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Bacteriologic profile and susceptibility pattern of mechanically ventilated paediatric patients with pneumonia

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ABSTRACT

Aim: Due to the current widespread bacterial resistance to many antibiotics – especially extended-spectrum β-lactams, carbapenems, and anti-pseudomonal drugs – therapy for severe pneumonia is very challenging. This study aimed to assess antimicrobial sensitivity patterns and optimisation of the antibiotic stewardship program applied at a university-affiliated paediatric intensive care unit (PICU).
Subjects and methods: This prospective cohort study included all patients aged 1 month to 12 years, admitted to the PICU with severe pneumonia episodes indicated for mechanical ventilation, and were followed up and investigated. Non-bronchoscopic bronchoalveolar lavage specimens were tested for positive microbiological yields and examined for their susceptibility pattern.
Results: Of 85 patients with 96 episodes, 69 of them yielded positive growth: 43 were community-acquired pneumonia episodes, 62.79% of which were of unidentified cause. The isolated bacteria were predominantly due to *Chlamydia pneumonia* (18.6%) followed by *Staphylococcus aureus* and its resistant form (9.3%). Hospital and ventilator-associated pneumonia were mainly related to Gram-negative bacteria (91.67% and 87.8%, respectively), especially *Klebsiella acinetobacter* and *Pseudomonas*. There was a significant increase in multi-drug resistance among Gram-negative bacteria, which was considered an independent risk factor of mortality ($P = 0.003$).
Conclusion: Severe community-acquired pneumonia was treated with macrolides in combination with vancomycin or linezolid if methicillin-resistant *S. aureus* was suspected. This was appropriate, in view of its causative agents and their susceptibility pattern. Hospital and ventilator-associated pneumonia caused by resistant Gram-negative organisms might have better outcomes by adding tigecycline or colistin in combination with fluoroquinolones. Owing to the widespread resistance of many Gram-negative bacteria, it is recommended that the antibiotic stewardship program be frequently updated.

1. Introduction

Pneumonia is considered to be the single largest cause of death in children. Worldwide, 35–40% mortality among children aged <5 years is attributed to the respiratory tract, accounting for 2.04 million deaths/year [1]. Geographically, most pneumonia studies are from the United States and Europe [2], with a paucity of information from Africa, although two-thirds of pneumonia-related mortality is reported from Africa and South Asia [3].

Acute respiratory infection (ARI) due to bacterial infections have become a global concern, especially because of the emergence of an increasing number of multidrug-resistant bacteria [4]. Therapy for severe pneumonia should not be postponed for the purpose of performing diagnostic studies [5]. The initial empiric therapy can be modified based on knowledge of local microbiological data, patient characteristics, and sensitivity pattern of expected pathogens of the institution [6].

The aim of the present study was to find the microbiological aspect isolated from patients with severe pneumonia indicated for mechanical ventilation. The study focused on the antimicrobial sensitivity pattern and patients' outcomes in terms of duration of mechanical ventilation (MV), length of paediatric intensive care unit (PICU) stay, and survival/mortality fate.

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2. Subjects and methods

This prospective cohort study was conducted in a tertiary care university-affiliated PICU from 1 May 2015 to 31 March 2018. The PICU comprised nine beds and eleven ventilators, where strict infection control measures were applied, including the ventilator bundle according to Center for Disease Control (CDC) guidelines [7]. Treatment of ventilator-associated pneumonia follows a local antibiotic stewardship program, developed since 2007 and updated based on the *Antibiotic Basics for Clinicians guidelines* (2012) [8] and is subject for revision whenever indicated. All children admitted to the PICU with severe pneumonia indicated for MV or those who developed a ventilator-associated pneumonia (VAP) during their PICU stay were screened. Patients with chronic heart and lung diseases, who were immune-compromised, or aged <1 month were excluded from this study. A sample size of 81 children with severe pneumonia on MV was required to detect a prevalence of bacterial pneumonia of 70%, alpha error 0.05%, and a precision of 10% [9].

