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Clinical and Radiographic Spectrum of Influenza A (H1N1) Infection and Its Association with Disease Severity

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ABSTRACT

Background: Influenza A (H1N1) infection remains an important cause of acute respiratory illness and viral pneumonia, with a wide spectrum of clinical severity ranging from mild disease to respiratory failure. For diagnostic purposes of H1NI, Chest imaging plays a crucial role in assessing pulmonary involvement and may provide valuable prognostic information when combined with clinical findings.

Objective: To evaluate the correlation between clinical and imaging findings and a worse clinical outcome in patients with a confirmed diagnosis of H1N1 influenza A virus.

Methodology: This multicenter observational study was included 140 patients with RT-PCR-confirmed H1N1 infection were included. All the patients' demographic data, clinical features, comorbidities, laboratory parameters, and imaging findings were recorded. The clinical outcomes were classified into good and worse (hospitalization and/or ICU admission). The statistical analysis included univariate and multivariate logistic regression to identify predictors of worse clinical outcomes.

Results: Worse clinical outcomes occurred in 42 patients (30.0%). The worst outcomes showed significantly higher frequencies of dyspnea (47.6% vs. 14.3%), diabetes mellitus (21.4% vs. 5.1%), and hypertension (31.0% vs. 13.3%). Poor outcomes were associated with 40.0% of patients with abnormal chest x-rays, whereas only 10.4% of patients with good outcomes had similar x-rays ($p < 0.001$). CT scan abnormalities were detected in 87.5% of severe cases, with strong associations of ground-glass opacities, consolidation, and diffuse bilateral lung involvement with disease severity.

Conclusion: Infectious influenza A (H1N1) clinical features and chest imaging, especially shortness of breath, associated diseases, and large radiographic or CT changes, were the most important factors for the sickness grade.

Keywords: Influenza A (H1N1); Chest Radiography; Computed Tomography; Disease Severity; Viral Pneumonia

Introduction

Globally, the influenza A (H1N1) virus remains a leading cause of acute respiratory illness, with a significant impact on seasonal epidemics and healthcare utilization. The virus has become an established seasonal pathogen that can cause significant morbidity, hospitalization, and intensive care unit (ICU) admissions, especially among adults with underlying comorbidities, even though the 2009 pandemic marked its emergence as a global public health threat. The need for early identification of patients at risk of unfavorable outcomes is highlighted by the fact that H1N1 infection is still linked to serious pulmonary complications, such as viral pneumonia and acute respiratory distress syndrome (ARDS), despite advancements in vaccination strategies and antiviral therapies.[1,2]

H1N1 infection can present clinically in a variety of ways, from self-limiting influenza-like illness to rapidly worsening respiratory failure. Fever, cough, myalgia, and dyspnea are common symptoms; in more severe cases, hypoxemia, chest pain, and a systemic inflammatory response may be present. Comorbid conditions like diabetes mellitus, hypertension, chronic lung disease, and immunosuppression significantly increase the risk of severe disease and poor clinical outcomes, according to several studies.[3,4] However, especially in busy emergency department settings, clinical assessment alone may not accurately predict disease severity at initial presentation.

When evaluating patients with suspected or confirmed viral pneumonia, chest imaging is essential. When patients present with respiratory symptoms, conventional chest radiography (CXR) is often the initial investigation because it remains the most widely available imaging modality. Consolidation, unilateral or bilateral pulmonary infiltrates, and, less frequently, pleural effusion are typical radiographic findings in H1N1 infection. However, the sensitivity of chest radiography may be limited in cases of early or mild disease.[5]

Computed tomography (CT) of the chest offers better sensitivity and detailed descriptions of lung involvement in viral infections. Ground-glass opacities, consolidation, thickening of the bronchial walls, and widespread lung involvement are common in patients with H1N1 pneumonia. These conditions are believed to show damage to the alveoli and inflammation. Recent studies have pointed out the value of CT findings for predicting outcomes. They show that extensive lung involvement raises the chances of respiratory failure, ICU admission, and longer hospital stays. Therefore, combining imaging results with clinical data may improve early risk assessment and help with management choices.

Over the past 10 years, greater focus has been placed on identifying imaging and clinical signs that predict disease severity in viral pneumonia, especially with new respiratory viruses. Different studies also strengthened the notion that chest imaging is an important tool for predicting outcomes in influenza-related pneumonia, including H1N1 infection.[2,5,9] However, most of these studies come from high-income countries, and data on South Asian populations remain limited.

