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# Prevalence and clinical correlates of peripheral artery disease in patients undergoing hemodialysis: a cross-sectional study from Palestine

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## Abstract

**Background** Peripheral artery disease (PAD) is a common but underrecognized complication among patients with end-stage renal disease (ESRD) receiving hemodialysis. PAD contributes substantially to morbidity and mortality, yet data from Palestine are lacking. This study aimed to estimate the prevalence of PAD and examine its association with clinical and laboratory characteristics in hemodialysis patients.

**Methods** A cross-sectional study was conducted between February and November 2023 at the dialysis center in a large tertiary accredited teaching hospital, the main referral center in the northern West Bank, Palestine. A total of 278 patients undergoing regular hemodialysis were enrolled. PAD was diagnosed using the ankle–brachial index (ABI) measured by handheld Doppler ultrasound;  $ABI \leq 0.90$  indicated PAD. Demographic, clinical, and laboratory data were collected from patient interviews and medical records. Multivariable logistic regression was used to identify factors associated with PAD and to estimate adjusted odds ratios with 95% confidence intervals.

**Results** PAD was detected in 150 of 278 patients (54%). The mean age was  $57 \pm 16$  years, and 176 (63.3%) were male. Hypertension was present in 236 (84.9%), diabetes mellitus in 147 (52.9%), and cardiac disease in 85 (30.6%). PAD was significantly associated with older age ( $p=0.01$ ), longer dialysis duration ( $p=0.03$ ), hypertension ( $p=0.025$ ), diabetes ( $p=0.023$ ), cardiac disease ( $p=0.008$ ), and lower serum phosphorus levels ( $p=0.03$ ). No significant associations were observed with gender ( $p=0.448$ ), smoking ( $p=0.836$ ), prior myocardial infarction ( $p=0.074$ ), stroke ( $p=0.170$ ), physical activity ( $p=0.688$ ), vascular access type ( $p=0.688$ ), duration of hypertension ( $p=0.281$ ), or duration of diabetes

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( $p=0.165$ ). In a multivariable logistic regression model, dialysis duration remained significantly associated with PAD (adjusted OR 1.08 per year, 95% CI 1.01–1.16,  $p=0.031$ ).

**Conclusions** PAD prevalence was high among hemodialysis patients in this Palestinian cohort, and longer dialysis duration emerged as a significant correlate of PAD. Routine ABI screening—particularly in patients with longer dialysis vintage—may enable earlier detection and management of PAD, potentially reducing adverse cardiovascular outcomes. Further longitudinal studies are warranted to identify causal pathways and inform preventive strategies.

**Keywords** Peripheral arterial disease, End-Stage renal disease, Hemodialysis, Ankle–Brachial index, Diabetes mellitus, Hypertension, Cardiovascular disease, Palestine

## Introduction

Peripheral artery disease (PAD) is characterized by atherosclerotic narrowing of the peripheral arteries and is recognized as a significant contributor to global morbidity and mortality [1]. The ankle–brachial index (ABI) is widely applied in clinical settings as a non-invasive method for detecting the presence and severity of PAD [2]. Prevalence rates of PAD are considerably higher among individuals with advanced symptoms—such as rest pain, ulcers, or gangrene—compared with those presenting with intermittent claudication [3].

End-stage renal disease (ESRD) occurs when kidney function declines to a point where survival is not possible without dialysis or kidney transplantation [4]. While transplantation generally offers the most favorable outcomes, most patients remain on dialysis, which is associated with profound cardiovascular and coagulation abnormalities [5]. Patients with ESRD face an increased risk of cardiovascular disease [6], which accounts for more than half of all deaths in this population [7]. Importantly, conditions that compromise cardiovascular health, such as PAD, may alter biomarker levels in ways that signal worsening ESRD [6].

Although the prevalence of PAD among hemodialysis patients has been extensively investigated worldwide, no such studies have been conducted in Palestine. Given the growing dialysis population in the region, understanding the burden of PAD is essential for guiding preventive interventions, tailoring patient care, and reducing cardiovascular complications. Moreover, given its descriptive, cross-sectional design, this study aims to characterize the prevalence of PAD and its clinical and laboratory correlates among hemodialysis patients, rather than to establish causal relationships.

**Aim of the study** The present study was conducted to (1) investigate the clinical characteristics and laboratory findings of patients on hemodialysis, (2) evaluate ESRD patients using ABI to diagnose PAD, and (3) compare patients with and without PAD with respect to their clinical and laboratory characteristics.

## Materials and methods

### Study design and setting

This was a descriptive cross-sectional study conducted between February and November 2023 at the dialysis center in a large tertiary accredited teaching hospital in Palestine. The hospital is the main referral facility for the dialysis population in the northern West Bank, Palestine. The study was reported in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines [8] (see Supplementary File 1 for checklist).

