Research Article

Archives of Infectious Diseases & Therapy

The Clinical Characteristics and Outcome of H1N1 Pneumonia Patients with and without Acute Renal Injury

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Submitted: 03 May 2017; **Accepted**: 09 May 2017; **Published**: 12 May 2017

Abstract

Background: *Currently, little information exists about the impact of kidney injury and resource utilization in the form of renal replacement therapy in critically ill patients with II1N1 infections.*

Objectives: *Clarification of clinical characteristics and outcome of acute renal injury in patients with MINI pneumonia.*

Patients and Methods: *40 patients who were living in or visitors to Makkah region, admitted to the hospital and revealed confirmatory MINI injection, pneumonia and acute renal injury, were submitted to real-time reverse transcriptase-polymerase chain reaction (rRT-PCR). Severity of illness was assessed by using the Acute Physiology and Chronic Health Evaluation (APACHEJ II, Sequential Organ Failure Assessment (SOFA) score, Multiple Organ Dysfunction Score, and partial arterial 02pressure to the fraction of inspired 02 on high flow oxygen mask(PaOj/FIO?). Another severity score related to theseverity of pulmonary infiltrates (XRChest score) was used and Co-morbidities were recorded.*

Results: *77.5%ofthe patients had subjective fever, 72.5% chills, 97.5% cough, 90%fatigue, 82.5% headache, 80% nasal congestion, 70%sore throat, 85% myalgia, 40% ear pain, 37.5% nausea, 20% vomiting. Symptoms severity score of median 19 with range from 14-24. APACHEII score 26.3±9.7, SOFA score 97±3.8, MOD score 9+4.All patients had pneumonia confirmed radiological!}' with XR-chest score 13.4±3.6. The findings on chest radiographs were consisted with acute respiratory distress syndrome that required mechanical ventilation for 19 out of40 patients, only4 of them survived.*

Conclusion: *Acute renal injury is an adding impact of increasing the mortality rate of HINI pneumonial patients and may be related directly to the infection by this virusor complication to it which may be explained by severe hypoxia secondary to severe acute lung injury, multi-organ dysfunction. A high mortality in middle and old-aged patients with underlying medical co-morbidities was associated with higher Symptoms Severity, APACHE II, SOFA, MODS, and XRC scores.*

Recomondations: *Early recognition of the diseaseas well as prompt medical attention to provide opportunities aiming to limit the progression of the illness and to reduce the mortality. Prospective and controlled clinical trials are needed for clarifying the effectiveness of early treatment and protection by using H1N1 vaccination.*

KEYWORDS: Clinical Characteristics Outcome of HlNl-Pneumonia-Acute renal injury-APACHEII-SOFA-MODS.

INTRODUCTION

Currently, little information exists about the impact of kidney injury and resource utilization in the form of renal replacement therapy in critically ill patients with HlNl infections [1]. Patients admitted to the intensive care units (ICUs) with acute renal injury are at increased risk of mortality, prolonged ICU and hospital stay, and the development of chronic kidney disease [2]. During the severe adult respiratory syndrome corona virus outbreak, kidney injury and the need for dialysis were uncommon [3]. As of 21 March 2010. Worldwide, more than 213 countries and overseas territories had reported laboratory confirmed cases of pandemic influenza HlNl 2009, including over 16931 deaths [4]. World Health Organization (WHO) declared pandemic ofHlNl on 11 June 2009 [4]. Genomic analysis of this new 2009 virus indicated that it to be a reasserted virus containing genes from influenza A virus strains endemic in (mainly Eurasian) swine, avian species and humans [5]. The pandemic2009 influenza A(HlNl) virus caused wide spread transmission in the United States and other countries. The centers for disease control and prevention (CDC)

estimate that 43 millions to 89 million infections occurred in USA from April 2009 through April 10, 2010 with mid-range estimates of 274000 H1N1- related hospitalizations and 12470 deaths [6]. Children, young adults, pregnant women, and individuals with underlying chronic medical conditions appear to have a higher risk of hospital admission and critical illness when infected with the pandemic virus [7]. Serologic studies suggest that most children and young adults do not have preexisting cross-reactive antibodies against 2009 HlNl and that they are highly susceptible to infection [8]. A recent epidemiological study from the USA found that 40% of all hospitalized patients on admission had finding consistent with pneumonia on chest radiography [9]. It is difficult to compare the spectrum of illness and outcomes for 2009 HlNl and seasonal influenza A infections because most reports of 2009 HlNl influenza have been based on surveillance reports, particularly those for hospital admissions and fatalities [10].

