

## Clinical and Laboratory Profile of H1n1 Influenza in Children and Adolescents in Tertiary Care Centres

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### Abstract

**Introduction:** Influenza viral infections cause a broad array of respiratory diseases that are responsible for significant morbidity and mortality in children.

Influenza A viruses also have potential to cause periodic global Pandemics with higher penetration of illness than seasonal epidemics. Swine origin Influenza has become the first pandemic of the 21st century. The currently circulating strain of swine origin influenza virus, the H1N1 strain has undergone triple reassortment and contains genes from the avian, swine and human viruses. This virus was first reported in Mexico in April 2009 and spread to various countries worldwide. Higher morbidity (27236 cases) and mortality (981 deaths) have been reported from India. As per WHO, the Pandemic influenza A (H1N1) virus is now considered as seasonal virus.

**Objectives:** (1) To know the pattern of clinical presentation of H1N1 influenza in children. (2) To know the risk factors predisposing to serious illness in H1N1 influenza in children. (3) To analyse the laboratory profile of children with H1N1 influenza infection.

**Methodology:** A hospital based cross sectional observational study was conducted from March 2017 to March 2019. The study had ethical clearance from Institute ethical committee. All suspected cases were confirmed by RT-PCR performed at Institute of preventive medicine, Narayanguda and Fever hospital, Nallakunta. A total of 80 H1N1 positive patients from tertiary care centres (Niloufer hospital, Gandhi hospital, Fever hospital) were studied during a period of 24 months.

Data was analysed using SPSS software and using chi square tests.

**Results:** Comparison of mean age, gender and clinical presentation of H1N1 influenza infected children showed that maximum number of cases were below 2 years with slight male predominance. The most common clinical presentation was fever (100%) and most (80-96%) had respiratory symptoms. Abnormal chest X Ray findings with bilateral involvement in 49% cases and lobar consolidation in 10.6 % cases. Of all the cases, 18.6% required CPAP and 13.3% required ventilatory support.

**Conclusion:** Demographic profile according to present study showed more cases in February and March. The rate of reported cases and hospitalisation rates were highest among children less than 2 years. In our study, more than 90% of positive cases met the definition of influenza like illness.

Factors predicting the severity of illness were presence of congenital heart disease, lung disease, immunosuppression, malnutrition. Abnormal chest X Ray and Arterial Blood Gas values and requirement of mechanical ventilation predicted poor outcomes.

**Keywords:** Children, Influenza; H1N1 infection; RT-PCR; Epidemic; Pandemic; Antigenic drift and shift; pneumonia; Influenza like illness; Malnutrition, anemia; Acidosis; Mechanical ventilation.

## Introduction

### Case Definitions

The following definitions have been provided by the United States Centers for Disease Control and Prevention:

1. Influenza like illness (ILI) is defined as fever [temperature 100°F (37.8°C) or more] with cough / sore throat without a known cause other than influenza.
2. A confirmed case of pandemic H1N1 influenza A is an individual with an ILI with laboratory confirmed H1N1 influenza A virus, detected by real-time reverse transcriptase (rRT)-PCR or culture.
3. Pandemic H1N1 influenza A may be suspected in an individual who does not meet the definition of confirmed pandemic H1N1 influenza A, and has an ILI and an epidemiologic link.

## Virology

### Influenza Subtypes

Clinical influenza can be caused by several different influenza subtypes, though H1N1 is the most common subtype in both swine and human infections. Human cases of swine H3N2 influenza A virus infection has been reported rarely.<sup>4</sup> Other subtypes that have been circulating in pigs include H1N2, H3N1, and H3N2.

### Influenza Virus 3 Types

Type A	Type B	Type C
Causes significant disease: epidemics, global pandemics	Causes significant disease: milder epidemics	Does not cause significant disease
Infects both humans and other species	Limited to humans	Limited to humans
Frequent antigenic variations	Infrequent antigenic variations	Antigenically stable

### Aims and Objectives

1. To know the pattern of clinical presentation of H1N1 influenza in children.
2. To know the risk factors predisposing to serious illness in H1N1 influenza in children.
3. To analyse the laboratory profile of children with H1N1 influenza infection.

