

# Prevalence and factors associated with hematuria among adult population in Tumbes, Peru

## Prevalencia y factores asociados con hematuria en población adulta en Tumbes, Perú

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### ABSTRACT

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**Objectives:** To estimate the prevalence and to explore potential factors associated with hematuria in adults living in Tumbes, northern Peru. **Methods:** Secondary analysis using data from a population-based study conducted between 2017 and 2018. The dependent variable was hematuria, defined using a dipstick ( $\geq 1+$ ). The potential associated factors included demographic variables (sex, age, education level, etc.), socioenvironmental variables (access to drinking water, regular work in hot environments, etc.), and clinical variables (history of lithiasis, hypertension etc.). An exploratory Poisson regression model was built to report prevalence ratios (PR) and 95% confidence intervals (95%CI). **Results:** Data from 1514 participants were analyzed, mean age 45.1 years, and 835 (55.2%) women. Hematuria (prevalence: 8.9%; 95%CI: 7.5%-10.5%) was more common among women (PR: 1.89; 95%CI: 1.11-3.21); among those aged 30-49 years (PR: 1.98; 95%CI: 1.03-3.79); among those with a history of nephrolithiasis (PR: 1.70; 95%CI: 1.14-2.53), with a history of leptospirosis (PR: 5.41; 95%CI: 1.73-16.99), with diabetes mellitus (PR: 1.90; 95% CI: 1.17-3.08); and in those with a moderate/severe reduced glomerular filtration rate (PR: 3.09; 95% CI: 1.28-7.48). **Conclusion:** Hematuria is relatively common in adults in Tumbes. Being female, aged 30 to 49 years, a history of nephrolithiasis, leptospirosis, diabetes mellitus, and a decreased glomerular filtration rate were factors associated with hematuria. Our results suggest the need to evaluate appropriate methods for identifying hematuria, especially in high-risk groups.

**Keywords:** Hematuria; Prevalence; Risk factors; Adult; Epidemiology (source: MeSH NLM)

### RESUMEN

**Objetivos:** Estimar la prevalencia y explorar los factores asociados a hematuria en adultos de Tumbes, en el norte del Perú. **Materiales y métodos:** Análisis de datos de un estudio poblacional realizado entre 2017 y 2018. La variable dependiente fue hematuria, definido usando tira reactiva ( $\geq 1+$ ). Los potenciales factores evaluados fueron variables demográficas, socioambientales y clínicas. Se construyó un modelo de regresión de Poisson exploratorio para reportar razones de prevalencia (RP) e intervalos de confianza al 95% (IC95%). **Resultados:** Se analizó los datos de 1514 participantes, edad media de 45,1 años, y 835 (55,2%) mujeres. La hematuria (prevalencia: 8,9%; IC95%: 7,5%-10,5%) fue más frecuente en mujeres (RP: 1,89; IC 95%: 1,11-3,21); en aquellos con 30-49 años (RP:1,98; IC 95% 1,03-3,79); en aquellos con antecedente de nefrolitiasis (RP: 1,70; IC 95%: 1,14-2,53), con historia de leptospirosis (RP: 5,41; IC95% 1,73-16,99), con diabetes mellitus (RP: 1,90; IC95%: 1,17-3,08); y en aquellos con tasa de filtración glomerular moderada/ severamente reducida (RP: 3,09; IC95%: 1,28-7,48). **Conclusión:** La hematuria es relativamente común en adultos en Tumbes. Ser mujer, tener 30 a 49 años, historia de nefrolitiasis, de leptospirosis, de diabetes mellitus, y la disminución de la tasa de filtración glomerular estuvieron asociados con mayor prevalencia de hematuria. Nuestros resultados sugieren la necesidad de evaluar métodos adecuados para la identificación de hematuria, principalmente en grupos de riesgo.

**Palabras clave:** Hematuria; Prevalencia; Factores de riesgo; Adulto; Epidemiología (fuente: DeCS Bireme).

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## INTRODUCTION

Hematuria is one of the most common and at the same time most underestimated clinical findings in medical practice. Far from being an isolated finding, its presence can be the first indication of potentially serious pathologies, such as urinary tract infections, chronic kidney disease or even urological neoplasia [1]. Hematuria is classified as macroscopic, visible to simple view, and microscopic, detected only by laboratory testing, and the latter can have clinical implications as important as evident hematuria [2]. Although traditional diagnosis is based on microscopic analysis ( $\geq 3$  erythrocytes per high-power field), the use of test strips is now accepted as an accessible tool for initial detection (screening) [3,4].