The aim of this study was clarification of clinical characteristics and outcome in patients infected with HlNl Pandemic virus with acute renal injury.

PATIENTS AND METHODS

The source population included 60 patients (whatever citizens and residents living in or visitors to Makkah region),.admitted to HGH and revealed confirmatory HlNl infection, pneumonia and then subdivided into two groups; first group 40 HlNl pneumonia patients with features of acute renal injury, and second group 20 HlNl pneumonia patients, without features of acute renal injury (as control group). The study carried throughout the period between (20 September 2009 and 24 August 2011). The patients complained of subjective fever, chills, cough, flu-like symptoms and had influenza HlNl virus subtype-specefic RNA diagnosed through nasopharyngeal swabs which were submitted to real-time reverse transcriptase polymerase chain reaction (rRT-PCR). After taking the consent for screening and testing for influenza A infection. Patients with illness duration of 8 days or more were excluded due to the potential for false-negative influenza test results after prolonged illness [11].

Retrospectively the clinical data were collected from the original files as well as reviewing the medical charts, radiological and laboratory results. Diagnoses without radiographic confirmation were excluded to limit misclassification due to lack of standardized clinical criteria for pneumonia diagnosis. Severity of illness was assessed by using the Acute Physiology and Chronic Health Evaluation (APACHE) II, Sequential Organ Failure Assessment (SOFA) score, Multiple Organ Dysfunction Score (MODS), and partial arterial o_2 pressure to the fraction of inspired o_2 on high flow oxygen mask ($Pa0_2/FI0_2$) which was calculated on admission [12]. A subjective severity score was calculated for adults based on self-reported severity of 12 symptoms: cough, subjective fever, chills, fatigue, nasal congestion, wheezing, vomiting, headache, muscle aches, sore throat, ear pain, and nausea. Each symptom was scored on a 4-point scale (0=absent; l=mild; 2=moderate; 3=severe). The severity score was calculated by summing the points for the 12 individual symptoms. Possible scores ranged from l (a single mild symptom) to 36 (all symptoms severe) [13]. Another severity score related to the severity of pulmonary infiltrates (XR Chest score); each lung was divided into four equal quadrants and each quadrant was scored on a scale of 0-3 (0=normal; l=subtle increased interstitial markings; 2=prominent interstitial opacities;3=confluent interstitial and acinar opacities), with maximum score of 24 for both lungs [14]. International Classification of Diseases, Ninth Revision, Clinical Modification diagnosis codes were used to estimate the incidence of influenza-like illness for adults included (487 “Influenza”, 078.8 “Other specified viral and chlamydial diseases”, 780.6 “fever”, 079.9” Unspecified viral and chlamydial infections”, or 465.6”Acute upper respiratory tract infection”).Co-morbidities were recorded as the presence of one or more of the following chronic medical disorders: chronic obstructive pulmonary disease (COPD), asthma, chronic kidney disease (CKD), ischemic heart disease (IHD), hypertension (HT), diabeted mellitus (DM), Steroids and immunosuppressive drugs, pregnancy, and obesity [15].

STATISTICAL ANALYSIS

The continuous variables were presented as mean ± standard deviation (SD) or median and range. Data entry were performed by using SPSS 12.00software and assessed by analysis of Mann-Whitney U-testto identify the differences between groups, with statistical significance set at P-value<0.05.

RESULTS

The variables and characteristics of the two groups of patients were collected in the table 1, while comparative study between survived (Gr.lA) and non-survived (Gr.lB) patients of the first group was presented in the table 2. None of the patients had history of seasonal influenza, pneumococcal vaccine within the last year or history of use of any antiviral therapy as prophylaxis a month before the onset of symptoms. The bacterial cultures of the blood and sputum samples collected within the first day of admission were negative in all patients of the present study. No evidence of secondary pathogen on admission, but nosocomial infection more than fourty eight hours after admission were developed in 4 out 40 patients of group1, (10%) .As regards to comparison of patients of both groups, no statistical significance related to symptoms whatever separately or totally according to the symptoms severity scores (tab.l) while statistically significant between the two groups regards to parameters, tab.l. APACHE II score in gr.l was 26.3±9.7 and in gr.2 was 14.1±5.3, (P-value < 0.005, not shown in the table 1) (5,6,8-11,14&15). All patients had pneumonia confirmed radiologically with XR chest score. 4±3.6 (gr.l), 10±1.3 (gr.2). The findings on chest radiographs were consisted with acute respiratory distress syndrome that required mechanical ventilation for 19 out of 40 patients of gr.l. Table 2, represent the comparative study between patients of group 1A & IB (Survived and Non-survived patients among the first group).

