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Research Article

Multidrug Resistant Bacteria in Respiratory Associated Infections at a Major Hospital in Khartoum, Sudan

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Abstract

Introduction: Respiratory associated infections caused by MDR bacteria are main reason for morbidity and mortality in the ICU, specially in a third world country such as Sudan where the basic health care practices are lacking, self medication is a norm and policies and guidelines are merely ink on paper, in this paper we take a glance at the situation of respiratory associated infections caused be MDR bacteria during the first year of the COVID-19 pandemic.

Methodology: A retrospective record review of culture results of all types of wound swabs referred to this private major hospital from 1 June 2020 to 31 December 2020 was conducted. The hospital is considered one of the few hospitals in Khartoum that conduct good microbiological procedures. This is a study based on bacteriological laboratory records review in which we have extracted a total of 77 respiratory samples (sputum, BAL, endotracheal aspiration and pulmonary fluids) culture reports using data extraction sheet. We considered all records documented during the stated time period.

Results: Out of the 77 isolated organisms, 75 (97%) were multi drug resistant (four or more) (Table 1). Poly infection was present in this study with 12 (16%) cases reported, all of which were multidrug resistant. *K. pneumoniae* showed the highest rate of isolation with 22 (29%), along with full resistance (100%) to ceftazidime, ceftriaxone, amoxiclav, aztreonam, cefepime and piperacillin, with (86%) resistance to meropenem and (75%) to co-trimoxazole. *A. baumannii* was aggressively resistant to almost all antimicrobials, showing complete resistance to meropenem, imipenem, ceftazidime, ceftriaxone, amoxiclav, aztreonam, cefepime, co-trimoxazole, ciprofloxacin and piperacillin. With high level of resistance to amikacin (90%) and (89%) to gentamycin. The only effective drug being colistin. *P. aeruginosa* appeared resistant (100%) to amoxiclav, cefepime and co-trimoxazole, and elevated rates to piperacillin (90%), aztreonam (80%), ceftriaxone (88%) and ceftazidime (75%). *S. aureus* was the most frequently isolated all of which being multi drug resistant, showing (100%) resistance to penicillin, amoxicillin, amoxiclav, ampicillin and ciprofloxacin, and high level of resistance to gentamycin, erythromycin and amikacin (80%), (86%) and (80%) respectively.

Conclusion: *K. pneumoniae* showed the highest rate of isolation and fully resistant (100%) to ceftazidime, ceftriaxone, amoxiclav, aztreonam, cefepime and piperacillin, with (86%) resistance to meropenem and (75%) to co-trimoxazole. For it and *A. baumannii* the only effective drug being colistin. *S. aureus* was the most frequently isolated all of which being multi drug resistant, showing (100%) resistance to penicillin, amoxicillin, amoxiclav, ampicillin and ciprofloxacin and high level of resistance to gentamycin, erythromycin and amikacin (80%), (86%) and (80%) respectively.

Keywords: *Multidrug Resistance; Acinetobacter baumannii; MRSA; Antimicrobial Therapy*

Abbreviations

MDR: Multidrug Resistance; AMR: Antimicrobial Resistance; MRSA: Methicillin Resistant *S. aureus*; VRE: Vancomycin Resistant *Enterococcus*

Introduction

Antibiotics are the key for the control of upper and lower respiratory tract infections. The crisis of antibiotic resistance is a major concern to clinical practice because it increases the mortality rates, clinical failure and longer hospital stays [1].

In 2017, the World Health Organization released the list of pathogens for which research and development into antimicrobial therapies are needed [2]. This list contains pathogens that are often implicated in respiratory tract infections, *Acinetobacter baumannii*, *Pseudomonas aeruginosa*; *Enterobacteriaceae*, including *Klebsiella pneumoniae* and *E coli*, *Staphylococcus aureus* (methicillin resistant, vancomycin intermediate, and vancomycin resistant); *Streptococcus pneumoniae*; and ampicillin-resistant *Haemophilus influenzae* [2,3]. In addition to *Moraxella catarrhalis*, which is frequently resistant to b-lactams.

