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Original Article

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Proportion of MDR/XDR and PDR in an ICU of Tertiary Care Hospital: Are Newer Treatment Options Enough?

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ABSTRACT

Background: The resistance among pathogenic organisms to different antimicrobial drugs has emerged as a cause of public health threats all over the world. Antimicrobial resistance has been identified as one of the main concerns affecting health and the health economy in several reports, including those from the World Health Organization (WHO), the Infectious Diseases Society of America (IDSA), and the UK government. Among gram-negative bacteria, members of *Enterobacteriaceae* such as *E. coli*, *Klebsiella* sp., *Enterobacter* sp., *Proteus* sp. and among non-lactose fermenters, *Pseudomonas* sp., *Acinetobacter* sp. have been associated with multidrug-resistant bacterial infections.

Methods: All clinical specimens (blood, respiratory samples, skin and soft tissue infections samples and urine samples) received in the Microbiology laboratory from various ICUs during the study period (January 2019 to December 2020) were included in the study. Retrospective analysis was performed.

Results: Out of 21208 samples received 4514 samples were culture positives among which 2103 (46.5%) were from ICUs. Among the isolates, multidrug-resistant organisms (MDROs) were more than extensive drug-resistant (XDR) and pan-drug-resistant (PDR). Blood specimens only showed MDRs, no XDRs or PDRs, showing lesser antibiotic pressure whereas respiratory, skin, and soft tissue and urine specimens showed MDRs and PDRs, this may be due to positive antibiotic pressure due to overuse or misuse of antibiotics.

Conclusion: This study highlights the fact that the burden of MDRs is more compared to XDR and PDRs which gives a ray of hope to still reduce these MDRs. It also enforces the need to prevent the emergence of XDRs and PDRs through proper infection prevention control practices and antibiotic stewardship programs and judicious use of available antibiotics.

Key-words: Extensive drug-resistant, Multidrug resistance, Pan drug resistance, Antibiogram, Antibiotic Stewardship Program

INTRODUCTION

Patients in critical care units are subjected to advanced antibiotics and face a heightened risk of infections with multidrug-resistant organisms, leading to increased mortality rates, higher hospitalization costs, and extended duration of hospital stays. While antibiotic resistance affects the global economy, the examination of its burden has been insufficiently explored in low and middle-income countries (LMICs). The increase in population income, reduction in drug prices, and lack of regulation in sales have contributed to a surge in antibiotic usage, resulting in elevated resistance rates [1]. Globally spreading antibiotic resistance in bacteria has put treatment and results for diseases acquired in

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healthcare facilities at risk [2]. Antimicrobial resistance has been identified as one of the main concerns affecting health and the economy in several official publications, including those from the World Health Organization (WHO), the Infectious Diseases Society of America (IDSA), and the UK government [2]. Enterobacteriaceae such as *E. coli, Klebsiella* sp*., Enterobacter* sp*., Proteus* sp. and among non-lactose fermenters, *Pseudomonas* sp., *Acinetobacter* sp. are the major culprits causing multidrug-resistant bacterial infections? Standardized criteria for MDR, XDR, and PDR microorganisms have been proposed by the Centers for Disease Control and Prevention (CDC), Atlanta, and the European Center for Disease Control (ECDC). Guidelines defined multidrug resistance (MDR) as resistance to at least one agent in three or more antimicrobial groups. PDR was defined as non-susceptibility to all agents in all antimicrobial categories, whereas extensively XDR was defined as non-susceptibility to at least one agent in all but two or fewer antimicrobial categories specified.[3]

There are very limited treatment options which are available to the treating clinicians. No new drugs are there in the pipeline. Pharmaceutical companies are not investing much in the research and development of newer molecules. The newer drugs that are being introduced are combinations of previous molecules or slight changes in their structure leading to a new product [4,5].

