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Original Article

The burden of viral infections in pediatric intensive care unit between endemic and pandemic coronavirus infections: A tertiary care center experience

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ABSTRACT

Objectives: To measure the prevalence of viral infections, length of stay (LOS), and outcome in children admitted to the pediatric intensive care unit (PICU) during the period preceding the COVID-19 pandemic in a MERS-CoV endemic country.

Methods: A retrospective chart review of children 0–14 years old admitted to PICU with a viral infection.

Results: Of 1736 patients, 164 patients (9.45%) had a positive viral infection. The annual prevalence trended downward over a three-year period, from 11.7% to 7.3%. The median PICU LOS was 11.6 days. Viral infections were responsible for 1904.4 (21.94%) PICU patient-days. Mechanical ventilation was used in 91.5% of patients, including noninvasive and invasive modes. Comorbidities were significantly associated with intubation (P-value = 0.025). Patients infected with multiple viruses had median pediatric index of mortality 2 (PIM 2) scores of 4, as compared to 1 for patients with single virus infections ($p < 0.001$), and a median PICU LOS of 12 days, compared to 4 in the single-virus group ($p < 0.001$). Overall, mortality associated with viral infections in PICU was 7 (4.3%). Patients with viral infections having multiple organ failure were significantly more likely to die in the PICU ($p = 0.001$).

Conclusion: **V**iral infections are responsible for one-fifth of PICU patient-days, with a high demand for mechanical ventilation. Patients with multiple viral infections had longer LOS, and higher PIM 2 scores. The downward trend in the yearly rate of PICU admissions for viral infections between the end of the MERS-CoV outbreak and the start of the COVID-19 pandemic may suggest viral interference that warrants further investigations.

1. Introduction

Viral infections represent significant causes of morbidity and mortality in pediatric intensive care units (PICU) [1–3]. The prevalence of PICU admissions due to viral respiratory tract infections is reported at approximately 17.9–20% [1,2].

Exploring the various viruses causing PICU admissions may help in understanding the local epidemiology and planning health care resources. This is of particular importance during seasonal crises or infectious disease outbreaks, such as the COVID-19 pandemic [4,5]. As the pandemic expanded, fear of burdening healthcare facilities was significant for both patients and healthcare authorities [6,7].

While previous research indicated that few cases of Middle East Respiratory Syndrome Coronavirus (MERS-CoV) in children were observed, it remains mainly a disease of adults, similar to what was observed in the COVID-19 pandemic [8,9]. Still, few children had severe

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course, with poor outcome in either MERS-CoV or COVID-19 patients hospitalized with comorbidities [8–10]. Similarly, while common respiratory viruses cause a self-limiting disease in children, it can still result in many PICU admissions [4,11].

The literature regarding viral infection prevalence in our region is limited, so we aimed to measure this prevalence among children admitted to the PICU and to describe associated outcomes.

2. Materials and methods

This retrospective cohort study was conducted in the PICU at King Khalid University Hospital, Riyadh, Saudi Arabia, with data collected. Our PICU is medical and surgical ICU. We admit variety of cases including trauma, infections, post-surgical cases, neurosurgical procedures, and medical cardiac cases. We don't admit post-surgical cardiac cases. We included all patients up to 14 years of age from June 2015 to October 2018who were admitted to the PICU with a viral infection. We defined diagnosis of viral infection as positive evidence of virus presence in human body samples, detected either by immunofluorescence or by real-time polymerase chain reaction (PCR) tests, and the presence of symptoms supportive of the corresponding viral disease. The viral testing was performed based on the clinical indication and PICU team's assessment. The initial viral screening was done using immunofluorescent testing for Influenza, Parainfluenza, Respiratory syncytial and Adenovirus (Respiratory viral screening and identification Mab, Vircell, Granada, Spain). If the initial immunofluorescent testing was negative, samples were processed using PCR testing for Influenza (Cepheid Xpert Flu Assay, Cepheid, California, United States), MERS-CoV (RealStar® MERS-CoV RT-PCR Kit, Altona diagnostics Hamburg, Germany) and multiplex PCR testing for Adenovirus, Coronavirus 229E, Coronavirus HKU1, Coronavirus NL63, Coronavirus OC43, MERS-CoV, Human Metapneumovirus, Rhinovirus, Enterovirus, Influenza A and B, Parainfluenza 1–4, Respiratory syncytial virus (Biofire respiratory panel, bioMérieux, Marcy-l'Étoile, France).

