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Human Respiratory Syncytial Virus and Hospitalization of Young Children with Lower Respiratory Tract Infection in Marrakech, Morocco

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Abstract Although respiratory syncytial virus (RSV) infection is one of the leading causes of Acute Lower Respiratory Tract Infections (ALRTI) and death in young children worldwide, little is known about the burden of this pathogen in Morroco. Our Objectives is to determine the prevalence of RSV infection in children hospitalized with ALRTI. From January to Decembre 2018, nasopharyngeal swabs were collected from 217 children, not older than 24 months of age, and positively tested for RSV using a real-time PCR multiplex assay. From 217 of collected specimens, 49 were tested positively for RSV infection. Eighty four percent of collected samples were collected from children having an age under 6 months; female children were predominant (55.10%), median age was 3.6 months. Higher positivity rate was observed in February that typically features the coldest temperatures of the year (24 cases). In 21 cases RSV was co-detected with at least one of the others virus. Respiratory distress, pneumonia and bronchiolitis were the most common diagnoses of al hospital admissions. Our data demonstrated that RSV remains important viral etiological agent causing severe acute respiratory infections on infant in Marrakech.

Keywords: *acute lower respiratory infections, children, infants, human respiratory syncytial virus,hospitalization*

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1. Introduction

Acute lower respiratory infection (ALRI) remains one of the leading causes of hospitalization, morbidity and mortality in infants and children worldwide [1]. The etiology of ALRIs is diverse and complicated [2]. Viruses play an important role , especially in infants younger than 2 years [3]. A recent study conducted in the US found that respiratory viruses were much more common in children hospitalized with pneumonia than bacteria with at least one virus detected in 65% of enrolled children [4].

In early childhood, respiratory syncytial virus (RSV) is the main etiologic agent of infections of the lower respiratory tract and is related to several clinical pictures such as bronchiolitis, pneumonia, ashmatic bronchitis, and cause death [5]. A meta-analysis by shi and colleagues were estimated that globally in 2015 [6], 33·1 million episodes of RSV-ALRTI, resulted in about 3·2 million hospital admissions, and 59600 in-hospital deaths in children younger than 5 years. In children younger than 6 months, 1·4 million hospital admissions, and 27 300 in-hospital deaths were due to RSV-ALRI. About 45% of hospital admissions and in- hospital deaths due to RSV-ALRTI occur in children younger than 6 months [6].

In Morocco, a middle-income country in north Africa, to date, there is no surveillance system to monitor and assess RSV incidence in pediatric populations. This study was conducted to investigate the epidemiological and clinical features of RSV among children aged under 2 years admitted with ALTRI to CHU Mohammed IV Pole Mere Enfant from January to Decembre 2018.

2. Materials and Methods

2.1. Study Design and Patient Population

This prospective study was conducted from January to Decembre 2018 at the Hospital Arrazi , CHU Mohammed VI in Marrakech, Morocco.

Children aged less than 2 years admitted to Arrazi hospital with respiratory symptomatology suggesting lower respiratory tract infection (such as cough, rhinorrhea, pharyngalgia, expectoration, nose/throat congestion, shortness of breath, abnormal breathing sounds or dyspnea) were enrolled and tested for RSV using à multiplex PCR assay.

Chest radiography was performed for all patients.

The patient's clinical presentations or diagnoses were recorded from patient's medical records by attending physicians.

2.2. Specimen Collection

Nasopharyngeal aspirates were collected and combined in transport medium from all the enrolled children by qualified medical personnel following standard operating procedures. The specimens were immediately transferred to the Clinical Laboratory of the Arrazi's Hospital for respiratory pathogen detection.

2.3. Specimen Detection

Each specimen was tested for viruses and atypical bacteria with FilmArray Respiratory Panel (FA-RP) according to the manufacturer's instructions. The FA-RP is an FDA certified multiplex PCR that can detect 17 viruses: (respiratory syncytial virus (RSV); para-influenza virus types 1–4 (PIV1–4); influenza A and B viruses (InfA(H1,H1-2009,H3), InfB); adenovirus (ADV); human Metapneumovirus (hMP); human coronaviruses (HCoV-229E, HCoV-OC43, HCoV-NL63 and HCoV-HKU1); human rhinovirus/Enterovirus (HRV/ETV); human bocavirus (HBoV)) and 3 atypical bacteria (*Mycoplasma pneumoniae* (MP); and *Chlamydophila pneumoniae* (CP), *Bordetella pertussis* (BP)) responsible for respiratory tract infections.

