



ANALYSIS OF INTRAVENOUS ANTIBIOTIC PRESCRIBING IN INTENSIVE CARE UNITS: A THREE-YEAR RETROSPECTIVE STUDY OF CEPHALOSPORIN PRESCRIBING IN JORDAN ROYAL MEDICAL SERVICES HOSPITALS

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Submitted on: 16.10.2025;

Revised on: 25.10.2025;

Accepted on: 28.10.2025

ABSTRACT:

Introduction: Intravenous antibiotic prescribing in intensive care units (ICUs) represents a vital component of antimicrobial stewardship programs particularly in the specialized healthcare settings. The Jordan Royal Medical Services (JRMS) hospitals serve varied patient populations with variable clinical and health related needs and therefore necessitating a careful analysis of antibiotic utilization in order to augment therapeutic outcomes and minimize any resistance development.

Methods: A retrospective analysis will be conducted using prescription data obtained from Princess Haya Military Hospital, Queen Rania Pediatric Hospital and Queen Alia Heart Institution pharmacy department system covering the period from January 2019 to December 2021 and additional data will be collected on patient demographics including age and gender, prescribed medication type, and temporal distribution and the statistical analysis will employ descriptive statistics and trend analysis to identify any potential patterns in antibiotic utilization which will be followed by a subgroup analysis which will be performed to study age-specific and gender-specific prescribing across different hospital settings.

Results: A total of 7,261 intravenous cephalosporin prescriptions were recorded during the study period. Ceftriaxone was the most frequently prescribed antibiotic (39.3%), followed by Cefoxitin (21.0%), Cefazidime (20.5%), and Cefotaxime (19.2%). Prescribing patterns varied significantly across hospitals: Queen Alia Heart Institution accounted for 52.5% of total prescriptions (mainly Cefoxitin, used for cardiac surgical prophylaxis) while Queen Rania Pediatric Hospital primarily prescribed Cefotaxime (59.7%) reflecting pediatric treatment standards. Temporal analysis showed a decline in antibiotic prescriptions during 2020 (an 18.2% decrease) followed by recovery in 2021 (16.0% increase), reflecting the impact of the COVID-19 pandemic on clinical operations. Demographic analysis revealed higher antibiotic use among male patients (69.3%) and notable prescribing peaks among pediatric (0–18 years) and elderly (66+ years) populations, indicating age-specific susceptibility to severe infections.

Keywords: Intravenous cephalosporins, Intensive Care Units (ICUs), Antimicrobial stewardship, Antibiotic utilization, COVID-19 pandemic

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Indian Research Journal of Pharmacy and Science; 44(2025); 3385- 3395
Journal Home Page: <https://www.irjps.in>

1. INTRODUCTION:

The administration of Intravenous antibiotics particularly in high acuity settings and environments such as the intensive care units is one of the most important aspects of modern medicine and in this regard the Jordan Royal Medical Services (JRMS) network of hospitals and institutions aims to provide an essential and holistic healthcare services to their active and retired military members, children and other patients with complex conditions, this complex network create a unique fully integrated clinical setting that fosters the ongoing clinical research and cross discipline comparative analyses of the prescription and use of antibiotics, empirical treatment and the increasing patterns of microbiological resistance in antibiotics and varying epidemiological factors.

Cephalosporin antibiotics family constitute a basic and a foundation corner stone for antimicrobial therapy in intensive care settings due to this group broad-spectrum activity and its good safety profiles and these medications signify different generations of cephalosporins each of with a very distinct and a separate pharmacological characteristics and features, different range of activity and clinical applications all of which function to making understanding their utilization patterns very essential for the optimizing and enhancing of therapeutic outcomes while at the same time minimizing and eliminating the risk of antimicrobial resistance development.

2019 to 2021 was marked by a substantial and significant global healthcare challenges in which the COVID-19 pandemic served as one of the largest and unprecedented challenges to the healthcare system worldwide and this timeframe also provides a very exceptional lens through which we can examine the antibiotic prescribing behaviors during both the routine and usual clinical practice and during those extraordinary circumstances and challenges of the COVID-19, changes associated with the pandemic in the dynamics of patient population clinical acuteness, along with the therapeutic tactics, infection mitigation strategies, and the cardinal infection control measures which instituted the primary determinants of a set of rules of antibiotics prescribed, intersect with mechanisms that are much in need of further study.