2.1. Definitions

Enrolment of patients depended on CDC criteria for diagnosis of pneumonia on MV, depending on clinical, laboratory, and radiologic findings [10]. According to the origin of infection, enrolled patients were classified into:

- Community-acquired pneumonia (CAP): ventilator-associated pneumonia with the infection occurring outside hospital or

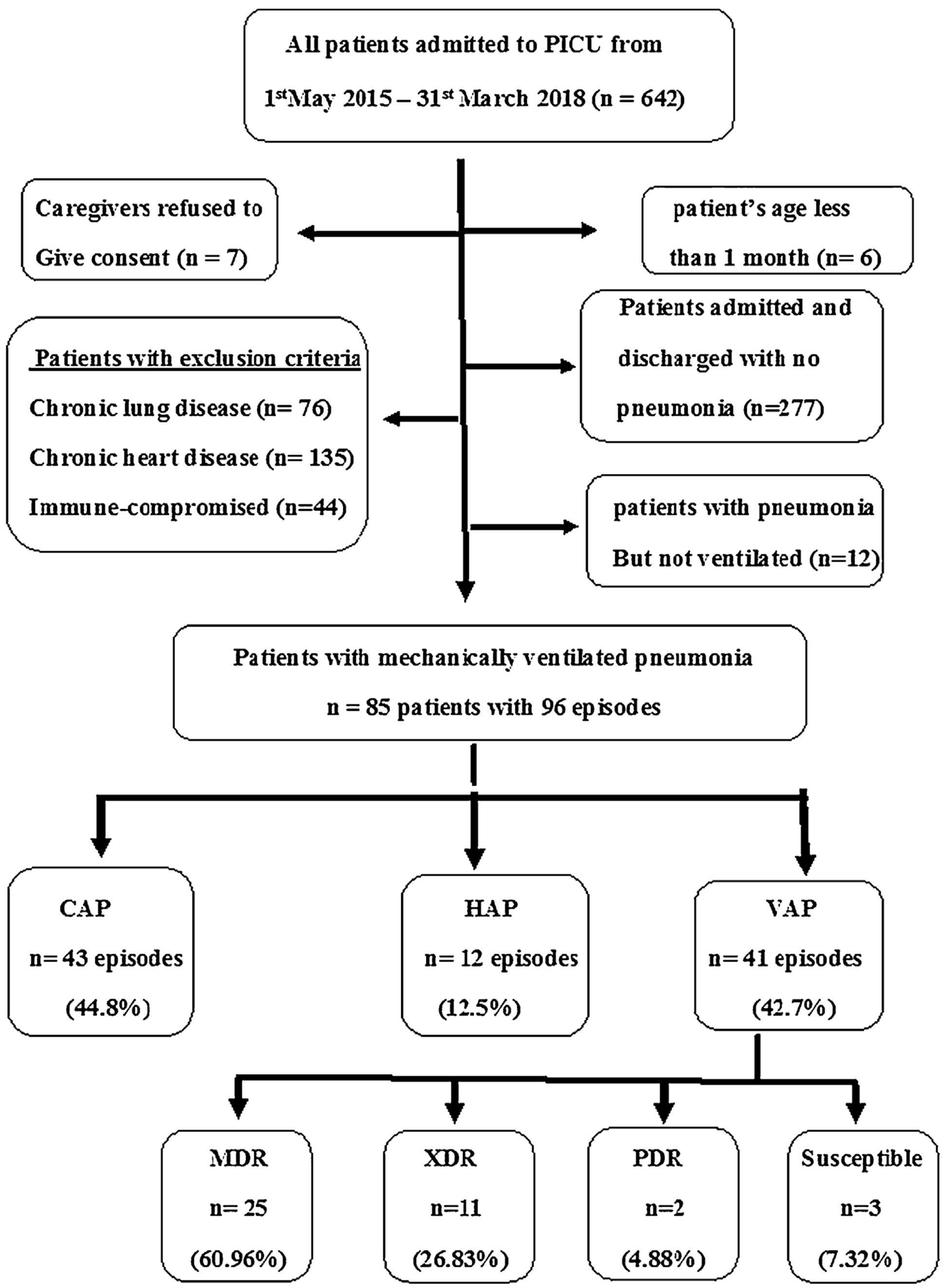

Fig. 1. Record strategy of recruitment of the studied population.
PICU, paediatric intensive care unit; CAP, community-acquired pneumonia; HAP, hospital-acquired pneumonia; VAP, ventilator-acquired pneumonia; MDR, multidrug resistant; XDR, extensively drug resistant; PDR, pan drug resistant

within the first 48 h of admission to hospital in a patient with no history of visiting any healthcare facility for the preceding 90 days.

- Hospital-associated pneumonia (HAP): ventilator-associated pneumonia with the infection occurring ≥48 h after hospital or healthcare facility admission.
- Ventilator-associated pneumonia (VAP): infection occurring ≥48 h from PICU admission and attachment to MV [11].