2.4. Statistical Analysis

Descriptive statistics were presented as frequency (percentage) or median and IQR where appropriate. Data were analyzed using Microsoft Excel 2013 and STATA version 10.0.

2.5. Ethical Considerations

Since the analysis used only de-identified and aggregated hospitalization and laboratory data, this study was considered to be exempt from human subjects' ethics review.

3. Results

3.1. Study Population and Age Distribution of Patients Who Have Positive RSV

From 217 paediatric patients hospitalized with ALTRI. 49 patients (22.58%) were positive for RSV. The female to male ratio was 1.22 (27/22) in patients who are RSV positive. The patient ages ranged from 0 to 2 years, with a median age of 3.6 months (range 0.07-24 months); 83.67% patients were under 6 months of age (~6 mo), 10.20% patients were 6–12 months of age (~12 mo), 6.12% patients were 1–2 years of age (~2 yr) (Table 1).

Table 1. Distribution of RSV among age group

Age groups	< 6 months, n=41	6months-1years, n=5	1-2years, n=3	All ages, n=49
	No.(%)	No.(%)	No.(%)	No.
positive	41 (83.67)[a]	5(10.20)[a]	3(6.12)[a]	49
single	24 (58.53)[b]	3(60)[b]	1(33.33)[b]	28
mixed	17 (41.46)[b]	2(40)[b]	2(66.66)[b]	21

[a]Case number and percentage among all positive cases.
[b]Case number and percentage by age groupe.

Table 2. Prevalence of respiratory pathogens in 217 children with ALRTI

Virus	No (217)	%
HRV only	56 (35< 6months)	25.80 (62.50 <6months)
RSV only	49 (24< 6months)	22.58 (51.02 <6months)
ADV only	2	0.92
HEV	1	0.46
Influenza virus (A/B) only	1	0.46
Parainfluenza (1-4) only	8	3.68
hMP only	10	4.60
Coronavirus only	2	0.92
Atypical bacteria	No	%
MP only	2	0.92
CP only	1	0.46
BP only	7	3.22
Copathogenes	N	%
virus –virus	120	55.29
virus -bacteria	12	5.52

There was a significant difference in RSV prevalence between patients < 6 months (41/49) and those > 6 months (8/49). A total of 11 children (28%) required intensive care included two neonates. In addition, no pathogens were identified in 36 patients (16.58%), while respiratory viruses other than RSV were found in 122 (56.22%) of children. Among the respiratory virus other than RSV, the most identified virus was Rhinovirus (25.80%) followed by hMP (4.60%) and PIV 1-4(3.68%) (Table 2).

3.2. Seasonal Outbreaks of VRS

Seasonal distributions of RSV were estimated by admission dates for the included children. RSV had a high prevalence during the cold season in Winter, the epidemic peak of RSV seasonal infection for our population was occured in February (Figure 1).

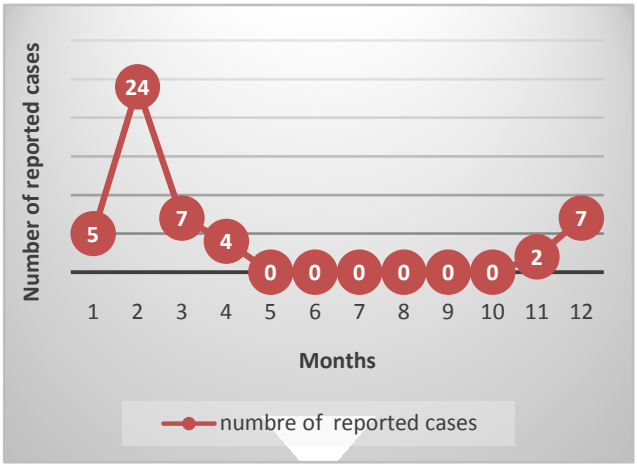

Figure 1. Seasonal distribution of VRS from January to Decembre 2018

3.3. Codetection with Common Respiratory Pathogens in Patients Who Are RSV Positive

RSV was detected in 28 (57.14%) specimens as a single pathogen, viral co-detection were common. there were 21 specimens in which 2 or more pathogens were detected, representing 42.85 % of the specimens. Of these co-detection, the RSV-HRV coinfection was the most frequent with 14 samples (accounting for 66.66% of all coinfection samples). A 4 samples showed infection with 3 pathogens, in 3 samples were RSV-HRV-ADV (Table 1, Table 3). RSV-atypical bacterial coinfection were not found in our study.

