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Pattern of Antibiotics Prescription and alignment with antibiotic susceptibility test results in The Intensive Care Unit in the Eastern Region of Saudi Arabia

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Abstract

BACKGROUND: The rising prevalence of multi-drug-resistant bacteria (MDRB) poses a significant challenge, particularly in intensive care units (ICUs), requiring strategic interventions to combat its impact. poses significant challenges in intensive care units (ICUs). In Saudi Arabia, limited data exist regarding MDRB prevalence and antibiotic prescribing practices in ICU settings.

OBJECTIVES: This study aims to determine the pattern of antibiotic prescribing and its alignment with the susceptibility test result among ICU patients in the Eastern Region of Saudi Arabia.

METHOD. This retrospective, cross sectional study included patients aged 18 years and older, admitted to the ICU in Dammam Medical Complex, Saudi Arabia and with a confirmed bacterial infection from 1st January to 31st December 2019. Descriptive statistics were used to describe the included patients, whereas for comparison, the student-T test for continuous variables and Chai-square test for binary regression was used. Statistical analyses were performed using Statistical Package for the Social Sciences (SPSS) software version 23.

RESULT: Among 277 patients (mean age: 49 (SD: 22) years, 56% male), Methicillin-resistant Staphylococcus aureus (MRSA) and Acinetobacter accounted for 76% of included cases. Only 17.3% of patients received antibiotic prescriptions that corresponded accurately to sensitivity test results. Carbapenems and polymyxins were the most frequently prescribed antibiotics, raising concerns due to their use even in cases with evidence of resistance.

CCONCLUSION: The low rate of alignment between antibiotic prescription and the susceptibility test result raises concerns towards suboptimal prescribing practices which potentially exacerbates resistance issues and negatively impacts on patient outcomes. Implementing strategies that incorporate local antibiograms and integration with the susceptibility test findings are essential steps toward optimizing antibiotic prescriptions, reducing resistance, and improving clinical outcomes for ICU patients with bacterial infections.

Keywords. Antibiotics, multi-drug resistance bacteria, intensive care unit, pattern of use, appropriateness.

Introduction

The increasing pattern of multi-drug-resistant bacteria (MDRB) remains as an important challenge when providing the care for seriously ill patients, particularly those within the intensive care units (ICUs).[1, 2] The World Health Organization (WHO) has classified antibiotic resistance as a critical public health threat, emphasizing the need for rigorous antimicrobial stewardship programs to optimize prescribing practices and mitigate the emergence of resistant bacterial strains.[3] Antibiotic resistance have become a significant concern in Saudi Arabia, with studies indicating that pathogens such as Methicillin-resistant Staphylococcus aureus (MRSA) and Acinetobacter baumannii are prevalent in ICU settings, complicating treatment protocols and negatively affecting care outcomes.[4, 5]

Inappropriate prescribing of antibiotics which often driven by diagnostic uncertainties and the urgent nature of care in ICU settings contributes significantly to the increasing prevalence of antibiotic resistance.[6, 7] A recent study revealed that empirical antibiotic prescriptions frequently do not align with local resistance profiles, leading to treatment failures and poor clinical outcomes in ICU care settings.[8] This finding highlights the essential need to utilize antibiotic sensitivity data to inform prescribing choices.

The relationship between antibiotic prescription and the results of antibiotic susceptibility tests is often poorly investigated, leading to a reliance on empirical therapies that may not align with local resistance patterns.[9] In the Eastern Region of Saudi Arabia, data describing the pattern antibiotic prescription and its alignments with the antibiotic susceptibility tests remains inadequate to support health authorities to fully address this global concern. Therefore, this study aims to address this gap by evaluating the pattern of antibiotic prescribing, identifying the prevalence of the prescription alignment with susceptibility test among patients admitted to ICU care setting. By addressing these aims, this study targets to highlight areas for improvement in antibiotic stewardship and provide a foundation for future interventions aimed at enhancing clinical outcomes for patients with MDRB infections. Understanding these patterns is crucial for developing tailored strategies that not only improve individual patient management but also contribute to broader public health efforts to overcome antibiotic resistance issues.

Methods

Ethical Consideration and Study population

Ethics approval was obtained from the Institutional Review Board (IRB) at Dammam Medical Complex (DMC) (Approval number PH-36, Approval date 19/11/2024). Due to retrospective nature of the study, waiving to collect approval consent were sought from the IRB. The collected data was anonymised to maintain patient confidentiality. The inclusion criteria were patients aged 18 years and above, admitted to ICU and had a confirmed diagnosis with bacterial infection during 1st of January till 31st of December 2019. Patients younger than 18 years old, pregnant woman, admitted to medical or surgical wards, admitted to ICU but not diagnosed with bacterial infection, and admitted to ICU outside the study period were excluded from the study.

