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Original Research Article

Mortality Predictors in Influenza Pneumonia: A Prospective Study in a Tertiary Care Hospital

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Abstract

Objectives: Influenza causes annual seasonal epidemics around the world. Periodically, genetically novel strain of influenza circulates worldwide, causing an influenzas pandemic. The present study aims to assess the clinical profile, prognosis of the disease and outcome in influenza positive patients during 2017-2018 epidemics in Kashmir, so that epidemiology of the disease could be known, and high-risk groups can be identified.

Methods: All influenza positive patients, confirmed by RT -PCR method, admitted in ICU / Isolation ward in SHER –I-KASHMIR INSTITUTE OF MEDICAL SCIENCES SOURA KASHMIR during epidemic of influenza (2017-2018) were studied, the data collected was analyzed.

Results: During the study period there were 124 influenza positive admissions. The age group most affected was 20-59 years males (49.2%) and females (50.8%). There were 30 deaths; mortality was high in rural population 73.33% (n=22) and patients with underlying comorbidities. Common presenting symptoms were fever, cough, breathlessness, sore throat.

Conclusion: Swine flu influenza infection took its heaviest toll in terms of human lives and economy because the young and productive population was mostly affected. Patients with co-morbid conditions and pregnant women were the susceptible population and thus preventive and therapeutic interventions should be directed to them. Early vaccination of high-risk groups and high index of suspicion in the symptomatic patients and chemoprophylaxis accordingly can save many human lives.

Keywords: Influenza, Prognosis of Disease, Epidemic, Population

Introduction

Influenza is a vaccine-preventable disease and a major cause of morbidity and mortality in developed and developing countries [1,2] in temperate regions of the Northern and Southern Hemispheres, influenza activity has been well described with its typical seasonality [3] and annual epidemics associated with excess deaths from influenza.

Few data are available to assess the epidemiology and burden of influenza in tropical and developing countries [4].

Improved understanding of the temporal and geographic circulation of influenza viruses and the impact of influenza among populations living in tropical and subtropical regions is essential for the development of influenza prevention and control strategies. A novel influenza A (H1N1) virus emerged in mid-April 2009 and spread rapidly among humans worldwide [5,6]. It always had potential to cause widespread pandemics whenever a new type of Influenza strain appeared in the human population and then spread easily from person to person [7]. In April 2009, a new strain of Influenza virus A H1N1, commonly referred to as "swine flu," began to spread in several countries around the world. The recent H1N1 virus strain has been found to be closely related to the swine flu virus, but with a genetic composition that is quite different from the earlier known isolates. This novel virus presented genetic characteristics that had not been previously identified in Influenza A in humans, swine or poultry [8,9]. India confirmed its first case on 16 May 2009, when a man travelling from New York via Dubai and Delhi tested positive for the H1N1 Influenza virus in Hyderabad [10]. The second case was reported by the National Institute of Virology (NIV), Pune, in a mother and son duo from Chennai on 1 June 2009 [7].

There are three known types of influenza viruses, labelled A, B and C. These are further divided into subtypes based on the variety and the combination of two surface proteins: hemagglutinin (HA) and neuraminidase (NA). Several combinations of HA and NA subtypes are possible. Currently, influenza A (H1N1) and A (H3N2) are the circulating seasonal influenza A virus subtypes. In addition, there are two type B viruses that are also circulating, the Victoria and the Yamagata lineages. Type C influenza causes milder infections and is associated with sporadic and localized outbreaks [11]. Influenza viruses may undergo mutations by antigenic drift or antigenic shift [12]. The antigenic drift produces a new virus strain that is new to our immune system, even in individuals who have been previously exposed through infection or vaccination. The antigenic shift is a sudden change which results in a new influenza subtype or a virus with a combination of HA or NA that has emerged from an animal species that is so different from the same subtype in humans that most people do not have immunity to the new virus. Such a 'shift' occurred in the spring of 2009. A new H1N1 virus emerged to infect people and quickly spread causing a pandemic. Globally, within only three months, the documented cases rose to 277,607 persons and the fatalities to 3,205 [13].

