

Diagnostic Cut off The S. LDH In Cases of Pneumonia Caused By Pandemic 2009 H1N1 Influenza Virus At Tertiary Care Hospital

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Abstract

Introduction: Global pandemics with high mortality and morbidity occur when a virulent new viral strain emerges, against which the human population has no immunity. estimate the serum biochemical parameters especially serum LDH in suspected patients of swine flu and to compare these biochemical parameters in RT-PCR positive cases of swine flu with suspected cases of swine flu that are RT-PCR negative.

Objectives:

Material and methods :hospital based observation descriptive study conducted on adult patients (n=150), admitted or took consultation at Medicine OPD of SMS Hospital during one Year period of the analysis (January 2015 to 2016) and tested for the presence of (H1N1) infection based on clinical suspicion n seeking consultations for flu like symptoms were screened and these were categorized as Guidelines provided by Ministry of Health & Family Welfare on categorization of Seasonal Influenza cases during screening for home isolation, testing, treatment and hospitalization (Revised on 18.10.2016.were enrolled

At first all individuals Patients with Influenza like illness , age >14 years with informed consent to participate in the study Patients having other conditions that can cause LDH abnormalities like Myocardial Infarction, Hemolytic anemia, Ischemic cardiomyopathy, Liver disease such as hepatitis, Muscle injury, Muscular dystrophy, Pancreatitis, Viral meningitis, Encephalitis, Hypothyroidism were excluded.

Statistical analysis :students 't' test and chi-square test Roc curve were used for analysis

Result: serum LDH level was significantly higher in H1N1 positive patients and higher serum LDH level along with high serum CPK level and high blood sugar level may need intensive care and treatment compared to low value of these parameters in respiratory illness patients at time of H1N1 influenza epidemics, however larger studies are needed to establish this hypothesis. ROC curve analysis A \geq 736 unit To area under the curve (AUC = 0.65) optimal cut- off value of LDH, with a sensitivity of 53 % and a specificity of 73%, was determined with SE 0.04 .

Keywords :H1N1 influenza, LDH optimal cut- off value

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I. Introduction

Global pandemics with high mortality and morbidity occur when a virulent new viral strain emerges, against which the human population has no immunity. .In 2015, the outbreak became widespread throughout India.¹The state of Rajasthan,. In the first 3 month of 2015 (up to 8th April) a total no of 6597 H1N1 Positive cases and 406 fatal cases reported in Rajasthan which was highest in India.² A major challenge in clinical practice of intensive care and emergency medicine is early detection and prognosis of severe community respiratory infections, as well as the differentiation between viral and bacterial infections, with a consequent impact on the inappropriate use of antibiotics, bacterial resistance, mortality, and costs The recent pandemic by influenza A (H1N1) virus⁽²⁾ has reinforced the importance of biomarkers that might assist the clinician in diagnosis and management of patients with severe community-acquired pneumonia and acute respiratory failure. 4 Lactate dehydrogenase (LDH) is a protein that normally appears throughout the body in small amounts many cancers can raise LDH levels, so LDH may be used as a tumor marker, but at the same time, it is not useful in identifying a specific kind of cancer. Measuring LDH levels can be helpful in monitoring treatment for cancer. Noncancerous conditions that can raise LDH levels include heart failure, hypothyroidism, anemia, pre-eclampsia, meningitis, encephalitis, acute pancreatitis, HIV and lung or liver disease. Tissue breakdown releases LDH, and therefore LDH can be measured as a surrogate for tissue breakdown, e.g. hemolysis.⁵The use of biomarkers has given support to the management of sepsis and respiratory failure patients, including the decision to use antibiotics⁽⁶⁻⁸⁾

This study was conducted with the objectives to estimate the serum biochemical parameters especially serum LDH in suspected patients of swine flu and to compare these biochemical parameters in RT-PCR positive cases of swine flu with suspected cases of swine flu that are RT-PCR negative. So rationale of study is to assess the utility of serum LDH (Lactic dehydrogenase) enzyme and other surrogate markers in clinical assessment, prognostication and treatment of influenza H1N1 positive patients. Knowing clinical predictors for pneumonia caused by this virus might be helpful in early treatment. This study was conducted with the aim to estimate the level of serum LDH in suspected patients of swine flu and to compare levels of S. LDH in RT-PCR positive cases of swine flu with S. LDH of suspected cases of swine flu that are RT-PCR negative. To detect other biochemical and pathological abnormality in patients diagnosed with swine flu (RT-PCR positive).

II. Material And Methods

This hospital based observation descriptive study conducted on adult patients (n=150), who were admitted or took consultation at Medicine OPD of SMS Hospital during one Year period of the analysis (January 2015 to till sample size completed) and tested for the presence of (H1N1) infection based on clinical suspicion n seeking consultations for flu like symptoms were screened and these were categorized as Guidelines provided by Ministry of Health & Family Welfare on categorization of Seasonal Influenza cases during screening for home isolation, testing, treatment and hospitalization (Revised on 18.10.2016.were enrolled in after taking informed consent. The decision to hospitalize suspected patients was based on comorbidity, symptom severity, hypoxia or radiographic evidence of pneumonia and absence of social support. At first all individuals Patients with Influenza like illness at Medicine OPD and emergency age >14 yearswith informed consent to participate in the studyPatients having other conditions that can cause LDH abnormalities likeMyocardial Infarction, Hemolytic anemia,Ischemic cardiomyopathy,Liver disease such as hepatitis, Muscle injury,Muscular dystrophy, Pancreatitis, Viral meningitis, Encephalitis, Hypothyroidism were excluded.

