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ONLINE BRIEF COMMUNICATION

Pattern of Viral Infections among Infants and Children Admitted to the Paediatric Intensive Care Unit at Sultan Qaboos University Hospital, Oman

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أنماط العدوى الفيروسية بين الرضع والأطفال المنومين في وحدة العناية المركزة للأطفال في مستشفى جامعة السلطان قابوس، سلطنة عمان

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ABSTRACT: ***Objectives:*** The aim of this study was to describe the pattern of viral infections in infants and children admitted to the Paediatric Intensive Care Unit (PICU) at Sultan Qaboos University Hospital (SQUH) in Muscat, Oman. ***Methods:*** A retrospective review of patient records was carried out on all patients admitted to the PICU between January 2011 and December 2012. In order to detect viruses, polymerase chain reaction (PCR) technology was used to detect viruses in nasopharyngeal aspirates, tracheal aspirates, plasma, stool and urine samples. All infants and children below 13 years old, who were admitted to the PICU at SQUH during the study period and with confirmed viral infections, were included in the study. ***Results:*** A total of 373 infants and children were admitted to the PICU during the study period. Viruses were detected in 34 patients. The most frequently detected viruses were cytomegalovirus (CMV) in 29.4%; this virus was noted predominantly in immuncompromised patients (80%, $P = 0.023$) and was associated with increased mortality (50%, $P = 0.031$) and prolonged PICU stay (70%, $P = 0.045$). Fatalities before discharge were recorded in 23.5% of the patients. The most frequent risk factors for viral infections were an age of <12 months old (47.1%), assisted ventilation/intubation (52.9%) and a prolonged PICU stay (55.9%). ***Conclusion:*** The results of this study found that CMV was the most common viral infection among infants and children admitted to the PICU in SQUH. CMV was also the leading cause of mortality.

Keywords: Viral Diseases; Viruses; Cytomegalovirus; Respiratory Syncytial Viruses; Infants; Children; Oman.

الملخص: الهدف: هدفت هذه الدراسة الي وصف أنماط الالتهابات الفيروسية لدى الرضع والأطفال المنومين في وحدة العناية المركزة للاطفال في مستشفى جامعة السلطان قابوس بمسقط، سلطنة عمان. **الطريقة:** تم ادراج جميع المرضى الذين تم تنويمهم في وحدة العناية المركزة للأطفال بين يناير 2011 وديسمبر 2012. تم استخدم سلسلة تفاعل البلمرة للكشف عن الفيروسات في عينات من البلعوم، القصبة الهوائية، البلازما، البراز والبول. وقد تم إدراج جميع الرضع والأطفال أقل من عمر 13 سنة والذين تم تنويمهم فى وحدة العناية المركزة بمستشفي جامعة السلطان قابوس خلال فترة الدراسة والذين ثبت وجود االتهابات فيروسية لديهم. **النتائج:** تم قبول عدد 373 طفل في وحدة العناية المركزة للأطفال خلال فترة الدراسة. وقد تم الكشف عن وجود التهاب فيروسي في 34 مريضا من بينهم. كان الفيروس المضخم للخلايا هو الاكثر شيوعآ (29.4%)؛ وقد لوحظ وجود هذا الفيروس بصورة أكبر في المرضى ذوي المناعة المنخفضة (80%، P = 0.023) وكان وجودة مرتبطا مع زيادة معدل الوفيات (50%، P = 0.031) والإقامة لفترات طويلة في العناية المركزة (70%، P = 0.045). وسجلت حالات الوفاة قبل الخروج من الوحدة في 23.5% من المرضى. لوحظ ان صغر السن في الأطفال الاقل من 12 شهرآ هو اكثر العوامل ارتباطا بالعدوى الفيروسية (47.1%)، و الاحتياج للتنفس الاصطناعي (52.9%) والإقامة لفترات طويلة في العناية المركزة (55.9%). **الخلاصة:** اثبتت نتائج هذه الدراسة أن الفيروس المضخم للخلايا هو الأكثر شيوعا بين الرضع والأطفال المنومين في العناية المركزة في مستشفى جامعة السلطان قابوس وهو يمثل السبب الرئيسي للوفيات.