2.2. Sampling and microbiological testing

Two non-bronchoscopic bronchoalveolar lavage specimens were collected upon diagnosis and before the start of empiric antibiotics [12]. The following was performed from non-bronchoscopic bronchoalveolar lavage specimens:

- Gram-stained film to show the presence of polymorphonuclear cells, bacteria and fungi if present.
- Semi-quantitative culture on blood and MacConkey's agar plates. Growth of bacterial colonies of count $\geq 10^4$ colony-forming unit (CFU)/mL were considered significant. Full identification of these colonies was achieved using colonial morphology, Gram-stained film, and the appropriate set of biochemical reactions.
- Culture on modified chocolate agar plates supplemented by isovitalex (BD, USA) and bacitracin antibiotic (300 μg/mL) was used for the selective isolation of *Haemophilus influenzae* (after incubation in 5–10% CO2 at 35–37 °C for 24–48 h).
- Culture on Sabouraud dextrose agar plates was performed to identify candida species. Further confirmation was achieved with Gram-stained film.

Antibiotic susceptibility testing was performed for all significant bacterial isolates by the disc diffusion method using Clinical Laboratory Standards Institute guidelines [13]. Resistance pattern was stratified according to Magiorakos et al. [14] into:

- *Multidrug resistant* (MDR):organisms that acquire non-susceptibility to at least one agent in three antimicrobial categories.
- *Extensively drug resistant* (XDR): organisms that are non-susceptible to at least one agent in all but two or fewer antimicrobial categories.
- *Pan drug resistant* (PDR): organisms that are non-susceptible to all agents in all antimicrobial categories.

The serum specimen was used for detecting immunoglobulin IgM to *Mycoplasma pneumoniae* and *Chlamydia pneumoniae* by means of an enzyme-linked immunosorbent assay (ELISA) (Ridascreen, Germany) according to the manufacturer's recommendations.

2.3. Statistical analysis

Analysis was performed using statistical package for social science SPSS program (version 21) [15]. Kolmogrov–Smirnov test of normality revealed significance in the distribution of the

Table 1
Demographic data and comparison between survival and non-survival groups.

Characteristic	Total N = 85 patients	Survival N = 56 (65.88%)	Non-survival n = 29 (34.12%)	Test of significance (*P*-value)
Age, months, median (IQR)	7.00 (3.00–24.00)	5.00 (2.00–17.50)	17.00 (4.00–53.00)	*P* = 0.047*
Sex: n (%)				
- Males	47 (55.29%)	30 (53.57%)	17 (85.62%)	*P* = 0.657
- Females	38 (44.71%)	26 (46.43%)	12 (41.38%)	
Weight for age (Z score), median (IQR)	−1.4 (−3.30 to 0.10)	−1.40 (−3.30 to 0.05)	−1.40 (−3.20 to 0.10)	*P* = 0.908
PIM2 score, median (IQR)	17.50 (3.90–37.00)	13.00 (2.50–34.50)	33.90 (13.40–45.60)	*P* = 0.02*
PELOD† score, median (IQR)	3.00 (1.00–13.00)	2.00 (1.00–10.50)	11.00 (1.00–20.80)	*P* = 0.014*
Misuse of antibiotics, n (%)	59 (69.41%)	42 (62.69%)	17 (58.62%)	*P* = 0.707
Comorbid conditions, n (%)**	37 (43.50%)	18 (32.21%)	19 (65.52%)	*P* = 0.003*
Neurological	27 (31.76%)			
Renal	8 (9.41%)			
Endocrinal	1 (1.18%)			
Gastrointestinal	2 (2.35%)			
Nutritional	5 (5.88%)			
Burn	1 (1.18%)			
Cause of last pneumonia episode				$P_{(MC)} = 0.003$*
- Unidentified	27 (28.13%)	24 (42.86%)	3 (10.34%)	
- Gram-positive	6 (6.25%)	3 (5.36%)	2 (6.90%)	
- Gram-negative	49 (51.04%)	18 (32.14%)	22 (75.86%)	
- Atypical	8 (8.33%)	7 (12.50%)	1 (3.45%)	
- Fungal	5 (5.21%)	3 (5.36%)	1 (3.45%)	
- Gram-negative and atypical	1 (1.04%)	1 (1.79%)	0 (0.00%)	
Length of stay, days, median (IQR)	13.00 (7.00–30.00)	10.00 (6.50–26.00)	21 (12.00–51.00)	*P* = 0.02*
Days on MV, median (IQR)	10.00 (4.00–30.00)	6.00 (3.00–24.50)	18.00 (12.00–51.00)	*P* = 0.004*
Type of infection during pneumonia episodes (n = 96) (%)				$P_{(MC)} = 0.002$*
- CAI	43 (44.79%)	36 (64.29%)	7 (24.14%)	
- HAI	12 (12.50%)	6 (10.71%)	6 (20.69%)	
- VAP	41 (42.71%) ***	14 (25.00%)	16 (55.17%)	
Susceptibility pattern of organism isolated by NBBAL (n = 61)		n = 36	n = 25	$P_{(MC)} = 0.041$*
- Susceptible	6 (9.84%)	6 (16.67%)	0 (0.00%)	
- MDR	35 (57.38%)	21 (58.33%)	14 (56.00%)	
- XDR	18 (29.51%)	9 (25.00%)	9 (36.00%)	
- PDR	2 (3.28%)	0 (0.00%)	2 (8.00%)	

