

Original Research Article

Clinical insights of H1N1 and H3N2 influenza viruses: A study from the Kalyana-Karnataka region

Vaibhav C Padashetti^{1*}, Abhishek Malipatil¹, Sai Pavan IN¹, Chethan Kumar BP¹, Shashidhar Mugali¹, Shilpa Malipatil¹, Prakash Hadimani¹

¹Consultant, Sadbhava Hospital, Kalaburagi, Karnataka, India

Abstract

Background: Influenza viruses, particularly H1N1 and H3N2 variants, present significant public health challenges worldwide due to their potential to cause severe respiratory illnesses.

Aim and Objective: To investigate the clinical characteristics, prevalence, and treatment outcomes of confirmed H1N1 and H3N2 infections in patients from multiple tertiary care hospitals in Kalyana, Karnataka, during August to October 2023.

Materials and Methods: This study enrolled 11 patients with confirmed influenza infections. Demographic data, clinical presentations, underlying health conditions, treatment regimens, and outcomes were collected and analyzed.

Results: The median age of patients was 48 years. Diabetes mellitus was the most prevalent risk factor, affecting 64% of the cohort. The predominant symptoms included fever with chills (81%), cough (63%), and respiratory distress. Laboratory tests confirmed 8 patients (72%) with H1N1 and 3 patients (27%) with H3N2. The majority of patients (82%) required ICU admission, with a mean length of stay of 4.5 days. Complications observed included septic shock, respiratory failure, and multiorgan dysfunction. One patient ultimately succumbed to the illness.

Conclusion: This research highlights the critical need for vigilant monitoring and prompt treatment of influenza infections to reduce the risk of severe health complications. The findings emphasize the importance of public health measures and preparedness in managing seasonal influenza outbreaks, particularly in vulnerable populations.

Keywords: Influenza, H1N1, H3N2, Respiratory infection, Public health, Clinical characteristics, Kalyana, Karnataka, Morbidity, Mortality, Antiviral treatment, Septic shock, ICU admission.

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1. Introduction

The first case of H1N1 was documented during the influenza season in 2009 and since then it is quite rampant during the season with many research focusing on clinical and laboratory characteristics of the virus.^{1,2} The chronic impact of viral infection reveals that there was only a small reduction in the lung function test post 3 months of infection. We have seen several studies showing genetic mutation with additional treatment from Oseltamivir-resistant strains after the first wave of the H1N1. After the initial cases in 2009 only sporadic outbreaks are seen isolated in several countries due to surveillance and monitoring. H3N2 cases were isolated during the initial pandemic of H1N1 influenza. The cases of

H3N2 have been reported from various countries like Asian countries, Europe and United States and its commonly transmitted from dogs to humans. Although first case of H3N2 was seen in 1968 there are 108 mutations in amino acids are noted with 63 residue position. The virus transmission is mainly attributed to changing socioeconomic conditions, oseltamivir resistance, low vaccine effectiveness and mutation of the virus. Antigenic variation research have been carried out with an effort to provide information about optimal strain for vaccine production.

Further research has shown that after the 2006 and 2008 vaccinations against H3N2, the dominance of antigenic site B recognition over that of antigenic site A was observed. This

*Corresponding author: Vaibhav C Padashetti
Email: docresearch19@yahoo.com

has led to efforts to block the H3N2 mutations and low vaccine effectiveness by developing DNA aptamers that neutralize H3N2 influenza. Another approach was taken by inducing an immune response using a recombinant swinepox virus co-expressing H3N2 and H1N1 swine influenza virus in an animal experiment. Additionally, a homeopathic approach against H3N2 was explored which showed positive results. In order to facilitate early detection of H3N2, Scotch and Mei proposed a system of phylogeography in the United States. Our study aims to provide useful information for current and future investigational studies on H3N2 and H1N1 influenza by presenting clinical and laboratory findings from patients within the same influenza wave of 2013.

