Clinical and Epidemiological Profile of H1N1 Influenza A in Kashmiri Children

Aasiya Unjum[1], Aijaz Ahmed Bhat[2], Zul Eidain Hassan[3], Irshad Ahmad Bhat[4]

ABSTRACT

Introduction: Individuals of all ages can be affected by the influenza virus and it can produce repeated infections throughout life. We aimed to describe the clinical and epidemiological profile of Kashmiri children infected with H1N1 influenza A virus.

Material and methods: It was a hospital based prospective observational study done on infants and children under the age of 16 years admitted to paediatric wards and ICU and children under 16 years of age attending OPD with the diagnosis of influenza like illness. Basic epidemiological details like age, sex, residential status, date and time of admission to the hospital, history of close contact and clinical details like coexisting morbid conditions, date and time of first symptoms etc were collected.

Results: Surveillance for influenza A (H1N1) virus revealed an overall sero-positivity of 19.4% (50 confirmed cases from 258 ILI patients). Among confirmed cases 22 were in category A, 16 were in category B and 12 were in category C. Mean age of lab confirmed cases was 7.6 +/- 4.4 years and 56% (n=28) of the confirmed cases were males. Thirty-eight 38 (76%) belonged to rural population and 12 (24%) cases were from urban areas. Influenza A (H1N1) infection in children peaked during winter months (November to February).

Conclusion: Influenza A (H1N1) paediatric patients are characterized by self-limiting, uncomplicated, febrile respiratory illness and make an over-all recovery with minimal complications.

Keywords: ILI, Influenza, H1N1

INTRODUCTION

The communicability of influenza is high and annual epidemics of varying severity can be caused. The attack rate of influenza can be substantially higher during certain epidemic years and among certain populations.[1-4]

Influenza is an acute infectious disease caused by a member of the ortho-myxovirus family. Outbreaks of influenza usually occur in the winter in temperate climates. Pandemics of influenza are associated with influenza virus type A or B. Type B influenza usually causes milder illness and type C virus is associated with still minor symptoms.

Majority of influenza virus infections in children are self-limited. However, in certain populations, influenza may be severe, particularly in young children those with chronic medical conditions. In children aged <2 years, influenza may lead to hospitalizations for lower respiratory tract disease, nonspecific febrile illness, or central nervous system complications.[5,6,7] In addition to this, young children are known to shed larger quantities of influenza virus for longer periods of time and this may contribute to the spread of influenza within a community or household.[8-12]

In April 2009 a novel influenza A H1N1 virus was discovered first in Mexico and then in United States (US)[13,14] which was originally referred to as "Swine Flu" because of the similarity of its genome to swine genome. It was found that this new virus had gene segments from the swine, avian and human flu virus genes and genetic reassortment in pigs which acted as a reservoir was proposed as a mechanism.[15,16,17] This virus spread rapidly worldwide, and hence the World Health Organization (WHO) declared swine flu as a pandemic to the maximum alert level of '6'.[18]

In May 2009 in India, the first confirmed case of 2009 pandemic H1N1 influenza A virus in India was reported from Hyderabad.[19] The State of Jammu and Kashmir is located in the northernmost part of the Indian Union between 32˚17" and 36˚58" latitude and 73˚26" and 80˚30" longitude. The Province of Kashmir is composed of twelve districts with an estimated population of four million people. Kashmir has a temperate climate, and respiratory illnesses constitute the bulk of hospital visits and admissions during the winter and spring months, either in the form of acute respiratory illnesses or as exacerbations of chronic lung diseases.[20]

The reasons for the recrudescence in Kashmir area are not clear; however, it is possible that the exposure of those not affected in the previous pandemic may be responsible due to absence of immunity. Furthermore, there is a likelihood of emergence and spread of antigenically drifted variants of A/H1N1pdm09 in the area[21] especially in younger children who are at an increased risk of developing severe disease.

This study was conducted with objective to study the clinic-epidemiological characteristics of children who were infected with H1N1 influenza A virus. The study helped in understanding the different clinical and epidemiological characteristics of H1N1 influenza A in a temperate zone like Kashmir to help further for future management of the infection and deciding the timing of vaccination campaign in

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this region where data on influenza is relatively scarce

Study aimed to describe the clinical profile of Kashmiri children infected with H1N1 influenza A virus and to describe the epidemiological profile of Kashmiri children infected with H1N1 influenza A virus.