Antimicrobial resistance can be exchanged between bacteria, for instance by mobile genetic elements; environmentally acquired; or through mutation due to selective pressures of the drugs themselves. There are various mechanisms resistance, including reduced permeability of the cell envelope, active efflux of the drug from the bacterial cell, modification or destruction of the antibiotic and alteration of the drug's target within the bacterial cell. *Haemophilus influenzae*, *Streptococcus pneumoniae*, *Mycobacterium tuberculosis* and *Pseudomonas aeruginosa* are frequently implicated in respiratory infections [2].

Often manifesting with low to none susceptibility to multiple classes of antibiotics. Some mechanisms of resistance, such as the b-lactamases that confer resistance to penicillins, carbapenemase and related drugs are widespread in clinical isolates [4].

Thus, there is a dire need for local resistance prevalence in order to guide empirical prescription. Therefore, this study was designed to identify the bacterial profile Respiratory associated infections I one private hospital in Khartoum, a study reported in one hospital is not necessarily reflecting the status of others, this is as far as an individually carried and self-funded research has come to determine the antibiotic susceptibility and resistance patterns among these pathogens in our locality. Respiratory associated infection caused by MDR bacteria are a main reason for morbidity and mortality in the ICU, specially in a third world country such as Sudan where the basic health are lacking.

Methodology

Study design and period: A retrospective record review of culture results of all types of wound swabs referred to this private major hospital from 1 June 2020 to 31 December 2020 was conducted. The hospital is considered one of the few hospitals in Khartoum that conduct good microbiological procedures.

Data collection: This is a study based on bacteriological laboratory records review in which we have extracted a total of 77 respiratory samples (sputum, BAL, endotracheal aspiration and pulmonary fluids) culture reports using data extraction sheet. We considered all records documented during the stated time period.

Isolation and identification of pathogens

The hospital microbiology laboratory received the clinical specimens (sputum, BAL, endotracheal aspiration and pulmonary fluids) during the course of routine diagnostic work up from patients. Specimens were inoculated on 5% Blood Agar and MacConkey Agar and incubated overnight aerobically at 37°C. identification of some isolates was performed based on the colonial morphology, Gram stain, and routine biochemical tests such as catalase, indole, Kilgler Ion agar, oxidase test, Motility test, Urease test, citrate test, DNase test and Litmus milk.

Antimicrobial susceptibility testing

Antimicrobial susceptibility was done by Kirby Baeur method as per the (CLSI) guidelines, using Muller Hinton agar (Hi-Media, Mumbai) and antimicrobial discs (bioanalyse, Turkey and Hi-Media, Mumbai).

The following antimicrobial agents were used: cefepime (30), Ceftazidim (30), cefuroxime (30), ciprofloxacin (5), amoxiclav (30), cephalexin (30), meropenem (10), gentamicin (10), amikacin (30), aztreonam (30), ceftriaxone (30) and colistin (10). The inhibition zones diameter was measured and data were reported as susceptible and resistant.

Ethical consideration: Approval was obtained from the lab director and administrator after submitting and presenting the research proposal.

Data processing and analysis: Data regarding antimicrobial susceptibilities, and resistance determinants were entered into a computer program. Data were analyzed using Excel and interpreted according to percentage.

Results

Out of the 77 isolated organisms, 75 (97%) were multi drug resistant (four or more) (Table 1). Poly infection was present in this study with 12 (16%) cases reported, all of which were multidrug resistant (Table 2).

