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Evaluation of empiric therapy appropriateness, resistance patterns, and mortality in *Pseudomonas aeruginosa* infections in Jordan

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Abstract

Aim: This study aimed to investigate the susceptibility patterns of *Pseudomonas aeruginosa* strains, examine infection characteristics, and evaluate the appropriateness of empiric antibiotic therapy. Additionally, the study sought to identify factors influencing 30-day all-cause mortality in patients with *Pseudomonas aeruginosa* infections.

Methods: This was a retrospective study conducted at Jordan University Hospital from January 2018 to March 2024. Adult patients (\geq 18 years) with confirmed *Pseudomonas aeruginosa* infections were included. Data were collected from medical records, focusing on demographics, infection characteristics, antibiotic treatment, and outcomes. The susceptibility patterns of *Pseudomonas aeruginosa* isolates were classified as multidrug-resistant (MDR) or non-MDR. Logistic regression was used to identify factors associated with 30-day mortality.

Results: A total of 210 patients were included in the study, with 106 males (50.5%) and 104 females (49.5%). The majority of infections were community-acquired (n = 178, 84.8%), with the respiratory tract being the most common infection site (n = 81, 38.6%). Nearly half of the *Pseudomonas aeruginosa* isolates were MDR (n = 99, 47.1%). Empiric antibiotic therapy was administered to all patients, with imipenem-cilastatin (55.7%), vancomycin (35.7%), and piperacillin-tazobactam (26.7%) being the most commonly used antibiotics. Of the 210 patients, 32.4% (n = 68) received inappropriate empiric therapy. The 30-day all-cause mortality rate was 4.9% (n = 10). Multivariate analysis revealed that non-localized infections, such as bacteremia and sepsis, were strongly associated with increased mortality [adjusted odds ratio (AOR) = 17.455, P < 0.001].

Conclusions: This study highlights the high prevalence of MDR *Pseudomonas aeruginosa* infections, especially in community-acquired cases, and emphasizes the need for improved antimicrobial stewardship. The significant proportion of patients (32.4%) receiving inappropriate empiric therapy calls for better

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guidance in antibiotic prescribing practices. The key predictor of mortality was infection localization, indicating the importance of early intervention for systemic infections to reduce mortality rates.

Keywords

Pseudomonas aeruginosa, multidrug-resistant, antibiotic resistance, mortality predictors, Jordan

Introduction

Multidrug-resistant (MDR) bacteria present a significant global health threat, complicating the treatment of infections and leading to increased healthcare costs and patient risks [1, 2]. Among these, *Pseudomonas aeruginosa* is particularly concerning due to its ability to thrive in healthcare settings and its natural resistance to many antibiotics [3]. The overuse and misuse of antibiotics are major contributors to the rise of resistant strains [4], highlighting the need for urgent action in antibiotic stewardship and infection control [5].

Healthcare environments, especially hospitals, are particularly vulnerable to MDR bacteria. High patient turnover, invasive procedures, and the frequent use of medical devices create conditions conducive to the spread of these pathogens [6]. Healthcare-associated infections (HAIs) are especially dangerous for immunocompromised patients, worsening an already critical situation [7]. Effective infection control practices, such as maintaining hygiene and sterilization, are crucial for preventing the spread of these harmful bacteria [8].

In the Middle East, the prevalence of *P. aeruginosa* infections is alarming, driven by factors such as high rates of chronic diseases and inadequate infection control measures [9]. The misuse of antibiotics further exacerbates the issue, promoting the development of resistant strains [10, 11]. As treatment options for *P. aeruginosa* are limited by the rise of MDR strains, healthcare providers are increasingly resorting to combination therapy, which involves using multiple antibiotics to enhance effectiveness [12].

Despite the significant impact of *P. aeruginosa* infections, there is a notable lack of research focused on susceptibility patterns and treatment practices in Jordanian hospitals. This gap in knowledge makes it difficult to develop effective infection control strategies tailored to the region. Therefore, this study aimed to investigate the susceptibility patterns of *P. aeruginosa* strains, examine infection characteristics, and evaluate the appropriateness of empiric antibiotic therapy. Additionally, the study sought to identify factors influencing 30-day all-cause mortality in patients with *P. aeruginosa* infections.

