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Original Research Article

The hospital-based incidence of influenza infection in children with type C symptoms: an observational study

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ABSTRACT

Background: Influenza, a contagious respiratory illness, poses a significant threat to children, especially those with severe symptoms (Category C). This study aimed to investigate the hospital-based incidence, clinical profile, and outcomes of influenza in pediatric patients.
Methods: This prospective cross-sectional study was conducted from June 2019 to August 2021, enrolling 220 children (6 months to 18 years) with category C influenza-like symptoms. Influenza was diagnosed via reverse transcription polymerase chain reaction (RT-PCR) using nasopharyngeal and oropharyngeal swabs. Clinical data, laboratory findings, and treatment outcomes were analyzed.
Results: Influenza was detected in 47 (21.63%) patients, with peak incidence in October 2019 and February 2020. No cases were recorded in 2021. No significant differences were observed between influenza-positive and-negative groups in demographics or clinical symptoms. ICU admission was higher in the influenza-positive group (14.9% vs. 1.7%). Mortality was significantly higher in influenza-positive patients (12.8% vs. 1.2%). Vaccination rates were low (2.3%).
Conclusions: Influenza poses a considerable health burden in children with severe respiratory symptoms, with increased mortality in positive cases. The marked decline in influenza cases during the COVID-19 pandemic highlights the effectiveness of public health measures. Clinicians should consider influenza in the differential diagnosis of children with severe respiratory illness, particularly during winter. Low vaccination rates emphasize the need for improved vaccination strategies.

Keywords: Pediatric influenza, RT-PCR, Respiratory illness, Vaccination

INTRODUCTION

Influenza, commonly known as the flu, is a highly contagious respiratory illness primarily caused by influenza viruses A or B. These viruses target the upper respiratory tract, encompassing the nose, throat, bronchi, and lungs, and in severe cases, can affect other organs like the heart, brain, and muscles. This globally prevalent infection manifests as seasonal epidemics, contributing significantly to annual morbidity and mortality, with a dramatic surge in fatalities during pandemics. Transmission occurs through respiratory droplets dispersed by infected individuals during coughing or sneezing. While most cases resolve within days, high-risk groups, including pregnant women and those with compromised immune systems, are susceptible to complications and even death. Symptomatically, individuals may experience high fever, body aches, headaches, severe malaise, dry cough, sore throat, and a runny nose, necessitating clinical differentiation from the common cold using clinical assessment.[1]

Influenza viruses, belonging to the *Viridae* family, infect individuals of all ages and are known for their high communicability, causing annual epidemics of varying severity. Major outbreaks are associated with influenza A and B, with influenza A typically presenting with severe symptoms.[2] Influenza A virus, an enveloped virus with a single-stranded, negative-sense RNA genome, is categorized into subtypes based on hemagglutinin (HA) and neuraminidase (NA) proteins, critical for viral invasion and release. These proteins also serve as key targets for antiviral drugs and vaccines.[3] The complex genomic structure of influenza viruses, including their segmented RNA and various structural and non-structural proteins, plays a crucial role in their replication and pathogenesis.[4] The nomenclature of influenza virus strains follows a standardized format, denoting genus, host species, location, isolate number, year of isolation, and HA and NA subtypes for influenza A.[5] Antigenic drift and shift, driven by point mutations and genetic reassortment, respectively, contribute to the virus ability to evade host immunity, leading to sporadic outbreaks and pandemics.[6]

Historically, influenza has caused numerous epidemics and pandemics, with the 1918-1919 Spanish flu being among the deadliest events in human history.[1] More recent pandemics, such as the 1957 H2N2, 1968 H3N2, and 2009 H1N1, have indicated reemergence and the virus' ongoing threat.[7]

The epidemiological features of influenza, including its zoonotic potential and transmission dynamics, highlight the complex interplay between human, animal, and avian hosts.[5] The pathogenesis of influenza involves a combination of host and viral factors, with the virus replicating in respiratory epithelial cells and causing a range of clinical manifestations.[8] Clinical diagnosis relies on symptom assessment, with laboratory confirmation through rapid diagnostic tests and molecular assays being crucial for specific cases.[1]

Patient categorization and treatment guidelines, such as those issued by the ministry of health and family welfare government of India, help manage influenza cases based on symptom severity and risk factors.[9] Severe cases (Category C), marked by breathlessness, chest pain, and other critical symptoms, require immediate hospitalization.[10-13] Complications, particularly respiratory issues like pneumonia, contribute to influenza-related morbidity and mortality, especially in vulnerable populations.[14]

Treatment options, primarily limited to NA inhibitors, face challenges due to drug resistance.[15] Vaccination remains the most effective strategy for preventing influenza and its complications, necessitating continuous adaptation to evolving virus strains.[16] The impact of influenza extends beyond individual health, affecting public health systems and economies through increased healthcare utilization and lost productivity.[17]

Objectives

Objectives were to study hospital based incidence of influenza in patients with category C flu like symptoms.