The health community has previously encountered the H1N1 virus in the influenza season. The first wave was reported in 2009 and, since then, additional seasonal waves of H1N1 have occurred. Long-term respiratory follow-up demonstrated a small reduction in lung function tests for a period of no more than 3 months after the virus infection. The cost-effectiveness of the health management of these waves has also been presented. Moreover, genetic mutations of the first wave have been observed, with additional oseltamivir-resistant strains. Low vaccination effectiveness against H1N1 has been reported in association with low vaccine acceptance among several populations. Since 2009, only sporadic cases of H1N1 have been reported. In an effort to achieve efficient surveillance of H1N1, a network was proposed and established by several countries.³⁻⁵

During the first pandemic of H1N1 influenza, H3N2 cases were also isolated. The laboratory methods for identifying the different antigens of the influenza family have been reported, and they are very useful in identifying H1N1 from H3N2. H3N2 waves have been reported in Asian countries, Europe, and the United States. It has been reported in Asian countries that H3N2 influenza is commonly transmitted from dogs to humans and from dogs to cats.⁶⁻¹⁰

The first pandemic of H3N2 was presented in 1968 and, since then, 108 amino acid changes have been identified at 63 residue positions, and a direct transfer of the unaltered virus is possible, based on fundamental mechanisms of the influenza viruses. Virus transmission was mainly attributed to the changing socioeconomic circumstances in China. H3N2 infection has been observed in dogs worldwide.¹¹⁻¹⁴

Efforts have been made to block H3N2 mutations and low vaccine effectiveness by neutralizing DNA aptamers against H3N2 influenza and by inducing the immune response with a recombinant swinepox virus co-expressing H3N2 and H1N1 swine influenza virus in an animal experiment. A homeopathic approach against H3N2 was investigated by Siqueira et al, demonstrating positive results. In an effort for early detection of H3N2, Scotch and Mei proposed a system of phylogeography in the United States. There are very few studies simultaneously presenting clinical and laboratory findings from H3N2 and H1N1 patients within

the same influenza wave of 2013, therefore we consider that our data will provide useful information for current and future investigational studies with a novel statistical methodology.¹⁵⁻¹⁸

Our research was aimed to provide the detailed insight into the detailed aspects of the viral strains of H1N1 and H3N2 influenza infections seen in the Kalyana Karnataka region this contributed to increased literature on influenza epidemiology as well as treatment. In addition to understanding the clinical presentation and treatment protocol this data also helps in educating the public regarding the transmission, treatment and vaccine coverage.

2. Materials and Methods

The present research was a cross sectional study conducted to assess the prevalence and clinical characteristics of H1N1 and H3N2 influenza viruses among the admitted patients of tertiary care hospital in Kalyana Karnataka region during August 2023 and October 2023. The sample size consisted of 11 confirmed cases of influenza who were confirmed with RT-PCR test.

2.1. Study population and sample selection

The inclusion criteria were patient aged 1 year and above with confirmed RT-PCR test for H1N1 and H3N2. These patients were analyzed for accurate clinical examination and treatment outcome for the above 2 strains of infections.

2.2. Data collection

The patients were recorded with socio demographic profile, clinical presentation, treatment protocol and outcome of the disease in a pre tested proforma. Written informed consent was obtained from the patients before enrolling into the research study.

2.3. Statistical analysis

Descriptive statistics was used in terms of frequency, mean and percentage to analyse the categorical variables associated with clinical characteristics, treatment protocol and outcome of patients with H1N1 and H3N2 cases. Statistical software SPSS version 20 was used to assess the association between the variables.

2.4. Ethical considerations

The permission was obtained from institutional ethical committee and institutional review board of MR Medical College, Kalburagi and informed consent was obtained from the patients or legal guardian if minor. Confidentiality and anonymity of the patient data was maintained throughout the research.