### Study population, inclusion, and exclusion criteria

The dialysis center served a total of 320 patients with ESRD receiving maintenance hemodialysis during the study period. Of these, 278 patients were enrolled. Patients were eligible if they were on regular hemodialysis and provided informed consent. Exclusion criteria included active ankle or leg infection, a history of deep venous thrombosis, lymphadenitis (enlarged lymph nodes due to infection, as documented in medical reports), or vasospasm (as noted in medical reports).

### Sample size and sampling technique

A census sampling technique was applied, targeting all patients at the dialysis center ( $N=320$ ). After applying the exclusion criteria and accounting for non-participation, 278 patients were included in the final analysis. This approach ensured near-complete coverage of the dialysis population at the facility.

### Variables and definitions

Data collected included demographic variables (age, sex), clinical comorbidities (hypertension, diabetes mellitus, cardiac disease, prior myocardial infarction, stroke), and lifestyle factors (smoking, alcohol use, physical activity). Smoking status was categorized as current, former, or never smoked, based on established definitions [9]. Smoking status was self-reported, which may be subject to recall or social-desirability bias. Hypertension was classified according to international blood pressure thresholds [10] and body mass index (BMI) was calculated as weight in kilograms divided by height in meters

squared, categorized according to World Health Organization (WHO) criteria [11]. Dialysis-related variables included dialysis duration (in years) and type of vascular access (arteriovenous fistula, arteriovenous graft, or central venous catheter). Dialysis vintage (duration on hemodialysis, in years) was extracted from medical records and analyzed as a continuous variable. Laboratory parameters included serum creatinine, blood urea nitrogen (BUN), electrolytes (calcium, sodium, potassium, phosphorus), parathyroid hormone (PTH; reference range 15–65 pg/mL) [12], iron indices (serum iron, ferritin, transferrin saturation, total iron binding capacity), albumin, and lipid profile, where available [13]. Interpretation of mineral metabolism parameters (phosphorus and PTH) was guided by KDIGO recommendations for chronic kidney disease–mineral and bone disorder (CKD-MBD) [14].

## Outcomes

The primary outcome was the prevalence of PAD among patients on hemodialysis, defined as  $ABI \leq 0.90$ . Secondary outcomes included associations between PAD and clinical as well as laboratory characteristics.

## Data collection tools and measurement

PAD was assessed using the ABI, which was measured according to the standard protocol [9] using a portable handheld bidirectional Doppler device available at the hospital hemodialysis unit. Our ABI protocol is consistent with contemporary PAD guidelines, which recommend ABI as a first-line diagnostic test for lower extremity PAD in high-risk populations such as patients with diabetes and chronic kidney disease [15, 16]. Measurements were performed before dialysis while the patient was supine and after 5–10 min of rest. To minimize measurement bias, this standardized protocol was used for all ABI measurements, ensuring consistency in patient positioning and rest time prior to data collection. Systolic blood pressure was recorded in the brachial artery of the arm without vascular access and in the dorsalis pedis and posterior tibial arteries of both legs. ABI was calculated by dividing the higher ankle systolic pressure by the higher brachial systolic pressure, and the lowest value for each patient was used. An  $ABI \leq 0.90$  indicated PAD, and values between 0.91 and 1.30 were considered normal [11]. In line with contemporary PAD guidelines, ABI values  $> 1.30$  are typically interpreted as suggesting non-compressible arteries due to medial arterial calcification, particularly in patients with diabetes or chronic kidney disease [15, 16]. However, in our cohort, no participant had an  $ABI > 1.30$ ; therefore, no “non-compressible” category was present, and all analyses were restricted to ABI values  $\leq 1.30$ , comparing PAD ( $ABI \leq 0.90$ ) versus non-PAD ( $ABI > 0.90$ ).

Blood samples were drawn before dialysis sessions to measure serum creatinine, urea, electrolytes, calcium, phosphorus, glucose, C-reactive protein (CRP), lipid profile, iron indices, intact parathyroid hormone, hemoglobin, and complete blood count. The Doppler device used for ABI measurement demonstrated good accuracy, with systemic error  $< 6\%$ .

## Statistical analysis

Data were analyzed using SPSS version 22 [17]. Continuous variables were expressed as mean  $\pm$  standard deviation (SD) or median (interquartile range), while categorical variables were reported as frequencies and percentages. Independent-samples t-tests or Mann–Whitney U tests were used to compare continuous variables, and Pearson’s chi-square test or Fisher’s exact test was applied for categorical variables. Missing values were defined as user-missing in SPSS and excluded from analyses using a complete case approach. Reliability testing was considered for scales; however, as most variables were drawn from objective clinical and laboratory data, no internal consistency measures, such as Cronbach’s alpha, were applicable. To identify factors associated with PAD, we fitted a multivariable binary logistic regression model with PAD status ( $ABI \leq 0.90$  vs.  $> 0.90$ ) as the dependent variable. Covariates were selected a priori based on clinical relevance and previous literature and included age (per 10-year increase), sex, dialysis duration (years), hypertension, diabetes mellitus, current smoking, cardiac disease, and serum phosphorus (per 1 mg/dL). Hypertension, diabetes, cardiac disease, and current smoking were entered as binary variables (yes/no). The model was estimated using complete-case analysis after exclusion of observations with missing values ( $n = 265$ ). Results are presented as adjusted odds ratios (aORs) with 95% confidence intervals (CIs) and p-values. Model fit was evaluated using the Hosmer–Lemeshow goodness-of-fit test and pseudo-R<sup>2</sup> statistics. Statistical significance was set at a p-value  $< 0.05$ .