Table (1): Comparative Study between Demographic Features and Clinical Characteristics of the Confirmed H1N1 Pneumonia Patients With and Without Acute Renal Injury.

Characteristics/Variables	Gr.(l) no=40	Gr.(2) no=20
l-Age(yrs)	45±21	44±19
2-Sex(M/F)	23/17	12/8
3-Symptoms(#pts/%)		
Subjective fever	31/77.5	15/75
Chills	29/72.5	15/75
Cough	39/97.5	19/95
Fatigue	36/90	17/85
Nasal congestion	32/80	15/75
Vomiting	08/20	5/25
Wheezing	24/60	10/50
Sore throat	28/70	13/65
Ear pain	16/40	7/35
Headache	33/82.5	16/80
Myalgia	34/85	16/80
Nausea	15/37.5	6/30
4-Symptoms Severity Score, median(range)	19(14-24)	17(12-21)
5-lnterval days from symptoms to admission	4.3+1.7	2.911.6*
6-lnterval days from admission to discharge/death	10.9±4.2	6.1±1.9*s
7-lnterval days from admission to acute kidney injury	4.1±23	NA
8-XRChest-score	19.4±3.6	10±1.3*
9-$Pa0_2/Fi0_2$	169 ±73	203194*
10-Risk factors/comorbidities	35/40	6/20*
11-APACHEII score	26.3±9.7	14.1±5.3*
12-SOFA score	9.7±3.8	NA
13-MODS	9±4	NA
14-Serum creatinine(mg/dl)	5.1±1.9	1.1+0.6*
15-Creatfnine clearance(ml/min)	17±3.4	92±7.6*

APACHE=Acute Physio logy and Chronic Health Evaluation, SOFA= Sequential Organ Failure Assessment score, MODS= Multiple Organ Dysfunction Score, and PaO_2=partial arterial o_2 pressure
*=Pvalue < 0.05 (significant). NA=not applicable

Table (2): Comparative Study between Survived and Non -survived Patients With HlNl Pneumonia and Acute Renal Injury.

Characteristics/Variables On Hospital Arrival	Gr.lA (no=25)	Gr.lB (no=15)	P-value
Age in yrs*	39.4(14-66)	43.1(29-79)	0.53
Sex—M/F	19/6	6/9	0.67
Days from symptoms to admission*	2.3(2-5)	5.9(4-8)	0.0001
Other medical comorbidities#	7/25	14/15	0.02
Hypotension not responding to rVFs#	8/25	15/15	0.004
Renal replacement therapy#	13/25	11/15	0.57
Initial $PadO_2$*	93(43-121)	62(37-89)	0.05
Initial PaO_2/FiO_2	248(98-301)	131(79-229)	0.03
PH*	7.41(7.33-7.49)	7.29(7.11-7.47)	0.317
Mechanichal ventilation#	4/25	15/15	0.005
XR-Chest score*	13.1(6-14)	18.7(12-24)	0.0001
APACHE II score*	18(8-20)	34(24-44)	0.00005
SOFA score*	6(4-8)	14(10-16)	0.00002
MOD score*	4(4-8)	14(8-16)	0.0001
LDH (U/L)*	258(212-430)	1673(1112-2003)	0.005
Serum creatinine(mg/dl)*	3.2(2.9-5.6)	7.8(5.1-11.8)	0.0002
Creatinine clearance(ml/mln)*	59(48-69)	11(10-23)	0.0005

Gr.lA= Survived patients, Gr .1B= Non -survived patients, APACHE=Acute Physiology and Chronic Health Evaluation, S0FA= Sequential Organ Failure Assessment score, MODS= Multiple Organ Dysfunction Score, and PaO/FiOj=partial arterial o_2 pressure/flow index of or *=median (range), # = number/total.

