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CEPHALOSPORIN PRESCRIBING IN INTENSIVE CARE UNIT SETTINGS OF THE JORDANIAN ROYAL MEDICAL SERVICES HOSPITALS: A COMPREHENSIVE ANALYSIS OF TRENDS AND IMPACT ON ANTIMICROBIAL RESISTANCE ACROSS FOUR MAJOR HOSPITALS.

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ABSTRACT

Introduction: The escalating incidence of antimicrobial resistance (AMR) and the increasing complexity of patient circumstances necessitate vigilant monitoring and optimization of antibiotic administration. Cephalosporins are a class of broad-spectrum antibiotics extensively utilized in the treatment of serious infections, particularly within intensive care units (ICUs). Nonetheless, cephalosporins broad-spectrum efficacy also presents the risk of overutilization, leading to the emergence of resistance. The hospitals of the Jordanian Royal Medical Services (JRMS), which deliver medical care to military members and their families, represent a signific setting for analyzing cephalosporin utilization.

Objective: This study seeks to analyze the usage patterns of five intravenous cephalosporins (Cefazolin, Cefotaxime, Cefoxitin, Ceftazidime, and Ceftriaxone) in the ICUs of four prominent hospitals within the Jordanian Royal Medical Services (Princess Haya Military Hospital, King Hussein Medical Hospital, Queen Alia Heart Institute, and King Talal Military Hospital) during the years 2020-2021. The study aims to identify patterns of cephalosporin consumption, investigate hospital-specific variances in antibiotic preferences, and examine the possible influence of these changes on antimicrobial stewardship initiatives within JRMS hospitals.

Methodology: This study will collect and analyze retrospective data obtained from the medical electronic records of patients admitted to the ICU 's of the four JRMS hospitals during 2020 - 2021 to evaluate the usage of the five selected cephalosporins in the ICUs. The data will concentrate on the yearly amounts of each cephalosporin administered in each facility. The investigation will include exploring antibiotic usage data over a two-year span along with the discrepancies among facilities. The consumption data will be organized by year and hospital, and the overall usage for each medication will be computed. Statistical techniques will be utilized to detect substantial alterations in consumption patterns and to compare utilization among other hospitals. The study will also examine hospital-specific factors, including patient demographics and hospital specialization, to enhance the knowledge of prescribing habits and the potential consequences of heightened antibiotic consumption on antimicrobial resistance will also be examined, along with recommendations for future antimicrobial stewardship initiatives in JRMS institutions. This study's findings will yield significant insights for enhancing antibiotic utilization in ICU environments and enhancing patient outcomes.

KEYWORDS: Cephalosporin usage, intensive care units, antimicrobial resistance, antibiotic consumption, Jordanian Royal Medical Services, antimicrobial stewardship, hospital prescribing patterns, cefazolin, cefotaxime, cefoxitin, ceftazidime, ceftriaxone.

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INTRODUCTION:

The cephalosporin class of antibiotics has proven fundamental in the management of bacterial infections since its introduction in 1945. These β-lactam antibiotics are divided into various generations, each distinguished by specific antibacterial spectra and therapeutic uses. Cephalosporins are preferred in hospital environments owing to their extensive efficacy, limited toxicity, and resistance to specific β-lactamase enzymes [1]. Infections in intensive care units (ICUs) frequently involve multidrug-resistant organisms and serious complications such as sepsis or pneumonia; as a result, cephalosporins are routinely employed to manage these critical situations [2].

The ICU setting presents distinctive challenges regarding antibiotic prescription. Patients in the ICU frequently exhibit immunocompromised states, endure comorbidities, and possess a heightened susceptibility to hospital-acquired infections (HAIs). The selection of an antibiotic must reconcile the necessity for swift, broad-spectrum efficacy with the potential for promoting antimicrobial resistance (AMR) [3]. This delicate equilibrium highlights the necessity of comprehending utilization trends to guarantee that prescribed medications conform to evidence-based recommendations and institutional standards.

