among the population, and plays a part in the usual seasonal epidemics of influenza.⁽⁹⁾ The global 2009 H1N1 virus led to extensive

transmission among the United States and other countries, and accounted for approximately 61 million cases, 274,000 hospital admissions, and 12,470 deaths.^{(10),(11)}

Till now, internationally over 214 countries and territories have reported lab-confirmed cases of H1N1, with 17,919 deaths⁽¹²⁾, as well as enormous economic effect covering both direct and indirect expense.⁽¹³⁾ In a new case series, the lag between the manifestation of the symptoms and starting the treatments has been linked to unfavorable results.⁽¹⁴⁾ As regards the patients diagnosed with influenza, longitudinal reviews are required to draw an estimation of the fraction of cases that advance to death, respiratory failure, or need extended hospitalization.⁽¹⁵⁾ The earliest case of swine flu (H1N1) in Pakistan, confirmed by laboratory testing, was found on the 10th of August 2009, with occasional cases reported every year thereafter. Pakistan was afflicted by the H1N1 epidemic from winter 2015 until February 2016, during when over 240 confirmed cases were reported.⁽¹⁾ But regarding hospitalizations of the affected patients, its clinical manifestations and outcomes, limited studies have been carried out in Pakistan. Our aim was to evaluate the clinical manifestations and results in patients admitted to the hospital having H1N1 influenza virus infection. The objectives of this research were to evaluate the clinical features and its outcomes in H1N1 influenza patients being treated at NWGH & RC, Peshawar.

Methods

All patients with confirmed or suspected H1N1 who reported from January 2018 till December 2019 at the Department of Medicine & Allied, Northwest General Hospital & Research Centre (NWGH & RC), Peshawar, Pakistan were recruited to the study.

Participants were enrolled to the study based on early respiratory symptoms and clinical suspicion as assessed by the physician and/or positive results of the rapid real-time polymerase chain reaction. A structured questionnaire was used to collect data on demographics, underlying medical conditions, smoking history, duration of hospital stay, clinical laboratory data, outcome, and personal history. Participants were observed till either death or discharge from the hospital, whichever happened first. Patients were admitted in accordance to the hospital's admission policy and treated in the isolation rooms meant specifically for either suspected or confirmed patients of H1N1. Blood samples for biochemical analysis were collected on the day of admission. They were all given fever medications, fluid therapy, antivirals, oxygen therapy, as well as noninvasive ventilation and invasive mechanical ventilation as per individual needs.

Statistical analysis was performed using SPSS software (version 23; SPSS, Chicago, IL, USA). Distribution of variables was assessed by histograms. Results are expressed as mean (standard deviation SD) and percentage, or frequency for continuous and categorical variable respectively. Comparison of continuous variables was done via the independent Student's *t* -test while that of categorical variables was done via the chi-square test. A two-sided P value less than 0.05 was used to show statistical significance.

The hospital ethics committee granted this study ethical approval (Ref#: IRB-EB/NWSM/696/2020). All participants provided informed written consent.

Results

A total of 39 cases reported at the NWGH & RC during the specified study period. Their mean age was 52(15.8) years and female to male ratio was 1:1.29 (Males: 43.6% and Females: 56.4%). All patients in the study developed cough. The next most common symptom was shortness of breath in 37 patients (95%), followed by fever in 36 (92.3%), chest pain and sore throat in 31 (79.5%) each, **Table 1** .

The different co-morbidities amongst patients and the patients' outcomes are presented in **Table 2**. Hypertension [21 (53.8%)] was reported as the most common comorbidity followed by diabetes [11 (28.2%)] and chronic kidney disease [3 (7.7%)]. Smoking history was positive for 3 (7.7%) patients. Amongst all participants, 30 (76.9%) survived and were discharged while 09 (23.1%) passed away (**Table 2**).

Table 3 presents the results of biochemical analysis performed on blood samples collected on the day of admission. Mean Hb level was 13.19 (2.12) g/dl. Both the pO₂ and pCO₂ levels were below the normal

reference range ($<83\text{mmHg}$ and $<40\text{mmHg}$ respectively). CRP [12.84 (9.44) mg/dl], ESR [45.60 (26.11) mm/1st hour] and Troponin I [2411.59 (9903.25) ng/l] were also raised above the normal reference values. Real time Polymerase Chain Reaction (PCR) was positive in 36 (92.3%) patients as shown in **Figure 1**.