The prevalence of hematuria among adults varies widely, from 0.2% to 31% [5,6]; however, in screening studies, hematuria may be found in 4% to 5% of asymptomatic adults screened [7]. Figures such as these may mask more complex clinical realities, where hematuria is only the top of the iceberg. In Iran, for example, one study showed a prevalence of hematuria in the general population and in children of 16.4% and 1.6%, respectively [8], whereas in cases related to urolithiasis, this figure can rise to 84% [8]. In Japan, a prevalence of long-term hematuria after operation among benign prostatic hyperplasia patients of 7.4% was reported after analyzed retrospectively clinical data [9].

Besides estimating hematuria frequency, it is crucial to understand the clinical and social factors associated with that condition. Thus, hematuria has been linked to highly prevalent chronic conditions such as arterial hypertension, diabetes mellitus, urinary lithiasis, and chronic kidney disease [5, 7]. In addition, in vulnerable populations such as rural residents, women, and older adults, there may be additional risk factors such as urinary tract infections [10]. In resource-constrained settings, extreme heat and dehydration have also been proposed as relevant factors, especially in areas with limited access to health services [11].

Hematuria is clinically relevant due to its potential association with common chronic diseases; therefore, identifying its prevalence and related factors can facilitate timely diagnosis and management. Among these diseases, chronic kidney disease stands out, with an estimated prevalence of 13% to 21% in Peru and responsible for 2% of deaths [12]. Thus, this research acquires social importance, given the potential impact on a population with socioeconomic challenges and limited access to health services. Currently, in Peru and in other Latin American settings, there is limited information on the prevalence of hematuria at the population level, especially in asymptomatic adults.

Therefore, we take advantage of the Disadvantaged Populations eGFR Epidemiology (DEGREE) Study dataset, a multi-country initiative using information from 11 countries, some of them in Latin America (Chile, Ecuador, Guatemala, Nicaragua, and Peru), to estimate the prevalence and explore the factors associated with hematuria among adults residing in the Tumbes region, in northern Peru.

## METHODS

### **Study design and site**

This work is a secondary analysis using data from the DEGREE Study [13], an observational, cross-sectional, population-based study conducted in the Tumbes region between November 2017 and May 2018. The study was conducted in Tumbes, a region located in northern Peru. This region was selected as site for the DEGREE Study because 10% of the population are agriculture workers, contamination of Puyango river, the main source of water, and warm climate comparable with other countries in the study. Tumbes is the warmest region on the coast, with a tropical arid climate, and an average annual temperature of 25.3°C and a humidity of 76% [14]. According to the National Institute of Statistics and Informatics (INEI), in 2017, the population in Tumbes was approximately 225 thousand inhabitants, with an urban and rural population of 93.6% and 6.4% respectively [15].

As previously reported, the DEGREE study followed a standardized protocol for several countries in the world [16], which sought to estimate the prevalence of chronic kidney disease (CKD) in adults living in urban and rural areas, with special emphasis on socio-environmental factors.

### **Study population**

The original study included adults ( $\geq 18$  years old), habitual residents (with at least 6 months living in the study area), selected through stratified random sampling by geographic area (urban/rural) and sex (maximum 60% women), using the 2014 regional census as the sampling frame. Participants with limited mobility that would prevent their transfer or evaluation, and pacemaker users, were excluded due to restrictions related to the complementary study procedures. For the present analysis, only those records with complete information on the dipstick test and, therefore, hematuria results, were considered.

## Procedures

All participants provided informed consent before being enrolled in the study. Data collection was conducted through home visits, including the administration of a structured questionnaire developed for the DEGREE Study and the collection of biological samples (blood and urine), following standardized international protocols. The survey was administered using electronic tablets with the REDCap platform, allowing for accurate and controlled collection in real time. Staff were trained in interviewing, digital recording, sample collection, biosafety, and anthropometric procedures.