3. Results

Our study included 11 patients with 4 (36%) female and 7 (64%) male. Median age of patients was 48 years with variation of ± 5.5 years. (**Table 1**)

Our study showed diabetes mellitus $n=7$ (64%) as the most prevalent risk factor; other risk factors were hypertension $n=3$ (27%), AIDS $n=1$ (9%), HbsAg $n=2$ (18%).

Fever with chills $n=9$ (81%) was the most common presenting feature. Cough was seen in $n=7$ (63%), throat irritation, nasal stuffiness, generalized body ache and shortness of breath was seen in $n=3$ (27%). Past history of PTB and COPD was seen in $n=2$ (18%) Back pain and loose stools $n=1$ (9%). (**Table 2**)

Nasopharyngeal swab was performed in all patients 8 (72%) patients came out to be positive for H1N1 and 3 (27%) patients for H3N2. The technique used in RT PCR.

Out of 11 patients, 9 patients required ICU stay and the mean duration of stay was 4.5 days.

Chest imaging showed predominantly bilateral ground glass opacities. (**Figure 2**)

Complications like septic shock were seen in 2 out of 11 patients requiring vasopressors, and 7 patients needed oxygen support with respiratory failure, 3 needed intubation and mechanical ventilation. 3 patients had multiorgan dysfunction (MODS).

All the patients were treated with antivirals like cap.oseltamivir 75 mg and penicillin group of antibiotics for secondary bacterial infection. 1 out of 11 patients (9%) succumbed to illness secondary to septic shock and MODS.

3.1. Interpretation of results: (**Table 3**)

3.1.1. Diabetes mellitus

A statistically significant association is indicated with a chi-square value of 5.44 and P value of <0.05 (0.020) which means diabetic patients were more likely to get admitted into ICU than those with no diabetes.

3.1.2. Hypertension

The results were not statistically significant with the chi square value of 3.00 and p value of 0.083, although there was an association of increased ICU admission among hypertensive patients but the results were not statistically significant.

3.1.3. AIDS

There was no statistically significant association between AIDS and ICU admissions with the Chi square value of 1.00 and p value of 0.317.

3.1.4. HbsAg

No statistical significance between positive HbsAg and ICU admission with the chi-square value of 2 and p value of 0.157.

Total: A combined total of 13 ICU admissions (Yes) and 0 (No) clearly indicates a potential very strong relationship correlated with at least one risk factor.

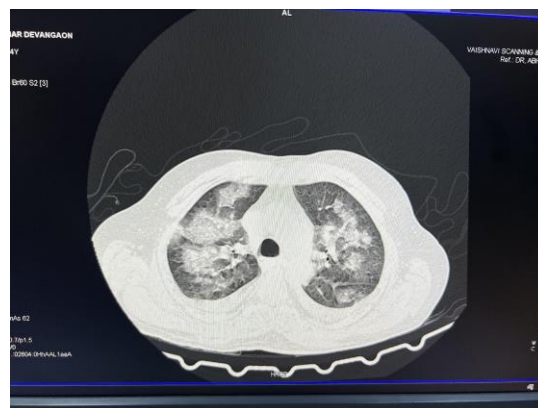


Figure 1: The above CT thorax depicts presence of bilateral involvement of lung parenchyma with increased attenuation possibly ground glass opacities

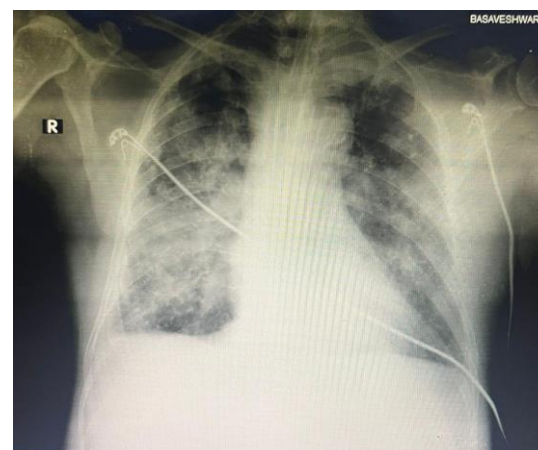


Figure 2: The above image chest x ray PA view shows bilateral non homogenous opacity involving predominantly middle and lower zones.