MATERIAL AND METHODS

It was a hospital based prospective observational study from April 2014 to March 2015. The study was conducted in Post Graduate Department of Paediatrics at GB Pant Hospital, an associated Tertiary Care Hospital of Government Medical College Srinagar (with the catchment area of both rural and urban populations)

Study Population: Infants and children under the age of 16 years admitted to paediatric wards and ICU and children attending OPD with the diagnosis of ILI.

Methods

All children with ILI attending our hospital during the study period were included in the study. ILI in a child was defined as acute febrile respiratory illness i.e. reported or documented fever (37.5 degree Celsius and above) and one of the following symptoms: cough, sore throat, body ache, shortness of breath, nasal discharge at onset or within 7 days of close contact with a person who had ILI or confirmed case of H1N1 influenza A virus infection or within 7 days of travel to a community where there has been one or more confirmed case of H1N1 influenza A.[22,23]

Data collected from the patients included their basic details like age, sex, residential status, date and time of admission to the hospital, clinical details like coexisting morbid conditions date and time of first symptoms etc.

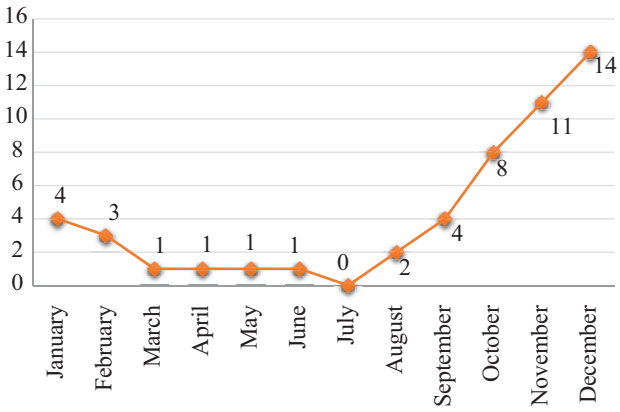
Details like the presence and type of influenza syndrome, duration between onset of illness and diagnosis, duration of treatment in the hospitals and intensive care units were also recorded.

History of close contact with a confirmed case of influenza A (H1N1) or recent travel to an area where there had been confirmed cases was recorded. All the cases screened were categorized as per guidelines of National Health and family welfare and WHO into category A, B and C.[24]

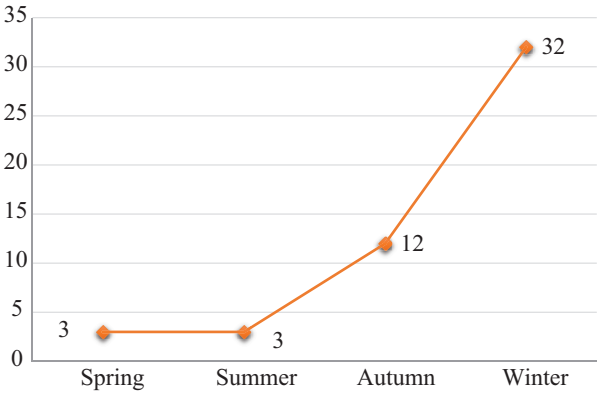
H1N1 influenza A virus was detected with the use of a real time RT-PCR assay in accordance with the protocol from the US centres for Disease Control and Prevention, as recommended by the WHO.[25] Those children who were suspected of being infected were investigated by taking two swabs: One from the nasopharynx and other from the pharynx for detection of virus by real time RT-PCR assay. 5–10 nasopharyngeal samples were taken each week and tested for influenza A (H1N1). Results were available after 24 hours. CBC, Chest Radiograph and Blood culture was done whenever indicated. Children were treated with oseltamivir as per the available guidelines issued by the Ministry of Health, Government of India.[26]

RESULTS

Surveillance for influenza A (H1N1) virus revealed an overall sero-positivity of 19.4% (50 confirmed cases from 258 ILI patients) Among confirmed cases 22 were in category A, 16 were in category B and 12 were in category C.