For bacterial co-infection, we reported the results of the initial cultures that were done after PICU admission. For sepsis, we applied the current definition of pediatric sepsis [12,13]. The causes of sepsis could be bacterial if there is a bacterial co-infection, while viral sepsis was considered if only a viral pathogen was identified [14,15].

Descriptive statistics including mean, standard deviation, frequencies, and percentages were used. Bivariate statistical analysis was carried out using the chi-square test for categorical variables while continuous variables were analyzed using Student's-t and Mann-Whitney tests for parametric and non-parametric data, respectively. Multivariate logistic regression analysis was used to assess the combined and individual association between virally infected PICU patients' key relevant demographic, clinical characteristics for their association with intubation and mechanical ventilation. A p-value <0.05 and 95% CI were used to report the statistical significance and precision of the results, respectively. Data were analyzed using SPSS version 24.0 statistical software.

This study was approved by the King Saud University Institutional Review Board (IRB) (#E-19-4146), and consent was waived, given the retrospective design.

3. Results

The total number of PICU admissions was 1736, including 164 cases (9.45%) viral infection. The annual prevalence trended downward over the study period, from 11.7% to 7.3% as illustrated in Fig. A. The proportions of virally infected children admitted to the PICU across the months of the year differed significantly for the three analyzed years ($p < 0.001$) (Fig. B).

The demographic and clinical characteristics of children with viral infection in the PICU are shown in Table 1. Most patients (91.5%) required respiratory support/mechanical ventilation. Almost half of these patients required invasive ventilation (n = 77, 47.0%), while 18 (11.0%) needed high-frequency oscillatory ventilation (HFOV). Table 2 summarizes the comparison of noninvasive ventilation (NIV) and conventional ventilation among the studied cohort. The multivariate logistic regression analysis revealed that comorbidities were significantly associated with a requirement for invasive mechanical ventilation (p-value 0.025), as shown in Table 3. The most common comorbidities in the intubated group were respiratory (16.9%), central nervous system (CNS; 6.5%), and cardiovascular system (CVS; 3.9%) comorbidities; while the most comorbidities in the NIV group were respiratory (5.5%), CNS (1.4%), and prematurity (1.4%). For intubated patients, there was no mortality in the group with positive tracheal aspirate cultures. However, their median length of stay (LOS) = 23.5 (IQR 25.79) days was higher than the group with negative tracheal aspirate cultures (median LOS = 6 (IQR 7) days); $p < 0.001$.

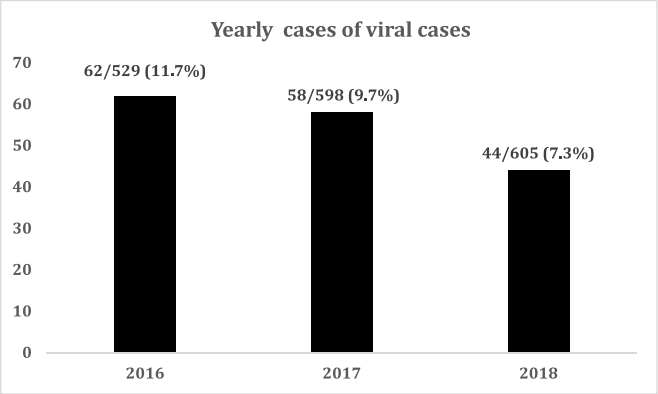

Fig. A. Number of viral infection cases per year and its corresponding prevalence among PICU admissions for three years.

