BMC Infectious Diseases

RESEARCH Open Access

Fecal carriage of extended-spectrum β-lactamase-producing, and carbapenem-resistant gram-negative bacteria among hemodialysis patients in a palestinian tertiary care hospital

Abdullah Janem[1†], Dawod Jawabreh[1†], Yaqoot Anabseh[1†], Mohammed Jawabreh[2], Zaher Nazzal[1], Adham Abu Taha[2,3*] and Mohammad Qadi[2*]

Abstract

The study explores the presence of extended-spectrum β-lactamase-producing Gram-negative bacteria (ESBL-GNB) and carbapenem-resistant Gram-negative bacteria (CR-GNB) in the stool of hemodialysis patients, reflecting a significant concern amid rising antibiotic resistance. This cross-sectional study included 137 outpatients conducted from October to December 2023 at An-Najah National University Hospital. Samples were incubated on appropriate MacConkey-based agar for bacterial analysis, and potential risk factors were evaluated using logistic regression. Out of 137 stool samples, 116 (84.7%) were positive for ESBL-producing bacteria, and 8 (5.8%) for carbapenem-resistant bacteria. Age of the patients (aOR: 1.068; *p*: 0.012), hypertension (aOR: 15.582; *p*: 0.0107), ischemic heart disease (aOR: 5.381; *p*: 0.040), the timing of the dialysis shift (aOR: 8.864; *p*: 0,005), and the level of blood urea nitrogen (aOR: 1.049; *p*: 0.045) were independently associated with ESBL-GNB colonization. Carbapenem-resistant bacteria colonization presented an inverse association with ischemic heart disease (aOR: 0.052; *p*: 0.041). This study highlights a significant prevalence of ESBL-GNB colonization linked with age and comorbidities such as hypertension. An inverse association of CR-GNB colonization with ischemic heart disease was observed, suggesting a complex interplay between patient health status and antibiotic-resistant bacterial colonization.

Keywords Antimicrobial resistance, Extended-spectrum β-lactamase, Carbapenem-resistant, Fecal colonization, Hemodialysis, Fecal indicator bacteria, Transmissible infections, Transmitted drug resistance

†Abdullah Janem, Dawod Jawabreh and Yaqoot Anabseh contributed equally to this work.

*Correspondence:
Adham Abu Taha
aabutaha@najah.edu
Mohammad Qadi
m.qadi@najah.edu

[1]Department of Medicine, Faculty of Medicine and Health Sciences, An-Najah National University, Nablus 4439, State of Palestine
[2]Department of Biomedical Sciences, Faculty of Medicine and Health Sciences, An-Najah National University, Nablus 44839, State of Palestine
[3]Department of Pathology, An-Najah National University Hospital, Nablus 44839, State of Palestine

Introduction

Antimicrobial resistance poses a serious threat to global healthcare systems, especially when it comes from multidrug-resistant gram-negative bacteria (MDR-GNB). In patient care settings, the prevalence of certain bacteria has increased dramatically over the past 20 years, particularly carbapenem-resistant gram-negative bacteria (CR-GNB) and extended-spectrum β-lactamase-producing gram-negative bacteria (ESBL-GNB) [1–4]. The Centers for Disease Control and Prevention (CDC) has classified these bacteria as serious dangers, which are made worse by the notable pause in the development of antibiotics [5, 6]. The quick rise of CR-GNB, which shows resistance to most antibiotics, further jeopardizes the few available treatment choices, which are mostly limited to last-resort medications like carbapenems [7, 8]. The requirement for a thorough understanding of the incidence and infection rates of CR-GNB and ESBL-GNB in feces underscores how serious this issue is in hospital settings, where fecal carriage raises the risk of subsequent infections.

In light of end-stage renal disease (ESRD), an advanced stage of chronic kidney disease (CKD), this research is extremely important. Because of compromised immune systems and dysbiosis of the gut flora, patients with ESRD are more vulnerable to potentially deadly infections including infections caused by MDR pathogens [9–11]. After cardiovascular illnesses, infections rank as the second most common cause of death for ESRD patients in the US [12, 13]. There is an urgent need for targeted study in this field because the survival rates of ESRD patients infected with CR-GNB are significantly lower than those of individuals who are not [14]. Studies examining the frequency of fecal CR-GNB in the Palestinian environment are noticeably lacking. Nevertheless, closing this gap is essential to create efficient control mechanisms and enhance patient outcomes.

According to recent literature and published studies, patients on hemodialysis are more likely to encounter multidrug-resistant microorganisms, especially gram-negative bacteria [15, 16]. Furthermore, ESBL-GNB and CR-GNB colonization among hemodialysis patients have been studied extensively, showing varying carriage rates in different geographic areas [17–19]. Asymptomatically colonized patients may play a crucial role as reservoirs for infection spread, potentially contributing to the rising incidence of clinical infections caused by these resistant bacteria [20, 21]. These individuals are expected to have a high presence of fecal bacteria due to regular hospital visits, frequent contact with medical staff and equipment, consumption of hospital food, and the frequent use of antibiotics [18, 22].