Cephalosporins are classified into generations according to their chronological development and spectrum of activity. First-generation cephalosporins (e.g., Cefazolin) are effective against gram-positive bacteria and are primarily utilized for surgical prophylaxis and mild infections [1]. Second-generation cephalosporins (e.g., Cefotaxime) widened coverage to encompass certain gram-negative organisms, rendering them appropriate for moderate infections such as intra-abdominal or gynecological infections. Third-generation cephalosporins (e.g., Cefoxitin, Ceftazidime, and Ceftriaxone) provide enhanced efficacy against gram-negative bacteria and exhibit increased resistance to β-lactamases [1]. They are commonly employed in ICUs due to their effectiveness against severe infections, such as meningitis, bloodstream infections, and healthcare-associated infections. Their broad spectrum of activity, ease of administration, and favorable safety profile render them a preferred option for empiric therapy while awaiting microbiological results. The excessive use of these antibiotics has been associated with the development of resistant pathogens, including *Escherichia coli*, *Klebsiella pneumoniae*, and *Pseudomonas aeruginosa* [4,5].

In Jordan, the Jordanian Royal Medical Services (JRMS) delivers healthcare services to members of the military, their families, and other populations. JRMS stands as a prominent institution in the field of tertiary care within the country, managing multiple major hospitals. Each of these facilities is integral to the provision of specialized medical services, including ICU services, catering to a diverse patient population [6,7]. Due to the significant importance of managing infections within intensive care units, cephalosporins are among the most frequently prescribed antibiotics in these environments. Their usage patterns frequently differ according to the clinical specialties of the hospital, the demographics of the patient population, and the types of infections that are typically encountered.

The patterns of antibiotic usage in intensive care units are influenced by the clinical requirements of patients, as well as the prescribing tendencies of healthcare providers, institutional protocols, and overarching national guidelines [8]. Comprehending these patterns is crucial for enhancing antibiotic utilization, reducing antimicrobial resistance, facilitating effective resource distribution, and guiding policy formulation. Analyzing trends in cephalosporin consumption is essential for informing interventions aimed at promoting appropriate prescribing practices and minimizing unnecessary usage. The overuse or misuse of antibiotics, especially broad-spectrum forms, plays a significant role in the emergence of antimicrobial resistance. Therefore, tracking usage patterns is an essential aspect of effective antimicrobial stewardship initiatives [3]. Hospitals, particularly those functioning within public healthcare frameworks such as JRMS, are required to optimize their limited resources. Through the analysis of usage data, health administrators are equipped to make evidence-based decisions regarding procurement and inventory management. Analysis of usage patterns can significantly enhance the formulation of clinical guidelines that are specifically aligned with local epidemiological data and resistance profiles.

The objective of this study is to investigate the use of five intravenous cephalosporins (Cefazolin, Cefotaxime, Cefoxitin, Ceftazidime, and Ceftriaxone) within the intensive care units of four prominent JRMS hospitals during the timeframe of 2020 to 2021. This research will conduct a thorough analysis of hospital-specific data to evaluate overall trends in cephalosporin consumption. It will identify prescribing preferences for those particular drugs across the various hospitals and investigate potential factors that may influence these patterns, including

hospital specialization and modifications in clinical guidelines.

The results of this study carry considerable importance for antimicrobial stewardship initiatives within JRMS and may provide a framework for analogous evaluations in other healthcare systems. This research provides a comprehensive analysis of cephalosporin utilization, contributing significantly to the overarching objective of optimizing antibiotic management within intensive care units. The findings aim to improve patient outcomes while tackling the pressing global issue of antimicrobial resistance.

METHOD:

This research employed a retrospective observational methodology to examine the usage patterns of five intravenous (IV) cephalosporins (Cefazolin, Cefotaxime, Cefoxitin, Ceftazidime, and Ceftriaxone) within the ICUs of four prominent hospitals in the Jordanian Royal Medical Services (JRMS). The hospitals selected for this analysis, including Princess Haya Military Hospital, King Hussein Medical Hospital, Queen Alia Heart Institute, and King Talal Military Hospital, play pivotal roles in delivering tertiary care throughout Jordan. The study encompassed the years 2020 and 2021, with an emphasis on analyzing hospital-specific prescribing patterns, overall consumption trends, and the year-to-year variations in drug utilization.

The data utilized in this study were sourced from the official records of the JRMS pharmacy. The records presented comprehensive data regarding the number of patients who were administered cephalosporin in the intensive care units throughout the study duration. The data were thoroughly disaggregated by hospital and year, facilitating a thorough analysis of usage trends at both the individual hospital and system-wide levels.