IQR, Interquartile range; PIM2, Pediatric Index of Mortality; MV, mechanical ventilation; PELOD†, pediatric logistic organ dysfunction score (the worst value during the length of stay) **: One patient could have more than one symptom; CAI, community-acquired infection; HAI, hospital-acquired infection; VAP, ventilator-associated pneumonia; ***: Some patients have more than one VAP episode; MDR, multidrug resistant; XDR, extensively drug resistant; PDR, pan drug resistant.
$_{(MC)}$, Monte Carlo correction for *P*-value of Pearson χ^2 test.
*Statistically significant ($P < 0.05$).

variables, so non-parametric statistics were adopted. Data were described using minimum, maximum, median and interquartile range. Categorical variables were described using frequency and percentages. Comparisons were carried out between two studied independent variables using Mann–Whitney U test. The χ^2 test was used to test association between qualitative variables. Monte Carlo and Yate's (continuity) correction were carried out when indicated. The binary (Cox) logistic model was used to estimate the probability of death based on independent variables. The calibration was assessed by directly comparing the observed and customised predicted mortality across subcategories of risk. The Hosmer–Lemeshow goodness-of-fit test was used, where $P \geq 0.1$ indicated acceptable calibration. Histograms and clustered bar chart were used accordingly. An alpha level was set to 5%, with a significance level of 95% and a beta error accepted up to 20%, with a power of study of 80%.

2.4. Ethical statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and national research committees and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The university ethical committee approved the study design in February 2015 (IRB: 00007555–FWA: 00018699). Informed consent was obtained from all patients' caregivers for the purpose of publication, with assurance of confidentiality of personal data.

3. Results

A total of 642 patients were admitted to the PICU during the period 1 May 2015 to the end of March 2018. After verifying the exclusion and inclusion criteria, 85 patients who were candidates for MV developed 96 episodes of pneumonia: 44.8% were CAP, 12.5% were HAP, and the remaining 42.7% were VAP (Fig. 1).

Table 1 shows the characteristics of the studied population and comparison between survived and non-survived subgroups. Statistically significant risk factors related to mortality were: older age, higher Paediatric Index of Mortality (PIM2) and paediatric logistic organ dysfunction (PELOD) scores, presence of comorbid conditions, origin of pneumonia, and infection with MDR organisms ($P = 0.047$, $P = 0.02$, $P = 0.014$, $P = 0.003$, $P = 0.002$, and $P = 0.041$, respectively).

Table 2 shows the microbial organisms isolated from 96 episodes of MV pneumonia. The majority of episodes acquired from the community (n = 43) had unidentified organisms (62.79%) followed by *C. pneumoniae* (18.6%), and the most common isolated bacteria were Gram-positive (11.62%). On the other hand, HAP and VAP were associated with Gram-negative bacteria (91.67% and 87.8%, respectively). *Klebsiella pneumoniae* was predominant among HAP (83.33%), while Klebsiella and *Acinetobacter baumannii* were equally represented among VAP (26.83% each). Fungal infection was more detected among VAP and all were of *Candida albicans* species (four of five cases). Mycoplasma was tested serologically and was negative for all of the studied population. Regarding the susceptibility pattern, MDR organisms were the most prevailing pattern among CAP, XDR organisms were more common among HAP, and PDR organisms appeared only among the VAP group. Eight cases developed more than one pneumonia episode, as shown in Table 3. Every episode was diagnosed based on the CDC criteria, including clinical manifestations, change in ventilator settings, accompanied by new radiological finding of pulmonary infiltrates, and rise of laboratory markers [10].