This study aims to determine the prevalence of ESBL-GNB and CR-GNB fecal carriage among hemodialysis patients in a Palestinian tertiary care hospital. In addition, we aim to identify risk factors for ESBL-GNB and CR-GNB fecal colonization. This study will contribute positively to the global effort in managing MDR pathogens in high-risk groups and improve the regional understanding of antimicrobial resistance.

Methods

Study design and setting

A cross-sectional study was conducted from October to December 2023 at Najah National University Hospital (NNUH), Nablus, to investigate the fecal carriage prevalence of ESBL-GNB and CR-GNB among hemodialysis patients. NNUH is a not-for-profit teaching hospital and specialized medical center that includes a Kidney Disease Treatment Center. This facility has 100 hemodialysis beds and 6 peritoneal dialysis beds, divided into four units to deliver outpatient hemodialysis treatment for around 276 individuals. The hospital is recognized as the primary center for hemodialysis in the northern governorates of Palestine, serving patients from across the West Bank [23].

Participants and sample size

All outpatients undergoing hemodialysis at the hospital from October to December 2023 were included in the study upon providing informed consent and agreeing to provide a single fecal sample. Exclusion criteria comprised patients < 18 years, in-patients undergoing hemodialysis, unable or unwilling to provide a single fecal sample, an imminent switch to peritoneal dialysis, mental illness, and any medical condition that could affect bowel function or compromise the accuracy of the study results. The total number of the population upon starting the study was 276 patients. However, after applying the inclusion and exclusion criteria, 233 of the patients were eligible. The sample size was calculated using a population of the 233 eligible patients with a confidence level of 95%, a margin of error of 5%, and an assumed population proportion of 50% (the prevalence of fecal carriage of ESBL-GNB and CR-GNB among hemodialysis patients in our setting was unknown, and this value provides the maximum sample size for a conservative estimate). Based on these parameters, the minimum required sample size was calculated to be 146 patients. However, of the 233 eligible patients, only 159 agreed to participate, with 137 providing fecal samples (see Fig. 1).

Microbiological screening

Stool samples from 137 patients were collected for the screening process. Swabs from each sample were streaked onto three different MacConkey agar plates. The first plate was supplemented with 1 μg/ml cefotaxime for detecting ESBL-GNB, the second plate with 1 μg/ml meropenem to screen for CR-GNB, and the

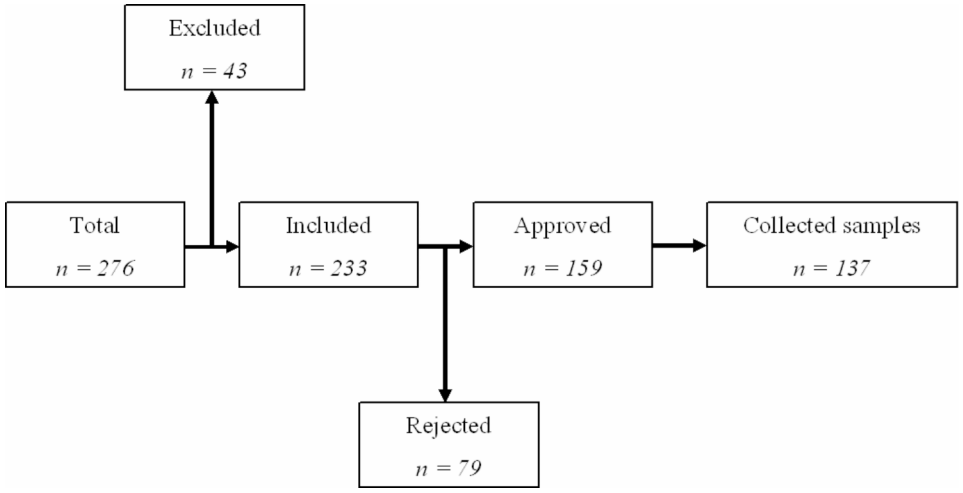

Fig. 1 Inclusion of patients and sampling

third MacConkey agar plate contained no antibiotics. All plates were incubated at 37 degrees for 24–48 h [14, 15, 26].

Clinically confirmed strains (ESBL-GNB and CR-GNB) and *E. coil* ATCC 25,922 were used as controls for the prepared media in each preparation [24, 25]. Antibiotics used in this study were purchased from Sigma Aldrich, while the media were purchased from Oxoid. Media with antibiotics were prepared as described in the Clinical and Laboratory Standard Institute (CLSI) 2023 and as described in the literature [24–26].

Data collection

Potential risk factors for the colonization by CR-GNB and ESBL-GNB were identified based on existing literature and the clinical rationale [14, 17–19, 27–33]. Baseline demographic data including age and gender were obtained from hospital medical records. Laboratory results were collected from routine monthly lab reports. Other variables assessed included comorbidities such as hypertension, diabetes mellitus, ischemic heart disease, congestive heart failure, cerebrovascular accidents, cancer, fractures, and previous surgeries. Additionally, anticoagulant use, vascular access type, dialysis shift timing (morning or evening), frequency of dialysis sessions per week, and duration of hemodialysis in months were recorded. The dependent variable was whether the patient's stool culture tested positive or negative for CR-GNB and/or ESBL-GNB based on culture results.