Clinical characteristics were compared between the survivors and non-survivors (**Table 4**). There was no significant difference between the age ($p=0.8$), gender distribution ($p=0.6$), smoking status ($p=0.5$), length of hospital stay ($p=0.6$) and duration of symptoms ($p=0.2$). Comparison of different comorbidities showed that although the proportion of patients having respiratory failure was higher in non-survivors than in the survivors, the difference was not statistically significant [n (%): 9 (100) vs. 21 (70.00), $p = 0.1$, respectively]. In contrast, the proportion of patients who developed renal failure ($p=0.02$, secondary infection ($p<0.001$) and septic shock ($p=0.03$) was significantly higher amongst the non-survivors compared to that amongst survivors. Furthermore, a significantly higher proportion of non-survivors required Ionotropic support ($P<0.001$) and ventilator support ($p=0.001$) than the survivors while a similar proportion of non-survivors and survivors required oxygen support ($p=0.6$).

Discussion

Our study findings reveal that a total of 39 confirmed or suspected cases of H1N1 presented to the hospital from January 2018 till December 2019. Clinical features included fever, shortness of breath, cough, chest pain, body aches and sore throat. The most commonly occurring comorbidities were hypertension, diabetes, and chronic kidney disease. Biochemical profile of these patients showed low levels of pO_2 and pCO_2 whereas CRP, ESR and Troponin I were raised above the normal reference values. Of the 39 participants, 30 (76.9%) survived while 09 (23.1%) did not survive. Comparison of the clinical parameters of survivors and non-survivors showed that non-survivors had significantly higher risk of renal failure, ionotropic disturbances, secondary infection, septic shock, and respiratory problems, requiring non-invasive ventilation and invasive mechanical ventilation.

In a study conducted by Ijaz M et. al, length of hospital stays had a significant impact on the survival of patients ($p=0.006$) with patients expiring significantly earlier than the survivors.⁽¹⁾ In our study, no such pattern was seen. This could be due to almost similar duration of stay in both survivors and death patients in our setup. The longer stay pertains to the patient developing hospital acquired infections and hence an increased chance of death. In another study by Kumar TCN, similar results to ours were found ($p=0.254$).⁽²²⁾

In our study 36.67% survivors required ventilatory support while the remaining did not. All patients that died were on ventilatory support. A similar picture was seen in the study conducted in the same setup in 2017.⁽¹⁾ Patients requiring ventilatory support showed a significantly high mortality in other studies too ($p<0.05$).⁽²³⁾ Previously a similar study in China reported comparable results⁽¹⁶⁾. Deaths were reported in 10 (14.7%) of the patients while the clinical manifestations were mainly cough in 60 (88%), respiratory problems in 31 (46%), and myalgia in 18 (27%) patients. Another study by Chudasama R, et al⁽¹⁷⁾ was conducted in 1726 patients in India. Similar symptoms were reported amongst these patients [cough (93.9%), pyrexia (90.8%), shortness of breath (66.5%) and sore throat (59.9%)] while death was reported in 127 (24.9%) out of the total patients.

Fajardo-Dolci G, et al⁽¹⁸⁾, in his study, described the comorbidities amongst patients with H1N1. Results from the study showed metabolic syndrome (40%), cardiovascular disease (21%), hypertension (20%) and diabetes mellitus (20%) as the main chronic medical conditions amongst these patients. These study findings are in line with our results where hypertension and diabetes were present in 53.8% and 28.2% of the patients respectively. Major clinical manifestations reported by Fajardo-Dolci G, et al⁽¹⁸⁾ were pyrexia (84%), cough (85%), shortness of breath (75%) and muscle pain (30%). Similar findings have been documented by other research studies as well⁽¹⁹⁾ ⁽²⁰⁾.

A study was conducted in intensive care unit patients of H1N1 where the biochemical profile of all patients was similar to that of our study with significant differences seen in only the creatinine levels (1.9mg/dl compared to 1.14mg/dl). All other biochemical markers were in the same limits⁽²¹⁾. CRP levels in our study were found to be higher compared to a study conducted by Ijaz M et.al while all the other biochemical

parameters showed a similar trend⁽¹⁾.