مفتاح الكلمات: الأمراض الفيروسية؛ الفيروسات؛ الفيروس المضخم للخلايا؛ فيروس الجهاز التنفسي المخلوي؛ الرضع؛ الأطفال؛ عمان.

Viral infections are common among children and most cases are categorised as mild infections. However, some cases require hospital admission in intensive care or high dependency units. Viral infections may be among the underlying causes for the high rates of morbidity among hospitalised children, especially in paediatric intensive care units (PICUs).[1] Nosocomial respiratory and systemic viral infections cause significant morbidity and mortality, particularly among hospitalised children with underlying cardiorespiratory diseases or immunodeficiencies.[2,3] Infections acquired in intensive care units (ICUs) account for high morbidity and mortality rates and cause considerable expense. Infection and sepsis are the leading causes of death in non-cardiac ICUs and account for 40% of all ICU expenditures.[4]

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Cytomegalovirus (CMV) infections have been shown to lead to significant disease in immunocompromised hosts.[5,6] Research has shown that critically ill patients, traditionally considered to be immunocompetent, may also be at risk of contracting CMV.[5] Septic insult as a result of bacterial or fungal infections has the potential to promote the release of immunomodulatory cytokines and lead to the reactivation of CMV.[5,7–9] Additionally, respiratory syncytial virus (RSV) infections are the leading cause of lower respiratory tract infections such as bronchiolitis and bronchopneumonia.[10] RSV infections lead to the intermediate or intensive care admission of approximately 1–2% of each annual birth cohort in Switzerland.[11]

Understanding the pattern of viral infections is important as this knowledge will help improve infection control practices and limit the spread of disease within PICUs. The objective of this study was to characterise the pattern and risk factors of viral infections among infants and children admitted to the PICU in Sultan Qaboos University Hospital (SQUH), Muscat, Oman.

Methods

Patient records from the PICU at SQUH were retrospectively reviewed to identify infants and children with viral infections admitted to the PICU between January 2011 and December 2012. All patients below 13 years old who were admitted to the PICU during the study period and who had confirmed viral infections were included in the study. These included immunodeficient patients (both primary and secondary immunodeficiencies), patients on steroids and haematological cases. Patients with viruses that were not isolated and subjects known to have viral infections before admission were excluded from the study.

Data extracted from the records included demographic characteristics; clinical diagnosis; number and types of virus isolated; duration of assisted ventilation; duration of stay in the PICU, and patient outcome. A stay of less than seven days was considered to be a short stay.[12]

Viruses were isolated from nasopharyngeal aspirate (NPA), tracheal aspirate (TA), plasma, stool or urine. Viral studies were not taken routinely and were undertaken only on a clinical basis in patients suspected of viral infections. For the purpose of this study, the viruses were grouped into two major categories: respiratory viruses and systemic viruses. Some patients underwent a respiratory virus panel while others underwent a systemic viral panel. Respiratory system samples (NPA and TA) were collected in disposable mucus extractors (Vygon SA, Écouen, France) and systemic samples (blood, urine and stool) were collected in plain containers. Samples were processed by polymerase chain reaction (PCR) for viral detection using three kits (Fast-Track Diagnostics Ltd., Sliema, Malta). The PCR FTD® Viral Gastroenteritis kit was used to detect norovirus G1, norovirus G2, astrovirus, rotavirus, adenovirus and sapovirus. The FTD® ACE kit was used to detect CMV, Epstein-Barr virus (EBV) and adenovirus. The FTD® Respiratory Pathogens 21 kit was used to detect influenza A; H_1N_1; influenza B; rhinovirus; coronaviruses NL63, 229E, HKU1 and OC43; parainfluenza viruses 1, 2, 3 and 4; human metapneumoviruses A and B; RSV A and B; adenovirus; enterovirus; parechovirus; human bocavirus, and mycoplasma *pneumoniae*.

Data were analysed using the Statistical Package for Social Sciences (SPSS), Version 19 (IBM Corp., Chicago, Illinois, USA). Fisher's exact test was used to test the significance of the results at the 5% level.

As this study was retrospective, it did not require ethical approval.