Statistical methods

The data was entered and analyzed using the Statistical Package for Social Sciences (IBM-SPSS) software, version 29. Categorical variables were described using absolute and relative frequencies. The distribution of continuous variables was tested, and variables were reported as mean and standard deviation or as median (interquartile range) according to the normality of distribution. A logistic regression model was used for univariate and multivariate analysis, and measures of association (odds ratio: OR) were reported with their corresponding 95% confidence intervals (CI). All statistical analyses were conducted using two-tailed tests, and statistical significance was determined by a p-value below 0.05. The reported p-values were rounded to three decimal places.

Ethical considerations

This study was approved by the Institutional Review Board (IRB) of An-Najah National University (Ref: Med. Sept. 2023/2). The IRB reviewed all aspects of the study protocol, including procedures for accessing and utilizing patient clinical information. The study was also approved by the clinical research center of An-Najah National University Hospital. All collected data were employed exclusively for this clinical research project and were maintained with strict confidentiality. Patient data and hospital details were anonymized through a coding system, allowing access to the information only for authorized research staff to maintain confidentiality. Written informed consent was obtained from each participant before their inclusion in the study. The research methodology followed all relevant ethical guidelines and regulations.

Results

Participants and clinical characteristics

The study included a diverse group of hemodialysis patients, with male patients constituting a majority at 56.9%. The age of participants ranged widely from 19 to 87 years, with an average age of 59.31 ± 13.96 years (see Table 1). Most patients received hemodialysis three times per week, with a slightly higher representation from the

Table 1 Demographic and clinical profiles of participants

Variable	*N* (%)
Age (years), median and IQR	61 (51.5–69.0)
Dialysis duration (months), median and IQR	34 (15.5–66.5)
Gender	
Male	78 (56.9)
Female	59 (43.1)
Comorbidities	
HTN	119 (86.9)
DM	81 (59.1)
IHD	58 (42.3)
CHF	25 (18.2)
CVA	17 (12.4)
Cancer	1 (0.7)
Fracture	8 (5.8)
Surgery	69 (50.4)
Dialysis shift	
Morning	79 (57.7)
Evening	58 (42.3)
Sessions per week	
< 3	11 (8.0)
≥ 3	126 (92.0)
Vascular access	
CVC	20 (14.6)
AVF	117 (85.4)
Anticoagulant use	99 (72.3)

HTN: hypertension; DM: diabetes mellitus; IHD: ischemic heart disease; CHF: congestive heart failure; CVA, cerebrovascular accidents; CVC, central venous catheter; AVF: arteriovenous fistula

morning shift at 57.7%. The arteriovenous fistulas (AVF) stood out as the most common type of vascular access among the subjects. Hypertension (HTN) was notably the most prevalent comorbidity followed by diabetes, affecting 86.9% and 59.1% of the cohort respectively, highlighting their significance as comorbid conditions in the population under study, as shown in Table 1.

Colonization rates and comorbidities of hemodialysis patients harboring ESBL and carbapenem-resistant gram-negative bacteria

In the cross-sectional study, out of 137 hemodialysis patients, 116 patients (84.7%) were colonized with ESBL-GNB. The median age of these colonized patients was 62.00 years. The group consisted of 67 male patients (57.8%) and 49 female patients (42.2%). Among the colonized patients, 104 (89.7%) had hypertension, 69 (59.5%) had diabetes mellitus, and 54 (46.6%) had ischemic heart disease. Other comorbidities included congestive heart failure in 25 patients (21.6%), cerebrovascular accident in 17 patients (14.7%), cancer in 1 patient (0.9%), and fractures in 7 patients (6.0%). Surgical history was reported in 63 patients (54.3%). The median duration of dialysis among the colonized patients was 33.00 months (interquartile range 14.50 to 67.00 months). Morning dialysis shifts were attended by 71 patients (61.2%), while 45 patients (38.8%) attended evening shifts. A total of 109 patients (94.0%) underwent three or more dialysis sessions per week. Vascular access via arteriovenous fistula was present in 100 patients (86.2%), and central venous catheters were used in 16 patients (13.8%). Anticoagulant use was noted in 83 patients (71.6%). Laboratory measurements showed a median blood urea nitrogen level of 53.20 mg/dL, white blood cell count of 6.90×10^9/L, hemoglobin level of 10.90 g/dL, calcium level of 9.00 mg/dL, and phosphate level of 4.51 mg/dL, as shown in the supplementary table.

