Risk factors for a poor outcome among children admitted with clinically severe pneumonia to a university hospital in Rabat, Morocco

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SUMMARY

Objectives: Data on prognostic factors among children with severe pneumonia are scarce in middle-income countries. We investigated prognostic factors for an adverse outcome among children admitted to the Hôpital d'Enfants de Rabat, Morocco with World Health Organization-defined clinically severe pneumonia (CSP).
Methods: Children aged 2–59 months admitted to the hospital and fulfilling the CSP definition were recruited into this 13-month prospective study. A poor prognosis was defined as death, a need for intensive care, or a Respiratory Index of Severity in Children (RISC) score ≥3. Multivariate logistic regression was performed to ascertain independent predictive factors for a poor prognosis.
Results: Of the 689 children included in this analysis, 55 (8.0%) required intensive care and 28 died (4.0%). Five hundred and two (72.8%) children were classified as having a good prognosis and 187 (27.2%) as having a poor prognosis. A history of prematurity (odds ratio (OR) 2.50, 95% confidence interval (CI) 1.24–5.04), of fever (OR 2.25, 95% CI 1.32–3.83), living in a house with smokers (OR 1.79, 95% CI 1.18–2.72), impaired consciousness (OR 10.96, 95% CI 2.88–41.73), cyanosis (OR 2.09, 95% CI 1.05–4.15), pallor (OR 2.27, 95% CI 1.34–3.84), having rhonchi on auscultation (OR 2.45, 95% CI 1.58–3.79), and human metapneumovirus infection (OR 2.13, 95% CI 1.13–4.02) were all independent risk factors for an adverse outcome, whereas a history of asthma (OR 0.46, 95% CI 0.25–0.84) was the only independent risk factor for a positive outcome.
Conclusions: The early identification of factors associated with a poor prognosis could improve management strategies and the likelihood of survival of Moroccan children with severe pneumonia.
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1. Introduction

Acute respiratory infections (ARI) remain the leading cause of death in young children in low- and middle-income countries, accounting for almost 1.4 million annual deaths, with around one sixth of the deaths occurring in children under the age of five.[1] Indeed, the death toll imposed by respiratory infections represents a massive burden for the fragile health systems in the developing world, where over 90% of all global deaths occur,[2] and this cannot be sufficiently emphasized. Respiratory infections cause a variety of clinical syndromes, of which pneumonia – perhaps the most paradigmatic and severe of all – is the most commonly associated with an adverse outcome, causing over 90% of all deaths.[3]

Pneumonia is typically caused by bacterial agents, with *Streptococcus pneumoniae*[4] and *Haemophilus influenzae* type b (Hib)[5] being the two most frequent underlying aetiologies. Respiratory viruses are typically the causes of upper and lower respiratory infections with a more benign course, although their pathogenic potential can sometimes be comparable to that of bacteria or even worse; respiratory syncytial virus (RSV) is one of the most common viruses involved in severe childhood disease.[6] Whatever the underlying cause, case-fatality rates among under-fives hospitalized with pneumonia are reported to be around 19%.[7]

In the developing world, currently existing interventions to reduce pneumonia-related morbidity and mortality include the implementation of anti-pneumonia vaccines through the Expanded Programme on Immunization during infancy,[8] and the adequate diagnosis and prompt treatment of clinical cases with antibiotics, in accordance with the Integrated Management of Childhood Illnesses (IMCI) algorithms,[9] under the assumption that in such settings the majority of severe pneumonia cases are of bacterial origin.

Despite the increasing availability of preventive vaccines, morbidity amongst those children who do become infected remains high, possibly in relation to the many challenges faced in the diagnosis and management in resource-constrained settings. The early identification of risk factors for a poor outcome among pneumonia patients could help prioritize the management of those patients with an uncertain prognosis and perhaps increase their likelihood of surviving. Previous studies have described a series of factors including young age of the patient (or the patient's mother), malnutrition, anaemia, or the confirmation of grunting, cyanosis, or chest indrawing, among others, as harbingers of a negative outcome.[10–13]

Scarce and limited epidemiological, clinical, and microbiological data are available regarding paediatric respiratory tract infections in the Kingdom of Morocco, a middle-income country in north-western Africa, although the World Health Organization (WHO) estimates that up to 26.5% of all deaths in children aged 1–59 months are secondary to pneumonia.[14] In this analysis, part of a wider surveillance project on the aetiology of paediatric respiratory infections, we aimed to describe factors associated with a poor outcome among hospitalized children under the age of five admitted to a Moroccan reference hospital with a diagnosis of WHO-defined severe pneumonia.