A thorough history, clinical examination and complete socio-demographic information were taken from study population, If any case fits in the case definition then samples should be collected according to the sample collection guidelinesand laboratory data were obtained.All the Included participants was evaluated for Clinical presentations and laboratory results were recorded. A diagnosis of pneumonia was made if the patients had any one of the following signs or symptoms: tachypnea (respiratory rate > 60 breaths/minute if the person was less than 2 months of age, 50 breaths/minute if 2–12 months of age, 40 breaths/ minutes if 1–5 years of age, 30 breaths/minute if 5–10 years of age, and 24 breaths/minute if > 10 years of age), dyspnea/chest pain, lung crepitation or consolidation signs upon physical examination, oxygen saturation at room air > 95% plus abnormal chest radiographic finding compatible with pneumonia. Investigations:Respiratory specimens : RT-PCR for H1N1,SERUM LDH,RBS, CPK, CRP, RFT, L CBC, DLC, ESR,Chest X ray,Arterial blood gas analysis,Other relevant investigations Respiratory specimens including: bronchoalveolar lavage, tracheal aspirates, nasopharyngeal or oropharyngeal aspirates as washes, and nasopharyngeal or oropharyngeal swabs. Swab specimens should be collected only on swabs with a synthetic tip (such as polyester or Dacron) and aluminium or plastic shaft. Swabs with cotton and wooden shafts are not recommended. Specimens collected with swabs made of calcium alginate are acceptable.

III. Stastical Analysis

The Data was entered in MS excel sheet. Student's t-test to compare normally distributed continuous variables, Chi-square test was used to analyze dichotomized variables. ROC curve were used to find out LDH optimal cut of value. P Value <0.05 is considered significant.

IV. Observations

Of these (150) patients, 75 had positive PCR test results for H1N1 virus. The diagnosis of pneumonia was made for 51 (11.56%) patients. Baseline clinical features and laboratory results for H1N1 patients without and with pneumonia are shown in Table 1. Most clinical variables were comparable between both groups most of the patients were in the age group of 21-40 years (41.3 % and 50.7% respectively). The mean age of H1N1 positive subjects was higher (41.90 years) as compared to H1N1 negative subjects, H1N1 negative group had more males (52%) as compared to H1N1 positive group, but the difference was not statistically significant ($p=1.000$). Significantly more number of H1N1 positive patient required admission to the ICU (48%) as compared to H1N1 negative patients (10.7%), ($p<0.001$).More H1N1 positive patients (62.7%) belonged to Rural area as compared to H1N1 negative patients (53.3%), ($p=0.321$). Most of the H1N1 positive and H1N1 negative patients belonged to low socioeconomic status (34.7% and 36% respectively). ($p=0.652$). significantly more H1N1 positive patients (68%) had shortness of breath at presentation as compared to H1N1 negative patients (44%). ($p=0.005$). Presence of fever and cough was not significantly different in both groups. mean systolic and diastolic blood pressure was not significantly different but mean blood sugar level was higher in H1N1 positive patients (123.9 mg/dl) as compared to H1N1 negative patients (73 mg/dl). ($p<0.001$). mean

LDH level was significantly higher in H1N1 positive patients (919.38 U/L) as compared to H1N1 negative patients (641.38 U/L) with p value=0.008 Above table shows that mean CPK level was higher in H1N1 positive patients (407.06 U/L) as compared to H1N1 negative patients (247 U/L). Application of t test revealed that this difference was statistically significant ($p=0.073$). ECG abnormality was found in significantly more H1N1 positive patients (68%) as compared to H1N1 negative patients (49%). pneumonitis was statistically significant more in H1N1 positive patients (82.2%) as compared to H1N1 negative patients (57.3%) ($p=0.002$).

mean blood urea level was higher in H1N1 negative patient (43.85 mg/dl) as compared to H1N1 positive patient (40.29mg/dl), ($p=0.416$) mean serum creatinine level was higher in H1N1 negative patient (2.51 mg/dl) as compared to H1N1 positive patient (1.189mg/dl), ($p=0.296$) mean serum LDL level was higher in H1N1 negative patient (94.08 mg/dl) as compared to H1N1 positive patient (78.82mg/dl), and this difference was found to be statistically significant ($p=0.009$) mean serum HDL level was not found to be significantly different between H1N1 negative patient (36.85 mg/dl) and H1N1 positive patient (36.45mg/dl), $p=0.701$. mean serum HDL level was not found to be significantly different between H1N1 negative patient (154.19 mg/dl) and H1N1 positive patient (153.80mg/dl), $p=0.979$.

mean serum total cholesterol , level was higher in H1N1 negative patient (146.64 mg/dl) as compared to H1N1 positive patient (138.11mg/dl), but this difference was not found to be statistically significant ($p=0.206$)