The variables examined in the study encompassed the total number of patients received each cephalosporin, hospital-specific utilization rates, year-over-year changes, and the comparative usage of first-, second-, and third-generation cephalosporins. The analysis of these variables was designed to clarify patterns of preference among prescribers, variations in consumption across hospitals, and temporal trends that may signify shifts in clinical practice or alterations in hospital policies. Particular emphasis was placed on the application of third-generation cephalosporins, considering their significant importance in managing severe infections within intensive care unit environments.

The analysis of data was performed using Microsoft Excel. The total utilization of each cephalosporin across all hospitals was systematically calculated to evaluate overall prescribing trends. An analysis was conducted to assess the contribution of each hospital to the overall utilization of each medication, aiming to identify preferences specific to each site. The comparative analysis conducted among the four hospitals yielded valuable insights regarding the potential impact of clinical specialization on the selection of cephalosporins. For instance, the Queen Alia Heart Institute, which specializes in cardiology, was anticipated to exhibit distinct usage patterns in comparison to general hospitals such as King Hussein Medical Hospital.

Comparative analyses across years were conducted to assess temporal variations in medication utilization. The percentage changes in utilization for each cephalosporin across the various hospitals were carefully calculated for the years 2020 and 2021. The data were categorized according to cephalosporin generation to assess trends in the utilization of narrow-spectrum compared to broad-spectrum antibiotics. This analysis was essential for evaluating the alignment of prescribing practices with antimicrobial stewardship objectives, especially regarding the appropriate consumption of third-generation cephalosporins.

Along with quantitative analysis, we also took into account contextual factors, including the specialization of hospitals and the influence of local prescribing guidelines. The aforementioned factors were utilized to analyze the variations in cephalosporin utilization among different hospitals. The focus on cardiothoracic procedures at Queen Alia Heart Institute may account for a greater dependence on particular antibiotics for surgical prophylaxis, in contrast to general medical facilities that may favor broad-spectrum agents to address a more diverse array of infections.

RESULTS:

This study presents a comprehensive analysis of the utilization patterns of five cephalosporins within the four JRMS hospitals during the years 2020 and 2021. The data indicate significant variations in prescribing practices across hospitals, shifts in drug utilization over time, and preferences for particular generations of cephalosporins.

Overall Utilization Trends: Ceftriaxone was identified as the most commonly dispensed cephalosporin across all hospitals, representing 2,847 patients, which constitutes 53.1% of the overall usage. The notable preference for Ceftriaxone underscores its importance as a broad-

spectrum antibiotic frequently employed in the management of severe infections within intensive care unit environments [9]. After Ceftriaxone, Cefoxitin emerged as the second most dispensed medication, accounting for 1,192 patients, which represents 22.2% of the total usage. Ceftazidime followed closely in third place, with 712 patients, corresponding to 13.3% of the overall usage. Cefotaxime and Cefazolin exhibited the lowest dispensing rates, with total utilizations recorded at 536 (10.0%) and 73 (1.4%) patients, respectively (Figure 1).