Study Design, Data collection and handling

This is a retrospective, cross-sectional descriptive study. Once the patient was identified, data on demographics, medical history, microbiology, and antibiotic prescriptions were obtained from patient records. Antibiotics were classified according to the Anatomical Therapeutic Classification (ATC) system to facilitate their presentation.[10]

Antibiotic prescriptions were evaluated against the clinical records to confirm the indication of the prescribed antibiotic based on the reported pathogen in the culture test, antibiotic susceptibility test results, and according to the management guidelines [11]. Antiviral, antituberculosis, antifungal, prophylactic antibiotic prescriptions, antibiotics used for off-label, non-antimicrobial indications, such as prokinetic use, were excluded, as were cases with missing or incomplete patient records. Patients presenting with antibiotic prescriptions were categorised as either treatment or prophylaxis according to the information presented in the patients' medical records, and prophylactic treatment was excluded from the study.

In this study, patients were categorized into different categories. First, patients were categorized based on the referred ward into medical, surgical, burn and emergency department. Second classification were based on the collected sample types into wound swap, nasal swap, chest secretion, urine, and blood samples.

Statistical analysis

Descriptive statistics were used to describe the mean and standard deviation (SD) for continuous variables and the frequency and percentage (%) for binary variables. For comparison, the student-T test for continuous variables and Chai-square test for binary variables were used. Statistical analysis was performed using SPSS-v.26, whereas the GraphPad-Prism was used for figure generation.

Result

Patients Characteristics

This study included 277 patients identified with a bacterial infection. The average age was mean (SD); 49 (22) year and the majority of them were male individuals (56%) (Table 1). 19% of the patients were identified with diabetes mellitus, 8% with chronic kidney diseases, and 5% with peptic ulcer diseases. The data revealed that the majority of the patients were referred to ICU from surgical wards (42%) and emergency department (34%).

Table 1: Characteristics of the patients included.

Characteristics	Total cohort (n = 277)
Age, mean (± SD)	49 (22)
Gender,	
Male, n (%)	156 (56)
Female, n (%)	121 (44)
Diabetes mellitus, n (%)	52 (19)
Chronic kidney diseases, n (%)	23 (8)
Peptic ulcer diseases, n (%)	14 (5)
Congestive heart failure, n (%)	3 (1)
Myocardial infraction, n (%)	2 (1)
Chronic obstructive pulmonary diseases, n (%)	2 (1)
Solid tumour with metastasis, n (%)	1 (0.4)
Dementia, n (%)	1 (0.4)
Wards,	
Burn wards, n (%)	8 (3)
Emergency department, n (%)	95 (34)
Medical wards, n (%)	54 (20)
Surgical wards, n (%)	120 (43)

SD: Standard deviation

Common Reported bacteria

The data showed that 71% (n = 196) of the cohort had a bacterial culture test (Table 2). The analysis showed that the majority of the collected samples were wound swap (n = 87) and chest secretion samples (n = 66) (Table 2). Interestingly, Table 2 shows that MRSA (n = 106) and Acinetobacter (n = 105) bacteria were the most commonly identified pathogen in the collected samples.

Table 2: Prevalence and types of collected samples for culture and sensitivity test among the included patients

Characteristics	Total (n = 277)
Culture test completed,	
Yes	196 (71%)
No	81 (29%)
Sample Types,	
Blood sample	51
Wound swap	87
Chest secretion	66
Nasal swap	51
Urine sample	22
Reported microorganism,	
Methicillin resistance staph-aureus	106
Acinetobacter	105
Klebsiella	33

Pseudomonas	28
Enterococcal	4
Serratia	3
Providence	2
Proteases	2

Figures present the total number of tests completed. As patients could have more than one sample collected and diagnosed with more than one microorganism concurrently, they may be included into more than one class.

Further analyses were conducted to determine the difference in the pattern of pathogen reporting among different hospital wards and among different type of the collected samples (Figure 1). Interestingly, **Error! Reference source not found.** shows that MRSA was reported from nasal swap samples (37%) and wound swap samples (34%), were Acinetobacter were reported from wound swap samples (37%) and chest secretion (26%) more often compared to other reported pathogen ($P < .01$). However, no difference was observed among different referring wards in terms of reported pathogen (Figure 1).

