

Research Article

Patterns of Viral Pathogens Causing Upper Respiratory Tract Infections in Children Under 13 Years Old: A Retrospective Analysis

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Abstract

Background: Respiratory viral infections strain healthcare globally, accounting for 15% of encounters in the UAE. However, seasonal prevalence in the region remains unclear. This hospital-based study aims to understand viral causes of upper respiratory tract infections (URTIs) in children under 13, focusing on influenza and RSV.

Methods: We conducted a retrospective chart review at Hatta Hospital in Dubai, collecting data from pediatric patients under 13 years old with URTI diagnoses from 2022 to 2023. Nasopharyngeal aspirate samples were analyzed using a multiplex chain reaction (mPCR) assay to identify viral pathogens. Data were collected from the hospital's emergency department, walk-in clinic, and admitted patients.

Results: During the study period, 2714 samples were analyzed, with 1870 (69%) testing positive for any respiratory pathogen. Most infected individuals were males (56.7%), aged between 1 and 3 years (37.9%). Single viral infections were predominant (85.3%), with 27.3% attributed to Human Enterovirus/Rhinovirus, 26.6% to Influenza A, and 10.2% to respiratory syncytial virus (RSV). The RSV season was observed to span from August to December, peaking in October, while Influenza A had semi-seasonal peaks in June and October. Hospital admissions varied significantly between single (21%) and multiple viral infections (27%). Of 340 children hospitalized with single viral infections, 28.2% were infected with Human Enterovirus/Rhinovirus, 16.7% with RSV, and 13.5% with Influenza A.

Conclusion: The study provides insights into viral epidemiology among children in the UAE, highlighting the high prevalence and seasonal peaks of viral pathogens. Awareness of these trends can reduce unnecessary streptococcal testing and antibiotic overuse. Understanding the seasonal patterns aids in optimizing prophylactic measures and vaccination strategies for RSV and influenza, benefiting high-risk infants and children.

Keywords: Hatta Hospital, seasonality, respiratory tract infections, prevalence, influenza, RSV, vaccination

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1. Introduction

Acute respiratory infections (ARIs) represent a major worldwide health challenge, predominantly caused by respiratory viruses [1, 2]. These viral infections account for 15% of all pediatric healthcare visits in the United Arab Emirates (UAE) [3]. Infants and preschoolers in developed countries usually face 6-10 viral infections annually, while those of school age and teenagers typically experience 3-5 such illnesses each year. [4, 5].

Prompt detection of viral causes is crucial to reduce inappropriate use of antibiotics, start suitable antiviral treatment, and limit spread further [6]. The epidemiology of respiratory viruses linked to acute infections has been well-studied in temperate climates [1, 7, 8]. However, there is limited research on the subject in tropical and subtropical areas, despite some studies addressing local climate and latitude effects [9-12].

In the UAE, limited information is available on the patterns and clinical features of respiratory viral infections [13, 14]. Studies from nearby countries are also limited and often focus on specific groups [15]. Even with the existence of seasonal flu vaccine and respiratory syncytial virus (RSV) prevention for infants at high risk, these viruses continue to be major factors contributing to morbidity and mortality [7, 9, 16-19]. Recent advancements, such as maternal vaccination for RSV [20, 21] and the development of Nirsevimab, a long-acting monoclonal antibody providing season-long protection for infants, offer promising new strategies for reducing the burden of RSV [22, 23]. However, the lack of vaccines and effective antiviral treatments for many other respiratory viruses further emphasizes the need for a thorough understanding of respiratory virus epidemiology, which is crucial for public health preparedness.

RSV and influenza exhibit a clear winter seasonal pattern in temperate climates, while their activity trends are highly variable in tropical areas [24, 25]. Understanding influenza's seasonality is vital for guiding vaccine policy decisions and monitoring new virus strains [26, 27]. Despite the increasing availability of influenza vaccines in middle-income countries, the complex seasonal behavior of the virus poses challenges in developing effective vaccination strategies [27, 28]. The monthly administration of palivizumab for high-risk infants requires precise timing aligned with local virus circulation trends [29].

The literature shows a broad range of frequencies for respiratory virus co-infections, often reported between 10% and 20%, and sometimes as high as 60% [30-34]. Growing evidence highlights the importance of mixed infections, particularly co-infections with other viruses, with interactions being recognized directly, indirectly, and through immunological pathways [35]. However, the clinical significance of these viral co-infections in disease presentation remains unclear. While some research has associated viral co-infections with increased severity, including higher rates of hospitalization and intensive care admissions [36-38], the issue remains controversial as several other studies indicate no increase in patient morbidity [39-45]. It is also important to note that bacterial co-infections, which frequently accompany viral respiratory infections, can complicate clinical outcomes. Bacterial co-infections are well-documented to exacerbate the severity of viral illnesses, contributing to higher morbidity and mortality rates, and should be considered when evaluating the overall impact of co-infections in respiratory diseases.

2. Materials and Methods

2.1. Overview

This study employed a retrospective chart review methodology, focusing on the medical records of pediatric patients presented to Hatta Hospital with features of upper respiratory tract infections (URTI) between 2022 and 2023. The study included all pediatric patients aged under 13, who sought care at the hospital's emergency department, pediatric and family medicine walk-in clinic, or were admitted to the pediatric ward with a URTI and had confirmed viral infections through multiplex polymerase chain reaction (mPCR). The collected data encompassed demographic details, hospitalization status, molecular pathogen detection, co-infections, and recording of the month of the infection.