## Ethical approval

Ethical approval was obtained from the Institutional Review Board (IRB) of An-Najah National University (Med.Sept.2023/16). Study design and objectives were explained to participants, and written informed consent was obtained from all adults. For minors, consent was obtained from parents or guardians. The study was conducted in accordance with the ethical principles of the Declaration of Helsinki and institutional guidelines.

## Results

### Participant characteristics

Of the 320 patients receiving maintenance hemodialysis at the dialysis center during the study period,

**Table 1** Baseline demographic and clinical characteristics of Hemodialysis patients (N=278)

Characteristic	Frequency n (%) / Mean $\pm$ SD
Age categories (years)	
0–17	6 (2.1)
18–44	48 (17.3)
45–64	126 (45.3)
65–84	95 (34.2)
≥85	3 (1.1)
Age in years	57 $\pm$ 16
Gender	
Male	176 (63.3)
Female	102 (36.7)
Smoking status	
Current	91 (32.4)
Former	41 (14.7)
Never	146 (52.5)
BMI (kg/m <sup>2</sup> )	27 $\pm$ 6
Alcohol use	
Yes	0 (0)
No	278 (100)
Physical activity	
Mobile	252 (90.6)
Immobile	26 (9.4)
Medical history	
DM	147 (52.9)
No DM	130 (46.8)
DM duration (years)	18 $\pm$ 9
HTN	236 (84.9)
No HTN	42 (15.1)
HTN duration (years)	14 $\pm$ 9
Cardiac disease	85 (30.6)
History of myocardial infarction	19 (6.8)
History of stroke	39 (14.0)
Dialysis-related	
Dialysis duration (years)	4 $\pm$ 4
Vascular access type	
AVF	244 (87.8)
AVG	2 (0.7)
Catheter	32 (11.5)
CCI	4 $\pm$ 2

Data are presented as n (%) or mean  $\pm$  standard deviation (SD), as indicated. Abbreviations: BMI, body mass index; DM, diabetes mellitus; HTN, hypertension; AVF, arteriovenous fistula; AVG, arteriovenous graft; CCI, Charlson comorbidity index

278 met the inclusion criteria and were enrolled in the study (Table 1). The mean age was 57  $\pm$  16 years, with the majority between 45 and 64 years (45.3%). A small subset of patients were younger than 18 years (n=6; age range 7–16 years), reflecting adolescents with end-stage renal disease receiving chronic hemodialysis at the center. Most participants were male (63.3%). The mean BMI was 27  $\pm$  6 kg/m<sup>2</sup>. Nearly one-third (32.4%) were current smokers, and 9.4% were immobile. Hypertension was present in 236 patients (84.9%) with a mean duration of

**Table 2** Laboratory parameters of Hemodialysis patients

Variable	N	Mean $\pm$ SD
Calcium (mg/dL)	267	8.87 $\pm$ 0.85
Sodium (mmol/L)	268	133.1 $\pm$ 14.4
Phosphorus (mg/dL)	267	4.86 $\pm$ 1.43
Potassium (mmol/L)	265	4.82 $\pm$ 0.76
Parathyroid hormone (pg/mL)	270	409.7 $\pm$ 473.9
White blood cells ( $\times 10^9$ /L)	270	7.02 $\pm$ 2.21
Platelets ( $\times 10^9$ /L)	271	192.3 $\pm$ 62.6
Hemoglobin (g/dL)	270	10.3 $\pm$ 1.6
Transferrin saturation (%)	268	32.4 $\pm$ 16.0
Total iron binding capacity (μg/dL)	268	198.6 $\pm$ 38.7
Iron (μg/dL)	268	63.1 $\pm$ 27.8
Ferritin (ng/mL)	246	1055.6 $\pm$ 605.5
Albumin (g/dL)	268	3.90 $\pm$ 0.39
Creatinine (mg/dL)	268	9.04 $\pm$ 2.83

Data are presented as mean  $\pm$  standard deviation (SD). The number of patients varies by variable because some laboratory tests were not performed for all participants; analyses were conducted on available cases using a complete-case approach

**Table 3** Prevalence of PAD based on ABI classification

ABI classification	Frequency n (%)
Abnormal ABI ( $\leq 0.90$ ) (PAD present)	150 (54.0)
Normal ABI ( $> 0.90$ ) (PAD absent)	128 (46.0)