## Materials and Methods

*Setting:* Patients admitted with diagnosis of H1N1 influenza in tertiary care center, Hyderabad were evaluated in the study

*Ethical Committee Approval:* Institute ethical committee approved the study

*Study design:* Cross sectional observational study

*Duration of Study:* 24 months

*Inclusion Criteria:* All children diagnosed with H1N1 influenza diagnosed by RT-PCR

*Exclusion criteria:* Those who have not given consent

*Sample Size:* 75 cases

*Period of Study:* 2017 (March)-2019 (March)

*Target Population:* All children below the age of 18 years.

## Methodology

A hospital based cross sectional observational study was conducted from March 2017 to March 2019. The study had ethical clearance from Institute ethical committee. All suspected cases were confirmed by RT-PCR performed at Institute of preventive medicine, Narayanguda and Fever hospital, Nallakunta. A total of 80 H1N1 positive patients from tertiary care centres (Niloufer hospital, Gandhi hospital, Fever hospital) were studied during a period of 24 months. A confirmed case of pandemic H1N1 influenza A is defined as an individual with an ILI with laboratory confirmed H1N1 influenza A virus detected by RT-PCR. During this period the clinical profile and laboratory profile of H1N1 cases was analysed.

Data was analysed using SPSS software and using chi square test. The clinical parameters with which the child presented were assessed. The lab parameters included Hemoglobin%, leucocyte count, Platelet count, Renal parameters, Arterial Blood gases, Chest Radiography.

### Statistical analysis

Following statistical method has been employed in the present study. Pearson correlation coefficient and Fisher Exact test calculator was used with contingency tables.

## Observations and Results

### Case distribution

**Table 1:** Time Distribution of Cases

Time period	Cases
March	11
April	8
May	–
June	–
July	5
August	7
September	9
October	6
November	5
December	5
January	6
February	13

**Table 2:** Age Distribution of Cases.

Age distribution	No. of cases (%)
<6 mo	10 (13.3%)
6mo - 1yr	18 (24%)
1 to 2yrs	20 (26.6%)
w2 to 5 yrs	12 (16%)
> 5 yrs	15 (20%)

**Table 3:** Sex Distribution of Cases

Total cases	No. of cases	% of cases
Males	40	53.4%
Females	35	46.6%

**Table 4:** Clinical Manifestations.

Symptoms	Percent	Symptoms	Percent
Cold	54%	Headache	5%
Cough	80%	Eye congestion	25%
Fever	100%	Cyanosis	7%
SOB	96%	Inability to feed	49%
Sore throat	5%	Drowsiness	20%
Vomitings	57%	Hemoptysis	0%
Diarrhea	45%	Somnolence	22%
Seizures	18%	Skin rash	1%

Cough, Fever and Shortness of breath were the main clinical features associated with almost all of the cases.

Of all the cases 18% (15) cases presented with seizures out of which 9 children had febrile seizures while 6 children had Encephalitis picture with altered sensorium. All children with Encephalitis presentation succumbed to death.

**Table 5:** Risk Factors.

Risk factor	Percentage of cases	P value
Asthma	0%	
Tuberculosis	0%	
Congenital heart disease	4%	<0.05
Diabetes	0%	
Renal anomalies	0%	
Immunodeficiency	0%	

**Table 6:** Malnutrition.

Nutritional status	
Normal	39%
PEM Grade 1	11%
PEM Grade 2	23%
PEM Grade 3	4%
SAM	14%

Lab Parameters In H1n1 Influenza Patients.

**Table 7:** Hemoglobin Level (Anemia).

	<7	7-9.9	10-10.9	>/=11
No. of cases	7	39	15	14
% of cases	11%	49%	20%	20%

#### Renal Parameters

Of all the cases, 8% (7) cases were associated with deranged renal parameters. Deranged renal parameters at admission was significantly associated with mortality with a P value 0.0001.

#### Leucocyte Count

Of all the cases, 25 (33%) cases were associated with leucocytosis (>11000) and leukopenia in 24% (18) cases. Leucocytosis was significantly associated with mortality with a P value of 0.0053.