Healthcare professionals collected nasopharyngeal specimens using flocked fiber tip swabs. These samples were placed in universal viral transport media and sent to the microbiology laboratory to be processed using mPCR.

The United Arab Emirates (UAE) is located on the Arabian Peninsula and experiences a desert climate characterized by extreme heat, low humidity, and minimal rainfall. During the summer months (June to September), temperatures frequently rise above 40°C–50°C, driving people to stay indoors. Virus transmission can sometimes increase in enclosed spaces due to close contact, limiting exposure to large outdoor gatherings and environmental factors like pollution, which may otherwise contribute to the spread of respiratory viruses. Furthermore, air-conditioned indoor environments, if properly ventilated, can help in reducing the circulation of pathogens, potentially lowering the risk of viral transmission in such conditions. In the autumn (October to November), as temperatures moderate to 25°C–35°C, an increase in indoor gatherings was observed, coinciding with the onset of the respiratory virus season. Winter (December to February) is the coolest period, with temperatures ranging from 12°C to 24°C, and is associated with the highest incidence of respiratory infections such as influenza and RSV due to increased indoor activity. A gradual increase in temperatures was observed during Spring (March to May), leading to decline in respiratory viral activity [46, 47].

Hatta Hospital, established in December 2010 as an upgrade from the Hatta Health Center, is a multispecialty community hospital under the Dubai Health umbrella. Located in Hatta, approximately 130 km from Dubai, the hospital serves a population of around 40,000 residents in Hatta and the surrounding areas. The facility covers an area of 10,430 square meters and offers 73 beds, providing both primary and secondary care services. Its comprehensive medical services include internal medicine, pediatrics, surgery, cardiology, neurology, obstetrics and gynecology, and specialized care such as a NICU and a clinical diabetes center. Hatta Hospital is accredited by the Joint Commission International (JCI) and recognized as a Baby-Friendly Hospital Initiative (BFHI) facility, reflecting its commitment to high standards of healthcare quality and patient safety.

2.2. Statistical Analysis

The characteristics of the study participants were summarized using frequencies and percentages. The Chi-square test (X^2) was employed to analyze gender differences based on participant characteristics and to explore the relationship between admission status, the number of infecting viruses, and age groups. Additionally, an independent t-test was utilized to assess differences in the duration of hospitalization based on the number of infecting viruses. Statistical significance was defined as $p \leq 0.05$. All data analyses were performed using IBM SPSS Statistics for Windows, Version 28.0 (Armonk, NY: IBM Corp).

3. Results

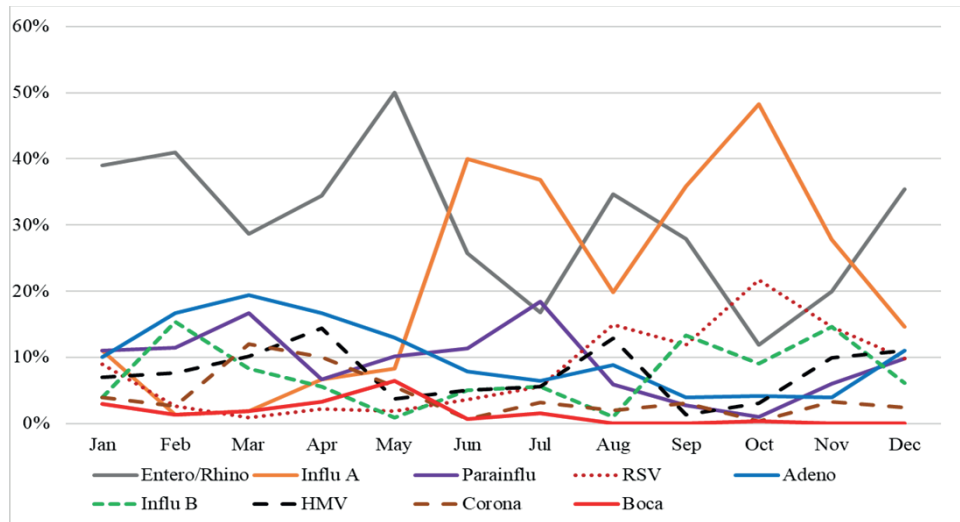
Within the specified study duration, 2714 samples underwent mPCR assay, with 1870 (69%) testing positive for any respiratory pathogen.

A total of 1870 infants and children under 13 years old fulfilled the inclusion criteria. Among them, 1061 (56.7%) were males, 709 (37.9%) were aged between 1 and 3 years, 1596 (85.3%) were infected with a single virus, while 274 (14.7%) had multiple viral infections. A total of 416 (22.2%) required hospitalization (Table 1).

Table 1: Characteristics of the study participants, n = 1870.

| Variables | Frequency (%) |
|---------------------------------|---------------|
| Gender | |
| Female | 811 (43.4) |
| Male | 1059 (56.6) |
| Age group, years | |
| < 1 | 346 (18.5) |
| 1–3 | 708 (37.9) |
| 4–6 | 413 (22.1) |
| 7–12 | 403 (21.4) |
| Number of viruses | |
| 1 | 1596 (85.3) |
| ≥ 2 | 274 (14.7) |
| Admission duration, days | |
| 0 | 1454 (77.8) |
| 1–2 | 250 (13.4) |
| > 2 | 166 (8.8) |
| Year | |
| 2022 | 1211 (64.8) |
| 2023 | 659 (35.2) |

Human Enterovirus/Rhinovirus remained prevalent throughout the year, while Adenovirus was common from February to May, with its peak in March (Figure 1).