There is also the revival of older molecules that were not used because of related side effects [6,7]. In this scenario, it becomes very important for any hospital to have data on the prevalence of organisms along with their sensitivity. Data also helps any hospital to have a strong antibiotic stewardship program [8]. Antibiogram helps in deciding the empirical antibiotic before the actual result of cultures is available. Once the sensitivity is available antibiotics can be chosen as per the report.

MATERIALS AND METHODS

Study Design: Retrospective study

Study period: January 2019 to December 2020

Definitions- Acquired resistance to at least one agent in three or more antimicrobial categories was referred to as multidrug resistance (MDR).

According to the definition of XDR, a bacterial isolate is only susceptible to one or two antimicrobial categories if it is not susceptible to at least one agent in the remaining two or fewer categories.

Non-susceptibility to all drugs in all antimicrobial groups, including polymyxins, was the definition of PDR [9].

Inclusion Criteria- All clinical specimen (blood, respiratory samples, skin and soft tissue infections samples and urine samples) received in the Microbiology laboratory from various ICUs during the study period was included in the study.

Exclusion Criteria- Duplicate isolates obtained from different samples of the same patient were excluded from the study.

Methodology- All the clinical specimens were analyzed retrospectively during the study period for organisms isolated in each category of specimens and their antibiotic susceptibility was analyzed. Results are tabulated in percentage and proportion of MDR, XDR and PDR organisms in various specimens from ICUs during the study period were analyzed and expressed as percentages and graphs and were compared with various published data.

Since it is a retrospective analysis, all specimens were processed according to the standard accepted culture procedure using blood agar, chocolate agar and Mac Conkey agar. Blood cultures were taken in an automated blood culture system (Bactec9120 BD). The isolates were identified using Vitek 2C (biomereiux). Antibiotic susceptibility testing was done using both manual and automated sensitivity systems using Vitek 2C interpreted using CLSI M100 S23 guidelines.[10] The antibiotics tested were aminoglycosides like gentamicin, amikacin and netilmicin, cephalosporins like ceftriaxone, ceftazidime and cefipime, carbapenems like meropenem, imipenem and doripenem and others like cefepime tazobactum, colistin, polymyxin B, tigecycline, minocycline and ceftriaxone sulbactum EDTA.

Statistical Analysis- The study conducted the statistical analysis using SPSS-27 and calculated the frequencies and percentages using MS Excel. The continuous data has been expressed as mean +/- SD, while discrete data has been expressed in the form of frequency. The level of significance was $p<0.05$.

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RESULTS

Out of 21208 samples received from January 2019 to December 2020 at the microbiology laboratory, 4514 samples were culture positives. Out of 4514 culture positives 2103(46.5%) were from ICUs. Isolates are shown in Table 1 (Blood isolates and Urine isolates), and Table 2 (Respiratory isolates, and Skin and soft tissue isolates). Data revealed that *Klebsiella sp.* is most prevalent in blood isolates, *Acinetobacter* sp. is most prevalent in Respiratory and skin and soft tissue infections samples and *E coli* is the most prevalent isolate in urine samples. XDR and PDR are more prevalent in *Klebsiella* sp., *Pseudomonas* sp., and *Acinetobacter* sp. XDR/MDR/PDR from the above-mentioned samples are summarized in Table 3. Fig. 1-4 illustrates the sensitivity of the isolates that were taken from the four categories.

Table 1: Isolates from Blood and Urine specimens

Isolates from clinical specimens	Blood (%)		Urine (%)	
Isolates	**No**	**%**	**No**	**%**
Acinetobacter sp.	23	10	35	6
Aspergillus sp.	23	10	-	-
Candida sp.	47	21	145	24
Enterococcus sp.	22	10	77	13
E. cloacae	5	2	9	1
E. coli	29	13	130	21
K. pneumoniae	57	26	109	18
NLF	15	7	19	3
P. aeruginosa	10	4	70	11
S. aureus	15	7	16	3
Total	223	100	610	100