Data are presented as n (%). PAD was defined as ankle–brachial index (ABI)  $\leq 0.90$ ; ABI  $> 0.90$  was considered normal (non-PAD). Abbreviations: PAD, peripheral artery disease; ABI, ankle–brachial index

14  $\pm$  9 years, and diabetes mellitus in 147 (52.9%) with a mean duration of 18  $\pm$  6 years. Cardiac disease was reported in 85 patients (30.6%), while 19 (6.8%) had a prior myocardial infarction and 39 (14.0%) a history of stroke. The mean dialysis duration was 4  $\pm$  4 years. The majority of patients (87.8%) had an arteriovenous fistula as vascular access, while 11.5% had catheters.

### Laboratory findings

Mean laboratory values included serum calcium 8.9  $\pm$  0.9 mg/dL, phosphorus 4.9  $\pm$  1.4 mg/dL, potassium 4.8  $\pm$  0.8 mmol/L, sodium 133  $\pm$  14 mmol/L, and albumin 3.9  $\pm$  0.4 g/dL. The mean hemoglobin level was 10.3  $\pm$  1.6 g/dL. Median parathyroid hormone levels were markedly elevated (409 pg/mL), and mean ferritin was also high (1056 ng/mL). The number of observations for each laboratory parameter varied slightly due to missing tests; denominators for each variable are reported in Table 2. Other hematologic and biochemical parameters are also reported in the table.

### Prevalence of PAD

According to ABI measurements, 150 patients (54.0%) had PAD, while 128 (46.0%) had normal ABI values (Table 3). No patient in this cohort had an ABI  $> 1.30$ ; thus, no cases with clearly non-compressible

arteries were identified, and all patients fell into the PAD (ABI  $\leq 0.90$ ) or non-PAD (ABI  $> 0.90$ ) categories.

#### Associations with clinical characteristics

PAD was significantly more common among older patients (median age 63 vs. 60 years,  $p=0.01$ ) and those with longer dialysis duration (median 3 vs. 2 years,  $p=0.03$ ). Hypertension (89.3% vs. 79.9%,  $p=0.025$ ), diabetes mellitus (59.3% vs. 45.7%,  $p=0.023$ ), and cardiac disease (37.3% vs. 22.7%,  $p=0.008$ ) were significantly more frequent in patients with PAD. No significant associations were observed with gender ( $p=0.448$ ), smoking ( $p=0.839$ ), physical activity ( $p=0.688$ ), vascular access type ( $p=0.688$ ), history of myocardial infarction ( $p=0.074$ ), or stroke ( $p=0.170$ ) (Table 4). Obesity

( $\text{BMI} \geq 30 \text{ kg/m}^2$ ) was present in 49 of 150 patients with PAD (32.7%) and 39 of 128 patients without PAD (30.5%), and was not significantly associated with PAD ( $p=0.79$ ).

#### Associations with laboratory parameters

Among laboratory variables, only serum phosphorus levels were significantly associated with PAD, with lower mean phosphorus in patients with PAD compared with those without PAD ( $4.68 \pm 1.44$  vs.  $5.06 \pm 1.41 \text{ mg/dL}$ ,  $p=0.030$ ). Other biochemical markers—including calcium, sodium, potassium, hemoglobin, creatinine, ferritin, albumin, white blood cell count, platelet count, transferrin saturation, total iron-binding capacity, iron, and parathyroid hormone—also demonstrated no significant differences between PAD and non-PAD groups (Table 5).

**Table 4** Association of PAD with clinical characteristics

Variable	PAD present (ABI $\leq 0.90$ ), n (%)	PAD absent (ABI $> 0.90$ ), n (%)	p-value
Age, median (range), years	63 (58–70)	60 (53–64)	<b>0.01</b>
Gender			
Male	98 (65.3)	78 (60.9)	0.448
Female	52 (34.7)	50 (39.1)	
Smoking status			0.839
Current	51 (34.0)	39 (30.7)	
Former	22 (14.7)	19 (15.0)	
Never	77 (51.3)	69 (54.3)	
BMI			0.792
Non-obese (BMI $< 30$ )	89 (69.5)	101 (67.3)	
Obese (BMI $\geq 30$ )	39 (30.5)	49 (32.7)	
HTN	134 (89.3)	102 (79.9)	<b>0.025</b>
HTN duration, median (range), years	10 (10–20)	10 (6–20)	0.281
DM	89 (59.3)	58 (45.7)	<b>0.023</b>
DM duration, median (range), years	20 (10–25)	17.5 (10–20)	0.165
Cardiac disease	56 (37.3)	29 (22.7)	<b>0.008</b>
Previous myocardial infarction	14 (9.3)	5 (3.9)	0.074
Previous stroke	25 (16.7)	14 (10.9)	0.170
Physical activity			0.688
Mobile	135 (90.0)	117 (91.4)	
Immobile	15 (10.0)	11 (8.6)	
Dialysis duration, median (range), years	3 (2–5)	2 (1–4)	<b>0.03</b>
Type of vascular access			0.688
AVF	134 (89.3)	110 (85.9)	
AVG	1 (0.7)	1 (0.8)	
Catheter	15 (10.0)	17 (13.3)	