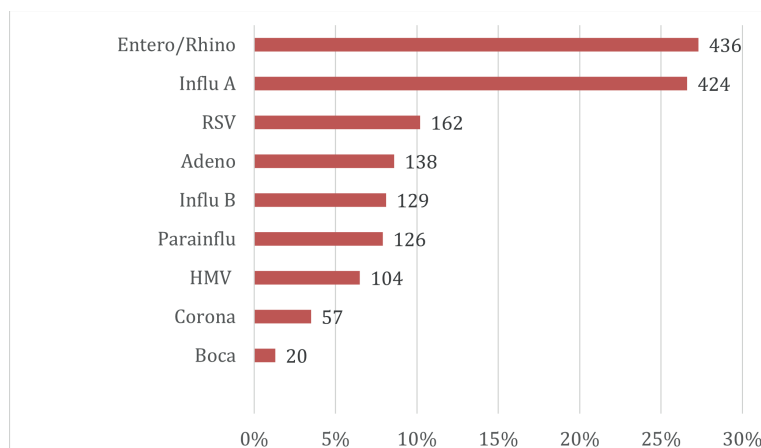


Adeno: Adenovirus; Corona: Coronavirus, MPV: Human metapneumovirus, Influenza A: Influenza A, Influenza B: Influenza B, Rhino/Entero: Human rhinovirus/Enterovirus, Parainfluenza: Parainfluenza virus, RSV: Respiratory syncytial virus, Boca: Bocavirus

Figure 1: Monthly distribution of respiratory viral pathogens in 2022-2023, n = 1596.

Here, RSV showed a seasonal pattern, with infection rates exceeding 10% between August and December, with a rise in peak during October. Influenza A displayed two peaks, first in June and then in October. Conversely, Influenza B was predominantly observed during the winter months, with no significant increase noted in the summer. (Figure 1)

Figure 2 depicts the incidence of different viruses detected throughout the study period. Among the nine most common viruses, Enterovirus/Rhinovirus accounted for 27.3% of cases, while Influenza A comprised 26.6%, and RSV A + B represented 10.2%.

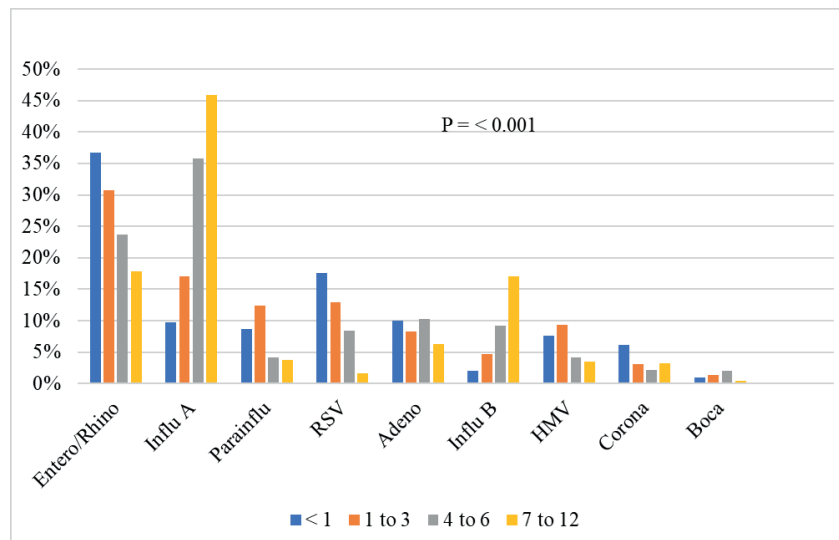


Adeno: Adenovirus, Corona: Coronavirus, MPV: Human metapneumovirus, Influenza A: Influenza A, Influenza B: Influenza B, Rhino/Entero: Human Enterovirus/rhinovirus, Parainfluenza: Parainfluenza virus, RSV: Respiratory syncytial virus, Boca: Bocavirus

Figure 2: Number and percentage of the single viruses caused URTIs, 2022-2023, n = 1596.

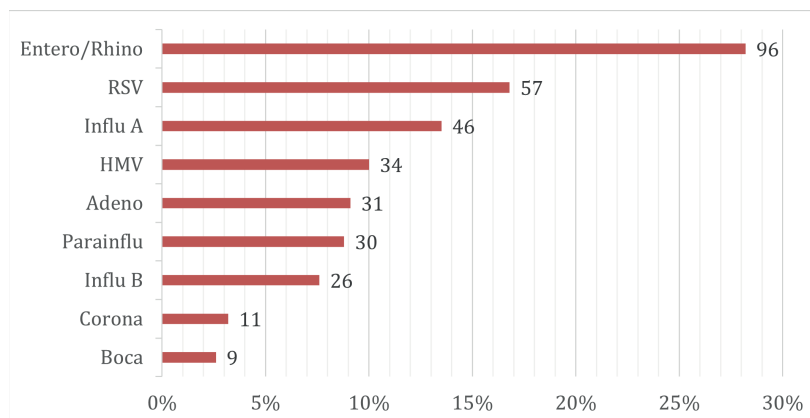
Figure 3 illustrates that the incidence of Human Enterovirus/Rhinovirus and RSV tends to be higher among infants, decreasing with age, whereas the opposite trend was observed for Influenza A and B, with their incidence increasing as age advances. Among the 340 children admitted to the hospital for single

viral URTIs, 28.2% were diagnosed with Human Enterovirus/Rhinovirus, 16.7% had RSV A + B, and 13.5% were found to have Influenza A (Figure 4). Bocavirus had the highest admission rate at 45%, followed by RSV at 35% and Human Metapneumovirus at 33%, while Influenza A had the lowest at 11%. As expected, admission rates decreased with age, with the highest rate observed among infants under 1 year old (37%) and those aged between 1 and 3 (25%) ($p < 0.001$).