In the same cohort, 8 out of 130 hemodialysis patients (5.8%) were colonized with CR-GNB. The colonized patients had a median age of 66.00 years, with an interquartile range of 58.50 to 68.50 years. This group included 4 male patients (50.0%) and 4 female patients (50.0%). All colonized patients (8 patients, 100.0%) had hypertension, and 7 patients (87.5%) had diabetes mellitus. Ischemic heart disease was present in 2 patients (25.0%), congestive heart failure in 2 patients (25.0%), and cerebrovascular accident in 2 patients (25.0%). One patient (12.5%) had a history of cancer, and none had fractures. Four patients (50.0%) had undergone surgery. The median duration of dialysis was 37.50 months for the colonized group. Morning dialysis shifts were attended by 6 patients (75.0%), and evening shifts by 2 patients (25.0%). Seven patients (87.5%) received three or more dialysis sessions per week. Vascular access was established via arteriovenous fistula in 7 patients (87.5%) and via central venous catheter in 1 patient (12.5%). Anticoagulant therapy was used by 6 patients (75.0%). Laboratory values indicated a median blood urea nitrogen level of 39.05 mg/dL, white blood cell count of 6.43×10^9/L, hemoglobin level of 10.65 g/dL, calcium level of 9.28 mg/dL, and phosphate level of 2.98 mg/dL, as shown in the supplementary table.

ESBL-GNB carriage & risk factors

Out of 137 stool samples that were collected throughout the duration of the study, 116 samples exhibited growths for ESBL-GNB (84.7%). Univariate analysis showed that the age, hypertension, ischemic heart disease, and BUN were positively or negatively associated with ESBL-GNB colonization. These variables maintained their association with colonization by ESBL-GNB even after adjusting the multivariate analysis for the confounding variables in this study to discern the nuanced relationships between various factors and the fecal carriage of ESBL-GNB producing bacteria among hemodialysis patients in the university hospital. The results revealed compelling associations after adjusting for potential confounding variables. The analysis uncovered that age played a significant role (aOR: 1.068; *p*: 0.012) with older

individuals exhibiting a higher prevalence of ESBL-GNB colonization. Gender emerged as an insignificant factor (aOR: 0.291; *p*: 0.102) after adjusting for potential confounding variables. This indicates that, when considering other relevant variables, there is no statistically significant difference in the likelihood of ESBL colonization between male and female patients.

Among the tested comorbidities only HTN and ischemic heart disease (IHD) appeared as statistically significant associated with increased odds of ESBL-GNB colonization. For hypertension, the adjusted odds ratio (aOR) was 15.582, with a *p*-value of 0.017, indicating a substantial independent association. Similarly, ischemic heart disease exhibited an aOR of 5.381, with a *p*-value of 0.040, signifying a significant correlation. These results suggest that hemodialysis patients with hypertension or ischemic heart disease are at a notably higher risk of harboring ESBL-GNB producing bacteria in their fecal flora (see Table 2).

The timing of the dialysis shift revealed as a significant factor (aOR: 8.864; *p*: 0,005), specifically, patients undergoing hemodialysis during the morning shift exhibited a markedly higher probability of ESBL-GNB colonization. This finding suggests that the morning dialysis session is independently associated with an increased likelihood of ESBL-GNB colonization compared to other shifts when accounting for other relevant variables. From the evaluated laboratory parameters only, BUN stood out as a significant indicator (aOR: 1.049; *p*: 0.045), this underscores the clinical relevance of BUN as a potential biomarker for bacterial colonization risk (see Table 2).

CR-GNB carriage & risk factors

In terms of CR-GNB only 8 were found to be colonized with CR-GNB, representing an 5.8% prevalence. After adjusting the potential confounding variables in the multivariate analysis. The results revealed a significant association only with IHD playing a notable role (aOR: 0.052; *p*: 0.041). This low adjusted odds ratio (aOR) signifies a robust inverse correlation, indicating that hemodialysis patients with IHD are at a significantly lower risk of harboring CR-GNB in their fecal flora. This finding underscores the potential protective effect of IHD against CR-GNB colonization in this specific patient population (see Table 3).

Discussion

In this study, a high prevalence of colonization by ESBL-GNB (84.7%) was found in patients on hemodialysis, and they are higher than those found in other studies. In a

Table 2 Univariate and multivariate analysis for identification of factors associated with colonization by ESBL-GNB in hemodialysis patients