Materials and methods

Study design and setting

This retrospective study was conducted at Jordan University Hospital (JUH), the first academic teaching hospital in Jordan, with a 550-bed capacity. The study aimed to investigate adult patients (aged 18 years and older) hospitalized with *P. aeruginosa* infections. It involved a review of electronic medical records for patients who tested positive for *P. aeruginosa* from January 2018 to March 2024.

Inclusion and exclusion criteria

The study included adults aged 18 years and older who were diagnosed with *P. aeruginosa* infections and admitted to the hospital during the study period. Exclusion criteria were applied to ensure the accuracy of the analysis. Patients with incomplete medical records, those lacking susceptibility testing data, individuals with polymicrobial infections, and patients who were transferred out of the hospital before receiving empirical antibiotic therapy were excluded from the study. This approach enabled us to assess the appropriateness of empiric antibiotic therapy initiated during the hospital stay.

Data collection

Data for all eligible patients were collected through a review of their medical records. The collected data included demographic information such as age, gender, admission date, and the total duration of hospitalization. Clinical details were also gathered, including the department of admission, site of infection acquisition, the season of infection acquisition, admitting diagnosis, comorbid conditions, previous colonization, any recent hospitalizations within the past three months, antimicrobial use, and the use of corticosteroids or immunosuppressants prior to infection acquisition. Additionally, information on invasive medical procedures before infection was obtained. The study also collected details about the primary infection site, specimen retrieval, empirical antibiotic therapy (including initiation date, specific antibiotics used, dosage, and duration), susceptibility testing results, adjustments to therapy based on culture outcomes, and the 30-day all-cause mortality rate.

Study outcomes

The study aimed to assess several key outcomes related to *P. aeruginosa* infections. One of the primary outcomes was the susceptibility patterns of the *P. aeruginosa* strains, which were classified into four categories based on resistance: non-MDR strains, which are sensitive to all tested antibiotics or resistant to only one agent in one or two antimicrobial drug classes; and MDR strains, which exhibit resistance to antibiotics in at least one agent in three or more antimicrobial drug classes. These classes are aminoglycosides, monobactams, cephalosporins, cephalosporin with beta-lactamase inhibitors, penicillins, fluoroquinolones, polymyxins, carbapenems, and glycylcyclines. Another key outcome was the evaluation of management practices, particularly the appropriateness of empirical antibiotic therapy. This included an assessment of the timely initiation of treatment, the choice of antibiotics, dosages, and the duration of therapy. The study also focused on 30-day all-cause mortality, aiming to identify factors that influence mortality within 30 days of infection.

Ethical considerations

The study adhered to the ethical guidelines established by the World Medical Association's Declaration of Helsinki. The research protocol was approved by the Institutional Review Board at JUH (Approval number R023/28293). Patient confidentiality was ensured by anonymizing all medical records, and as the study was retrospective, direct patient contact was not involved. Consequently, informed consent was not required for this study.

Statistical analysis

Data were analyzed using IBM SPSS Statistics for Windows, Version 26.0 (IBM Corp., Armonk, NY, USA). Descriptive statistics were used to summarize categorical variables with frequencies and percentages, and continuous variables with means and standard deviations. Continuous variables were tested for normality using the Shapiro-Wilk test before performing statistical comparisons. Chi-square test was used to evaluate the relationship between previous medication use (immunosuppressant/chemotherapy, antibiotics, and corticosteroids) and the presence of MDR versus non-MDR *P. aeruginosa*. Moreover, logistic regression analysis was conducted to identify independent factors associated with 30-day all-cause mortality. Variables with a *P*-value less than 0.250 in simple logistic regression were included in multiple logistic regression analysis. Prior to this, potential multicollinearity among variables was assessed, ensuring that the Pearson correlation coefficient between any two variables was less than 0.9. A *P*-value of < 0.05 was considered statistically significant.

Results

A total of 1,484 cases with positive *P. aeruginosa* isolates were screened, of which 1,274 cases were excluded as they did not meet the inclusion criteria. These include: 459 cases with polymicrobial infections or co-infections, 174 cases were < 18 years of age, 148 cases with inadequate susceptibility testing results, 143 cases with incomplete medical records, 137 cases involved recurrent infections, 118 cases of patients

who left the hospital without receiving empiric antibiotic therapy, and 95 cases were treated as an outpatient. As such, a total of 210 cases were included and analyzed (14.1%) (Figure 1).