Adeno: Adenovirus, Corona: Coronavirus, MPV: Human metapneumovirus, Influenza A: Influenza A, Influenza B: Influenza B, Rhino/Entero: Human rhinovirus/Enterovirus, Parainfluenza: Parainfluenza virus, RSV: Respiratory syncytial virus, Boca- Bocavirus

Figure 3: Age-specific distribution of single viral pathogens in 2022-2023.

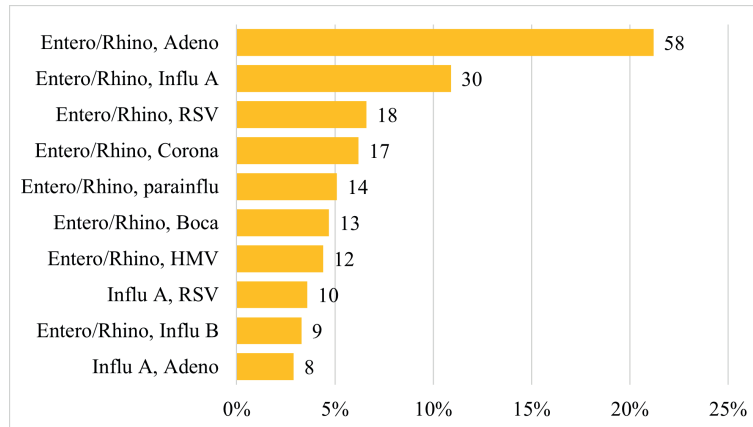


Adeno: Adenovirus, Corona: Coronavirus, MPV: Human metapneumovirus, Influenza A: Influenza A, Influenza B: Influenza B, Rhino/Entero: Human rhinovirus/Enterovirus, Parainfluenza: Parainfluenza virus, RSV: Respiratory syncytial virus, Boca: Bocavirus

Figure 4: Numbers and percentage of URTI admissions due to single viral pathogens in 2022-2023, $n = 340$.

Most co-infections involve Human Enterovirus/Rhinovirus, with co-infection with Enterovirus/Rhinovirus and Adenovirus being the most common (21%), followed by co-infection with Enterovirus/Rhinovirus and Influenza A (11%), and then Enterovirus/Rhinovirus and RSV (7%) (Figure 5). The primary viral co-infections leading to admission are Human Enterovirus/Rhinovirus with Adenovirus (31%), followed by Human Enterovirus/Rhinovirus with RSV (11%), and Human Enterovirus/Rhinovirus with Bocavirus (8%).

Hospital admissions varied significantly between those caused by a single virus (21%) and two or more viruses (27%), $P = 0.043$ (Figure 6). Table 2 highlights a notable variation in the length of hospital stay between cases with a single viral infection and those with two or more viral infections, with a P-value of 0.004.



Adeno: Adenovirus, Corona: Coronavirus, MPV: Human Metapneumovirus, Infl A: Influenza A: Infl B: Influenza B, Rhino/Entero: Human rhinovirus/Enterovirus, Parainflu: Parainfluenza virus, RSV: Respiratory syncytial virus, Boca: Bocavirus

Figure 5: Number and percentage of viral coinfections caused URTIs in 2022-2023, $n = 274$.

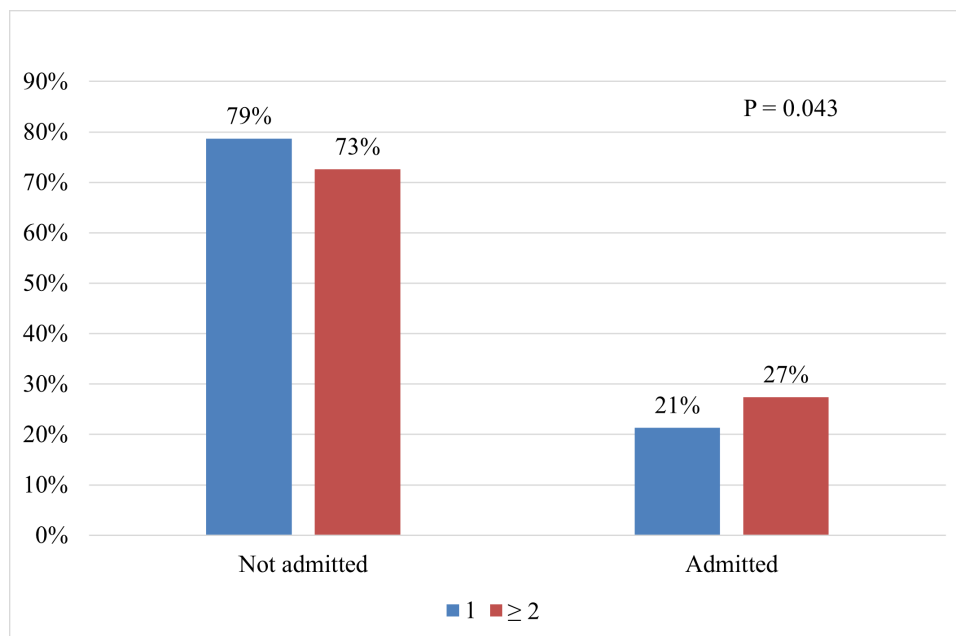


Figure 6: Percentages of admission status based on number of viruses.