Data are presented as n (%) or median (range), as appropriate. Comparisons between PAD and non-PAD groups were performed using chi-square or Fisher's exact test for categorical variables and independent-samples t-tests or Mann-Whitney U tests for continuous variables. Statistical significance was defined as  $p < 0.05$ . Abbreviations: PAD, peripheral artery disease; ABI, ankle-brachial index; BMI, body mass index; HTN, hypertension; DM, diabetes mellitus; AVF, arteriovenous fistula; AVG, arteriovenous graft

#### Multivariable logistic regression analysis

In a multivariable logistic regression model including age (per 10-year increase), sex, dialysis duration, hypertension, diabetes, current smoking, cardiac disease, and serum phosphorus, dialysis duration was the only variable significantly associated with PAD (Table 6). Each additional year on hemodialysis was associated with a 7–8% higher odds of PAD (adjusted OR 1.08, 95% CI 1.01–1.16,  $p=0.031$ ). Age, hypertension, diabetes, cardiac disease, smoking, and sex no longer reached statistical significance after adjustment, and the inverse association with serum phosphorus showed only a non-significant trend (adjusted OR 0.84 per 1 mg/dL increase, 95% CI 0.69–1.01,  $p=0.061$ ). The model demonstrated acceptable calibration (Hosmer–Lemeshow  $p=0.536$ ), though the explained variance was modest (Nagelkerke  $R^2 = 0.104$ ), consistent with an exploratory, descriptive analysis.

#### Discussion

This cross-sectional study demonstrated a high prevalence of PAD among hemodialysis patients in northern Palestine, with 54% of participants affected. PAD was significantly associated with older age, longer dialysis duration, hypertension, diabetes mellitus, cardiac disease, and lower serum phosphorus levels, while no associations were observed with gender, smoking, physical activity, prior myocardial infarction, stroke, or vascular access type.

Although ABI is a widely recommended and practical tool for PAD detection, it has important limitations in ESRD. Arterial media calcification, which is frequent in patients with diabetes and chronic kidney disease, can lead to falsely elevated or non-compressible ABI values [15, 16]. In our cohort, no patients had ABI  $> 1.30$ , so we did not identify a clearly “non-compressible” subgroup; nonetheless, misclassification due to calcification

**Table 5** Association of PAD with laboratory parameters

Variable	PAD present (ABI $\leq 0.90$ ), (n=144)	PAD absent (ABI $> 0.90$ ), (n=123)	p- value
Calcium (mg/dL), mean $\pm$ SD	8.85 $\pm$ 0.85	8.88 $\pm$ 0.86	0.822
Sodium (mmol/L), mean $\pm$ SD	131.7 $\pm$ 18.6	134.6 $\pm$ 6.3	0.102
Phosphorus (mg/dL), mean $\pm$ SD	4.68 $\pm$ 1.44	5.06 $\pm$ 1.41	<b>0.030</b>
White blood cells ( $\times 10^9$ /L), mean $\pm$ SD	7.07 $\pm$ 2.15	6.95 $\pm$ 2.27	0.673
Platelets ( $\times 10^9$ /L), mean $\pm$ SD	193.9 $\pm$ 66.4	190.6 $\pm$ 60.2	0.631
Hemoglobin (g/dL), mean $\pm$ SD	10.37 $\pm$ 1.58	10.24 $\pm$ 1.56	0.494
Creatinine (mg/dL), mean $\pm$ SD	8.81 $\pm$ 2.54	9.31 $\pm$ 3.11	0.141
Potassium (mmol/L), median (range)	4.7 (4.4–5.3)	4.85 (4.0–5.3)	0.973
Total iron binding capacity ( $\mu$ g/dL), median (range)	193 (176–218)	201 (170–226)	0.805
Iron ( $\mu$ g/dL), median (range)	57 (44–77)	57 (45–76)	0.383
Transferrin saturation (%), median (range)	28.5 (23–36)	31.1 (23–38)	0.776
Parathyroid hormone (pg/ mL), median (range)	232 (137–425)	189 (115–376)	0.524
Ferritin (ng/mL), median (range)	842 (557–1400)	960 (651–1516)	0.752
Albumin (g/dL), median (range)	3.88 (3.66–4.05)	3.90 (3.60–3.90)	0.870

