Clinical profile of Respiratory Syncytial Virus (RSV) bronchiolitis in the intensive care unit at a Tertiary Care Hospital

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Abstract

RSV (Respiratory Syncytial Virus) is the most common cause of bronchiolitis among newborns worldwide. Although many risk factors for RSVinfections in newborns have been proposed, there is still a need to further investigate the profile of RSV positive children who required ICU admission to be able to better identify children at risk. Moreover, increasing evidences suggest that genetic variations of the host response can influence the outcome of some infectious diseases such as RSV-induced bronchiolitis. In this study, we have investi-gated the risk factors associated with RSVinfection in Saudi children admitted to the pedi-atric intensive care unit (PICU) of a tertiary university hospital. We have noticed that prematurity is associated with increased severity of RSV infection. Thirty seven percent of the infants admitted in the PICU were found to be of premature birth. Moreover, children with pulmonary pathology and cardio-vascular abnormalities were also more prone to RSV in-fection. The clinical characteristics of these patients and the over-all outcome of the PICU admission were discussed. The seasonality of RSV admissions in the PICU at a teaching tertiary care hospital was also reported herein.

Introduction

Human Respiratory Syncytial Virus is the most common cause of severe viral respiratory tract infection among children worldwide. Bronchiolitis, the main outcome of RSV infection, leads to numerous hospital admissions for children under the age of five [1]. The global burden of RSV is estimated at 64 million cases and around 16000 deaths annually [2]. In Saudi Arabia, a previous study on Saudi children showed that 79% of the children admitted to King Khalid University Hospital (KKUH) with acute respiratory tract infections were diagnosed with RSV infection [3]. Most of RSV infections are usually mild and require minimal hospital stay; however, some children are severely affected requiring pediatric ICU admission and onger hospital stay.

Several studies have identified prematurity, chronic lung disease, congenital heart disease, immunodeficiency and other pre-existing co-morbidities as significant risk factors for severe RSV infection among children [4-7]. Alongside these risk factors, it is also important to determine the clinical pattern and outcome of severe RSV infections. Jamjoom et al. noted that the median hospital stay for RSV infection in KKUH is 5 days [8]. However, this covered only one season and general ward admissions. It has been reported that a history of apnea or hypoxia on admission significantly contributed to the duration of the hospital stay and admission to intensive care [6]. Seasonality is also a distinct characteristic of RSV. Temperate climates haveRSV outbreaks during late fall, winter and spring. Tropical countries have RSV spread related to temperature and rainfall [9]. The exact reason for the seasonality for RSV infection is still unknown. One study indicated that temperature partly explains the year to year variability in RSV activity [10].

Currently, the previous studies on Saudi children reported cases of SV in the winter months [3,5].

Although many risk factors for RSV infections in new-borns have been proposed, there is still a need to further investigate the profile of these ICUadmitted-RSV positive children in order to identify children at risk and hence be able to better control related complications. Moreover, there is increasing evidence that genetic variation of the host response can influence the outcome of some infec-tious diseases [11,12]. Genetic variation was shown to influence the outcome of RSV-induced bronchiolitis [13].

In this study, we have investigated the risk factors associated with RSV infection in Saudi children admitted to the PICU of KKUH. We also made sure to document the clinical characteristics of these patients and the overall outcome of the PICU admission. The seasonality of RSV admissions in the PICUof that Saudi hospital was also reported herein.

Materials and Methods

The study population consisted of 70 Saudi children ad-mitted to the PICU of the KKUH from January 2003 to January 2009 in Riyadh, Kingdom of Saudi Arabia. There were another 24 patients admitted at that period (total 94) but we were not able to retrieve their records for technical reasons.KKUH is a 740-bed tertiary, university hospital with a PICU capacity of 7 beds. The following information was obtained: age on admission, gender, gestational age, and infant nutrition. The respiratory rate, auscultation findings, oxygen saturation, blood pH, presence of chest wall retractions and cyanosis upon admission were noted. Children diagnosed with bronchiolitis but not admitted to the PICU were excluded.

Clinical factors such as prematurity, chronic lung disease and congenital heart disease were investigated through the recorded clinical histories. Other pre-existing diseases such as immunodeficiency and congenital anatomical abnormalities were also monitored. The social conditions of the child such as possible exposure to passive smoking, family history of atopy, number of siblings and if the patient had a twin were also accounted for.

Study Design

This is an observational, retrospective study. All clinical information of the patients was retrieved from their documented charts. Data was collected from the medical records section of the hospital.

