

Brief Report

Clinical and Epidemiological Characteristics of Pandemic Influenza A/(H1N1) in Hospitalized Pediatric Patients at a University Hospital, Istanbul, Turkey

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Summary

Background: The aim of this study was to describe the clinical and epidemiological characteristics of pandemic influenza in hospitalized children.

Methods: A total of 114 patients with suspected H1N1 virus infection were hospitalized, and nasal swabs were sent to National Influenza Reference Laboratory for confirmation of pandemic influenza A (H1N1) virus infection by rRT-PCR assay.

Results: Forty-six female and 68 male patients were included in the study. Age of the patients ranged from 40 days to 16 years. Clinical and/or radiological pneumonia were detected in 96% of all. Sixteen patients required mechanical ventilation due to hypoxemia. Previously healthy children required mechanical ventilation and oxygen therapy more than patients with chronic diseases. Elevated levels of CRP and LDH in patients with respiratory distress and patients who required mechanical ventilation were statistically significant.

Conclusion: Our study showed that progress of pandemic influenza infection in previously healthy children is as severe as their counterparts with chronic underlying diseases.

Key words: pandemic influenza (H1N1), children, pneumonia.

Introduction

A new strain of pandemic influenza A (H1N1) virus has emerged in Mexico in April 2009 [1]. On 11 June 2009, WHO declared the first pandemic of the 21st century [2]. The index case reported on 16 May 2009 in Turkey was a USA resident travelling from Tennessee to Iraq through Ataturk Airport in Istanbul [3]. The first case in our pediatric clinic was detected on 26 October 2009 in a 4-year-old patient with epilepsy and respiratory distress.

In this study, the clinical and epidemiological characteristics of patients hospitalized at Pediatric Infectious Diseases Division between 26 September and 26 November 2009 with the preliminary and laboratory confirmed diagnosis of pandemic influenza are presented.

Materials and Methods

The patients who presented to Pediatrics Emergency Polyclinic during 26 October and 26 November 2009 with flu complaints were evaluated according to the pandemic influenza or H1N1 case management algorithm of the Turkish Health Ministry [4].

Children >2 years, all children who were under medical therapy due to a chronic disease or who were immune compromised were regarded as at-risk patients. The patients who did not belong to one of these groups were regarded as 'previously' healthy patients.

Nasopharyngeal swabs were taken only from 68 out of 114 hospitalized patients due to shortage of viral transport medium supply. Commercial viral transport medium (ViroCult, Medical Wire &

Equipment Co., England) was supplied by Ministry of Health and samples were sent to National Influenza Reference Laboratory located at Istanbul Faculty of Medicine.

The data of all patients were evaluated with a computer package program, SPSS 14.0 for Windows.

Results

An average of 312 (120–600) patients was presented to Pediatric Emergency Clinic with flu complaints during 26 October and 26 November 2009 per day. A total of 114 patients with serious disease presentation were hospitalized. Out of 68 nasopharyngeal samples sent for laboratory testing, 58 were positive for pandemic Influenza A (H1N1) virus, two were positive for Influenza A H3N2 and eight were negative for influenza.

The mean of age distribution of the patients was 6 years and 8/12-months old (ranged from 40-day olds to 16-year olds; Fig. 1). Forty percent of the patients ($n=46$) were females, and 60% of the patients ($n=68$) were males.

The patients presented to the emergency clinic on an average of 4 days ($SD \pm 3$ days) after the onset of the symptoms (Table 1). Of the hospitalized patients,

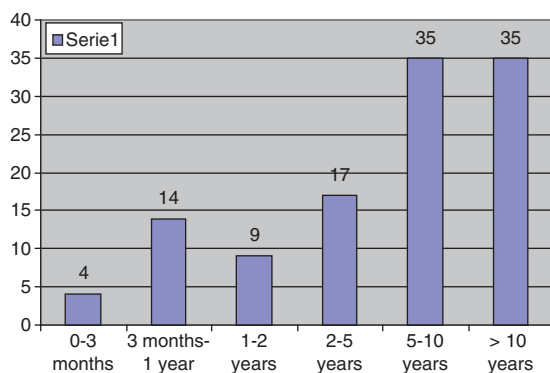


FIG. 1. Age distribution of the patients.

