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Respiratory Syncytial Virus Infection in Young Malaysian Children

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ABSTRACT

Respiratory syncytial virus (RSV) is the most important agent causing respiratory illness in the young paediatric age group.

Objective: To determine the clinical profile and risk factors for respiratory distress in young Malaysian children with RSV infection.

Method: The study was a retrospective review of 185 children below the age of 24 months hospitalised with RSV infection. Respiratory distress at admission was categorised into mild, moderate and severe using a modified respiratory distress assessment instrument (RDAI) score.

Results: RSV infection occurred most frequently in the 3 – 6 months age group with a male predominance. A small number of patients had extrapulmonary symptoms of diarrhoea (8%) and seizures (7%). Forty-seven patients (25%) had an underlying illness. The majority of patients (63%) had mild respiratory distress. All patients (8%) with severe respiratory distress required intensive care and 80% of them required assisted ventilation. The overall mean duration of hospital stay was 7.0 ± 5.0 days. There was only one death. Risk factors associated with respiratory distress included age less than 3 months, a family history of bronchial asthma and presence of an underlying disease.

Conclusion: The majority of Malaysian children with RSV infection had a mild illness but a small number of them who developed severe illness had a higher incidence of respiratory failure requiring assisted ventilation.

Keywords: respiratory syncytial virus (RSV), respiratory distress, risk factors

INTRODUCTION

Respiratory syncytial virus is an important organism in children with lower respiratory tract infection. In urban Malaysian children diagnosed with lower respiratory tract infection namely bronchiolitis, croup and pneumonia, RSV was isolated in the nasopharyngeal secretion of between 18% – 22% of these patients[1,2]. In addition to the constellation of respiratory symptoms caused by RSV, extrapulmonary manifestations like seizures, shock and apnoea have also been extensively described in the literature[3,4]. RSV is usually a self-limiting respiratory disease with a very low mortality. Nonetheless, severe RSV disease is increasingly recognised especially in the high risk patient groups ie. premature infants, immunodeficient patients, patients with chronic lung disease and congenital heart disease[5].

The objective of this study was to determine the clinical epidemiology, clinical profile and outcome in young Malaysian children less than two years of age admitted to the Department of Paediatrics, University Hospital Kuala Lumpur, with RSV chest infection. We also studied the degree of respiratory distress on admission and identified the various clinical risk factors that could contribute to severe RSV.

MATERIAL AND METHODS

Patient population

University Hospital Kuala Lumpur (UHKL) is situated in the heart of the Klang Valley and provides clinical services to a predominantly urban population and tertiary referral services to the nation. This is a retrospective study where all patients with RSV chest infection were admitted over a three-year period between 1 January 1993 and 31 December 1995. Only patients between the ages of 0 – 24 months on admission with clinical features of lower respiratory tract infection ie. cough, tachypnoea, breathlessness, crepitations and rhonchi on auscultation, were included in the final analysis. The patients' records were then traced and reviewed individually.

RSV isolation

Nasopharyngeal secretion was collected from patients using a sterile mucus extractor with a suction apparatus leading into a specimen tube. This was packed in ice and sent to the Virology Laboratory. RSV was identified by immunofluorescence, viral culture or both. Nasopharyngeal secretions were first washed, smeared on slides and dried; after which, 12 uL of RSV screen identification monoclonal antibody was applied. After a 30 minute incubation at 37°C, the slides were then washed with phosphate buffered saline (PBS) and then fluorescein isothiacyanate (FITC) conjugated goat anti mouse serum was applied followed by incubation and examination under a fluorescence microscope at 400X magnification. For viral isolation, nasopharyngeal secretions were treated for one hour with antibiotics prior to inoculation into

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MDCK cells, Vero cells and Hep-2 cells. These cells were incubated at 33°C and checked daily for cytopathic effects as an indication of RSV isolation.

Respiratory distress assessment instrument (RDAI) score

The clinical condition of the patients upon admission was also evaluated with the use of a modified respiratory distress assessment instrument (RDAI) score[6,7] (Table I). Each patient's parameter was given a score based on the clinical status on admission and then added up, giving the RDAI score. The categories of respiratory distress were reflected by the modified RDAI score with 0 – 4 denoting mild respiratory distress and a RDAI score of 5 – 8 and 9 – 12 denoting moderate and severe respiratory distress respectively. The patients' clinical profile of the different categories were then studied to identify if the individual clinical factors conferred risk for respiratory distress.