RSV-associated admission was defined as children that where diagnosed with bronchiolitis and admitted directly to the pediatric ICU. Confirmation ofRSV infection was based on the analysis of nasopharyngeal aspirates using direct immunofluorescent technique (IMAGEN) (Oxoid, Cambridgeshire, UK).

Virology studies, white blood cell count and chest x-rays upon admission were documented. Interventions noted were oxygen supplementation, mechanical ventilation and medications used. Other outcomes considered were respiratory failure, bacterial pneumonia, sepsis and death. Length ofPICU stay and entire hospital stay were collected from the admission data of the PICU. Seasonality was based on the admission dates.

Results

Ninty-four patients diagnosed with bronchiolitis where admitted in the PICU from January 2003 to January 2009. Only 70 charts were available for clinical review. The only information available to us for the other 24 patients was their age and diagnosis. They all were under 6 months of age and all recovered except one patient who had severe combined immunodeficiency (SCID) diagnosed with bronchiolitis. The data collected for the 70 patients are summarized in Table 1.

Fifty-one males and 19 females were included in the study with 1: 2.6, male to female ratio. Sixty-two % (44 patients) were born full-term and 48% were pre-term, (less than 36 weeks); 48.5% (n= 34) were fully breast fed while 51% (n=36) were formula fed.

Several co-morbid conditions were reported at the time of RSV admission. These were prematurity (n = 26, 37%), pulmonary conditions (n=13, 18.5%), cardiac abnormalities (n= 16, 22.8%), neurological (n=4, 5.7%) and Trisomy 21 (n=3, 4.2%). There were also 4 cases which had previous admissions due to neonatal sepsis.

Nine children were results of multiple births (twins) and 77% of the patients had older siblings, with an average of 2 siblings; 38.6% reported to have positive family history of atopy or bronchial asthma.

The medical record at the emergency room was the basis for the clinical presentation data collected. Almost half of these patients presented with a history of apnea (n=27), cyanosis (n=31) and labored breathing (chest wall retraction, n= 34). Majority of these patients were previously healthy children, however, they presented with severe respiratory infection upon admission. The median oxygen saturation via arterial blood gas was 96%, blood pH was documented at 7.329 (median) and white blood cell count was 11.

All patients received supplemental oxygen, either via na-sal cannula or oxygen hood, 38.6% of those admitted were hooked to a mechanical ventilator. Majority (97.1%) of these children also received inhaled bronchodilators and antibiotics (98.5) despite the viral etiology. Corticosteroids (61.4%) and antipyretics (50%) were given to half of these patients. Four patients went into respiratory arrest, warranting cardio-pulmonary resuscitation while in thePICU.
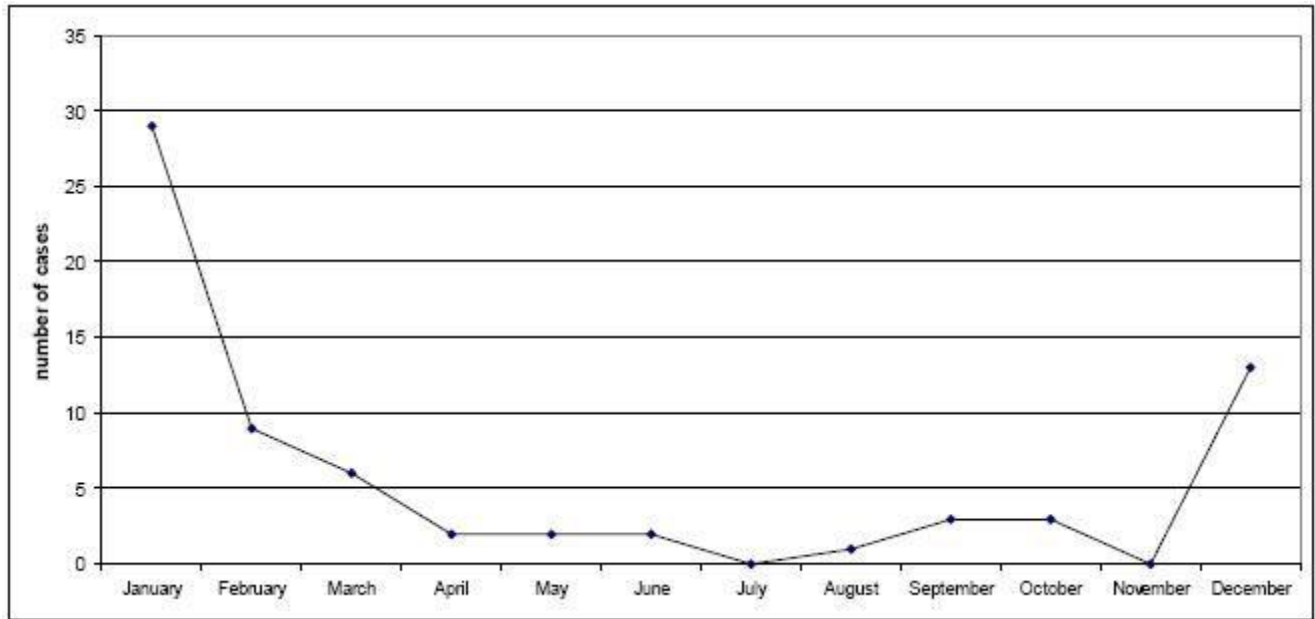
Respiratory failure was reported in 26 patients (37%). Twenty-five children also had concomitant bacterial pneumonia, supported by lab diagnosis and chest x-ray findings. Eleven of the patients developed sepsis. Only one mortality was documented. This patient was premature and had Down's syndrome, patent ductus arteriosus, and persistent pulmonary hypertension. He eventually developed pulmonary hemorrhage, septic shock and multiple-organ failure. This infant stayed in the PICU for 25 days.