Demographic factors particularly age and gender have been regularly identified as important determining factors of antibiotic prescribing patterns in several healthcare settings, age-related differences in pharmacokinetics, disease vulnerability and clinical presentation and symptoms manifestation can significantly influence antibiotic selection and their dosing strategies and similarly, gender-related variations in infection patterns, healthcare-seeking behaviors and treatment responses may also contribute to an observable differences in antibiotic utilization patterns.

The three hospitals within the JRMS system represent diverse clinical environments with unique patient populations and therapeutic challenges, Princess Haya Military Hospital primarily serves military personnel and their families and potentially encountering general infection, Queen Rania Pediatric Hospital focuses exclusively on pediatric patients which require specialized considerations for their antibiotic selection based on age-appropriate dosing, safety profiles and pediatric-specific infection patterns and Queen Alia Heart Institution specializes in cardiac care where antibiotic selection must consider potential drug interactions, cardiac-specific complications and perioperative prophylaxis requirements.

The present inquiry submits a systematic appraisal of antibiotic prescribing dynamics across the JRMS platform, thereby advancing the empirical discourse on antimicrobial stewardship in tertiary care settings. By elucidating the prevailing utilization trends, the investigation delineates the determinants of prescribing variability, the concordance with established guidelines, and the downstream clinical and microbiological impact. The resultant dataset affirms the interdependence of local epidemiological, demographic, and prescribing culture factors, thereby supplying a granular basis for calibrated change. Anchored in the triadic model of policy, pedagogy, and practice, the exposition anticipates informing the formulation of governing protocols, the design of targeted educational curricula, and the refinement of bedside antibiotic decision algorithms, with the synergistic aim of optimizing therapeutic efficacy, preserving microbial resilience, and augmenting the overall quality of patient care within the institution.

2. LITERATURE REVIEW:

2.1 Cephalosporin Antibiotics in Critical Care:

Cephalosporin antibiotics have went through significant development and changes since their creation with each generation offering new and distinct pharmacological advantages and clinical applications from the previous generation, the four agents which are analyzed in this study (ceftriaxone, ceftazidime, cefoxitin and cefotaxime) represent different generations and highlight the therapeutic diversity of the cephalosporin family as a whole and therefore understanding their pharmacological profiles is essential for interpreting prescribing patterns and evaluating their clinical appropriateness.

Ceftriaxone is a third generation cephalosporin and it is one of the most broadly used antibiotics worldwide and this antibiotic broad-spectrum activity, long half-life, once-daily dosing regimens and its capability to provide a reliable coverage against both the gram-positive and gram-negative pathogens (1), all these features combined with its excellent tissue penetration make ceftriaxone highly effective in the treatment of respiratory tract infections, urinary tract infections and sepsis and thereby establishing its role as a preferred choice in intensive care settings (2).

Although Ceftazidime is classified as a third-generation cephalosporin, it is notably distinguished by potent activity against *Pseudomonas aeruginosa*, a predominant pathogen in healthcare-associated infections. Consequently, it is frequently employed in the treatment of ventilator-associated pneumonia and other nosocomial syndromes; however, the agent's pharmacokinetic characteristics mandate administration in multiple daily doses and such a dosing regimen may influence the prescribing patterns of both clinicians and the healthcare team and also the clinical utility of Ceftazidime must be judiciously tempered by the prevailing local resistance patterns and by a thorough assessment of patient-specific variables.

Cefoxitin is a second generation cephalosporin which provides stability against beta-lactamases and wide coverage against anaerobic organisms (5) and these properties make it particularly valuable in surgical prophylaxis and intraabdominal infections which are conditions that are frequently encountered in ICU patients (6) and its established role in cardiac surgery further illustrates how cephalosporins are

integrated into specialty specific prescribing protocols.

Cefotaxime is also another third-generation agent and is pharmacologically similar to ceftriaxone but it differs in its dosing requirements and clearance mechanisms (7) yet it is effective against a broad spectrum of organisms and is especially appropriate in pediatric populations due to its well-documented safety profile (8) which explains its extensive use in pediatric intensive care units and its role in managing severe systemic infections.

