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A comparison of human metapneumovirus and respiratory syncytial virus WHO-defined severe pneumonia in Moroccan children

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SUMMARY

Acute respiratory infections remain the principal cause of morbidity and mortality in Moroccan children. Besides bacterial infections, respiratory syncytial virus (RSV) and human metapneumovirus (hMPV) are prominent among other viruses due to their high prevalence and association with severe clinical episodes. We aimed to describe and compare RSV- and hMPV-associated cases of WHO-defined severe pneumonia in a paediatric population admitted to Morocco's reference hospital. Children aged 2–59 months admitted to the Hôpital d'Enfants de Rabat, Morocco meeting WHO-defined severe pneumonia criteria were recruited during 14 months and thoroughly investigated to ascertain a definitive diagnosis. Viral prevalence of RSV, hMPV and other viruses causing respiratory symptoms was investigated in nasopharyngeal aspirate samples through the use of molecular methods. Of the 683 children recruited and included in the final analysis, 61/683 (8·9%) and 124/683 (18·2%) were infected with hMPV and RSV, respectively. Besides a borderline significant tendency for higher age in hMPV cases, patients infected with either of the viruses behaved similarly in terms of demographics, patient history, past morbidity and comorbidity, vaccination history, socioeconomic background and family environment. Clinical presentation on arrival was also similar for both viruses, but hMPV cases were associated with more severity than RSV cases, had a higher risk of intensive care need, and received antibiotic treatment more frequently. RSV and hMPV are common and potentially life-threatening causes of WHO-defined pneumonia in Moroccan children. Both viruses show indistinctive clinical symptomatology, but in Moroccan children, hMPV was associated with a more severe evolution.

Key words: Human metapneumovirus, respiratory syncytial virus, pneumonia, Morocco, children.

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INTRODUCTION

Acute respiratory infections (ARI) remain the leading cause of disease and death in young children in

low- and middle-income countries, accounting for almost 1·4 million annual deaths, i.e. almost a fifth of all deaths in children aged <5 years worldwide [1]. Over 90% of these pneumonia-associated deaths in young children occur in developing countries [2] and are mainly secondary to bacterial infection [3]. However, the increasing availability of molecular diagnostic techniques, confirming the presence of respiratory viruses in at least 50–60% of pneumonia episodes requiring hospitalization [4, 5], is progressively exposing the significance and burden of these pathogens as a global health threat. Commonly diagnosed respiratory viruses in the developing world include, among others, respiratory syncytial virus (RSV), rhinovirus (RV), human metapneumovirus (hMPV), human bocavirus, influenza and parainfluenza viruses and adenovirus [6, 7]. RSV and hMPV are prominent among viruses due to their high prevalence and association with severe clinical episodes. Indeed, RSV is believed to cause an estimated 3·4 million annual hospital admissions, and between 66 000 and 199 000 deaths, accounting for at least one in every five ARI episodes in children aged <5 years [8]. The burden and consequences of paediatric hMPV infections are much more poorly known, probably on account of its more recent characterization dating back to 2001 [9], but many reports have clearly documented its high burden, pathogenicity, and comparability to RSV in terms of associated severe outcomes [10–16].

In this respect, there is a paucity of data available regarding the role of these two viruses in causing ARIs in the Kingdom of Morocco, a middle-income country in North-western Africa. We hereby aim to describe and compare the roles and characteristics of RSV and hMPV in causing WHO-defined severe pneumonia in children aged 2–59 months admitted to a tertiary referral Moroccan paediatric hospital [17].

MATERIALS AND METHODS

Study setting and procedures for recruited children

This prospective study was conducted from November 2010 to December 2011 at the Hôpital d'Enfants de Rabat (HER), in Morocco's capital. Children aged 2–59 months admitted to HER with respiratory symptomatology were identified and approached for recruitment if they fulfilled the WHO definition of clinical severe pneumonia (CSP) [18, 19], i.e. history of cough or reported breathing difficulty and increased respiratory rate adjusted according to age [19], together with chest indrawing. Children were excluded if the principal reason for hospital admission was a non-respiratory illness or a condition not caused by respiratory illness, or in the event of evidence of a foreign body in the respiratory tract. After parents had signed an informed consent, recruited children underwent standardized procedures upon admission, including pulse oximetry (Bionics Palm Care®, Seoul, South Korea), an antero-posterior chest X-ray, nasal and pharyngeal swabs for diagnosis of bacterial infection/carriage, and a nasopharyngeal aspirate (NPA) for diagnosis of respiratory viruses by molecular techniques. A minimum of 2 ml venous blood was also collected for blood culture, full blood cell count and biochemistry, including C-reactive protein (CRP), and procalcitonin (PCT).