2. Materials and methods

2.1. 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 symptoms were identified and approached for recruitment if they fulfilled the WHO definition of clinically severe pneumonia (CSP),[15,16] namely a history of cough or reported breathing difficulty and increased respiratory rate (RR) according to age,[16] together with chest indrawing. After parents had signed an informed consent form, recruited children underwent standardized procedures upon admission, including pulse oximetry (Bionics PalmCare), an anteroposterior chest X-ray, nasal and pharyngeal swabs for the diagnosis of bacterial infection/carriage, and nasopharyngeal aspirates (NPA) for the diagnosis of respiratory viruses. A minimum of 2 ml venous blood was also collected for blood culture, full blood cell count, and biochemical determinations, including C-reactive protein (CRP) and procalcitonin (PCT).

2.2. Definitions and clinical groups established

Admission and discharge diagnoses were coded using the International Classification of Diseases, 10th Revision (ICD-10).[17] Hypoxemia implied an oxygen saturation (SaO_2) <90%. Fever was defined as an axillary temperature of $\geq$37.5 °C. Nutritional status was based on weight-for-age Z scores (WAZ), calculated using the least mean square method and the 2000 Centers for Disease Control and Prevention (CDC) growth reference.[18] Invasive bacterial disease implied the isolation of one or more non-contaminant bacteria in blood or pleural fluid.

For the purpose of this specific analysis, we defined two prognostic groups utilizing a composite definition based on outcome (discharged alive vs. in-hospital death), requirement for admission to the intensive care unit (ICU), and 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 (LRTI), based on parameters such as oxygen saturation, respiratory signs including indrawing or wheezing, and nutritional status.[19] Thus, we defined a good prognosis as a RISC score <3, no need for admission to the ICU, and a discharge from hospital on the grounds of clinical improvement. In contrast, a poor prognosis was defined as the occurrence of a death outcome, or an ICU admission, or a RISC score of $\geq$3.

2.3. Laboratory methods

The full laboratory methods of the general study from which this analysis has been performed are detailed elsewhere.[20] Blood samples were cultured using an automated blood culture system (BD Bactec; BD, New Jersey, USA), and bacterial isolates identified by Phoenix Automated Microbiology System (PHX system; BD) or colony morphology and biochemical tests. The detection of *S. pneumoniae* and *H. influenzae* type B was also studied by real-time PCR using a published in-house assay.[21]

The presence of DNA/RNA of influenza viruses A and B, RSV A and B, parainfluenza viruses (PIV) 1, 2, 3, and 4, rhinovirus (RV), adenovirus (ADV), enterovirus (EV), coronaviruses (CoV) 229E, NL63, and OC43, human metapneumovirus (hMPV), *Mycoplasma pneumoniae*, *Chlamydophila pneumoniae*, and *Bordetella pertussis* in nasopharyngeal aspirates was also systematically investigated by means of the TrueScience RespiFinder Pathogen Identification Panel (Applied Biosystems, New York, USA).

2.4. X-ray interpretation

Chest X-rays were interpreted independently by two paediatricians following a WHO-designed X-ray interpretation protocol.[22] 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.

2.5. 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., Santa Clara, CA, USA). Statistical analyses were done using Stata 11 (StataCorp., College Station, TX, USA). Study variables were counted and summarized in frequency tables. Means with corresponding standard deviations (SD) or medians and interquartile ranges are presented for normally and non-normally distributed variables, respectively. Multivariate logistic regression was performed with good prognosis/poor prognosis as the outcome, using an automated backward and forward stepwise estimation. Variables previously shown in the literature to

be related to a poor prognosis and other available data were investigated. All variables that were associated with an adverse outcome at a significance level of $p < 0.10$ in the univariate analysis were included in the initial model. The significance level for removal from the model was set at $p = 0.06$ and that for addition to the model at $p = 0.05$. The strength of association was determined by estimating the odds ratio (OR) and the 95% confidence intervals (CI).