Results

There were 373 infants and children admitted to the PICU between January 2011 and December 2012. Of these, a total of 34 (9.12%) were found to have confirmed viral infections. Viral infections were identified among 47.1% of the infants below 12 months old.

The most frequently isolated virus was CMV (n = 10; 29.4%) followed by RSV (n = 7; 23.3%), rotavirus (n = 7; 23.3%) and EBV (n = 6; 20.0%). The least frequently isolated viruses were the influenza B virus (n = 2; 5.9%), astrovirus (n = 2; 5.9%), rubella virus (n = 2; 5.9%), influenza A virus (n = 1; 2.9%) and norovirus (n = 1; 2.9%). Dual or multiple co-infections were found in five cases (14.7%).

Respiratory viruses were identified in 29.4% of the cases. The most common was RSV, either in isolation (14.7%) or as a co-infection (5.9%) with CMV. EBV and CMV were also commonly identified as co-infections. Other viruses, such as the influenza viruses and the rubella virus, were mostly detected as single infections.

Table 1 depicts the demographic characteristics and clinical parameters of infants and children with viral infections. The age of the patients ranged from two months to 13 years old with a mean of 2.6 ± 3.2 years. There were more males (61.8%) than females with a male to female ratio of 1.6:1. A substantial

Table 1: Demographic and clinical characteristics of paediatric intensive care unit-admitted infants and children with viral infections (N = 34)

Characteristics	n	%
Gender		
Male	21	61.8
Female	13	38.2
Age		
<12 months	16	47.1
12 months – <5 years	12	35.3
≥5 years	6	17.6
Immunocompromised		
Yes	16	47.1
No	18	52.9
Intubated		
Yes	18	52.9
No	16	47.1
Duration of intubation		
<7 days	6	33.3
≥7 days	12	66.7
Duration of stay		
Short stay (<7 days)	15	44.1
Long stay (≥7 days)	19	55.9
Number of viruses isolated		
1	29	85.3
2	5	14.7
Type of virus isolated		
Respiratory	10	29.4
Systemic	24	70.6
Virus isolated*		
CMV	10	29.4
RSV	7	23.3
Rotavirus	7	23.3
EBV	6	20
Other**	8	23.5
Management/antivirus therapy		
Yes	10	29.4
No	24	70.6
Outcome		
Discharged alive	26	76.5
Fatality	8	23.5

*CMV = cytomegalovirus; RSV = respiratory syncytial virus; EBV = Epstein-Barr virus. *Categories are not mutually exclusive. **Influenza B virus (2, 5.9%), astrovirus (n = 2; 5.9%), rubella virus (n = 2; 5.9%), influenza A virus (n = 1; 2.9%) and norovirus (n = 1; 2.9%).*

Table 2: Clinical characteristics of paediatric intensive care unit-admitted infants and children with the four most frequently detected viral infections

Characteristics	Type of virus* n (%)			
	Rotavirus (n = 7)	CMV (n = 10)	EBV (n = 6)	RSV (n = 7)
Immunocompromised				
Yes	3 (42.9)	8 (80.0)	5 (83.3)	1 (14.3)
No	4 (57.1)	2 (20.0)	1 (16.7)	6 (85.7)
P value†	1.000	0.023	0.078	0.090
Duration of stay				
<7 days	4 (57.1)	3 (30.0)	3 (50.0)	3 (42.9)
≥7 days	3 (42.9)	7 (70.0)	3 (50.0)	4 (57.1)
P value†	0.067	0.045	1.000	1.000
Type of virus isolated				
Respiratory	0 (0.0)	1 (10.0)	1 (16.7)	7 (100.0)
Systemic	7 (100.0)	9 (90.0)	5 (83.3)	0 (0.0)
P value†	0.078	0.215	0.644	0.000
Outcome				
Discharged alive	7 (100.0)	5 (50.0)	3 (50.0)	6 (85.7)
Fatality	0 (0.0)	5 (50.0)	3 (50.0)	1 (14.3)
P value†	0.160	0.031	0.126	1.000