2.2 Demographic Factors in Antibiotic Prescribing:

Patient demographics are critical and vital determinant factors of antibiotic prescribing, pediatric patients require a weight-based dosing, age-appropriate preparations and enhanced monitoring due to developmental differences in drug metabolism and its clearance (9) and elderly patients by contrast may need dose modifications and changes due to renal impairment, increased drug sensitivity and the likelihood of drug-drug interactions (10).

Gender differences have also been reported, previous published studies suggest that women may receive antibiotics more often for certain types of conditions which may be possibly linked to their higher healthcare seeking behavior and attitude or to their greater susceptibility to specific types of infections (11) however in contrast to them men usually predominate in military or trauma-related contexts where infection risks differ and therefore the interactions between age and gender add more complexity since elderly women for instance usually show a higher rates of urinary tract infections whereas young men in military populations face different infectious exposures (12) and therefore and in this regards recognizing these dynamics is very important and essential for designing stewardship interventions that reflect and take into considerations real-world patient populations characteristics and features.

2.3 Hospital-Specific Prescribing Patterns: The type of hospital and its specialty focus often have a large and a big effect on how healthcare providers at the hospital prescribe drugs, military hospitals often face and have unique infection risks such as exposure to deployment and trauma-related infections which may lead to a personalized empirical prescribing approaches (13), pediatric

hospitals usually prioritize child-specific dosing protocols and evidence-based guidelines while also trying to reduce unnecessary exposure to antibiotics in order to reduce resistance development(14), cardiac specialty hospitals usually and typically should prioritize perioperative prophylaxis, the prevention of device-related infections and the meticulous evaluation of drug-drug interactions with other cardiac therapies (15).

2.4 Temporal Trends and Pandemic Impact:

Antibiotic prescribing changes over time in response to emerging resistance trends, the updated clinical guidelines and stewardship initiatives, the COVID-19 pandemic disrupted these patterns globally and some healthcare systems have reported reduced antibiotic use due to lower patient admissions while others noted an increased prescribing which is usually out of concern for bacterial co-infections in COVID-19 patients (16) and hence this broader temporal trends continue to be shaped by the global rise of antimicrobial resistance, guideline-based prescribing and enhanced monitoring systems (17,18) and therefore evaluating these trends is vital and critical to assess stewardship effectiveness and ensure that prescribing practices remain aligned with the evolving clinical challenges.

3. METHODOLOGY:

3.1 Study Design and Setting: This retrospective and cross-sectional study analyzed intravenous antibiotic prescribing patterns in the intensive care units of three hospitals within the Jordanian Royal Medical Services network of hospitals and clinics, the study period stretched from January 2019 to December 2021 and encompassing three complete years of prescription data and this selected timeframe provided adequate data for temporal trend analysis while apprehending the potential impact of the COVID-19 pandemic on prescribing practices.

The three participating hospitals in this study represent distinct clinical environments and settings within the JRMS system: Princess Haya Military Hospital (PHMH) which serves Jordan military personnel and their families, Queen Rania Pediatric Hospital (QRPH) which is specializing in pediatric care and Queen Alia Heart Institution (QAH) which focuses on cardiac and cardiovascular diseases, providing a comprehensive view of antibiotic

prescribing patterns across different clinical specialties.

3.2 Data Collection and Variables: Prescription data were extracted and collected from the electronic health records and pharmacy information systems of the three participating hospitals and the collected dataset included several information on patient demographics, medication details, prescription dates and prescribing departments.

The primary and main variables of interest in this study included patient age, gender, prescribed medication, prescription date and hospital and age was categorized to five groups: 0-18 years (pediatric), 19-35 years (young adult), 36-50 years (middle-aged adult), 51-65 years (older adult) and 66+ years (elderly) and this age stratification and grouping was selected and designed to capture any clinically relevant age related differences in antibiotic prescribing patterns while also maintaining sufficient sample sizes for statistical analysis.

3.3 Statistical Analysis: Descriptive statistics were employed and calculated for all variables of interest including their frequencies and percentages and temporal trend analysis was also conducted in order to identify any significant changes in prescribing patterns over the study period, also the monthly and yearly prescription counts were analyzed in order to identify seasonal variations and long-term trends and then the potential effect and impact of the COVID-19 pandemic was assessed by comparing the resulted prescribing patterns between 2019 (pre-pandemic), 2020 (pandemic onset) and 2021 (ongoing pandemic response) furthermore subgroup analyses were performed to examine prescribing patterns within specific demographic groups and hospital settings including age-stratified and gender-stratified comparisons.