Definitions and clinical groups

All children fulfilled the WHO CSP definition upon admission. However, upon discharge, a study clinician was responsible for reviewing the patient's chart, laboratory and chest X-ray results, and providing a final diagnosis. Discharge diagnoses were coded using ICD-10 [20]. All cases were categorized upon discharge in one of five self-exclusive clinical syndrome groups which included 'pneumonia', 'bronchiolitis', 'bronchitis/asthma', 'laryngotracheitis (croup)' and 'all other diagnoses'. No patient could therefore be classified in more than one group. Hypoxaemia implied an oxygen saturation (SaO_2)<90%. Fever was defined as an axillary temperature of $\geqslant$37·5 °C. Nutritional status was based on weight-for-age Z scores (WAZ), calculated using the least mean square method and the 2000 CDC growth chart [21]. Invasive bacterial disease implied the isolation of $\geqslant$1 non-contaminant bacteria in blood or pleural fluid. The Respiratory Index of Severity in Children (RISC) score, a simple and validated clinical score predicting the probability of death in children with lower respiratory tract infections (LRTIs), based on parameters such as oxygen saturation, respiratory signs such as indrawing, or wheezing, and nutritional status [22] was utilized to rank severity in study children. Case-fatality rates (CFRs) were calculated for the different diagnoses as the number of patients who died with that diagnosis divided by the total number of patients with known outcome admitted with that diagnosis. These CFRs represent in-hospital mortality. Cases evaluated at the emergency department but not resulting in hospitalization were excluded.

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Laboratory methods

The full laboratory methods of the general study from which this analysis has been performed have been detailed elsewhere [17]. Briefly, blood samples were cultured using an automated blood culture system (BD Bactec®, BD, USA), and bacterial isolates identified by Phoenix Automated Microbiology System (PHX system, BD) or colony morphology and biochemical tests. The presence of *Streptococcus pneumoniae* in NAs and in blood samples was investigated by real-time PCR according to a published home-made assay [23].

Detection of DNA/RNA of hMPV, RSV (A and B), and other viral pathogens [influenza (A and B), parainfluenza virus (1–4), RV, adenovirus, enterovirus and coronavirus (229E, NL63 and OC43)] in NPAs was systematically investigated for all recruited patients by means of the TrueScience® RespiFinder Pathogen Identification Panel (Applied Biosystems, USA), a multiplex PCR-based automated system. This methodology has previously been used in similar populations (children with respiratory symptoms) yielding high positivity rates and virus signatures in around 90% of cases [24, 25]. Careful was taken when processing samples to avoid cross-contamination. Every PCR run included positive and negative controls (as provided in each kit by the manufacturers) to guarantee the reliability of results. In addition, a NPA aliquot from 163 of the patients that tested positive for human RV (the most commonly detected virus in the study population) were shipped to the School of Paediatrics and Child Health (University of Western Australia) in Perth, for quality control, and human RV was successfully genotyped in 157 (96·3%) of those cases. Results of viral molecular testing were not made available to clinicians in charge of the study patients, who decided their clinical management on a case-to-case basis, and according to their clinical judgement.

HIV testing was only performed in patients with clinical signs/symptoms suggestive of immunosuppression, as prevalence of HIV infection in Moroccan children is thought to be <0·5% [26].

X-ray interpretation

Chest X-rays were independently interpreted by two paediatricians following a WHO-designed X-ray interpretation protocol [27]. Discordant results were resolved through a third reading. Evidence of consolidation and/or pleural effusion was defined as 'endpoint pneumonia'. Other radiological endpoints included interstitial infiltrates or normal radiographs.

Data management and statistical analysis

All study questionnaires were double-entered into a study database using a program written in Filemaker Pro 12 (Filemaker Inc., USA). Statistical analyses were performed with Stata v. 11 (Stata Corp., USA). Study variables were counted and summarized in frequency tables. Qualitative variables were compared using χ^2 test or Fisher's exact test. Means of normally distributed variables were compared using the Student's t test (binary) or ANOVA (more than two categories). For non-normally distributed variables, medians and interquartile ranges are presented, and the Wilcoxon rank sum or other non-parametric tests were used to assess differences. P values <0·05 were considered statistically significant.