DISCUSSION

The present study of critically ill patients with HlNl showed that the disease affected middle aged patients most of them with underlying chronic medical disorders (41 out of 60, 68.33%). The patients fulfilled the criteria of acute respiratory distress syndrome and acute renal injury. 15 out of 40 died (37.5%), 14 patients out of them had past history of medical co morbidities (93.3%). The most common cause of death was acute respiratory distress syndrome (ARDS)/ multiorgan dysfunction syndrome. There was significant variation in the reported mortality rates of HlNl, ranging from 11 to 69% and higher in older patients and those who required renal replacement therapy (RRT) [16]. The probable contributing factors for death in the present study including the late presentation to hospital (5.9 days) in comparison to survivors (2.3 days), P-value=0.0001. Also, the present study reported higher APACHE II, SOFA, MODS, XRC scores in the group of non-survivors. The potential explanation for variability in mortality rates may be a pure bias with regard to the population reported, as the hospital of the present study offers a referral service to many secondary and districts hospitals and the present study population, therefore represented the more serious end of the spectrum of the affected individuals. Co-infection with other respiratory pathogenic viruses could also explain the high pathogenicity among the patients of the present study, especially those who died. H5N1 infection was reported to have a very aggressive variety of influenza with severe viremia [17]. Respiratory distress requiring respiratory support even up to intubation and mechanical ventilation which developed in 19 patients (47.5%). and they had a median oxygen saturation of 79%., only 4 of them survived, with median serum creatinine 3.2 (range 2.9-5.6) and creatinine clearance 59 (range48-69), in comparison to 15 non-survived patients with median serum creatinine7.8 (range 5.1-11.8) and creatinine clearance 11 (range 10-28), (P-value < 0.0002& 0.0005 respectively). That reflects clear observation of the impact of severe renal injury in increasing the mortality rate of HlNl pnuemonia patients submitted to mechanical ventilation in comparison to patients with mild renal injury. The etiology of acute renal injury is due to acute tubular necrosis may be related to hypo perfusion, rhabdomyolysis in the setting of severe systemic inflammatory response syndrome, renal vasoconstriction and hypoxemia of acute lung injury [18,19]. Some authors have suggested that infection with HlNl pneumonia is the cause of acute renal injury inspite there is no documented direct cytopathic renal injury.

The study of Belongia, et al., 2010 reported that comparisons of severity by influenza A strain could have been influenced by antiviral therapy, vaccination, and the differences in health care seeking behavior and reported that antiviral therapy was unlikely to explain any differences between 2009 HlNl and H3N2 outcomes, since the proportion of infected participants receiving antiviral therapy was similar [20]. Influenza vaccine may have also reduced the occurrence of serious outcomes in vaccinated patients with seasonal HlNl or H3N2 strains but not those with 2009 HlNl infections, since monovalent HlNl vaccine was first available in the population when HlNl infections were peaking in mid October [21]. Certain studies have suggested that certain racial or ethnic

groups experienced higher rates of hospital admission or other complications because of 2009 HlNl infection [22], but the patients of the present study of Makkah region were of multi-nationality characteristics.

The present study has certain limitations as it was a retrospective, limited number of cases and single-hospital observational study. Also the focus on critically ill patients may not show the important presenting features in less severe cases and that may give impression of over presentation or under-presentation of certain co morbidities. Pneumonia prevention should be an increased focus of Hajj medicine. Vaccination against seasonal and pandemic influenza strains in addition to Pneumococcal vaccine should be considered for at-risk patients before Hajj. Intra-pilgrimage frequent hand washing, and potentially the wearing off ace masks for patients with early symptoms, should be a future focus of Hajj medicine in order to reduce the burden of respiratory tract infection. Also, improvements in pilgrim living conditions with less spatial crowding and decreased density of pilgrims in shelters in Mina may decrease the incidence of transmission of severe pneumonia in Hajj and should be explored further. Beyond the period of Hajj, patients who have returned from the pilgrimage (and clinicians evaluating them) should be vigilant for signs of pneumonia [23]. In conclusion, acute renal injury is an adding impact of increasing the mortality rate of H1N1 pneumonia critically ill patients and may be related directly to the infection by this virus or complication to it which may be explained by severe hypoxia secondary to severe acute lung injury, multi-organ dysfunction. A high mortality in middle and old-aged patients with underlying medical co-morbidities was associated with higher Symptoms Severity, APACHE II, SOFA, MODS, and XRC scores. The present study recommended early recognition of the disease as well as prompt medical attention to provide opportunities aiming to limit the progression of the illness and to reduce the mortality. Prospective and controlled clinical trials are needed for clarifying the effectiveness of early treatment and protection by using HlNl vaccination.

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