No significant difference was observed according to mean SGOT level ($p=0.343$) mean SGPT level was higher in H1N1 positive patient (141.88 U/L) as compared to H1N1 negative patient (110.09 U/L), ($p=0.542$) mean alkaline phosphatase level was higher in H1N1 positive patient (119.19 IU/L) as compared to H1N1 positive patient (106.77 IU/L), ($p=0.400$) mean serum bilirubin level was higher in H1N1 negative patient (1.09 mg/dl) as compared to H1N1 positive patient (0.93mg/dl) $p=0.162$ mean serum direct bilirubin level was not significantly different among H1N1 negative patient (0.51 mg/dl) and H1N1 positive patient (0.42mg/dl), ($p=0.164$) mean serum potassium level was higher in H1N1 positive patient (4.30 meq/l) as compared to H1N1 negative patient (4.12meq/l), but this difference was not found to be statistically significant ($p=0.090$) mean serum sodium level was not significantly different among H1N1 negative patient (138.33 meq/l) and H1N1 positive patient (138.27meq/l), ($p=0.949$)

mean hemoglobin level was not significantly different among H1N1 negative patient (11.62 g/dl) and H1N1 positive patient (11.82g/dl), ($p=0.616$) mean TLC was lower in H1N1 positive patient (8.82) as compared to H1N1 negative patient (11.55), and this difference was found to be statistically significant ($p=0.003$) mean platelet count was not significantly different among H1N1 negative patient (1.89 lakh/dl) and H1N1 positive patient (2.06 lakh/dl), ($p=0.295$). mean ESR was not significantly different among H1N1 negative patient (37.11mm in 1st hr) and H1N1 positive patient (44.65mm in 1st hr), ($p=0.105$) Receiver operating characteristic ROC for LDH showing (1-specificity) on the X axis and sensitivity on Y Axis excersing different cut off value to land at the choice the most apposite cut off point and which provide the greatest sum of sensitivity and specificity. Table illustrate sensitivity, specificity ,1- specificity(False positivity rate) of LDH at diverse level appropriate for H1N1 positivity (RT PCR positive cases).As the level of LDH increases ,sensitivity lessens and specificity enhances. The optimum cut off value was obtained by points of test values that grants the highest Youden Index that is (SN+SP)-1 . ROC curve analysis was performed to determine the optimal cut-off values of significant variables (LDH) detected between the two groups (Figure 1). A ≥ 736 unit Toarea under the curve (AUC = 0.65) optimal cut- off value of LDH, with a sensitivity of 53 % and a specificity of 73%, was determined with SE 0.04 .

V. Discussion

Influenza pandemics have been associated with increased morbidity and mortality. The hospital based descriptive analytic comparative study was conducted in the Department of General Medicine, S.M.S hospital, Jaipur most of the patients were in the age group of 21-40 years (41.3 % and 50.7% respectively Of these (150) patients, 75 had positive PCR test results for H1N1 virus. The diagnosis of pneumonia was made for 51 (11.56%) patients. **Serap Duru et al.**⁹ Thirty-one (15 female, 16 male) of 51 patients RT-PCR test were positive for Influenza A(H1N1) virus infection. Among hospitalized patients, most of the H1N1 positive and negative patients were in the age group of 21-40 years (41.3 % and 50.7% respectively). It has been proposed that elderly persons may have some level of cross-protection against H1N1 infection from preexisting antibodies against other influenza A (H1N1) viruses, as suggested by serologic studies of the seasonal influenza viruses.¹⁰ In the present study, females had more H1N1 positive cases Vs H1N1 negative cases (49.3% vs 48%) as compared to males where H1N1 positive cases Vs H1N1 negative cases (50.7% vs 52%) were found but the difference was not statistically significant. This is comparable to study of **Nancy M. Abdelaty**¹⁰ where Male/Female% was (36/64) in H1N1 positive vs. (56/44) in H1N1 Negative. **Amir Shlomai et al.**¹¹ found Gender (Male/Female)% 55.4/44.6, 57.9/42.1 in H1N1 positive vs Negative patients.

In our study 122 out of 150 patient had hospitalized (app. 81%). (29.3%) had severe disease and required ICUs and mechanical ventilation while (52%) had non severe disease and admitted in ward. Out of 44 patients in ICU 36 patients was found to be H1N1 positive. All patients requiring ventilatory support had significant respiratory involvement in the form of pneumonia, Acute Respiratory Distress Syndrome (ARDS) and respiratory failure. X-ray chest showed bilateral pulmonary infiltrates in all the patients. Review of all the investigations done revealed that 16/36 patients, developed extra-pulmonary organ dysfunction during the course of disease. 35% of the patients developed cardiovascular compromise, manifesting as hypotension and shock, requiring inotropic support (13.8%) of the patients developed deranged renal status with raised levels of blood urea and serum creatinine.

