Research Paper
Clinical Characteristics and Underlying Medical Conditions Among Hospitalized Children and Adult Patients With Seasonal Influenza

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ABSTRACT

Background: Influenza is a respiratory infection that causes a wide range of symptoms, from mild symptoms to a significantly impaired disease.

Objective: This study aims to examine demographic characteristics, clinical features, and underlying medical conditions in children and adults hospitalized with laboratory-confirmed influenza.

Methods: This was a retrospective comparative study on 333 adults and 102 children hospitalized with symptoms of acute respiratory tract infection and seasonal influenza confirmed by reverse transcription polymerase chain reaction (RT-PCR) in three university hospitals, in Qazvin City, Iran, during two influenza seasons (March 2017 and February 2019).

Findings: Most clinical manifestations of influenza were similar among adults. A significant difference was observed among the two groups in terms of 1) a greater proportion of male patients in children (66.7%) and female patients in adults (58.6%); 2) adults were more exposed to risk factors than children (median 1 vs. 0); 3) a greater proportion of children presenting influenza-related encephalopathy (38.2% vs. 26.7%) and upper respiratory signs compared to adults; 4) a greater proportion of adults presenting lower respiratory signs and symptoms compared to children. The most common underlying conditions were asthma and diabetes mellitus (DM) in adults and diabetes mellitus (DM) and cancer in children. The duration of hospitalization had a significant relationship with the number of risk factors (r=0.219, P<0.001).

Conclusion: In summary, influenza-related encephalopathy and upper respiratory signs are more prevalent in children, and in contrast, adults are more likely to have underlying medical conditions than children with seasonal influenza.

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1. Introduction

The influenza virus is a critical cause of respiratory illness among children and adults [1]. An estimated 20%–30% of children and 5%–10% of adults are infected with the influenza virus, which causes 3–5 million severe cases besides 250,000 - 500,000 deaths annually [2, 3]. It causes significant morbidity and mortality, especially at the extreme ends of the age spectrum. Infants, young children, and people 65 years of age and older account for the highest rates of influenza-related hospital admissions. Other high-risk groups for this disease include pregnant women, and people with serious medical illnesses [4]. Influenza is a seasonal respiratory infection that causes a wide range of symptoms, from mild symptoms to a significantly impaired disease. Symptoms of influenza include fever, cough, body pain, headache, sore throat, and gastrointestinal and neurological complications [5]. This illness is mostly self-limited; thus, a large proportion of infected patients do not admit themselves to hospitals. Influenza patients usually have a high-grade fever or at least two symptoms of respiratory disease [6]. A probable case of influenza is defined as a patient with a fever (>38°C) and at least two respiratory symptoms, while the result of a positive reverse transcription polymerase chain reaction (RT-PCR) test confirms the diagnosis of influenza [7].

To our knowledge, no previous reports of a comparison between adult and younger patients with influenza were observed. In this paper, we present our experience resulting from direct participation in the management of children and adults admitted to three tertiary referral teaching hospitals with influenza A and B. The current study was conducted to describe the demographic characteristics, clinical features, and underlying diseases of these patients and to compare these data among hospitalized children and adult patients with seasonal influenza.

2. Materials and Methods

Study design

This is a retrospective comparative study on adults and children hospitalized with symptoms of acute respiratory tract infection and finally, laboratory-confirmed seasonal influenza attending emergency departments and admitted to three university Hospitals (Bou Ali Sina, Velayate, and Qods Hospitals), Qazvin City, Iran, in two influenza seasons (28 march 2017 and 27 February 2019). These hospitals serve as the pediatric and adult tertiary referral centers in the Qazvin area and the surrounding region. We reviewed the charts of all patients, and finally, our patients were divided based on age to ≥15 years (adult group) and <15 years (children's group) due to dramatic differences according to demographic characteristics and risk factors. Qazvin Province with a population of 1,143,178 (according to the latest national census) is located on the southern margin of the Alborz mountain range at a latitude range of 35° 24' and 36° 48' N. At least 90% of children hospitalized due to acute respiratory tract infections in the Qazvin Province were in Qods pediatric hospital.