*CMV = cytomegalovirus; EBV = Epstein-Barr virus; RSV = respiratory syncytial virus. *Tests of significance were performed against other cases where the virus was not isolated. †P values were computed using Fisher's exact test.*

proportion of the patients were immunocompromised (n = 16; 47.1%). More than half of the cases (n = 18; 52.9%) required assisted ventilation. A total of 12 patients (66.7%) required intubation for more than seven days with a mean duration of 10.5 ± 10.5 days. Antiviral therapy was prescribed for 10 patients (29.4%). Over half of the patients (n = 19; 55.9%) stayed in the PICU for more than seven days with a mean duration of 10.6 ± 11.9 days. There were eight fatalities before discharge (23.5%). Over the study period, the overall mortality rate in the PICU was 2.97%.

A high percentage of CMV cases (n = 8; 80.0%) were immunocompromised (*P* = 0.023). CMV infection was also significantly associated with a long stay in the PICU (70%, *P* = 0.045) and mortality at discharge (50%, *P* = 0.031). Out of the seven cases of RSV, four (57.1%) had a long PICU stay and the majority (n = 6; 85.7%) were alive upon discharge [Table 2].

Discussion

The current study aimed to characterise the pattern of viral infections among infants and children admitted to the PICU in SQUH over a two-year period. Viral infections were identified among 9.12% of all admissions. It is unclear if the patients with isolated viruses were asymptomatic carriers.

The most commonly isolated virus was CMV (29.4%), followed by RSV, rotavirus and EBV. This is comparable to the findings of Ziemann *et al.* who observed CMV infections in 36% of the critically ill adult patients studied.[9] Risk factors for CMV infections in the current study included immunosuppression, mechanical ventilation and prolonged PICU stay. However, systemic viral infections in cases requiring prolonged intubation may lead to ventilation-associated pneumonia, resulting in increased morbidity and mortality among these patients. CMV infection was also associated with increased mortality. These results were higher than those observed in a study by Limaye *et al.*, in which CMV infections were recorded in 35% of patients with a mortality rate of 28.6%.[13]

Respiratory viruses were identified in 29.4% of the cases and the most commonly isolated virus was RSV, either alone or as a co-infection. Similar results were found in previous studies which observed rates of infections between 11–15%.[14,15] These rates are higher in comparison to a study by Leung *et al.* which identified RSV in 117 RSV-associated PICU admissions (2.4%).[16] This low percentage may be attributable to the fact that the majority of RSV-infected children do not require PICU support.[16] A study performed in Kenya by Berkley *et al.* found a higher percentage of respiratory viruses in comparison to the current study. Respiratory viruses were detected in 56% of participants, with RSV representing 34% of cases and other viruses showing similar percentages.[17]

The current study found co-infections in 14.7% of patients, which is similar to another local study in Oman by Khamis *et al.* which found dual or multiple infections in 18% of patients.[18] Of these, RSV infections were found in 22% of patients,[18] which is again comparable to the results found in this study (23.3%). These high rates can be explained by the effect of winter seasonality on RSV-associated PICU admissions.

The deaths recorded as outcomes among eight patients were not attributable to a single factor; however viral infection was associated with increased mortality.

This study has several limitations. As the data was collected retrospectively, there were some missing data and it was not possible to differentiate between nosocomial and community-acquired viral infections. Future prospective studies are recommended to identify how many days post-admission viruses are isolated in order to determine if they are hospital- or community-acquired. Additionally, specimens were not taken in a standardised manner among all children admitted to the PICU. Furthermore, the lack of a control group limits the interpretation of the results as it is not possible to establish the prevalence or generalise the results to the entire population of Oman. Future studies should investigate how many patients are negative for viral infections so as to determine the prevalence. By determining the baseline prevalence, improvements in infection control can be assessed.

Conclusion

CMV was the most common virus among infants and children admitted to the PICU in SQUH, followed by RSV, rotavirus and EBV. CMV infections were associated with increased mortality and prolonged PICU stay. The most frequent risk factors for viral infection included an age of <12 months old, immune deficiencies and a prolonged PICU stay. This is the first study in Oman to focus on this emerging topic. More detailed studies are recommended to determine the prevalence of viral infections in Oman.

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