Nancy M. Abdelaty et al¹⁰ found that there was higher rate of transfer to the ICU, mechanical ventilation and death among patients with positive H1N1 suggesting that pandemic (H1N1) 2009 infection tends to be a relatively serious disease in a significant proportion of hospitalized patients. Eighteen (10.2%) of (H1N1) Positive cases had radiologically confirmed pneumonia vs 5 (9.2%) in negative cases. In (H1N1) Positive cases, seven patients (3.97%) required admission to an intensive care unit, because of respiratory failure, 4 patients' required mechanical ventilation and 1 patient required NIPV. Five of the ICU admitted patients had recovered from the acute illness and 2 died.

Amir Shlomai et al¹¹ were found that (36%) were found positive. These patients tended to be younger and had significantly fewer comorbidities. In addition, they had a significantly higher frequency of fever (94%), cough (86%) and myalgia (29%). Furthermore, age < 65 years and cough were independent predictors for pandemic (H1N1) 2009 virus positivity in a multivariate regression analysis. Notably, (21.5%) had acute respiratory insufficiency requiring treatment in the intensive care unit.

In this study, significantly more number of H1N1 positive patient required admission to the ICU (48% vs 10.7%) , (68% vs 44%) had shortness of breath at presentation as compared to H1N1 negative patients respectively ($P < 0.001$). Presence of fever and cough was not significantly different in both groups. The clinical spectrum of novel H1N1 infection is still being defined, but both self-limited illness and severe outcomes, including respiratory failure and death, have been observed. **Nancy M. Abdelaty et al.¹⁰** observed that in the United States surveillance, most confirmed cases of H1N1 infection have been characterized by self-limited, uncomplicated febrile respiratory illness and symptoms similar to those of seasonal influenza (cough, sore throat, rhinorrhea, headache, and myalgia), but approximately 38% of cases have also involved vomiting or diarrhea, neither of which is typical of seasonal influenza.

Present study shows that more H1N1 positive patients (62.7%) belonged to Rural area and low socioeconomic status ($p = 0.652$). similar with **Hilary Placzek et al.¹²**

A. Liapikou et al.¹³ found that 58 patients were hospitalized with H1N1 infection, of which 52% presented with flu-like symptoms and had a benign course. Nearly 30% had one or more underlying medical conditions. A total of 28 of the 58 patients (48%) presented with pneumonia, and there were 7 intensive care admissions, but no deaths. Four patients developed acute respiratory distress syndrome (ARDS) and therefore required mechanical ventilation. The patients with pneumonia were older (36 vs 26, $p = 0.003$), more hypoxemic (39% vs 7%, $p = 0.01$)

Mean systolic blood pressure was not significantly different in H1N1 positive (114.16 mmHg) and negative patients (111.44). ($p = 0.232$). mean LDH level was significantly higher in H1N1 positive patients (919.38 U/L) as compared to H1N1 negative patients (641.38 U/L) (p value = 0.008). High level of serum LDH may correlate with immune system over-reaction to the viral infection, leading to cytokine activation, which triggers inflammation and lung damage that can lead to multiple organ failure and death. Serum LDH and CPK values were very high, and there was a great incidence of obesity.¹⁴

Nancy M. Abdelaty et al.¹⁰ compared with patients who had suspected 2009 pandemic influenza A (H1N1) virus, patients with confirmed 2009 pandemic influenza A (H1N1) virus had lower total leukocyte, neutrophil, and lymphocyte counts and higher lactate dehydrogenase and creatine phosphokinase levels at presentation. These patients may have had a higher viral load at presentation, which may have led to the apparent worsening of laboratory values. This observation may correlate with immune system over-reaction to the viral infection, leading to the so called cytokine storm, which triggers inflammation and lung damage that can lead to multiple organ failure and death.¹⁶

ROC curve analysis was performed to determine the optimal cut-off values of significant variables (LDH) detected between the two groups (Figure 1). A ≥ 736 unit To area under the curve (AUC = 0.65) optimal cut-off value of LDH, with a sensitivity of 53% and a specificity of 73%, was determined with SE 0.04.

S. Reyes et al.¹⁵ found that Risk factors for in-hospital mortality in the whole group were A/H1N1 (b) etiology and LDH > 600 IU/L (OR 4.1) when adjusting for PSI, and hypoxemia (OR 4.2) when adjusting for CURB 65 (AUC 0.81). Heart disease (OR 27.4) and LDH > 600 IU/L (OR 10.5) were risk factors for in-hospital mortality in A/H1N1(b) patients (AUC 0.81). They concluded that Leukopenia, multilobar infiltrates, CRP < 10 mg/dl and age < 60 years were independently associated with A/H1N1(b) etiology. Pandemic A/H1N1(b)

increased mortality pneumonia. Heart disease and LDH > 600 were independently associated with mortality in A/H1N1(p) pneumonia.¹⁵ found that LDH behaved as a better biomarker than CRP to predict mortality, keeping its independent association in a multivariate analysis.¹⁶

A. Liapikou et al.¹⁷ found presented higher serum levels of alanine aminotransferase (SGOT) (43.2 vs 25.5, $p=0.01$), creatine phosphokinase (CPK) (418 vs 127.5, $p=0.01$) and lactate dehydrogenase (LDH) (345 vs 171, $p=0.002$) than the other patients hospitalized with H1N1. They observed that H1N1 influenza can cause pneumonia devoid of bacterial infection, with prognostic factors for its development being high serum levels of LDH at admission and the smoking habit.

