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UNNECESSARY USE OF ANTIMICROBIALS – COMPARISON OF THE PREDICTIVE PERFORMANCE OF QSOFA AND APACHE SCORE FOR EVALUATION OF DISEASE PROGNOSIS PATTERNS IN CRITICAL ILLNESS

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Abstract: *In critical care, accurate prognosis assessment, including antimicrobial therapy, is vital for guiding treatment decisions. The Acute Physiology and Chronic Health Evaluation (APACHE) and quick Sequential Organ Failure Assessment (qSOFA) scores are widely used for predicting patient outcomes. Yet, their relative performance and potential implications for antimicrobial stewardship need further exploration.* ***Objective:*** *To evaluate the disease prognosis patterns in critically ill patients by comparing the predictive performance of APACHE and qSOFA scores and to explore their correlation with antimicrobial misuse.* ***Methods:*** *A comparative study was conducted at the National Hospital and Medical Center in Lahore from January to November 2023. The study included 138 critically ill patients. Demographic information, clinical parameters, and medical history were collected, explicitly focusing on APACHE and qSOFA scores recorded at admission and during follow-up. Statistical analysis, including Pearson's and Spearman's correlation coefficients and logistic regression models, was performed using RStudio to assess the predictive ability of these scores for disease progression and patient outcomes.* ***Results:*** *The analysis revealed a moderate positive correlation (r=0.51) between qSOFA and APACHE-II scores, suggesting that both scores align in assessing the severity of illness in critically ill patients. The predictive models indicated that combining qSOFA and APACHE-II scores enhanced the accuracy of predicting critical outcomes, such as shortness of breath (SOB), with a combined model AUC of 0.659 compared to 0.601 for the APACHE-II model alone.* ***Conclusion:*** *The findings underscore the value of integrating multiple clinical scoring systems in managing critically ill patients. Such integration can aid in more judicious use of antibiotics, potentially mitigating the risk of antimicrobial resistance. The study advocates incorporating these insights into clinical guidelines and decision-making processes in critical care settings.*

Keywords: APACHE score, antimicrobial stewardship, critical care, disease prognosis, ICU, patient outcomes, qSOFA score, ventilator-associated pneumonia.

Introduction

The proliferation of antibiotic misuse and overutilization within intensive care units (ICUs) and high-dependency units (HDUs) represents a pressing and escalating issue in the care of critically ill individuals. These units constitute pivotal domains within healthcare delivery, catering to patients afflicted with severe medical pathologies necessitating specialized and attentive management. Despite their historical acclaim for revolutionizing the treatment of bacterial infections, antibiotics now manifest as a double-edged sword within these critical care environments.(1) In recent years, the misuse of antibiotics within ICUs and HDUs has escalated, propelled by a multitude of contributing factors. Among these factors is the urgency inherent to critical care environments, where quick decision-making is frequently essential to counteract life-threatening infections.(2)

In critical care, healthcare providers frequently face the imperative to promptly commence treatment, often resorting to prescription potent antibiotics as a precautionary measure, irrespective of precise diagnostic confirmation. This preemptive strategy is motivated by concerns regarding potential inadequate pathogen coverage or the emergence of resistant microbial strains. Although intended to safeguard patient health, this practice contributes significantly to antibiotic overuse, exacerbating the global challenge of antibiotic resistance.(3) Antibiotic misuse in critical care settings fuels the proliferation of drug-resistant bacteria, exacerbating the challenge of effectively treating infections. Consequently, routine medical procedures and surgical interventions become more precarious due to the heightened probability of encountering postoperative infections resistant to conventional antibiotic therapies.(4)

Furthermore, the excessive utilization of antibiotics in ICUs and HDUs subjects patients to avoidable side effects and adverse responses. Given the compromised immune status and organ impairments frequently observed in critically ill patients, their vulnerability to the harmful impacts of potent antibiotics is heightened.(5) These adverse effects span from minor gastrointestinal disturbances to more severe complications, including antibiotic-induced organ toxicity.(6) The economic ramifications of antibiotic misuse in critical care settings are substantial. Ineffectively prescribed antibiotics drive up healthcare expenditures, as hospitals must address not only the direct costs of the