Demographic and clinical information

We extracted demographic information, clinical features at presentation, underlying medical conditions already known to be risk factors for influenza-related clinical complications, and duration of hospitalization from the patient record review.

Laboratory tests

Seasonal influenza of patients confirmed using RT-PCR. At each site, one nasal swab and one throat swab were collected from each enrolled child and adult. A specimen was defined as influenza-positive if RT-PCR assays were positive for influenza A or B.

Statistical analysis

We compared the data of the adult group and the children group with seasonal influenza. Patient clinical data were not normally distributed and were statistically analyzed using nonparametric statistics, the Mann–Whitney U test. The Chi-square test or Fisher's exact test was used to compare categorical variables between groups. The correlation between the duration of a hospital stay and the number of risk factors was measured by Spearman's rank correlation coefficient. A two-sided P of less than 0.05 was considered to indicate statistical significance. All statistical analyses were performed with SPSS software, version 25.

3. Results

We identified 435 patients (333 adults and 102 children) admitted with seasonal influenza during the previous two influenza seasons. While seasonal influenza viruses were detected year-round in Qazvin Province, seasonal influenza viruses were most common during the fall and winter. Influenza activity began to increase in October, and the "peak month of flu activity" during these 2 years was December (the month with the highest percentage of respiratory specimens testing positive for influenza virus infection during that influenza season).

Demographic characteristics

Table 1 presents the characteristics of the 435 patients. The characteristics of hospitalized adults were similar at each site and in each study year, so we present cumulative results.

Clinical manifestations

Common symptoms included ague (86.3% of the children and 77.5% of the adult), and cough (74.5% of children and 82.9% of the adult). Most children and adults (62.7% and 63.4%, respectively) with seasonal influenza presented with an influenza-like illness with at least a fever and cough.

Symptoms in the remaining patients were lethargy without fever; gastrointestinal symptoms include diarrhea with or without vomiting, fever and altered level of consciousness, and fever and seizures. Most clinical manifestations of influenza were similar between the two groups, except for myalgia, sore throat, sputum, chest pain, headache, and vertigo which were more prevalent among the adults, and rhinorrhea, post nasal drip (PND), imbalance, and seizure that were more prevalent in children. Upper respiratory signs were more prevalent in children, and a greater proportion of adults showed lower respiratory signs and symptoms. Neurological manifestations were diagnosed in 45.7% of the patients (43.1% of children vs. 46.5% of adults). Most neurological manifestations were seizures and imbalance in children and headache and vertigo in adults, the frequency of these manifestations did not differ significantly between the two groups. Influenza-related encephalopathy was suspected in 38.2% of children and 26.7% of adults with vertigo, imbalance, seizure, and an altered level of consciousness; the frequency of this diagnosis differed significantly between the two groups (P=0.026). Differences exist in sex distribution. When stratified by age and sex, male children and female adults were the most affected demographic groups.

Underlying medical conditions

Table 2 presents the distribution of important risk factors for severe influenza. Adults were more likely to have seasonal influenza than children (P < 0.001). Underlying medical conditions already known to be risk factors for severe influenza was present in 28 (27.5%) of the children and 232 (69.7%) of the adults admitted with seasonal influenza (overall, 59.8% of patients). Overall, the most common underlying medical conditions were asthma, diabetes mellitus (DM), and ischemic heart disease (IHD) in adults and DM, cancer, and cystic fibrosis in children.

The median duration of hospital stay was 4 days for the children and 5 days for adults (both within the interquartile range of 3–7 days). No significant differences were observed between the two groups in the duration of hospital stay (P=0.067). The number of risk factors was significantly correlated with the duration of hospital stay (r=0.243, P<0.001). Influenza A accounted for 75.6% of infections. Unfortunately, most laboratory results were not available to the clinicians before the patients were discharged.