Present study we found that mean CPK level was higher in H1N1 positive patients (407.06 U/L) as compared to H1N1 negative patients (247 U/L). Application of t test revealed that this difference was statistically significant ($p=0.073$). similar finding were observed in

Nancy M. Abdelaty et al.¹⁶**Bárbara Borgatta et al.**⁶⁴

Present study shows that mean blood sugar level was higher in H1N1 positive patients (123.9 mg/dl) as compared to H1N1 negative patients (73 mg/dl). Application of t test revealed that this difference was statistically significant ($p<0.001$). Our results are consistent with those of recent studies indicating that the mean BSL (blood sugar level) of H1N1 patients on admission is a simple and feasible indicator to predict the disease tendency; however, more information and clinical data are required to investigate whether the prognosis of H1N1 pneumonia will benefit from plasma glucose control and regulation.

Our study shows that mean serum potassium level was higher in H1N1 positive patient (4.30 meq/l) as compared to H1N1 negative patient (4.12 meq/l), ($p=0.09$ NS). And also mean serum sodium level was not significantly different among H1N1 negative patient (138.33 meq/l) and H1N1 positive patient (138.27 meq/l), ($p=0.949$)

Our study shows that mean SGOT, SGPT, alkaline phosphatase, serum bilirubin level was higher in H1N1 positive patient (225.69 U/L) as compared to H1N1 negative patient (116.13 U/L), but this difference was not found to be statistically significant similar finding were observed with **Papic et al.**¹⁸**Zarogoulidis et al.**¹⁹

Despite the multi-systemic effects of influenza A/H1N1 virus, the occurrence of hepatic injury during the natural course of the infection remains a matter of debate.²⁰ it can be assumed that influenza A/H1N1 virus is -or at least could be a hepatotropic virus.

Our study found mean serum LDL and total cholesterol higher in H1N1 negative patient as compared to H1N1 positive patient a ($p=0.009$). Mean serum HDL and serum TG level level was not different between H1N1 negative patient (36.85 mg/dl) and H1N1 positive patient Our study results are not consistent with previous literature and it may due to is lipid profile estimation is done at time of admission or OPD consultation, serial LDL level monitoring was not done. However, more information and clinical data are required to investigate whether the low level of serum LDL affects disease progress and outcome.

Memon et al.²⁰ reported that after injection with bacterial lipopolysaccharide, zymosan, or turpentine, LDL contained increased amounts of conjugated dienes and lipid hydroperoxides, as well as lysophosphatidyl choline. Considering these and our own observations, we suspect that the changes in LDL seen by **Memon et al.** were secondary to changes in HDL induced by the APR. These modifications in HDL may have evolved to provide an oxidative environment to promote host defense in combating viral infection.

Our study found that mean TLC was significantly lower in H1N1 positive patient as compared to H1N1 negative patient, mean hemoglobin, platelet count, ESR was not significantly different among H1N1 negative and H1N1 positive patient **T.M. Tumpey et al.**²¹ In accordance, this suggests that certain pathogenic strains of influenza virus might severely harm the immune system, resulting in disseminated and lethal disease. Therefore, we suggest that CPK, LDH, leukopenia, neutropenia and lymphopenia during hospitalization in severely ill H1N1 infected patients might serve as a surrogate marker for the severity of the disease and its prognosis.

Persons with pneumonia caused by H1N1 virus infection were shown to have dramatically high levels of LDH, particularly in persons who died. In our study, serum LDH levels > 500 U/L were significantly more common in patients with pneumonia, as analyzed by univariate analysis However, these levels were not an independent factor for H1N1 pneumonia. High levels of LDH may be associated with critically ill H1N1 patients but are not a predictor for H1N1 pneumonia²²⁻²³

Nancy M. Abdelaty et al.¹⁶ patients with confirmed 2009 pandemic influenza A (H1N1) virus had lower total leukocyte, neutrophil, and lymphocyte counts and higher lactate dehydrogenase and creatine phosphokinase levels at presentation. **Nancy M. Abdelaty et al** reported 21.4% of patients had leukopenia, and 68.1% of adults and 92.3% of children had lymphopenia. None of the patients had thrombocytopenia. The lymphopenia was transient. In the same context, both leukocytosis and leukopenia were reported in hospitalized patients in California.