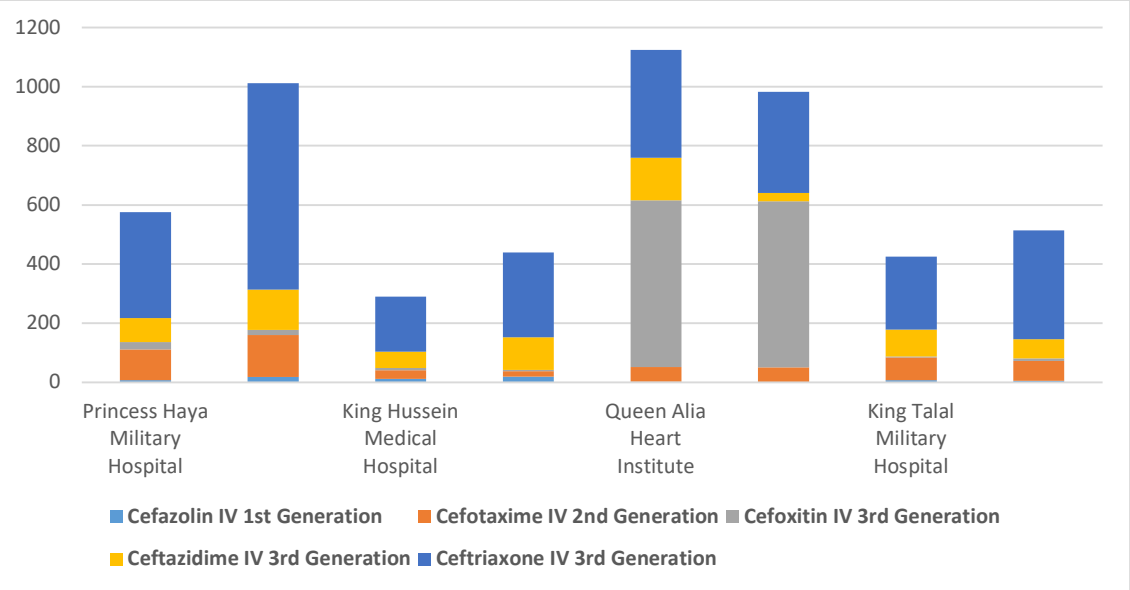

Figure 1: Frequency and distribution of Cefotaxime and Cefazolin in study hospitals

Hospital-Specific Utilization: Each hospital exhibited unique prescribing patterns influenced by its specialization, clinical practices, and the characteristics of its patient population.

At Princess Haya Military Hospital, Ceftriaxone was the most frequently utilized antibiotic, accounting for 1,056 patients, which represents 68.3% of the hospital's total patient. This was followed by Cefotaxime, which was administered to 246 patients, corresponding to 15.5% of the total. Cefoxitin and Ceftazidime represented a limited proportion, while Cefazolin was utilized to a minimal extent, with a total of 26 patients receiving this treatment. This observation indicates a significant tendency towards the utilization of third-generation cephalosporins for the management of complex infections within this healthcare facility.

King Hussein Medical Hospital exhibited greater equity in the distribution of cephalosporins; however, Ceftriaxone continued to be the most frequently dispensed, with a total of 473 patients (53.8%). Cefoxitin was administered to 131 patients, accounting for 14.9% of the total, while Ceftazidime was utilized in 165 patients, representing 18.7%. This data indicates a significant diversity in therapeutic requirements within the general hospital environment. Cefazolin was the least utilized agent, with a total of only 31 patients receiving prescriptions over the two-year period.

The data from Queen Alia Heart Institute reveals distinctive dispensing patterns, highlighting Cefoxitin as the most frequently administered antibiotic, utilized by 1,125 patients, which constitutes 57.2% of the hospital's overall total. This highlights its primary function in perioperative prophylaxis, considering the hospital's focus on cardiothoracic surgical procedures. Ceftriaxone was administered to 705 patients, accounting for 35.8% of the cases, whereas the utilization of Ceftazidime and Cefotaxime was significantly lower. The utilization of Cefazolin was minimal, as evidenced by the documentation of only two patients throughout the study duration.

The utilization of Ceftriaxone at King Talal Military Hospital was observed in 613 patients, accounting for 56.6% of the hospital total cases. In comparison, Ceftazidime was administered to 157 patients, representing 14.7%, while Cefotaxime was utilized in 142 patients, making up 13.2% of the total. Cefoxitin was utilized in only 12 patients (1.1%) at this hospital, indicating a significantly lower usage compared to the Queen Alia Heart Institute. This

observation highlights the variability in antibiotic preferences among different healthcare facilities.

Year-over-Year Changes: From the year 2020 to 2021, there was a notable increase in the total consumption of cephalosporins, rising from 2,414 patients in 2020 to 2,946 patients in 2021, which corresponds to an overall increase of 22%. The observed increase was uniform across all hospitals and the majority of cephalosporins, although the extent of variation was dependent on the specific drug and healthcare facility.

The data indicates that ceftriaxone experienced a significant rise, with the number of patients increasing from 1,154 in 2020 to 1,693 in 2021, reflecting a 46.6% growth. The observed increase was particularly significant at Princess Haya Military Hospital and King Hussein Medical Hospital, indicating an escalating dependence on this third-generation cephalosporin for managing infections in the ICU setting. The utilization of Cefoxitin exhibited a relatively stable trend, with a mere 0.5% increase observed over the two-year period.

The utilization of Ceftazidime has increased by 34.5%, largely attributed to heightened demand at Princess Haya Military Hospital and King Talal Military Hospital. Cefotaxime demonstrated a more modest increase of 7.6%, indicating its more restricted utilization within ICU treatment protocols. It is noteworthy that the utilization of Cefazolin experienced a significant increase during this timeframe, although its overall contribution remained relatively modest.