Clinical measurements included height, weight, and blood pressure, using calibrated equipment. Blood pressure was evaluated using an automatic blood pressure monitor (OMRON HEM-780, Tokyo, Japan). Three measurements were taken five minutes after a resting period and at least five minutes apart between evaluations. A fasting blood sample (8 to 12 hours) was obtained to estimate glucose and creatinine levels. A urine sample was also analyzed with a dipstick, assessing hematuria, proteinuria, pH, and urine specific gravity. Participants were instructed to collect a clean-catch midstream urine sample to minimize contamination from external bacteria and cells. Ideally, the sample was taken early in the morning before eating or working. After that, the fieldworker immersed the test strip into the well-mixed urine sample for approximately 10-15 seconds ensuring all reagent pads were covered. Then, the strip was held horizontally to prevent chemicals from adjacent pads from mixing. A color chart from the dipstick container was provided to compare the color change on each pad, especially in this case, for the presence of blood cells. Findings were registered, and after that, the strip was discarded. The entire process was carried out under biosecurity and quality control standards.

## Variables

The outcome variable was the presence of hematuria, defined as the detection of blood in urine using a dipstick (COMBUR 10 Test M, Roche, Germany) with a reading of at least 1+ as a positive test, according to the results of the DEGREE urinalysis study.

Additionally, we explored whether certain variables were associated with hematuria, grouped into sociodemographic, environmental and occupational, as well as personal and clinical history variables. The sociodemographic variables included in the analysis were age, grouped into four categories (18-29, 30-49, 50-69, and  $\geq 70$  years); sex (male or female); and education level, classified as primary (0-6 years of schooling), secondary (7-11 years), and higher education (12 years

or more). Monthly household income was also included, categorized according to the minimum living wage at the time of the study (<850 PEN and  $\geq 850$  PEN), as well as the setting (urban or rural).

Among the environmental and occupational exposure conditions, we evaluated access to drinking water (yes or no), whether the participant regularly worked in hot environments (yes or no), and whether they had been exposed to pesticides (yes or no), based on self-reported occupational history.

Regarding personal and medical history, we assessed tobacco use in the past 12 months (never, previously, and currently); alcohol consumption, assessed as the intake of at least six alcoholic drinks per month (yes or no); physical activity levels, evaluated using the short version of the International Physical Activity Questionnaire (IPAQ) and categorized as low vs. moderate/high; and regular use of nonsteroidal anti-inflammatory drugs (NSAIDs), a recognized risk factor for kidney disease (yes or no). We also considered history of nephrolithiasis (yes or no) and leptospirosis (yes or no); and body mass index was also evaluated and categorized according to international guidelines (normal:  $<25 \text{ kg/m}^2$ , overweight:  $25 \text{ to } <30 \text{ kg/m}^2$ , and obesity  $\geq 30 \text{ kg/m}^2$ ). The diagnosis of arterial hypertension (yes or no) was defined as the self-report of a previous medical diagnosis or current medication or based on blood pressure measurements (systolic  $\geq 140 \text{ mmHg}$  or diastolic  $\geq 90 \text{ mmHg}$ ), whereas the diagnosis of diabetes mellitus (yes or no) was defined by self-report of a previous medical diagnosis or use of specific medication or a fasting glucose value  $\geq 126 \text{ mg/dL}$ . Finally, a marker of renal function was also included, assessed by the estimated glomerular filtration rate (eGFR) using the CKD-EPI (Chronic Kidney Disease – Epidemiology Collaboration) formula [17]. Based on the results, three categories of renal function were defined: moderate or severe renal dysfunction ( $<60 \text{ ml/min/1.73 m}^2$ ), mild renal dysfunction ( $60\text{-}90 \text{ ml/min/1.73 m}^2$ ), and normal ( $\geq 90 \text{ ml/min/1.73 m}^2$ ).

## Statistical analysis

An anonymized database was created, and the analysis was performed using STATA version 16.0 software (StataCorp, College Station, TX, USA).

The characteristics of the study sample were described using absolute and relative frequencies for categorical variables, whereas measures of central tendency and dispersion (mean and standard deviation) were used for numerical variables. The prevalence of hematuria was determined and reported, along with 95% confidence intervals (95%CI). Comparisons based on the presence or absence of hematuria were performed using the Chi-square test.