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antibiotics but also the subsequent expenses associated with treating antibiotic-resistant infections and mitigating their repercussions.(7)

Effective collaboration and communication within healthcare teams are crucial in mitigating antibiotic misuse. Interdisciplinary coordination involving intensivists, infectious disease specialists, microbiologists, and pharmacists is instrumental in formulating evidence-based protocols for antibiotic administration in critical care settings. Routine evaluations of antibiotic prescriptions and feedback mechanisms enforce adherence to these protocols and promote a culture of prudent antibiotic utilization.(8)

QSOFA, an acronym for Quick Sequential Organ Failure Assessment, is a streamlined variant of the Sequential Organ Failure Assessment (SOFA) score.(9) It is a rapid bedside tool for identifying patients at risk of developing sepsis or septic shock. Comprising three criteria, QSOFA flags patients with two or more of these criteria as being at heightened risk of unfavorable outcomes. These criteria encompass a respiratory rate exceeding 22 breaths per minute, altered mental status indicated by a Glasgow Coma Scale (GCS) score of 14 or lower, and hypotension characterized by a systolic blood pressure of 100 mm Hg or lower. In contrast, APACHE, short for Acute Physiology and Chronic Health Evaluation, represents a severity-of-disease classification system utilized in intensive care settings. It aids in gauging the severity and prognosis of critically ill patients by considering various physiological parameters and additional factors.(10) Higher APACHE scores generally correlate with a more severe clinical condition.

Methodology

This comparative research study was conducted at the National Hospital and Medical Center in Lahore city from January 2023 to November 2023. It received approval from the Institutional Review Board (IRB) of the National Hospital and Medical Center Institute, adhered to ethical standards, and all participants provided written informed consent (ref no. NHMC/HR/1045).

The study cohort consisted of 138 critically ill patients admitted to the ICU and HDU during the specified period. Upon arrival at the emergency department, these patients were identified based on their critical illness status.

The primary objective was to evaluate disease prognosis patterns in critically ill patients by comparing the predictive performances of the APACHE scores and the qSOFA scores. These scores were recorded upon admission and on the completion of the third and fifth days to investigate potential correlations with antimicrobial misuse among the critically ill population.

Data collection encompassed demographic information, clinical parameters, and medical history, including APACHE and qSOFA scores at specified time points. This approach facilitated a comprehensive analysis of each scoring system's ability to predict disease progression and outcomes.

The study included a broad and diverse patient population to ensure comprehensive coverage within its scope. Participants consisted of individuals admitted to the Intensive Care Unit (ICU) and High Dependency Unit (HDU) due to critical illness, regardless of gender and age. However, certain patient groups were excluded to maintain the study's focus and validity. Patients who presented with revision cases indicated previous interventions were excluded to prevent confounding study outcomes. Additionally, individuals with post-traumatic critical illness were excluded, as the trauma could independently influence prognosis and antimicrobial use. Finally, patients younger than 17 were excluded, aligning with ethical considerations concerning the study's focus on adult populations.

We summarized the study population's clinical parameters, medical history, and treatment data. Continuous variables were expressed as mean ± standard deviation (SD), while categorical variables were presented as frequencies and percentages. This approach provided an overview of the participants' demographics, clinical presentations, and medical histories.

We visualized the distribution of APACHE-II and qSOFA scores using histograms and density plots. This enabled the identification of patterns in disease severity among the study population. The distributions were analyzed for skewness, modality, and overall spread to infer the severity levels present within the cohort.

We calculated Pearson's and Spearman's correlation coefficients to understand the relationship between qSOFA and APACHE-II scores. Pearson's correlation coefficient assessed the linear relationship, while Spearman's correlation evaluated the monotonic relationship between the scores. This analysis helped to elucidate whether higher severity levels, as indicated by one scoring system, were associated with higher levels in the other.

We employed logistic regression models to predict the probability of specific outcomes based on qSOFA and APACHE-II scores separately and combined. The outcomes were chosen based on their relevance to critical illness and potential influence on antimicrobial use. Model performance was assessed using the Area Under the Receiver Operating Characteristic (ROC) Curve (AUC), which quantifies the model's ability to discriminate between patient outcomes.