TABLE 1
The symptoms of the patients

Symptom	n (%)
Fever	114 (100)
Cough	97 (85)
Vomiting	34 (30)
Respiratory difficulty	30 (26)
Myalgia	23 (20)
Headache	21 (18)
Rhinorrhoea	16 (14)
Diarrhoea	15 (13)
Sore throat	9 (8)

84 had pneumonia, 16 had acute asthmatic attack, 2 were epileptic, 1 had hepatitis and 13 patients were in the risk group. Sixteen patients needed mechanical ventilator support due to signs of hypoxemia.

Laboratory and radiological findings

The C-reactive protein (CRP) was negative in 40 patients ($<5 \text{ mg l}^{-1}$). The CRP was positive in 75% of patients with respiratory difficulty, and it was positive in 21.9% of the patients without respiratory difficulty. This difference was found statistically meaningful ($p < 0.00$, $p < 0.05$). Lactate dehydrogenase (LDH) levels were recorded for 60 patients and the average LDH level was 644 U l^{-1} ($SD \pm 409$). The average LDH level was 963 U l^{-1} ($SD \pm 707$) in patients receiving mechanical ventilator support, and it was 538 U l^{-1} ($SD \pm 158$) in patients who were not intubated. This difference was regarded as statistically meaningful ($p = 0.04$, $p < 0.05$). The abnormal laboratory findings of the patients are listed in Table 2.

Blood culture that was taken from all patients was negative. Basal interstitial infiltration was common in the posterior to anterior (PA) chest radiograms of the patients (Figs 2–5).

Treatment and complications

Oseltamivir was administered to all patients. The treatment of one patient was stopped due to high levels of the liver transaminase at the presentation, one patient with hepatitis received zanamivir treatment.

Comparison of patients with and without a chronic disease

The ratio of patients with chronic disease was 56% (Table 3).

Fifty (44%) patients had no underlying diseases. Pneumonia was found in 96% of these patients. Eighteen (36%) out of 50 patients developed respiratory difficulty, 12 needed mechanical ventilation support. Rate of respiratory difficulty and need for mechanical ventilation were higher in patients with no underlying diseases compared to their counterparts with underlying diseases and this was statistically meaningful ($p = 0.01$, $p < 0.05$) (Fig. 6). There were no deaths in either group of patients.

Discussion

Pandemic (H1N1) virus was confirmed in 58 (85%) out of 68 nasopharyngeal samples sent to the laboratory. Two of the samples were confirmed as influenza A/H3N2 and no influenza was detected in eight samples. The reason for no detection of influenza in the nasopharyngeal samples of these eight patients might be related to delayed referral to the hospital hence

TABLE 2
Abnormal laboratory findings

Abnormal laboratory finding	Patient, <i>n</i> (%)	Respiratory difficulty, <i>p</i> -value	Mechanical ventilator support, <i>p</i> -value
CRP >5 mg l ⁻¹	74/114 (65)	<0.001	<0.001
Lactate dehydrogenase >480 U l ⁻¹	32/60 (53)	0.08	0.04
Lymphopenia <1000 mm ³	34/114 (30)	0.254	0.186
Creatinine kinase >300 U l ⁻¹	6/31 (19)	0.350	0.171
Hypertransemia AST >38 U l ⁻¹	15/82 (18)	0.340	0.429
Hyponatremia <135 mmol l ⁻¹	20/114 (17.5)	0.618	0.636
Hypophosphatemia <3.0 mg dl ⁻¹	11/80 (13)	0.316	0.708
Neutropenia <1500 mm ³	11/114 (10)	0.552	0.482

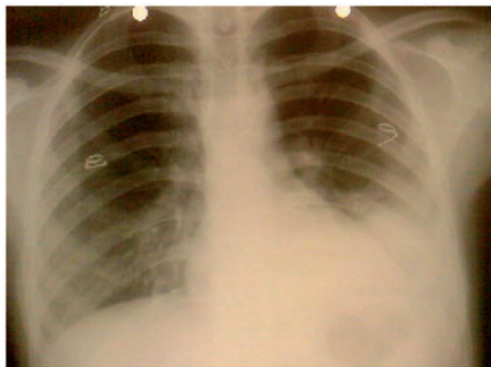


FIG. 2. Bilaterally consolidated areas at the inferior lobes.