Fig. 2 shows the clustered bar chart of susceptibility pattern stratified within the organisms isolated in non-bronchoscopic bronchoalveolar lavage. The PDR organisms were detected only among *Acinetobacter* species, and *Streptococcus pneumoniae* isolates were all susceptible.

Fig. 3A shows the bar chart representing the susceptibility pattern of *K. pneumoniae.* It was found to be highly resistant to the majority of antibiotics, and moderately resistant to tigecycline (62%), colistin (57%), and fluoroquinolones (48–57%).

Fig. 3B shows the bar chart representing the susceptibility pattern of *A. baumannii.* It was found to be totally resistant (100%) to extended-spectrum penicillins and cephalosporins; and moderately resistant to aminoglycosides (54%) and fluoroquinolones (62%). The least resistance was reported with tigecycline (23%) and colistin (15%).

Table 2
Microbial organisms isolated during pneumonia episodes (n = 96).

Organisms	TOTAL n = 96 100%	CAP N = 43 44.79%	HAP N = 12 12.50%	VAP N = 41 42.71%
Unidentified organisms	27 (28.13%)	27 (62.79%)	0 (0.00%)	0 (0.00%)
Gram-positive bacteria	**6 (6.25%)**	**5 (11.62%)**	**0 (0.00%)**	**1 (2.44%)**
• MRSA	2 (2.08%)	2 (4.65%)	0 (0.00%)	0 (0.00%)
• *Staphylococcus aureus*	3 (3.13%)	2 (4.65%)	0 (0.00%)	1 (2.44%)
• *Streptococcus pneumoniae*	1 (1.04%)	1 (2.33%)	0 (0.00%)	0 (0.00%)
Gram-negative bacteria	**49 (51.04%)**	**2 (4.65%)**	**11 (91.67%)**	**36 (87.8%)**
• *Klebsiella pneumoniae*	21 (21.88%)	0 (0.00%)	10 (83.33%)	11 (26.83%)
• Acinetobacter	12 (12.5%)	1 (2.33%)	0 (0.00%)	11 (26.83%)
• *Pseudomonas aeruginosa*	9 (9.38%)	0 (0.00%)	0 (0.00%)	9 (21.95%)
• *Escherichia coli*	3 (3.13%)	1 (2.33%)	1 (8.33%)	1 (2.44%)
• Citrobacter	1 (1.04%)	0 (0.00%)	0 (0.00%)	1 (2.44%)
• Proteus	1 (1.04%)	0 (0.00%)	0 (0.00%)	1 (2.44%)
• Enterobacter	1 (1.04%)	0 (0.00%)	0 (0.00%)	1 (2.44%)
• Stenotrophomonas	1 (1.04%)	0 (0.00%)	0 (0.00%)	1 (2.44%)
Chlamydia pneumoniae	8 (8.33%)	8 (18.60%)	0 (0.00%)	0 (0.00%)
Mixed *Chlamydia pneumoniae* and Acinetobacter	1 (1.04%)	0 (0.00%)	1 (8.33%)	0 (0.00%)
Fungal infection: *Candida albicans* susceptibility pattern of isolates[a] n = 61	5 (5.21%)	1 (2.33%)	0 (0.00%)	4 (9.76%)
• Susceptible	6 (9.84%)	3 (37.50%)	0 (0.00%)	3 (7.32%)
• MDR	35 (57.38%)	5 (62.50%)	5 (41.67%)	25 (60.98%)
• XDR	18 (29.51%)	0 (0.00%)	7 (58.33%)	11 (26.83%)
• PDR	2 (3.28%)	0 (0.00%)	0 (0.00%)	2 (4.88%)

The bold values represent the total of gram negative bacteria that is stratified below into different organisms.
[a] Patients with chlamydia were serologically diagnosed and not tested for susceptibility. CAI, community-acquired infection; HAI, hospital-acquired infection; MRSA, methicillin-resistant *Staphylococcus aureus*; MDR, multidrug resistant; XDR, extensively drug resistant; PDR, pan drug resistant.

Table 3
Characterisation of cases with multiple episodes of pneumonia (n = 11 episodes).