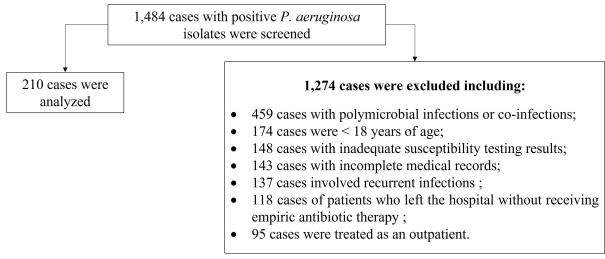


Figure 1. Enrollment flowchart of P. aeruginosa cases

The study cohort, as shown in Table 1, consisted of 210 patients, with a nearly balanced gender distribution: 106 males (n = 106, 50.5%) and 104 females (n = 104, 49.5%). Approximately one-quarter of the patients were aged 65 years or older (n = 54, 25.7%). Regarding smoking status, 31.9% (n = 67) were current smokers, 7.1% (n = 15) were ex-smokers, and the majority, 61.0% (n = 128) were non-smokers. The majority of patients had public insurance coverage (n = 202, 96.2%), while only a small minority (n = 8, 3.8%) had private insurance.

Parameter	Frequency (%)	
Gender		
Male	106 (50.5)	
Female	104 (49.5)	
Age categories (years)		
< 35	41 (19.5)	
35-44	43 (20.5)	
45–54	29 (13.8)	
55-64	43 (20.5)	
≥ 65	54 (25.7)	
Smoking status		
Non-smoker	128 (61.0)	
Ex-smoker	15 (7.1)	
Smoker	67 (31.9)	
Health status		
Healthy	36 (17.1)	
With chronic illnesses	174 (82.9)	
Most common chronic illnesses		
Diabetes mellitus	75 (35.7)	
Hypertension	74 (35.2)	
Bronchiectasis	25 (11.9)	
Myocardial infarction	21 (10.0)	
Insurance type		
Public	202 (96.2)	
Private	8 (3.8)	

Table 1. Patient demographics and medical characteristics (*n* = 210)

In terms of health status, 82.9% (n = 174) of the cohort had chronic medical conditions. The most common chronic conditions were diabetes mellitus type II (n = 75, 35.7%), hypertension (n = 74, 35.2%), bronchiectasis (n = 25, 11.9%), and myocardial infarction (n = 21, 10.0%).

The majority of infections were community-acquired (n = 178, 84.8%), while 15.2% (n = 32) were hospital-acquired infections. The primary sites of infection were the respiratory tract (n = 81, 38.6%), skin and soft tissue (n = 48, 22.9%), and urinary tract (n = 40, 19.0%).

Infections occurred most frequently during the winter and fall seasons (n = 61 each, 29.0%). Within the three months prior to infection acquisition, 39.5% of patients (n = 83) had been hospitalized, and 39.5% (n = 83) had received antibiotics. Approximately 6.2% (n = 13) of patients had been exposed to major surgery, and 5.2% (n = 11) had undergone urethral stenting before infection acquisition.

Among the tested *P. aeruginosa* isolates, nearly half (47.1%, n = 99) were MDR pathogens. Regarding treatment outcomes, 4 patients (out of 210) were lost to follow-up during the 30-day period (discharged against medical advice). Of the remaining 206 patients, the 30-day all-cause mortality rate was 4.9% (n = 10), while 95.1% (n = 196) survived. Detailed information is presented in Table 2.

Parameter	Frequency (%)	
Source of infection acquisition [#]		
Community-acquired	178 (84.8)	
Hospital-acquired	32 (15.2)	
Primary site of infection		
Respiratory tract	81 (38.6)	
Skin and soft tissue	48 (22.9)	
Urinary tract	40 (19.0)	
Surgical site	15 (7.1)	
Bloodstream	7 (3.3)	
Bone	5 (2.4)	
Others	14 (6.7)	
Season of infection acquisition		
Winter	61 (29.0)	
Spring	45 (21.4)	
Summer	43 (20.5)	
Fall	61 (29.0)	
Hospitalization within the last three months		
No	127 (60.5)	
Yes	83 (39.5)	
Use of antibiotics within the last three months	S	
No	127 (60.5)	
Yes	83 (39.5)	
Use of corticosteroids within the last three m	onths	
No	177 (84.3)	
Yes	33 (15.7)	
Previous immunosuppressant/chemotherapy	use within the last three months	
No	198 (94.3)	
Yes	12 (5.7)	
Invasive procedures prior to infection acquisi	tion	
No	167 (79.5)	
Major surgery	13 (6.2)	
Double J stent	11 (5.2)	
Others ^a	19 (9.0)	