The most commonly identified viruses were RSV, influenza H1N1, and MERS-CoV, with percentages of 77.4%, 17.7%, and 11%, respectively. Other viruses included rhinovirus (2.4%), enterovirus (1.8%), human metapneumovirus (1.2%), influenza B (1.2%), adenovirus (0.6%), and bocavirus (0.6%). Of the total cohort, 21 patients (12.9%) were positive with more than one virus. Out of these 21 patients, 71.4% had influenza and MERS-CoV, 14.2% had rhinovirus and enterovirus, 9.5% had RSV and influenza, and 4.8% had human metapneumovirus and bocavirus. Table 4 summarizes the comparison between patients with single versus multiple viral infections.

Patients with viral infections had a mean and median PICU LOS of 11.6 and 5 days, respectively, compared to a mean and median of 5.19 and 3 days, respectively, for all PICU admissions during the study period. The burden of viral infection in terms of PICU patient-days revealed that viral infections were responsible for 1904.4/8680 (21.94%) PICU patient-days.

The overall mortality rate associated with viral infections was 4.3%. Mortalities included three cases with influenza H1N1; one of them had an order of "do not resuscitate-DNR", one with Adenovirus, and one patient with co-infection of influenza H1N1 and MERS-CoV. In addition, two patients died with RSV; one of them had an order of "DNR", while the second patient had a bacterial co-infection with bloodstream Gram-negative sepsis.

Although the annual prevalence of viral cases differed across the study period, the annual mortality did not vary significantly ($p = 0.940$). The bivariate analysis comparing survivors and non-survivors showed that patients with multiple systems failure were significantly more likely to die ($p = 0.001$) (Table 5).

4. Discussion

Common viral infections represent a significant burden in the PICU

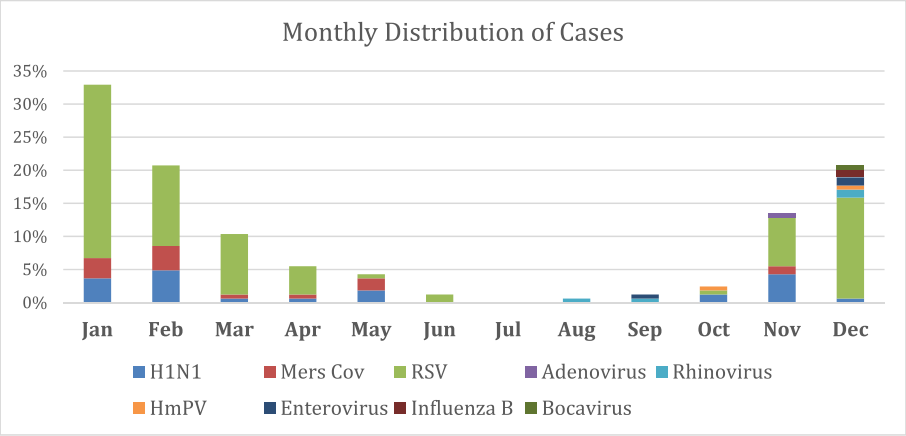

Fig. B. The percentage of monthly distribution cases admitted to the PICU with viral infections for the three years combined (2016–2018). The proportions of virally infected children admitted to the PICU across the months of the year differed significantly for the three analyzed years when chi-squire test was applied ($p < 0.001$).

Table 1
Demographic and clinical characteristics of children with viral infection in the pediatric intensive care unit (Number = 164).