Table 2: Duration of admission by the number of viruses.

| No. of viruses | Admission duration, days, (mean ± SD) | t value | P value |
|----------------|---------------------------------------|---------|---------|
| 1 | 0.54 ± 1.20 | -2.887 | 0.004 |
| ≥ 2 | 0.76 ± 1.45 | | |

4. Discussion

The high rate of positive viral identification in our study (69%) was consistent with the elevated rates observed in children with respiratory symptoms globally and in our region, including 78.3% in Dubai, 60% in Egypt, and 61% in Riyadh [14, 15, 19]. However, our findings are notably higher than those from a study conducted at Sheikh Khalifa Specialty Hospital (SKSH) in Ras Al Khaimah emirate, where the positivity rate was 37.2%. The lower rate in that study may be attributed to the inclusion of adults, who generally show lower positivity rates compared to children.

The hospitalization rate in our study was 22.2%, which is relatively high compared to other studies where rates generally range from 1% to 10%, with some reporting up to 15% in high-risk groups [48, 49]. This higher rate may be partly due to a lower threshold for admission, particularly for observation, and it is important to recognize that our research did not investigate comorbidities, which could also contribute to the elevated rate; however, further studies are needed to explore these factors more thoroughly.

Human Enterovirus/Rhinovirus emerged as the most common virus causing URTI in our cohort, consistently present across the year, with RSV and Influenza A coming after. This trend aligns with previous pediatric data from the UAE [13-14]. However, this contrasts with findings from the Kingdom of Saudi Arabia, in which RSV was the predominant virus among children, with Human Enterovirus/Rhinovirus coming next [50, 51].

In our study, Human Enterovirus/Rhinovirus was the leading cause of hospital admissions, accounting for 28.2% of cases. Although the specific reasons for admission were not the primary focus, it is common in clinical practice to admit children with viral URTIs due to factors such as poor oral intake, persistent fever, and family anxiety. These concerns often necessitate hospital admission for close monitoring and supportive care, underscoring the significant clinical impact of these viruses.

In our study, we found that the prevalence of influenza increases with age. This finding may hold clinical significance for practitioners, particularly when considering empirical Tamiflu prescription. While older age groups may be more commonly prescribed Tamiflu due to the higher prevalence observed, it is important to note that influenza can be more severe in younger patients, who are also more likely to be admitted. Therefore, clinicians should remain vigilant in assessing the need for antiviral treatment in infants and younger children, despite the lower prevalence in these age groups.

We observed a semi-seasonal pattern in Influenza A infection rates, with peaks occurring during winter months, possibly due to lower temperatures and specific humidity levels [12]. Additionally, a secondary peak in June was noted, consistent with patterns reported in a previous study in the UAE and in regions at similar latitudes, such as Taiwan and Nepal [9, 13]. This summer peak may be linked to increased activities within enclosed spaces during the hot months and reduced relative humidity, both of which are associated with higher viral illness rates [52, 53]. In contrast, Influenza B infections showed a different pattern, with rates beginning to increase in September and peaking in November, without a notable peak during the summer.

Our data also revealed that the RSV season, characterized by an infection rate above 10%, occurred between August and December, reaching its highest point in October. This timing is similar to findings

from a study conducted in Dubai before the COVID-19 pandemic in 2019 [14]. In the United States and other regions with comparable climates, the RSV season usually begins in the fall and reaches its peak during the winter months, based on pre-pandemic data from 2014 to 2017 [54]. However, the COVID-19 pandemic disrupted these patterns, with an unusual rise in RSV cases in the spring of 2021, reaching its peak in July [55]. It remains uncertain when these patterns will normalize.

Our research identified a 14.6% rate of concurrent viral infections, aligning with previous reports [8]. Human Enterovirus/Rhinovirus was frequently found in these cases, consistent with literature findings [8, 56]. Coinfection with Influenza A and Enterovirus/Rhinovirus was the second most common, despite some studies suggesting a negative correlation between these two viruses [7, 57]. While Enterovirus/Rhinovirus is often detected in co-infections, its exact role in driving the severity of illness requiring hospitalization remains complex and multifactorial. It is challenging to determine whether Enterovirus/Rhinovirus was the primary cause of the symptoms leading to admission or if the other co-infecting viruses, such as Adenovirus, Influenza A, or RSV played a more significant role. Further studies are needed to clarify the individual contributions of each virus in such co-infections.

Additionally, our analysis showed that hospitalization rates were higher for multiple viral infections than for single viral infections. This finding aligns with research from the United States, which also observed increased hospitalization rates in cases of dual infections compared to single infections [32]. While some recent studies have presented mixed results, with a few showing no significant difference in disease severity between single and viral co-infections [36-56], our study highlights that even modest differences in admission rates and duration, though statistically significant, can have important implications. These differences may impact hospital capacity, resource allocation, and patient outcomes, especially in health-care settings with limited resources. Thus, even small variations in clinical outcomes could be clinically relevant when considered within the broader context of healthcare management and patient care.

There are several limitations to this research. First, its retrospective nature may have missed some URTI cases at the hospital. Second, the findings may not fully represent the actual impact of URTIs in the community, as mild cases often do not seek medical care and may self-treat. Community-based epidemiological studies are needed to address this gap. Lastly, as the study was conducted in one health facility, our results may not be applicable to the broader UAE population.

5. Conclusions

This comprehensive study, conducted at Hatta Hospital in Dubai, sheds light on the viral epidemiology, affecting children over two full calendar years. The detection of a significant presence of viral pathogens in children presenting with fever, combined with the observed monthly spikes in viral activity, underscores the need for heightened physician awareness. Such awareness is critical to reducing unwarranted tests for streptococcus and avoiding the overuse and misuse of antibiotics.