The pandemic was declared, by the World Health Organization (WHO), as officially over in August 2010. From then on, the H1N1 virus has become a regular flu virus which circulates seasonally and causes outbreaks in different areas of the world. Asian countries have been receiving global attention because of the risk of emerging infectious diseases with pandemic potential; in fact, most antigenic shifts in the influenza virus rise from Asia. In India, in just the first two and a half months of 2015, the number of reported cases of swine flu was 27,000 and 1,500 deaths in the country [14]. The State of Jammu and Kashmir is in the northernmost part of the Indian Union. It lies between 32.17" and 36.58" North altitude; and East to West, between 73.26" and 80.30" longitude. The Province of Kashmir, within the State of Jammu and Kashmir, is composed of twelve districts with an estimated population of four million people. The province borders Pakistan, China, and Afghanistan.

Previous investigations have shown that the seasonality of the influenza virus depended on the hemisphere of the geographical area, with local variations depending mainly on transmission factors [15,16]. Moreover,

sentinel surveillance of influenza has shown distinct peaks across India [17,18]. In Delhi, the peaks of influenza activity coincide mainly with the monsoon season, followed by a minor peak in winter in both urban and rural settings [17]. In Northern India, the virus demonstrates peak activity during the winter months which extend from December till March [16]. As there are very limited studies relating to Influenza H1N1 and its epidemiology in the Indian situation, this study aimed to study the clinic epidemiologic profile of patients found positive for Influenza H1N1 at SHER-I-KASHMIR INSTITUTE OF MEDICAL SCIENCE SOURA.

Material and Method

Sher-i-Kashmir Institute of Medical Sciences is a 650-bedded facility and constitutes the main tertiary care cum referral center for the respiratory cases for the valley of Kashmir. One hundred and twenty-four patients with acute respiratory illness (ARI) that presented to the Internal & Pulmonary Medicine Department of Sher-i-Kashmir Institute of Medical Sciences, Srinagar, over a period of 4 months from December 01 to March 14, 2018, were enrolled for the study. Nasal and throat swabs were collected from participants at enrollment for testing by reverse-transcription polymerase chain reaction for influenza A and B viruses, and those positive for influenza A viruses were further subtyped for A/H1N1pdm09, A/H3N2, and seasonal H1N1 using US Centers for Disease Control and Prevention (CDC) protocols.

Results

During December 2017–March 2018, 124 patients hospitalized with influenza confirmed cases were enrolled for study. Of these, 61 (49.2%) patients were male and 63(50.8%) were female. Most of the patients in present study were from rural area 67.75% (n=84). Most common age group affected was 41-59(38.7%). Most common symptom was fever followed by cough 92.7% (n=115). More than 90% patients were having associated comorbidities with most common comorbidity hypertensive heart disease 35%(n=44), diabetes 17.74%(n=22), COPD 16.93%(n=21), malignancy 12.09%(n=15) and pregnancy 10.48%(n=13). 59.67% (n=74) had anemia with hemoglobin <12 and 21.77% (n=27) had hemoglobin <8, table 1. 27.44% had leucopenia (n=34) and 20.96% (n=26) had leukocytosis table 2. Out of 124 patients admitted 85.5% had hypoxia (n=106) with most common radiological finding infiltrates followed by ARDS table 3, It was also found that 36.29% (n-45) had azotemia. In present 30 out of 124 patients expired, most of deceased person were male (n=19) and were from rural area (n=22) as shown in table 4. Most common comorbidities among deceased person were malignancy (n=5) followed by COPD and diabetes four patient were pregnant and one had CLD. Patients with age group 20-40 had high mortality (n=11) followed by age group of more than or equal to 60yrs (n=10), among the deceased Patients 17 patient's chest X ray was showing ARDS and 10 had infiltrates and 3 had consolidation as shown in table 5.