Ethics

The protocol and informed consent documents were approved by the Ethics Committee of the Hospital Clinic (Barcelona, Spain), and by the Comité d'Éthique de la Recherche Biomédicale (Départ no. 1252, 16 Déc 2009) of the Faculty of Medicine in Rabat.

RESULTS

Of the 3202 children aged 2–59 months with respiratory symptoms seen at HER during the 14-month study period, only 1334 (42%) were hospitalized, of these 683 (51%) who fulfilled WHO CSP criteria and the rest of the inclusion criteria were included in the final analysis. Nasopharyngeal carriage of at least one respiratory virus in the nasopharynx was almost universal (628/683, 91·9%). Mixed (double, triple, quadruple or even quintuple) infections occurred in 40% of the hospitalized patients. RV was the most commonly detected virus (360 cases, 52·7%), followed by RSV (124 cases, 18·2%) and Adenoavirus (17%), and 61 (8·9%) of inpatients had a hMPV infection. Of RSV-positive infections, 68 (54·8%) were single RSV-A infections, nine (7·3%) single RSV-B infections, and the remaining 47 (37·9%) mixed RSV-A/RSV-B infections. A single case in this series presented with a mixed hMPV-RSV infection, and was excluded from the analysis (Fig. 1). This case occurred in an

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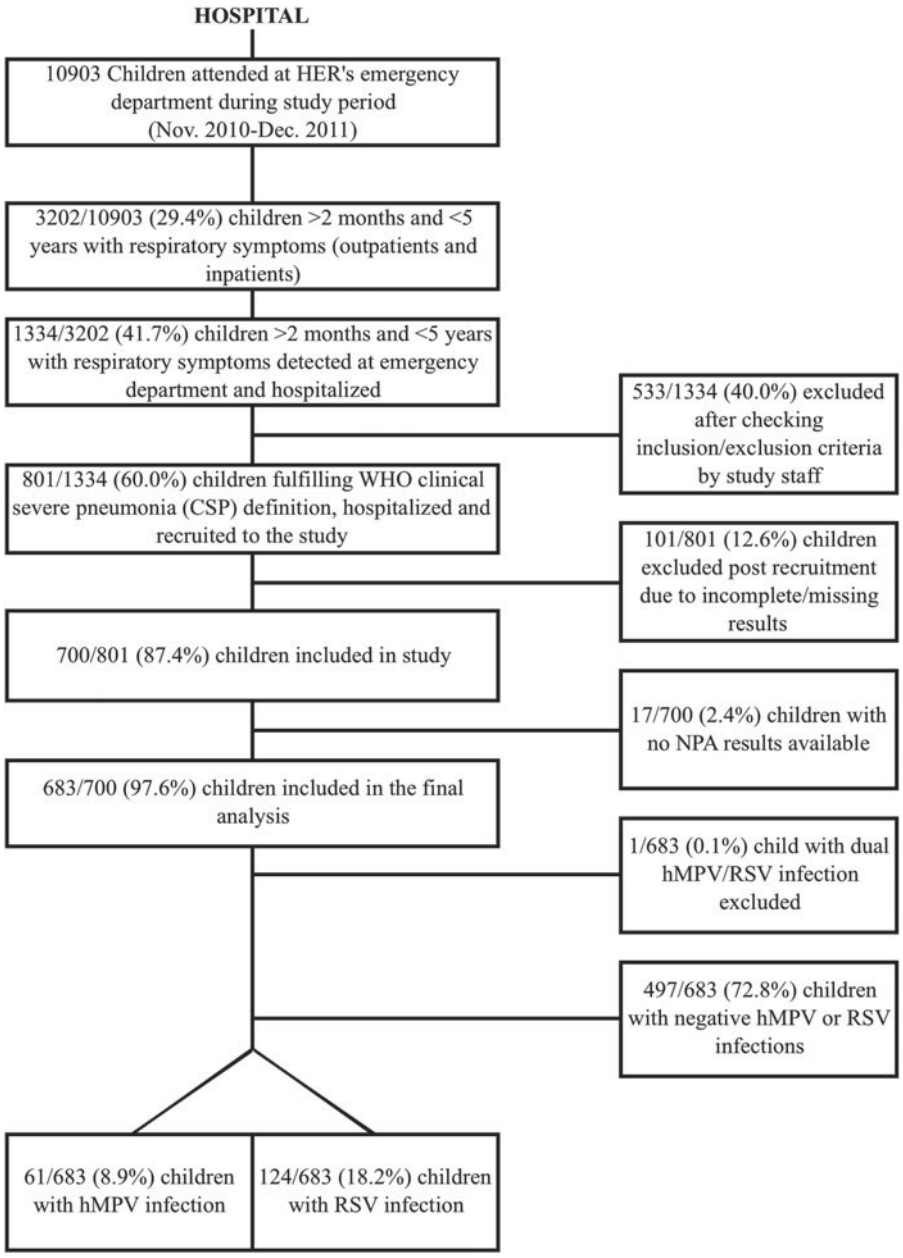