**Table 1.** Characteristics of the study population by the presence of hematuria

Characteristics	(N = 1514) n (%)	Hematuria		p-value
		No (N=1379) n (%)	Yes (N=135) n (%)	
<b>Sex</b>				<0.001
Male	679 (44.8)	639 (94.1)	40 (5.9)	
Female	835 (55.2)	740 (88.6)	95 (11.4)	
<b>Age (years)</b>				0.104
18 - 29	291 (19.4)	275 (94.5)	16 (5.5)	
30 - 49	661 (44.0)	595 (90.0)	66 (10.0)	
50 - 69	410 (27.3)	373 (91.0)	37 (9.0)	
70+	140 (9.3)	124 (88.6)	16 (11.4)	
<b>Education level (years)</b>				0.454
Primary (0 - 6)	556 (36.7)	500 (89.9)	56 (10.1)	
Secondary (7 - 11)	624 (41.2)	571 (91.5)	53 (8.5)	
Superior (12+)	334 (22.1)	308 (92.2)	26 (7.8)	
<b>Monthly income</b>				0.801
<850 PEN	842 (65.9)	767 (91.1)	75 (8.9)	
≥850 PEN	436 (34.1)	399 (91.5)	37 (8.5)	
<b>Setting</b>				0.017
Rural	754 (49.8)	700 (92.8)	54 (7.2)	
Urban	750 (50.2)	679 (89.3)	81 (10.7)	
<b>Access to drinking water</b>				0.046
No	830 (54.8)	767 (92.4)	63 (7.6)	
Yes	684 (45.2)	612 (89.5)	72 (10.5)	
<b>Working in a hot environment</b>				0.022
No	1083 (71.5)	975 (90.0)	108 (10.0)	
Yes	431 (28.5)	404 (93.7)	27 (6.3)	
<b>Exposure to pesticides</b>				0.004
No	1201 (79.3)	1081 (90.0)	120 (10.0)	
Yes	313 (20.7)	298 (95.2)	15 (4.8)	
<b>Regular use of NSAIDs</b>				0.511
No	733 (48.4)	664 (90.6)	69 (9.4)	
Yes	781 (51.6)	715 (91.6)	66 (8.4)	
<b>History of nephrolithiasis</b>				0.015
No	1276 (84.3)	1172 (91.9)	104 (8.1)	
Yes	238 (15.7)	207 (87.0)	31 (13.0)	
<b>History of leptospirosis</b>				0.036
No	1498 (99.6)	1365 (91.1)	133 (8.9)	
Yes	6 (0.4)	4 (66.7)	2 (33.3)	
<b>Tobacco use</b>				0.031
Never	780 (51.5)	697 (89.4)	83 (10.6)	
Previously	560 (37.0)	517 (92.3)	43 (7.7)	
Currently	174 (11.5)	165 (94.8)	9 (5.2)	
<b>Alcohol consumption</b>				0.229
No	1369 (90.4)	1243 (90.8)	126 (9.2)	
Yes	145 (9.6)	136 (93.8)	9 (6.2)	
<b>Physical activity level</b>				0.013
Moderate/High	330 (21.8)	312 (94.6)	18 (5.4)	
Low	1184 (78.2)	1067 (90.1)	117 (9.9)	
<b>Body mass index</b>				0.832
Normal	450 (29.7)	407 (90.4)	43 (9.6)	
Overweight	659 (43.5)	603 (91.5)	56 (8.5)	
Obesity	405 (26.8)	369 (91.1)	36 (8.9)	
<b>Hypertension</b>				0.390
No	1178 (77.8)	1069 (90.8)	109 (9.2)	
Yes	336 (22.2)	310 (92.3)	26 (7.7)	
<b>Diabetes mellitus</b>				<0.001
No	1382 (91.3)	1273 (92.1)	109 (7.9)	
Yes	132 (8.7)	106 (80.3)	26 (19.7)	
<b>Renal function</b>				0.033
Normal	1236 (81.6)	1131 (91.5)	105 (8.5)	
Mild dysfunction	252 (16.6)	228 (90.5)	24 (9.5)	
Moderate/severe dysfunction	26 (1.7)	20 (76.9)	6 (23.1)	

PEN: Peruvian currency; NSAIDs: Non-steroid anti-inflammatory drugs.