Receiver Operating Characteristic (ROC) curves were generated for each logistic regression model to evaluate its discriminative ability regarding the outcomes of interest. The AUC values were calculated to quantify each model's accuracy, with higher values indicating better predictive performance.

To further explore the associations between clinical scoring systems and patient outcomes, we conducted the Welch two-sample t-test, which was used to compare mean APACHE-II scores between two groups defined by the presence or absence of SOB, a critical outcome indicative of disease severity. We also conducted the chi-square test, which assessed the association between categorized qSOFA scores ('High' vs. 'Low') and the presence of SOB. This test determined whether the distribution of scores was related to the critical outcome.

The statistical testing was conducted in RStudio.

Results

The clinical parameters and medical history are listed in Table 1. The mean age of the participants was 66.09 ± 15.02 years. There were 73 (52.9%) males and 65 (47.1%) females. Systolic blood pressure averaged 126.92 mmHg (±26.86), while diastolic blood pressure averaged 72.89

mmHg (±14.77). The mean pulse rate was 94.04 ± 20.86 beats per minute. Participants exhibited an average body temperature of 98.44°F (±1). The respiratory rate had a mean value of 20.77 ± 5.78 breaths per minute. Oxygen saturation levels averaged 94.99% (±3.1).

Table 1. Clinical Parameters and Medical History (N=138).

Variable	Mean	Standard Deviation
	Clinical Parameters	
Age	66.09	15.02
Systolic BP	126.92	26.86
Diastolic BP	72.89	14.77
Pulse	94.04	20.86
Temperature	98.44	1
Respiratory Rate	20.77	5.78
Oxygen saturation	94.99	3.1
	Medical History	
Total leukocyte count	13.09	8.56
Inflammatory markers	14.96	17.36
Unit	1.78	0.41
Glasgow coma scale	13.36	2.44
hematocrit	36.57	6.71
Creatinine	2.07	2.39
Serum sodium	135.27	6.91
Serum potassium	4.32	0.88
Mean arterial pressure	89.07	18.63
PaO2/FiO2 ratio	521.5	582.05
APACHE Score	16.71	9.53
APACHE Mortality	21.56	24.57
QSOFA Score	0.93	0.87

In the medical history data, the total leukocyte count exhibited a mean value of 13.09 ± 8.56. Inflammatory markers had a mean value of 14.96 ± 17.36. The Glasgow Coma Scale had a mean value of 13.36 ± 2.44. Hematocrit levels averaged 36.57 ± 6.71. Creatinine levels exhibited a mean value of 2.07 ± 2.39. Serum sodium levels showed a mean value of 135.27 ± 6.91. Serum potassium levels had a mean value of 4.32 ± 0.88. The mean arterial pressure averaged 89.07 ± 18.63. The PaO2/FiO2 ratio had a mean value of 521.5 ± 582.05. The APACHE score exhibited a mean value of 16.71 ± 9.53. APACHE mortality showed a mean value of 21.56 ± 24.57. The qSOFA score had a mean value of 0.93 ± 0.87 (Table 1)

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Table 2. Patient Presentation and Treatment Overview.

Variable	Yes (Count, %)	No (Count, %)
Clinical Presentation		
Ionotropic support	32, (23.19%)	106, (76.81%)
Previous culture/sensitivity	7, (5.07%)	131, (94.93%)
Fever	43, (31.16%)	95, (68.84%)
SOB	64, (46.38%)	74, (53.62%)
Altered state of consciousness	43, (31.16%)	95, (68.84%)
Loose Motions	7, (5.07%)	131, (94.93%)
Unconsciousness	2, (1.45%)	136, (98.55%)
Right-sided body weakness	4, (2.90%)	134, (97.10%)
Aphasia	2, (1.45%)	136, (98.55%)
Lower limb swelling	4, (2.90%)	134, (97.10%)
Abdominal pain	9, (6.52%)	129, (93.48%)
RTA	3, (2.17%)	135, (97.83%)
Hemoptysis	1, (0.72%)	137, (99.28%)

