Scientific Research Publishing

Health, 2019, 11, 609-620
http://www.scirp.org/journal/health
ISSN Online: 1949-5005
ISSN Print: 1949-4998

Factors Associated with Asymptomatic Proteinuria in Adult Nigerians. A Community-Based Study

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How to cite this paper: Onodugo, O., Ezeala-Adikaibe, B.A., Orjioke, C., Onodugo, P.N., Ijoma, U.N., Chime, P., Mbadiwe, N., Onyekonwu, C., Anyim, O.B., Obumneme-Anyim, I.N., Young, E., Nwatu, C.B., Okoye, J.U. and Nwobodo, M.U. (2019) Factors Associated with Asymptomatic Proteinuria in Adult Nigerians. A Community-Based Study. *Health*, **11**, 609-620.
https://doi.org/10.4236/health.2019.116051

Received: April 29, 2019
Accepted: May 31, 2019
Published: June 3, 2019

Abstract

Introduction: Early detection of proteinuria is early detection is a cost-effective method of assessing individuals with and without risk factors for chronic renal disease. Proteinuria is common in adults and may present a clinical challenge in the absence of obvious renal disease or risk factors especially in the tropics. Few studies in Nigeria have assessed the prevalence of proteinuria in adults using the dipstick method. The aim of this study was to document the prevalence of proteinuria among residents of a community in Enugu, south east Nigeria. **Methods:** This was a cross-sectional descriptive study carried out in an isolated urban slum settlement in Enugu, south east Nigeria. Dipstick testing of freshly voided early morning mid-stream urine samples was done to detect proteinuria. For database management and statistical analyses, SPSS version 23 was used. **Results:** A total of 262 individuals were recruited for the study, 165 (63%) females and 97 (37%) males. The participants' age ranged from 18 to 90 years, averaging 43.7 ± 15.5. Trace amounts of protein were detected in urine samples of 225 (85.9%) individuals. Significant proteinuria was detected in 3.8% of the participants and was significantly higher 40 - 49-year-olds (6%). p = 0.02 and 0.02 respectively. Significant correlates of proteinuria were lower diastolic blood pressure and current tobacco use. Lower body mass index weakly correlated with proteinuria. **Conclusion**: The prevalence of significant early morning proteinuria in a community-based study in Enugu was 3.8%. Significant correlates of proteinuria included low diastolic blood pressure and tobacco use. Community

based awareness programs targeted at prevention of chronic renal diseases should be incorporated in public health programs.

Keywords

Proteinuria, Chronic Renal Disease, Risk Factors, Nigeria

1. Introduction

The presence of detectable protein in urine (proteinuria) is common in adults and especially in the elderly [1] and may present a clinical challenge for physicians in the absence of obvious renal disease especially in the tropics. Apart from established causes, proteinuria may be seen in malaria and other common tropical infections [2] and tobacco users [3] [4] [5]. Proteinuria is an established predictor of developing renal disease. It has been associated with a two-fold increase in the risk of developing hypertension in renal disease [1] [2]. It is also an indirect marker for arterial diseases and a risk factor for dementia, stroke as well as poor prognostic factor in cardiovascular disease [6] [7] [8] [9]. Using proteinuria as the first step in screening for renal disease in both subjects with or without risk factors for chronic renal disease is an established protocol in hospital practice [10], however, the same cannot be said of the general population. A study done about 2 decades ago in the US considered early detection of urine protein not to be cost-effective in individuals without risk factors [11], nevertheless, screening for proteinuria is considered to be cheap in some developing countries [12] where it remains a cheap but high yielding investigation for patients presenting in crowded general adult medical outpatient clinics. The use of early morning urine sample is thought to achieve greater consistency in the assessment of proteinuria but it has not achieved widespread acceptance [13].

Causes and risk factors for proteinuria in adults and the elderly are numerous and include hypertension, obesity, smoking and elevated systolic blood pressure [1] [7] [14]. Generally, it has been estimated that about 5% of the general population would develop proteinuria, 15% of whom who may develop renal disease [15]. Few studies in Nigeria have assessed the prevalence of proteinuria in adults [16] [17] [18] [19] using the dipstick method. Ulasi *et al.* [16] reported a 19% prevalence of proteinuria in a community survey while Arogundade *et al.* [17] and Abene *et al.* [18] reported a prevalence of 29.7% and 8.4% respectively. In a study from the northern part of Nigeria, a prevalence of 20.2% was found among undergraduates [19]. Studies outside the country have reported lower prevalences among the general adult population [5] [7] [14] [20] [21] [22] [23] [24]. Screening for proteinuria in the general populace has frequently been used to detect cases of possible chronic renal disease in Nigeria [16] [17] [18] [19] because of availability, reliability and ease of use. The aim of this study was to document the prevalence of proteinuria among residents of a community in Enugu, south east Nigeria.