2.6. 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 Recherché Biomédicale (Départ No. 1252–16Déc2009) of the Faculty of Medicine in Rabat.

3. Results

Out of almost 11 000 children seen in the emergency department of HER during the 13-month study period, 700 under the age of five were recruited into the study. Six hundred and eighty-nine (98.4%) of these children had all the necessary outcome data for inclusion in this specific risk factor analysis (Figure 1). There were 28 deaths among these 689 patients (4.0%), and 55 children (8.0%) required transfer to the ICU. The mean RISC score for the overall study population was 1.36 (SD 1.34). With regard to the two established risk groups, 502 (72.8%) children were assigned to the good prognosis group and 187 (27.2%) to the poor prognosis group (Figure 1).

The socio-demographic characteristics and health history factors of the patients according to the prognosis group are shown in Table 1. Patients with a worse outcome were significantly younger; no difference was found regarding gender. No significant differences were seen in terms of any seasonality of admission in relation to outcome (data not shown). A history of having been born prematurely, having received antibiotics preceding admission, or having an already known co-morbidity had a significant

Figure 1. Study flowchart.

association with a poorer outcome, while a history of previous admission for LRTI or wheezing was strongly associated with a good prognosis. Finally, being exposed to tobacco smoking at home was also significantly associated with a worse outcome.

In terms of the current admission history and other clinical indicators, patients with a worse outcome were clearly more severely ill on admission (including a significantly higher mean temperature, heart rate, and respiratory rate, and a lower oxygen saturation) and had a significantly longer history of symptoms (Table 2). They were also significantly more likely to have required antibiotics during hospitalization (OR 8.75, $p < 0.001$). Their nutritional status was also significantly poorer, with up to 16.5% (30/182) being severely malnourished. In terms of respiratory signs, only wheezing was significantly more common among children with a good prognosis. Radiologically confirmed pneumonia was again much more frequent (32.9% vs. 14.5%, $p = 0.001$) amongst children with a poorer outcome, and hospitalizations were significantly more prolonged in this group (9.96 days vs. 4.31 days, $p = 0.001$).

Laboratory and microbiology findings also showed important differences between the two groups, with children with a worse outcome being significantly more anaemic and more frequently demonstrating elevated biomarkers of infection (PCT and CRP). Importantly, no differences were seen according to the outcome group in the mean white blood cell count or in the prevalence of leukopenia or leukocytosis (Table 3). As expected, cases of bacteraemia were significantly more frequent among the group with a poor outcome, and so were infections with hMPV. In contrast, infections with RV appeared to be associated with a good outcome ($p = 0.001$).

The multivariate analysis of factors associated with the prognosis (Table 4) showed that a history of prematurity (OR 2.50, 95% CI 1.24–5.04), of fever (OR 2.25, 95% CI 1.32–3.83), living in a house with smokers (OR 1.79, 95% CI 1.18–2.72), impaired consciousness (OR 10.96, 95% CI 2.88–41.73), cyanosis (OR 2.09, 95% CI 1.05–4.15), pallor (OR 2.27, 95% CI 1.34–3.84), having rhonchi on auscultation (OR 2.45, 95% CI 1.58–3.79), and hMPV infection (OR 2.13, 95% CI 1.13–4.02) were all independent risk factors for an adverse outcome, whereas a history of asthma (OR 0.46, 95% CI 0.25–0.84) was the only independent risk factor for a positive outcome.