Cases	Time interval between episodes	Organism	Susceptibility pattern
Case 1			
Episode 1		Acinetobacter	XDR
Episode 2	30 days	Pseudomonas	MDR
Episode 3	15 days	Acinetobacter	PDR
Case 2			
Episode 1		Pseudomonas	MDR
Episode 2	14 days	*Klebsiella pneumoniae*	XDR
Episode 3	20 days	Pseudomonas	MDR
Case 3			
Episode 1		Pseudomonas	MDR
Episode 2	20 days	Acinetobacter	PDR
Case 4			
Episode 1		Acinetobacter	MDR
Episode 2	12 days	*Staphylococcus aureus*	Susceptible
Episode 3	15 days	Pseudomonas	Susceptible
Case 5			
Episode 1		Sterile	
Episode 2	6 days	Candida	MDR
Case 6			
Episode 1		Sterile	
Episode 2	10 days	*Klebsiella pneumoniae*	MDR
Case 7			
Episode 1		Pseudomonas	MDR
Episode 2	20 days	*Klebsiella pneumoniae*	MDR
Case 8			
Episode 1		Sterile	
Episode 2	5 days	*Klebsiella pneumoniae*	XDR

MDR, multidrug resistant; XDR, extensively drug resistant; PDR, pan drug resistant.

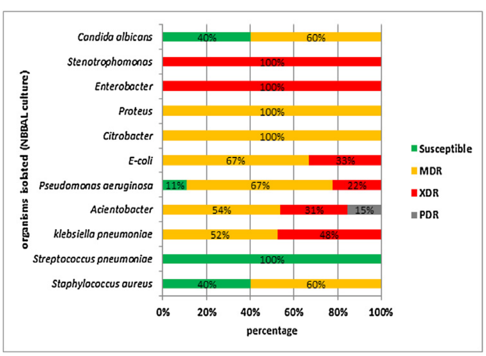

Fig. 2. Clustered bar chart of susceptibility pattern of organisms isolated in non-bronchoscopic bronchoalveolar lavage during pneumonia episodes.
MDR, multidrug resistant; XDR, extensively drug resistant; PDR, pan drug resistant

Fig. 3C shows the bar chart representing the susceptibility pattern of *Pseudomonas aeruginosa*. The organism was found to be highly resistant to anti-pseudomonas penicillin, carbapenems, and fluoroquinolones. Again, the least resistance was reported with colistin (22%) and tigecycline (11%).

Fig. 3D shows the bar chart representing the susceptibility pattern of *Staphylococcus aureus*. It was found to be moderately resistant to macrolides, aminoglycosides, fluoroquinolones, and all *Staphylococcus* isolates were sensitive to vancomycin and linezolid.

Multiple logistic regression modelling shows that pneumonia caused by MDR and XDR organisms was a statistically significant independent risk factor of mortality, regardless of the number of organ failures represented by the PELOD score. Pan drug resistant organisms were reported in two patients; both of them eventually died but the regression analysis for PDR was inapplicable due to low event rate. Infection with MDR organisms increased death probability by 6.6 times, while infection with XDR organisms increased the death probability by 9.0 times (Table 4).

4. Discussion

The current study is considered unique in providing detailed characteristics and clinical outcomes of paediatric patients with severe pneumonia indicated for MV from multiple origin: either community, healthcare or ventilator-associated pneumonia. This study revealed the difference between CAP causative organisms and those organisms causing HAP and VAP. Community-acquired pneumonia was attributed to unidentified organisms, possible viruses, in the majority of cases (62.79%) followed by *C. pneumoniae* (18.6%), and the commonest bacteria isolated were Gram-positive (11.62%). Healthcare-associated pneumonia and VAP showed more prevalent Gram-negative bacteria (91.67% and 87.8%, respectively) and less Gram-positive bacteria (2.44%) compared with CAP. Mortality significantly differed according to the causative agent and its origin ($P = 0.003$ and $P = 0.002$, respectively). The most common Gram-positive organism isolated from CAP was *S. aureus*, while the most prevalent Gram-negative organism isolated from HAP was *K. pneumoniae*; *Klebsiella* and *Acinetobacter* were equally represented in VAP.