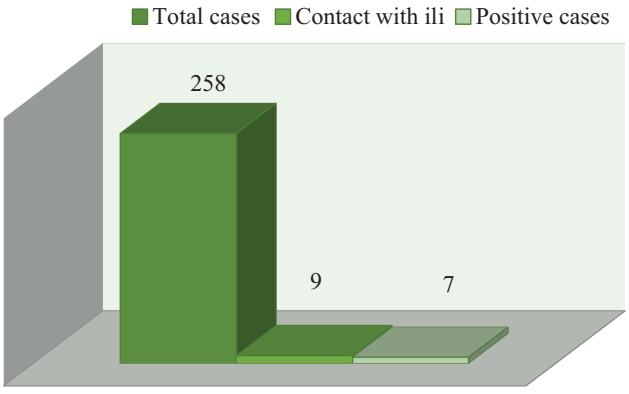


Line diagram showing the distribution of confirmed cases as per month



Spring: March, April, May
Summer: June, July, August
Autumn: September, October
Winter: November, December, January, February

Line diagram showing the seasonal trend of h1n1 influenza A



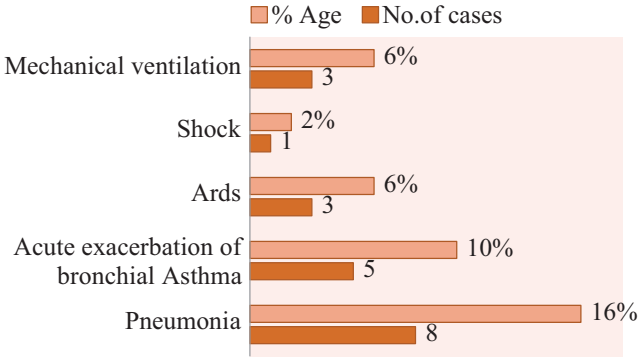
Column diagram showing the no. of children who tested positive after contact with a case of ili

Only 10% (n=5) of the confirmed cases were below the age of 2 years. 90% (n=45) of the confirmed cases were between 2 and 16 years of age [(24% (n=12) between 2 to 5 years,26% (n=13 between 6 to 9 years and 40% (n=20) between 10 to 16 years of age.]

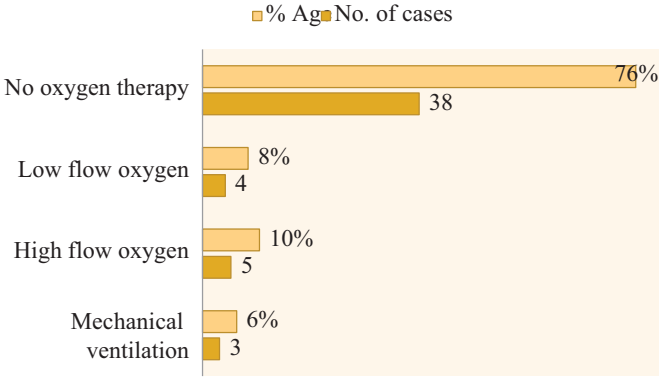
Mean age of lab confirmed cases was 7.6 +/- 4.4 years and 56% (n=28) of the confirmed cases were males.

Characteristics	Hospitalized N = 12	Not hospitalized N = 38	P value
Age (y) mean	4.4+/ -3.5	8.6 +/- 4.2	0.003
Underlying co morbid condition	11 (64.7%)	6 (35.3%)	<0.001
Symptoms			
High grade fever	8 (42.1%)	11 (57.9%)	0.038
Breathlessness	4 (9.5%)	38 (90.5%)	<0.001
Cyanosis	9 (19.1%)	38 (80.9%)	0.01
Lower chest indrawing	3 (7.3%)	38 (92.7%)	<0.001
Tachypnoea	3 (7.3%)	38 (92.7%)	<0.001
Wheezing	6 (15.8%)	32 (84.2%)	0.025
Crepitations	9 (19.1%)	38 (80.9%)	0.01
Reduced air entry	7 (100%)	0 (0.0%)	<0.001
Interval between onset of symptoms and initiation of oseltamivir	6.0 +/- 0.6 days	4.4 +/- 0.8 days	<0.001