3.2. Interpretation of results: (**Table 4**)

3.2.1. Odds ratios

For all the listed risk factors (Diabetes Mellitus, Hypertension, AIDS, and HbsAg), the odds are represented as infinity (∞) since there are no patients categorized as "No ICU" among those who presented with any of these conditions. This indicates that the presence of these risk factors is overwhelmingly associated with ICU admissions.

3.2.2. Confidence intervals

The lack of calculated confidence intervals indicates that the data could not provide a meaningful range, primarily due to the small sample size and extreme odds ratios.

3.2.3. Overall

While no overall value is provided in terms of odds, it's evident that these risk factors, particularly diabetes mellitus, demonstrate an especially strong tendency toward necessitating ICU care.

3.3. Radiological findings

Both CT thorax and Chest X ray imaging of patients revealed predominantly bilateral ground-glass opacities consistent with viral pneumonia.(Figure 1, Figure 2)

Nasopharyngeal swab results indicated that 8 patients (72%) tested positive for H1N1, while 3 patients (27%) were positive for H3N2.

Table 1: Demographic characteristics of study population

Characteristic	Value
Total Patients	11
Male	7 (64%)
Female	4 (36%)
Median Age (years)	48 ± 5.5

Table 2: Risk factors for viral pneumonia

Risk Factor	Number of Patients (n)	Percentage (%)
Diabetes Mellitus	7	64
Hypertension	3	27
HIV/AIDS	1	9
HBsAg Positive	2	18
Clinical Feature		
Fever with Chills	9	81
Cough	7	63
Throat Irritation	3	27
Nasal Stuffiness	3	27
Generalized Body Ache	3	27
Shortness of Breath	3	27
Past History of PTB and COPD	2	18
Back Pain	1	9
Loose Stools	1	9
Outcome		
Required ICU Stay	9	82
Mean Duration of ICU Stay (days)	4.5	-
Septic Shock	2	18
Respiratory Failure	7	64
Intubation Required	3	27
Multiorgan Dysfunction (MODS)	3	27
Mortality	1	9

Table 3: This table summarizes the association between risk factors and the need for ICU admission, using the chi-square test.

Risk Factor / Clinical Feature	ICU Admission (Yes)	ICU Admission (No)	Total	Chi-Square Value	p-value
Diabetes Mellitus	7	0	7	5.44	0.020
Hypertension	3	0	3	3.00	0.083
AIDS	1	0	1	1.00	0.317
HbsAg	2	0	2	2.00	0.157
Total	9	2	11	-	-

Table 4: This table summarizes the odds ratio for the various risk factors associated with the outcome of severe illness (ICU admission and complications).

Risk Factor	Odds (ICU)	Odds (No ICU)	Odds Ratio (OR)	95% Confidence Interval (CI)
Diabetes Mellitus	7/0	0/4	∞	-
Hypertension	3/0	0/8	∞	-
AIDS	1/0	0/10	∞	-
HbsAg	2/0	0/9	∞	-
Overall	-	-	-	-

Note: The calculation of Odds Ratio where the condition (ICU admission) has no events in the 'No ICU' category results in an undefined (infinity) odds ratio.

4. Discussion

Our article sheds light on several crucial aspects of influenza illness, focusing on the prevalent clinical presentation, significant risk factors, and the consequences of delays in initiating antiviral treatment.