In Pakistan, seasonal influenza significantly affects respiratory health. However, there is limited published data linking clinical features, imaging results, and disease severity in H1N1 infections. Differences in patient demographics, existing health conditions, access to healthcare, and diagnostic methods highlight the need for evidence specific to this region. It is crucial to understand the range of imaging results and how they relate to clinical outcomes in the local population. This knowledge will help improve early diagnosis, triage, and resource use.

The present study was conducted with the aims to assess the clinical and imaging aspects of Influenza A (H1N1) infection. It will explore the relationship between specific clinical features, chest imaging results, and disease severity in patients at a tertiary care hospital in Multan, Pakistan. By identifying readily available indicators of poor clinical outcomes, this research aims to support timely decision-making and improve the management of patients with H1N1 infection.

Objective

To evaluate the correlation between clinical and imaging findings and a worse clinical outcome in patients with a confirmed diagnosis of H1N1 influenza A virus.

Methodology

This multicenter observational study was conducted from January 2021 to March 2022 at Nishtar Medical University Hospital in Multan and Bahawal Victoria Hospital in Bahawalpur, two tertiary care teaching hospitals in Southern Punjab, Pakistan. For this study, ethical approval was obtained from the Institutional Review Boards of Nishtar Medical University, Multan. Because the study was observational, informed consent was waived, and patient confidentiality was carefully maintained throughout the study.

Adult patients aged 18 and older with a confirmed diagnosis of Influenza A (H1N1) were eligible for inclusion. H1N1 infection was confirmed using real-time reverse transcription polymerase chain reaction (RT-PCR) on nasopharyngeal or oropharyngeal swab samples. Patients were included if they had a chest X-ray and/or a chest computed tomography (CT) scan within 48 hours of diagnosis. Exclusion criteria included patients with bacterial or fungal lung infections, known active pulmonary tuberculosis, pre-existing interstitial lung disease, incomplete medical records, or missing follow-up data.

For study purpose, demographic and clinical information

were collected from hospital medical records using a standardized data collection form. The data collected included age, sex, symptoms at presentation (fever, cough, dyspnea, chest pain), existing health conditions (diabetes, hypertension, chronic obstructive pulmonary disease, immunosuppression), vital signs at admission, oxygen saturation on room air, and laboratory results such as total leukocyte count and C-reactive protein (CRP). Clinical outcomes were classified as good (discharge from the emergency department or ward without requiring intensive care) or worse, requiring hospitalization, ICU admission, or both.

Chest X-rays were performed on digital systems in standard posteroanterior views, with portable anteroposterior views obtained for critically ill patients as needed. Chest CT scans were performed on multidetector CT scanners with patients lying on their backs at full inspiration. Images were reconstructed with thin-section protocols and assessed in lung and mediastinal windows. Intravenous contrast was administered only when necessary, not routinely for all patients.

Two consultant radiologists with experience in lung imaging independently reviewed all imaging studies, unaware of the clinical outcomes. Chest X-ray findings were classified as normal or abnormal, with abnormalities further divided into pulmonary infiltrates, consolidation, and pleural effusion. CT findings were evaluated according to the Fleischner Society glossary, including ground-glass opacities, consolidation, bronchial wall thickening, pleural effusion, and the distribution of lung involvement (unilateral, bilateral, focal, or diffuse). If the reviewers disagreed, they reached a consensus through joint review.

Statistical analysis used SPSS software (version 26.0). Continuous variables were checked for normality and expressed as mean ± standard deviation or median with interquartile range, as applicable. Categorical variables were shown as frequencies and percentages. Comparisons between patients with good and worse outcomes were made with the Chi-square test or Fisher's exact test for categorical variables and the Student's t-test or Mann-Whitney U test for continuous variables. Variables with p-values < 0.10 in the univariate analysis were included in a multivariate logistic regression model to identify independent predictors of worse outcomes. Odds ratios (ORs) with 95% confidence intervals (CIs) were calculated, and a p-value of 0.05 or less was considered statistically significant.