**Table 8:** Leucocyte Count.

	N(%)
Normal	32(42%)
Leucocytosis	25(33%)
Leucocytopenia	18(24%)

**Table 9:** Radiographic Findings.

X Ray findings	No. of cases(%)
Normal	25 (33%)
Bilateral diffuse infiltrates	37 (49%)
Lobar Consolidation	8 (10.6%)
ARDS	5 (6.6%)

**Table 10:** Arterial Blood Gases

	Normal	Acidosis
No. of cases	52	13
% of cases	69%	17.3%

ABG was not done in 10 cases.

Respiratory and Metabolic acidosis at admission time was significantly associated with mortality with P value <0.00001.

**Table 11:** Complications.

	No. of cases	% of cases
Pneumonia	26	34%
ARDS	5	6%
MODS	8	10%
Sepsis with Shock	6	6%

About half of the positive cases had complications and of all the complications, Pneumonia was found in 26%, ARDS in 5%, MODS in 8% and Septic Shock in 6%.

**Table 12:** Ventilatory Requirement.

	CPAP	Ventilator
No. of cases	14 (18.6%)	10 (13.3%)

**Table 13:** Ventilatory Requirement And Outcome.

	Alive	Dead	Total
Ventilator used	4	8	12 cases
Not used	63	0	63 cases

Ventilator requirement was an independent risk factor correlating with higher mortality rate and poor prognosis in H1N1 patients. P value <0.01.

## Discussion

Clinical and laboratory profile of H1N1 positive children was studied in the age group below 18 years. The study population included 75 children positive for H1N1 Influenza. The study was conducted during the period of March 2017 to March 2019.

The 2009 pandemic of H1N1 Influenza rapidly spread globally, causing significant mortality and morbidity. It was first pandemic since 1968. This outbreak involved more than 170 countries and spread over many continents with more than one lakh people affected. The reason for the rapid spread is because many people have mild symptoms and don't seek treatment and those who seek treatment don't officially get tested and most of the times, it is

only hospitalized people who get tested.

H1N1 is a flu virus and spreads between people in the same way that seasonal flu viruses spread, that is, through droplets or fomites. Incubation period is around 2-7 days.

Symptoms of H1N1 are flu like symptoms, Fever, cough, coryza, headache, myalgia, and joint pain. Less common symptoms are vomiting, diarrhea, conjunctivitis, and parotitis.

In this present study, admission rate was more in February and March with 32% cases being admitted in the two months. Similar findings were observed in the study conducted by Sujatha et al.

**Table 14:** Comparison of mean age distribution of present study with similar studies.

Study	Mean age
Present study	3yrs +/- 2.5 yrs
Das et al	7.5 +/- 3.5 yrs
Hema Gupta et al	3.5 yrs

Mean age distribution was 3+/-2.5 years. Maximum number of cases were below 2 years. This finding correlates with the age distribution of other studies.

**Table 15:** Comparison of gender distribution of present study with similar studies.

Study	Males%	Females%
Present study	53.4%	46.6%
Sujatha et al	61%	39%
SheoPratap et al	60%	40%

Sex distribution of cases is with slight male predominance (53.4%) and females (46.6%).

**Table 16:** Comparison of clinical manifestations of cases in present study with similar studies.

Study	Fever	Cough	SOB	Seizures	Sore throat
Present study	100%	80%	96%	18%	5%
Sujatha et al	90%	90%	23%	2%	3%
Ramya HS et al	100%	100%	18.6%	-	17.1%
Pushpalatha et al	100%	97.5%	73.1%	-	17%

All of the children had fever (100%) and most of them had cough and Shortness of breath (80% and 96%). This finding coincided with other studies.

Of the 18% of cases which presented with seizures in the present study, 9 children had febrile seizures and recovered while 6 children had prolonged encephalopathy with encephalitis picture. All children with Encephalitis presentation succumbed

to death.

Of all the cases 4% of the cases were associated with congenital heart disease with increased risk of mortality in such association with P value <0.05. One child was a known case of steroid dependent nephrotic syndrome presented with Pneumonia with throat swab positive for H1N1.

