

Hospitalization patterns and outcomes of infants with Influenza A(H1N1) in Kuwait

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Abstract

Introduction: Infants represent an important risk group for influenza associated hospitalizations and mortality. This study evaluated the clinical presentations, hospitalization course and outcome of infants hospitalized with the pandemic influenza A H1N1 [Influenza A(H1N1)pdm09] in relation to their previous health status.

Methodology: We conducted a retrospective chart review of hospitalized infants with laboratory-confirmed Influenza A(H1N1)pdm09 infection in two hospitals in Kuwait. Demographic characteristics, pre-existing high-risk medical conditions, clinical presentations, complications and mortality were analyzed. Previously healthy infants' data were compared with infants with pre-existing high-risk medical conditions for severity of the illness and outcome.

Results: We identified 62 infants comprising 32% of all admissions with Influenza A(H1N1)pdm09. The median age \pm SD was 7 ± 4 months. Nineteen (31%) had pre-existing high-risk medical conditions. Complications were documented in 53% of previously healthy infants compared to 47% in high-risk infants. Mean duration of hospitalization was 4.9 days in healthy infants and 6.7 for infants with high-risk medical conditions. Bacterial pneumonia complicated 7% of previously healthy infants compared to 26% with high-risk conditions ($P = 0.03$). Four infants (6.5%) required admission to the intensive care unit (ICU), of whom three had high risk medical condition.

Conclusion: The majority of hospitalized infants with Influenza A(H1N1)pdm09 were previously healthy. Prolonged hospitalization, ICU admission and mortality were more observed in infants with high-risk medical conditions. According to the latest Advisory Committee on Immunization Practices (ACIP) recommendations, annual influenza vaccination is recommended for any child six months of age and older, particularly those with risk factors.

Key words: Influenza A; H1N1; infants; Kuwait

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Introduction

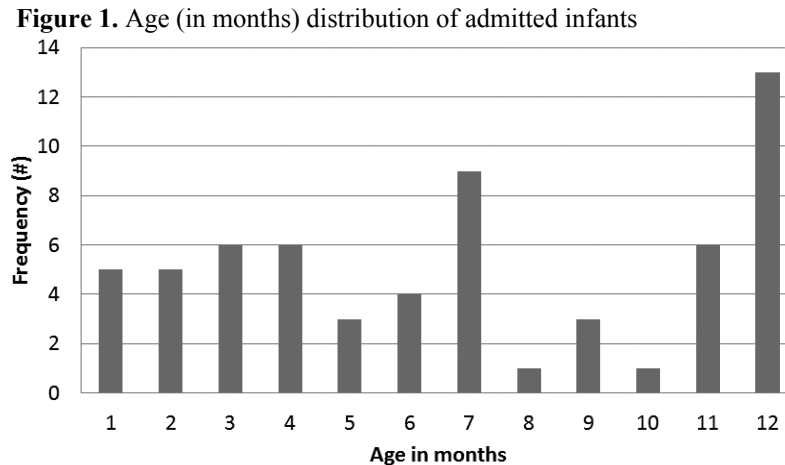
Influenza is a common cause of illness in children. Infants and young children without chronic or serious medical conditions are at increased risk for hospitalization during influenza seasons [1]. The Advisory Committee on Immunization Practices (ACIP) recommends an annual influenza vaccination for any child 6 months of age and older, particularly those with high-risk medical condition [2].

In June 2009, the World Health Organization declared Influenza A(H1N1)pdm09 as a pandemic infection. During the pandemic, the highest rate of hospitalization was seen among infants [3,4].

There are several clinicoepidemiologic studies of Influenza A(H1N1) in children that included infants among their population. Only two studies described

exclusively hospitalized infants with Influenza A(H1N1)pdm09 [5,6]. The first is a descriptive report of a series of 10 young infants within the first two months of life but not infants in the first year of life. The second is a French study of hospitalized infants less than six months of age.

The objective of this retrospective analysis was to describe the clinical manifestations, hospitalization course and outcome of infants one year old or younger hospitalized with the Influenza A(H1N1)pdm09 in Kuwait and, to compare the pattern of hospitalization between previously healthy infants and infants with underlying health conditions.



Methodology

Study design and patient population

The study population consisted of infants one year of age or younger with laboratory confirmed Influenza A(H1N1)pdm09. All infants were hospitalized in two hospitals in Kuwait between August 2009 and January 2010. Diagnosis of Influenza A(H1N1)pdm09 was confirmed by testing nasopharyngeal swab specimens with the use of the reverse-transcriptase polymerase chain reaction (RT-PCR) assay. The medical records of the patients were retrospectively reviewed after obtaining Ministry of Health and the hospital board's ethical approval. All infants included in the study received the conjugate pneumococcal vaccine as part of the national immunization program.