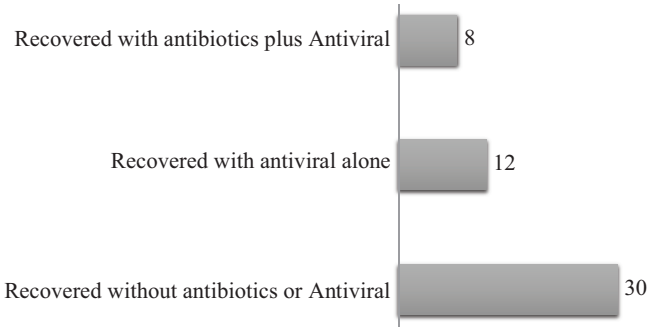
Table-1:



Bar diagram showing the complicatons that developed during the course of illness in lab confirmed cases



Bar diagram showing requirement of respiratory support in lab confirmed cases



Bar diagram showing the medications needed for recovery in confirmed cases

District Srinagar had 12 (24%), Anantnag had 7 (14%), Sopore had 4 (8%), Pulwama had 2 (4%), Bandipora had 3 (6%), Handwara had 1 (2%), Ganderbal had 2 (4%), Shopian had 6 (12%), Budgam had 5 (10%), Baramullah had 6 (12%) and Kupwara had 2 (4%) confirmed cases.

Among the confirmed cases 38 (76%) belonged to rural population and 12 (24%) cases were from urban areas.

In our study influenza A (H1N1) infection in children peaked during winter months (November to February).

Contact History

A total of 9 children had history of contact with a case of ILI within past 7 days out of which 7 tested positive for H1N1 Influenza A which was statistically significant (p value :0.0001).

Clinical Profile

37 of the 50 children with H1N1 Influenza presented with an ILI (fever and cough with or without additional signs or symptoms). Presenting symptoms in the remaining 13 children were fever and seizures (1), fever and diarrhoea (3), fever with vomiting (4), fever with vomiting and headache (2). Three children presented with gastrointestinal symptoms alone consisting of isolated vomiting (1) and vomiting with diarrhoea (2). One of these children had severe diarrhoea.

One child had clinical seizure and exhibited altered consciousness at the height of fever. EEG in this patient showed focal slowing. Examination of CSF yielded normal results. There was no recurrence in the illness upon follow up.

Fever (100%) was the most common symptom followed by cough (80%), nasal discharge (60%), sore throat (44%), body ache (26%), headache (18%) and vomiting (18%) as depicted by the column diagram below. (Figure 9). Subjective symptoms such as headache body ache and sore throat were assessed in children over 5 years of age only.

Underlying Comorbid Conditions

Underlying Co Morbid conditions known to be risk factors for severe influenza were present in 14 (28%) of the children who tested positive for H1N1 influenza A out of which 9 were admitted to the hospital as depicted by the diagrams below (Figure 10 - 12). Pulmonary disease was the most

common Co morbid condition noted in children who tested positive for H1N1 Influenza A. Out of 10 patients with underlying pulmonary disease, 8 had Bronchial Asthma,1 had Acute Bronchiolitis and 1 had Cystic fibrosis. One patient who tested positive for H1N1 influenza A had Spastic Quadriplegia with Aspiration pneumonitis. A patient with Nephrotic Syndrome, on steroids, admitted with the diagnosis of Left basal consolidation with empyema thoracis tested positive for H1N1 influenza A. Two patients who tested positive had underlying cardiac disease (TOF and VSD).

Complications

Pneumonia was the most common complication among the children who tested positive for H1N1 influenza A.

Eight (8) children had radiographic changes compatible with pneumonia. Among these 5 had radiographic findings of bilateral peribronchial markings with hyperinflation. In 2 children chest radiograph showed bilateral symmetrical and multifocal areas of consolidation and 1 child had left basal consolidation on chest radiograph.

In one child with spastic quadriplegia and radiographic evidence of pneumonia blood culture yielded Klebsiella Pneumoniae. Three (3) children with clinical and radiographic features suggestive of ARDS required mechanical ventilation. 1 child among these required vasoactive support for shock.

Severity of Illness and Outcomes

Mean duration of symptoms at consult was 4.6 days. 12 out of 50 children who tested positive for H1N1 influenza A were hospitalized. 8 patients among those who were hospitalized were admitted to paediatric ICU. The mean duration of hospital stay was 6.3 +/ - 1.8 days. Patients who were admitted to the paediatric ICU had a longer stay in the hospital. Median duration of stay in the paediatric ICU was 9 days.