Variables	Frequency (%)	Variables	Frequency (%)
Sex		Principal admitting diagnosis	
Male	113(68.9)	Bronchiolitis	119(72.6)
Female	51(31.3)	Pneumonia	22(13.4)
Age (months), mean (SD)	20.03 (34.83)	Asthma	2(1.2)
1–6 Months	76(46.3)	BRUE	2(1.2)
>6–12 Months	35(21.3)	Cardiomyopathy	1(0.6)
>12–18 Months	12(7.3)	Heart Failure	1(0.6)
>18 Months	41(25)	Encephalitis	1(0.6)
Weight (Kg), mean(SD)	8.40 (5.5)	Thalassemia major	1(0.6)
Height (meter), mean (±SD)	0.72 (±0.21)	Other[a]	15(9.1)
Body Mass Index, mean (±SD)	**15.1 (±2.5)**	**Respiratory Failure**	137(83.5)
PICU Length of stay days	11.6	**Sepsis**	7(4.3)
Mean(±SD)	11.6 (±31.5)	**Endotracheal Intubated**	77(47)
median(Qrt.1, Qrt.3)	5 (3,9.8)	**Mechanical Ventilation**	
PIM 2, mean(±SD)	2.68 (±6.8)	NIV	73(44.5)
Immune-compromised status	6(3.7)	Conventional Ventilation	59(36)
Comorbidities	41(25)	HFOV	18(11)
Types of comorbidities[b]		Not ventilated	14(8.5)
Respiratory	17(10.4)	**Use of (iNO)**	6(3.7)
Others	8(4.9)	**Survival**	
CNS	6(3.7)	Survived	157(95.7)
CVS	3(1.8)	Deceased	7(4.3)
Prematurity	3(1.8)		
Genitourinary	2(1.2)		
Multisystem	2(1.2)		

PIM 2:Pediatric Index of Mortality 2; CNS: Central Nervous System; CVS: Cardiovascular System; BRUE: Brief Resolved Unexplained Event; NIV Noninvasive Ventilation; HFOV: High Frequency Oscillatory Ventilation; LOS: Length of Stay in Pediatric Intensive Care Unit, iNO: inhaled Nitric Oxide.

[a] Inhaled foreign body; Congenital lung anomaly; Breath holding attacks; Pneumonitis; Septic shock; Seizure; VACTERL association; Inborn error of metabolism, Muscular dystrophy, Immune deficiency.

[b] Types of comorbidities include the following examples: asthma, cerebral palsy, seizure disorders, ventricular septal defect, and end-stage renal disease.

[16]. Our study explored the prevalence and types of viral infections in a tertiary PICU setting over three-year period. Viral infections represented 9.45% of PICU admissions. The yearly prevalence showed a downward

Table 2
Comparison between patients with noninvasive ventilation and patients required invasive mechanical ventilation.

	NIV (n = 73)	CMV/HFOV (n = 77)	p-value
Sex			
Male	53(72.6%)	52(67.5%)	
Female	20 (27.4%)	25 (32.5%)	$0.498^{\chi 2}$
Age (months), mean (SD)	14.9 (28.3)	22.6 (38.9)	0.167^{t}
Weight (Kg), mean (SD)	6.85 (3.6)	8.94 (6.1)	0.012^{t}
Height (meter), mean (SD)	0.66 (0.16)	0.73 (0.23)	0.026^{t}
Body Mass Index, mean (SD)	14.91 (2.6)	15.20 (2.4)	0.502^{t}
PIM 2, median	4	8	0.002^{U}
PICU Length of stay (days), median	5.62 (4.9)	19.02 (44.7)	$<0.001^{U}$
Admitted with Sepsis			
No	71 (97.3%)	73 (94.8%)	$0.726^{\chi 2}$
Yes	2 (2.7%)	4 (5.2%)	
Comorbidity			
None	63 (86.3%)	48 (62.3%)	$0.001^{\chi 2}$
At least one	10 (13.7%)	29 (37.7%)	
Ex-Prematurity	1 (1.4%)	1 (1.3%)	$0.97^{\chi 2}$
Immune-compromised status	0	3 (3.9%)	$0.263^{\chi 2}$
Survival outcome	72 (98.6%)[a]	72 (93.5%)	$0.237^{\chi 2}$

[a] One patient died in this group without intubation due to a Do Not Resuscitate order. CMV: conventional mechanical ventilation, HFOV: High Frequency Oscillatory Ventilation; NIV: Noninvasive Ventilation. PIM 2: Pediatric Index of Mortality 2. ^{t} The T –test was applied; ^{U} The Mann-Whitney test was applied, $^{\chi 2}$ The Chi square test was applied.