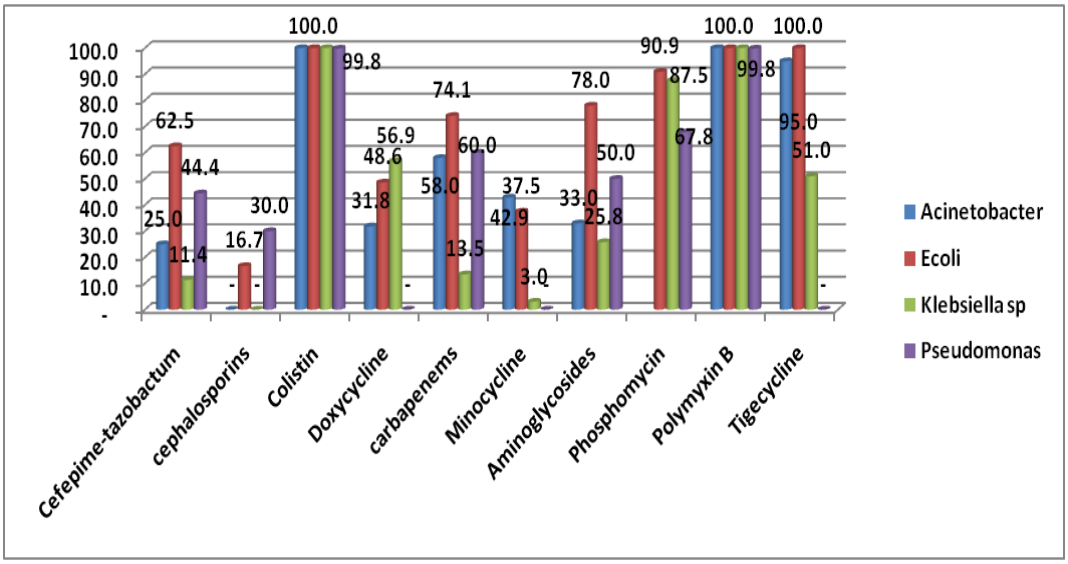

Fig. 1: Sensitivity pattern in blood isolates (%)

Table 2: Isolates from Respiratory specimens and Skin & soft tissue specimens

Isolates from clinical specimens	Respiratory specimens (%)		Skin and soft tissue specimens (%)	
Isolates	**No**	**%**	**No**	**%**
Acinetobacter sp.	33	36	42	12
Aspergillus sp.	10	1	3	1

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Candida sp.	80	9	31	9
Enterococcus sp.	-	-	31	9
E. cloacae	7	1	3	1
E. coli	37	4	80	23
K. pneumoniae	280	31	70	20
NLF	53	6	16	5
P. aeruginosa	81	9	31	9
S. aureus	28	3	39	11
Streptococcus sp.	6	1	9	3
Total	915	100	355	100