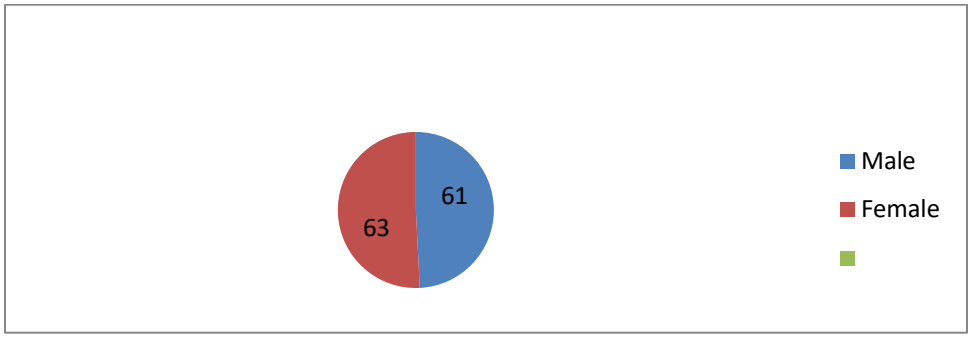


Figure 1

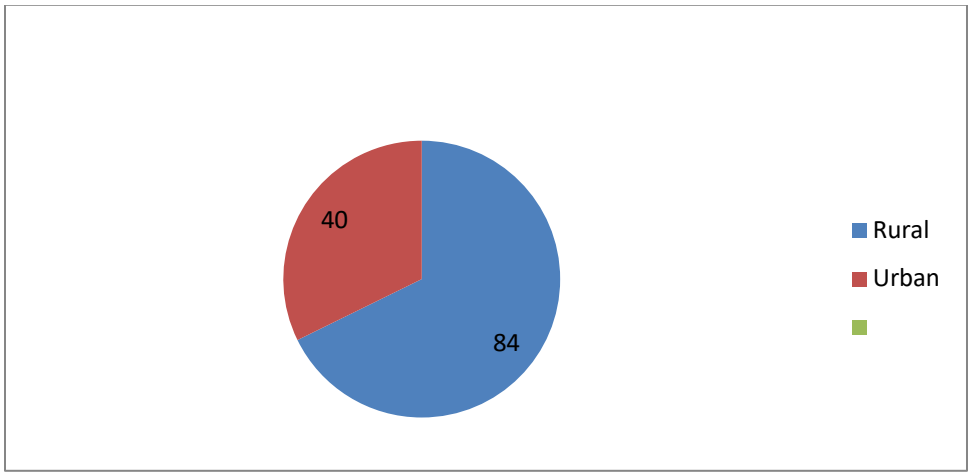
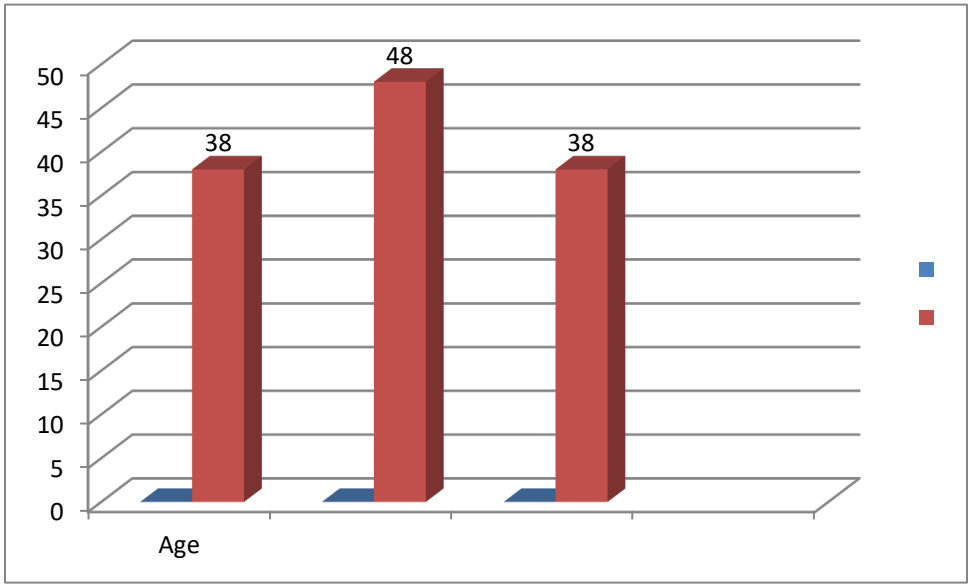