Fig. 1. Study flowchart. HER, Hôpital d'Enfants de Rabat; hMPV, human metapneumovirus; NPA, nasopharyngeal aspirate; RSV, respiratory syncytial virus.

11-month-old male child, who was hospitalized for 4 days, did not require intensive care, and received antibiotics on account of a high white blood cell count, high CRP and PCT values, and a chest X-ray compatible with lobar consolidation.

Seasonality

RSV cases presented a very clear seasonal pattern, with over 98% cases occurring between November and April (coinciding with the coldest and least humid months), while hMPV cases were predominantly detected in two peaks, one occurring during the spring months (March–June) and the other from October to December (but only in the second year) (Fig. 2).

Baseline demographics and health history

The baseline socio-demographic and health history factors for each of the two viral groups (RSV *vs.* hMPV) are shown in Table 1. Of note, hMPV cases

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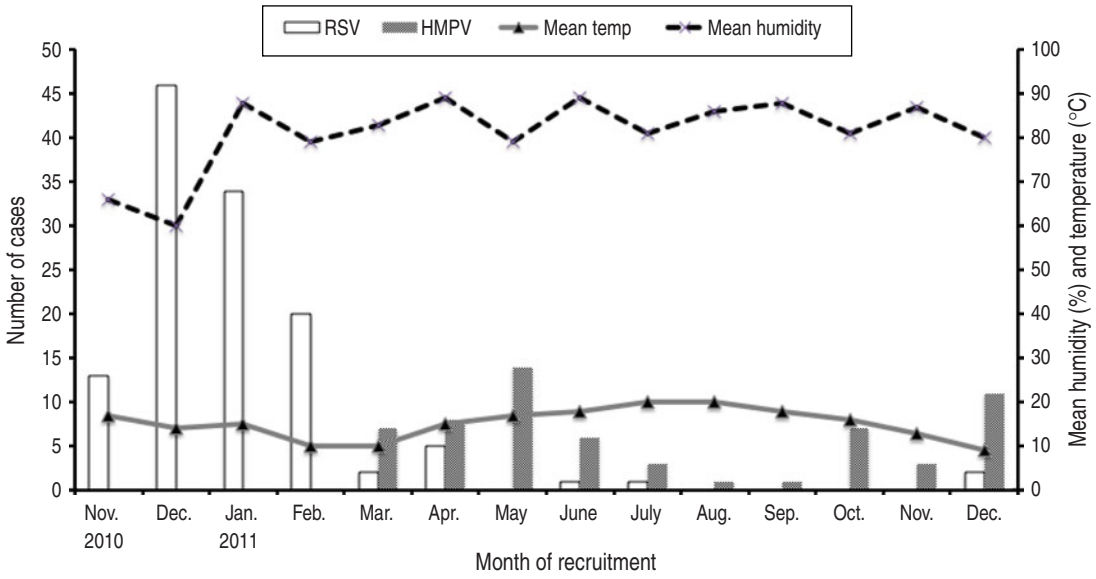

Fig. 2. Number of cases of respiratory syncytial virus (RSV) and human metapneumovirus (hMPV) according to month of recruitment, in relation to humidity and temperature.

were on average older (median age 15 months *vs.* 10 months), although differences did not reach statistical significance ($P = 0{\cdot}072$). Cases of both viruses were otherwise very similar in terms of demographics, patient history, past morbidity and comorbidity, vaccination history, socioeconomic background and family environment.