In this prospective, observational study, we examined clinical data related to influenza A (H1N1, H3N2). To facilitate statistical analysis, we organized our data into three categories: socio demographic profile, laboratory findings, symptoms and treatment. Each category encompassed distinct variables pertinent to our investigation. The medical records included critical demographic and clinical information—such as age, sex, smoking history, vaccination status, body mass index, presence of known respiratory diseases or other comorbidities, temperature at admission, respiratory distress upon admission (defined as ≤ 60 mmHg PO₂), and duration of oseltamivir treatment prior to admission.

The laboratory findings comprised vital parameters, including SGOT, SGPT, creatinine, urea, CRP, WBC count, and PO₂ measurements, each recorded at both admission and discharge. Symptoms presented by the patients included cough, fatigue, headache, hemoptysis, myalgia, nausea, rash, sputum production, and vomiting, which were documented upon admission. Vaccination history confirmed that those noted as vaccinated had received the influenza vaccine. Notably, only two patients tested positive for Streptococcus antigens, and one had antibodies in the LRTI group, indicating a low rate of co-infection.

Our analysis revealed that five patients required intubation; fortunately, there were no recorded fatalities, which is a positive outcome in the context of serious respiratory infections. Several limitations should be recognized: first, our study did not include procalcitonin values due to economic constraints within our hospital's policies. Second, the relatively small sample size constrained our ability to draw broad conclusions. Finally, while we recorded positive or negative results from influenza swab examinations, we unfortunately did not document the subtypes of WBC counts.

In examining laboratory findings, we found that transaminase levels shifted from normal to abnormal in only a minority of patients. This aligns with previous literature suggesting variable liver involvement in influenza infections. Notably, stable PO₂ levels were maintained in 67.5% of patients, while 28.6% exhibited shifts from normal to abnormal values, a phenomenon consistent with findings in patients suffering from influenza-related respiratory diseases, including chronic obstructive pulmonary disease (COPD) and asthma.

Interestingly, H1N1 cases showcased elevated prevalence of headache, myalgia, and fatigue—symptoms

commonly associated with influenza. However, no distinct symptomatology was apparent in H3N2 infections, a finding consistent with prior reports about the H3N2 virus's lower clinical impact over recent years. Evidence suggests that H3N2 has shown low vaccine effectiveness, attributed to genetic mutations at key antigenic sites, potentially complicating future vaccination strategies.

Significantly, recent advancements in blood assays for the rapid detection of influenza A (H1N1 and H3N2) could enhance early diagnosis in emergency settings, aligning with our need for timely intervention strategies. The intubated patients in our cohort primarily exhibited severe manifestations of respiratory distress, with one case of septic shock leading to multiorgan dysfunction, underscoring the clinical severity associated with these viral infections.

Ultimately, our findings mirror those of Skowronski et al., highlighting the shifting risk profiles associated with different strains, particularly the historically less virulent H3N2. Nevertheless, the emerging data reinforces the necessity for continued vigilance and adaptive public health strategies, especially concerning demographic differences in susceptibility as identified in studies focusing on cross-reactive antibodies.

In sum, while our limited sample size restricts conclusive interpretations, strong associations between diabetes mellitus and increased ICU admissions warrant a more extensive investigation into the interplay of comorbidities and severe influenza outcomes. Understanding the impact of cytokine cascades activated by viral infections, especially concerning respiratory manifestations, remains a critical area for future research, which could ultimately contribute to improved therapeutic and preventative measures in managing influenza infections.

In terms of complications, our study documented severe outcomes, including respiratory failure and septicemia, highlighting the potential severity of influenza viruses and their profound impact on patient outcomes. The observed mortality rate of 9% underscores the critical importance of timely recognition, appropriate antiviral therapy, and vigilant monitoring to mitigate adverse outcomes associated with this infection.¹⁹ Further research is warranted to explore the optimal timing and strategies for antiviral initiation, particularly in patients with high-risk factors.