Previous reports showed that lymphopenia and thrombocytopenia were related to severity of H1N1 virus infection.^{10,11} In our study, both factors were not associated with pneumonia.²²⁻²³

Our study found that ECG abnormality was found in significantly more H1N1 positive patients (68%) as compared to H1N1 negative patients (49%). Cardiovascular involvement in acute influenza infection can occur through a myocardium direct effect or through exacerbation of previous disease. Cardiac conditions associated with influenza include myocarditis, pericarditis, myocardial infarction, congestive heart failure and sudden death. Influenza-associated cardiac conditions are typically short-lived and reversible.^{15,24}

S. Reyes et al.¹⁵ analyze the risk factors to predict influenza A/H1N1 infection in patients with pneumonia, and the impact of this etiology on mortality during a pandemic period. They found Heart disease (OR 27.4) and LDH > 600 IU/L (OR10.5) were risk factors for in-hospital mortality in A/H1N1(b) patients (AUC 0.81). They concluded that Heart disease and LDH > 600 were independently associated with mortality in A/H1N1(b) pneumonia.¹⁵

In our study 122 out of 150 patient had hospitalized (app. 81%). 44 out 150 (29.3%) had severe disease and required ICUs and mechanical ventilation .Out of 44 patients in ICU 36 patients was found to be H1N1 positive. All patients requiring ventilatory support had significant respiratory involvement in the form of pneumonia, Acute Respiratory Distress Syndrome (ARDS) and respiratory failure. **Nancy M. Abdelaty et al.**¹⁶ found in their study that Eighteen (10.2%) of (H1N1) Positive cases had radiological confirmed pneumonia vs 5 (9.2%) in negative cases. In (H1N1) Positive cases, seven patients (3.97%) required admission to an intensive care unit, because of respiratory failure, 4 patients required mechanical ventilation and 1 patient required NIPV. Five of the ICU admitted patients had recovered from the acute illness and 2 died.

Pnar Nercis KOAR et al.⁵ In the chest X-rays, the most common pathology was patchy consolidations with a prevalence of 27%. Bilateral symmetrical involvement was observed in 42% of the cases..

VI. Conclusions

mean serum LDH,CPK, blood sugar, Serum potassium (K⁺) level ,urea and creatinine was significantly high in H1N1 positive patients as compared to H1N1 negative patients. On review of liver function test hepatic enzymes were higher in H1N1 positive patients but were not statistically significant. Serum LDL level was significantly low in H1N1 positive patients. However, more information and clinical data are required to investigate whether the low level of serum LDH significantly affects clinical assessment, disease severity and prognosis of H1N1 pneumonia.

Bibliography

- [1]. Rajasthan declares swine flu epidemic". Business Standard. 13 February 2015. Retrieved 22 February 2015
- [2]. www.mapsofindia.com/maps/mapinnews/swine-flu-india.html
- [3]. Suresh Rewar, Dashrath Mirdha, Prahlad Rewar. Treatment and Prevention of Pandemic H1N1 Influenza, Annals of Global Health, VOL. 81, NO. 5, 2015 Pandemic H1N1 Influenza,September -October 2015: 645 – 65
- [4]. *Einstein(SãoPaulo) vol.9 no.1 SãoPaulo Jan./Mar. 2011*<http://dx.doi.org/10.1590/s1679-45082011ao1878>
- [5]. M. Drent, N.A.M. Cobben, R.F. Henderson, E.F.M. Wouters, M. van Dieijen-Visser. Usefulness of lactate dehydrogenase and its isoenzymes as indicators of lung damage or inflammation. Eur Respir J, 1996(9):1736–1742.
- [6]. Rello J, Rodríguez A, Ibañez P, Socías L, Cebrian J, Marques A, Guerrero J, Ruiz-Santana S, Marquez E, Del Nogal-Saez F, Alvarez-Lerma F, Martínez S, Ferrer M, Avellanas M, Granada R, Maraví-Poma E, Albert P, Sierra R, Vidaur L, Ortiz P, Prieto del Portillo I, Galván B, León-Gil C; H1N1 SEMICYUC Working Group. Intensive care adult patients with severe respiratory failure caused by Influenza A (H1N1) virus in Spain. Crit Care. 2009;13(5):R148. [[Links](#)]
- [7]. Shapiro NI, Trzeciak S, Hollander JE, Birkhahn R, Otero R, Osborn TM, et al. A prospective, multicenter derivation of a biomarker panel to assess risk of organ dysfunction, shock, and death in emergency department patients with suspected sepsis. Crit Care Med. 2009;37(1):96-04. [[Links](#)]
- [8]. Hausfater P, Juillien G, Madonna-Py B, Haroche J, Bernard M, Riou B. Serum procalcitonin measurement as diagnostic and prognostic marker in febrile adult patients presenting to the emergency department. Crit Care. 2007;11(3):R60. [[Links](#)]
- [9]. Serap Duru, Yavuz Köker, Çağla Uyanusta, Nasibe Şencan, Başak Altaş, Nurhan Albayrak et al. Clinical Analysis in Influenza A (H1N1) Virus Patients. Tur Toraks Der2012; 13: 45-9.
- [10]. Nancy M. Abdelaty et al. Risk factors and prognostic criteria in 230 patients with influenza A (H1N1) infection. Egyptian Journal of Chest Diseases and Tuberculosis 2013; 62: 1–8.
- [11]. Amir Shlomai, Amir Nutman, Taly Kotlovsky et al. Predictors of pandemic (H1N1) 2009 virus positivity and adverse outcomes among hospitalized patients with a compatible syndrome. IMAJ 2010; 12: 622–627.
- [12]. Hilary Placzek, Lawrence madoff. Effect of Race/Ethnicity and Socioeconomic Status on Pandemic H1N1-Related Outcomes in Massachusetts. American Journal of Public Health January 2014;(104)1: 31-38.
- [13]. A. Liapikou, G. Hardavella, N. Koulouris, M. Alchanatis. Preliminary analysis of adult patients with 2009 H1N1 influenza hospitalized in a University Department in Athens, May–August 2009. ARCHIVES OF HELLENIC MEDICINE: ISSN 11-05-3992.
- [14]. *Einstein (São Paulo) vol.9 no.1 São Paulo Jan./Mar. 2011* <http://dx.doi.org/10.1590/s1679-45082011ao1878>
- [15]. Reyes S, Montull B, Martínez R, Córdoba J, Molina JM, Martí V, Martínez A, Ramírez P, Menéndez R. Risk factors of A/H1N1 etiology in pneumonia and its impact on mortality. Respir Med. 2011 Sep;105(9):1404-11.
- [16]. ZHANG Peng-jun, CAO Bin, LI Xiao-li, LIANG Li-rong, YANG Shi-gui, GU Li et al. Risk factors for adult death due to 2009 pandemic influenza A (H1N1) virus infection: a 2151 severe and critical cases analysis. Chin Med J 2013;126 (12): 2222-2228.