Figure 2



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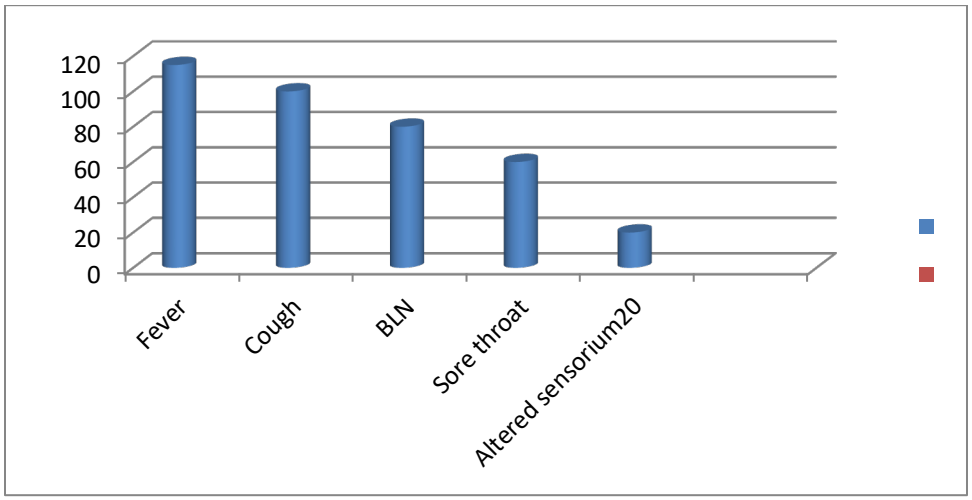

Figure 4

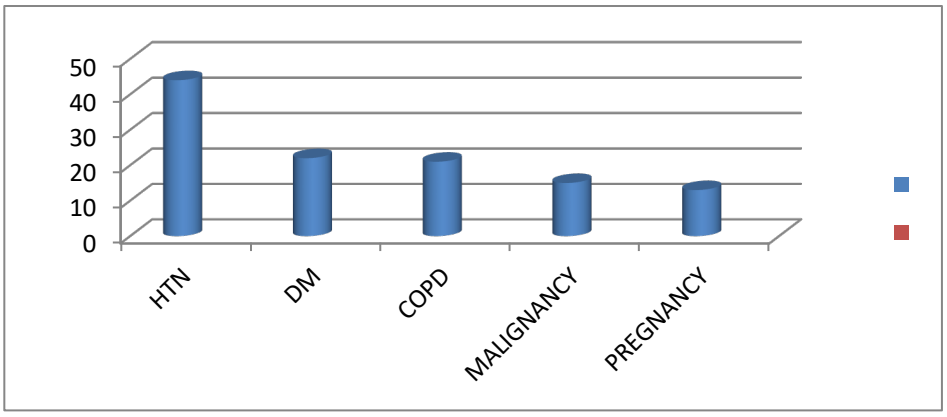

Figure 5

Table 1: Hemoglobin of the patients

Hemoglobin	No. of Patients	Percentage
<8	27	21.77%
8-12	47	37.9%
>12	50	40.32%

Table 2: White blood cell count of study population

WBC	No. of Patients	Percentage
<4	34	27.41%
4-12	64	51.61%
>12	26	20.96%

Table 3: Radiological manifestation, shock and MODS

Manifestation	No. of Patients (n)
Infiltrates	60
Consolidation	20
ARDS	26
Shock	24
MODS	20

Table 4: No of deaths as per gender and geographic distribution

No.of deaths	Males	Females	Rural	Urban
30	19	11	22	8
24.19%	63.33%	36.66%	73.33%	26.66%

Table 5: Radiological manifestation, shock and MODS in expired patients

Manifestation	No. of Patients died
ARDS	17
Consolidation	3
Infiltrates	10
Shock	16
MODS	12

Discussion

The present study was aimed to assess the clinical profile, factors, prognosis of the disease and outcome in influenza positive patients so that epidemiology of the disease could be known, and high-risk groups can be identified. The study was done on 124 influenza positive patients who were admitted in SKIMS hospital, Srinagar during epidemic 2017-2018. Among 124 studied patients males were 61 (49.2%) and female were 63 (50.8%), 84 (67.75%) from rural and 40(32.25%) from urban, most common age group effected was 20-59(n=86) 69.35%.our study is supported by study of Surinder [19] who also found the similar result that influenza infection predominantly affected females and the younger age group and study done by shyam Mathur *et al* [20] who found that rural population are more commonly effected than urban.

Most common clinical manifestation was fever followed by cough and breathlessness Rashmi Ranjan Das *et al* [21] in their study showed that fever was the most common symptom, followed by cough D.B. Kadam *et al* [22] in their study of H1N1 positive patients in Pune concluded that fever was the most common symptom (95%) followed by cough (88%). and breathlessness (77%). More than 90% patients were having associated comorbidities Due to presence of co-morbid condition; immune system of them was compromised. Infection of influenza in already compromised immune system lead to rapid in-crease in viral load.