The study also reveals a semi-seasonal trend in influenza infections within the UAE, suggesting a possible need for ongoing influenza vaccination efforts and booster shots. These preventative measures

are vital for lessening the impact of influenza, especially among individuals at high risk. Moreover, a comprehensive national dataset is required to fully establish the semi-seasonal trend of influenza in the region.

The insights gained from this research are invaluable for healthcare providers and public health officials in anticipating the start of the season for influenza and RSV. This information is crucial for the timely implementation of preventive measures and vaccination programs, particularly aimed at protecting vulnerable infants and children.

Acknowledgment

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Statement of Ethics

This study did not involve any human participants or animals directly. It was a retrospective analysis based solely on existing medical records. Ethical approval for the use of these records was obtained from the relevant institutional review board and ethics committee. All patient data were anonymized to ensure confidentiality and privacy.

Ethical Approval

Ethical and regulatory approval was obtained from the Dubai Scientific Research Ethics Committee (Ref: DSREC-03/2023_10 on March 23, 2023, and amendment ref: DSREC-01/2024_06 on Jan 10, 2024) and the Institutional Review Board of Mohammed Bin Rashid University of Medicine and Health Sciences (DAHC-MBRU-IRB-2023-036 on Jan 10, 2024).

Informed Consent Statement

As this study was a retrospective analysis utilizing anonymized medical records, no direct contact with patients was made, and informed consent from participants was not required. The study was conducted in accordance with ethical guidelines, and approval was obtained from the relevant institutional review board and ethics committee, which waived the need for informed consent.

Conflict of Interests

Authors declare that there are no conflicts of interest.

Artificial Intelligence (AI) Disclosure Statement

In the preparation of this manuscript, the authors utilized AI-based writing assistance tools to enhance language clarity, grammar, and overall readability. The usage of this tool was limited to editorial assistance and did not influence the research content, interpretation, or conclusions.

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Author Contribution

Dr. Sabir Salah A. Salih, led the research project, coordinated the manuscript preparation, and managed communication with the journal. Dr. Mohammad Abdullatif Al Bana, Dr. Nourhan Rashid Howidi, and Dr. Sadaf Binu Manaf, were responsible for data collection. Dr. Babiker A. Abdalkafi, Dr. Rikaz A. A. Bizzari, and Dr. Abdulrahiman Ch. House, were responsible for data analysis.

Data Sharing Statement

Data sets are included in the published article.

References

- [1] Fendrick AM, Monto AS, Nightengale B, Sarnes M. The economic burden of non-influenza-related viral respiratory tract infection in the United States. *Arch Intern Med*. 2003 Feb;163(4):487–494.
- [2] Schnell D, Gits-Muselli M, Canet E, Lemiale V, Schlemmer B, Simon F, et al. Burden of respiratory viruses in patients with acute respiratory failure. *J Med Virol*. 2014 Jul;86(7):1198–1202.
- [3] Loney T, Aw TC, Handysides DG, Raghil A, Ian B, Michal G, et al. An analysis of the health status of the United Arab Emirates: The 'Big 4' public health issues. *Glob Health Action*. 2013;6:20100.
- [4] Glezen P, Denny FW. Epidemiology of acute lower respiratory disease in children. *N Engl J Med*. 1973 Mar;288(10):498–505.
- [5] Heikkinen T, Järvinen A. The common cold. *Lancet*. 2003 Jan;361(9351):51–59.
- [6] Sanghavi SK, Bullotta A, Husain S, Rinaldo CR. Clinical evaluation of multiplex real-time PCR panels for rapid detection of respiratory viral infections. *J Med Virol*. 2012 Jan;84(1):162–169.
- [7] Tanner H, Boxall E, Osman H. Respiratory viral infections during the 2009-2010 winter season in Central England, UK: Incidence and patterns of multiple virus co-infections [PMC free article]. *Eur J Clin Microbiol Infect Dis*. 2012 Nov;31(11):3001–3006.