Statistical analysis

Data gathered from the study was entered into a statistical programme SPSSWin Version 61.3. The Students t test was used to compare quantitative data and the significant differences between proportions were compared using the Chi square test. A p value of less than 0.05 was considered to be significant. Multiple logistic regression analysis with the elimination of confounding factors was used to study the various risk factors independently for association with moderate and severe respiratory distress as defined by the RDAI score. The relative risk estimate of the individual clinical factors for respiratory distress was described as an odds ratio (OR). The 95% confidence interval was then calculated as between $e^{\log OR - 1.96\ SE(\log OR)}$ and $e^{\log OR + 1.96\ SE\ (\log OR)}$.

RESULTS

Clinical profile of RSV chest infection

A total of 185 patients fulfilled the inclusion criteria and were enrolled into the final analysis. The incidence of RSV chest infection was highest in the 3 – 6 months age group, with a mean age of 8.9 ± 6.0 months and a median age of 7.5 months. Seventy-eight percent of the patients were less than 12 months old (Fig 1). There was a predominance of male patients (M:F 1.5:1). Malays made up 56% of the patients followed by an equal proportion of Chinese (19%) and Indians (21%).

Table II shows the main clinical features of the patients studied. A small number of the patients also had extrapulmonary symptoms with 13 (7%) of them having seizures and another 14 (8%) had diarrhoea. Cyanosis was seen in only 22 (12%) patients. Auscultatory findings of crepitations compared to rhonchi (66% vs 35%) predominated the clinical signs. Forty seven (25%) of them had an underlying illness (Table III).

Using the modified RDAI score, 117 (63%) patients had mild respiratory distress and 53 (29%) patients had moderate respiratory distress. All 15 (8%) patients who had severe respiratory distress were admitted to the Paediatric Intensive Care Unit (PICU), of whom 12 (80%) required assisted ventilation for respiratory failure.

The overall mean duration of hospital stay was 7.0 ± 5.0 days with a range of 2 – 30 days and a median of 5.0 days. The one death that occurred as a direct result of RSV chest infection, was a 5-month-old Indian child, who developed acute respiratory distress syndrome (ARDS) and had an underlying primary immunodeficiency.

Risk factors for respiratory distress

The mean age at admission for patients with moderate and severe respiratory distress was much younger compared to patients with only mild respiratory distress. Clinical factors that also appeared to be associated with respiratory distress included a family history of bronchial asthma and the presence of an underlying illness. The sex, ethnic distribution and whether patients were being breast-fed at the time of illness, did not influence the degree of respiratory distress (Table IV).

Using multivariate analysis in this group of patients, clinical factors that were significantly associated with respiratory distress included age of less than 3 months on admission, a family history of bronchial asthma and the presence of an underlying illness, especially prematurity less than 36 weeks (Table V). Patients with an underlying illness were also more proned to prolonged hospital stay (11.0 ± 6.7 days) though this was not observed in patients with a family history of bronchial asthma (7.3 ± 4.5 days).

Table I – Modified respiratory distress assessment instrument (RDAI) score[6,7]

Clinical Parameter	Score 0	Score 1	Score 2	Score 3
Respiratory rate	less than 40 per minute	between 40 – 60 per minute	between 60 – 70 per minute	more than 70 per minute
Use of accessory muscle	none	one accessory muscle used	two accessory muscles used	three or more accessory muscles used
Colour/Cyanosis	Pink in room air/no cyanosis	Cyanosed when crying	Pink with oxygen supplement or cyanosed in room air	Cyanosed with oxygen or cardiorespiratory arrest
Auscultation finding	normal	Decreased air entry No rhonchi	Decreased air entry Rhonchi heard	Silent chest