**Table 2.** Factors associated with hematuria: crude Poisson regression models

Characteristics	PR crude (95%CI)
<b>Sex</b>	
Female (vs. male)	<b>1.93 (1.35 – 2.76)</b>
<b>Age (years)</b>	
30 – 49 (vs. 18 – 29)	<b>1.82 (1.07 – 3.08)</b>
50 – 69 (vs. 18 – 29)	1.64 (0.93 – 2.89)
70+ (vs. 18 – 29)	2.08 (1.07 – 4.03)
<b>Education level</b>	
Secondary (vs. primary)	0.84 (0.59 – 1.21)
Superior (vs. primary)	0.77 (0.50 – 1.21)
<b>Monthly income</b>	
850+ PEN (vs. <850 PEN)	0.95 (0.65 – 1.39)
<b>Setting</b>	
Urban (vs. rural)	<b>1.49 (1.07 – 2.07)</b>
<b>Access to drinking water</b>	
Yes (vs. no)	<b>1.39 (1.01 – 1.92)</b>
<b>Working in a not environment</b>	
Yes (vs. no)	<b>0.63 (0.42 – 0.94)</b>
<b>Exposure to pesticides</b>	
Yes (vs. no)	<b>0.48 (0.28 – 0.81)</b>
<b>Regular use of NSAIDs</b>	
Yes (vs. no)	0.90 (0.65 – 1.24)
<b>History of nephrolithiasis</b>	
Yes (vs. no)	<b>1.60 (1.10 – 2.33)</b>
<b>History of leptospirosis</b>	
Yes (vs. no)	<b>3.75 (1.20 – 11.8)</b>
<b>Tobacco use</b>	
Previously (vs. never)	0.72 (0.51 – 1.03)
Currently (vs. never)	<b>0.49 (0.25 – 0.95)</b>
<b>Alcohol consumption</b>	
Yes (vs. no)	0.67 (0.35 – 1.30)
<b>Physical activity level</b>	
Low (vs. moderate/high)	<b>1.81 (1.12 – 2.93)</b>
<b>Body mass index</b>	
Overweight (vs. normal)	0.89 (0.61 – 1.30)
Obesity (vs. normal)	0.93 (0.61 – 1.42)
<b>Hypertension</b>	
Yes (vs. no)	0.84 (0.55 – 1.26)
<b>Diabetes mellitus</b>	
Yes (vs. no)	<b>2.50 (1.69 – 3.68)</b>
<b>Renal function</b>	
Mild (vs. normal)	1.12 (0.73 – 1.71)
Moderate/severe (vs. normal)	<b>2.72 (1.32 – 5.61)</b>

Estimates in bold are significant ( $p < 0.05$ )

PEN: Peruvian currency; NSAIDs: Non-steroid anti-inflammatory drugs; PR: Prevalence ratio.

Potential associated factors (age, sex, setting, access to drinking water, etc.) were evaluated using crude Poisson regression models and robust variance, using

the hematuria variable as the outcome, and reporting prevalence ratios (PR) and 95% CIs. To determine potential associated factors, as this was an exploratory model, all variables included in the crude models, independent of p-values, were listed as possible factors associated with our dependent variable of interest. The results of the multivariable model are displayed graphically using a forest plot, which shows the RP and 95% CI for each variable studied. Overdispersion was evaluated in all our models by calculating a dispersion parameter, a value greater than 1 was considered overdispersion. Finally, multicollinearity was evaluated using the variance inflation factor.