METHODS

This was a prospective cross-sectional study which was conducted in the postgraduate department of pediatrics and neonatology, Sher I Kashmir institute of medical sciences, Srinagar over a period of 2 years. Children from six months to 18 years of age, with type C influenza like symptoms (high fever, severe sore throat, breathlessness, chest pain, drowsiness, hypotension, hemoptysis, cyanosis, irritability, refusal of feeds and worsening of underlying condition) admitted in department from June 2019 to August 2021were enrolled for study. Patients with type A/B category of influenza-like symptoms were excluded. A detailed medical history and physical examination were conducted on each patient, documenting demographics, vaccination status, pre-existing conditions, and symptom duration. Examination included anthropometric measurements, vital signs (pulse, blood pressure, heart rate, capillary refill time, oxygen saturation), and assessments for respiratory distress and dehydration. A thorough systemic examination was also performed. All patients underwent influenza testing via RT-PCR using combined oropharyngeal and nasopharyngeal swabs, processed at the state level viral research and diagnostic laboratory. Samples were collected in viral transport medium, transported under a cold chain, and stored at -70°C. Viral RNA was extracted using a silica spin column-based kit, and RT-PCR was performed using TaqMan chemistry with CDC/WHO primers and probes on an applied biosystems 7500 fast Dx system. Positive results were defined as growth curves crossing the threshold within 36 cycles, using a pooled positive RNA control from the national institute of virology, Pune. Additional investigations, including complete blood counts, kidney and liver function tests, serum calcium, blood sugar, venous blood gases, and chest X-rays, were performed and recorded. Statistical analysis was conducted using SPSS version 20.0, with normality testing via Shapiro-Wilk test. Parametric data were presented as mean±SD, and non-parametric data as median (IQR). Nominal data were presented as frequency (percentage). Student's t test and Mann-Whitney U-test were used for parametric and non-parametric data analysis, respectively. A $p<0.05$ was considered statistically significant.

RESULTS

This prospective cross-sectional study, conducted from June 2019 to May 2021, analyzed hospital-based influenza incidence in 220 pediatric patients with severe respiratory symptoms (Category C). Of these, 47 (21.63%) tested positive for influenza via RT-PCR. Demographic features of patients admitted are given in Table 1 and 2. No significant differences were observed

between influenza-positive and-negative groups regarding gender (p=0.983), age (p=0.811), anthropometric measurements (height, weight, BMI>0.05), parental education (p=0.480), occupation (p=0.555), or socioeconomic status (p=0.669). Influenza positivity peaked in October 2019 (46.80%) and February 2020 (53.19%), with no cases recorded in 2021 (Table 3). Clinical profiles were similar across both groups. Common symptoms included fever (85-89%), cough (85-87%) and breathlessness (51%). No statistically significant differences were noted in prevalence of fever, cough, vomiting/diarrhea, sore throat, breathlessness, crepitations, wheeze, hemoptysis, cyanosis, nasal flaring, irritability, drowsiness, chest retractions, or chest pain (p>0.05). Vitals (respiratory rate, heart rate, SpO_2) also showed no significant differences (p>0.05). ICU admission was higher in influenza-positive group (14.9%) compared to negative group (1.7%) (Table 4). Baseline laboratory parameters (hemoglobin, total leukocyte count, absolute neutrophil count, absolute lymphocyte count, platelets, pH, bicarbonates) were comparable between groups (p>0.05). Chest X-ray findings (normal, bilateral infiltrates, consolidation) did not significantly differ between groups (p=0.063).

Chronic underlying illnesses were present in 14.89% of influenza-positive and 11.50% of influenza-negative patients (p=0.545). Cardiac disorders were the most common comorbidity in influenza-positive cases. Treatment patterns, including oral and intravenous antibiotics, antiviral therapy (oseltamivir), oxygen supplementation, and nebulization, were similar between groups (p>0.05). However, mortality was significantly higher in the influenza-positive group (12.8%) compared to the negative group (1.2%) (p<0.001). Vaccination rates were low in both groups, with only 2.3% of total cohort vaccinated. No significant difference in vaccination status was observed between groups (p=0.468) (Table 5).

Table 1: Gender distribution of the patients.

Gender	Influenza positive, (n=47) (%)	Influenza negative, (n=173) (%)	P value
Male	26 (55.3)	96 (55.5)	0.983
Female	21 (44.7)	77 (44.5)	

Table 2: Age and anthropometric indices of the patients.

Variables	Influenza positive, (n=47)	Influenza negative, (n=173)	P value
	Median (IQR)	**Median (IQR)**	
Age (in months)	36.0 (69)	24.0 (70)	0.811
Height (in cm)	87.0 (38)	82.0 (35)	0.948
Weight (in kg)	14.0 (13)	12.0 (12)	0.956
BMI (Kg/m^2)	19.0 (2)	19.0 (2)	0.292

Table 3: Incidence of influenza by year and month.