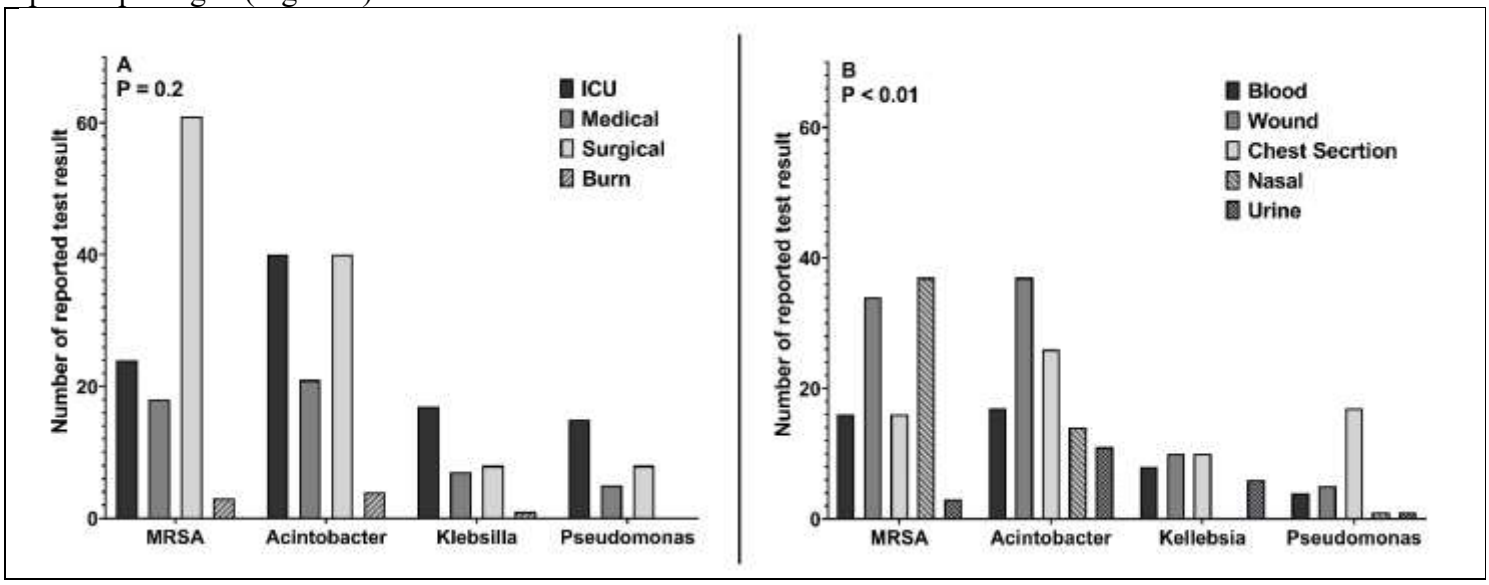

Figure 1: Pattern of the most reported multi-drug-resistant bacteria classified as; *Panel A according to the hospital wards, Panel B according to the collected sample types. P: represents P-value generated from Chi-square statistical test. MRSA: Methicillin resistance staph aurous, ER: Emergency department.*

In addition, the data revealed that ten culture tests reported two microorganisms, and one test reported three microorganisms (pseudomonas, Acinetobacter and klebsiella). The combination was common among pseudomonas (two tests with Acinetobacter and one test with either E. coli, providence, MRSA, and proteases), Acinetobacter (either MRSA, Klebsiella and enterococcal) and E. coli (with Serratia) (data not shown).

Common reported susceptible antibiotics

Further analysis was performed to identify the pattern of most commonly antibiotics reported from the antibiotic susceptibility test. A total of 168 antibiotic susceptibility test were successfully conducted for samples that have underwent complete cultural identification test (Table 3). Table 3 shows that fluroquinolone (n = 51 test), polymyxin (n = 45), aminoglycoside (n = 43), lincosamide (n = 40), sulfamethoxazole and trimethoprim combination (n = 30) and carbapenem (n = 25) were the most common reported susceptible antibiotics. The analysis revealed that 22 samples had failed the antibiotic susceptibility test as the identified bacteria were resistant to the tested antibiotics. However, 69 samples reported only one susceptible antibiotic, 41 reported susceptibility to two antibiotics, 25 reported susceptibility to three antibiotics and 11 reported susceptibility to four antibiotics to the identified microorganism (Table 3).

Table 3: Prevalence of completing the sensitivity test and the pattern of reported sensitive antibiotics

Characteristics	total
Sensitivity test completed,	
Yes	168
No	28
Reported sensitive antibiotics	
Tetracycline	4
Penicillin with beta-lactamase inhibitor	7
3rd generation cephalosporine	1
Carbapenem	25
Sulfamethoxazole and trimethoprim combination	30
Lincosamide	40
Aminoglycoside	43
Fluroquinolone	51
Glycopeptide	11
Polymyxin	45
Linezolid	10
Pattern of sensitivity report	
Resistance	22
One antibiotic	69
Two antibiotics	41
Three antibiotics	25
Four antibiotics	11

Figures present the total number of tests completed. As patients could have more than one microorganism reported in their sensitivity test concurrently, they may be included into more than one antibiotic class.

Furthermore, another analysis was conducted to determine the pattern of reporting multiple susceptible antibiotics was conducted and the result is presented in Supplementary Materials (Table S1).