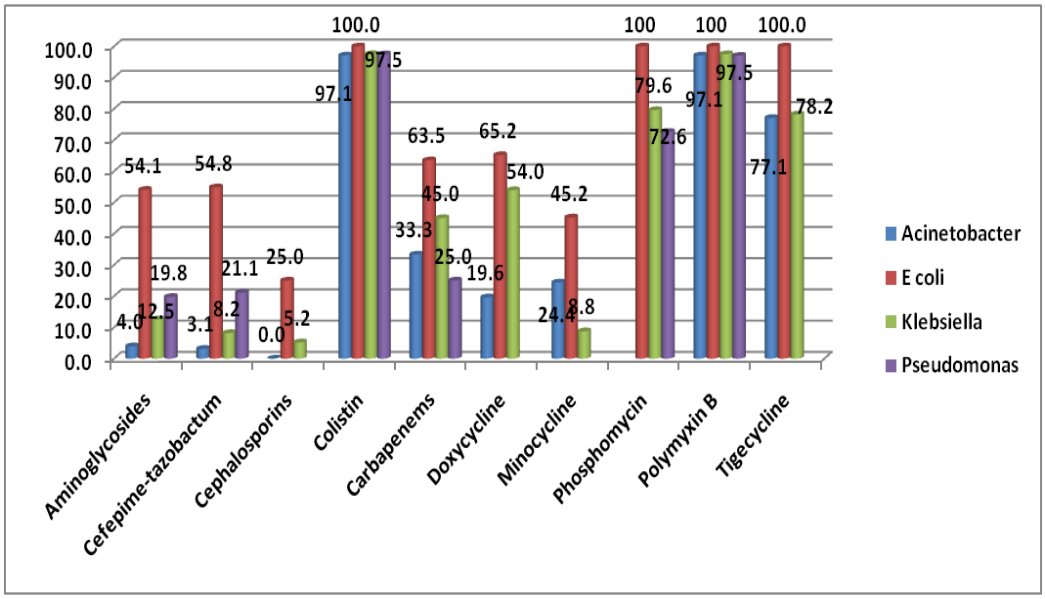

Fig. 2: Sensitivity pattern in respiratory isolates (%)

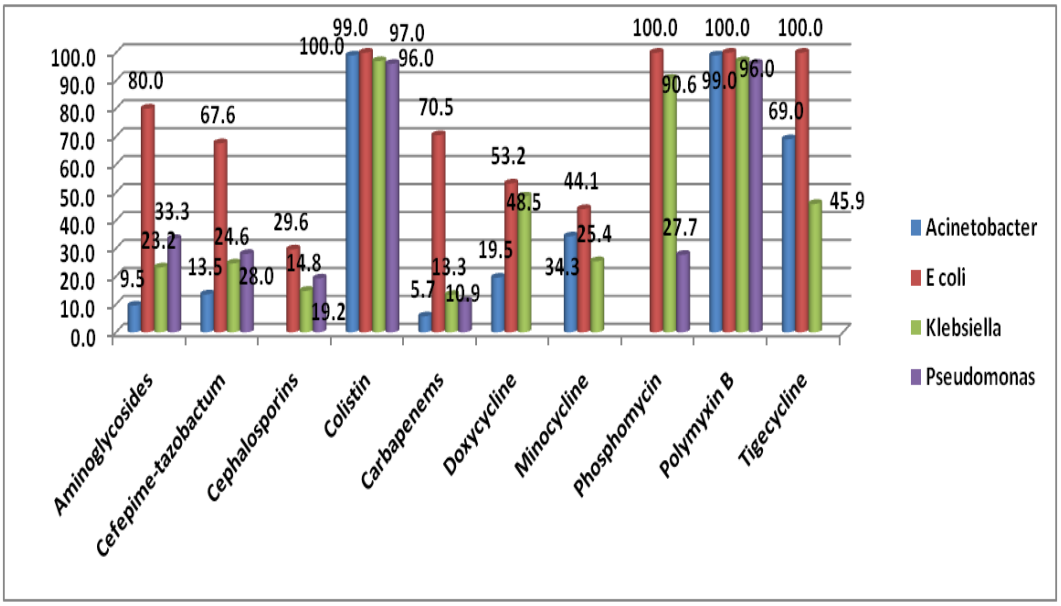

Fig. 3: Sensitivity pattern in skin & soft tissue infections (%)

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Table 3: Proportion of Resistance in percentage among the Isolates

Samples	Resistance	*Acinetobacter* sp.	*E. coli*	*Klebsiella* sp.	*Pseudomonas* sp.
Blood	XDR	0	0	0	0
	MDR	42	25.9	43.1	40
	PDR	0	0	0	1
Respiratory	XDR	0	0	0	0
	MDR	66.7	36.5	55	75
	PDR	2.9	0	2.5	2.5
SSTI	XDR	0	0	0	0
	MDR	94.3	29.5	86.7	89.1
	PDR	1	0	3	4
Urine	XDR	0	0	0	0
	MDR	90	32.6	81.9	75
	PDR	2	0	2	3.5