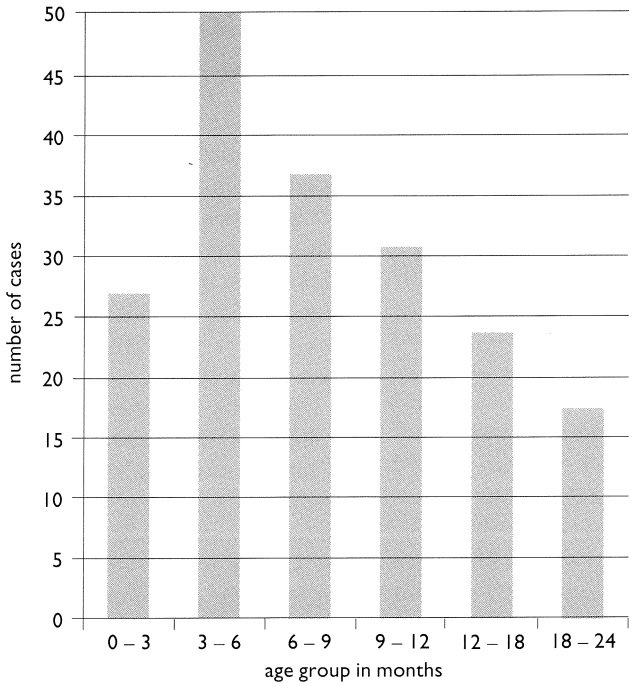

Fig 1 – Number of RSV chest infection cases for different age groups (n = 185).

Table II – Frequency distribution of clinical features in Malaysian children with RSV chest infection

Clinical features	Number of patients	Frequency (%)
Clinical symptoms		
Fever	150	82
Cough	175	93
Coryza	169	91
Breathlessness	129	70
Poor feeding	133	72
Diarrhoea	13	7
Seizure	14	8
Family history of bronchial asthma	57	30
Clinical signs		
Cyanosis	22	12
Tachypnoea*	155	84
Chest recession	126	66
Crepitations on auscultation	123	63
Rhonchi on auscultation	64	35

* Tachypnoea is defined as a respiratory rate more than 50 per minute between the ages of 1 – 12 months and a respiratory rate of more than 40 per minute between the ages of 12 – 24 months.

Table III – Frequency of underlying illness in Malaysian children with RSV chest infection (n = 47)

Underlying illness	Number of patients	Frequency (%)
Prematurity (less than 36 weeks gestation)	19	40
Congenital heart disease	10	21
Chronic lung disease	3	6
Immunodeficiency	2	4
Others: Cerebral palsy, infantile spasm, spinal muscular atrophy, aplastic anaemia, Russel silver syndrome	13	29

DISCUSSION

The clinical scenario in Malaysia is no different from that in most countries where respiratory diseases remain one of the most common causes of morbidity in the young paediatric patient. Clinicians generally recognise the importance of RSV infection in the local population but local published data on this illness is generally confined to a small number of epidemiological surveys[1,2,8].

The majority of our patients were less than 1 year of age, indicating that RSV is most commonly associated with respiratory illness in infancy. There was a preponderance of male patients which is comparable to previously published data[9]. The ethnic distribution of our patients is a reflection of the ethnic groups that sought treatment and hospital care in UHKL. Interestingly, 4% of them were Indonesians and they represent an increasing number of foreigners who now reside in the urban areas in Malaysia.

Cough followed by coryza, fever, poor feeding and breathlessness were the more common symptoms in Malaysian children with RSV chest infection. A small number of our patients had extrapulmonary manifestations which included seizures and diarrhoea. It is now recognised that the pathology of RSV infection is no longer confined to the respiratory system and an increasing number of extrapulmonary system involvement is being reported. Seizures seen in this study could be a reflection of the incidence of febrile seizure and neurological manifestation of RSV infection is well documented among Malaysian children. RSV has been isolated in the cerebrospinal fluid of children with meningitis and encephalitis[10,11]. The neurotropic effect of RSV has also been demonstrated in animal studies[12]. Diarrhoea on the other hand, has not been extensively described in the literature. Unfortunately, there were no attempts made to identify or isolate RSV in our patients' stools and only 5 patients had their stools sent for viral studies as the diarrhoea appeared to be transient. Other extrapulmonary manifestations of RSV infection described in the literature included myocarditis, heart block, exanthem and hypothermia[3,13,14].