Data extraction

The following data were collected: demographic characteristics, pre-existing high-risk medical conditions, clinical features at presentation, complications, hematologic and radiologic findings, therapeutic measures and outcome. Data from previously healthy infants were compared with that of infants with pre-existing high-risk medical conditions for the severity of the illness and outcome.

Definition of complications

Bacterial pneumonia was defined either by a positive blood culture or lobar consolidation on chest X ray or bronchopneumonia associated with leukocytosis. Viral pneumonia was defined with negative blood culture or a chest X ray with a diffuse interstitial infiltrate. Febrile convulsion was defined as convulsion associated with fever in the absence of a primary brain disease or associated neurological

deficit. Neutropenia was defined as an absolute neutrophil count of (ANC) $\leq 1.5 \times 10^9/L$.

Statistical analyses

Data entry and statistical analysis were performed using SPSS 16.0 for Windows (SPSS Inc., Chicago, IL USA). The data was presented in frequency and proportions. Descriptive statistics such as mean and median were used to calculate age and length of hospitalization and fever duration. Student's *t* test was used to identify the differences between means, with statistical significance set at $P < 0.05$. We used χ^2 to test the association between two categorical variables in clinical characteristics and complications between the previously healthy and the underlying risk group. We used exact Fisher two-sided *P* values and 95% confidence intervals to evaluate differences between the two groups when given supportive respiratory therapy (beta agonist, inhaled steroids, and systemic steroids).

Results

A total of 62 infants were hospitalized with confirmed Influenza A(H1N1)pdm09 in the two hospitals during the study period. This number comprised 32% of all pediatric admissions with the infection.

The median age \pm SD was 7 ± 4 months. Figure 1 shows the distribution of the ages of admitted infants. There were 33 (53%) infants above the age of six months. Forty were (64.5%) males and 22 (35.5%) were females. The peak of admissions was during the months of October and November (81%). There were 43 (69%) previously healthy infants. The remaining 19 infants had the following pre-existing high-risk medical conditions: bronchial asthma (14),

Table 1. Clinical characteristics of admitted infants

Clinical feature	Healthy infants N = 43 # (%)	High-risk infants N = 19 # (%)	P value
Fever	42 (98)	17 (89)	NS
Mean temperature on admission \pm SD	38.2 \pm 0.8°C	38.5 \pm 0.5°C	NS
Days of fever \pm SD	3.7 \pm 2 days	3.4 \pm 2.5 days	NS
Vomiting	10 (23)	5 (26)	NS
Diarrhea	7 (16)	3 (16)	NS
Respiratory distress	7 (16)	7 (37)	NS
Cough	32 (76)	16 (84)	NS
Rhinorrhea	28(65)	9 (47)	NS
Tachypnea	6 (14)	4 (21)	NS
Wheezes	4 (9)	6 (32)	0.03
Throat congestion	2 (3)	-	NS
ICU admissions	1 (2)	3 (16)	0.05
Mortality	-	1 (5)	NS

congenital heart disease (3), neurological disease (2), and hematological condition (1). The mean duration of hospitalization \pm SD was 4.9 \pm 3.5 days in previously healthy infants and 6.7 \pm 6.3 days for infants with high-risk medical conditions. The difference between the two groups was not statistically significant. The frequencies of clinical presentations on admission are summarized in Table 1.

The hematological findings were as follows: mean white blood count (WBC) was 10.9 \pm 7 x 10⁹ /L. The mean absolute neutrophil count (ANC) was 4.7 \pm 5.9 x 10⁹ /L. The mean absolute lymphocyte count (ALC) was 4 \pm 2 x 10⁹ /L. Mean platelet count was 333.5 \pm 128 x 10⁹ /L. There was no association between hematological findings when comparing previously healthy and high-risk infants. Chest radiographs were performed in 32 (50%) infants; 21 (49%) were done in previously healthy and 11 (58%) in infants with an underlying medical condition. The most common finding in all infants was interstitial pneumonia in 14 (74%).

Complications occurred in 23 (53%) of the previously healthy infants and in 9 (47%) of the infants with an underlying medical condition. The list of complications in each group is shown in Table 2. Fifty percent of these complications were in infants older than 6 months of age. Only one infant had a positive blood culture for *Streptococcus pneumoniae*.

Four children (6.5%) were admitted to the intensive care unit (ICU), of whom three needed artificial ventilation. Their ages were 3, 4, 7 months

and one year respectively. One infant was previously healthy and the other three had high-risk medical conditions (bronchial asthma, congenital heart disease, and spinal muscular atrophy). There was only one death in the series in a three-month-old female with spinal muscular atrophy type I.