Nutritional status of the children in the present study was normal in 39%. 14% were with Severe Acute Malnutrition. SAM is a significant risk factor for serious outcome with P value 0.0248.

Among the laboratory parameters, Severe Anemia was found in 11%. About half of the children had moderate anemia. Leucocytosis was found in 48% cases and leucopenia in 24% cases with significant risk of prolonged hospitalisation and increased risk of serious outcome in children with leucocytosis (p value 0.0053). Similar finding was observed in a study by Hema Gupta et al where children had leucocytosis more than leukopenia and leucocytosis associated with prolonged hospital study in their study. Of all the cases, 8% of the cases were associated with deranged renal parameters. Deranged renal parameters at admission was significantly associated with mortality with a P value 0.0001.

**Table 17:** Comparison of Chest X-ray of present study with similar studies.

Study	Normal	Bilateral infiltrates	Lobar consolidation	ARDS
Present study	33%	49%	10.6%	6.6%
Aviram et al	60%	27%	13%	-
Pushpalatha et al	18.2%	81.8%	-	-

Chest X Ray findings were normal in 33% children.

ARDS picture in 6.6% cases. And it was significantly associated with mortality with a statistical significance of <0.00001.

Acidosis (both metabolic and respiratory) was found in 17.3% of cases. Blood gases have been found to predict mortality with Respiratory and Metabolic acidosis being significantly associated with mortality (P value <0.0001).

**Table 18:** Comparison of common complications in present study with similar studies.

Study	Common Complication
Present study	Pneumonia (34% cases)
Aasiya Unjum et al	Pneumonia

Pneumonia was the most common complication observed in the present study in 34% cases. Similar finding was observed in study conducted by Aasiya Unjum, Aijaz Ahmed et al. ARDS, MODS and Septic shock were other complications.

Of all the cases, 14 cases (18.6%) required CPAP support and 10 cases (13.3%) required Ventilatory support.

	CPAP	Ventilator
No. of cases	14 (18.6%)	10 (13.3%)

While all the children with CPAP recovered, only 4 out of 12 ventilated cases recovered. The remaining 8 succumbed to death.

**Table 19:** Outcome Of Mechanical Ventilation In Present Study.

	Alive	Dead	Total
Ventilator used	4	8	12 cases
Not used	63	0	63 cases

Ventilator requirement was an independent risk factor correlating with higher mortality rate and poor prognosis in H1N1 influenza patients with a P value <0.01.

## Conclusion

- The number of cases reported were more in February and March.
- The rate of reported cases and hospitalisation rates were highest among children <2 years.
- H1N1 cases were distributed almost equally in both the sexes with slight male preponderance.
- In our study more than 90% of positive cases met the definition of Influenza like illness (fever + cough/sorethroat).
- The risk of severe outcome was associated with the presence of one or more underlying comorbid conditions.
- Coexisting Congenital heart disease was associated with severe outcome with a significant P value (<0.05). One case was associated with steroid dependant nephrotic syndrome.
- In this study, 39% children had good nutritional status.
- 14% of all the cases were with Severe Acute Malnutrition. SAM was significantly associated with mortality with P value 0.0248.

- H1N1 pneumonia was found to have bilateral diffuse infiltrates in 49% cases.
- 33% of cases had normal radiograph findings.
- Lobar involvement with consolidation was observed in 10.6% of cases.
- ARDS picture in 6.6% cases. And it was significantly associated with mortality with a statistical significance of <0.00001.
- Blood gases have been found to predict mortality with Respiratory and Metabolic acidosis being significantly associated with mortality (P value <0.0001).
- About half of the affected children had moderate anemia.
- 11% had severe anemia.
- Leucocytosis was observed more commonly than leukopenia and also a more better predictor of increased hospital stay.
- In this study, deranged renal parameters at admission time were significantly associated with mortality.
- Of all the cases, 18.6% required CPAP and 13.3% required Ventilatory support. Requirement of mechanical ventilation is an important predictor of mortality.

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