Generation-Based Analysis: During the study period, third-generation cephalosporins were the predominant agents utilized, representing a substantial 88.6% of the total patient population. Ceftriaxone accounted for 61.4% of the total usage of third-generation antibiotics, with Cefoxitin at 25.7% and Ceftazidime at 12.9%. The utilization of first- and second-generation cephalosporins, specifically Cefazolin and Cefotaxime, appears to be significantly lower, indicating an apparent preference for broad-spectrum antibiotics in intensive care unit environments.

Hospital Contributions to Total Usage: The Queen Alia Heart Institute accounted for the highest utilization of cephalosporins, representing 38.5% of the total patient population. This was followed by Princess Haya Military Hospital at 29.5%, King Hussein Medical Hospital at 14.1%, and King Talal Military Hospital at 18.0%. The significant role of Queen Alia Heart Institute in overall medication consumption can be primarily linked to its substantial utilization of Cefoxitin, highlighting the impact of hospital specialization on prescribing behaviors.

DISCUSSION:

The results of this study offer valuable insights into the utilization patterns of cephalosporins within the ICUs of four prominent hospitals in the Jordanian Royal Medical Services (JRMS). The findings underscore significant trends and present essential considerations concerning antibiotic preferences, prescribing practices, and the wider implications for antimicrobial stewardship within the JRMS healthcare system.

The investigation demonstrated a significant prevalence of third-generation cephalosporins, representing 88.6% of the overall cephalosporin consumption. Ceftriaxone, recognized as the most frequently dispensed medication, accounted for over half of the total consumption, specifically 53.1%. The observed preference can be attributed to the broad-spectrum activity of Ceftriaxone, along with its flexibility in addressing a variety of severe bacterial infections frequently seen in intensive care units, including community-acquired pneumonia, meningitis, and septicemia [4]. The extended half-life and the convenience of once-daily dosing render it especially appealing for intensive care unit environments, where the efficiency and simplicity of administration are paramount [9].

Cefoxitin and Ceftazidime, both classified as third-generation cephalosporins, exhibited significant utilization, nevertheless with distinct patterns specific to individual hospitals. The primary application of Cefoxitin at Queen Alia Heart Institute is likely indicative of its significance in surgical prophylaxis for cardiothoracic procedures. Conversely, Ceftazidime, noted for its superior efficacy against Pseudomonas aeruginosa, may have been employed more commonly in healthcare settings experiencing elevated incidences of multidrug-resistant infections.

The findings highlight the considerable impact of hospital specialization on the utilization of cephalosporins. The Queen Alia Heart Institute, specializing in cardiology, demonstrated a significant dependence on Cefoxitin, which constituted 57.2% of its overall utilization. This is consistent with the hospital's focus on perioperative prophylaxis, as the spectrum of activity of Cefoxitin offers significant advantages [1]. In contrast, Princess Haya Military Hospital and King Hussein Medical Hospital demonstrated a more favorable attitude towards the use of Ceftriaxone, indicative of their diverse patient demographics and the necessity to

address a more extensive array of systemic infections.

The balanced use of various cephalosporins at King Hussein Medical Hospital indicates a more varied prescribing strategy, presumably shaped by the hospital's overall medical and surgical patient load. Meanwhile, King Talal Military Hospital exhibited a fairly uniform distribution of third-generation cephalosporins, with significant utilization of Ceftazidime and Cefotaxime alongside Ceftriaxone. The variation observed in prescribing practices may suggest a more individualized strategy for antibiotic selection, influenced by patient-specific considerations and the characteristics of the infections being treated.

The year-over-year increase in cephalosporin usage, rising from 2,414 patients in 2020 to 2,946 patients in 2021, indicates a significant growth of 22% in the total patient population. This trend prompts a number of significant concerns. The observed increase may be attributed in part to a rise in ICU admissions or the expansion of services within JRMS hospitals. Additionally, it may suggest evolving prescribing practices, including an increasing dependence on broad-spectrum antibiotics. The notable rise in Ceftriaxone utilization, quantified at 46.6%, indicates a growing tendency towards this medication, likely attributable to its broad applicability and efficacy. Nonetheless, this trend highlights the imperative for careful antimicrobial stewardship, given that the excessive use of third-generation cephalosporins correlates with the emergence of antibiotic resistance. The consistent utilization of Cefoxitin over the two-year period indicates its function as a specialized therapeutic agent, rather than serving as a broad-spectrum alternative.