Data are presented as mean  $\pm$  standard deviation (SD) for approximately normally distributed variables and median (interquartile range) for skewed variables. The number of patients varies by variable due to missing laboratory data; analyses were conducted on available cases using a complete-case approach. Comparisons between PAD and non-PAD groups were performed using independent-samples t-tests or Mann–Whitney U tests, as appropriate. Statistical significance was defined as  $p < 0.05$ . Abbreviations: PAD, peripheral artery disease; ABI, ankle–brachial index

**Table 6** Multivariable logistic regression analysis of factors associated with PAD

Variable	Ad- justed OR (Exp(B))	95% CI for OR	p- value
Age (per 10-year increase)	1.14	0.95–1.37	0.168
Female sex (vs. male)	0.82	0.46–1.47	0.505
Dialysis duration (per 1-year increase)	1.08	1.01–1.16	<b>0.031</b>
Hypertension (yes vs. no)	1.51	0.69–3.31	0.306
Diabetes mellitus (yes vs. no)	1.44	0.82–2.53	0.201
Current smoker (yes vs. no)	1.33	0.73–2.41	0.349
Cardiac disease (yes vs. no)	1.45	0.80–2.61	0.218
Serum phosphorus (per 1 mg/dL increase)	0.84	0.69–1.01	0.061

Model adjusted for all variables listed. PAD coded as 1 (PAD present, ABI  $\leq 0.90$ ) vs. 0 (no PAD, ABI  $> 0.90$ ). Complete-case analysis (n=265). Hosmer–Lemeshow  $p = 0.536$ ; Nagelkerke  $R^2 = 0.104$ ; overall correct classification 58.9%. Abbreviations: PAD, peripheral artery disease; OR, odds ratio; CI, confidence interval; HTN, hypertension; DM, diabetes mellitus

remains possible and should be considered when interpreting the findings.

The prevalence observed in this study is higher than reports from other regions, where prevalence rates in hemodialysis populations typically range from 17% to 48% [18, 19]. Our findings align with those of R Matsuzawa, N Aoyama and A Yoshida [20], who also reported elevated prevalence among hemodialysis patients, suggesting that patients with ESRD are particularly vulnerable to atherosclerotic complications. The prevalence of PAD in our cohort (54%) lies at the upper end of, and in fact exceeds, most published estimates in hemodialysis populations, where reported rates generally range from about 17–48% depending on diagnostic criteria and case mix. Studies from Europe and Japan using ABI-based definitions have typically reported PAD prevalence between 26% and 39% among patients on maintenance hemodialysis [21–25]. This comparatively high prevalence may reflect the broader cardiovascular risk profile of the Middle East and North Africa (MENA) region, where the burden of diabetes, hypertension, dyslipidemia, and cardiovascular disease is substantial and often exceeds that of many high-income settings [26–29]. In Palestine specifically, diabetic and hypertensive nephropathy are leading causes of end-stage renal disease, and chronic kidney disease is highly prevalent among patients with diabetes, indicating a heavy concentration of vascular risk factors in the dialysis population [30, 31]. At the same time, local studies have documented challenges in access to cardiovascular prevention and specialized care under conditions of resource constraint and political instability, which may further limit early detection and management of PAD and related comorbidities [32, 33]. Several factors may help explain the high prevalence in our cohort, including the high burden of diabetes and hypertension, and the relatively older age of the population. In addition, context-specific barriers to cardiovascular prevention and limited access to structured PAD screening in low-resource settings may further contribute to late detection and higher disease burden. Finally, our study was conducted in a single tertiary dialysis center that serves as a referral facility for complex cases; this case-mix may over-represent patients with advanced comorbidity, so the observed PAD prevalence might be higher than in the broader Palestinian hemodialysis population, and the findings should be generalized with appropriate caution.

Consistent with previous studies, older age was a significant predictor of PAD [21]. This association likely reflects the cumulative effects of vascular aging, comorbidities, and exposure to dialysis-related factors. The duration of hemodialysis was also associated with PAD, supporting findings by JH Liu, CC Chang, SM Wang, CY Chou, YF Yang, YL Liu, HH Lin and CC Huang [34], who suggested that prolonged dialysis may contribute

to vascular calcification, oxidative stress, and chronic inflammation.

Hypertension and diabetes were strongly associated with PAD in our study, consistent with findings from the Dialysis Outcomes and Practice Patterns Study (DOPPS) and several other reports [35, 36]. Chronic hyperglycemia and hemodynamic stress may accelerate atherosclerosis, explaining the observed associations. Similarly, cardiac disease was more common in patients with PAD, in line with earlier studies highlighting the close link between coronary artery disease and PAD [36, 37].

Although several laboratory parameters were abnormal in this cohort—including elevated parathyroid hormone, high ferritin, and anemia—none differed significantly between PAD and non-PAD groups in our cross-sectional analysis. Prior work in hemodialysis has shown mixed results: higher ferritin has been associated with worse baseline ABI and PAD progression [38], and ferritin elevations correlate with adverse cardiovascular outcomes [39], while anemia has been linked to PAD incidence and progression [40]. The absence of significant associations in our cohort may reflect limited statistical power to detect modest differences or variability across populations.