The mean age of children who were hospitalized was lower (4.4 +/- 3.5 years) compared to those who required ambulatory care (8.6+/-4.2 years). (p-value: 0.003). 66.6% of hospitalized were aged below 5 years.

Children aged 5 years or less, those with underlying co morbid conditions and symptoms like high grade fever, wheezing, crepitations, breathlessness and those having longer interval between the onset of symptoms and initiation of antiviral therapy were at a higher risk of hospitalization.76% (n=38) of the children who tested positive for H1N1 Influenza A did not require supplemental oxygen therapy. 10% (n=5) required high flow oxygen. 8% (n=4) required low flow oxygen therapy and 6% (n=3) required mechanical ventilation.

Among 5 patients who experienced Acute exacerbation of bronchial asthma, 3 required High Flow Oxygen for bronchospasm.

A total of 8 patients were admitted to Paediatric ICU among which 3 had acute exacerbation of bronchial asthma,1 had cystic fibrosis and required high flow oxygen, 3 had features of ARDS and required mechanical ventilation. One had nephrotic syndrome with left sided empyema.

Patients requiring supplemental oxygen therapy and mechanical ventilation had a longer duration of hospital stay compared to those who did not receive supplemental oxygen therapy. Mean duration of hospital stay for positive cases who did not require supplemental oxygen therapy 5.7 days. It was 6.5 days for those who received low flow oxygen therapy, 8.4 days for those requiring high Flow Oxygen and 10 days for those who required mechanical ventilation.

Antimicrobial Therapy

Oseltamivir was started in 20 (40%) out of 50 patients at 4.9 +/- 1.0 days after the onset of illness. Remaining 30 children had a mild illness and recovered without the administration of oseltamivir or antibiotics. This comprised of 8 children admitted to the ICU and 4 children who were admitted to the wards. 8 children who received oseltamivir were quarantined at home. 4 out of these 8 patients presented to the hospital with first episode of wheezing and were managed with salbutamol nebulization. 1 had severe sore throat, 2 had high grade fever with cough and nasal stuffiness .1 had Diabetes mellitus controlled on insulin presenting to the OPD with high grade fever and severe sore throat.

The time interval between the onset of symptoms and initiation of antiviral therapy was higher (6.0 ± 0.6 days) for those who were hospitalized compared to those who received ambulatory care (4.4 ±0.8 days).

In patients admitted to the ICU (n=8) antibiotics were also started due to increased severity of the illness. Rest of the children (n=12) received oseltamivir alone for recovery.

5 patients received ceftriaxone alone in addition to antiviral therapy. 2 received ceftriaxone and vancomycin and 1 received ceftriaxone and amikacin.

Laboratory Investigations and Chest Radiography:66% (n=33) children had normal leukocyte counts. 20% (n=10) had mild leukopenia (TLC<5000/mm^3) and 14% (n=7) had leucocytosis (TLC > 11000/mm^3). 2 patients had thrombocytopenia (platelets <150000/mm^3). On Chest radiograph the most common finding was prominent peri-bronchial markings with hyperinflation. (Observed in 8 patients). 4 patients had bilateral symmetrical and multifocal areas of consolidation on chest radiograph.

Blood cultures were drawn in all the hospitalized patients. 1 patient had culture positive sepsis. (Klebsiella pneumoniae).

DISCUSSION

Our study is a hospital based descriptive study conducted at GB Pant Children's Hospital, Srinagar, which is the capital of Kashmir province. With the emergence of pandemic influenza, A (H1N1) virus in India, we sought to determine the prevalence, clinical presentation and epidemiological profile of H1N1 Influenza A among the children presenting to our hospital with ILI.