- [17]. A. Liapikou, G. Hardavella, N. Koulouris, M. Alchanatis. Preliminary analysis of adult patients with 2009 H1N1 influenza hospitalized in a University Department in Athens, May–August 2009. ARCHIVES OF HELLENIC MEDICINE: ISSN 11-05-3992.
- [18]. Charalampos Seretis, Emmanuel Lagoudianakis, Nikolaos Salemis, Apostolos Pappas, George Gemenetzi, Fotios Seretis et al. Liver Biochemistry During the Course of Influenza A/H1N1 Infection. Gastroenterology Research 2013;6(3):103-105.
- [19]. Papic N, Pangercic A, Vargovic M, Barsic B, Vince A, Kuzman I. Liver involvement during influenza infection: perspective on the 2009 influenza pandemic. Influenza Other Respi Viruses. 2012;6(3):e2-5.
- [20]. Memon RA, Staprans I, Noor M, Holleran WM, Uchida Y, Moser AH, Feingold KR, Grunfeld C. Infection and inflammation induce LDL oxidation in vivo. Arterioscler Thromb Vasc Biol. 2000 Jun;20(6):1536-42.
- [21]. T.M. Tumpey, X. Lu, T. Morken, S.R. Zaki, J.M. Katz et al. Depletion of lymphocytes and diminished cytokine production in mice infected with a highly virulent influenza A (H5N1) virus isolated from humans, J. Virol. 74 (2000) 6105–6116.
- [22]. Ko JH, Kim JH, Kang JH, Kim JH, Eun BW, Kim KH, Hong JY, Oh SH, 2012. Characteristics of hospitalized children with 2009 pandemic influenza A (H1N1): a multicenter study in Korea. J Korean Med Sci 27: 408–415.
- [23]. Ornek T, Yalcın FD, Ekin S, Yalcın S, Yemis, en M, 2011. Pneumonia in patients with novel influenza A (H1N1) virus in southeastern Turkey. Wien Klin Wochenschr 123: 106–111.
- [24]. Mamas MA, Fraser D, Neyses L. Cardiovascular manifestations associated with influenza virus infection. Int J Cardiol 2008; 130:304-9.
- [25]. Pınar Nercis KOŞAR, Zeliha KOÇAK TUFAN, Elif ERGÜN, Hasan YİĞİT, Uğur KOŞAR and Ali Pekcan DEMİRÖZ. Chest radiography and computed tomography findings of cases with pandemic influenza A (H1N1/09) infection. Turk J Med Sci 2012; 42 (5): 787-795.

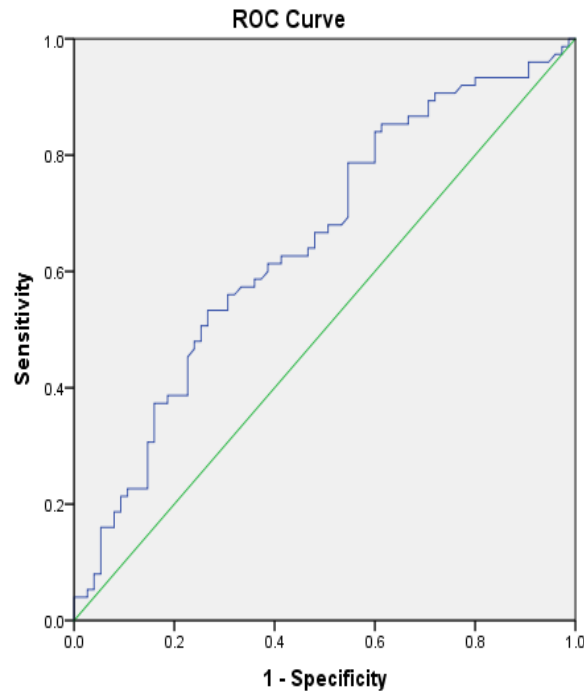
Table 1 Baseline characteristics of patients infected with pandemic 2009 H1N1 influenza virus with and without pneumonia*