RSV caused a mild self-limiting disease as two-thirds of our patients had only mild respiratory distress on admission. Eight percent of our patients required intensive care and the majority of them needed assisted ventilation for respiratory failure. A previous local study showed a slightly higher incidence of PICU requirement of 12%, and more than two-thirds of them required assisted ventilation[15]. This observation is in sharp contrast with children in more developed nations, where severe RSV infection requiring PICU care occurred in about 15% of cases and 40% – 50% of them required assisted ventilation[16,17]. The incidence of an underlying illness or risk factor for severe RSV infection in our population of 25% is comparable to the studies mentioned[16]. This observation suggests that although only a smaller number of our patients developed severe RSV infection, however they also developed respiratory failure and required ventilatory support. This finding may be possibly explained by the shortage of PICU

Table IV – Patient clinical parameters and categories of respiratory distress in chldren with RSV infection

Clinical parameter	Respiratory distress			p value
	Mild	Moderate	Severe	
Mean age (months)	10.5 ± 6.3	6.3 ± 4.4	5.3 ± 3.7	0.001
Age less than 6 weeks	4%	9%	27%	0.001
Age less than 3 months	10%	28%	40%	0.009
M : F ratio	1.54	1.52	1.1	ns
Ethnic group M : C : I*	2.9 : 1 : 1.1	5.1 : 2 : 1	2.5 : 1 : 1	ns
Breastfeeding	24%	25%	47%	ns
Family history of bronchial asthma	23%	43%	40%	0.03
TWBC on admission (10^9/L)	13.3	12.4	12.0	ns
Presence of underlying illness	11%	40%	87%	0.0001

M : C : I = Malay : Chinese : Indian
* Indonesians excluded
ns – not significant

Table V – Multiple logistic regression analysis of independent risk factors associated with respiratory distress in 185 patients

Independent variable	n	OR	95% CI	p value
Age less than 3 months	32	4.5	1.2 – 17.6	0.001
Family history of asthma	57	4.0	1.4 – 9.1	0.003
Underlying illness	47	6.6	1.5 – 29.1	0.0001
Prematurity [gestation < 36 weeks]	19	5.1	1.0 – 25.0	0.02

OR = odds ratio
CI = confidence interval

beds and facilities in our unit. Patients with severe RSV-infection might have been nursed in the non-intensive care areas and then only transferred to the PICU when their respiratory status deteriorated, at which time, they would have required intubation and assisted mechanical ventilation for respiratory failure. However, the mortality rate of RSV infection in Malaysian children remains low and is no different from other populations.

A younger age, especially patients less than 3 months old, a history of prematurity of less than 36 weeks, a family history of bronchial asthma and the presence of an underlying illness, appeared to be associated with respiratory distress in Malaysian children admitted with RSV infection. The majority of patients who required PICU care had at least one of the risk factors described. It has been well recognised that severe RSV infection requiring PICU care occurs in about 30% of patients with an underlying illness as compared to only 7% in patients who were previously healthy[16]. These patients tended to have a longer hospital stay, PICU stay and a longer need for oxygen supplementation[18].

Breastfeeding did not appear to protect these children from respiratory distress although various reports have suggested a protective role of breastfeeding against severe RSV disease[19]. Interestingly in our patients, those with a family history of bronchial asthma appeared to have increased risk for respiratory distress but did not have a longer duration of hospital stay. It would appear that the respiratory distress in this group of children with a risk of atopy resolved more rapidly. Reversible inflammatory changes of the airways could have contributed significantly to the initial respiratory distress in this group of patients.

This clinical overview of RSV infection provides an insight into the clinical variability or lack of it in Malaysian children, as compared to that reported in the literature. This study is however, retrospective in nature and the various clinical data collected was a review of observations made by different clinicians with different levels of training and experience. Overall, the majority of Malaysian children with RSV chest infection had a mild illness but a smaller proportion of them who developed severe illness appeared to have a higher incidence of respiratory failure that required intubation and ventilatory support. The risk factors identified in this study which predisposed children with RSV infection to respiratory distress may serve as a guide to clinicians in recognising categories of patients who require general or intensive care admission. With improvement in medical care in Malaysia and the increasing number of survivors with an underlying chronic illness, severe RSV disease may perhaps be more commonly encountered in the future.

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