In summary, our study has highlighted the important clinical features and its outcomes in H1N1 influenza patients in a hospital setting in Pakistan. Major clinical features were fever, shortness of breath, cough, chest pain, body aches and sore throat while most commonly occurring comorbidities were hypertension, diabetes, and chronic kidney disease. Biochemical profile of these patients showed low levels of pO₂ and pCO₂ whereas CRP, ESR and Troponin I were raised above the normal reference values. Non-survivors had significantly higher risk of renal failure, ionotropic disturbances, secondary infection, septic shock, and respiratory problems, requiring non-invasive ventilation and invasive mechanical ventilation.

CONCLUSION

Patients with H1N1 influenza infection have increased risk for advancement of illness, particularly patients of older age, having renal failure, or those who are admitted with secondary infection.

RECOMMENDATION

Increased usage of tetravalent influenza vaccine may prove useful in the prevention of future cases of influenza and its consequent hospitalizations.

CONFLICT OF INTEREST

Authors have no conflicts of interest to declare.

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Table 1: Demographics and Symptoms of Patients with confirmed or suspected H1N1

Characteristics

	No. of Patients & Percentages n (%)
Age [years (SD)]	52 (15.8)
Gender	Gender
Male	17 (43.6%)
Female	22 (56.4%)
Symptoms	Symptoms
Fever	36 (92.3%)
Shortness of Breath	37 (95%)
Cough	39 (100%)
Chest Pain	31 (79.5%)
Body Aches	31 (79.5%)
Sore throat	31 (79.5%)

Table 2: Co-morbidities and Outcomes of Patients having H1N1 Influenza

Variables	No. of Patients & Percentages n (%)
Co-morbidities	Co-morbidities
Hypertension	21 (53.8%)
Diabetes Mellitus	11 (28.2%)
Chronic Kidney Disease	3 (7.7%)
Smoking	
Current Smokers	3 (7.7%)
Non-Smokers	36 (92.3%)
Outcomes	Outcomes
Discharged	30 (76.9%)
Expired	9 (23.1%)

Table 3: Biochemical profile of confirmed and suspected cases of H1N1.

Variables	Units	Mean (SD)
Hemoglobin (Hb)	g/dl	13.19 (2.12)
White Blood Cell Count (WBC)	$\times 10^3$ u/L	9.42 (4.92)
Platelets (PLT)	$\times 10^9$ /L	215.90 (103.73)
pH	-	7.44 (0.07)
pO ₂	mmHg	64.42 (19.46)
pCO ₂	mmHg	33.74 (8.77)
C-Reactive Protein (CRP)	mg/dl	12.84 (9.44)
Erythrocyte Sedimentation Rate (ESR)	mm/1 st hour	45.60 (26.11)
Serum Creatinine	mg/dl	1.14 (0.92)
Blood Urea	mg/dl	46.30 (37.55)
Alanine Transaminase (ALT)	U/L	39.27 (23.74)
Albumin	g/dl	3.12 (0.68)
Troponin I	ng/l	2411.59 (9903.25)

Table 4: Comparison of Clinical Features Between Survivors and Non-survivors of H1N1

Characteristics	Survivors (30)	Non-survivors (9)	p-Value
Age [years (SD)]	52.03 (15.80)	51.33 (17.31)	0.8
Gender	Gender	Gender	0.6
Male, n (%)	13 (43.33)	4 (44.44)	
Female, n (%)	17 (56.67)	5 (55.56)	
Smoking	Smoking	Smoking	0.5
Smoker, n (%)	2 (6.67)	1 (11.11)	
Non-smoker, n (%)	28 (93.33)	8 (88.89)	
Length of Hospital Stay (days)	7.53 (4.42)	6.78 (4.94)	0.6
Duration of Symptoms [days (SD)]	7.30 (3.02)	8.56 (5.00)	0.2
Respiratory Failure, n (%)	21 (70.00)	9 (100)	0.1
Renal Failure, n (%)	6 (20.00)	6 (66.67)	0.02
Ionotropic Support, n (%)	3 (10.00)	8 (88.89)	<0.001
Secondary Infection, n (%)	19 (63.33)	9 (100)	0.03
Septic Shock, n (%)	3 (10.00)	9 (100)	<0.001
Ventilator Support, n (%)	11 (36.67)	9 (100)	0.001
Oxygen (O ₂) Support, n (%)	22 (73.33)	7 (77.79)	0.6

Figure 1: PCR Results amongst patients with confirmed or suspected H1N1

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