Table 3. Distribution of copathogens in patients who are RSV positive

Copathogens virus – virus	Numbre of patients (21)
2 pathogens:	17
RSV+HRV	14
RSV+ADV	1
RSV+hMPV	1
VRS+Influenza 3	1
3 pathogens :	4
RSV+HRV +ADV	3
RSV+hMPV+PIV3	1

3.4. RSV and Clinical Characteristics

We analysed the clinical presentation of 49 patients who have positive RSV. The main clinical features in this patients included dyspnea (83.67%), acute distress respiratory (34.69%), pneumonia (40.81%) bronchiolitis (26.53%), fever (20.40%), cough (20.40%) and cyanosis (14.28%) (Table 4). Of 49 children with RSV positive 09 infants was admitted to an intensive peadiatric care unit and 02 newborn admitted to an intensive neonate care.

Table 4. Clinical characteristics in infants younger than 2 years with RSV infection who are RSV positive

Symptoms/diagnosis	Patients with RSV, n=49
Dyspnea	41
Acute respiratory distress	17
Fever	10
Cough	10
Runny nose	01
Cyanosis	07
Sepsis	02
Wheezing	4
Pneumonia*	20
Bronchiolitis	13
Atelectasis *	01
Acute respiratory failure	09

*by chest radiograph.

4. Discussion

To the best of our knowledge, this is the first paper investigating the role of RSV in children under 2 years old hospitalized with LRTIs in Marrakech and the one of rare study about RSV in Morocco. In this study, RSV was detected in 22.58% of children with ALRTIs admitted to Hospital Arrazi from January to Decembre 2018, this provide that RSV is a one of a major respiratory pathogen, after HRV, in children under 2 years old hospitalized with ALRTIs, especially children younger than 6 months (83.67%). This results are in concordance with rares previous studies conducted in Morocco that reported the same prevalence [7,8]. Several studies proved that the prevalence of this pathogen decreased with age owing to the maturation of the immune system [9]. The frequency of RSV in female children was higher when compared to one recorded on male, and that is not consistent with findings from previous studies [10]. The seasonal climate is an important factor that can affect pathogen transmission. Wet and cold weather are factors of risk for RSV infection. Therefore, in temperate climates (Morocco's climate), RSV activity peaks in cold winter months especially in February (24 cases /49), However, in tropical and subtropical areas, RSV infection primarily increases in the summer months [11]. Viral-atypical bacterial co-infection were not found in our study. However, in this target population, mixed respiratory virus had a proportion of 45% (of all cases) with RSV/HRV was the most frequent combinations. It has been suggested that multiplex PCR techniques demonstrate high detection rate of viral co-infections [12].

Clinical presentations of respiratory infections may be overlapping and could not discriminate between

respiratory viruses. However, identified RSV in infants tended to have more severe symptoms, particularly those in the 0-6 months of age group [13]. Worldwide, RSV pneumonia is the second cause of postnatal infant death after malaria, causing 137,000 deaths each year (equal to 6.7% of all newborn deaths) [14]. In our population, 40.81% of peadiatric patients had a pneumonia, 34.69% had acute respiratory distress and 26.53% had bronchiolitis. In addition, the RSV-positive children in our study were more likely to require oxygen therapy (8/49), or intensive care (11/49) suggesting that these children have severe LRTI disease. Paediatric intensive care was available to all infants in University Hospital Center. In a cross-sectional study of healthy-community-based infant age < 1 year without acute respiratory illness or comorbidities, RSV was rare (<2%) in nasal swabs [15] that suggested that RSV is a real pathogen in children and cause severe respiratory infections .

Knowledge of the epidemiology of RSV has an important impact. The World Health Organization has been concerned with the burden of RSV and has initiated RSV surveillance using the Global Influenza Surveillance and Response System platform [16]. Such actions in our country are important in obtaining baseline information for evaluating future vaccination programs, and understanding global trends and distributions of RSV.

5. Conclusion

Our data demonstrated that RSV remains an important viral etiological agent causing severe acute respiratory infections among infants in Marrakech. Further surveillance, is required to understand better the risk factors of RSV infection and are critical to successfully implement prevention, control, and treatment strategies in this area.

List of Abbreviations

ALRTI: Acute Lower Respiratory Tract Infections
RSV: Respiratory Syncytial virus
PCR: Polymerase Chain Reaction
FA-RP: Film Array Respiratory Panel
PIV-1-4: Para-influenza Virus types 1-4
Inf A: Influenza A Virus
ADV: Adenovirus
hMP: human Metapneumovirus
HCoV-: human Coronavirus
HRV: human Rhinovirus
HBoV: human BocaVirus
MP: Mycoplasma pneumonia
CP: Chlamydia pneumonia
BP: Bordetella pertussis

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