Afterward, a univariate analysis using Chi-square test was conducted to assess the difference in the pattern of antibiotic susceptibility test results among different identified pathogens, referred wards, and sample types. Figure 2 presents that the antibiotic susceptibility test results differ among different identified pathogens. lincosamide (n = 38) and fluroquinolone (n = 35) were the most reported susceptible antibiotics for MRSA, polymyxin (n = 31) and aminoglycoside (n = 11) for Acinetobacter, aminoglycoside (n = 13) and carbapenem (n = 6) for Klebsiella and aminoglycoside (n = 7) and polymyxin (n = 6) for pseudomonas (Figure 2). Interestingly, lincosamide (n = 30) and floruoquinolone (n = 28) were the most reported susceptible antibiotics from samples collected from patients referred from surgical wards, polymyxin (n = 16) and aminoglycoside (n = 11) from ER, and polymyxin (n = 11) and fluroquinolone (n = 11) from medical wards (**Error! Reference source not found.**). Finally, Figure 2 represents that lincosamide (n = 23) and fluroquinolone (n = 23) were most reported susceptible antibiotics from wound swap samples, aminoglycoside (n = 18) and fluroquinolone (n = 13) from chest secretion samples, and polymyxin (n = 11) and fluroquinolone (n = 11) from blood samples.

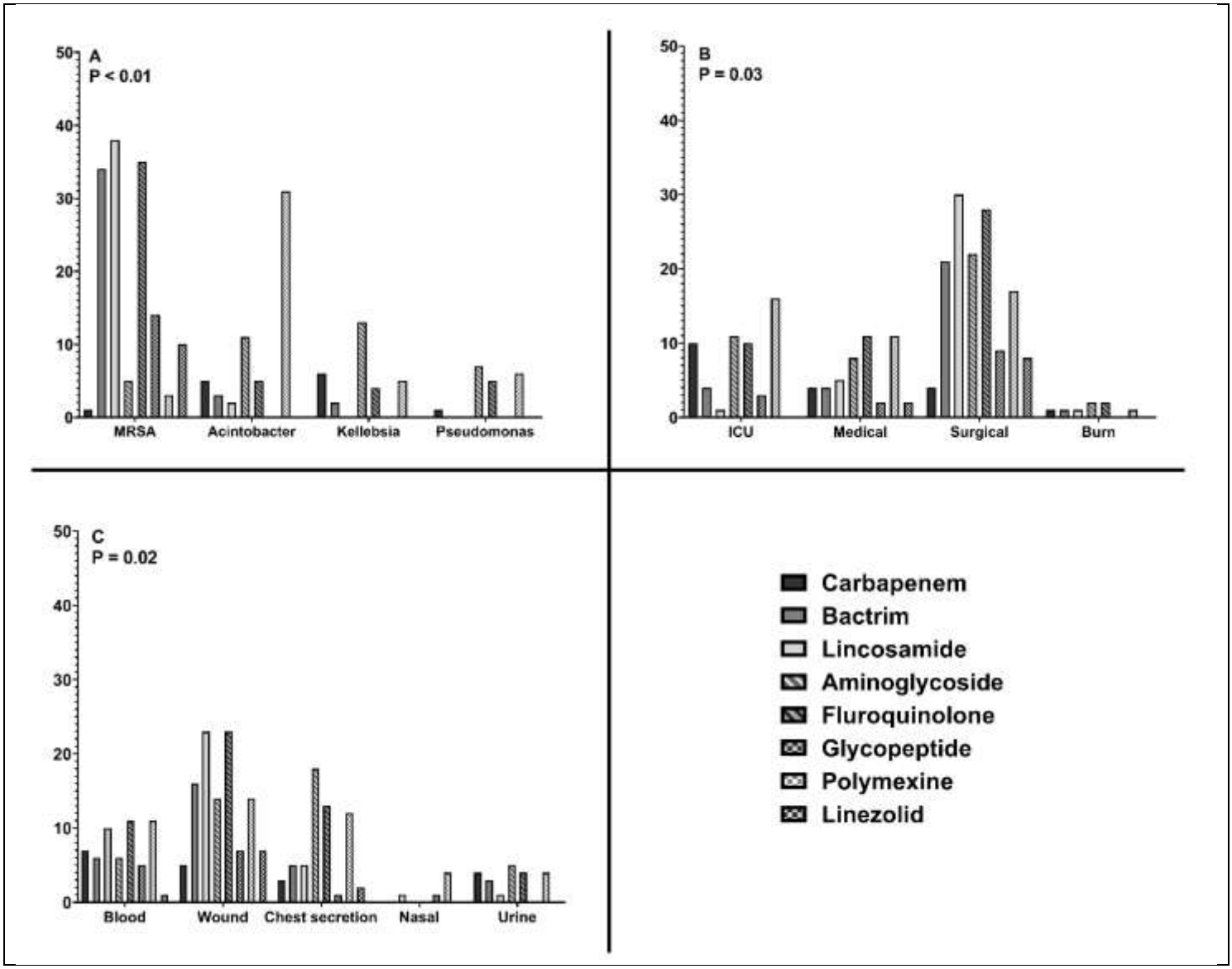

Figure 2: The pattern of antibiotic reported from the sensitivity test. *Panel A illustrates the pattern among different reported microorganisms, Panel B illustrates the pattern among different referred hospital wards, Panel C illustrates the pattern among different sample types. MRSA; Methicillin resistance staph aurous, ER; Emergency department*