Variable		ESBL-GNB					
		Univariate analysis			Multivariate analysis		
		OR	95%CI	*p*-value	OR[a]	95%CI	*p*-value[a]
Age (years)		1.054	1.02–1.09	0.002*	1.068	1.01–1.12	0.012*
Gender	Male	1.243	0.49–3.16	0.647	0.291	0.07–1.28	0.102
	Female	1	-	-	1	-	-
Comorbidities	HTN**	3.467	1.13–10.62	0.023*	15.582	1.63–149.34	0.017*
	DM**	1.101	0.43–2.82	0.841	0.326	0.06–1.93	0.216
	IHD**	3.702	1.17–11.67	0.019*	5.381	1.08–26.76	0.040*
	Fracture**	1.284	0.15–11.01	0.819	1.008	0.07–15.46	0.996
	Surgery**	2.972	1.08–8.20	0.030*	1.961	0.42–9.05	0.388
Dialysis time (months)		0.998	0.99–1.01	0.769	1.002	0.99–1.02	0.773
Shift of dialysis	Morning	2.564	0.99–6.67	0.054	8.864	1.91–41.15	0.005*
	Evening	1	-	-	1	-	-
Sessions per week	≥ 3	3.664	0.97–13.86	0.056	2.958	0.40–21.97	0.289
	< 3	1	-	-	1	-	-
Vascular access	AVF	1.471	0.44–4.93	0.532	0.965	0.18–5.26	0.967
	CVC	1	-	-	1	-	-
Anticoagulants**		0.786	0.27–2.32	0.663	0.509	0.10–2.56	0.413
Labs	BUN	1.040	1.01–1.07	0.017*	1.049	1.00–1.10	0.045*
	WBC	1.154	0.93–1.44	0.202	1.045	0.78–1.40	0.771
	HGB	0.904	0.63–1.30	0.581	0.735	0.43–1.27	0.267
	Calcium	0.78	0.41–1.49	0.451	0.521	0.20–1.36	0.182
	Phosphate	1.231	0.88–1.73	0.231	1.528	0.86–2.70	0.145

ESBL, extended-spectrum β-lactamase; GNB, Gram-negative bacilli; HTN, hypertension; DM, diabetes mellitus; IHD, ischemic heart disease; CVC, central venous catheter; AVF, arteriovenous fistula; BUN, blood urea nitrogen; WBC, white blood cells; Hgb, hemoglobin.[a] Adjusted values *Significant values are marked with an asterisk. **Reference: No

Table 3 Univariate and multivariate analysis for identification of factors associated with colonization by CR-GNB in hemodialysis patients

Variable		CR-GNB					
		Univariate analysis			Multivariate analysis		
		OR	95%CI	*p*-value	OR[a]	95%CI	*p*-value[a]
Age (years)		1.035	0.98–1.10	0.258	1.062	0.97–1.16	0.198
Gender	Male	0.743	0.18–3.10	0.683	1.674	0.27–10.49	0.582
	Female	1	-	-	1	-	-
Comorbidities	CHF**	1.536	0.291–8.10	0.613	5.846	0.43–78.71	0.183
	DM**	5.203	0.62–43.52	0.128	5.786	0.44–76.36	0.182
	IHD**	0.435	1.08–2.24	0.319	0.052	0.00–0.89	0.041*
	CVA**	2.533	0.47–13.71	0.281	3.479	0.41–29.67	0.254
	Surgery**	0.985	0.236–4.107	0.983	0.697	0.11–4.26	0.696
Dialysis time (months)		0.990	0.98–1.01	0.389	0.995	0.97–1.02	0.708
Shift of dialysis	Morning	2.301	0.45–11.84	0.319	4.929	0.69–35.05	0.111
	Evening	1	-	-	1	-	-
Sessions per week	≥ 3	0.588	0.07–5.27	0.635	0.815	0.04–16.33	0.894
	< 3	1	-	-	1	-	-
Vascular access	AVF	1.209	0.14–10.39	0.863	1.462	0.08–25.42	0.794
	CVC	1	-	-	1	-	-
Anticoagulants		1.161	0.22–6.02	0.859	1.754	0.01–5.80	0.786
Labs	WBC	0.897	0.65–1.25	0.516	0.775	0.48–1.25	0.296
	HGB	0.862	0.51–1.45	0.576	0.803	0.42–1.55	0.515

CR, carbapenem-resistant; GNB, Gram-negative bacilli; CHF, congestive heart failure; DM, diabetes mellitus; IHD, ischemic heart disease; CVA, cerebrovascular accidents; CVC, central venous catheter; AVF, arteriovenous fistula; WBC, white blood cells; Hgb, hemoglobin. [a] Adjusted values. *Significant values are marked with an asterisk. **Reference: No

study conducted in Colombia, the prevalence of ESBL-GNB in hemodialysis patients was 41.2% [18]. Similarly, in an Iranian study involving hemodialysis patients, the ESBL-GNB rate was 48.6% [19]. Furthermore, our observed rates outweigh those of ESBL-GNB colonization in the general population, which are as high as 12.3% [27,34].

For CR-GNB the prevalence was low (5.8%) compared to other studies. In Colombia, a study conducted on hemodialysis patients found that CR-GNB colonization prevalence was 11.5% [18]. In China, for example, the prevalence of CR-GNB in inpatients of a tertiary care hospital closely aligned with our study at 6.6% [17]. For the general population around the world, the prevalence of CR-GNB colonization was high reaching 6.9% [35].

This study showed a significant presence of ESBL-GNB colonization among hemodialysis patients, particularly linked to advanced age and specific underlying health conditions. Age emerged as a critical factor, with colonization becoming more likely as patients aged, which differs from previous findings indicating no correlation with age [17, 18, 28]. This aligns with the notion that older patients may have a higher cumulative risk of exposure to hospital environments or a diminished immune response, leading to greater vulnerability. The strong association between ESBL-GNB colonization and comorbidities such as hypertension and ischemic heart disease suggests a complex interplay between the patient's overall health status and susceptibility to bacterial colonization. Patients with such comorbidities have frequent contact with healthcare, frequent hospital visits, and receive different groups of drugs, which increases the risk of colonization by resistant bacteria [36], or could expose them to immune response alterations due to potential interactions between medications used for treatment [37], The exact mechanisms behind this relationship warrant further investigation.