### Ethical considerations

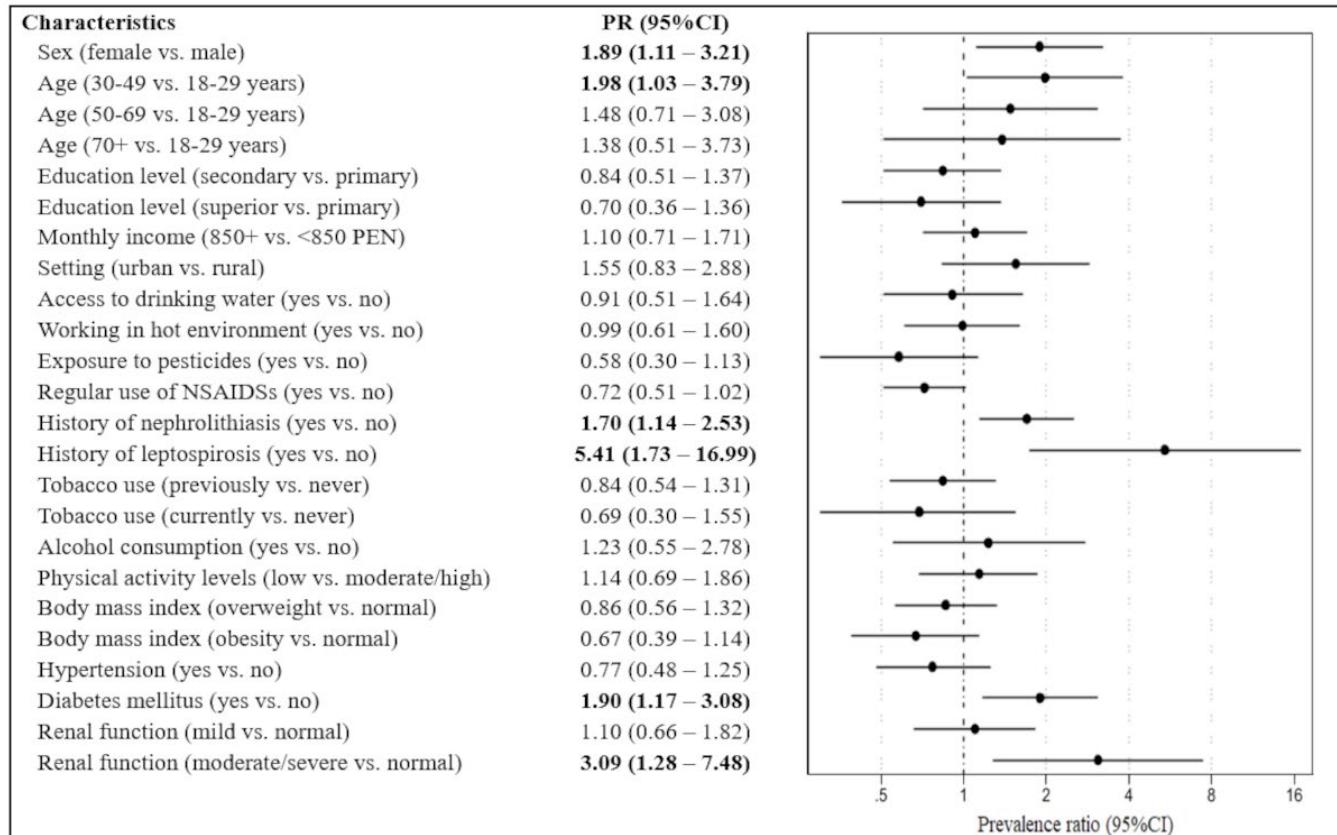
The original study was approved by the Ethics Committee of the Universidad Peruana Cayetano Heredia and the London School of Hygiene and Tropical Medicine. For this secondary analysis, approval was obtained from the Ethics Committee of the Universidad Científica del Sur (Code: PRE-15-2024-00045). Anonymity, confidentiality, and compliance with bioethical principles were ensured during the whole process.

### RESULTS

A total of 1,818 subjects were contacted and invited to participate, but only 1,514 (83.3%) consented to be enrolled in the study. The mean age was 45.1 years; 835 (55.2%) were women; 624 (41.2%) had secondary education; and 842 (55.6%) had incomes under 850 soles.

According to the dipstick results, 135 participants (8.9%; 95%CI: 7.5%–10.5%) had hematuria. The description of the characteristics of the study population according to the presence of hematuria is shown in Table 1. In the crude model, a significant association was evident between hematuria and being female, aged 30 to 49 years, urban residents, those with access to drinking water, a history of nephrolithiasis or leptospirosis, those with low levels of physical activity, those with diabetes mellitus, and those with moderate to severe glomerular filtration rate impairment (Table 2).

In the multivariate model (Figure 1), hematuria was more frequent in women than in men (PR: 1.89; 95%CI: 1.11–3.21); among those aged 30–49 years (PR: 1.98; 95%CI: 1.03–3.79); among those with a history of nephrolithiasis (PR: 1.70; 95%CI: 1.14–2.53); those with a history of leptospirosis (PR: 5.41; 95%CI: 1.73–16.99); those with diabetes mellitus (PR: 1.90; 95%CI: 1.17–3.08); and those with a moderate/severely reduced glomerular filtration rate (PR: 3.09; 95%CI: 1.28–7.48). Overdispersion was not present in the models (overdispersion parameter <1), and the variance inflation factor was <5 in the multivariable model.