Table 3
Multivariate logistic regression analysis of the viral-infected PICU patients' association with intubation and mechanical ventilation.

	B	S.E.	Adjusted Odds Ratio	95% C.I.for (O.R)		p-value
				Lower	Upper	
Sex = Male	−.197	.398	.821	.376	1.789	.619
Age (months)	.002	.006	1.002	.990	1.014	.742
Body Mass Index score	.059	.075	1.061	.916	1.228	.432
PICU Length of stay (days)	.086	.030	1.090	1.027	1.157	.004
Survival	1.799	1.317	6.046	.457	79.916	.172
Presented with respiratory failure	.459	.621	1.582	.468	5.346	.460
With comorbidity ≥ 1	1.046	.467	2.846	1.139	7.110	.025
Constant	−2.153	1.470	.116			.143

Table 4
Comparison of patients with single viral infection versus multiple viral infection.

Variables	Single (N = 143)	Multiple (N = 21)	p-value
Sex			
Male	97 (67.8%)	16 (76.2%)	0.44 $^{\chi 2}$
Female	46(32.2%)	5(23.8%)	
Age (months), mean(±SD)	17.55 (31.6)	36.94 (49.7)	0.096 ^{t}
Body Mass Index: Mean(±SD)	15.1 (2.4)	15.1 (3.1)	0.97 ^{t}
PIM 2, Median	1	4	<0.001^{U}
PICU Length of Stay (days), Median	4	12	<0.001^{U}
Mechanical Ventilation			
NIV	67 (51.5%)	6 (30%)	0.073$^{\chi 2}$
Conventional Ventilation	63 (48.5%)	14 (70%)	
Use of Inhaled Nitric Oxide (iNO)	5 (3.5%)	1 (4.8%)	1$^{\chi 2}$
Comorbidities	29 (20.3%)	12 (57.1%)	<0.001 $^{\chi 2}$
Type of comorbidity			0.008$^{\chi 2}$
Respiratory	15 (10.5%)	2 (9.5%)	
Others	4(2.8%)	4(19%)	
CNS	3(2.1%)	3(14.3%)	
CVS	2(1.4%)	1(4.8%)	
Prematurity	2 (1.4%)	1 (4.8%)	
Multisystem	2 (1.4%)	0	
Genitourinary	1(0.71)	1(4.8%)	
Prematurity	2 (1.4%)	1 (4.8%)	0.84$^{\chi 2}$
Immune-compromised status	1 (0.7%)	2 (9.5%)	0.052$^{\chi 2}$
Survival outcome	138 (96.5%)	19 (90.5%)	0.485$^{\chi 2}$

PIM 2: Pediatric Index of Mortality 2, NIV: Noninvasive Ventilation, CNS: Central Nervous System; CVS: Cardiovascular System. ^{t} The T –test was applied; ^{U} The Mann-Whitney test was applied, $^{\chi 2}$ The Chi square test was applied.

Table 5
Comparison between survived and deceased patients among children admitted to the PICU with viral infection.