Clinical history, anthropometrics and physical examination findings

Both viral infections showed a few differences in terms of clinical history, anthropometrics, and physical examination findings of the children (Table 2). hMPV cases referred a significantly commoner history of fever and runny nose on admission than RSV cases, and were significantly more frequently pale on arrival (22·9% *vs.* 9·7%, $P = 0{\cdot}015$). In terms of respiratory signs, RSV cases wheezed more (70·2% *vs.* 52·5%, $P = 0{\cdot}018$) and had a significantly higher mean respiratory rate (64·6 *vs.* 59, $P = 0{\cdot}009$).

Laboratory results

Laboratory results also showed some differences between the two groups, with a higher proportion of anaemic patients in the RSV group (19·2% *vs.* 5·9%, $P = 0{\cdot}032$), a significantly lower mean haemoglobin reading on admission (10·4 g/l *vs.* 12·1 g/l, $P = 0{\cdot}004$) while hMPV cases presented a higher proportion of elevated CRP (>5 mg/dl) (36·1% *vs.* 21·8%, $P = 0{\cdot}041$). hMPV cases were twice as frequently infected with pneumococci in their nasopharynx (29·5% *vs.* 12·9%, $P = 0{\cdot}006$), and were significantly more often viral mono-infections than RSV cases (49·2% *vs.* 29·0%, $P = 0{\cdot}007$). Both viruses co-existed frequently with other respiratory viruses (RV, coronavirus, influenza, parainfluenza virus or adenovirus), with only parainfluenza co-infections being more commonly seen in hMPV cases (14·7% *vs.* 5·6%, $P = 0{\cdot}038$) (Table 3).

Clinical evolution and outcome, chest X-ray findings and management

Regarding clinical syndromes, RSV was more commonly associated to bronchiolitis episodes (41·1% RSV *vs.* 6·6% hMPV, $P < 0{\cdot}001$), while the reverse was seen in the associations with laryngotracheitis (hMPV 9·8%, RSV 0%, $P < 0{\cdot}001$). Importantly, although hMPV was more frequently associated with pneumonia episodes (42·6% *vs.* 31·4%, $P = 0{\cdot}135$) or bronchitis/asthma (39·3% *vs.* 25·8%, $P = 0{\cdot}060$) none of these differences showed statistical significance. Chest X-ray findings were also similar between the two groups (Table 4). In terms of management, RSV-infected patients received more bronchodilator treatment ($P = 0{\cdot}011$), while hMPV patients received more corticosteroids ($P = 0{\cdot}001$) and antibiotics ($P = 0{\cdot}048$). There were no differences in oxygen needs or

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Table 1. *Baseline socio-demographic characteristics and health history of recruited patients with RSV and hMPV infections*

	RSV cases ($n = 124$)	hMPV cases ($n = 61$)	P value
Demographic			
Age, months, median (IQR)	10 (4–24)	15 (7–25)	0·072
Group age <12 months	65/124 (52·4)	25/61 (41·0)	0·143
Sex, female	46/124 (37·1)	26/61 (42·6)	0·469
Patient history			
Prematurity	14/124 (11·3)	3/61 (4·9)	0·158
Breastfeeding ⩾6 months	59/124 (48·0)	32/61 (52·5)	0·566
Past morbidity and comorbidity			
Previous admission for ARI	31/124 (25·0)	17/61 (27·9)	0·676
History of wheezing or asthma	18/124 (14·5)	15/61 (24·6)	0·092
Antibiotic preceding admission	44/124 (35·5)	19/61 (31·2)	0·558
Existing comorbidity	2/124 (1·6)	2/60 (3·3)	0·453
Vaccination history			
Adequate vaccination for age	103/124 (83·1)	47/61 (77·0)	0·326
⩾1 dose of Hib vaccine	120/124 (96·8)	58/61 (95·1)	0·571
⩾1 dose of pneumococcus vaccine	16/124 (12·9)	14/61 (22·9)	0·081
Proxy of socioeconomic level			
High parent's education level	14/124 (11·3)	10/61 (16·4)	0·331
Both parents unemployed	19/124 (15·3)	11/61 (18·0)	0·638
Medical insurance	26/124 (21·0)	10/59 (17·0)	0·523
Family environment			
Smoking exposure at home	52/124 (41·9)	22/60 (36·7)	0·494
Number of persons in the house >6	46/124 (37·1)	23/61 (37·7)	0·936
Rooms in the house ⩽2	83/124 (66·9)	47/61 (77·0)	0·157