Table 1: Clinical characteristics of patients

Variable	Gender	Percentage	Number of cases (n=70)	Median
	Male	72.8	51	
	Female	27.1	19	
Age (months)	median			2
Gestational Age	Term	62.8	44	
	Pre-term	37.1	26	
Infant Nutrition	Breast-fed	48.5	34	
	Not Breast-fed	51.4	36	
Pre-existing Co-Morbidities				
Prematurity		37.1	26	
Pulmonary	BPD/HMD	14.2	10	
	Bronchial asthma	4.2	3	
Cardio-vascular	PDA	12.85	9	
	ASD/VSD	5.7	4	
	PFO	2.85	2	
	Coarctation of the aorta	1.4	1	

		%	n	
Neurological		5.7	4	
previous history of neonatal sepsis		5.7	4	
Trisomy 21		4.2	3	
Social Factors				
	Twin/Multiple Birth	12.85	9	
	with older siblings	77	54	
	(+)family history of atopy	38.6	27	
Clinical Presentation				
	Cyanosis	44.2	31	
	Apnea	38.5	27	
	chest wall retractions	48.5	34	
	oxygen saturation			96
	blood pH			7.329
	white blood cell count			11
Intervention	Oxygen therapy	100	70	
	mechanical ventilation	38.6	27	
	Bronchodilators	97.1	68	
	Antibiotics	98.5	69	
	Corticosteroids	61.4	43	
	CPR	5.7	4	
Complications	respiratory failure	37	26	
	bacterial pneumonia	36	25	
	Sepsis	15.7	11	
	Death	1.4	1	
Length of Hospital Stay				11
Length of PICU Stay				3

Figure 1: Seasonality of RSV infection.

Seasonality

From a span of five years, the earliest RSV cases ap-peared in October and the last cases were documented as late as April. Peak RSV admissions were from December to February. In the year 2004, there were noted sporadic RSV cases in the summer months, (May-June). December 2006 and January 2007 had the most number of cases (n=18), this appears to be a severe RSV outbreak (Figure 1).

Discussion

RSV is the major cause of severe respiratory tract infections for children under the age of 5 [1.3-9]. It has been previously noted that 79% of hospital admissions due to acute respiratory infections among Saudi children are caused by RSV infection [3]. These infections outcomes could be as simple as common cold or at its worst, causing significant morbidity and mortality. We report here, for the first time, the trend, outcome and seasonality of RSVbronchioitis among ICU admission in Saudi children.

This five-year survey of PICU admission due to RSV infections observed an increased susceptibility of infants less than one year of age. This is in consistent with a previous study on Saudi children which found a significant association between bronchiolitis and lower age groups (0-6 months) [3]. The median age of the study group was 2 months old. Our results are also similar to those from other countries and emphasize the role of RSV as the major cause of bronchiolitis especially in infants less than 6 months of age [14-16].