4. Discussion

The burden and impact of acute LRTIs in Morocco has not been sufficiently addressed. The few available publications[23–26] have patchily presented data on specific microorganisms or generic laboratory findings, but to our knowledge, this project has been the first to comprehensively describe the burden, aetiology, and clinical characterization of severe paediatric pneumonia in a tertiary referral Moroccan hospital.[20] In this setting, paediatric respiratory disease results in unacceptably high associated case-fatality rates (28 deaths, giving a case-fatality rate (CFR) of 4.0%, which is towards the upper bound of what has previously been described for similar or even poorer settings, ranging from 0.8% to 4.8%[7,27]) and affects mostly infants.[7] About a quarter of the patients recruited into this study could be classified as having a poor prognosis, and 8% of these patients required intensive care. Importantly, the management of these patients seems to have been adequately matched to the severity of their symptoms, with a good availability of intensive care and a very high coverage of oxygen and antibiotics, including broad-spectrum ones.[20,28] Nosocomial infections, which in other settings may be an important cause of in-hospital mortality, appear to have played a moderate role in this series, as only about 14.2% of the patients (4/28) had an admission duration longer than 10 days.
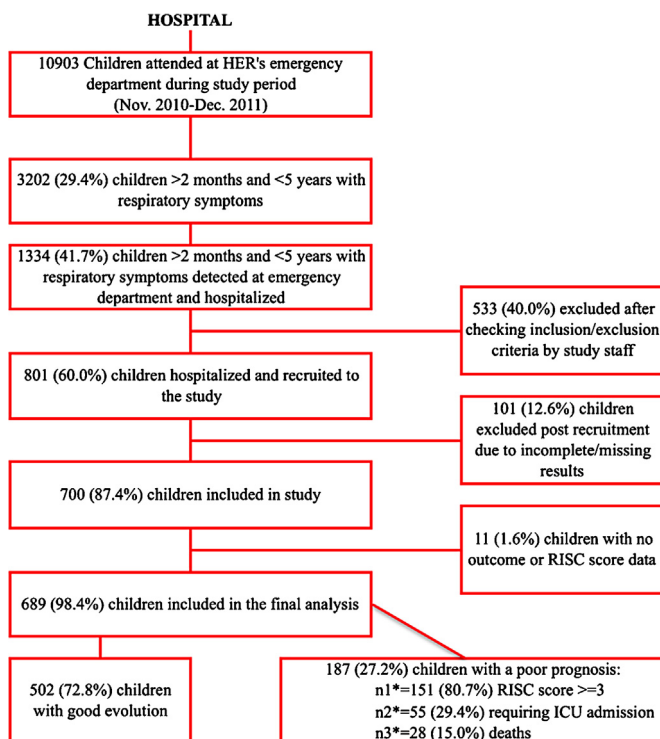
Table 1
Baseline socio-demographic characteristics of recruited patients, according to the prognosis group[a]

	Good prognosis (n = 502)	Poor prognosis (n = 189)	OR (95% CI)	p-Value
Demographic characteristics				
Age, months, mean ± SD	23.40 ± 14.80	16.00 ± 12.10		0.001
Age <12 months	123 (24.50)	89 (47.59)	2.80 (1.97–2.98)	0.001
Female sex	187 (37.25)	62 (33.16)	0.84 (0.59–1.19)	0.32
Patient history				
Prematurity	28 (5.59)	23 (12.30)	2.37 (1.33–4.33)	0.003
Breastfeeding ≥6 months	308 (61.72)	109 (58.30)	0.87 (0.62–1.22)	0.41
Vitamin A supplementation	461 (91.83)	168 (89.84)	0.79 (0.45–1.40)	0.67
Past morbidity and co-morbidity				
Previous admission for ARI	182 (36.25)	39 (20.86)	0.46 (0.31–0.68)	0.001
History of wheezing or asthma	164 (32.67)	22 (11.76)	0.27 (0.17–0.44)	0.001
Antibiotic preceding admission	136 (27.09)	68 (36.36)	1.54 (1.08–2.20)	0.018
Existing co-morbidity	13 (2.60)	12 (6.50)	3.06 (1.37–6.83)	0.016
Vaccination history				
Adequate vaccination status according to age	438 (87.43)	158 (84.95)	0.81 (0.50–1.31)	0.39
At least one dose of Hib vaccine	492 (98.01)	181 (96.80)	0.61 (0.22–1.70)	0.34
Proxy of socioeconomic level				
Parents with high level of education	68 (13.55)	24 (12.83)	0.94 (0.57–1.55)	0.93
Medical insurance	137 (27.30)	40 (21.40)	0.72 (0.48–1.08)	0.28
Father's occupation status	396 (79.68)	145 (79.23)	0.97 (0.64–1.47)	0.89
Mother's occupation status	60 (11.98)	20 (10.70)	0.88 (0.51–1.50)	0.64
Family environment				
Smoking exposure at home	192 (38.32)	87 (46.52)	1.04 (1–1.97)	0.05
Number of persons in the house >6	189 (37.65)	75 (40.11)	1.11 (0.80–1.57)	0.55
Rooms in the house >3	164 (32.67)	72 (38.50)	1.30 (0.91–1.83)	0.15

OR, odds ratio; CI, confidence interval; SD, standard deviation; ARI, acute respiratory infection; Hib, *Haemophilus influenzae* type b.
[a] Results are *n* (%), unless stated otherwise.