**Figure 1.** Factors associated with hematuria: exploratory Poisson regression model

Estimates in bold are significant ( $p<0.05$ )

PEN: Peruvian currency; NSAIDs: Non-steroid anti-inflammatory drugs; PR: Prevalence ratio.

## DISCUSSION

The findings of this study, based on a population-based sample of adults in Tumbes, reveal that 8.9% of participants had hematuria. This condition was more common among women, people aged 30 to 49, those with a history of nephrolithiasis, leptospirosis, type 2 diabetes mellitus, and those with a moderately or severely decreased glomerular filtration rate.

Evidence on the prevalence of hematuria in the general population is scarce. In other contexts, studies have been conducted in specific populations, such as those with acute renal failure and tranexamic acid use [18], or in those with prostate cancer [19]. Comparisons of urine strip and microscopic hematuria have been conducted. For example, a study in Ireland prospectively compared dipstick vs. microscopy urine analysis on 1000 consecutive samples and, using both tests, reported a prevalence of hematuria of 18.5%, whereas 68.7% did not have that condition, with a dipstick sensitivity of 86% and a specificity of 85% [20]. However, this was a sample of urological out-patients in a hospital in Dublin.

In Iran, a systematic review including 25 manuscripts, but only three in the meta-analysis, reported a prevalence of hematuria of 16.4% in the general population, with

variations according to demographic characteristics and health conditions [6]. This estimate doubled the one reported in our study. Nevertheless, in a different study conducted in a rural population in southwestern Iran, it was reported that 229 (33.9%) of 676 people had hematuria assessed using a dipstick, but only 28 (4.1%) had hematuria with microscopy [21].

On the other hand, a study conducted in Nigeria with 2077 people who attended for a medical check-up (between 15-88 years old) found a prevalence of hematuria of 15.9%, using optical microscopy (3 or more red blood cells per high power field) [22]. The Prospective Epidemiological Research Studies in Iran (the PERSIAN study) conducted in more than 10 thousand subjects between 35 and 70 years old and using microscopy, reported a prevalence of hematuria of 34.1% [5]. In the Latin American region, many studies have been conducted in specific populations. Thus, a study in Zuni population of Mexico, prevalences of hematuria above 30% were reported if measured by evaluating traces (dipstick), while using another definition ( $\geq 50$  red blood cells per microliter of urine), this estimate fell to 17.8% [23]. Similarly, using urine samples from in- and outpatients from a nephrology unit of a hospital university in Brazil, a study reported a prevalence of hematuria of 39.0% [24], very high compared to our population-based results.

According to the literature, women have a higher prevalence of hematuria than men [6, 21, 22], similar to our findings. This may be explained by hormonal factors in women related to the onset of hematuria, such as decreased estrogen, which limits the production of antimicrobial peptides that alter the integrity of the urothelial lining, predisposing to urinary tract infections [25], which have been shown to be a common cause of hematuria [26,27].

Related to age, unlike our study, which showed a higher prevalence of hematuria in people aged 30 to 39 years, a study from São Paulo (Brazil) showed a higher prevalence of hematuria in elderly adults, mainly due to urinary tract neoplasms, as well as the deterioration of kidney function associated with aging [26]. In this age group, some comorbidities such as hypertension, diabetes mellitus and, especially, chronic kidney disease, significantly increase the risk of developing hematuria [28,29].

Two different clinical variables, a history of nephrolithiasis and leptospirosis, were associated with a higher prevalence of hematuria. Hematuria, usually microscopic but sometimes visible, is the most frequent consequence of the passage of a kidney stone through the walls of the urinary tract [27]. Moreover, stone formation can manifest as obstruction, infection, and renal failure, all of which can cause hematuria. Equally important, leptospirosis can produce acute interstitial nephritis with tubular inflammation and necrosis, in addition to glomerular damage, which facilitates the filtration of erythrocytes into the urine, may manifest clinically as hematuria [30,31]. Leptospirosis is relatively common in various locations in Peru, especially in the Amazon and in rural areas [32].