4. RESULTS AND DISCUSSION:

4.1 Overall Prescribing Patterns: The analysis included 7,261 intravenous antibiotic prescriptions across the three JRMS hospitals during the study period and this substantial dataset provided strong evidence for examining prescribing patterns and demographic influences on antibiotic utilization and demonstrates the significant role these four cephalosporin antibiotics play in intensive care management within the JRMS system (table 1).

Table 1: Intravenous antibiotic prescriptions across the three JRMS hospitals

Medication	Prescriptions
Ceftriaxone	2,854
Cefoxitin	1,527
Ceftazidime	1,486
Cefotaxime	1,394

Ceftriaxone appeared as the most regularly prescribed antibiotic accounting for 2,854 prescriptions accounting for 39.3% of the total which aligns with the global trends in cephalosporin utilization and use in which its favorable pharmacokinetic characteristics including the long half-life and the once daily dosing regimen makes it a preferred choice for empirical therapy in critically ill patients and also this medication's wide spectrum of activity against both the gram-positive and gram-negative bacteria in addition to its good tissue penetration and safety profile also are likely to contribute to this widespread adoption and use across all three hospital settings.

Cefoxitin was second in the prescription frequency with 1,527 prescriptions and accounting for 21.0% of the total and then followed closely by Ceftazidime with 1,486 prescriptions and accounting for 20.5% of the total and Cefotaxime with 1,394 prescriptions which accounted for 19.2%

of the total and this resulted relatively balanced distribution among these three antibiotics suggests that each medication serves distinct clinical functions within the JRMS system with selection likely influenced and affected by the specific patient characteristics and infection types and institutional protocols.

4.2 Hospital-Specific Prescribing Patterns:

Significant variations and discrepancies in the prescribing patterns were detected in all the three study hospitals which reflecting their diverse patient populations and different clinical specialties, Queen Alia Heart Institution showed the highest prescription with 3,813 prescriptions that accounted for 52.5% of the total prescriptions then followed by Princess Haya Military Hospital which prescribed 2,060 prescriptions and accounted for 28.4% of the total and then followed by Queen Rania Pediatric Hospital with 1,388 prescriptions accounting for 19.1% of the total (table 2).

Table 2: Intravenous antibiotic prescriptions per hospital

Hospital	Prescriptions
Queen Alia Heart Institution	3,813
Princess Haya Military Hospital	2,060
Queen Rania Pediatric Hospital	1,388

The unduly disproportionately high prescription volume at Queen Alia Heart Institution is likely reflective of several factors that are unique to the cardiac care nature of this hospital since cardiac patients repeatedly require prolonged ICU stays and undergo multiple surgical measures and face an increased risk of healthcare associated infections due to the presence and use of invasive devices and preexisted complex medical conditions, additionally this institution's role as a tertiary referral center for cardiac care may also result in a higher concentration of critically ill patients who are requiring intensive antibiotic therapy.

The prescribing patterns at Queen Alia Heart Institution shows a marked and noticeable preference for Cefoxitin which accounted for 1,470 prescriptions (38.5% of this hospital's total) and this preference likely reflects the medication's role in surgical prophylaxis for cardiac procedures and its effectiveness against anaerobic bacteria which is commonly encountered in post-surgical infections and also this institution's focus on cardiac surgery and other interventional procedures would naturally lead to the increased utilization of antibiotics especially those antibiotics with proven and documented efficacy as surgical prophylaxis antibiotics and those that are known to be effective in perioperative infection management (table 3).