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Left-sided body weakness	7, (5.07%)	131, (94.93%)
Medical Treatment		
No comorbidities	115, (83.33%)	23, (16.67%)
Diabetes mellitus	71, (51.45%)	67, (48.55%)
Hypertension	88, (63.77%)	50, (36.23%)
Ischemic heart diseases	38, (27.54%)	100, (72.46%)
Chronic kidney diseases	19, (13.77%)	119, (86.23%)
Chronic liver diseases	7, (5.07%)	131, (94.93%)
Asthma	12, (8.70%)	126, (91.30%)
Chronic pulmonary diseases	6, (4.35%)	132, (95.65%)
Cerebrovascular diseases	11, (7.97%)	127, (92.03%)
Dementia	4, (2.90%)	134, (97.10%)
Wegner's granulomatosis	1, (0.72%)	137, (99.28%)
Chronic myeloid leukemia	1, (0.72%)	137, (99.28%)
Benign prostatic hyperplasia	5, (3.62%)	133, (96.38%)
Bipolar disorder	1, (0.72%)	137, (99.28%)
Hemorrhoids	1, (0.72%)	137, (99.28%)
Secondary polycythemia	1, (0.72%)	137, (99.28%)
Medical Treatment (Injections)		
Meropenem	57, (41.30%)	81, (58.70%)
Moxifloxacin	37, (26.81%)	101, (73.19%)
Levofloxacin	16, (11.59%)	122, (88.41%)
Linezolid	3, (2.17%)	135, (97.83%)
Vancomycin	5, (3.62%)	133, (96.38%)
Ceftriaxone	32, (23.19%)	106, (76.81%)
Acyclovir	3, (2.17%)	135, (97.83%)
Piperacillin Tazobactam	22, (15.94%)	116, (84.06%)
Clarithromycin	1, (0.72%)	137, (99.28%)
Metronidazole	15, (10.87%)	123, (89.13%)
Cefoperazone	1, (0.72%)	137, (99.28%)
Vibramycin	1, (0.72%)	137, (99.28%)
Azithromycin	3, (2.17%)	135, (97.83%)
Ampicillin	3, (2.17%)	135, (97.83%)
	Medical Treatment (Conditions)	
Meningitis	1, (0.72%)	137, (99.28%)
Parkinsonism	1, (0.72%)	137, (99.28%)
Ciprofloxacin	1, (0.72%)	137, (99.28%)
Depression	3, (2.17%)	135, (97.83%)
Rheumatoid arthritis	3, (2.17%)	135, (97.83%)
Pulmonary fibrosis	1, (0.72%)	137, (99.28%)
Teicoplanin	2, (1.45%)	136, (98.55%)
QSOFA Mortality	37, (26.81%)	101, (73.19%)

The clinical presentation data reported various symptoms among the participants (Table.2). Ionotropic support was observed in 32 cases (23.19%). Fever was noted in 43 instances (31.16%). Shortness of breath (SOB) was reported in 64 cases (46.38%). A state of altered consciousness was documented in 43 cases (31.16%). Additionally, symptoms such as loose motions, unconsciousness, right-sided body weakness, aphasia, lower limb swelling, abdominal pain, road traffic accidents (RTA), and left-sided body weakness

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were observed in varying frequencies, ranging from 1.45% to 6.52%.

In the medical treatment data, several conditions were reported among the participants. Notably, 115 individuals, constituting 83.33% of the sample, had no comorbidities. Diabetes mellitus was observed in 71 cases (51.45%). Hypertension was documented in 88 instances (63.77%). Ischemic heart diseases were reported in 38 cases (27.54%). Chronic kidney disease was noted in 19 cases (13.77%). Similarly, various other conditions such as chronic liver diseases, asthma, chronic pulmonary diseases, cerebrovascular diseases, dementia, Wegner's granulomatosis, chronic myeloid leukemia, benign prostatic hyperplasia, bipolar disorder, hemorrhoids, and secondary polycythemia were observed in the dataset, with prevalence rates ranging from 0.72% to 8.7% (Table 2).

Several medications were administered to the participants who received medical treatment via injections. Specifically, 57 individuals (41.3%) received Meropenem. Moxifloxacin was administered to 37 participants (26.81%). Similarly, Levofloxacin was prescribed to 16 individuals (11.59%). Other medications such as Linezolid, Vancomycin, Ceftriaxone, Acyclovir, Piperacillin Tazobactam, Clarithromycin, Metronidazole, Cefoperazone, Vibramycin, Azithromycin, and Ampicillin were also administered, with varying prevalence rates ranging from 0.72% to 15.94% (Table 2).