In this analysis, we aimed to identify patient risk factors (socio-economic, clinical, and laboratory) upon arrival that could guide the clinician's response and help tailor the scarce resources for improved patient management. Such factors, extensively described in the pneumonia literature[10–13,19,29–34] and currently being specifically investigated as part of the PERCH (aetiology of pneumonia) multisite case–control study,[35] may change according to the local or regional epidemiology of LRTI, warranting locally

Table 2
Clinical history, physical examination findings on admission, and outcome of recruited patients, according to the prognosis group[a]

	Good prognosis (n = 502)	Poor prognosis (n = 189)	OR (95% CI)	p-Value
History of the current disease				
Time interval between onset and admission (Days): mean ± SD	3.40 ± 4.29	5.56 ± 7.85	NA	0.001
History of fever	312 (62.28)	157 (83.96)	3.17 (2.06–4.87)	0.001
History of cough	495 (98.80)	182 (97.85)	1.08 (1.04–1.13)	0.35
History of runny nose	390 (77.84)	139 (74.33)	0.82 (0.56–1.21)	0.33
History of vomiting	249 (49.70)	101 (54.01)	1.19 (0.85–1.67)	0.31
History of diarrhoea	80 (15.97)	57 (30.48)	2.31 (1.56–3.42)	0.001
Difficulties breastfeeding	141 (30.79)	121 (67.22)	4.61 (3.19–6.67)	0.001
Impaired consciousness	3 (0.60)	17 (9.09)	16.63 (4.81–57.45)	0.001
Symptoms and signs on admission				
Malnourished (WAZ < −1 SD)	118 (23.89)	86 (47.25)	2.85 (1.99–4.07)	0.001
WAZ > −1 SD	376 (76.11)	96 (52.75)	0.35 (0.24–0.5)	0.001
WAZ < −1 to > −3 SD	111 (22.47)	56 (30.77)	1.53 (1.05–2.24)	0.02
WAZ < −3 SD	7 (1.42)	30 (16.48)	13.73 (5.91–31.89)	0.001
Axillary temperature, °C, mean ± SD	37.65 ± 0.83	38.07 ± 0.88	NA	0.001
Hyperpyrexia (axillary temperature >39 °C)	50 (9.98)	45 (24.32)	2.90 (1.84–4.56)	0.001
Respiratory rate, per min, mean ± SD	58.68 ± 12.54	61.14 ± 17.98	1.01 (1–1.02)	0.04
Heart rate, per min, mean ± SD	125.86 ± 22.73	131.12 ± 24.61	1.01 (1–1.02)	0.008
Oxygen saturation, %, mean ± SD	95.37 ± 3.12	93.31 ± 6.35	NA	0.001
WHO oxygen desaturation <90%	17 (3.53)	35 (19.44)	6.58 (3.50–12.38)	0.001
Cyanosis	22 (4.38)	40 (21.40)	5.93 (3.34–10.52)	0.001
Pallor	55 (11)	61 (32.62)	3.93 (2.56–6.04)	0.001
Nasal flaring	367 (73.11)	139 (74.33)	1.07 (0.73–1.57)	0.74
Wheezing	416 (82.87)	36 (19.22)	0.05 (0.02–0.10)	0.001
Crackles	40 (7.97)	34 (18.18)	2.56 (1.56–4.22)	0.001
Rhonchi	215 (42.83)	138 (73.80)	3.76 (2.55–5.53)	0.001
Radiologically confirmed pneumonia	64 (14.48)	47 (32.87)	2.89 (1.84–4.52)	0.001
Outcome				
Received antibiotics during admission	139 (27.7)	144 (77.0)	8.75 (5.64–13.57)	0.001
Length of admission (Days): mean ± SD	5.24 ± 4.31	7.09 ± 9.96	NA	0.001
RISC score, mean ± SD	0.76 ± 0.80	2.98 ± 1.14	NA	0.001
Transferred to ICU	0 (0)	55 (29.41)	NA	0.001
Died	0 (0)	28 (14.97)	NA	0.001

OR, odds ratio; CI, confidence interval; SD, standard deviation; NA, Not applicable; WAZ, weight-for-age *Z* score; WHO, World Health Organization; RISC, Respiratory Index of Severity in Children; ICU, intensive care unit.
[a] Results are *n* (%), unless stated otherwise.