Kashmir, the northernmost part of India, has a temperate climate, and ILI'S here are so ubiquitous that nearly everyone has ILI at one time or the other during the months of fall and winter. Our data demonstrate that 2009A/H1N1 viral infection is associated with subset of children presenting with ILI in Kashmir. In this prospective study nasopharyngeal swabs of 258 children presenting to our hospital with ILI

were subjected to Real time RT PCR. Patients from both inpatient and outpatient departments were included in the study. The nasopharyngeal swabs yielded a seropositivity of 19.3%. In a study carried out in New Delhi by Rashmi Ranjan Das, Abdus Sami et al[27] the nasopharyngeal swabs yielded a seropositivity of 32.6%

The overall prevalence of H1N1 influenza A in Kashmir was lower than that observed in other cities in North India.[28,29,30] The reason for this could be that sample collection started late in the course of epidemic. Also the samples were collected in a tertiary care hospital where patients present late.

The mean duration of symptoms at consult in our study was 4.6 days. The justification for this could be that patients from rural areas and small towns were initially treated at local level by general practitioners but with no or little improvement they were referred to higher centre.

We found that majority of children who tested positive for H1N1 Influenza A belonged to rural population. This could be partly because most of the children presenting to our hospital belong to rural Areas. The percentage of urban population to total population in Kashmir being only 27.37%[31] and partly because of low health education in rural areas.

Mean age of children with laboratory confirmed H1N1 influenza A was higher (7.6 +/- 4.4 years) than the mean age of children who present with seasonal influenza[32] and males outnumbered females in our study. In a study done by Dawood FS, Jain et al[33] majority of children with pandemic influenza were between 10 and 18 years old.

The rate of hospitalization, however, was highest among children aged 5 years and less. Similar results were reported by Kathleen M Neuzil, Marier Griffin et al.[34] As with most of the other studies, in our study also patients generally presented with symptoms typical of influenza virus infection. The commonest symptoms were fever (100%), Cough (80%), nasal discharge (60%), sore throat (44%). Considerable number of patients (25%) presented with Gastro intestinal symptoms (Diarrhoea and vomiting). The findings of diarrhoea and vomiting in patients with seasonal flu are uncommon as compared to those diagnosed with H1N1 influenza A virus infection.[35] Similar results were also reported by Cynthia Seguerra, Cristan Q. Cabanilla et al in the study carried out in Philippine Children's Medical Centre.[36]

Most of the children with H1N1 influenza virus infection in our study developed a self-limiting uncomplicated febrile respiratory illness with only a minority developing severe complications requiring hospitalization.

Respiratory co morbidities pose the greatest risk for paediatric patients and these may lead to chronic medical conditions.

In our study Respiratory co morbidities were the most frequent cause of hospitalization with Bronchial asthma as the leading condition. Other respiratory Co morbidities were Cystic Fibrosis and Bronchiolitis. However, there are a few published paediatric data, particularly regarding the severity of asthma or the clinical course and outcome of children with asthma.

Pneumonia was the most frequent complication that developed during the course of illness. Three children went on to develop ARDS and required mechanical ventilation.

We presumed that that there is small group of children who are more adversely affected by this virus. However, we have insufficient numbers to identify the characteristics of this group.7 confirmed cases were linked to an index case through their household or a close friend. In a study carried out by E S Soteriades, M M Toumasi et al in Cyprus, 14 confirmed cases had a history of contact with a case of ILI.[37] Oseltamivir was administered in 20 out of 50 patients in our study and they started showing response to the drug by being afebrile within 48 hours. Oseltamivir was however administered later in the course of illness in our study because being a tertiary care hospital patient were referred to our hospital late. They initially sought consult from local physicians in the periphery. The rate of bacterial co infection was low in our study. Only one patient had culture proven sepsis and chest radiograph revealed non-specific findings. On chest radiography peribronchial markings with hyperinflation was the most common finding. This finding was in accordance with the study carried out by Edward Y. Lee, Alexander J. Mc Adam et al.[38] These observations of epidemiological risk factors, typical clinical features, response to therapy and prognosis could aid in the recognition, diagnosis and clinical management of H1N1 Influenza A in Kashmiri children.

CONCLUSION

Majority of the RT-PCR confirmed Influenza A (H1N1) pediatric patients are characterized by self-limiting, uncomplicated, febrile respiratory illness and make an over-all recovery with minimal complications. Regardless of the above we need to focus on the coming Influenza season and apply different methods including Influenza A(H1N1) vaccination in order to avoid severe cases among children which may inevitably occur due to the low level of immunity to the pandemic virus strains.

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