Unexpectedly, patients undergoing dialysis during the morning shift showed a higher probability of colonization. This could be due to various factors including the structure of staffing, the patient load, or differences in cleaning protocols between shifts that require more in-depth analysis. However, given that a majority of patients received dialysis during the morning shift regardless of their colonization status (57.7%) creating a slight disproportionate representation of patients in each shift, this association should be interpreted with caution as the data may be skewed and further studies with a more balanced sample distribution are needed to confirm this finding.

According to previous studies, the colonization of MDR increases with antibiotic exposure [17, 35, 38]. Interestingly, a previous study that researched factors associated with over-prescription of antimicrobials found that morning shift dialysis patients were exposed to higher rates of empiric antimicrobials while evening shift patients are less likely to receive immediate antimicrobial therapy, one hypothesis could be that these patients get

their evaluation deferred until they visit the emergency department or get hospitalized [39].

The observed inverse relationship between CR-GNB colonization and ischemic heart disease (IHD) in this study is a counterintuitive finding that challenges our conventional understanding. However, this finding is based on a small number of colonized patients ($n=8$), which limits the statistical power and validity of this association. The limited sample size makes it challenging to draw definitive conclusions, and the observed inverse relationship may be due to chance or unmeasured confounding factors. Therefore, this result should be interpreted with caution, and we cannot assert a causal relationship based on our data.

Moreover, the low prevalence of CR-GNB colonization in our cohort (5.8%) aligns with findings from other studies in the region. A recent study conducted in the West Bank, Palestine, reported a 17% prevalence of carbapenem-resistant Enterobacterales (CRE) among 600 randomly selected clinical samples collected from five governmental hospitals [40]. While this indicates that CRE is present in the region, the prevalence among hemodialysis patients may be lower. Our findings suggest that CRE colonization is relatively uncommon in this patient population, but due to the small number of cases, we cannot make strong assertions about risk factors such as IHD. Further studies with larger sample sizes are necessary to confirm or refute the observed association between CR-GNB colonization and ischemic heart disease. Such studies would help to better understand the epidemiology and risk factors of CRE colonization among hemodialysis patients in our region.

Limitations

While this study provides valuable insights into the fecal carriage of ESBL-GNB and CR-GNB among hemodialysis patients, several limitations should be acknowledged. Firstly, the single-center nature of the study conducted in An-Najah National University Hospital may limit the generalizability of our findings to broader population or healthcare settings. Nonetheless, hemodialysis patients share common characteristics that may facilitate the extrapolation of the study results to diverse dialysis settings. The self-collection of stool samples may be subject to variability in adherence and technique among participants, potentially influencing the accuracy and reliability of bacteria colonization screening. Additionally, the sample size may impact the precision of our estimates. It is imperative to acknowledge the absence of detailed medical records regarding the antibiotics prescribed for the hemodialysis patients in this study; the lack of comprehensive information on antibiotic usage hinders our ability to assess the potential impact of antibiotic exposure on the fecal carriage of ESBL-GNB and CR-GNB. In interpreting our results, it is crucial to recognize these limitations and consider their potential impact on the direction and magnitude of observed associations, emphasizing the need for cautious interpretation and further research to validate and extend our findings.

Despite the acknowledged limitations, this study is the first to investigate the prevalence of ESBL-GNB and CR-GNB colonization among hemodialysis patients in Palestine which possesses notable strengths that enhance the validity and relevance of our findings. First and foremost, the comprehensive multivariate analysis employed in this investigation allowed us to discern nuanced relationships between various factors and the fecal carriage of ESBL-GNB and CR-GNB among hemodialysis patients. The adjustment for potential confounding variables adds robustness to our results, providing a more accurate reflection of the independent associations identified. Additionally, the focus on a vulnerable population "hemodialysis patients" addresses an area of critical concern in infection control. The utilization of stool samples for bacterial screening, while subject to limitations, is a practical approach to capturing the prevalence of bacterial colonization. These strengths collectively contribute to the significance of this study, offering valuable insights into potential risk factors for bacterial colonization in hemodialysis patients and informing targeted strategies for infection prevention and patient management.

Implications and future directions

The findings highlight the importance of tailored interventions to reduce the risk of bacterial colonization and enhance patient care in hemodialysis settings. There is an imperative need for antimicrobial stewardship programs within renal units, the implementation of educational strategies regarding antibiotic use in the community, and effective infection prevention strategies in diverse healthcare settings. Future research should focus on larger, multicenter studies to further explore the risk factors associated with antibiotic-resistant bacterial colonization and to develop targeted interventions.