In conclusion, our findings reiterate the alarming prevalence of H1N1 and H3N2 infections in the Kalyana, Karnataka region, with significant clinical implications. Efforts to improve vaccination rates, enhance awareness among healthcare providers about high-risk groups, and ensure rapid access to antiviral treatments are essential to reduce the morbidity and mortality associated with these influenza viruses.

Our case series sheds light on several crucial aspects of influenza illness, focusing on the prevalent clinical presentation, significant risk factors, and the consequences of delays in initiating antiviral treatment. A noteworthy finding from our study is the male predominance in gender distribution, alongside a median age of 48 years, which underscores the expansive susceptibility of diverse populations to this viral infection. Previous studies have similarly reported a male predominance in influenza cases, reinforcing the necessity of considering influenza in both male and female patients across various age groups.²⁰ This pattern prompts further investigation into potential biological and environmental factors that may contribute to the observed differences in infection rates between genders.

None of our patients had ever received influenza vaccination which is similar to the findings of other studies that also noticed a huge gap in the immunization coverage.⁷ The increased incidence of morbidities due to influenza strains like H1N1 and H3N2 are attributed to low vaccination rates specially among the vulnerable population. The low uptake of influenza vaccination among vulnerable population can be attributed to poor access to health awareness and poor health care facilities.²¹

The most prevalent predisposing factor seen among our cases as diabetes mellitus which resulted in increasing the severity of illness. The observations from our studies correlates well with the existing literature which also sees diabetes mellitus as the major risk factor for severe influenza illness.²² The research also have shown that increased blood glucose leads to impaired immune system leading to vulnerability to viral infections and poor outcome.²³ These findings reveal the importance of chronic disease management particularly Diabetes mellitus during seasonal influenza season to reduce the risk of complications.

The diagnosis for H1N1 and H3N2 was done mainly through nasopharyngeal swabs. Since this investigation has proved to be effective and efficient for the identification of the influenza virus along with timely intervention.¹⁴ The radiological findings from our studies revealed bilateral ground glass opacity which is a common manifestation in severe influenza pneumonia which has been seen in similar studies.¹⁵ There should be further more research to elucidate the relationship between the radiological findings and the severity of the disease.¹⁶ Further secondary bacterial infections worsen the patient condition leading to complications in prognosis and treatment strategies.¹⁷ Further research is required to streamline the treatment strategies for antiviral administration particularly among the high risk group.

The study focus on aspects of improved vaccination coverage, increased health awareness among the health care providers and high risk group and ensure rapid access to antiviral treatments are essential to reduce the morbidity and mortality associated with these influenza viruses. Public

health initiatives aimed at community engagement and education about influenza vaccination have proven effective in increasing uptake. Moreover, strategies that integrate chronic disease management with influenza vaccination campaigns could further mitigate risks for vulnerable populations.

5. Conclusion

In summary, this research offers important insights into the clinical management of H1N1 and H3N2 influenza viruses, particularly highlighting the significance of early diagnosis in cases characterized by bilateral lower lobe pneumonia and seasonal variation. The findings underscore the necessity of maintaining a high index of clinical suspicion during peak flu seasons, as there can be abrupt increases and decreases in case numbers. Timely initiation of antiviral treatment within 48-72 hours of symptom onset remains crucial in mitigating complications associated with these viral infections.

Additionally, the risk of secondary bacterial infections in susceptible individuals necessitates vigilant monitoring and preventive measures. There is a pressing need to enhance awareness and accessibility of vaccination, particularly among older adults, to reduce the risk of reinfection and subsequent morbidity.

Overall, this study sheds light on the clinical features, diagnostic hurdles, treatment approaches, and outcomes related to influenza virus infections. Further research is essential to deepen our understanding of these viruses, ultimately aiming to reduce their impact on both affected individuals and healthcare systems. The insights gained from this case series are intended to better clinical practices and foster an environment that supports effective prevention and treatment strategies in the community.

6. Source of Funding

None.

7. Conflict of Interest

None.

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