	Survived (n = 157)	Deceased (n = 7)	p-value
Sex			
Female	49 (31.2%)	2 (28.6%)	NS$^{\chi 2}$
Male	108 (68.8%)	5 (71.4%)	
Age (months), mean(SD)	18.6 (33.9)	51.7 (41.7)	0.013 ^{t}
Weight (Kg), mean(SD)	8.17 (5.3)	12.88 (8.3)	0.186 ^{t}
Height (meter), mean(SD)	0.94 (0.24)	1 (0.001)	0.494 ^{t}
Body Mass Index, mean(SD)	**15.1 (2.5)**	**15.7 (2.6)**	0.537 ^{t}
PICU Length of stay days, median	5	13	0.5^{U}
Pediatric Index of Mortality-2, median	2.36	9.9	<0.001^{U}
Endotracheal intubation	72 (45.9%)	5 (71.4%)	0.348$^{\chi 2}$
Mechanical Ventilation type			
Non-ventilated	13 (8.3%)	1 (14.3%)[a]	0.257$^{\chi 2}$
Noninvasive mechanical ventilation	72 (45.6%)	1 (14.3%)[a]	
Invasive mechanical ventilation	72 (45.6%)	5 (71.4%)	
Sepsis	5 (3.2%)	2 (28.6%)	0.022$^{\chi 2}$
Respiratory Acute Failure	135 (86%)	2 (28.6%)	<0.001$^{\chi 2}$
Comorbidity	37 (23.6%)	4 (57.1%)	0.118$^{\chi 2}$
Prematurity	3 (1.9%)	0	NS$^{\chi 2}$
History of Respiratory Disease	15 (9.6%)	2 (28.6%)	0.326$^{\chi 2}$
Immune statues	2 (1.3%)	1 (14.3%)	0.284$^{\chi 2}$
Affected Body System			0.001$^{\chi 2}$
CNS	2 (1.3%)	0	
CVS	3 (1.9%)	0	
CVS and respiratory	3 (1.9%)	1 (14.2%)	
Respiratory	148 (94.3%)	3 (42.9%)	
Hematological	0	1 (14.3%)	
Multiple systems/Organ failures	1 (0.6%)	2 (14.3%)	
Bacterial co-infection[b]	43 (27.4%)	1(14.2%)	0.444$^{\chi 2}$

CNS: Central Nervous System; CVS: Cardiovascular System.
[a] These two patients died without intubation due to a Do Not Resuscitate order.
[b] These include pneumonia with positive bacterial growth from tracheal aspirate (20), bloodstream infection (12), urinary tract infection (6), and others such as bacterial growth from eye swab and wound cultures (6). ^{t} The T –test was applied;^{U} The Mann-Whitney test was applied, $^{\chi 2}$ The Chi square test was applied.

trend from 11% to 7%. This prevalence is lower than that described in studies from other countries, where their prevalence ranged from 17 to 20% [1,16,17]. Although the study design and inclusion criteria are important confounding factors when comparing these prevalence determinations, differences in prevalence or severity may exist between different locations even when applying the same study criteria, as Lonngren et al. illustrated in their comparison of the United Kingdom and South Africa study sites [3].