| | | H1N1 negative(N=75) | | H1N1 positive(N=75) | | P-Value |
|-----------------------|-------------|---------------------|------|---------------------|------|---------|
| | | N | % | N | % | |
| Age group (years) | ≤20 | 8 | 10.7 | 7 | 9.3 | 0.854 |
| | 21-40 | 38 | 50.7 | 31 | 41.3 | |
| | 41-60 | 20 | 26.7 | 25 | 33.3 | |
| | >60 | 9 | 12 | 12 | 16 | |
| | Mean Age | 38.29±15.96 | | 41.92±16.55 | | 0.174 |
| Sex | Female | 36 | 48 | 37 | 49.3 | 1.00S |
| | Male | 39 | 52 | 38 | 50.7 | |
| Residence | Urban | 35 | 46.7 | 28 | 37.3 | 0.321 |
| | Rural | 40 | 53.3 | 47 | 62.7 | |
| Clinical Category | ICU (C) | 8 | 10.7 | 36 | 48 | <0.001 |
| | OPD (A&B) | 26 | 34.7 | 2 | 2.7 | |
| | Ward (C) | 41 | 54.7 | 37 | 49.3 | |
| Socio-economic status | High | 23 | 30.7 | 28 | 37.3 | 0.652 |
| | Mid | 25 | 33.3 | 21 | 28 | |
| | Low | 27 | 36 | 26 | 34.7 | |
| Presenting complains* | Cough | 57 | 76 | 57 | 76 | 0.848 |
| | Fever | 58 | 77.3 | 63 | 84 | 0.408 |
| | SOB | 33 | 44 | 51 | 68 | 0.005 |
| ECG | Abnormal | 37 | 49.3 | 51 | 68 | 0.031 |
| | Normal | 38 | 50.7 | 24 | 32 | |
| Chest x ray | Pneumonitis | 43 | 57.3 | 60 | 82.2 | 0.002 |
| | Normal | 32 | 42.7 | 13 | 17.8 | |

Table No : 2 comparison of parameters in H1N1 positive and Negative groups

| | H1N1 negative(N=75) | H1N1 positive(N=75) | P-Value |
|-------------------------------|---------------------|---------------------|---------|
| | Mean±SD | Mean±SD | |
| systolic blood pressure | 114.16±14.5 | 111.44±13.2 | 0.232 |
| diastolic blood pressure | 73±12.16 | 71.2±10.09 | 0.325 |
| SUGAR | 73±12.16 | 123.91±51.25 | <0.001 |
| LDH level | 641.38±515.08 | 919.38±738.84 | 0.008 |
| CPK level | 247±335.5 | 407.06±689.98 | 0.073 |
| Blood urea level | 43.85±25.91 | 40.29±27.56 | 0.416 |
| serum creatinine level | 2.51±10.96 | 1.18±084 | 0.296 |
| serum LDL level | 94.08±36.31 | 78.82±34.52 | 0.009 |
| serum HDL level | 36.85±4.28 | 36.45±7.91 | 0.701 |
| serum TG level | 154.19±96.74 | 153.8±88.55 | 0.979 |
| serum total cholesterol level | 146.64±41.92 | 138.11±40.32 | 0.206 |
| SGOT level | 116.13±223.28 | 225.69±971.73 | 0.343 |
| SGPT level | 110.09±217.47 | 141.88±394.81 | 0.542 |
| alkaline phosphatase level | 106.77±92.41 | 119.19±87.86 | 0.4 |
| serum bilirubin level | 1.09±.74 | 0.93±.65 | 0.162 |
| serum direct bilirubin level | 0.51±.47 | 0.42±.3 | 0.164 |
| serum potassium level | 4.12±.62 | 4.3±.67 | 0.09 |
| serum sodium level | 138.33±5.69 | 138.27±5.69 | 0.949 |

| | | | |
|------------------|-------------|------------|-------|
| Hemoglobin level | 11.62±2.14 | 11.82±2.7 | 0.616 |
| TLC level | 11.55±6.22 | 8.82±4.61 | 0.003 |
| platelet count | 1.89±1.03 | 2.06±.95 | 0.295 |
| ESR | 37.11±25.65 | 44.65±30.7 | 0.105 |



Diagonal segments are produced by ties.

Table No:3

| Area Under the Curve | | | | |
|--|-------------------------|------------------------------|------------------------------------|-------------|
| Test Result Variable(s): LDH | | | | |
| Area | Std. Error ^a | Asymptotic Sig. ^b | Asymptotic 95% Confidence Interval | |
| | | | Lower Bound | Upper Bound |
| .650 | .045 | .002 | .562 | .737 |
| The test result variable(s): LDH has at least one tie between the positive actual state group and the negative actual state group. Statistics may be biased. | | | | |
| a. Under the nonparametric assumption | | | | |
| b. Null hypothesis: true area = 0.5 | | | | |

*Dr.arvind Laskeshar. "Diagnostic Cut off The S. LDH In Cases of Pneumonia Caused By Pandemic 2009 H1N1 Influenza Virus At Tertiary Care Hospital." IOSR Journal of Dental and Medical Sciences (IOSR-JDMS) 16.10 (2017): 92-99