Table 2. Medical information related to *P. aeruginosa* infections (*n* = 210)

Parameter	Frequency (%)	
Infection localization		
Localized	193 (91.9)	
Sepsis	12 (5.7)	
Bacteremia	5 (2.4)	
Resistance pattern of P. aeruginosa		
Non-MDR bacteria	111 (52.9)	
MDR bacteria	99 (47.1)	
30-days, all-cause mortality [^]		
Survived	196 (95.1)	
Died	10 (4.9)	

^a Foley, central venous line, endoscopy, venous access port, dialysis/acute renal replacement therapy, cystoscopy, ureteroscopy. [#] Community-acquired infections are those acquired within 48 hours of hospital admission, while hospital-acquired infections are those that become evident after 48 hours of hospitalization. [^] The percentages were calculated based on 206 individuals after excluding patients who were discharged against medical advice. MDR: multidrug-resistant

All patients in the study received empiric antibiotics (n = 210, 100.0%). The number of empiric antibiotics administered varied among patients: 21.0% (n = 44) received one antibiotic, while 44.3% (n = 93) received two antibiotics. In terms of the route of administration, the majority of patients were treated with intravenous antibiotics (n = 206, 98.1%). These findings are summarized in Table 3.

Table 3. Empirical ant	imicrobial therapy	received (<i>n</i> = 210)
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Parameter	Frequency (%)
Empiric antibiotics received	
Yes	210 (100.0)
No	0 (0)
Number of empiric antibiotics received	
1	44 (21.0)
2	93 (44.3)
3	49 (23.3)
≥ 4	24 (11.4)
Route of administration [#]	
Intravenous	206 (98.1)
Oral	166 (79.0)
Topical	4 (1.9)

[#] Patients could receive antibiotics via more than one route of administration, which is why the percentages for each route do not necessarily sum to 100%

The most frequently used empiric antibiotics were imipenem-cilastatin (55.7%), followed by vancomycin (35.7%), piperacillin-tazobactam (26.7%), and levofloxacin (24.3%) (Figure 2). When evaluating the appropriateness of the prescribed antibiotics, almost one-third of the patients (n = 68, 32.4%) received inappropriate initial antimicrobial therapy. Antibiotic prescriptions by infection type are presented in Table S1.

When evaluating predictors of mortality in patients with *P. aeruginosa* infection (Table 4), infection localization was significantly associated with 30-day all-cause mortality. Patients with non-localized infections, such as bacteremia and sepsis, were 17.45 times more likely to experience mortality compared to those with localized infections [adjusted odds ratio (AOR) = 17.455, *P* < 0.001].

When evaluating the relationship between previous medication use and the presence of MDR versus non-MDR *P. aeruginosa* infections (Table 5), recent antibiotic use is significantly associated with MDR infections (P < 0.001). In contrast, corticosteroid use does not show a significant correlation with MDR infections (P = 0.091). Furthermore, the use of immunosuppressants or chemotherapy is significantly linked to non-MDR infections (P = 0.029).

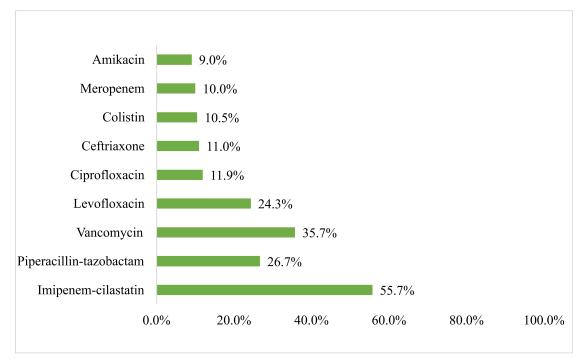


Figure 2. Distribution of the most frequently used empiric antibiotics (*n* = 210)

Table 4. Assessment of predictors associated with 30-days all-cause mortality in patients with P. aeruginosa infection	n
(<i>n</i> = 206)	