Several diagnoses were identified among participants receiving medical treatment for specific conditions. Notably, a small proportion of individuals, each constituting 0.72% of the sample, were diagnosed with meningitis, parkinsonism, Ciprofloxacin, and pulmonary fibrosis. Depression and rheumatoid arthritis were reported in slightly higher proportions, affecting 2.17% of participants each. Additionally, tecoplanin was prescribed to 2 individuals, representing 1.45% of the cases. A significant portion of the sample, comprising 26.81%, was identified as having a qSOFA mortality score (Table 2).

The histogram for APACHE-II scores shows most patients have lower scores, with a small number having much higher scores, indicating a range of disease severity among the study population. The distribution of qSOFA scores among the critically ill patient cohort exhibits a pronounced initial peak at 0, suggesting that a substantial portion of these individuals present with low severity levels by qSOFA criteria. The pattern suggests a bimodal distribution where patients predominantly exhibit non-critical clinical signs or progress to more severe markers, with fewer remaining at intermediate levels of severity. Such findings highlight the potential for qSOFA to delineate patient groups requiring differing levels of clinical attention, particularly in contexts assessing the risk of sepsis or similar critical outcomes (Figure 1).

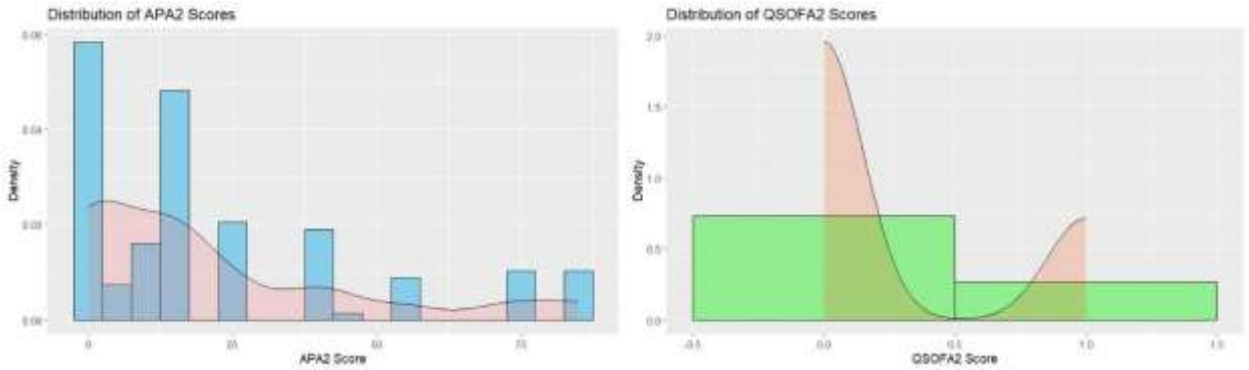

Figure 1. Histograms for APACHE-II and QSOFA Scores' Distribution.

The analysis revealed a moderate positive correlation between qSOFA and APACHE-II scores among critically ill hospitalized patients, as indicated by a Pearson's coefficient of 0.51. This suggests a linear relationship where patients with higher qSOFA scores, indicative of greater organ failure risk, also tend to have higher APACHE-II scores, reflecting more severe acute physiological disturbances. However, Spearman's correlation coefficient of 0.37 points to a weaker monotonic relationship, implying that the positive association may not strictly follow a linear pattern across the range of scores. This discrepancy could be attributed to the distribution of scores, outliers, or the inherently different aspects of patient health status that qSOFA2 and APACHE-II scores capture. Overall, the positive correlations support the premise that despite measuring distinct dimensions of patient health, both scoring systems share a relationship in reflecting patient severity in a critical care context.

The analysis revealed that the APACHE-II score model demonstrates a modest ability to discriminate between critically ill hospitalized patients with and without significant SOB, achieving an AUC of 0.601. This indicates a limited utility in using the APACHE-II score alone for guiding clinical decisions regarding antimicrobial use based on disease prognosis patterns.