Prior myocardial infarction and stroke did not differ significantly between groups, despite their known importance in cardiovascular morbidity. This may reflect low event numbers and potential survivor bias, as patients with severe events may have died before study enrollment, a phenomenon noted in other dialysis cohorts [21]. Likewise, smoking and gender—well-established PAD determinants in the general population—were not associated with PAD in our study. In hemodialysis patients, traditional risk factors may be overshadowed by non-traditional contributors such as uremia-related vascular calcification, inflammation, and dialysis vintage, which could explain these findings [41]. Although smoking is a well-established and powerful risk factor for peripheral artery disease in the general population, with recent large-scale analyses showing markedly increased PAD risk among current smokers and risk persisting years after cessation [42, 43], we did not observe a significant association in this hemodialysis cohort. Similar attenuation of smoking effects has been noted in chronic kidney disease and dialysis populations, where smoking clearly increases cardiovascular events and mortality but traditional risk factors only partially explain the vascular burden [44, 45]. In advanced chronic kidney disease (CKD) and end-stage kidney disease, uremia-related vascular calcification, mineral metabolism disorders, and chronic inflammation are major drivers of arterial damage and may overshadow the relative contribution of lifestyle factors such as smoking [46, 47]. In addition, smoking status in our study was based on self-report, which is vulnerable

to under-reporting and misclassification, particularly in settings where social desirability bias is likely; contemporary validation studies show that self-reported smoking can underestimate true smoking prevalence when compared with biochemical verification [48, 49]. Taken together, both biological overshadowing by uremic factors and potential misclassification of smoking exposure may help explain the absence of a detectable association between smoking and PAD in our analyses.

Lower serum phosphorus levels were significantly associated with PAD in our cohort, a finding supported by AM O'Hare, CY Hsu, P Bacchetti and KL Johansen [37]. This result is particularly noteworthy as it appears counterintuitive to the well-established role of hyperphosphatemia as a key driver of vascular calcification and adverse cardiovascular outcomes in patients with ESRD [50, 51]. This relationship may reflect complex mineral metabolism disturbances in ESRD, including secondary hyperparathyroidism, which can contribute to vascular calcification. However, other studies have reported inconsistent findings [21]. One potential explanation for this paradoxical association is the confounding effect of the malnutrition-inflammation-atherosclerosis (MIA) syndrome, where lower serum phosphorus may act as a marker of poor nutritional status—a potent risk factor for atherosclerotic disease in this population [52, 53]. This highlights the need for further research to clarify the complex role of phosphorus in PAD pathophysiology.

In unadjusted analyses, PAD was associated with older age, longer dialysis duration, hypertension, diabetes mellitus, and cardiac disease. However, in the adjusted multivariable logistic regression model, dialysis duration was the only variable that remained significantly associated with PAD, while other associations were attenuated and lost statistical significance. This pattern is consistent with prior work in dialysis cohorts, where longer dialysis duration has been linked to the presence or severity of PAD or low ABI after accounting for traditional risk factors, suggesting that cumulative dialysis exposure and the chronic uremic milieu may play a central role in PAD development [23, 54–56]. Taken together, these findings support the interpretation that much of the crude association between PAD and comorbidities in this hemodialysis population may be mediated or confounded by dialysis duration and overall cardiovascular burden, rather than by individual risk factors in isolation.

#### Strengths and limitations

This study is the first to investigate the prevalence and correlates of PAD among hemodialysis patients in Palestine, providing valuable data for a high-risk and under-represented population. The use of the ABI, a validated non-invasive diagnostic tool, strengthens the accuracy of PAD detection.

This study also has several important limitations. First, the cross-sectional design precludes any inference of causality; the analysis is purely descriptive, and both the univariable comparisons and multivariable logistic regression should be interpreted as exploratory and hypothesis-generating rather than evidence of formal associations or causal effects. In addition, because PAD was common in this cohort, the adjusted odds ratios from the logistic regression do not approximate risks or risk ratios and should be interpreted strictly as measures of association on the odds scale. Second, some clinically relevant variables—including medication use (e.g., anti-platelets, statins), PAD symptomatology, lipid profile, and inflammatory markers such as CRP—were not available, limiting evaluation of additional and potentially important risk factors. Third, although abnormalities in hemoglobin, ferritin, and parathyroid hormone were observed, the study was not powered to detect subtle differences in these markers between groups, and myocardial infarction and stroke events were relatively infrequent, which reduced statistical power for those comparisons. Fourth, as with most observational studies, residual confounding from unmeasured or incompletely measured factors cannot be excluded, even after multivariable adjustment. Fifth, smoking status was self-reported and may have been misclassified, which could partly explain the lack of association between current smoking and PAD. Sixth, dialysis adequacy parameters (Kt/V, urea reduction ratio) were not consistently available and thus could not be incorporated into the analyses, limiting our ability to examine the relationship between dialysis dose and PAD. Seventh, occupation and employment status were not collected, which restricted exploration of socioeconomic determinants and their potential contribution to PAD risk. Eighth, although PTH is biologically relevant to vascular calcification, missing data and the absence of significant differences between groups meant that PTH could not be robustly evaluated in multivariable models. Ninth, the study was conducted in a single tertiary dialysis center that functions as a referral facility for complex cases, and the cohort included a very small number of adolescent patients; together, these factors may limit generalizability and suggest that the findings should be interpreted primarily in the context of an adult, tertiary-care hemodialysis population. Finally, PAD diagnosis relied solely on ABI without toe–brachial index measurements or vascular imaging, which may underestimate or misclassify disease in patients with medial arterial calcification, a common phenomenon in ESRD.