Antibiotic prescription alignment with susceptibility test results

Further analysis to determine the alignment of the prescribed antibiotic with the susceptibility test result was performed. Table 4 shows that only 48 patients received an antibiotic prescription which align with susceptibility test result. The analysis also revealed that 36 patients were not prescribed an antibiotic therapy, 139 patients received a single antibiotic therapy, 87 received dual therapy, and 15 received a triple therapy (Table 4).

Beta-lactam antibiotics were the most prescribed antibiotics, as 72 patients received a carbapenem agent, 46 received a penicillin and beta-lactamase inhibitors combination and 19 received a cephalosporine agent (Table 4). Interestingly, the analysis revealed that polymyxin antibiotics (n = 72 patients), linezolid (n = 40), fluroquinolone (n = 34), glycopeptide (n = 27) and lincosamide (n = 24) were the among highest prescribed antibiotic classes (Table 4).

Table 4: Pattern of Antibiotic alignment with the sensitivity test result and prescribing pattern

Characteristics	Total
Alignment of antibiotic to the sensitivity test result	48
Total number of prescribed antibiotics for each patient	
Zero	36
One	139
Two	87
Three	15
Prescribed antibiotics	
Penicillin and beta-lactamase inhibitor	46
Carbapenem	72
Polymyxin	72
Linezolid	40
Fluoroquinolone	34
Lincosamide	24
Glycopeptide	27
Tetracycline	13
2nd generation cephalosporine	8
3rd generation cephalosporine	7
4th generation cephalosporine	4
Bactrim	2
Macrolide	6
Aminoglycoside	1
Imidazole derivative	2

Figures present the total number of tests result. As patients could have been prescribed more than antibiotic, they may be included into more than one antibiotic class.

Further analysis to assess the pattern of prescribing dual and triple antibiotic therapy was done and the result shows that carbapenem was commonly prescribed as dual combination with either linezolid or polymyxin and fluoroquinolone with lincosamide (Supplementary Materials Table S2).

Another analysis to assess the difference in the pattern of antibiotic prescribing among different reported microorganisms, different referred wards and different sample types. The analysis shows that there was no statistically significant difference within these three comparison levels (Figure 3).