Table 3: Frequency and distribution of Intravenous antibiotic prescriptions

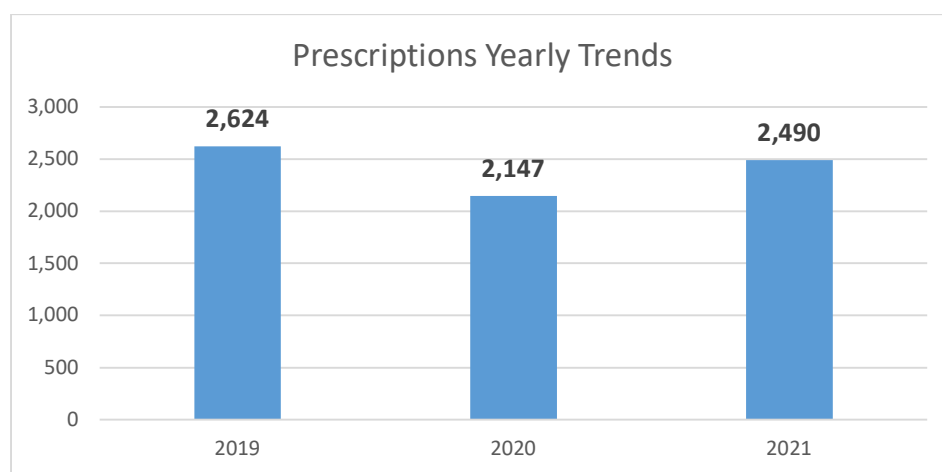
Medication	PHMH	QA Heart	QR Pediatric
Cefotaxime	410	155	829
Cefoxitin	52	1,470	5
Ceftazidime	282	1,028	176
Ceftriaxone	1,316	1,160	378

Princess Haya Military Hospital demonstrated and showed a somewhat more balanced antibiotic utilization pattern with Ceftriaxone leading at 1,316 prescriptions (63.9% of the hospital's total), this pattern likely reflects the diverse patient population served by this military hospital including both the routine medical cases and other trauma patients since the military setting may also influence prescribing patterns through specific protocols developed for deployment-related infections and trauma-associated complications.

Queen Rania Pediatric Hospital disclosed a distinctive antimicrobial prescribing trends that are aligned with the pediatric norms since cefotaxime was within this hospital the predominant agent that has been accrued 829 individual orders and thereby constituting 59.7% of the wide total and this datum markedly exceeds the corresponding cefotaxime distribution that has been observed with in the concurrent generalist settings thereby warranting scrutiny, also the predilection is plausible on the

grounds of the agent's extensive documented safety slate in the pediatric population combined with its potency against prevailing childhood pathogens all in turn making the comparatively restrained total volume of antibiotics prescribed within the center appears to be congruent with the recognized tendency of lower aggregate antibiotic exposure in children relative to adult patients which makes this phenomenon in a broad agreement with the widely prevailing pediatric antimicrobial stewardship directives that advocate the minimization of unexpected antimicrobial susceptibilities.

4.3 Temporal Trends and Pandemic Impact: The analysis of temporal trends revealed and showed significant variations in those antibiotic prescribing patterns over the three-year study period, the year 2019 recorded 2,624 prescriptions followed by a noteworthy decrease to 2,147 prescriptions in 2020 (18.2% reduction) and a subsequent increase to 2,490 prescriptions in 2021 (16.0% increase from 2020 (figure 1).

**Figure 1: Temporal Trends and Pandemic Impact**

The observed decrease in 2020 likely reflects the multifaceted and complex impact of the COVID-19 pandemic on healthcare delivery patterns and several factors may have contributed to this reduction: decreased elective procedures and routine

healthcare operation, the implementation of infection control procedures that reduced healthcare-associated infections and the potential changes in patient acuity and admission patterns in that era specially since the pandemic's impact on

healthcare systems worldwide already has been well-documented in which many institutions reported significant changes in their patient volumes and clinical practices.

The rebound in prescriptions which occurred during 2021 suggests a gradual and ongoing return to the pre-pandemic healthcare utilization patterns though the total remained below 2019 levels and also this recovery may reflect several factors: resumption and continuation of elective procedures, an increased understanding of COVID-19 management allowing for more routine care and potential changes in patient acuity or infection patterns that are related to the ongoing pandemic response.

Medication specific temporal trends revealed and showed an interesting and noteworthy patterns which warrant and deserve further discussion, Cefotaxime showed the most dramatic and significant change since its use decreased from 979 prescriptions in 2019 to 285 in 2020 (a 70.9% reduction) and then further declining to 222 in 2021 and this noteworthy pattern suggests that there was a significant shift away from this antibiotic during the pandemic period which could possibly be related to some changes in the types of infections encountered during this period or changes to the hospitals protocols (table 4).