Results

In the present study, 140 patients, who had laboratory-confirmed Influenza A (H1N1) infection, were included. Among them, 58 (41.4%) were female and 58.6% were male. The median age of the study cases was 47 years, with significantly higher ages in patients with worse outcomes (52 years [IQR: 36–67]) than in those with good outcomes (41 years [IQR: 28–55]; p = 0.021). Flu-like symptoms were common in both groups (93.9% in cases with good outcome and 95.2% in cases with worse

Table 1. Clinical characteristics according to clinical outcome

Variable	All patients (n=140)	Good outcome (n=98)	Worse outcome (n=42)	OR (95% CI)	p-value
Male sex	82 (58.6%)	60 (61.2%)	22 (52.4%)	0.70 (0.34–1.45)	0.339
Age >50 years	56 (40.0%)	31 (31.6%)	25 (59.5%)	3.19 (1.55–6.56)	0.001
Flu-like symptoms	132 (94.3%)	92 (93.9%)	40 (95.2%)	1.29 (0.28–5.98)	0.768
Dyspnea	34 (24.3%)	14 (14.3%)	20 (47.6%)	5.46 (2.39–12.45)	<0.001
Chest pain	12 (8.6%)	4 (4.1%)	8 (19.0%)	5.55 (1.55–19.8)	0.004
Any comorbidity	46 (32.9%)	25 (25.5%)	21 (50.0%)	2.92 (1.38–6.17)	0.004
Diabetes mellitus	14 (10.0%)	5 (5.1%)	9 (21.4%)	5.09 (1.56–16.6)	0.003
Hypertension	26 (18.6%)	13 (13.3%)	13 (31.0%)	2.92 (1.23–6.95)	0.013
Median CRP (mg/dL)	2.3	1.7	3.8	—	0.018
Temperature <37°C	48 (34.3%)	26 (26.5%)	22 (52.4%)	3.06 (1.47–6.37)	0.002

Table 2. Chest radiographic findings and association with outcome

Radiographic finding	Good outcome (n=58)	Worse outcome (n=40)	OR (95% CI)	p-value
Any abnormal CXR	6 (10.4%)	16 (40.0%)	5.73 (2.08–15.8)	<0.001
Pulmonary infiltrates	3 (5.2%)	8 (20.0%)	4.56 (1.12–18.6)	0.024
Consolidation	2 (3.4%)	6 (15.0%)	5.00 (0.97–25.7)	0.041
Pleural effusion	1 (1.7%)	3 (7.5%)	4.58 (0.46–45.3)	0.039

outcome) and did not differ significantly between groups. Dyspnea (47.6%) and chest pain (19.0%) were significantly more frequent among patients with worse outcomes. Among comorbidities, diabetes mellitus and hypertension showed a significant association with worse clinical outcomes. Median CRP levels were significantly higher in the worst outcome group (3.8), whereas body temperature at presentation was slightly lower in these patients (Table 1).

Results showed that Chest radiography was performed in 98 patients and found a significant association between abnormal radiographic findings and worse clinical outcomes. An abnormal chest X-ray was observed in 40.0% of patients with worse outcomes, compared with 10.4% in those with good outcomes, conferring nearly a six-fold increased risk of severe disease (OR 5.73, 95% CI 2.08–15.8; $p < 0.001$). Among specific radiographic patterns, pulmonary infiltrates were significantly more frequent in the worse outcome group (20.0% vs. 5.2%), and were associated with a more than four-fold increased odds of disease severity (OR 4.56, 95% CI 1.12–18.6; $p = 0.024$). Similarly, radiographic consolidation was predominantly observed in patients with worse outcomes, indicating a strong association with severe clinical course (OR 5.00, 95% CI 0.97–25.7; $p = 0.041$). Although pleural effusion was also significantly associated with disease severity (OR 4.58, 95% CI 0.46–45.3; $p = 0.039$) (Table 2).

Chest CT scans were performed on 55 patients, of whom 41 (74.5%) had abnormal results. Results showed that patients with CT abnormalities had worse clinical outcomes. An abnormal chest CT was found significantly more frequently among patients with worse outcomes than among those with good outcomes (87.5% vs. 56.5%), indicating a more than five-fold increased risk of severe disease (OR 5.40, 95% CI 1.39–21.0; $p = 0.012$). Among the different CT patterns, ground-glass opacities (GGO) were the most common abnormality and were significantly associated with disease severity (OR 3.84, 95% CI 1.24–11.9; $p = 0.018$). Pulmonary consolidation as seen on CT was also a strong indicator of worse clinical outcome (31.3% vs. 8.7%), which corresponds to a nearly five-fold increased odds of severe disease (OR 4.77, 95% CI 0.96–23.6; $p = 0.021$). A major and key radiological marker of severity, in this case, was the diffuse bilateral distribution of lung involvement (OR 4.17, 95% CI 1.19–14.6; $p = 0.004$) (Table 3).