Table 3
Laboratory and microbiology findings for the patients recruited, according to the prognosis group[a]

	Good prognosis (n = 502)	Poor prognosis (n = 189)	OR (95% CI)	p-Value
Biomarkers				
High PCT levels (>5 ng/ml)	98 (20.04)	92 (49.73)	3.94 (2.69–5.77)	0.001
High CRP levels (>5 mg/dl)	100 (20.16)	60 (32.61)	1.91 (1.30–2.80)	0.004
Haemogram				
WBC count, mean ± SD	15.82 ± 7.70	16.43 ± 8.01	NA	0.42
Abnormal WBC (<5 or >20, × 10⁹/l)	84 (23.33)	38 (25.85)	1.15 (0.74–1.79)	0.54
Haemoglobin, g/l, mean ± SD	11.62 ± 2.82	10.56 ± 1.87	NA	0.001
Anaemia <9 g/l	27 (7.44)	24 (16.11)	2.39 (1.32–4.32)	0.003
Biochemistry				
Creatinine, Micromol/L, mean ± SD	4.05 ± 0.53	4.46 ± 2.6	NA	0.34
Sodium, Micromol/L, mean ± SD	135.73 ± 3.9	136.72 ± 6.47	NA	0.42
Potassium, Micromol/L, mean ± SD	4.62 ± 0.55	4.64 ± 0.72	NA	0.88
Glycaemia, Micromol/L, mean ± SD	95.97 ± 40.61	114.5 ± 63.61	NA	0.12
Bacteraemia	10 (2.03)	14 (7.50)	3.9 (1.68–9.01)	0.006
PCR results, microorganism isolated				
Human metapneumovirus	33 (6.76)	27 (15.08)	2.48 (1.44–4.29)	0.007
Rhinovirus	282 (56.97)	72 (40.22)	0.50 (0.35–0.72)	0.001
Coronavirus	41 (8.28)	13 (7.26)	0.87 (0.45–1.66)	0.66
Bordetella pertussis	3 (0.61)	2 (1.12)	1.85 (0.31–11.16)	0.49
Mycoplasma	7 (1.41)	3 (1.68)	1.18 (0.30–4.61)	0.80
Influenza virus	14 (2.83)	10 (5.60)	2.03 (0.88–4.66)	0.08
Parainfluenza virus	92 (24.58)	44 (18.60)	1.43 (0.95–2.15)	0.08
Respiratory syncytial virus	93 (18.80)	32 (17.88)	0.94 (0.60–1.47)	0.78
Adenovirus	86 (17.37)	30 (16.76)	0.96 (0.61–1.51)	0.85

OR, odds ratio; CI, confidence interval; SD, standard deviation; NA, Not applicable; PCT, procalcitonin; CRP, C-reactive protein; WBC, white blood cell count.
  [a] Results are n (%), unless stated otherwise.

specific analyses. In this series, and similar to what other authors have already described, impaired consciousness,[10,13,33] cyanosis as a proxy of hypoxemia,[11–13,19,36] and pallor[13,34,37] were three clinical signs strongly and independently associated with a poor prognosis, together with the presence of rhonchi. Wheezing, normally associated with relatively benign LRTI (bronchitis and/or bronchiolitis), and usually considered less frequent in developing settings in comparison to rich countries,[38] was very common in our series (present in up to two-thirds of the patients) and highly associated with viral infections,[20] but carried a low associated CFR and risk of a poor outcome. Although wheezing was not included in the final multivariate model because of being part of the composite definition of the outcome (being part of the RISC score), we found that a history of asthma was the only protective factor against a negative outcome in our series.