Most studies concerned with CAP agree that Gram-positive organisms are the most prevalent organisms causing pneumonia in the community; *S. pneumoniae* is predominant in USA [15], Norway [16], India [17], and Malaysia [18]. Studies previously conducted in the Egyptian Delta [19] and Cairo [20] have revealed that *S. aureus* is the predominant organism among CAP, which was consistent with the present study. Regarding HAP and VAP, there is a worldwide agreement that Gram-negative bacteria are an increasing threat. *Acinetobacter*,*Klebsiella*, and *Pseudomonas* were estimated to be most commonly implicated in HAP [21–23]. Qureshi et al. noticed that Gram-negative bacteria were significantly associated with late-onset VAP ($P < 0.01$), whereas *Staphylococcus* was more common among early-onset VAP [23]. Kollef et al. explained this by the well-known fact that oropharyngeal and tracheal colonisation with *Pseudomonas* and enteric Gram-negative bacilli increases with length of hospital stay and severity of illness [11]. Aspiration of these organisms is higher in patients with

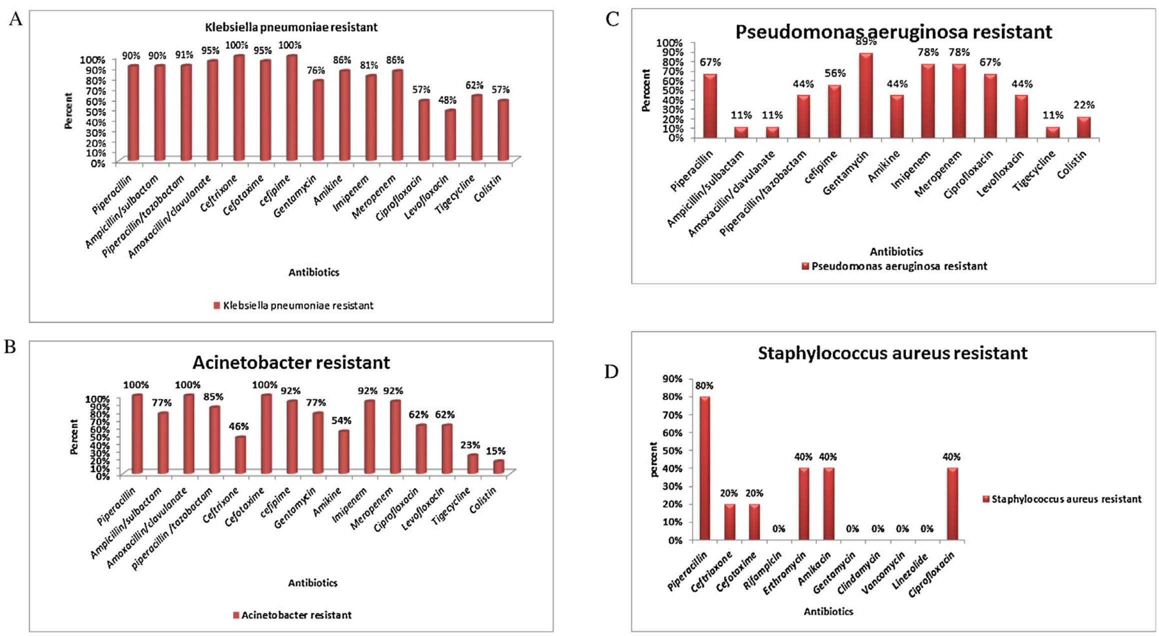

Fig. 3. (A) Bar chart of resistant pattern of *Klebsiella pneumoniae*. (B) Bar chart of resistant pattern of Acinetobacter. (C) Bar chart of resistant pattern of *Pseudomonas aeruginosa*. (D) Bar chart of resistant pattern of *Staphylococcus aureus*.

Table 4
Multiple logistic regression of the risk factors for mortality.

Predictor	Multivariate				
	B	SE	OR	95% CI	*P*-value
PELOD	0.072	0.029	1.075	1.015–1.139	0.014
NBBAL with MDR organisms	1.882	0.634	6.565	1.895–22.750	0.003
NBBAL with XDR organisms	2.192	0.724	8.953	2.166–37.011	0.002
NBBAL with PDR organisms	NA	–	–	–	–

OR, odds ratio; CI, confidence interval; PELOD, pediatric logistic organ dysfunction; MDR, multidrug resistant; XDR, extensively drug resistant; PDR, pan drug resistant; NA, not applicable due to low event rate.
*Statistically significant ($P < 0.05$).
The model was well calibrated (Hosmer–Lemeshow χ^2: 8.134, $P = 0.421$.

impaired levels of consciousness, blunted gag reflex, and higher rates of interventional procedures.