According to the univariate logistic regression analysis, the indicators of poor clinical outcomes included dyspnea, diabetes mellitus, chest pain, abnormal chest imaging, and diffuse bilateral lung involvement. The patients with either CXR or CT showing any abnormality had an almost 6-fold higher risk of a worse clinical outcome (OR 5.96, 95% CI 2.41–14.7; $p < 0.001$).

A multivariate logistic regression model was built to identify independent variables associated with the worst clinical trial outcome, while controlling for potential confounding factors. All variables with p-values < 0.10 in the univariate analysis, as well as those known to be clinically relevant, were included in the model. The Hosmer–Lemeshow goodness-of-fit test yielded $p = 0.64$, and Nagelkerke R^2 was 0.41 during this test (Table 4).

Discussion

The present multicenter study evaluated 140 patients with laboratory-confirmed Influenza A (H1N1) infection and demonstrated that 30.0% (n = 42) experienced a worse clinical outcome, including hospitalization and/or ICU admission. Our findings show that specific clinical symptoms, comorbidities, and radiographic and CT abnormalities were significantly associated with disease severity, highlighting the importance of early clinical and imaging assessment.

In our cohort, dyspnea was present in 47.6% of patients with worse outcomes compared to 14.3% in those with good outcomes, conferring more than a four-fold increased risk of severe disease (adjusted OR 4.12, 95% CI 1.68–10.10; $p = 0.002$). This finding is consistent with prior studies reporting dyspnea as a key clinical marker of severity in H1N1 pneumonia. Srinivas et al. reported that dyspnea and respiratory distress were significantly more frequent among patients requiring ICU care.[11] Jain et al. similarly demonstrated that dyspnea at presentation was strongly associated with hospitalization and the need for intensive care in pandemic H1N1 infection.[12] Kang et al. further showed that dyspnea correlated with extensive lung involvement on imaging and adverse outcomes.[13]

These observations collectively support dyspnea as a reliable early indicator of disease severity.

Comorbidities were present in 50.0% of patients with the worst outcomes and in 25.5% of those with the best outcomes (OR 2.92, 95% CI 1.38-6.17; p = 0.004). Among the worst-outcome group, diabetes was found in 21.4% of cases, whereas in the best-outcome group, it was only 5.1%. It was likewise an independent predictor of disease severity on multivariate analysis (adjusted OR 3.76, 95% CI 1.21-11.67; p = 0.022). Hypertension was also found to be considerably more prevalent among the cases with the poorest outcomes (31.0% vs. 13.3%; adjusted OR 2.28, 95% CI 1.01-5.18; p = 0.046). Kumar et al.,[14] Bramley et al.,[15] and Mertz et al.[16] have all reported similar associations between metabolic and cardiovascular comorbidities and severe H1N1 infection, indicating that the initial state of systemic inflammation and immune dysfunction may be the factors driving disease progression.

In our study, chest radiography was a principal modality that aided early risk stratification. Abnormal radiographic findings occurred in 40.0% of patients with worse outcomes, compared with 10.4% among patients with good outcomes, among those who had a chest X-ray. This corresponds to a risk of severity nearly six times higher (OR 5.73, 95% CI 2.08–15.8; p < 0.001). Pulmonary infiltrates were seen in 20.0% of patients with worse outcomes and in 5.2% with good outcomes, while radiographic consolidation was noted in 15.0% vs. 3.4%, respectively. The studies by Srinivas et al., Funaki et al.,[11,17,18] and Nicolini et al. have been cited in these findings, as they all indicated that early chest radiographic abnormalities, especially consolidation and bilateral opacities, correlated with increased disease severity and ICU admission.

The chest CT scans not only confirmed but also strengthened the association between imaging abnormalities and clinical severity. Abnormal CT scans were observed in 87.5% of patients with worse outcomes in our study, compared with 56.5% in patients with good outcomes, indicating a fivefold increase in the risk of severe disease (OR 5.40, 95% CI 1.39–21.0; p = 0.012). The most common CT abnormality was ground-glass opacity, which was found in 62.5% of patients with worse outcomes, compared with only 30.4% in the good-outcome group (OR 3.84, p = 0.018). Consolidation was observed in 31.3% vs. 8.7%, respectively. These CT findings are consistent with the typical imaging features of H1N1 pneumonia described by Ajlan et al. [19], Kang et al. [13], and Henzler et al. [20], in which greater alveolar involvement was associated with respiratory failure.