Table 4: Temporal Trends of antibiotic prescription

Medication	2019	2020	2021
Cefotaxime	452	416	526
Cefoxitin	356	590	581
Ceftazidime	979	285	222
Ceftriaxone	837	856	1,161

On the contrary Ceftriaxone demonstrated some degree of resilience during the pandemic period in which the prescriptions remained relatively stable in 2020 (856 prescriptions) compared to 2019 (837 prescriptions) and then showing a significant growth in 2021 (1,161 prescriptions), this pattern further reinforces and supports ceftriaxone's position as a useful first-line antibiotic that maintained its clinical relevance throughout the pandemic period.

4.4 Demographic Patterns in Antibiotic Prescribing: 4.4 Demographic Patterns in Antibiotic Prescribing: The analysis of demographic patterns revealed significant gender discrepancies in antibiotic prescribing with males receiving 5,034

prescriptions (69.3% of total) compared to females with 2,227 prescriptions (30.7%), this 2.3:1 male-to-female ratio was consistent and somewhat steady across all the four antibiotics which suggesting systematic factors rather than medication-specific preferences. Several factors may have contributed to this noted gender disparity, the military hospital component of the study population likely skews toward male patients given the demographics of military personnel, additionally certain cardiovascular conditions which requires intensive care may be more prevalent or widespread in males when compared to females particularly in middle-aged and elderly populations (figure 2).

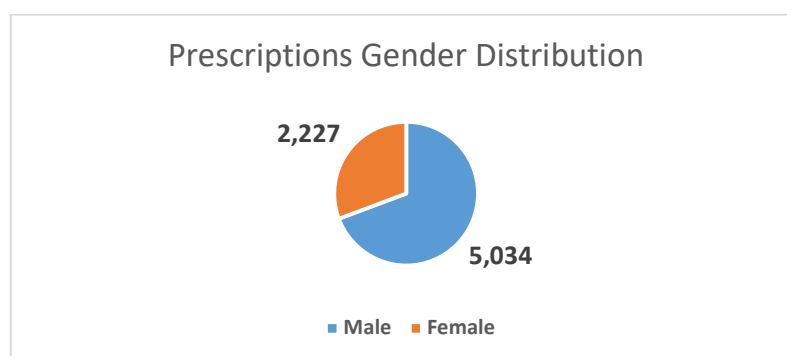


Figure 2: frequency of antibiotic prescription by gender

The antibiotic prescriptions utilization for both the 0 - 18 years of age as well as the 66+ age group recorded number of prescriptions for 2,164 and 2,756 respectively translating to 29.8 and 38.0 percent of the total. This bimodal distribution as identified in the age distribution analysis indicates that both children and the elderly are at an increased risk for serious infections that would necessitate intensive antibiotic treatment, which explains the noted peaks.

The noted elderly population's high prescription volume aligns with the well-established clinical patterns as advanced age is associated and linked to increased infection susceptibility and to more severe clinical presentations and elevated rates of healthcare-associated infections also the presence of multiple comorbidities, immunosenescence and the frequent healthcare exposures in elderly patients may contribute to their increased antibiotic requirements.

The considerable prescription volume in the pediatric age group (0-18 years) reflects the inclusion of Queen Rania Pediatric Hospital in the study but also it highlights the significant and high burden of serious infections in children requiring intensive care, pediatric patients in ICU settings often have complex medical conditions that predispose and expose them to infectious complications and therefore necessitating aggressive antibiotic therapy (figure 3).