What makes things worse is the increasing emergence of antimicrobial resistance that has reached a crisis stage. In fact, the narrow spectrum of antimicrobial resistance complicates the management of nearly every patient with VAP. Antimicrobial resistance increases the likelihood of an inadequate initial antibiotic regimen [25]. The current study shows that 62.5% of CAP were attributed to MDR, 58.3% of HAP were XDR, and the remaining (41.67%) were due to MDR organisms; there was an appearance of PDR organisms (4.88%) only among VAP. The resistant bacteria were significantly associated with mortality in this studied population ($P = 0.041$). Multivariate logistic modelling revealed that pneumonia caused by MDR and XDR organisms was an independent risk factor of mortality ($P = 0.003$, $P = 0.002$, respectively), while PDR was inapplicable because there were two cases of VAP acinetobacter; both of them died but statistically this was considered to be a low event rate. These results were in accordance with almost all recent studies. Mathot et al. stated that children with MDR infection in blood or lung had a case fatality rate 1.6 times higher than infection with a susceptible organism [26]. Qureshi et al. demonstrated a statistically significant mortality rate in late-onset VAP associated with deadly superbugs ($P < 0.05$) [24]. Kollef et al. declared that mortality increases by a factor of 2.6–6.4 in critically ill patients and exceeds 70% in ventilated patients with *Pseudomonas* or *Acinetobacter* [11]. This high mortality is attributed to increasing antibiotic resistance and administration of inappropriate empiric antimicrobial therapy.

To improve antibiotic decision-making initially prescribed to patients with severe pneumonia, it is preferred to locally identify the bacterial pathogens and their susceptibility pattern. The antibiotic stewardship program currently applied in this PICU setting advocates the use of a strong β-lactam combined with a macrolide or an anti-streptococcal quinolone for CAP, and if methicillin-resistant *S. aureus* is suspected, physicians are advised to use vancomycin or linezolid. In view of the present results, CAP was mostly attributed to unidentified organisms followed by *Chlamydia*, which enhances the choice of adding macrolides in the empiric therapy. In addition, CAP was attributed to *S. aureus*, which was found to be 100% sensitive to vancomycin and linezolid. Regarding HAP and VAP, the adopted program specifies that susceptible organisms should be treated with monotherapy: either cephalosporins, quinolones, or carbapenems, while patients at risk of MDR organisms should be treated with a combination of anti-pseudomonal penicillins/cephalosporins/carbapenems with quinolones or aminoglycosides. The antibiograms of the most commonly isolated organisms causing HAP and VAP are:

(1) *Klebsiella* showed a very high range of resistance to all β-lactams and aminoglycosides (75–100%) and around 50% resistance to tigecycline and colistin.
(2) *Acinetobacter* represented a more critical organism, showing isolates of PDR in the studied population. Again, *Acinetobacter* resistance averaged 60–100% to β-lactams and fluoroquinolones, while resistance to tigecycline and colistin were 23% and 15%, respectively.
(3) *Pseudomonas* also represented a similar pattern of susceptibility. A higher range of resistance (50–80%) was reported in anti-pseudomonas penicillins, cephalosporins, aminoglycosides and carbapenems compared with a range of 10–20% resistance to tigecycline and colistin. The same findings were approved by many studies [22,27].

Owing to the previous findings, the current authors advise that the guidelines for treatment of HAP and VAP be modified when MDR organisms are suspected. The adequate empiric antibiotic option might include tigecycline and colistin in appropriate dosage and duration in a combination with quinolones, in order to avoid failure of the empiric therapy and thus improve the outcome of these high-risk patients.

This study had some limitations. First, it was a single-centre study and because of the discrepancy in diagnosis of VAP, the results could not be generalised. Second, the lack of analysis of viruses causing pneumonia, due to economic reasons, might have been the cause of the relatively high number of cases with unidentified organisms. Moreover, the detection of atypical mycobacteria using serological tests, not culture, stopped the study from analysing its susceptibility pattern. However, it was clinically noticed that all cases with *Chlamydia* adequately responded to macrolides. Even with these limitations, the study provides important preliminary data that can be used for more focused adjustment of empiric antibiotic therapy.

5. Conclusion

This study describes the causative organisms of severe pneumonia. According to study data, HAP and VAP were significantly related to Gram-negative bacteria, especially *Klebsiella*, *Acinetobacter* and *Pseudomonas*. Multidrug-resistant Gram-negative bacteria were the most critical pathogens related to VAP. Colistin and tigecycline may be used in the successful combination of treatment of these MDR Gram-negative organisms, as they showed good in vitro activity against them. Local epidemiological data like this should be collected at all centres because this information can help to decrease morbidity and mortality. This would also help to reduce development of more resistant strains.

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None.

Competing interest

None.

Ethical approval

Ethical approval and informed consent were obtained

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