RSV, Respiratory syncytial virus; hMPV, human metapneumovirus; IQR, interquartile range; ARI, acute respiratory infection.
Values given are *n* (%) unless stated otherwise.

in mean duration of admission, but hMPV patients had a higher mean RISC score (1·8 *vs.* 1·5, $P = 0·025$), and were more commonly transferred to the intensive care unit (ICU) (11·5% *vs.* 3·2%, $P = 0·026$). There were seven deaths in the study, evenly distributed between the two groups (4/124 in the RSV group, with two cases of pneumonia, one of bronchiolitis and one of bronchitis; and 3/59 in the hMPV group, with two cases of pneumonia, one bronchiolitis; $P = 0·540$). No statistically significant differences could be detected between the deaths in each group.

DISCUSSION

This analysis, part of a larger study describing for the first time the aetiology and epidemiology of WHO-defined pneumonia in Morocco [17], confirms the high prevalence and importance in this country of both RSV and hMPV infections as causes of paediatric respiratory-related hospital admissions. Such data are of importance at the national level, but even more so at the regional level in Northern Africa, where few studies have specifically investigated and compared these two common viruses [28–32]. In our series, RSV infections were documented in 18·2% of all recruited children, whereas hMPV infections were half as common (8·9% of all patients). Importantly, and despite the high frequency of co-infections between RSV and hMPV with other common respiratory viruses, only one case of RSV/hMPV co-infection could be confirmed. This, together with the fact that a third of all RSV cases and up to a half of all hMPV infections occurred in the absence of other viral co-infections, confirms the pathogenicity of these two viruses and their potential to cause severe disease, with non-negligible associated CFRs ranging from 3·2% (RSV) to 5·1% (hMPV). However, the real relevance of the isolation of a pathogen in the nasopharynx (viral or bacterial) in causing the clinical

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Table 2. *Clinical history, anthropometrics and physical examination findings on admission of recruited patients with RSV and hMPV infections*

	RSV cases ($n = 124$)	hMPV cases ($n = 61$)	P value
History of the current disease			
Time interval between onset and admission (mean ± S.D.)	4·5 (5·6)	5·8 (8·6)	0·232
History of fever	93/124 (75·0)	54/60 (90·0)	**0·017**
Duration of cough, days (mean ± S.D.)	4·3 (4·3)	4·9 (5·6)	0·474
History of runny nose	92/124 (74·2)	54/60 (90·0)	**0·013**
History of vomit	75/124 (60·5)	29/60 (48·3)	0·119
History of diarrhoea	40/124 (32·3)	18/60 (30·0)	0·757
Difficulties to breastfeed/feed	53/117 (45·3)	30/59 (50·8)	0·486
Impaired consciousness	3/124 (2·4)	0/61 (0)	0·221
Anthropometrics			
Weight, kg (mean ± S.D.)	9·2 (3·1)	10·4 (3·8)	**0·030**
Malnourished	33/118 (28·0)	23/61 (37·7)	0·183
Severely malnourished (WAZ <–3 S.D.)	5/118 (4·2)	5/61 (8·2)	0·332
WAZ score (mean ± S.D.)	−0·24 (1·8)	−0·39 (1·7)	0·621
Symptoms and signs on admission			
Fever on admission	79/124 (63·7)	44/61 (72·1)	0·254
Hyperpyrexia (axillary temp. >39 °C)	19/124 (15·3)	16/61 (26·2)	0·075
Axillary temp., °C (mean ± S.D.)	37·9 (0·9)	38·1 (0·9)	0·165
Respiratory rate (mean ± S.D.)	64·6 (13·9)	59 (12·4)	**0·009**
Oxygen saturation, % (mean ± S.D.)	93·8 (3·8)	94·0 (5·8)	0·780
WHO oxygen desaturation <90%	13/116 (11·2)	8/57 (14·0)	0·592
Cyanosis	8/124 (6·5)	7/61 (11·5)	0·239
Pallor	12/124 (9·7)	14/61 (22·9)	**0·015**
Nasal flaring	83/124 (66·9)	48/61 (78·7)	0·098
Wheezing	87/124 (70·2)	32/61 (52·5)	**0·018**
Crackles	18/124 (14·5)	4/61 (6·6)	0·116
Rhonchi	78/124 (62·9)	38/61 (62·3)	0·936

RSV, Respiratory syncytial virus; hMPV, human metapneumovirus; WAZ, weight-for-age Z score.
Values given are n (%) unless stated otherwise.

picture in those patients is still debatable, as asymptomatic carriage is also a common phenomenon.