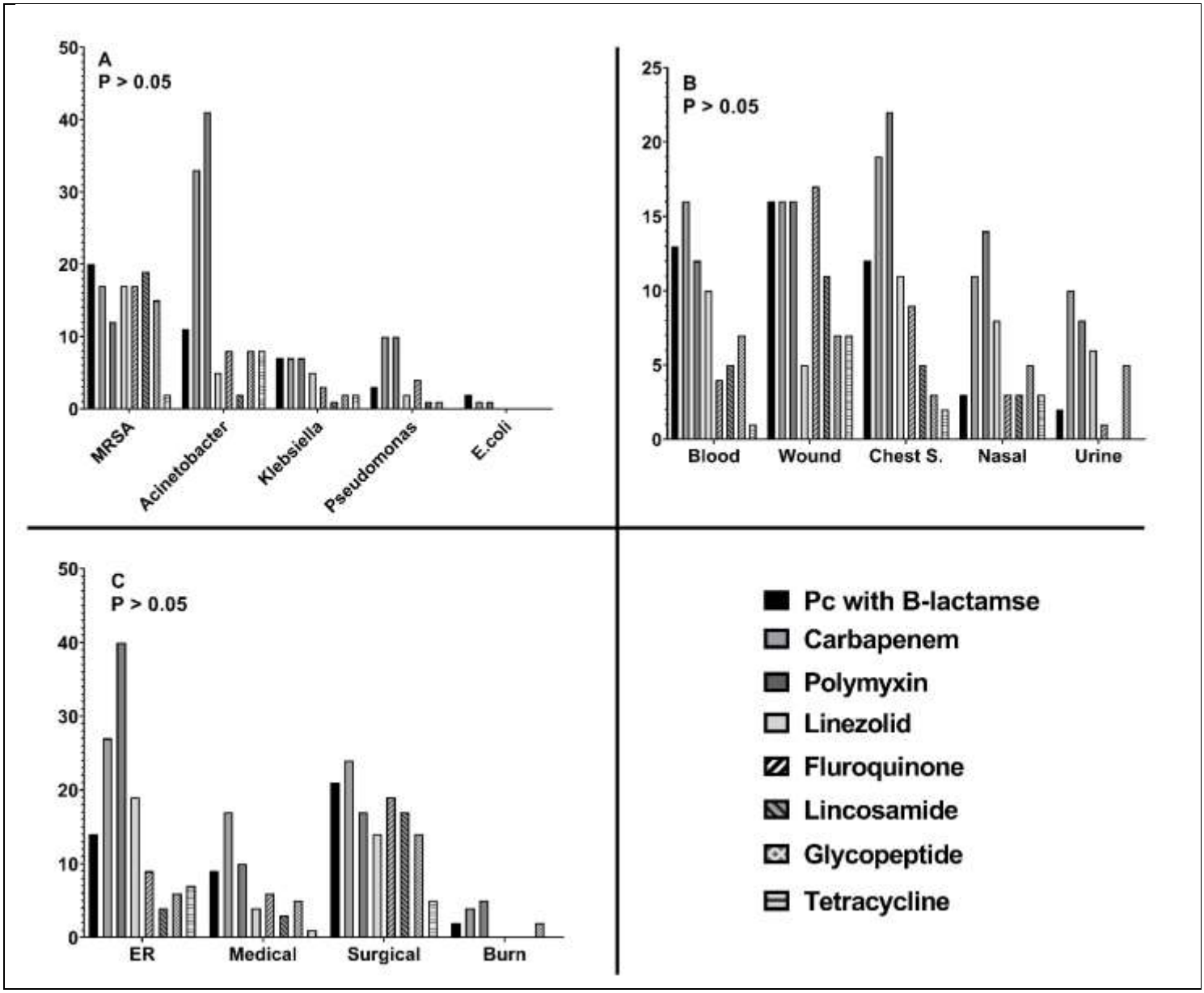

Figure 1: The prevalence and pattern of antibiotic prescribing. *Panel A shows the difference among different reported microorganisms, Panel B shows the difference among different hospital wards, Panel C shows the differences among different sample types. MRSA: Methicillin resistance staph aurous, ER: Emergency department, PC: Penicillin, C.S.: Chest secretion.*

The pattern of antibiotic prescription alignment with the susceptibility test result was assessed based on different categories. Figure 4 shows that there was no difference in the alignment pattern between different referred wards, common reported microorganisms and collected sample types. However, the analysis revealed that there was a difference in the pattern among common prescribed antibiotics, as lincosamide prescription presented a 50% alignment pattern to sensitivity test compared to linezolid (93%), penicillin (87%) and polymyxin (67%) classes ($P < .01$) (Figure 4)