4. Discussion

In this study, we investigated the demographic, clinical characteristics, and underlying medical conditions of seasonal influenza in Qazvin Province, Iran. In a surveillance study, Reukers et al. discovered that most cases in the 2017-2018 seasonal flu outbreak in the Netherlands occurred from October to May, and the epidemic lasted 18 weeks. The predominant type of influenza virus was influenza type B, but during the last weeks of the epidemic, influenza virus types A (H3N2) and A (H1N1) predominated [8]. In our study, the epidemic lasted 20 weeks from September to January, and the predominant type was type A. Another study reviewed the burden of seasonal influenza in the United States over 5 years beginning in 2010, finding that most cases of symptomatic community illness and outpatient medical visits attributable to seasonal influenza were in the 18-49 age group, while most patients admitted to the hospital with a diagnosis of influenza were in the age group above 65 years [9]. In our study, we did not investigate the number of symptomatic community illnesses and outpatient medical visits attributable to seasonal influenza, but because we covered all tertiary care hospitals admitting acute respiratory infections in the Province, our data regarding hospitalization regarding influenza is relatively acceptable. In our study, like the mentioned study, the predominant age in the adult group was >65 years.

A study in Australia between 2001 and 2013 estimated that the average annual seasonal influenza-attributable hospitalization rate was highest in the age group of > 65 years [10]. In a more up-to-date report from the U.S., the highest rate of hospitalization was in the age group above 65 years. The presenting clinical features of seasonal influenza in the pediatric age group in our study are like those described recently. A previous epidemiologic study found that the admission rate of children under 5 years old was higher than older children [11]. Older children may have had prior or cross-reactive immunity to influenza strains in previous seasons, which protected them against seasonal influenza. However, more community epidemiologic data are necessary to assist in interpreting the detected difference in the ages of admitted children.

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Table 1. Characteristics of patients (adults and children) admitted with seasonal Influenza in 2018-2019 (n=435)

Characteristics		No. (%)/Median (IQR)			P*
		Children	Adults	Total	
Age		4(2-6)	59(42-70)	50(19-66)	-
Gender	Male	68(66.7)	138(41.4)	206(47.4)	<0.001‡
	Female	34(33.3)	195(58.6)	229(52.6)	
Constitutional Symptoms	Ague	88(86.3)	258(77.5)	346(79.5)	0.054
	Myalgia	9(8.8)	182(54.7)	191(43.9)	<0.001‡
	Lethargy	21(20.6)	66(19.8)	87(20.0)	0.865
	Anorexia	13(12.7)	33(9.9)	46(10.6)	0.415
	Lymphadenopathy	1(1.0)	6(1.8)	7(1.6)	0.564
Upper and Lower Respiratory Signs and Symptoms	Sore throat	3(2.9)	43(12.9)	46(10.6)	0.004‡
	Throat erythema	29(28.4)	75(22.5)	104(23.9)	0.221
	Rhinorrhea	44(43.1)	68(20.4)	112(25.7)	<0.001‡
	Post-nasal drip (PND)	12(11.8)	16(4.8)	28(6.4)	0.012‡
	Cough	76(74.5)	276(82.9)	352(80.9)	0.060
	Sputum	23(22.5)	198(59.5)	221(50.8)	<0.001‡
	Tachypnea	0(0)	2(0.6)	2(0.5)	0.433
	Wheezing	3(2.9)	53(15.9)	56(12.9)	0.001‡
	Lung Crackles	23(22.5)	129(38.7)	152(34.9)	0.003‡
	Chest Pain	1(1.0)	54(16.2)	55(12.6)	<0.001‡
Gastrointestinal Symptoms	Diarrhea	9(8.8)	27(8.1)	36(8.3)	0.819
	Cramp	13(12.7)	24(7.2)	37(8.5)	0.079
	Vomit	27(26.5)	91(27.3)	118(27.1)	0.865
Neurological Signs and Symptoms	Vertigo	0(0)	41(12.3)	41(9.4)	<0.001‡
	Imbalance	9(8.8)	11(3.3)	20(4.6)	0.020‡
	Loss of consciousness	6(5.9)	39(11.7)	45(10.3)	0.091
	Delusions	1(1.0)	14(4.2)	15(3.4)	0.118
	Seizure	29(28.4)	6(1.8)	35(8.0)	<0.001‡
	Influenza-related encephalopathy	39(38.2)	89(26.7)	128(29.4)	0.026‡
	Headache	6(5.9)	88(26.4)	94(21.6)	<0.001‡
	Earache	3(2.9)	6(1.8)	9(2.1)	0.479