Conclusion

This study revealed a high prevalence of colonization by ESBL-GNB among hemodialysis patients in a Palestinian tertiary care hospital. Significant risk factors associated with ESBL-GNB colonization included advanced age, hypertension, ischemic heart disease, morning dialysis shifts, and elevated blood urea nitrogen levels. CR-GNB colonization was less prevalent, and an inverse association with ischemic heart disease was observed, though this finding should be interpreted with caution due to the small sample size. These results emphasize the critical need for enhanced surveillance and infection control

measures to prevent the spread of antibiotic-resistant bacteria in hemodialysis settings.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12879-024-10236-z.

Supplementary material 1

Acknowledgements
The authors would like to thank An-Najah National University (https://www.najah.edu/en/) for the technical support provided to publish the present manuscript.

Author contributions
A.J., D.J. and Y.A. data and sample collection, laboratory work, analysis and writing. M.J. data and sample collection. Z.N. analysis, study design and writing. A.A.T. and M.Q. conceptualization, supervising, study design, data collection, and writing. All authors reviewed the manuscript.

Funding
No fund, but this research was supported by An-Najah National University as part of a graduation degree project.

Data availability
The data used to support the findings of this study are included within the article.

Declarations

Ethics approval and consent to participate
This study was conducted with the full approval of the Institutional Review Board (IRB) at An-Najah National University (Ref: Med. Sept. 2023/2). The IRB reviewed all aspects of the study protocol, including procedures for accessing and utilizing patient clinical information. All collected data were employed exclusively for this clinical research project and were maintained with strict confidentiality. Patient data and hospital details were anonymized through a coding system, allowing access to the information only for authorized research staff to maintain confidentiality. Written informed consent was obtained from each participant before their inclusion in the study. The research methodology followed all relevant ethical guidelines and regulations.

Consent for publication
All authors approved the manuscript and gave their consent for submission and publication.

Competing interests
The authors declare no competing interests.

Received: 17 July 2024 / Accepted: 18 November 2024
Published online: 22 November 2024