Whether these prevalence variations are due to geographic locations and subsequent differences in weather or to the potential consequences of global climate change with variable location impacts is unclear. For instance, a longitudinal investigation in the Netherlands showed that the temperature and global radiation were the most frequently associated weather predictors for disease severity and PICU admissions among children with respiratory viruses [18]. These factors could partially explain the viral respiratory disease seasonal variations. However, these factors do not explain the changing annual prevalence in the same location, as these weather factors remain essentially unchanged locally [18]. By contrast, the potential change in clinical practices, and enhanced utilization of viral diagnostics could be other possible explanations for the increasing detection in developed countries [19–21]. While commercially available viral testing is constantly improving and advancing, we are not aware of any major advances or changes during the study period. However, while the access to new modalities of viral testing is one factor that might enhances detections in developed countries, the developed countries are more likely to maintain consistent access to testing, more efficient utilization, implementation and reliability of the facility are other importance factors as well. Another potential explanation may be the change in prevention strategy, such as change in palivizumab policy for high-risk group prophylaxis against RSV. Nationally, the age of targeted candidate for palivizumab was extended from 29-weeks of gestation up to 32-weeks in the later guidelines [22,23]. Still, the implementation of this change occurred only at end of 2018, which is less likely to affect the prevalence in our cohort that ended in 2018. Our study provides epidemiological data post MERS-CoV outbreak and pre-COVID19, where the burden of viral infection on pediatric critical care and outcome were explored. This would be of an interest to compare these data to the post-COVID 19 data and study the deference between the two eras. The downward trend of PICU admissions for viral infections between the end of the MERS-CoV outbreak and the start of the COVID-19 pandemic could be a thought-provoking for possible viral interference that warrants further investigations [24–27]. Reports have suggested potential viral interference between COVID-19 and other respiratory viruses that could be mediated by direct factors, such as cross-reactivity, or indirect factors, including changing personal behaviors or public health interventions [24–26]. In our study, the respiratory viruses were the most common, which were well-reported in the literature [1,3,28–33]. The variable forms of transmission could contribute to the higher respiratory system infection-susceptibility than other body systems [34].

In our study, we found that 12.8% of patients had multiple viral infections. This rate is comparable to rates reported previously (9.4–18%) [35–37]. Our data revealed a greater association with the severity of the disease in patients with multiple viral infections than with a single viral infection, as indicated by the pediatric index of mortality 2 (PIM 2) score. Kouni et al., similarly reported that viral co-infections might increase the severity of clinical presentation and the risk for hospitalization [29,38]. By contrast, another study showed that illnesses with multiple viral detections correlated with less severe

diseases [35]. These varying conclusions in different reports addressing the impact of multiple viral infections could reflect different populations or epidemiological factors, including the isolated pathogens. For example, in our cohort, most of the viral co-infection group had been infected with MERS-CoV, which could have impacted the outcome of this group.

In our cohort, the children with multiple viruses had longer PICU LOS compared to the children with a single virus infection. The significant association of higher severity scores and comorbidity in the multiple viral infection group could explain the longer LOS. While more invasive mechanical ventilation in the multiple-virus group could partially explain the longer LOS, but our analysis revealed only borderline statistical significance [29,38]. Our finding of higher PIM 2 scores, longer PICU LOS, and the associated comorbidities in the multiple viral infection group are in agreement with previous findings by Chauhan et al. [37]. Patients in the PICU with viral infections are also expected to potentially have complicated courses, especially in those patients with predisposing risk factors, such as bacterial co-infections or malignancy [39].The lack of statistical significance for the impact of the multiplicity of viral infections on the survival outcome in our study could be attributed to either a lack of a true association versus a shortcoming of our study for detecting this association due to sample size issues, or to overlooked confounding variables. Similar investigations did not report any statistically significant mortality differences either [19,35–38].

What predisposes a group to have coexisting multiple viral infections could be challenging to answer. Host factors, such as the presence of comorbidity, could play important roles, but environmental or immune-genetic factors cannot be excluded [39,40].

Different outcome indicators, such as the need for mechanical ventilation, LOS, and mortality rate, were assessed in our study. Multivariate logistic regression revealed a significant association between the presence of comorbidity and the need for intubation and mechanical ventilation upon viral infection. Different predisposing mechanism could be associated with increasing severity of viral infection in the presence of such comorbidities. For instance, following viral infection in asthma cases, the triggered airway inflammatory cascade may act as a double hit. Other example of comorbidity would be neuromuscular conditions associated with impaired clearance of respiratory secretions, such as cerebral palsy and muscular dystrophy. Additional examples of comorbidities include cardiac conditions that may induce lung changes, such as lesions with high left-to-right shunt, or heart lesions that are sensitive to changes in pulmonary vascular resistance and pulmonary blood flow, which could affect oxygenation and increase myocardial demand. In our cohort, RSV infection represents the highest proportion of viral infection, which might affects our outcome data, including intubation and PICU admission. This study represents data from our region and further studies from different centers will provide more insight and better understanding of our regional viral infection distribution.