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* Compared using χ² test/Fisher's exact test.

‡Statistically significant. P<0.05 was considered significant.

Abbreviations: IQR, interquartile range

Table 2. Prevalence of underlying medical conditions among patients admitted with seasonal Influenza in 2018-2019 (n=435)

Underlying Medical Conditions		No. (%)/Median (IQR)			P*
		Children	Adults	Total	
Metabolic	Diabetes mellitus	5(4.9)	78(23.4)	83(19.1)	<0.001‡
	Hypothyroidism	0(0)	17(5.1)	17(3.9)	0.020‡
	Hyperthyroidism	0(0)	5(1.5)	5(1.1)	0.213
	Chronic renal failure	1(1.0)	8(2.4)	9(2.1)	0.377
Cardiopulmonary	Asthma	3(2.9)	116(34.8)	119(27.4)	<0.001‡
	Chronic obstructive pulmonary disease	1(1.0)	20(6.0)	21(4.8)	0.038‡
	Ischemic heart disease	0(0)	67(20.1)	67(15.4)	<0.001‡
	Cardiac arrhythmia	0(0)	13(3.9)	13(3.0)	0.043‡
	Congestive heart failure	0(0)	5(1.5)	5(1.1)	0.213
Neurologic	Cerebrovascular accident	0(0)	25(7.5)	25(5.7)	0.004‡
	Parkinson and Alzheimer	0(0)	10(3.0)	10(2.3)	0.077
	Mental retardation	3(2.9)	7(2.1)	10(2.3)	0.621
	Miller Fisher	1(1.0)	0(0)	1(0.2)	0.070
Other Underlying	Pregnancy	0(0)	16(4.8)	16(3.7)	0.024‡
	Cancer	5(4.9)	6(1.8)	11(2.5)	0.081
	Immunodeficiency	3(2.9)	0(0)	3(0.7)	0.002‡
	Immunosuppressor medications	3(2.9)	3(0.9)	6(1.4)	0.122
	Cystic Fibrosis	9(8.8)	0(0)	9(2.1)	<0.001‡
	Number of risk factors	0(0-1)	1(0-1)	0(0-1)	<0.001‡
	Hospital stay	4(3-7)	5(3-7)	5(3-7)	0.067‡
Virus type	A, H1N1	36(35.3)	109(32.7)	145(33.3)	
	A, H2N2	24(23.5)	84(25.2)	108(24.8)	0.071
	A, H3N2	24(23.5)	52(15.6)	76(17.5)	
	B	18(17.6)	88(26.4)	106(24.4)	
Virus type (total)	A	84(82.4)	245(73.6)	329(75.6)	0.138
	B	18(17.6)	88(26.4)	106(24.4)	

* Compared using χ^2 test/Fisher's exact test.

† Compared using Mann-Whitney U test.

‡ Statistically significant. P<0.05 was considered significant.

Abbreviations: IQR, interquartile range

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In our study, male children were the most affected demographic group. Two main reasons may be considered for the current sex distribution, biological differences between males and females in the clinical course post-exposure/infection (a possible greater biological susceptibility to more severe manifestations), and differential health care-seeking/access behavior between males and females, leading to surveillance/detection bias. In a national surveillance study in Australia, a significant predominance of males existed in all subtypes of influenza in the age group of 0-14 years. In adults, most cases of diagnosed influenza were in female patients. The authors concluded that this predominance is related to health-seeking behavior and increased contact with young children [12]. In our patients, male predominance is seen for up to 22 years.