In contrast, a combined model incorporating qSOFA and APACHE-II scores improved the predictive performance, reflected by an AUC of 0.659. This enhancement suggests that considering multiple dimensions of patient severity—through both qSOFA and APACHE-II scores—yields a more accurate prediction of critical outcomes such as SOB, which may relate to decisions about antimicrobial therapy's necessity.

These findings highlight the complexity of predicting disease prognosis in critically ill patients and the benefits of a combined approach to risk stratification, particularly in optimizing antimicrobial use (Figure 2).

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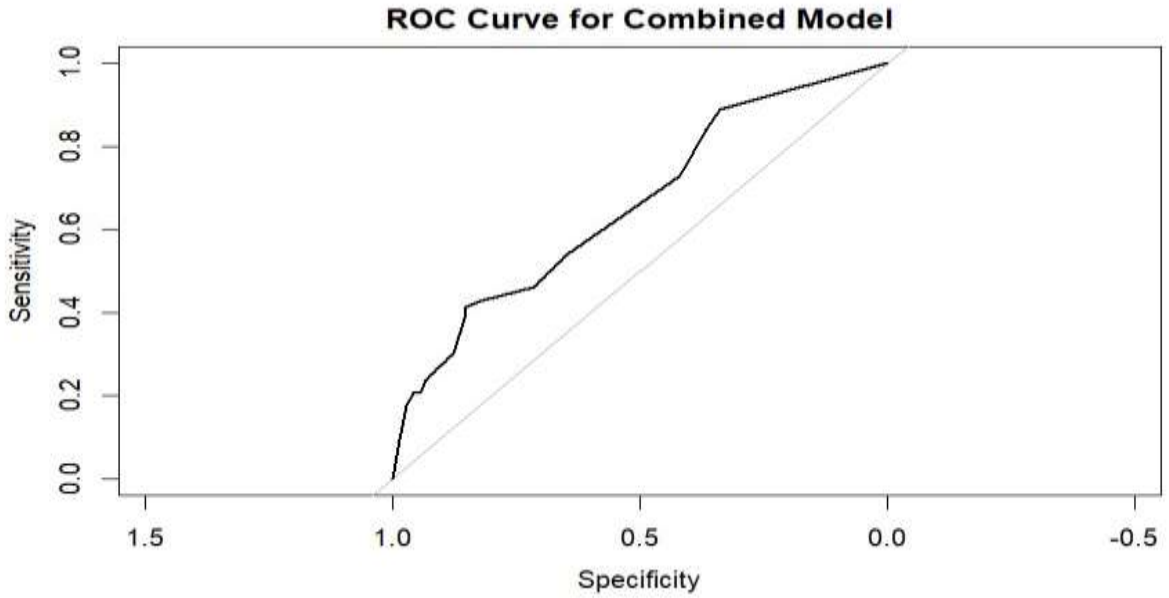

Figure 2. ROC Curve for the Combined Model- qSOFA and APACHE-II Depicting the Sensitivity and Specificity.

Our statistical analysis aimed to understand the relationships between clinical scoring systems (APACHE-II and qSOFA) and the presence of SOB among critically ill hospitalized patients. A Welch Two Sample t-test revealed a significant difference in APACHE-II scores between patients with and without SOB (P=0.01263), indicating that patients experiencing SOB tended to have higher APA2 scores. This finding underscores the potential of APACHE-II scores in identifying patients with more severe physiological disturbances.

In contrast, when qSOFA scores were categorized into 'High' and 'Low' groups, a Chi-Square test did not demonstrate a statistically significant association with SOB status (P=0.3946), suggesting the binary categorization of qSOFA scores might not be sensitive enough to detect variations in SOB presence within this patient cohort.

These results highlight the complexity of predicting clinical outcomes based on scoring systems and suggest that while APACHE-II scores may offer insights into patient severity, the binary categorization of qSOFA scores requires further evaluation for its utility in clinical decision-making regarding disease prognosis and treatment strategies.

Discussion

The misuse and overuse of antibiotics pose significant challenges in the critical care landscape of ICUs and HDUs. These settings demand rapid treatment decisions in the face of severe infections and the looming threat of antibiotic resistance. Our study delves into this issue by evaluating disease prognosis in critically ill patients and comparing the utility of APACHE and qSOFA scores in predicting the need for antibiotic therapy.