It has been clearly demonstrated that although young age is an independent risk factor for both pathogens [33, 34], hMPV occurs both in infancy and also at higher frequency than in RSV cases, in older children and at a higher mean age [11, 12, 16]. In our series, mean age on admission was also higher for hMPV patients, although statistical significance could not be achieved ($P = 0·07$). We were unable to find any other distinguishing features between the two viruses in terms of demographics, patient's history, vaccination history, family environment or socioeconomic background, and contrary to what other authors have described, we did not find differences in terms of underlying chronic comorbidities [11, 35]. What seemed to differ quite noticeably, as shown previously [12, 14, 16, 36], was the seasonal pattern of both viruses, with RSV showing a clear-cut transmission period coinciding with the cold and drier season (November–April) with hMPV concentrated in the remaining months of the year (March–December), with very little overlap.

It has also been argued that the clinical manifestations of hMPV are indistinguishable from those of RSV [33]. However, our analysis does pinpoint a few differences regarding the medical history and physical examination on admission, such as a higher frequency of children with runny nose or a history of fever for hMPV cases. Conversely, RSV-infected patients had significantly higher respiratory rates or greater frequency of wheezing than their comparator hMPV cases. Such minor differences may be linked to the fact that, in our series, and as described previously by other studies, RSV was significantly more frequently associated with bronchiolitis (41·1% *vs.* 6·6%,

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Table 3. *Laboratory and microbiology findings of recruited patients with RSV and hMPV infections*

	RSV cases ($n = 124$)	hMPV cases ($n = 61$)	P value
Biomarkers			
PCT (mean ± S.D.)	3·1 (11·5)	3·2 (10·6)	0·950
High PCT (>5 ng/ml)	39/121 (32·2)	21/60 (35·0)	0·710
CRP (mean ± S.D.)	2·8 (3·5)	3·5 (3·6)	0·156
High CRP (>5 mg/dl)	26/119 (21·8)	22/61 (36·1)	**0·041**
Haemogram			
WBC count (mean ± S.D.)	15·3 (10·1)	14·3 (6·9)	0·516
Abnormal WBC count, 10^9/l (<5 or >20)	21/77 (27·3)	8/51 (15·7)	0·125
Hb, g/l (mean ± S.D.)	10·4 (1·6)	12·1 (4·7)	**0·004**
Anaemia <9 g/l	15/78 (19·2)	3/51 (5·9)	**0·032**
Bacterial co-infections			
All-cause bacteraemia	6/120 (5·0)*	3/61 (4·9)†	0·981
Pneumococcus carriage in nasopharynx	16/124 (12·9)	18/61 (29·5)	**0·006**
Viral co-infections			
Viral monoinfection	36/124 (29·0)	30/61 (49·2)	**0·007**
Rhinovirus	32/124 (25·8)	17/61 (27·9)	0·765
Coronavirus	12/124 (9·7)	2/61 (3·3)	0·122
Influenza	2/124 (1·6)	0/61 (0)	0·319
Parainfluenza	7/124 (5·6)	9/61 (14·7)	**0·038**
Adenovirus	12/124 (9·7)	8/61 (13·1)	0·479

RSV, Respiratory syncytial virus; hMPV, human metapneumovirus; PCT, procalcitonin; CRP, C-reactive protein; WBC, White blood cell.

Values given are *n* (%) unless stated otherwise.

* *Staphylococcus aureus* ($n = 2$), *Pseudomonas aeruginosa* ($n = 1$), *Pseudomonas oryzihabitans* ($n = 1$), *Escherichia coli* ($n = 1$), *Streptococcus pneumonia* ($n = 1$).

† *Enterococcus faecalis* ($n = 1$), *Streptococcus pneumoniae* ($n = 1$), *Streptococcus* group C ($n = 1$).