Most importantly, the degree of lung involvement was a robust predictor of severity. In 46.9% of patients with the worst outcomes, diffuse bilateral lung involvement was noted, compared with 17.4% in patients with good outcomes. It remained an independent predictor on multivariate analysis (adjusted OR 3.97, 95% CI 1.42–11.10; p = 0.009). Similar observations were made by Agarwal et al. [21] and Koo et al. [2], who stressed that the widespread bilateral disease on imaging indicates substantial inflammation and corresponds to poor clinical outcomes in viral pneumonias.

From a clinical standpoint, the present study underscores the importance of combining uncomplicated clinical variables with high-quality imaging findings. The patients who exhibit breathing difficulties, several diseases at the same time, and abnormal chest imaging, particularly with the involvement of both lungs diffusely, are high-risk individuals who could get closer observation and even early care escalation, especially in healthcare settings that are not well equipped with resources, thus, the need for these people's high-risk factor close monitoring.

In summary, our research indicates that nearly a third of the H1N1-infected population suffered from worse clinical outcomes, and that among the disease course predictors, the breathing difficulty, the presence of diabetes, the history of hypertension, the abnormality in the chest X-ray pictures, the CT finding of ground-glass opacities, and the infiltration of the lung by air all over are major predictors of severity. Recognizing these signs

Table 3. CT findings according to clinical outcome

CT finding	Good outcome (n=23)	Worse outcome (n=32)	OR (95% CI)	p-value
Any abnormal CT	13 (56.5%)	28 (87.5%)	5.40 (1.39–21.0)	0.012
Ground-glass opacity	7 (30.4%)	20 (62.5%)	3.84 (1.24–11.9)	0.018
Consolidation	2 (8.7%)	10 (31.3%)	4.77 (0.96–23.6)	0.021
Bronchial thickening	9 (39.1%)	12 (37.5%)	0.94 (0.32–2.79)	0.912
Pleural effusion	1 (4.3%)	5 (15.6%)	4.07 (0.44–37.7)	0.047
Diffuse bilateral involvement	4 (17.4%)	15 (46.9%)	4.17 (1.19–14.6)	0.004

Table 4. Multivariate logistic regression analysis identifying independent predictors of worse clinical outcome in patients with Influenza A (H1N1) (n = 140)

Variable	Adjusted OR	95% CI	p-value
Age >50 years	2.41	1.09–5.36	0.031
Dyspnea at presentation	4.12	1.68–10.10	0.002
Diabetes mellitus	3.76	1.21–11.67	0.022
Hypertension	2.28	1.01–5.18	0.046
Chest pain	4.89	1.23–19.38	0.024
Elevated CRP (>3 mg/dL)	2.63	1.14–6.05	0.023
Any abnormality on CXR or CT	5.84	2.07–16.49	<0.001
Diffuse bilateral lung involvement (CXR/CT)	3.97	1.42–11.10	0.009

early may support timely risk stratification and the most appropriate management of patients with Influenza A (H1N1) infection.

Limitations

There are several limitations in this research that must be taken into account when interpreting the results. To start, the observational design limits the researcher's ability to infer causality between clinical or imaging findings and disease severity. In the second place, even though the research was conducted in two large tertiary care centers, it still reflects only a hospital-based population, which may make the results less applicable to patients with Influenza A (H1N1) managed in the community or with mild symptoms. Third, the decision to perform a chest CT was based on clinical factors rather than a uniform protocol, which may have led to the selection of more severe cases and introduced selection bias. Fourth, despite the interpretations being performed independently by seasoned radiologists, interobserver variability in image interpretation could not be entirely ruled out. In the end, the long-term follow-up data, which would have included post-discharge outcomes and residual pulmonary sequelae, were not analyzed, potentially leading to an underestimation of the overall clinical impact of severe H1N1 infection.

Conclusion

To sum up, the findings of this multicenter study show that around a third of patients with Influenza A (H1N1) infection had poor clinical outcomes, and that specific clinical and imaging features were strongly associated with disease severity. Major symptoms were dyspnea at the beginning, existing conditions, particularly diabetes and hypertension, and lung imaging with abnormalities. These were the strong indicators of the severe disease. In imaging, ground-glass opacities, consolidation, and diffuse bilateral lung involvement were the major markers of severity on chest X-ray and CT. The combination of early clinical evaluation with chest imaging can provide valuable prognostic information and support timely risk stratification and management, especially in resource-constrained health care systems. It is necessary to conduct prospective studies using standardized imaging protocols and longer follow-up to further refine severity prediction models and improve outcomes for patients infected with Influenza A (H1N1).

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