Parameter	30-days all-caus	30-days all-cause mortality (0: Survived, 1: Died)			
	COR	P-value [#]	AOR	<i>P</i> -value ^{\$}	
Age					
< 65 years	Reference	0.02	Reference	0.12	
≥ 65 years	4.625		3.406		
Gender					
Males	Reference	0.48			
Females	1.595				
Health status					
Healthy	Reference	0.99			
With chronic illnesses	0.000				
Source of infection acquisition					
Community-acquired	Reference	0.04^	Reference	0.36	
Hospital-acquired	4.000		2.136		
Site of infection					
Respiratory tract	Reference	0.91			
Others	0.930				
Hospitalization within the last the	nree months				
No	Reference	0.52			
Yes	1.531				
Use of antibiotics within the las	t three months				
No	Reference	0.99			
Yes	1.009				
Use of corticosteroids within the	e last three months				
No	Reference	0.18^	Reference	0.36	
Yes	2.571		2.416		
Previous immunosuppressant/o	chemotherapy use within	the last three months			
No	Reference	0.04^	Reference	0.74	
Yes	5.873		1.504		

Table 4. Assessment of predictors associated with 30-days all-cause mortality in patients with *P. aeruginosa* infection (*n* = 206) (*continued*)

Parameter	30-days all-caus	30-days all-cause mortality (0: Survived, 1: Died)			
	COR	P-value [#]	AOR	<i>P</i> -value ^{\$}	
Invasive procedures prior to	infection acquisition				
No	Reference	0.40			
Yes	0.407				
Infection localization					
Localized	Reference	< 0.001^	Reference	< 0.001*	
None localized	25.227		17.455		
Appropriateness of empiric	therapy				
Not appropriate	Reference	0.60			
Appropriate	0.709				
Type of antimicrobial resista	ance				
Non-MDR	Reference	0.39			
MDR	1.985				

[#] Using simple logistic regression;
^{\$} Using multiple logistic regression;
[^] Eligible for entry in multiple logistic regression;
^{*} Significant at 0.05 significance level. MDR: multidrug-resistant; COR: crude odds ratio; AOR: adjusted odds ratio

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Parameters	Non-MDR bacteria (<i>n</i> = 111)	MDR bacteria (<i>n</i> = 99)	<i>P</i> -value ^{\$}
Use of antibiotics	within the last three months		
Yes (<i>n</i> = 83)	31 (37.3)	52 (62.7)	< 0.001*
No (<i>n</i> = 127)	80 (63.0)	47 (37.0)	
Use of corticoster	oids within the last three months		
Yes (<i>n</i> = 33)	13 (39.4)	20 (60.6)	0.091
No (<i>n</i> = 177)	98 (55.4)	79 (44.6)	
Previous immunos	suppressant/chemotherapy use within the las	t three months	
Yes (<i>n</i> = 12)	10 (83.8)	2 (16.7)	0.029*
No (<i>n</i> = 198)	110 (51.0)	97 (49.0)	

^{\$} Using Chi-square test. ^{*} Significant at 0.05 significance level. MDR: multidrug-resistant

Discussion

This study offers an examination of *P. aeruginosa* infections at a tertiary teaching hospital in Jordan, focusing on clinical profiles, infection sources, antibiotic susceptibility patterns, and management strategies. The study found that the majority of *P. aeruginosa* infections (84.8%) were community-acquired, which contrasts with the traditional belief that *P. aeruginosa* is predominantly a hospital-acquired pathogen [13]. The primary infection sites were the respiratory tract (38.6%), skin and soft tissue (22.9%), and urinary tract (19.0%), which is consistent with *P. aeruginosa*'s preference for moist environments and areas with impaired defense mechanisms [14]. *P. aeruginosa* can colonize and multiply in hospital water systems such as sinks, showers, and water distribution, leading to biofilm formation. Inhalation of these droplets or direct contact with contaminated water can result in respiratory infections or colonization of the skin and soft tissues [15].

Early empiric therapy for high-risk patients was crucial, with most patients receiving combination antibiotic therapy. Clinicians favored imipenem-cilastatin and vancomycin, reflecting the need to provide broad-spectrum coverage for both Gram-negative and Gram-positive pathogens, especially MDR strains common in Jordan [14]. The study also highlighted concerning resistance patterns, particularly to ciprofloxacin (48.6%) and meropenem (49.8%), which are critical antibiotics for managing severe infections. Notably, colistin demonstrated the highest sensitivity, with only 3.4% resistance, highlighting its role as a last-resort therapy for MDR infections. However, the emerging resistance to colistin, even at low levels, signals a growing concern for its long-term efficacy [16].