In the present study, the mortality rate of the virally infected children was 4.3%, which is similar to the reported mortality rate of the general PICU population in our institution [41]. The mortality rate was previously reported to range from 2 to 7% in children with life-threatening respiratory virus infections [19,42,43]. Although pre-existing comorbidities were associated in our cohort with the need for invasive mechanical ventilation, they were not associated with higher mortality. In addition, the deceased group had a paradoxically older age, with a mean age of 51 months, versus 18 months in the survived group. A presentation of sepsis or acute respiratory failure on admission and the involvement of multi-organ failure were significantly associated with mortality in our cohort and other literatures as well [19,42,43]. Comorbidities, such as bacterial co-infection and immunodeficiency, have been reported as important factors associated with viral infection related mortality [42]. Most of the previous studies focused on a specific pathogen or a specifically affected system/disease, with mortality rates varying for different pathogens and diseases [44,45]. Our study scope focused on the burden of viral infection as a group, which provides different epidemiologic perspective, rather than investigating or linking specific outcome to a specific virus. Therefore, comparison of our mortality findings with other reports is challenging, as we included the pool of identified causative viral pathogens in our mortality analysis rather than specific mortality analysis for the identified viruses.

While researchers looked at the potential impact of viral infection during the COVID-19 pandemic or in the post-COVID-19 era; however, our study provides a distinct perspective and highlights the viral prevalence between MERS-CoV and COVID-19 peaks. The present study is one of the few regional reports published to date with relatively adequate sample size and focus on the burden and outcomes of children admitted to the PICU due to severe viral infections. Such regional data could highlight geographic differences playing a role in viral infection. Nevertheless, our study needs to be interpreted with consideration of its limitations, including that the data come from a single center. While the common virological screening within our institute is relatively adequate, the presence of other viruses could occasionally go undetected. The relatively low number of mortality cases was a limitation for performing multivariate logistic regression to further test for associations with mortality in our data set. Although the identification of specific virus-related outcomes could be of added value, this was beyond the study scope. Future large multicenter studies over long durations are recommended to clarify patterns of different viral infections among pediatric patients requiring PICU admission. This will be especially important post the COVID-19 pandemic and the potential reallocation of resources.

5. Conclusions

Respiratory viral infections are responsible for significant PICU admission days with a high demand for mechanical ventilation. Patients with multiple viral infections had longer PICU LOS, higher median PIM 2 scores, and more comorbidities. This study demonstrates the importance of planning public health policy implementation during the seasonal months of viral infections to account for the high PICU resource needs of these children. The downward trend and variability in the annual PICU admissions for viral infections between the end of the MERS-CoV outbreak and the start of the COVID-19 pandemic may signal viral interference that warrants further investigations.

Ethics approval

The institutional review board (IRB) of King Saud University approved this study (Approval No. E-21-5763).

Author contributions

Conceptualization, A.AE. and M.AZ.; Methodology, G.H. and Q.AM.; Validation, F.AS., M.AB. and A.AH.; Formal Analysis, A.AE.; Investigation, F.AF.; Data Curation, F.AF., S.AS.; Writing – Original Draft Preparation, N.AD.,Y.AJ.; Writing – Review & Editing, A.AE.,M.AZ.,G.H.,M.H.; Visualization, M.H.; Supervision, A.AE.

Statements and declarations

Authors have no financial or non-financial interests that are directly or indirectly related to the work submitted for publication, and the work had no financial funding.

Institutional review board statement

“The study was conducted according to the guidelines of the Declaration of Helsinki, and approved by the Institutional Review Board of King Saud University (protocol code #E-19-4146). Patient consent was

waived due to the retrospective design and removal of case identifier.

Declaration of competing interest

Authors have no conflict of interest to declare.

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