Bacteria	Total number isolated	MDR
P. aeruginosa	14	12
A. baumannii	21	21
K. pneumoniae	22	22
E coli	4	4
Moraxella spp	1	1
Enterobacter spp	1	1
Citrobacter spp	1	1
S. aureus	9	9
Enterococcus spp	1	1
CONS	1	3

Table 1: *MDR bacteria causing respiratory associated diseases.*

Bacteria	Num
K. pneumoniae and *A. baumannii*	4
K. pneumoniae and *P. aeruginosa*	2
P. aeruginosa and *A. baumannii*	1
A. baumannii and *Enterobacter spp*	1
K. pneumoniae and *S. aureus*	1
P. aeruginosa and *S. aureus*	1
K. pneumoniae and *Enterococcus spp*	1
P. aeruginosa and *CONS*	1
Total	12

Table 2: *Poly bacterial infections.*

K. pneumoniae showed the highest rate of isolation with 22 (29%), along with full resistance (100%) to ceftazidime, ceftriaxone, amoxiclav, aztreonam, cefepime and piperacillin, with (86%) resistance to meropenem and (75%) to co-trimoxazole. Luckily there was complete activity against it with colistin (100%).

A. baumannii was aggressively resistant to almost all antimicrobials, showing complete resistance to meropenem, imipenem, ceftazidime, ceftriaxone, amoxiclav, aztreonam, cefepime, co-trimoxazole, ciprofloxacin and piperacillin. With high level of resistance to amikacin (90%) and (89%) to gentamycin. The only effective drug being colistin.

P. aeruginosa appeared resistant (100%) to amoxiclav, cefepime and co-trimoxazole, and elevated rates to piperacillin (90%), aztreonam (80%), ceftriaxone (88%) and ceftazidime (75%) (Table 3).

Antibiotics	***K. pneumoniae* (n = 22)**	***A. baumannii* (n = 21)**	***P. aeruginosa* (n = 14)**	***E. coli* (n = 4)**	***Enterobacter* spp (n = 1)**	***Citrobacter* spp (n = 1)**	***Moraxella* spp (n = 1)**
Colistin	0%	0%	0%	0%	0%	0%	-
Meropenem	86%	100%	54%	0%	-	100%	-
Imipenem	60%	100%	46%	0%	-	100%	-
Aztreonam	100%	100%	80%	100%	100%	100%	-
Amikacin	70%	90%	43%	25%	100%	-	0%
Gentamicin	71%	89%	64%	25%	100%	0%	-
Ciprofloxacin	85%	100%	67%	100%	100%	100%	0%
Ceftazidime	100%	100%	75%	100%	100%	100%	-
Ceftriaxone	100%	100%	88%	100%	100%	-	100%
Amoclan	100%	100%	100%	100%	100%	100%	100%
Co-trimoxazole	75%	100%	100%	100%	100%	100%	-
piperacillin	100%	100%	91%	100%	-	100%	-
Cefepime	100%	100%	100%	100%	-	-	-
Erythromycin	-	-	-	-	-	-	100%
Daptomycin	-	-	-	-	-	-	100%
Ampicillin	-	-	-	-	-	-	100%

Table 3: *Antimicrobial characterization of gram-negative bacteria.*

E. coli on the other hand appeared susceptible (100%) to colistin, meropenem and imipenem. Along with amikacin and gentamycin with a sensitivity rate of (75%) And fully resistant to all other antibiotics.

Enterobacter spp appeared susceptible to colistin only, with *Citrobacter spp* being sensitive to only colistin and gentamycin.

Regarding gram-positive, *S. aureus* was the most frequently isolated all of which being multi drug resistant, showing (100%) resistance to penicillin, amoxicillin, amoxiclav, ampicillin and ciprofloxacin and high level of resistance to gentamycin, erythromycin and amikacin (80%), (86%) and (80%) respectively. The most effective drug was vancomycin. The *coagulase negative staphylococci (CONS)* were entirely resistant to penicillin, amoxiclav and co-trimoxazole, and sensitive to imipenem (100%).

Enterococcus spp was aggressively resistant to all antimicrobials, with only vancomycin for treatment (Table 4).