Years	Month	Influenza positive	Percentage (%)
2019	October	11	50
	November	5	22.72
	December	6	27.27
	Total 2019	22	46.8
2020	January	6	24
	February	10	40
	March	5	20
	November	4	16
	Total 2020	25	53.19
2021	All months	0	0
Overall total		47	100

Table 4: Clinical symptoms and signs in influenza positive and negative groups.

Symptom/ sign	Influenza positive, (n=47)		Influenza negative, (n=173)		P value
	N	**%**	**N**	**%**	
Fever	40	85.1	154	89	0.461
Cough	40	85.1	150	86.7	0.777
Breathlessness	24	51.1	89	51.4	0.963
Cyanosis	29	61.7	116	67.1	0.493
Irritability	25	53.2	85	49.1	0.622
Chest retractions	22	46.8	77	44.5	0.779
ICU admission	7	14.9	3	1.7	<0.001

Table 5: Treatment and outcome in influenza positive and negative groups.

Treatment/outcome	Influenza positive, (n=47)		Influenza negative, (n=173)		P value
	N	%	N	%	
Intravenous antibiotics	44	93.6	169	97.7	0.159
Oseltamivir (Antiviral)	9	19.1	34	19.7	0.938
Oxygen supplementation	44	93.6	152	87.8	0.611
Discharged	41	87.2	171	98.8	<0.001
Expired	6	12.8	2	1.2	<0.001
Vaccinated	2	4.3	3	1.7	0.468

DISCUSSION

In January 2010, the 2009 pandemic influenza (H1N1) had spread globally, causing significant morbidity and mortality.[18] Similarly, India reported a substantial number of cases and deaths. [19] This study aimed to investigate the hospital-based incidence, clinical profile, and outcomes of severe influenza (Category C) in pediatric patients admitted to the department of pediatrics and neonatology at our institution from June 2019 to May 2021. Our study revealed a 21.63% influenza positivity rate among 220 pediatric patients with severe respiratory symptoms. The median age of influenza-positive children was 36 months, compared to 24 months in the influenza-negative group, though this difference was not statistically significant. No significant differences were found in baseline demographics or anthropometric characteristics between the groups.

The incidence of influenza peaked during the winter months of October to February, consistent with previous reports of seasonal influenza outbreaks.[20] Interestingly, we observed a significant decline in influenza cases after 2019, coinciding with the COVID-19 pandemic. This observation aligns with numerous global studies reporting a substantial reduction in influenza activity during the pandemic.[21-23] The implementation of public health measures, such as social distancing and enhanced hygiene practices, likely contributed to this decline. Clinical features and routine laboratory investigations were non-specific and did not differentiate between influenza and other viral infections. While fever, cough, cyanosis, irritability, and chest retractions were more prevalent in the influenza-positive group, the differences were not statistically significant. These findings are consistent with previous studies reporting fever and cough as common influenza symptoms.[24] The low incidence of vomiting and diarrhea in our study is also in line with prior research.[25]

Children younger than five years and those with underlying comorbidities are at increased risk for severe influenza.[26,27] In our study, children with chronic underlying illnesses had a higher odd of influenza positivity, although this was not statistically significant. Cardiac disorders were the most common comorbidity in the influenza-positive group, while immunocompromised conditions more frequent in influenza-negative group.

Mortality was significantly higher in the influenza-positive group, particularly among children with underlying comorbidities. This finding is consistent with previous studies reporting increased severity and mortality in patients with comorbidities.[28] Treatment patterns, including intravenous antibiotics, antiviral therapy (oseltamivir), oxygen supplementation, and nebulization, were similar between the two groups. The low utilization of oseltamivir, often initiated beyond the recommended 48- hour window, may have impacted treatment outcomes. However, most patients recovered without complications, even without antiviral therapy, suggesting a benign course for many children. Vaccination rates were notably low in both groups, with over 97% of patients unvaccinated. This could be attributed to low socioeconomic status and limited access to influenza vaccines, which are not included in the universal immunization program in India.

Limitations

Our study has several limitations. First, the study population was relatively small and limited to a single center, potentially limiting the generalizability of our findings. Second, the retrospective nature of the study may have introduced bias. Third, the majority of patients were from families with lower parental education and socioeconomic status, potentially influencing healthcare-seeking behavior and outcomes.

CONCLUSION

This study reveals that influenza poses a significant health challenge to children, impacting both their well-being and that of their families. The most substantial illness burden was observed in children around three years old. Common clinical manifestations in influenza-positive patients included fever, cough, and cyanosis. The incidence of influenza exhibits seasonal variation, with a notable concentration during winter months. The markedly reduced influenza prevalence during the COVID-19 pandemic suggests that social distancing and enhanced hygiene practices are effective strategies for controlling influenza transmission. Children with pre-existing health conditions face a heightened risk of mortality from influenza compared to those without comorbidities. Vaccination rates among the study

population were alarmingly low. Therefore, clinicians should include influenza in the differential diagnosis for children presenting with fever, respiratory illness, or pneumonia, particularly during the winter season. While most cases follow a benign course, ongoing research is essential to comprehensively understand the clinical spectrum of influenza, thereby enabling the development of improved treatment guidelines.

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