- [8] Ambrosioni J, Bridevaux PO, Wagner G, Mamin A, Kaiser L. Epidemiology of viral respiratory infections in a tertiary care centre in the era of molecular diagnosis, Geneva, Switzerland, 2011-2012. *Clin Microbiol Infect.* 2014 Sep;20(9):O578–O584.
- [9] Bloom-Feshbach K, Alonso WJ, Charu V, Tamerius J, Simonsen L, Miller MA, et al. Latitudinal variations in seasonal activity of influenza and respiratory syncytial virus (RSV): A global comparative review. *PLoS One.* 2013;8(2):e54445.
- [10] Paynter S. Humidity and respiratory virus transmission in tropical and temperate settings. *Epidemiol Infect.* 2015 Apr;143(6):1110–1118.
- [11] Tang JW, Loh TP. Correlations between climate factors and incidence—a contributor to RSV seasonality. *Rev Med Virol.* 2014 Jan;24(1):15–34.
- [12] Tamerius JD, Shaman J, Alonso WJ, Bloom-Feshbach K, Uejio CK, Comrie A, et al. Environmental predictors of seasonal influenza epidemics across temperate and tropical climates. *PLoS Pathog.* 2013 Mar;9(3):e1003194.
- [13] Jeon JH, Han M, Chang HE, Park SS, Lee JW, Ahn YJ, et al. Incidence and seasonality of respiratory viruses causing acute respiratory infections in the Northern United Arab Emirates. *J Med Virol.* 2019 Aug;91(8):1378–1384.
- [14] Cureus. Seasonal prevalence of respiratory pathogens among children in the United Arab Emirates: A multicenter cross-sectional study in the Pre-COVID-19 Era. *Cureus.* 2023, September;15(9):e45204. <https://doi.org/10.7759/cureus.45204>
- [15] Albogami SS, Alotaibi MR, Alsahli SA, Masuadi E, Alshaalan M. Seasonal variations of respiratory viruses detected from children with respiratory tract infections in Riyadh, Saudi Arabia. *J Infect Public Health.* 2018;11(2):183–186.
- [16] Rockman S, Dyson A, Koernig S, Becher D, Ng M, Morelli AB, et al. Evaluation of the bioactivity of influenza vaccine strains in vitro suggests that the introduction of new strains in the 2010 Southern Hemisphere trivalent influenza vaccine is associated with adverse events. *Vaccine.* 2014 Jun;32(30):3861–3868.
- [17] Morikawa S, Kohdera U, Hosaka T, Ishii K, Akagawa S, Hiroi S, et al. Seasonal variations of respiratory viruses and etiology of human rhinovirus infection in children. *J Clin Virol.* 2015 Dec;73:14–19.
- [18] Kim JM, Jung HD, Cheong HM, Lee A, Lee NJ, Chu H, et al. Nation-wide surveillance of human acute respiratory virus infections between 2013 and 2015 in Korea. *J Med Virol.* 2018 Jul;90(7):1177–1183.
- [19] Writing Committee of the WHO consultation on clinical aspects of Pandemic (H1N1) 2009 influenza, Bautista E, Chotpitayasunondh T, et al. Clinical aspects of pandemic 2009 influenza A (H1N1) virus infection. *N Engl J Med.* 2010;362(18):1708-1719.
- [20] Munoz FM, Williams J, Herrera G, et al. Safety and immunogenicity of a respiratory syncytial virus prefusion F vaccine in pregnant women. *N Engl J Med.* 2019;381(23):2321–2334.
- [21] Ruckwardt TJ, Morabito KM, Graham BS. Immunological lessons from respiratory syncytial virus vaccine development. *Immunity.* 2019 Sep;51(3):429–442.

- [22] Hammitt LL, Dagan R, Yuan Y, Baca Cots M, Bosheva M, Madhi SA, et al.; MELODY Study Group. Nirsevimab for prevention of RSV in healthy late-preterm and term infants. *N Engl J Med*. 2022 Mar;386(9):837–846.
- [23] Griffin MP, Yuan Y, Takas T, Domachowske JB, Madhi SA, Manzoni P, et al.; Nirsevimab Study Group. Single-dose Nirsevimab for prevention of RSV in preterm infants. *N Engl J Med*. 2020 Jul;383(5):415–425.
- [24] Dowell SF. Seasonal variation in host susceptibility and cycles of certain infectious diseases. *Emerg Infect Dis*. 2001;7(3):369–374.
- [25] Stensballe LG, Devasundaram JK, Simoes EA. Respiratory syncytial virus epidemics: The ups and downs of a seasonal virus. *Pediatr Infect Dis J*. 2003 Feb;22(2 Suppl):S21–S32.
- [26] Richard SA, Viboud C, Miller MA. Evaluation of Southern Hemisphere influenza vaccine recommendations. *Vaccine*. 2010 Mar;28(15):2693–2699.
- [27] de Mello WA, de Paiva TM, Ishida MA, Benega MA, Dos Santos MC, Viboud C, et al. The dilemma of influenza vaccine recommendations when applied to the tropics: The Brazilian case examined under alternative scenarios. *PLoS One*. 2009;4(4):e5095.
- [28] Alonso WJ, Viboud C, Simonsen L, Hirano EW, Daufenbach LZ, Miller MA. Seasonality of influenza in Brazil: A traveling wave from the Amazon to the subtropics. *Am J Epidemiol*. 2007 Jun;165(12):1434–42.
- [29] Panozzo CA, Stockman LJ, Curns AT, Anderson LJ. Use of respiratory syncytial virus surveillance data to optimize the timing of immunoprophylaxis. *Pediatrics*. 2010 Jul;126(1):e116–e123.
- [30] Aberle JH, Aberle SW, Pracher E, Hutter HP, Kundi M, Popow-Kraupp T. Single versus dual respiratory virus infections in hospitalized infants: Impact on clinical course of disease and interferon-gamma response. *Pediatr Infect Dis J*. 2005 Jul;24(7):605–610.
- [31] Subbarao EK, Griffis J, Waner JL. Detection of multiple viral agents in nasopharyngeal specimens yielding respiratory syncytial virus (RSV). An assessment of diagnostic strategy and clinical significance. *Diagn Microbiol Infect Dis*. 1989;12(4):327–332.
- [32] Drews AL, Atmar RL, Glezen WP, Baxter BD, Piedra PA, Greenberg SB. Dual respiratory virus infections. *Clin Infect Dis*. 1997 Dec;25(6):1421–1429.
- [33] Brunstein JD, Cline CL, McKinney S, Thomas E. Evidence from multiplex molecular assays for complex multipathogen interactions in acute respiratory infections. *J Clin Microbiol*. 2008 Jan;46(1):97–102.
- [34] Follin P, Lindqvist A, Nyström K, Lindh M. A variety of respiratory viruses found in symptomatic travellers returning from countries with ongoing spread of the new influenza A(H1N1)v virus strain. *Euro Surveill*. 2009 Jun;14(24):19242.
- [35] DaPalma T, Doonan BP, Trager NM, Kasman LM. A systematic approach to virus-virus interactions. *Virus Res*. 2010 Apr;149(1):1–9.
- [36] Asner SA, Science ME, Tran D, Smieja M, Merglen A, Mertz D. Clinical disease severity of respiratory viral co-infection versus single viral infection: A systematic review and meta-analysis. *PLoS One*. 2014 Jun;9(6):e99392.