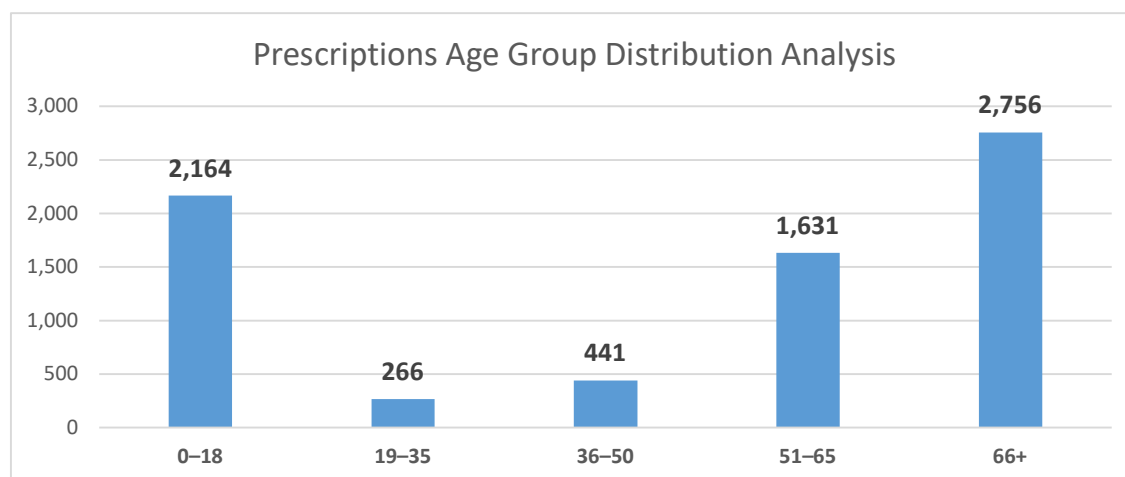


Figure 3: Frequency of antibiotic prescription by age groups

4.5 Medication-Specific Demographic Patterns:

The examination of the demographic characteristics found clinically pertinent relationships and associations, regarding Cefotaxime, within the age range of 0-18 the pediatric population had the highest preference with 1,149 prescriptions (82.4%

of total prescriptions) and this is probably indicative of the fact that the medication safety and effectiveness against the common bacterial pathogens of children including those associated with meningitis and sepsis (table 5).

Table 5: Frequency of antibiotic prescription by age group

Age Group	Cefotaxime	Cefoxitin	Ceftazidime	Ceftriaxone
0-18	1,149	137	373	505
19-35	16	37	43	170
36-50	17	134	78	212
51-65	41	686	393	511
66+	170	532	599	1,455

Ceftriaxone on the other hand possessed a somewhat more balanced age distribution yet it also showed a more remarkable strength in the elderly populations were it in the 66+ age group there were 1,455 prescriptions (51.0% of total ceftriaxone prescriptions) and this imbalance further reinforces the strong position of this medication as one of the most preferred empirical therapy for elderly patients which is more likely due to its broad-spectrum activity and due to its favorable dosing regimen that allow for some clinical advantage.

In addition Cefoxitin also has demonstrated an interesting pattern in which its utilization was the highest in the 51-65 age group (686 prescriptions and 44.9% of total prescriptions) and in the 66+ age

group (532 prescriptions, 34.8%) and this unique age distribution aligns with the medication's primary function and role as prophylactic and therapeutic agent for surgical site infections which are usually more frequent and faced in elderly patients whom undergoing cardiac and other surgical procedures.

The gender specific analysis revealed consistent male majority and predominance across all antibiotics with the ratio ranging from 1.7:1 for cefotaxime to 5.3:1 for cefoxitin, the particularly high male-to-female ratio for cefoxitin may reflect its extensive use in cardiac surgery in which male patients are more prevalent especially in older age groups (table 6).

Table 6: frequency of antibiotic prescription by gender

Medication	Female	Male
Cefotaxime	512	882
Cefoxitin	244	1,283
Ceftazidime	419	1,067
Ceftriaxone	1,052	1,802

5. CONCLUSIONS:

This analysis of intravenous antibiotic prescribing within the Jordan Royal Medical Services features and highlights the patterns of cephalosporin use across three hospital settings, Ceftriaxone arose as the dominant antibiotic which is reflective of its broad clinical applicability yet this widespread use underscores and support the need for stewardship programs to evaluate more targeted therapies.

Prescribing variations across hospitals generally aligned with clinical needs: cefoxitin use at Queen Alia Heart Institution corresponded to cardiac surgery protocols while cefotaxime use at Queen Rania Pediatric Hospital reflected and mirrored pediatric standards and therefore these patterns suggest that decisions were tailored to patient populations and their clinical indications.

The study also captured temporal trends during the COVID-19 pandemic which showed a decline in prescriptions in 2020 and a recovery in 2021 therefore emphasizing the system's adaptability during this period and the demographic analysis revealed and showed high antibiotic use in pediatric and elderly patients with a consistent male predominance that requiring further exploration.

Medication-specific trends also suggested largely appropriate practices such as cefotaxime in children and balanced ceftriaxone use across different age groups, nonetheless opportunities exist for enhancement and refinement through the development of standardized protocols and procedures, age-specific guidelines development and enhanced monitoring systems.

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CONFLICT OF INTEREST REPORTED: NIL; SOURCE OF FUNDING: NONE REPORTED