Antibiotics were administered to 33 (76%) of the previously healthy infants and 14 (73%) of the infants with pre-existing high-risk conditions. An antiviral agent (oseltamivir) was administered to all infants except one because of parental refusal. There were no documented adverse events from the drug. An inhaled beta-agonist was used in 11 (26%) of the previously healthy infants compared to 14 (74%) of the infants with a pre-existing high-risk condition (P 0.001, OR 8.15, 95% CI, 2.3-27.8). Inhaled steroids were used in 4 (9%) previously –healthy infants and 11 (58%) infants with pre-existing high-risk conditions (P < 0.0001, OR 13.4, 95% CI, 3.3-53). Systemic steroids were administered to 2 (5%), and 6 (32%) of the previously healthy infants and those with underlying health condition respectively (P 0.008, OR 9.5, 95% CI, 1.7-52).

Discussion

Thirty-two percent of the hospitalized children in Kuwait with pandemic Influenza A(H1N1)pdm09 were infants. This rate is higher than that previously reported from pandemic studies in the United States and Cyprus (6 and 17% respectively) [7,8]. A higher rate (52%) of hospitalization of infants with Influenza A(H1N1)pdm09 has been reported from Argentina [4]. Our finding of hospitalization with Influenza

Table 2. Complications in healthy infants & infants with underlying high-risk medical condition

Complication	Healthy N = 43	With medical condition N = 19	P value
Bacterial pneumonia	3 (7%)	5 (26%)	0.03
Viral pneumonia	8 (19%)	4 (21%)	NS
Febrile convulsions	5 (17%)	-	NS
Neutropenia	7 (16%)	-	NS
None	20 (47%)	10 (53%)	NS

A(H1N1)pdm09 is similar to the hospitalization rate in infants with seasonal influenza of 27%-29% observed in the United States [9]. These data would support that infants represent an important high-risk group for influenza-related hospitalization. The median age was seven months and infants older than six months of age represented 53% of all admitted infants, a result that was reported with seasonal influenza [10]. This is potentially due to loss of protection conferred by maternal influenza antibodies after six months of age [11].

Although the infants in this study had a wide range of presenting symptoms, fever, cough and rhinorrhea were the most common, and are similar to what has been reported in older children with Influenza A(H1N1)pdm09 [4,8]. To the contrary of what was previously reported that hospitalization rates are two to four times higher for high-risk infants [12], the majority of the hospitalized infants in our cohort were previously healthy. This might be explained by the higher incidence of complications seen in healthy infants necessitating hospitalization. The most commonly associated medical condition in hospitalized infants in our cohort was bronchial asthma, similar to what has been reported for seasonal influenza in infants and in older children with the Influenza A(H1N1)pdm09 [9].

The rate of respiratory complications such as bacterial and viral pneumonia and ventilation rates were significantly associated with high-risk medical conditions. This can explain the longer duration of hospitalization, higher rate of ICU admissions and mortality in these infants. The rate of bacterial pneumonia of 13% in our study is similar to that in reports of seasonal influenza [13] and in other studies in older children with Influenza A(H1N1)pdm09 [4].

None of the 61 infants in this report, including a seven-day-old newborn, who received oseltamivir had any adverse side effects. In one previous report,

oseltamivir was found to be safe for the treatment of influenza in infants younger than one year and was only associated with mild gastrointestinal symptoms in 50% of the treated infants [14].

This study, despite the small number of infants, confirms that most infants with Influenza A(H1N1)pdm09 were previously healthy and had a higher incidence of hospitalization for influenza-associated complications compared to infants with pre-existing high-risk medical conditions. However, the latter had longer duration of hospitalization, a complicated course, needed more supportive respiratory medications, and were associated with mortality.

Our findings suggest that, similar to infants with seasonal influenza, infants with the Influenza A(H1N1)pdm09 were at risk of hospitalization and complications in both previously healthy infants and infants with underlying high-risk condition. These findings concur with the latest ACIP recommendations that annual immunization with influenza vaccine is recommended for any child six months of age and older, particularly those with high-risk medical conditions [2]. Influenza vaccine is not licensed for children younger than six months of age. Protection against influenza in this age group can be attained by vaccinating women during pregnancy. A controlled observational study of influenza vaccine during pregnancy conducted from 2002-2005 has shown that there was a 41% reduction in the risk of laboratory-confirmed influenza and 39% reduction in the risk of ILI hospitalization for infants born to influenza vaccinated mothers [15].

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