Antibiotic resistance in *P. aeruginosa* was widespread, with 48% of isolates being MDR. These findings align with global trends and mirror those observed in Qatar, where similar resistance patterns were reported, emphasizing the increasing challenge of treating *P. aeruginosa* infections [17]. This highlights the need for effective antimicrobial stewardship programs to manage and limit the spread of resistant strains. Our study finds that recent antibiotic use is significantly associated with the presence of MDR *P. aeruginosa* infections. This can be explained by selective pressure, where frequent antibiotic use eliminates non-resistant bacteria, allowing resistant strains to survive and multiply [18]. Additionally, immunosuppressive therapies weaken the immune system, making patients more vulnerable to infections caused by non-resistant bacteria.

Despite the high resistance rates, the study found no significant difference in the 30-day mortality rate between patients infected with non-MDR strains and those infected with MDR strains. This is consistent with other research, which has indicated that MDR strains do not always lead to worse outcomes if treated promptly and effectively [19]. The key predictor of mortality in this study was infection localization, with non-localized infections such as bacteremia and septicemia significantly increasing the likelihood of death. This finding emphasizes the importance of early detection and treatment of systemic infections to improve patient outcomes [20].

The study also found that 32.4% of patients received inappropriate initial therapy, likely due to inadequate coverage of *P. aeruginosa* or resistance to prescribed antibiotics. This highlights the need for better utilization of antibiograms and rapid diagnostic tools to guide empirical therapy and optimize patient outcomes [21].

This study was conducted within a single tertiary teaching hospital in Jordan, which may limit the generalizability of the results to other healthcare settings. The retrospective design and exclusion of newer antibiotics, such as ceftazidime-avibactam and imipenem-cilastatin-relebactam, from the susceptibility testing may affect the completeness of the resistance patterns observed. Moreover, by restricting the study to hospitalized patients who received empirical antibiotic therapy during their hospital stay, outpatients were excluded. This exclusion may have led to an overestimation of resistance patterns. Consequently, the observed trends likely represented more severe infections requiring hospitalization, making it difficult to generalize the findings to milder cases managed in outpatient settings. Additionally, due to the retrospective nature of the study and incomplete documentation in the medical records, we did not evaluate the effect of empiric antibiotics on patient health conditions, focusing instead on the appropriateness of empiric therapy and 30-day mortality. Furthermore, the exclusion of polymicrobial or co-infection cases limits the understanding of the complexity and severity of infections involving multiple microbes. Future research should include these cases to provide a more comprehensive understanding and improve treatment strategies.

Conclusions

In conclusion, this study highlights the rising challenge of *P. aeruginosa* infections, particularly with increasing MDR. The high rate of community-acquired infections and widespread resistance emphasize the need for improved antimicrobial stewardship, early empiric therapy, and better use of rapid diagnostics. While no significant mortality difference was found between MDR and non-MDR strains, infection localization was a key predictor of death. The study emphasizes the importance of early intervention, the need for newer antibiotics in susceptibility testing, and further research to optimize treatment strategies for *P. aeruginosa* infections.

Abbreviations

MDR: multidrug-resistant

Supplementary materials

The supplementary table for this article are available at: https://www.explorationpub.com/uploads/ Article/file/1001312_sup_1.pdf.

Declarations

Author contributions

SS: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Validation, Visualization, Writing—original draft, Writing—review & editing. RI: Conceptualization, Investigation, Methodology, Validation, Visualization, Writing—original draft, Writing—review & editing. KAH: Conceptualization, Data curation, Methodology, Validation, Visualization, Writing—original draft, Writing—review & editing. RKAF: Conceptualization, Formal analysis, Investigation, Methodology, Project administration, Supervision, Validation, Visualization, Writing—original draft, Writing—review & editing.

Conflicts of interest

The authors declare that they have no conflicts of interest.

Ethical approval

The research protocol was approved by the Institutional Review Board at JUH (Approval number R023/28293).

Consent to participate

Due to the retrospective nature of the study, direct patient contact was not involved. Consequently, informed consent was not required for this study.

Consent to publication

Not applicable.

Availability of data and materials

Required information can be available upon request from the corresponding author (Rana Abu-Farha, r_abufarha@asu.edu.jo).

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