Antibiotic	*S. aureus* (n = 9)	*Enterococcus* spp (n = 1)	CONS (n = 3)
Vancomycin	0%	0%	50%
Meropenem	50%	100%	0%
Imipenem	25%	-	0%
Penicillin	100%	100%	100%
Ampicillin	100%	100%	-
Amoxiclav	100%	100%	100%
Ciprofloxacin	100%	-	33%
Gentamicin	80%	-	50%
Erythromycin	86%	100%	100%
Amikacin	80%	-	50%
Co-trimoxazole	20%	-	100%
Tetracycline	50%	100%	50%

Table 4: *Antimicrobial characterization of gram-positive bacteria.*

Discussion

A global crisis such as antimicrobial resistance is a major concern, especially for developing countries like Sudan, the health care system was already collapsing long before the consequences of the COVID-19 pandemic. And for that precisely, we should be addressing this very loud killer in ICU but chosen to be ignored by a capitalized system.

In our study, the highest isolation rates were observed in *K. pneumoniae* this is consistent with the studies conducted in Sudan [5] and several other papers from India and Nigeria [6,7] Gram negative bacteria predominated the organisms in this study, similar to the results of H Farida., *et al* [8].

The highest resistance of bacterial isolates was observed to third generation cephalosporins, piperacillin, Amikacin and even carbapenems in some cases. This is contradictory to previous study conducted in Sudan [5] and other documented in hospital-based study in Egypt [9].

We reported high rates of resistance to Co-trimoxazole this is in line with study from respiratory isolates in Nigeria [10]. The present study showed extremely high resistance of *Klebsiella, Pseudomonas aeruginosa* and *Acinetobacter* to cephalosporins. This is higher than that observed in a previous study from Sudan [5].

The emergence of carbapenem-resistant *A. baumannii* and *P. aeruginosa* has been an increasing problem in many parts of the world [11,12]. *A. baumannii* showed an extreme level of resistance to carbapenem and ESBL production was observed in this study, being completely resistant to all classes of antibiotics, this is considered high resistance rate when compared to two other studies in one of which reported by Muntasir., *et al.* and Khairy., *et al.* in Sudan and another one carried in Saudi Arabia [13-15]. although Khairy's study characterized the resistant strains genotypically we recommend that for future research. fortunately, resistance colistin resistant *A. baumannii* was not reported in this study, unlike other studies in Sudan [14] and worldwide [16-18], although, rationale use of colistin is highly recommended to reduce the possible emergence of resistance to such antibiotic.

We also reported *P. aeruginosa* having (54%) resistance to meropenem and (46%) to imipenem. Our results also showed *P. aeruginosa* had low resistant rates for ceftazidime (75%), cefepime (100%) and (88%) for ceftriaxone. The resistance levels of *P. aeruginosa* to ceftazidime and cefepime were higher than that in Sudan [5] but partially consistent with the one conducted in Nepal [19]. The reason

for this deviation in the time, as the bacteria is in a consistent state of evolution and samples being collected mostly from ICU patients; I hospitable environment for MDR bacteria.

Antimicrobial resistance development throughout the years could be associated with the increase in consumption of antibiotics. Many studies linked antimicrobial consumption and bacterial resistance [20]. Some antibiotics can revert to sensitive again in later years, this supports the fact that rotation of antibiotic classes minimize the emergence of resistance [21].

Conclusion

K. pneumoniae showed the highest rate of isolation and fully resistant (100%) to ceftazidime, ceftriaxone, amoxiclav, aztreonam, cefepime and piperacillin, with (86%) resistance to meropenem and (75%) to co-trimoxazole. For it and *A. baumannii* the only effective drug being colistin. *S. aureus* was the most frequently isolated all of which being multi drug resistant, showing (100%) resistance to penicillin, amoxicillin, amoxiclav, ampicillin and ciprofloxacin and high level of resistance to gentamycin, erythromycin and amikacin (80%), (86%) and (80%) respectively.

Recommendations:

1. Education of the staff on the resistance trends.
2. Establishment of clear guidelines for antimicrobial selection criteria.
3. Introduction of molecular techniques for the detection of antimicrobial resistance for its rapidness and reliability.
4. Improving documentation of medical records.

Conflict of Interest

All authors declared there is no conflict of interest.

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