When the viral load is high, the response to the treatment takes time and the co-morbid conditions get aggravated, leading to multi-organ failure or acute lung failure [23]. in the present study, thirteen females were pregnant. Pregnant women have been at higher risk for influenza associated morbidity and mortality [24-27]. Pregnant women if infected with H1N1, can rapidly develop a hemodynamic imbalance, which acutely affects lung function and facilitates the development of pneumonia, acute pulmonary edema, and other serious respiratory illness [28,29]. Pregnancy also reduces the ability of women to tolerate hypoxic stress, and thus in-creases risk of maternal and perinatal mortality.

Most common comorbidity was hypertensive heart disease (35%) followed by diabetes, COPD, malignancy and pregnancy (17.74%, 16.93%, 12.09%, 10.48%) respectively A study from the USA reported co-morbidities in 73 per cent of fatal cases; asthma, diabetes, heart, lung, neurologic diseases and pregnancy [30]; in addition, metabolic diseases, immunosuppressive conditions and neuromuscular disorders were reported from California [31].

Heart and respiratory diseases along with anemia, obesity and cancer were the common co-morbidities reported in Indian studies [32], We found that 59.67 %(n=74) patients had anemia with hemoglobin <12 the anemia in present study was higher as compared to study done by Hiren Jadawala *et al* [33] where they found anemia in 45.6% patients this difference can be attributed to poor nutrition, socioeconomic status**,** 51.61% (n=64) had normal leukocyte count, this was consistent with result showed by Hiren jadawala *et al* [33].

Out of 124 patients admitted 30 expired (24.19%) most of patients who expired where males (n=19) and from rural area (n=22) result was supported by study done by shyam mathur (20)*et al* who found higher rate of mortality in males and rural population. the morality rate in present study is higher than study done from other part of country The CFR was found to be 12.6 and 21 per cent in 2012 and 2013 in Western Rajasthan [34,35]. 1.8 per cent from south India 20 and 17.9 per cent in hospitalized patients at Jaipur [36]. this difference in CFR can be due to lack of awareness and delay in seeking medical advice. The reason for higher mortality

among rural population can be explained by living characteristics i.e., overcrowding, poor hygiene delay in seeking medical advice, and lack of awareness This view was supported by Rogelio Perez-Padella *et al* [37] in their study in Mexico who concluded that one contributing factor for death in the patients may have been delayed admission and delayed initiation of oseltamivir.

K. N. Bhatt *et al* [38] and D.B. Kadam *et al.* in their study concluded that higher mortality was associated with delayed presentation and late institution of oseltamivir. Most important contributing factor for increased mortality in present study was patients who presents with ARDS 56.66 %(n=17) this fact was supported by various studies. Louie J. K. *et al.* [39] in their study of H1N1 Influenza in California found that the most common causes of death were viral pneumonia and acute respiratory distress syndrome. D.B. Kadam *et al*. in their study of H1N1 positive patients in Pune concluded that patients who developed pneumonia and respiratory failure succumbed to death in more number.

A Puvanalingam *et al* [40] in their case study of the clinical profile of H1N1 swine flu influenza found that most common cause of death in patients was due to pneumonia and respiratory failure. this can be attributed to delay in starting oseltamivir because most of these patients received initial treatment outside the hospital, delay in diagnosis, poor vaccination, lack of awareness, mortality was also higher in patients with underlying comorbidities like malignancy 16.66%,diabetes 13.3%, COPD, pregnancy. Our result was supported by study done by Gerado chowel *et al* they also found higher mortality in patients with immunosuppression and diabetes, similar result were shown by study done by Hiren Jadawala *et al*, Diabetes and hypertension, IHD were co morbid condition and pregnancy was associated condition with H1N1 fatality.

Conclusion

Our study demonstrates that swine flu influenza infection took its heaviest toll in terms of human lives and economy because the young and productive population was mostly affected. The patients with co-morbid conditions and pregnant women were the susceptible population and thus preventive and therapeutic interventions should be directed to them. Primary prevention in form of vaccination and spread of herd immunity will help in combating this infection. Secondary prevention in form of early diagnosis and treatment, identifying alarming signs and symptoms such as severe breathlessness, tachypnea, and prompt referral to a Centre well equipped with ICU facilities can save lots of valuable human lives.

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