Pre-morbid conditions have been associated with increased severity of RSV infection [17-19]. Thirty-seven percents of the infants admitted to the PICUwere found to be of premature birth. Similarly, a Canadian study reported that prematurity was a factor in 20% of their cases [6]. Inadequate defense against infection and incomplete development of the airway are probably the most important mechanisms, which explain prematurity as a significant risk factor for severe RSV infection [18]. The premature infant has a lower number of alveoli and anatomic barriers to gas exchange leading to increased lethality due to bronchiolitis or any other pulmonary infection [18]. Maternal IgGs are found to have a protective role against RSV infection [20]. This transfer of antibodies occur at the latter part of gestation, therefore, premature infants hold a greater risk for RSV infection. The significant number of twins in the study is also within premature infants. These children are most probably not at risk because of multiple births but due to the complication of premature birth.

Prematurity has been significantly associated with RSV severity, however, premature infants that have pulmonary complications are at higher risk [18]. In the Canadian study, 6% of the cases had chronic lung disease due to prematurity. This finding consistently leads to the conclusion that pre-existing pulmonary conditions are risk factors for increased RSV severity.

Cardio-vascular abnormalities were found in 22.8% of the patients. These abnormalities result in high pulmonary blood flows, thus making the lung tissues susceptible to damage. Therefore, such patients are also at increased risk for severe RSV infection, explaining the high incidence among thePICU patients.

Aside from prematurity, pulmonary pathology and cardio-vascular abnormalities, there was a significant number of patients with neurological conditions (5.7%), a previous history of neonatal sepsis (5.7%) and Trisomy 21 (4.2%). Trisomy 21 is presently being considered as a risk factor forRSV. Children with Trisomy 21 have an abnormal physiology of the upper respiratory tract, which makes them prone to apnea [21]. When RSV afflicts these infants, apnea is easily triggered, hence leading to a more severe bronchiolitis. Previous neonatal sepsis usually affects the premature infants making them susceptible to RSV infections. Neurological conditions have not been significantly correlated with RSV infection. This relation-ship needs further investigation.

Cigarette smoking history was poorly documented, only one family admitted to cigarette smoking exposure. 38.6 % of the families however, had significant family atopy history. Bradley et al. found that family atopy, specifically maternal atopy, correlated with RSV severity [22]. Proper information dissemination is warranted to educate these families of the higher risk their children have for severe RSV. Seventy seven percent of the patients had older siblings present in the families. One study stated that older siblings and other family members usually contact the disease at the same time the infant is afflicted [23]. They may manifest as milder form of RSV that does not require clinical attention. Crowcroft et al. found that silent transmissions outside the affected family might be the source of RSV infection [23]. Therefore, during the peak season of RSV, parents should be aware of the significant risk of RSV that may transmit to the younger members of their families especially in large and extended families as occur in the Saudi society.

Approximately 50% of the patients admitted to the PICU presented with apnea, cyanosis and hypoxia. These complications occurred among patients without any pre-existing conditions. Therefore, severe RSV is not only a risk for infants with pre-existing conditions but also for healthy babies. Further investigations are warranted among these previously healthy infants for other underlying causes. Perhaps a more detailed medical and social history could help identify these unknown risk factors.

The majority of the infants received oxygen supplementation, bronchodilators and antibiotics. Despite being viral in nature, antibiotics were administered upon admission for the majority of patients (69%). Bloomfield et al. reported that only 0.6% of RSV broncholitis patients had documented bacteremia, and the risk is increased in those who were admitted to the pediatric ICU (2.9%). In addition to patients with nosocomial RSV infection (6.5%), and pre-morbid cyanotic congenital heart disease (6.6%) [24].

Despite of the high prevalence of co-morbid risk factor in this cohort, all patients except one recovered well which indicate good outcome after pediatricICU admission. The one mortality documented in this study had Down syndrome along with cardiac anomalies and prematurity that might indicate accumulative risk of multiple co-morbidities for the most serious outcome. Another patient among those who were unable to retrieve had SCID, which is a known risk for mortality in RSV infection.

Although most of the cases admitted to ICU were in the winter season, there were few cases reported in the summer season. Geographic and climate factors appeared to play major role in RSV seasonality that could be influenced by many factors including spread of virus, behavioral factors, or cyclic immunological susceptibility. The definite reasons for such periodicity and seasonality re-main unclear [20].

Conclusion

In this study, we have confirmed that prematurity, pulmonary pathology, neurological and cardiovascular abnormalities are associated with increased severity of RSV infection. Therefore, physicians should be aware that infants with pre-existing conditions are at risk for severe RSV infection and should have low threshold for ICU admission and urgent intervention. Although RSV infection is more prevalent in the winter season, high index of suspicion is needed for typical cases beyond this season. Prospective, multi-center studies, with standard documentation are needed to be able to fully investigate the burden of RSV among Saudi children.

Acknowledgments

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