References

1. Lautenbach E, Perencevich EN. Addressing the emergence and impact of multidrug-resistant gram-negative organisms: a critical focus for the next decade. Infect Control Hosp Epidemiol. 2014;35:333–5.
2. Kaye KS, Pogue JM. Infections caused by resistant gram-negative Bacteria: Epidemiology and Management. Pharmacotherapy. 2015;35:949–62.
3. Aiesh BM, et al. Epidemiology and clinical characteristics of patients with healthcare-acquired multidrug-resistant Gram-negative bacilli: a retrospective study from a tertiary care hospital. Sci Rep. 2024;14:3022.
4. Qadi M, Alhato S, Khayyat R, Elmanama AA. Colistin Resistance among Enterobacteriaceae Isolated from Clinical Samples in Gaza Strip. Canadian Journal of Infectious Diseases and Medical Microbiology 2021, 6634684.
5. CDC. The biggest antibiotic-resistant threats in the U.S. Centers Disease Control Prev 2022.https://www.cdc.gov/drugresistance/biggest-threats.html.
6. Hutchings MI, Truman AW, Wilkinson B. Antibiotics: past, present and future. Curr Opin Microbiol. 2019;51:72–80.
7. Hu F-P, et al. Resistance trends among clinical isolates in China reported from CHINET surveillance of bacterial resistance, 2005–2014. Clin Microbiol Infect. 2016;22(Suppl 1):S9–14.
8. Qadi M et al. Colistin and Antimicrobial Resistance among Gram-negative Bacteria isolated from Poultry in West Bank, Palestine. Palestinian Med Pharm J 9, (2024).
9. Kato S, et al. Aspects of immune dysfunction in end-stage renal disease. Clin J Am Soc Nephrol. 2008;3:1526–33.
10. Kallen AJ, Arduino MJ, Patel PR. Preventing infections in patients undergoing hemodialysis. Expert Rev Anti Infect Ther. 2010;8:643–55.
11. Vaziri ND, et al. Chronic kidney disease alters intestinal microbial flora. Kidney Int. 2013;83:308–15.
12. Johansen KL, et al. Epidemiology of Kidney Disease in the United States. Am J Kidney Dis. 2021;77:A7–8. US Renal Data System 2020 Annual Data Report:.
13. Vogelzang JL, et al. Mortality from infections and malignancies in patients treated with renal replacement therapy: data from the ERA-EDTA registry. Nephrol Dial Transpl. 2015;30:1028–37.
14. Bleumin D, et al. Carbapenem-resistant Klebsiella pneumoniae is associated with poor outcome in hemodialysis patients. J Infect. 2012;65:318–25.
15. Biehl LM, Schmidt-Hieber M, Liss B, Cornely OA, Vehreschild MJGT. Colonization and infection with extended spectrum beta-lactamase producing Enterobacteriaceae in high-risk patients - review of the literature from a clinical perspective. Crit Rev Microbiol. 2016;42:1–16.
16. Denholm JT, Huysmans M, Spelman D. Community acquisition of ESBL-producing Escherichia coli: a growing concern. Med J Aust. 2009;190:45–6.
17. Zhao Z, et al. Fecal carriage of carbapenem-resistant Enterobacteriaceae in a Chinese university hospital. Am J Infect Control. 2014;42:e61–64.
18. Salazar-Ospina L, Vanegas JM, Jiménez JN. High intermittent colonization by diverse clones of β-lactam-resistant Gram-negative bacilli suggests an excessive antibiotic use and different sources of transmission in haemodialysis patients. J Hosp Infect. 2021;107:76–86.
19. Hosseinzadeh-sohi N, Najar-Peerayeh S, Bakhshi B. Intestinal carriage of extended-spectrum β-lactamase and carbapenemase-producing Enterobacteriaceae in Hemodialysis patients. Jundishapur J Microbiol 15, (2022).
20. Calfee D, Jenkins SG. Use of active surveillance cultures to detect asymptomatic colonization with carbapenem-resistant Klebsiella pneumoniae in intensive care unit patients. Infect Control Hosp Epidemiol. 2008;29:966–8.
21. Tischendorf J, de Avila RA, Safdar N. Risk of infection following colonization with carbapenem-resistant enterobactericeae: a systematic review. Am J Infect Control. 2016;44:539–43.
22. Palacios-Baena ZR, et al. Risk factors for carbapenem-resistant Gram-negative bacterial infections: a systematic review. Clin Microbiol Infect. 2021;27:228–35.
23. Taher A, et al. Growing a peritoneal dialysis program in Palestine from zero to 178 patients in 5 years: a single-center experience. BMC Nephrol. 2023;24:21.
24. Kumar S, Vyas A. Utilization of MacConkey-Meropenem screening Agar for the detection of Carbapenem Resistanant Enterobacteriaceae in a tertiary care hospital. in (2018).
25. Wilson G, McCabe D. The use of antibiotic-containing agars for the isolation of extended-spectrum beta-lactamase-producing organisms in intensive care units. Clin Microbiol Infect. 2007;13:451–3.
26. Odeh Z, Abatli S, Qadi M, Radiology Department. A Potential Source of Multidrug-Resistant Microorganisms: A Cross-Sectional Study at Tertiary Hospital, Palestine. Can J Infect Dis Med Microbiol 2023, 4441338.
27. Tseng W-P, et al. Predicting Multidrug-Resistant Gram-negative bacterial colonization and Associated Infection on Hospital Admission. Infect Control Hosp Epidemiol. 2017;38:1216–25.
28. Leistner R, et al. Risk factors Associated with the community-acquired colonization of extended-spectrum beta-lactamase (ESBL) positive Escherichia Coli. An exploratory case-control study. PLoS ONE. 2013;8:e74323.
29. Garry S, Checchi F. Armed conflict and public health: into the 21st century. J Public Health (Oxf). 2020;42:e287–98.
30. Kattan R et al. Emergence of Klebsiella pneumoniae carbapenemase (blaKPC-2) in members of the enterobacteriaceae family in Palestine. Int Arabic J Antimicrob Agents 2, 2012.
31. Logan LK, Weinstein RA. The epidemiology of Carbapenem-Resistant Enterobacteriaceae: the impact and evolution of a global menace. J Infect Dis. 2017;215:S28–36.
32. Chiotos K, Han JH, Tamma PD. Carbapenem-Resistant Enterobacteriaceae infections in Children. Curr Infect Dis Rep. 2016;18:2.

33. Giannella M, et al. Risk factors for carbapenem-resistant Klebsiella pneumoniae bloodstream infection among rectal carriers: a prospective observational multicentre study. Clin Microbiol Infect. 2014;20:1357–62.
34. Pop-Vicas A, Strom J, Stanley K, D'Agata EM. C. Multidrug-resistant gram-negative bacteria among patients who require chronic hemodialysis. Clin J Am Soc Nephrol. 2008;3:752–8.
35. Rodríguez-Villodres Á, et al. Prevalence and risk factors for Multidrug-resistant organisms colonization in Long-Term Care facilities around the World: a review. Antibiot (Basel). 2021;10:680.
36. Moor CT, et al. Extended-spectrum beta-lactamase (ESBL)-producing enterobacteria: factors associated with infection in the community setting, Auckland, New Zealand. J Hosp Infect. 2008;68:355–62.
37. Mallat Z, Binder CJ. The why and how of adaptive immune responses in ischemic cardiovascular disease. Nat Cardiovasc Res. 2022;1:431–44.
38. Otter JA, et al. Individual- and community-level risk factors for ESBL Enterobacteriaceae colonization identified by universal admission screening in London. Clin Microbiol Infect. 2019;25:1259–65.
39. Snyder GM, et al. Factors associated with the receipt of antimicrobials among chronic hemodialysis patients. Am J Infect Control. 2016;44:1269–74.
40. Ibaideya MAT, Taha AA, Qadi M. Phenotypic and molecular characterization of multidrug-resistant Enterobacterales isolated from clinical samples in Palestine: a focus on extended-spectrum β-lactamase- and carbapenemase-producing isolates. BMC Infect Dis. 2024;24:812.

Publisher's note