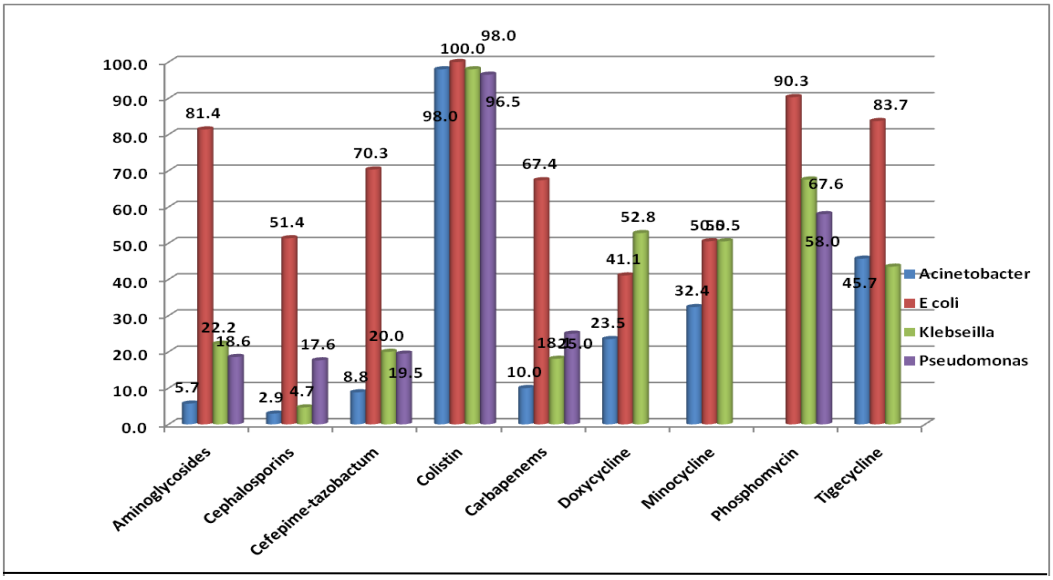

Fig. 4: Sensitivity pattern in urinary isolates (%)

DISCUSSION

This study shows that out of 21208 samples received from January 2019 to December 2020 at the microbiology laboratory, 4514 samples were culture-positive. In a study by Pattnaik *et al.*[3] at Kalinga Institute of Medical Sciences (KIMS), Bhubaneshwar Odisha, a total number of 912 Gram-negative bacterial isolates were obtained from 784 samples studied. Out of these, 375(41%) isolates were obtained from intensive care units (ICUs) and 537 isolates were from samples of clinical wards. A maximum number of isolates were obtained from urine samples (387/42.43%), followed by sputum (135/14.8%) and tracheal secretions (99/10.85%) [3]. Whereas in our study out of 4514 culture positives 2103 (46.5%) were from ICUs.

Among these 2103 isolates, 223 (10.6%) were blood isolates, 915 (43.5%) were Respiratory isolates,355 (16.8%) were skin and soft tissue isolates and 610 (29%) were urinary isolates respectively. In our study maximum number of isolates were contributed from respiratory specimens followed by urinary specimens respectively as published in other literature [11,12].

Our data revealed that *Klebsiella* sp. (26%) was most prevalent in blood isolates, whereas Acinetobacter sp. (36%) followed by *K. pneumoniae* (31%) were the most prevalent isolates in Respiratory specimens, skin and soft tissue samples and urine samples *E. coli* (23% & 21% respectively) were the most prevalent isolates like other studies [11,13]. According to a study by Pattnaik *et al.* [3], the most frequent gram-negative bacteria was *E. coli*

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(267/29.3%) followed by Klebsiella sp. (255/27.9%) and *Acinetobacter* sp. (141/15.5%). According to studies, by Agyepong *et al.* [14] (24.5%), Basak *et al.* [15] (35%), and Folgori *et al.* [16] (67.6%); the most common Gram-negative bacteria isolated was *E. coli* [3].