The study's descriptive synthesis outlines our patient cohort's demographic and clinical features, allowing for a deeper understanding of antibiotic use in critical care. Notably, the distribution of APACHE-II and qSOFA scores suggests a predominantly low severity level among our patients, with a distinct bimodal pattern for qSOFA scores. This pattern highlights the scores' potential to categorize patients based on severity, which is particularly relevant for assessing the risk of sepsis and guiding treatment decisions.

The correlation between qSOFA and APACHE-II scores, indicated by a Pearson's coefficient of 0.51, reveals a moderate positive linear relationship. This suggests that higher qSOFA scores, denoting increased organ failure risk, align with higher APACHE-II scores, which reflect severe physiological disturbances. However, Spearman's coefficient of 0.37 suggests this relationship is not strictly linear, pointing to the complexity of applying these scores to patient health status in a critical care context.

Our predictive modeling showed that integrating qSOFA and APACHE-II scores enhances predictive accuracy for critical outcomes such as SOB, with a combined model AUC of 0.659 surpassing the APACHE-II model's AUC of 0.601. This improvement highlights the value of an inclusive approach to severity assessment in critical care, particularly for guiding antimicrobial therapy decisions.

Moreover, our findings on the relationship between clinical scoring systems and SOB outcomes highlight the nuanced challenges of using these systems to predict clinical outcomes. While APACHE-II scores were significantly higher in patients with SOB, suggesting their potential to identify severe disturbances, the lack of significant association between qSOFA score categorization and SOB status indicates the need for refined scoring approaches to capture clinical variations among critically ill patients effectively.

Recent studies highlight the importance of a comprehensive plan to improve how antibiotics are used, teaching healthcare workers to use antibiotics wisely, improving diagnostic accuracy, and encouraging teamwork across different medical fields to follow proven guidelines for antibiotic use.(11-14) The introduction and use of better diagnostic tools, along with electronic health records and systems that help make clinical decisions, are crucial to targeting antibiotic treatment more effectively and prescribing antibiotics more appropriately.(15-17)

However, despite advancements in managing antibiotic use and technology, the issue of old prescribing habits and the

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global problem of antibiotic resistance still need ongoing attention through new ideas, research, and working together globally.(18) Finding new antibiotics and other ways to treat infections is critical to stay ahead of bacteria that are becoming resistant.(19-21) This continuous effort, along with vital programs for managing antibiotic use and teaching efforts, shows the global healthcare community's unified effort to tackle the misuse of antibiotics in places like ICUs.(22) This united approach is vital not just for improving patient care now but also for ensuring antibiotics remain effective for those needing them in the future.

While offering insights into the predictive capabilities of APACHE and qSOFA scores in the context of antimicrobial use in critically ill patients, this study has its limitations. Primarily, its observational nature and setting within a single center may limit the generalizability of the findings. Additionally, the reliance on specific inclusion and exclusion criteria, while necessary for study integrity, may restrict the applicability of results to broader patient populations. Though critical for assessing disease severity and prognosis, the study's focus on APACHE and qSOFA scores may overlook other factors influencing antimicrobial decision-making processes. Finally, the changing landscape of antibiotic resistance and advancements in diagnostic and therapeutic technologies highlight the need for ongoing research to adapt and refine critical care practices continually.

Conclusion

Our study dives into how APACHE and qSOFA scores can guide the use of antibiotics in critically ill patients, highlighting a key area where managing patient care meets the challenge of using antibiotics wisely. The findings suggest these scoring systems could lead to more intelligent, more targeted use of antibiotics, helping in the fight against antibiotic resistance. Despite some limitations, this research stresses the importance of using clinical scores to improve antibiotic decisions.

Declarations

Data Availability statement
All data generated or analyzed during the study are included in the manuscript.

Ethics approval and consent to participate.
Approved by the department concerned. (IRB-VEC-NDHL-0335/22)

Consent for publication
Approved

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Not applicable

Conflict of interest

The authors declared an absence of conflict of interest.

Authors Contribution

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Revisiting Critically
WAQAR KHALID
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Drafting & Concept & Design of Study

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