Finally, hematuria was common among participants with diabetes and chronic kidney disease with a markedly decreased filtration rate. Several studies have shown that the presence of diabetes more than doubles the likelihood of developing hematuria [7,9,23]. Diabetes may facilitate the development of hematuria due to the progressive kidney damage caused by chronic hyperglycemia. Thickening of the glomerular basement membrane, microangiopathy, and hyperfiltration alter the filtration barrier, allowing the passage of erythrocytes into the urine. Furthermore, the association between hematuria and chronic kidney disease (CKD) has been previously demonstrated. Thus, two different studies have shown that hematuria, even microscopic, is a risk factor for chronic kidney disease, and the results allow us to infer the association found in our study: in patients with CKD, glomerular structural changes and capillary fragility make hematuria more frequent [33]. This was confirmed in hospital settings, where in patients with moderate CKD, the prevalence of hematuria reached almost 30%, also being associated with a higher risk of progression and mortality [28].

This study provides evidence on the proportion of the population with hematuria, mostly asymptomatic,

in urban and rural Peru, in a setting where regional information is limited. Our findings highlight not only the influence of clinical and socioenvironmental factors, but also the urgent need to strengthen early detection to prevent kidney complications and improve the population's quality of life.

Although current guidelines recommend the use of high-power field microscopy to diagnose microhematuria [34], a structured evaluation should be performed, including physical examination, blood pressure measurement, and serum creatinine to assess risk factors for genitourinary malignancy (e.g., detailed smoking history), medical renal disease, gynecologic, and non-malignant genitourinary causes of microhematuria. International guidelines, such as the National Institute for Health and Care Excellence (NICE) [35], recommend that those aged  $\geq 50$  years may need diagnostic evaluation among urgent cases for visible hematuria. However, other guidelines consider different age cut points ( $\geq 45$  or  $\geq 60$  years). If these decisions are applicable to Peru is something that needs assessment. Such results will allow a risk-stratification of cases of hematuria as well as appropriate management.

This study has some strengths, primarily in the context of limited evidence in the region. The use of the DEGREE Study protocols ensures data quality through internationally standardized protocols. Furthermore, the study sample was randomly selected, ensuring representativeness and reflecting the characteristics of the population in Tumbes.

However, this study has some limitations that should be discussed. First, as a cross-sectional study, only association and not causality can be assessed; furthermore, reverse causality cannot be ruled out due to temporality issues. Second, the age of the data collected (pre-pandemic) may have changed; however, the results may be useful for understanding the problem. Although there may be significant changes in the prevalence of hematuria over time, the associated factors appear to be the same. Third, the ideal method for detecting hematuria is urine microscopy, considered the gold standard due to its high specificity and sensitivity in directly identifying red blood cells in urine [3,10]. However, the present survey used a urine strip, which introduces measurement bias, leading to an overestimation of the prevalence of hematuria due to false positives (e.g., myoglobinuria). For example, the urine strip in asymptomatic patients has a sensitivity  $<3\%$  and a PPV  $<0.2\%$  for detecting cancer, if none of those evaluated had any symptoms. As this was a population-based study, many participants were asymptomatic. Fourth, the data collection of the original study had significant limitations, as dichotomous (yes/no) questions were used for certain exposure factors, which prevented a more detailed exploration of these factors (duration, quantity, or times of exposure). Fifth, there is a potential selection bias, as only one region of Peru

was included, which may not be representative of the entire country. Finally, not all risk factors for hematuria, including the presence of neoplasia, diet, and others, were comprehensively assessed in the study.

Women, being aged 30 to 49 years, a history of nephrolithiasis, leptospirosis, diabetes mellitus, and a decreased glomerular filtration rate were associated with hematuria. Our results suggest the need to evaluate adequate methods for identifying hematuria, especially in groups at higher risk for this condition.

### Author contributions

Conceptualization: TSC-E, MCV-S, KMCC and AB-O. Methodology: AB-O. Formal analysis: AB-O. Investigation: TSC-E, MCV-S, KMCC and AB-O. Writing – Original draft: TSC-E, MCV-S and KMCC. Writing – Review and Editing: AB-O. Visualization: AB-O. All authors accepted the final content of the manuscript and approved this version for publication.

### Conflicts of interest statement

None to declare.

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### Data availability statement

Not applicable.

### Artificial Intelligence use statement

The authors declare that no artificial intelligence was used in any part of the manuscript preparation process.

### Supplementary material

None.

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