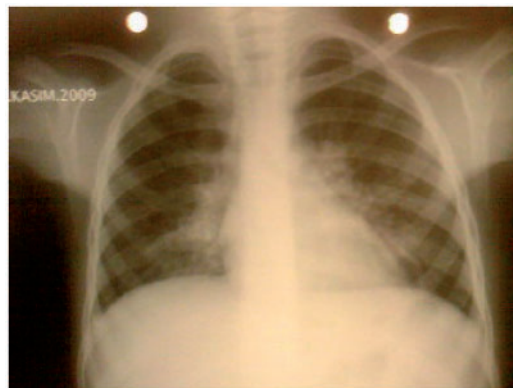


FIG. 4. Bilateral paracardiac infiltration.

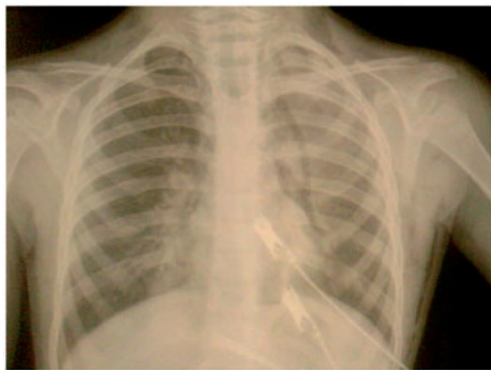


FIG. 3. Pneumomediastinum and paracardiac interstitial infiltration.



FIG. 5. Thoracic CT: consolidated areas, atelectasia and cavitations compatible with necrotizing pneumonia.

delayed sampling date which was >5 days after the onset of symptoms.

In this study, fever was the most common symptom (100%) followed by cough (85%), vomiting (30%), respiratory difficulty (26%). However, cough (98%) has been reported as the most

common symptom followed by fever (96%), fatigue (89%), headache (82%) and sore throat (82%) among adult patients [5, 6]. These data indicate that fever is a common symptom in children and

TABLE 3
Patients with chronic disease (n)

Asthma	16
Epilepsy	10
Immunodeficiency	9
Congenital metabolic disease	8
Bone marrow transplantation/liver transplantation/kidney transplantation	8
Immunosuppressive Therapy (chemotherapy or steroids)	6
Cystic fibrosis	4
Congenital heart disease	2
Diabetes	1
Total	64

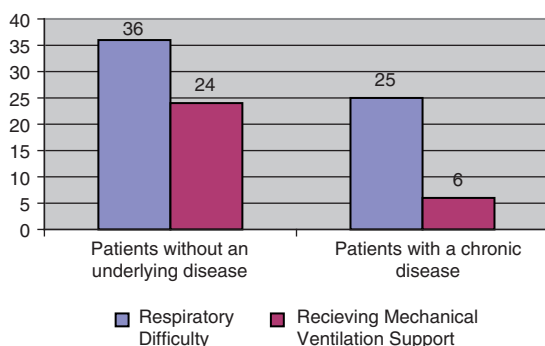


FIG. 6. Comparison of respiratory difficulty and mechanical ventilation support rates between patients with and without underlying diseases (%).

diversity of symptoms in children is limited compared with adults.

A total of 251 pediatric deaths have been reported to CDC [7, 8]. Bacterial culture samples of 89 patients revealed secondary bacterial co-infections in 28 (31.5%) samples. Although, the ratio of our patients with pneumonia was very high the blood cultures of these patients were sterile and there was no mortality in our cases. Our result supports the theory that cases associated with bacterial co-infection have high ratio of mortality as noted in the literature [9].

A study conducted during the pandemic with (H1N1) virus in Mexico by Padilla *et al.* [5] laboratory abnormalities reported as LDH elevation (100%), creatine kinase (CK) elevation (62%) and lymphopenia (61%). In this study, high CRP (65%), LDH (53%), CK (19%) and aspartate aminotransferase (AST) levels (18%) and lymphopenia (30%) were included. In patients with respiratory difficulty, and with the need of mechanical ventilator support, CRP and LDH elevations were found

statistically meaningful. These data suggest that these values could be used as indicators of serious disease in hospitalized patients with H1N1 infection.

Influenza infection has more serious consequences in people with chronic illness and >2 years [10]. However, in Mexico, deaths related to pneumonia occurred in previously young adults in patients hospitalized for pandemic (H1N1) virus infection [5]. Respiratory difficulty and need for mechanical ventilator support in patients who did not have any known underlying disease was higher than in patients with underlying disease. In accordance with the study conducted in Mexico [5], our study indicates that pandemic influenza may have a more serious progress in patients who were previously healthy.

Funding

Ethical Committee Consent of Istanbul Medical Faculty: 2009/2915-105.

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