According to the present study data, isolates from all specimens had MDRs, whereas only respiratory, skin and soft tissue specimens and urine specimens had PDR isolates and none of them had XDR isolates [17]. PDR isolates in urine samples many times can be contaminated therefore necessitates the importance of Infection Prevention and Control practices. Therefore, repeat sample collection by healthcare workers is recommended before initiation of therapy [18] Blood isolates showed, the highest MDRs in *Klebsiella* sp. (43.1%), followed by *Acinetobacter* sp. (42%) and *Pseudomonas* sp. (40%). Whereas in respiratory isolates highest MDRs were found in *Pseudomonas* sp. (75%), followed by *Acinetobacter* sp. (66.7%) and *Klebsiella* sp. (55%). In skin and soft tissue specimens, the highest MDRs were in *Acinetobacter* sp. (94.3%) followed by *Pseudomonas* sp. (89.1%) and *Klebsiella* sp. (86.7%). In urine specimens, the highest MDRs were in *Acinetobacter* sp. (90%) followed by *Klebsiella* sp. (89.1%) and *Pseudomonas* sp. (75%). In a study by Pattnaik *et al.* [3] at Kalinga Institute of Medical Sciences (KIMS), the Bhubaneshwar Odisha MDR strain most common was *Acinetobacter* sp. 71.63% followed by *Klebsiella* sp. 71% and *E. coli* 70.04%. In the study by Agyepong *et al.* [14] most common MDR bacteria were Acinetobacter sp. (100%) and *Pseudomonas* sp. (100%) whereas Basak *et al.* [15] (31.6%) and Tohamy *et al.* [19] (38.6%) in their studies showed *E. coli* as the most common MDR strain [14-16,20].

According to a study by Morshada *et al.* [21] Dhaka Bangladesh on wound infections *S. aureus* followed by *Pseudomonas* sp., and *E. coli* were the most prevalent organisms associated with wound infections. Among the Gram-negative bacteria isolated, *Proteus* sp. (75.9%) followed by *P. aeruginosa* (72.5%) showed the highest percentage of MDR and *Klebsiella* sp. (59.1%) followed by *E. coli* (59.6%) showed the lowest studies from India.

In the present study, the most common PDR isolates were Acinetobacter in respiratory specimens whereas in skin and soft tissue specimens most common PDR isolates were *Pseudomonas* sp. and in urine specimens most common PDR isolates were *Pseudomonas* sp. [22,23].

According to the study Pattnaik *et al.* [3] PDR (0.98%) strains, four were *Acinetobacter* sp. two strains of *Pseudomonas* sp., two strains of Proteus sp. and one strain of *Klebsiella* sp.

This study shows that long hospital stays in critical care units with added unnecessary antibiotic administration led to an increase in the spread of MDR pathogens. Thus, it is important to identify and characterize the shared risk factors that may be linked to intensifying MDR trends between ICU infections. A strong antimicrobial stewardship program to combat infection is the need of the hour. The older drugs that are used can be considered with combination therapy. [24]

CONCLUSIONS

In the present study out of 21208 samples received from January 2019 to December 2020 at the microbiology laboratory, 4514 samples were culture positives. Out of 4514 culture positives 2103 (46.5%) were from ICUs. Among the isolates MDRs were more than XDRs and PDRs. Blood specimens only showed MDRs, no XDRs or PDRs, showing rationale use of antibiotics and lesser antibiotic pressure. Whereas respiratory, skin & soft tissue and urine specimens showed MDRs and PDRs, this may be due to colonization of devices and skin with MDROs and PDROs in the hospital as well as due to positive antibiotic pressure due to overuse or misuse of antibiotics. 46.5% of the isolates were from ICUs where most of the patients were on ventilators, and urinary catheters and prone to bed sores which are commonly prone to early colonization as well and clinicians are under pressure to administer higher antibiotics even before proper indications. This study also highlights the fact that the burden of MDRs is more compared to XDR and PDRs which gives a ray of hope to still reduce MDRs, XDRs and PDRs through proper Infection Prevention Control practices and Antibiotic Stewardship programs and Judicious use of available antibiotics.

CONTRIBUTION OF AUTHORS

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