The clinical manifestations of influenza may differ between adults and children, in adults, a lower frequency of signs of upper respiratory tract dysfunction, imbalance, and seizure were observed. Although the results of our study indicate that adult patients show more neurological symptoms than children, influenza-related encephalopathy was more prevalent in children than in adults. The term "encephalopathy" implies that brain dysfunction exists in the absence of inflammation (delirium). The term encephalitis implies that "inflammation of the brain" is observed [13]. Children show more non-respiratory signs and symptoms than adults, including neurologic manifestations [14]. As evidence for this disparity, about three-quarters of all cases of influenza encephalopathy or encephalitis occur in children [15]. One explanation for the more prevalent encephalopathy in children may be reflected in delayed admission, leading to the progression of inflammation at presentation. Though symptomatic detection of influenza in children may often be difficult, diagnosis and treatment of this disease may be delayed in these patients.

The risk for complications or severe disease varies depending on an individual's age, comorbidities, influenza strain, and vaccination status [16, 17]. Medical conditions, such as severe asthma, lung or heart disease, immune deficiency, or DM may predispose an individual to increased influenza severity. Data on risk factors for serious influenza-related illnesses are essential to guide targeted influenza vaccination. This is especially crucial in under-resourced settings where flu vaccines are limited. In our study, the most common underlying medical conditions among hospital admissions were asthma, DM, and IHD in adults hospitalized with influenza and DM, cancer, and cystic fibrosis in children. In a prospective, hospital-based surveillance study, Tempia et al identified risk factors for seasonal influenza-associated hospitalization, such as extremes of age, pregnancy, asthma, chronic lung and heart diseases, DM, obesity, and HIV infection at three public hospitals in two provinces in South Africa [18], as previously described in studies, such as those by Dawood et al. and Bagdure et al. in the United States [19, 20].

The predominant complications from influenza for children are well-documented [21, 22]. Influenza can compromise medical comorbidities, leading to more severe outcomes, such as hospitalization and the requirement for higher-level care and/or death [23]. A recent review found that neurologic and immune disorders, prematurity, and ages younger than 2 years were strong risk factors for influenza-related hospitalization [24].

In the current study, the prevalence of asthma among children admitted with seasonal influenza was low compared to adults (2.9% vs. 34.8%). Most prior studies on seasonal influenza did not report asthma separately from other chronic lung diseases. The Riordan study suggested that asthma is a more significant risk factor for pandemic influenza requiring hospital admission than for seasonal influenza [25]. Asthma taboo is still a major concern in rural populations with lower socioeconomic status, which may lead to covering up the disease [26]. In some parts of Asia, asthma stigmatization is higher in populations with a lower literacy rate [27]. The stigma of an asthma diagnosis is higher in the pediatric age group, as seen in a study in China [28].

5. Conclusion

This study described clinical characteristics and underlying risk factors among hospitalized children and adults with seasonal influenza. In summary, significant differences were observed among the children and adults with seasonal influenza in terms of 1) a greater proportion of male children and female adults; 2) adults were more likely to have risk factors than children; 3) a greater proportion of children with influenza-related encephalopathy compared to adults; 4) a greater proportion of children with upper respiratory signs and a greater proportion of adults with lower respiratory sign and symptoms. The most common underlying medical conditions were asthma, DM, and IHD in adults and DM, cancer, and cystic fibrosis in children. Our results demonstrate the importance of generating additional data in this domain.

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Limitations

This study was limited by its retrospective design and lack of community epidemiological data. We cannot estimate hospitalization rates for seasonal influenza without population-based epidemiological data. This is an area for impending future research. Such studies should specifically focus on age and underlying medical conditions in particular.

Ethical Considerations

Compliance with ethical guidelines

The study was approved by the Research Ethics Board of Qazvin University of Medical Sciences (IR.QUMS. REC.1397.149). For this retrospective study, the requirement for individual patient consent was waived.

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