$P < 0·001$) [35, 37], while hMPV was more related to laryngotracheitis ($P < 0·001$) and (albeit non-significantly) to pneumonia [14, 35]. Similarly, although our data cannot support the hypothesis that hMPV may predispose or simply be more frequently associated with the risk of invasive bacterial disease, two findings should be mentioned in this respect, i.e. the significantly higher frequency of elevated (>5 mg/dl) CRP ($P = 0·041$) and pneumococcal nasopharyngeal carriage ($P = 0·006$) in hMPV-infected patients. Conversely, the low detection of pneumococci in the nasopharynx of RSV-infected patients (only 12·9% of cases) is of note, as some authors have proposed that RSV could be a predisposing agent for secondary bacterial infection in the airways of children [38–40]. However, and similarly to what other authors have found [41], our data do not confirm a major synergism between pneumococcus and RSV, and further studies are needed to clarify the real interaction between these two pathogens, particularly using better sampling methods that may be more helpful to disentangle the real contribution of isolates, such as lung aspirates [42, 43], or minimally invasive autopsies of the lung in post-mortem samples [44].

Despite mirroring quite closely the clinical presentation of RSV episodes on admission, hMPV infections are associated with a higher risk than RSV infections in terms of disease progression and hospital requirements. In our series, hMPV-infected patients were significantly more prone to receive antibiotics ($P = 0·048$), corticosteroids ($P = 0·001$, possibly in relation to their more frequent association with laryngotracheitis instead of with bronchiolitis), and transfer to the ICU ($P = 0·026$), and had a significantly higher mean RISC score (1·8 *vs.* 1·3, $P = 0·025$), suggesting a higher degree of severity and intra-hospital complications. Importantly, clinicians were not aware at the time of deciding upon the clinical management of these patients which viruses (if any) had been detected in the NPA of these children, and were causing the respiratory syndrome. This aligns with a previous analysis of this same series of patients in which hMPV infection was found to be the only independent

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Table 4. *Syndromic diagnosis, radiology endpoints and outcome of recruited patients with RSV and hMPV infections*

	RSV cases (n = 124)	hMPV cases (n = 61)	P value
Clinical syndromes upon discharge			
Pneumonia	39/124 (31·4)	26/61 (42·6)	0·135
Bronchiolitis	51/124 (41·1)	4/61 (6·6)	**<0·001**
Bronchitis/asthma	32/124 (25·8)	24/61 (39·3)	0·060
Laryngotracheitis	0/124 (0)	6/61 (9·8)	**<0·001**
Other diagnoses*	2/124 (1·6)	1/61 (1·6)	0·989
Radiology endpoints			
Normal chest X-ray	70/115 (60·9)	38/53 (71·7)	
Other infiltrates	17/115 (14·8)	5/53 (9·4)	0·380
Condensation/pleural effusion	28/115 (24·3)	10/53 (18·9)	
Outcome			
Required oxygen during admission	87/124 (70·2)	36/61 (59·0)	0·131
Required bronchodilators during admission	92/124 (74·2)	34/61 (55·7)	**0·011**
Required corticosteroids during admission	33/124 (26·6)	32/61 (52·5)	**0·001**
Received antibiotics during admission	56/124 (45·2)	37/61 (60·7)	**0·048**
Length of admission, days (mean ± S.D.)	6·0 (4·2)	7·3 (9·8)	0·192
RISC score (mean ± S.D.)	1·3 (1·3)	1·8 (1·5)	**0·025**
Transferred to ICU	4/124 (3·2)	7/61 (11·5)	**0·026**
Length of admission in ICU, days (mean ± S.D.)	4·0 (4·1)	18·2 (30·8)	0·396
Died	4/124 (3·2)	3/59 (5·1)	0·540

RSV, Respiratory syncytial virus; hMPV, human metapneumovirus; RISC, Respiratory Index of Severity in children; ICU, intensive care unit.
Values given are n (%) unless stated otherwise.
* Miscellaneous group of diseases including upper respiratory tract infections, other respiratory conditions or infections, congenital problems, other infections.

microbiological risk factor associated with an adverse outcome [45].

CONCLUSIONS

We have shown for the first time that both RSV and hMPV are common and potentially life-threatening causes of WHO-defined pneumonia in Moroccan children. Both viruses show indistinctive clinical symptomatology, but in our series, hMPV had a number of characteristics associated with a more severe evolution. Further studies are warranted to better characterize the nature and risk factors for these infections, in order to improve their early recognition and to guarantee better preventive and management strategies.

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DECLARATION OF INTEREST

None.

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