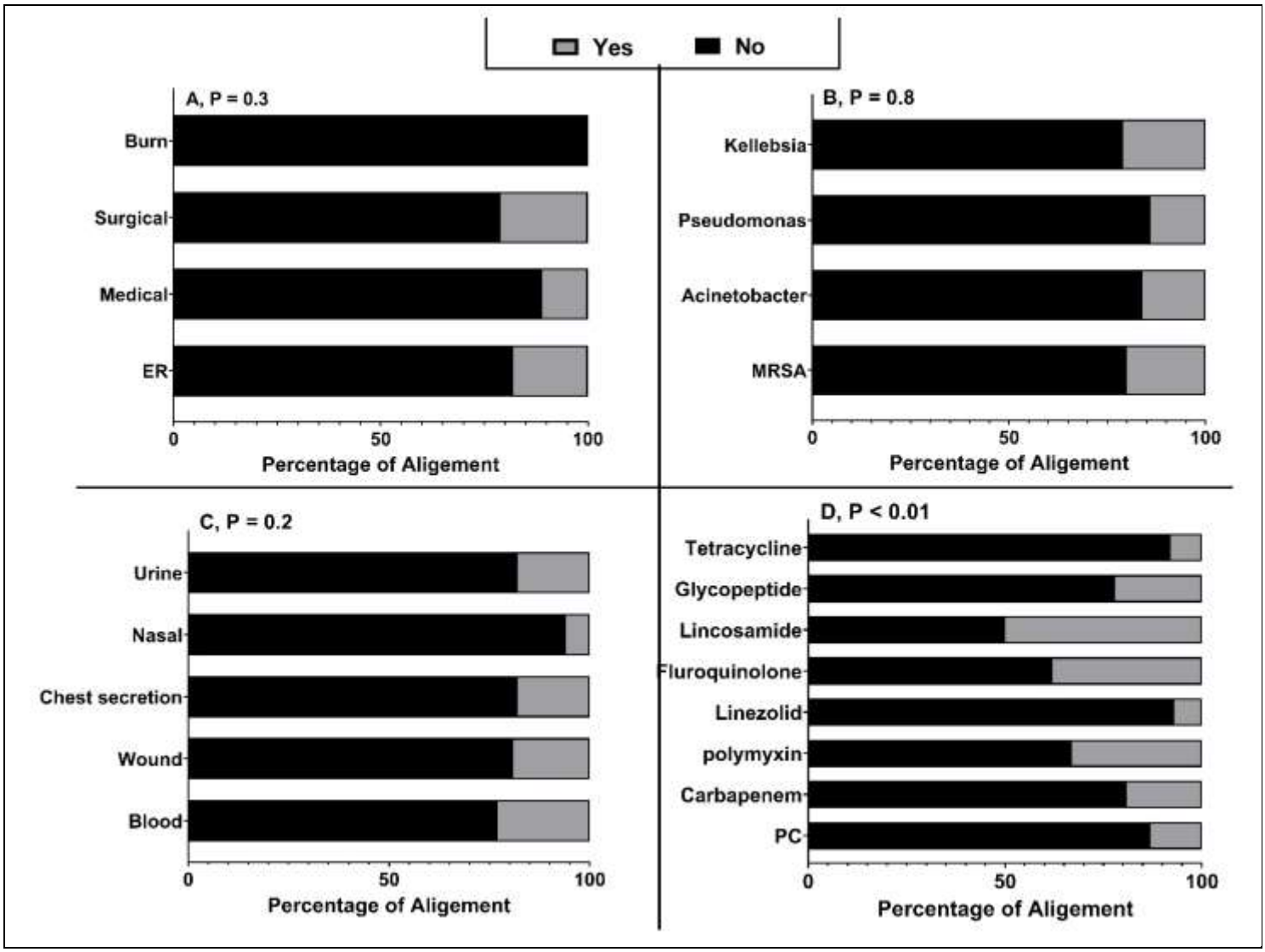

Figure 2: Pattern of antibiotic prescribing with the sensitivity test result. *Panel A illustrates difference in prescribing alignment pattern categorized per the hospital ward. Panel B illustrates difference in prescribing alignment pattern categorized per the reported microorganisms. Panel C illustrates differences in prescribing pattern categorized according to the type of collected samples. Panel D illustrates differences in prescribing pattern categorized according to common prescribed antibiotics. MRSA: Methicillin resistance staph aurous, ER: Emergency department, PC: Penicillin*

Discussion

Appropriate antibiotic prescription is essential in reducing unnecessary cost, improving patients' medical care and preventing development of MDRB.[8] One important finding from the current study is that MRSA and Acinetobacter were the most reported pathogen, together accounting for 74% of the included cases. This finding is not surprising as MRSA and Acinetobacter infections are among the top nosocomial infections worldwide and are largely associated with multi drug resistance and contributes to pneumonia, meningitis, septicaemia, wound and urinary tract infections.[6, 12] This observation is consistent with global trends reported by the Centre for Disease Control and Prevention (CDC) and the World Health Organization (WHO) which identify MRSA and Acinetobacter as major

pathogens in healthcare-associated infections.[13] The high prevalence of these organisms emphasizes the urgent need for ongoing surveillance and targeted interventions to mitigate the spread of resistant strains.

Furthermore, the analysis of antibiotic susceptibility test results revealed that fluoroquinolone and polymyxin were the most reported susceptible antibiotics. While 57% of the susceptibility test results indicated responsiveness to at least one antibiotic, the finding that 22 tests showed resistance to commonly tested antibiotics highlights the necessity for clinicians to tailor their prescribing practices based on local antibiotic susceptibility data. This finding aligns with recent study recommendations which call for the integration of local antibiograms in guiding empirical therapy.[14] Such an approach is vital in ensuring that treatment regimens are both effective and aligned with resistance patterns prevalent in the specific healthcare setting.

Interestingly, this study reported a low level of antibiotic prescription alignment with the susceptibility test results, as only 48 patients received an antibiotic prescription supported by susceptibility test, accounting for only 28% of the total cases. The most aligned antibiotics in the current study were lincasomide and fluoroquinolone, on the other hand linezolid and tetracycline were the most misaligned antibiotics. One reason for the misalignment can be contributed to the delay in getting susceptibility test results from diagnostic laboratory which could contributed to relaying on empirical prescription.[15, 16] Therefore, improving timely assessment of susceptibility tests and rapid delivery of test reports to physicians could improve alignment outcomes in the future. For instance, shifting to automated drug susceptibility machines such as BD phenoix and VITEK can provide rapid diagnosis of drug susceptibility compared to disk diffusion approach.[17, 18] In addition, holding seminars and workshops to improve communication of results and treatments between laboratories' personals and physicians could reduce cases of empirical treatments.