- [37] Semple MG, Cowell A, Dove W, Greensill J, McNamara PS, Halfhide C, et al. Dual infection of infants by human metapneumovirus and human respiratory syncytial virus is strongly associated with severe bronchiolitis. *J Infect Dis.* 2005 Feb;191(3):382–386.
- [38] Greensill J, McNamara PS, Dove W, Flanagan B, Smyth RL, Hart CA. Human metapneumovirus in severe respiratory syncytial virus bronchiolitis. *Emerg Infect Dis.* 2003 Mar;9(3):372–375.
- [39] Papadopoulos NG, Moustaki M, Tsofia M, Bossios A, Astra E, Prezerakou A, et al. Association of rhinovirus infection with increased disease severity in acute bronchiolitis. *Am J Respir Crit Care Med.* 2002 May;165(9):1285–1289.
- [40] Subbarao EK, Griffis J, Waner JL. Detection of multiple viral agents in nasopharyngeal specimens yielding respiratory syncytial virus (RSV). An assessment of diagnostic strategy and clinical significance. *Diagn Microbiol Infect Dis.* 1989;12(4):327–332.
- [41] Huang JJ, Huang TY, Huang MY, Chen BH, Lin KH, Jeng JE, et al. Simultaneous multiple viral infections in childhood acute lower respiratory tract infections in southern Taiwan. *J Trop Pediatr.* 1998 Oct;44(5):308–311.
- [42] Lazar I, Weibel C, Dziura J, Ferguson D, Landry ML, Kahn JS. Human metapneumovirus and severity of respiratory syncytial virus disease. *Emerg Infect Dis.* 2004 Jul;10(7):1318–1320.
- [43] Legg JP, Warner JA, Johnston SL, Warner JO. Frequency of detection of picornaviruses and seven other respiratory pathogens in infants. *Pediatr Infect Dis J.* 2005 Jul;24(7):611–616.
- [44] Richard N, Komurian-Pradel F, Javouhey E, Perret M, Rajoharison A, Bagnaud A, et al. The impact of dual viral infection in infants admitted to a pediatric intensive care unit associated with severe bronchiolitis. *Pediatr Infect Dis J.* 2008 Mar;27(3):213–217.
- [45] Palacios G, Hornig M, Cisterna D, Savji N, Bussetti AV, Kapoor V, et al. *Streptococcus pneumoniae* coinfection is correlated with the severity of H1N1 pandemic influenza. *PLoS One.* 2009 Dec;4(12):e8540.
- [46] UAE Ministry of Climate Change and Environment (MOCCA). The UAE State of Climate Report: A Review of the Arabian Gulf Region's Changing Climate & Its Impacts. UAE Ministry of Climate Change and Environment; 2021.
- [47] Cold temperature and low humidity are associated with increased occurrence of respiratory tract infections. Mäkinen TM, Juvonen R, Jokelainen J, et al. *Respir Med.* 2009;103:456–462.
- [48] Mansbach JM, Piedra PA, Teach SJ, Sullivan AF, Forgey T, Clark S, Camargo CA. Prospective multicenter study of viral etiology and hospital length of stay in children with severe bronchiolitis. *Arch Pediatr Adolesc Med.* 2012;166(8):700-706.
- [49] Hall CB, Weinberg GA, Iwane MK, Blumkin AK, Edwards KM, Staat MA, et al. The burden of respiratory syncytial virus infection in young children. *N Engl J Med.* 2009;360(6):588-598.
- [50] Fagbo SF, Garbati MA, Hasan R, AlShahrani D, Al-Shehri M, AlFawaz T, et al. Acute viral respiratory infections among children in MERS-endemic Riyadh, Saudi Arabia, 2012-2013. *J Med Virol.* 2017;89:195–201.

- [51] Farrag MA, Hamed ME, Amer HM, Almajhdi FN. Epidemiology of respiratory viruses in Saudi Arabia: Toward a complete picture. *Arch Virol.* 2019 Aug;164(8):1981–1996.
- [52] Fisman D. Seasonality of viral infections: mechanisms and unknowns. *Clin Microbiol Infect.* 2012 Oct;18(10):946–954.
- [53] Wei J, Li Y. Airborne spread of infectious agents in the indoor environment. *Am J Infect Control.* 2016 Sep;44(9 Suppl):S102–S108.
- [54] Rose EB, Wheatley A, Langley G, Gerber S, Haynes A; Centers for disease control and prevention. Respiratory Syncytial Virus Seasonality - United States, 2014-2017. *MMWR Morb Mortal Wkly Rep.* 2018 Jan;67(2):71–76.
- [55] Olsen SJ, Winn AK, Budd AP, Prill MM, Steel J, Midgley CM, et al. Centers for disease control and prevention. Changes in influenza and other respiratory virus activity during the COVID-19 Pandemic - United States, 2020-2021. *MMWR Morb Mortal Wkly Rep.* 2021 Jul;70(29):1013–1019.
- [56] Goka E, Vallely P, Mutton K, Klapper P. Influenza A viruses dual and multiple infections with other respiratory viruses and risk of hospitalisation and mortality. *Influenza Other Respir Viruses.* 2013 Nov;7(6):1079–1087.
- [57] Jacobs SE, Lamson DM, St George K, Walsh TJ. Human rhinoviruses. *Clin Microbiol Rev.* 2013 Jan;26(1):135–162.