#### Implications for practice and research

The high prevalence of PAD in this cohort underscores the importance of incorporating routine ABI screening into the care of hemodialysis patients. Early detection

may enable timely management of comorbidities and reduction of cardiovascular complications, which remain the leading cause of mortality in this group. The lack of association with some traditional risk factors highlights the role of non-traditional contributors in ESRD, emphasizing the need for individualized risk assessment. Future longitudinal studies should clarify causal pathways, evaluate the prognostic impact of anemia, iron status, and mineral metabolism, and assess the effectiveness of PAD-targeted interventions in dialysis populations.

#### Conclusion

This study revealed a high prevalence of PAD among patients with ESRD undergoing hemodialysis in northern Palestine, with more than half of the cohort affected. PAD was significantly associated with older age, longer dialysis duration, hypertension, diabetes mellitus, cardiac disease, and lower serum phosphorus levels, whereas no significant associations were observed with gender, smoking, prior myocardial infarction, stroke, or vascular access type. In the multivariable logistic regression model, however, longer dialysis duration was the only factor that remained significantly associated with PAD, suggesting that much of the crude association with other comorbidities may be related to overall cardiovascular and dialysis-related burden rather than to individual risk factors alone.

These findings highlight the importance of routine PAD screening using the ABI, a simple and non-invasive diagnostic tool that can help identify at-risk patients in hemodialysis units. Early recognition may support targeted management of comorbidities and contribute to reducing cardiovascular complications, which remain the leading cause of mortality in this population. Future research should employ longitudinal designs to clarify causal pathways and evaluate the prognostic significance of anemia, iron status, and mineral metabolism, as well as the effectiveness of PAD-focused interventions in dialysis care.

#### Abbreviations

ABI	Ankle–brachial index
aOR	Adjusted odds ratio
BMI	Body mass index
BUN	Blood urea nitrogen
CI	Confidence interval
CKD	Chronic kidney disease
CKD-MBD	Chronic kidney disease–mineral and bone disorder
CRP	C-reactive protein
DOPPS	Dialysis Outcomes and Practice Patterns Study
ESRD	End-stage renal disease
IRB	Institutional Review Board
KDIGO	Kidney Disease: Improving Global Outcomes
Kt/V	Dialyzer clearance of urea multiplied by dialysis time divided by volume of distribution of urea
MENA	Middle East and North Africa
PAD	Peripheral artery disease
PTH	Parathyroid hormone
SD	Standard deviation

SPSS	Statistical Package for the Social Sciences
STROBE	Strengthening the Reporting of Observational Studies in Epidemiology
WHO	World Health Organization

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## Supplementary Information

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Supplementary Material 1

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## Author contributions

SWZ, RMM, and MAN contributed equally to this work. They were responsible for conceiving and designing the study, collecting the data, and drafting the initial manuscript. AS assisted with data collection, statistical analysis, and interpretation of results. MMu, MH, and SS supervised the study and provided critical feedback on methodology and interpretation. LMZ supervised the data analysis and finalized the manuscript for submission. All authors reviewed and approved the final version and agree to be accountable for all aspects of the work.

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## Data availability

The datasets used and analyzed during the current study are available from the corresponding author upon reasonable request.

## Declarations

### Ethics approval and consent to participate

This study was approved by the Institutional Review Board of An-Najah National University (Approval number: Med.Sept.2023/16). The research was conducted in accordance with the Declaration of Helsinki and institutional ethical guidelines. All participants (or their parents/guardians for minors) received a clear explanation of the study objectives and procedures, and written informed consent was obtained prior to participation. Participation was voluntary, and patients were assured of their right to withdraw at any time without consequences for their care. Given the vulnerability of patients undergoing hemodialysis, particular attention was paid to ensuring comprehension and minimizing burden. All data were anonymized before analysis to protect confidentiality. As this was a cross-sectional observational study without any intervention beyond routine clinical care, prospective trial registration was not required.

### Consent for publication

Not applicable.

### Competing interests

The authors declare no competing interests.

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