Another important finding is the high prevalence of carbapenem and polymyxin prescriptions, even though the susceptibility test revealed simpler antibiotic instead. These drugs are considered as the last-resort option for patients with MDRB, particularly with polymyxin when considering its toxicity profile.[5, 19] Such pattern raises the risk of emerging new resistance bacterial strains and call for further future investigations to identify the underlaying reasons of such pattern to properly manage it.[20, 21]

This study reported a survival rate of 76% among patients with drug-resistant infections, however, there remains considerable opportunity for improvement in treatment strategies. The discrepancy between the high rates of inappropriate antibiotic prescribing and the observed clinical outcomes raises concerns about the potential for deteriorating patient conditions and the exacerbation of resistance. This issue was discussed extensively in previous studies, where a direct correlation between appropriate antibiotic use and improved clinical outcomes was clearly drawn.[3, 22, 23] Consequently, it is imperative that healthcare providers adhere strictly to established national and international guidelines which emphasize the importance of customizing antibiotic therapy based on local resistance data.[9]

This study is the first of its kind to report the pattern of antibiotic prescription and its alignment with the susceptibility test results among ICU patients in the Eastern Region of Saudi Arabia. One of the key strengths of this study is the retrospective design that ensures accurate capture of alignment of prescriptions with susceptibility test reports, as both physicians and personnel in diagnostic laboratories would not be prone to change their behaviour and practices due to knowledge of the study. Another strength of the current study is the inclusion of ICU patients, which deliver a crucial information for the health authorities to support any interventional approach to manage this issue in critical practice. The inclusion of detailed information, such as, sample types, referred wards, culture test results and sensitivity test results, added extra strength to the current study, as this information could help in better assessment of antibiotic prescription appropriateness and support local health authorities to tailor their intervention to support appropriate antibiotic prescription based on different patients' characteristics. Finally, findings from this study are significant not only for local healthcare providers but also for public health authorities, informing strategies to combat antibiotic resistance on a broader scale.

In terms of limitations, this study only represents DMC and more research are needed to investigate practices in different parts of the country. Although the data used in this study described patients five years ago, most, if not all of the findings remain relevant. Since the time of data collection there has been further strategies to increase the awareness of the potential risks of inappropriate antibiotic prescribing. In DMC, an implementation of new

antimicrobial stewardship program could have improved the overall prescribing appropriateness of such antibiotics ensuring effective use with minimal side effects and risk of resistant bacterial emergence.
Although more research is needed in the future to pinpoint and understand underlaying reasons of such practices, we anticipate that such misalignment rate could be due to heavy reliance on empirical treatments by physicians due to delays in receiving sensitivity reports. Which, if true, should be tackled urgently by shifting to automated approaches to assess drug susceptibility in diagnostic labs and implementing further improvements on communication chains between physicians and laboratory personnel to ensure rapid delivery of results to physicians.
Moreover, implementing an effective antimicrobial stewardship with a robust surveillance system to monitor local antibiotic resistance patterns will empower clinicians to make informed prescribing decisions. This approach can significantly improve patient outcomes by ensuring that empirical therapies are guided by current resistance data. Finally, educating clinicians about the importance of adhering to prescribed antibiotic regimens and the consequence of misuse is crucial in adopting a culture of responsible antibiotic use.

Conclusion

This study highlights a concerning prevalence of MRSA and Acinetobacter among ICU patients in the Eastern Region of Saudi Arabia. Only 17.3% of patients received antibiotic prescriptions that aligned with antibiotic susceptibility test results, indicating a significant misalignment which potentiate risk of exacerbating resistance and negatively impacting patient outcomes. The high rates of inappropriate antibiotic prescription emphasise on the need for enhanced antimicrobial stewardship programs that incorporate local antibiograms and facilitate timely communication of sensitivity test results. By enhancing the alignment of antibiotic therapy with sensitivity data, healthcare providers can optimize treatment effectiveness, reduce the emergence of resistant strains, and improve survival rates among ICU patients with bacterial infections.

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Conflict of interest

The authors have no potential conflicts of interest that might be relevant to the contents of this manuscript.

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Ethical approval and informed consent

The study was approved by the Institutional Review Board (IRB) at Dammam Medical Complex (DMC) (Approval number PH-36, Approval date 19/11/2024). All participants were deidentified. Due to retrospective nature of the study, waiving to collect approval consent were sought from the IRB. The collected data was anonymised to maintain patient confidentiality.

Data availability

The datasets analysed during the current study were uploaded with the manuscript.

Authors' contributions

Amira Albannai; Data collection, data analysis, evaluate and modify and approving final manuscript.
Rand Ashoor and Reem Ashoor: Data coding, data analysis, evaluate and modify and approving final manuscript.

Nida Alsaffar, Hawra Al-Ghafli, Yahya Aldawood, Wessam Alsaihati, Wadie A Alsaeed, Shyma Albrahim, Mukhtar J Alomar, Bader AlAlwan and Mashael N Alanazi: Support in writing the first draft of the introduction, methods, results, and discussion, interpreted the data, and evaluated and approve the final manuscript.
Aymen A. AlQurain: Data coding, data analysis, writing first draft, and evaluated and approve the final manuscript

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