The findings of this study underscore the essential requirement for comprehensive antimicrobial stewardship programs within the JRMS. The substantial dependence on third-generation cephalosporins, although clinically warranted in numerous instances, presents a considerable risk of fostering resistance in prevalent ICU pathogens. The rising utilization of Ceftriaxone necessitates careful consideration, given its overuse has been associated with the development of extended-spectrum beta-lactamase (ESBL)-producing bacteria.

The wise application of narrow-spectrum antibiotics, such as Cefazolin, in suitable clinical scenarios may significantly reduce this risk. The observation that Cefazolin constituted merely 1.4% of the total patient population, yet experienced a doubling in consumption from 2020 to 2021, may indicate an increasing acknowledgment of its effectiveness in targeted prophylaxis and therapeutic applications. Enhancing initiatives to advocate for its application in targeted indications may further strengthen stewardship objectives.

Considering the unique usage patterns identified at each hospital, it is imperative to implement customized antimicrobial stewardship strategies. At Queen Alia Heart Institute, stewardship initiatives may concentrate on enhancing the utilization of Cefoxitin for surgical prophylaxis, while ensuring compliance with evidence-based guidelines. In general hospitals such as King Hussein Medical Hospital, where a variety of cephalosporins are utilized, it is imperative for stewardship programs to underscore the significance of diagnostic stewardship. This approach is essential for informing antibiotic selection and reducing the reliance on unnecessary broad-spectrum coverage. The significant dependence on Ceftriaxone at Princess Haya Military Hospital and King Talal Military Hospital highlights the necessity for continuous education and surveillance to ensure that its advantages are weighed against the possible risks of resistance. Establishing tailored protocols within hospitals that emphasize the use of narrow-spectrum agents in suitable scenarios may significantly mitigate the unwarranted dependence on broad-spectrum alternatives.

The findings of the study possess significant implications for healthcare planning and the allocation of resources within the JRMS. The elevated use of third-generation cephalosporins underscores the necessity for ongoing investment in laboratory infrastructure to enhance microbiological diagnostics, thereby facilitating more precise antibiotic therapy. Furthermore, the provision of alternative agents, such as non-cephalosporin antibiotics, may enhance clinicians' ability to manage infections effectively and alleviate the reliance on cephalosporins as a therapeutic class.

CONCLUSIONS:

This investigation yielded significant findings regarding the utilization of cephalosporins within four prominent hospitals of the Jordanian Royal Medical Services (JRMS) during the period of 2020-2021. The results indicated a significant tendency towards third-generation cephalosporins, particularly Ceftriaxone, which comprised more than fifty percent of the study total patient population. This highlights the critical role of third-generation cephalosporins in the management of severe infections within intensive care unit environments. Nonetheless, the notable rise in Ceftriaxone consumption, coupled with the increasing overall use of cephalosporins, prompts concerns regarding the potential for overutilization

and its role in the emergence of antimicrobial resistance. Broad-spectrum antibiotics such as Ceftriaxone play a crucial role in the management of critical infections; however, their overuse may compromise their efficacy in the future.

The variations observed within hospitals underscore the significant impact of patient demographics and the specialization of the hospital on the selection of antibiotics. The increased utilization of Cefoxitin for surgical prophylaxis at Queen Alia Heart Institute, in contrast to the predominant preference for Ceftriaxone in other healthcare facilities, underscores these considerations. In summary, although third-generation cephalosporins play a vital role in intensive care unit environments, it is essential to align their application with the principles of antimicrobial stewardship. This study underscores the importance of ongoing surveillance, precision in diagnostics, and customized antibiotic prescribing strategies to mitigate the threat of antimicrobial resistance and maintain the efficacy of these essential medications.

Limitations of the Study: The study's primary limitation lies in its exclusive dependence on recorded data, which may not provide an accurate representation of actual antibiotic utilization within ICU environments. A notable limitation of this study is the absence of clinical correlation, as it does not incorporate patient-level data to evaluate the appropriateness of prescribed medications. In the absence of comprehensive clinical records, it is challenging to ascertain the appropriateness of the prescribed antibiotics in relation to the specific patient conditions, microbiological cultures, or resistance patterns. This limitation hinders the assessment of whether prescribing trends are consistent with optimal practices in antimicrobial stewardship and infection management. Despite these limitations, the results continue to hold significance in describing general the consumption trends and the prescribing tendencies specific to individual hospitals. Future investigations that integrate clinical data, patient outcomes, and resistance patterns will yield a more thorough comprehension of cephalosporin use in intensive care unit environments.

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