Young age (infants <12 months vs. older children) was also confirmed as a risk factor for a poor prognosis, as has been shown in other studies.[11,19,32,33] This sets the rationale for extra care when facing young infants with a respiratory

symptomatology, likely warranting a more conservative approach in terms of management.

Deficient nutritional status or low birth weight has clearly been established as a risk factor both for morbidity and mortality among LRTI patients.[10,19,30–33] In our series, a history of prematurity (intrinsically linked with a low birth weight) was independently associated with a high risk of dying. Similarly, under-nutrition, although not included in the final model because of being part of the outcome definition of the RISC score, was also found to be strongly associated with a higher likelihood of death, and was highly prevalent, affecting about a quarter of the recruited patients with a good outcome and almost half of those with a bad outcome. In recent years, Morocco has made important efforts to introduce programs for the prevention and management of childhood diseases, including the promotion of exclusive breastfeeding, supplementation of iron and vitamin A, and the introduction of anti-pneumonia vaccines, all of which may have an impact on the incidence of new malnutrition cases. However, malnutrition prevalence rates remain high in Morocco,[25,39] and unless adequately addressed, will continue to negatively affect the survival of patients with pneumonia.

Perhaps the most interesting finding in this analysis was the adverse outcome associated with the specific pneumonia cases secondary to hMPV. Among the 62 patients (9.1%) with this infection, seven (11.3%) required ICU admission, three died, and the mean RISC score was 1.84. The impact and real burden of this relatively newly described human virus needs to be investigated further,[40–42] but our data clearly show its pathogenicity potential and suggest that active surveillance for this virus should be maintained in Morocco.

Our study also confirmed the previously well-documented association of smoking in the household and an adverse outcome.[43,44] However, we were not able to confirm the association of certain well-known risk factors with a higher risk of death.[10–13] Indeed, parental education, lack of breastfeeding, vaccination status, unavailability of adequate medical care, co-morbidities and co-infections, metabolic acidosis, and other laboratory findings (leukocytosis, abnormal biomarkers, etc.), although assessed for some or the majority of outpatients, could

Table 4
Independent risk factors for a poor prognosis among admitted Moroccan children with WHO-defined severe pneumonia, according to multivariate analysis[a]

Risk factors for a poor prognosis	Adjusted OR	95% CI		p-Value[b]
		Lower	Upper	
History of prematurity	2.50	1.24	5.04	0.010
History of asthma	0.46	0.25	0.84	0.012
History of fever	2.25	1.32	3.83	0.003
Smoker at home	1.79	1.18	2.72	0.006
Pallor	2.27	1.34	3.84	0.002
Cyanosis	2.09	1.05	4.15	0.035
Rhonchi	2.45	1.58	3.79	<0.001
Impaired consciousness	10.96	2.88	41.73	<0.001
Human metapneumovirus infection	2.13	1.13	4.02	0.019

WHO, World Health Organization; OR, odds ratio; CI, confidence interval.
  [a] Other variables assessed in the model included having a chronic underlying disease, fever on admission, hyperpyrexia, crackles, diarrhoea, high C-reactive protein, high procalcitonin, bacteraemia, respiratory syncytial virus infection, and rhinovirus infection.
  [b] Likelihood ratio Chi-square test, 1 degree of freedom.

not be independently related to a poorer outcome, even though the study sample size was relatively large and the univariate association was evident. This does not limit the strength of our results, but, in our opinion, may express that in this setting their validity as prognostic markers appears less critical than in other settings. Our study suffers from further limitations, including the fact that it was conducted in an urban referral tertiary hospital with good accessibility to intensive care, a factor that may have influenced the outcome for some of these patients, thus underestimating the real impact that pneumonia may have in other less advantaged or more rural areas of the country.

In conclusion, the wide implementation of anti-pneumococcal and Hib vaccines and other known preventive measures will certainly result in a significant decrease in pneumonia-related morbidity and mortality globally. However, in regions where pneumonia remains a major cause of disease and death, the emphasis on early identification of risk factors known to be globally or locally associated with a poor outcome and the establishment of adequate case management strategies can make an enormous difference in the prognosis of these patients. In this respect, this study represents an important addition to the significant knowledge gaps related to paediatric pneumonia in Morocco, and more widely in the Maghreb area, and provides good evidence for new approaches to prevent and better manage this deadly disease.

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