2. Methods

This was a cross-sectional descriptive study carried out in an isolated urban slum settlement (Agu-Abor) in Enugu, the capital of Enugu State, south east Nigeria. Full description of the study protocol had been documented previously [25]. The inhabitants were surveyed over a 4-week period (August 12-September 9, 2013). This study was approved by the ethics committee of the University of Nigeria Teaching Hospital Ituku/Ozalla.

2.1. Study Protocol

A semi structured questionnaire was used to collect data on selected socio-demographic characteristics, lifestyle behaviors and medical history. Cases of hypertension, diabetes, epilepsy and other medical conditions were recorded based on previously published protocol. Substance use such as tobacco and alcohol in the past 4 weeks were also documented. Current use of alcohol was defined as use of any or all alcoholic beverages in the past 4 weeks. Level of education was the individual's highest formal educational attainment based on the Nigerian school system.

2.1.1. Sample Collection and Dipstick Testing

Urine samples were collected from randomly selected consenting adults 18 years and above. Freshly voided early morning mid-stream urine samples were collected at home by the participants after adequate sensitization on how the collection should be done. Samples were tested as early as 8-9 am the following day. Urine samples were collected from consecutive consenting adults 18 years and above. The urinalysis results of pregnant women (one person) and participants who had history of renal disease (none) were excluded from the final analysis. Dipstick testing was done using URS 11 urine analysis strips. Urine analysis strips were immersed in urine sample, quickly removed and read immediately by comparing the color change with that provided on the container chat. Excess urine was removed by running the edge of the strip against the rim of the container. Finally, the strip was held horizontally and compared to the color chart on the bottle label. The protein chart was read immediately in less than 60 seconds after dipping. The test kit is a reagent strip impregnated with a 0.1% m/m tetrabromphenol blue; 97.4% w/w buffer; 2.5% w/w non-reactive buffer and is based on the protein-error-of-indicators principle. A color matching any block greater than trace indicates significant proteinuria. The sensitivity of reagent strips is only 15% to 30% with a specificity of 97% to 100%. The dipstick provides a qualitative estimate of the degree of proteinuria and not absolute amounts. For the purpose of this study, samples with urine PH of 7 were regarded as false positive and were excluded. Participants were interviewed by teams of research assistants using the research questionnaire and results of the urine tests noted.

2.1.2. Inclusion and Exclusion Criteria

All consenting adults living in the locality were included. Pregnant women, sus-

pected cases of urinary tract infection and past medical history of renal disease were excluded.

2.2. Sample Size

The minimum sample size was calculated using the Cochran Equation [26],

$$N = Z^2(pq)/e^2$$

where: N = required sample size, Z = 1.96, p = 0.019 [16], q = 0.81 and e^2 = error limit of 0.05.

$N = (1.96)^2(0.019 \times 0.81)/0.0025 = 236$. Assuming 10% attrition rate an extra 40 participants were added giving a minimum sample size of 261 urine samples.

2.3. Statistical Methods

For database management and statistical analyses, we used the SPSS version 23 (IBM Corporation, New York, USA). Data were presented in tables and figures. For continuous variables, mean values and standard deviation were calculated. Rates were expressed as percentages. Categorical values were compared using the Chi-Square test. Mean age was compared using the independent t-test. In all, p-value < 0.05 was regarded as statistically significant. Conclusions were drawn at 95% confidence interval.

3. Results

3.1. General Characteristics of the Sample Population

Out of 298 samples that were collected, 262 (87.9%) had complete data and were analysed. Gender distribution showed that 165 (63%) were females and 97 (37%) were males with a male to female ratio of 1:1.7. The participants' age ranged from 18 to 90 years, averaging 43.7 ± 15.5. Males were older than females by about 9 years (mean age: 49.5 vs 40.4 years, p < 0.01). The peak age group of males and females was 50 - 69 and 20 - 29 years (40.2% and 49.7% respectively) (**Table 1**). Most participants achieved more than primary school education (54.2%) and more than 63% were employed in one trade or the other. The mean systolic and diastolic pressure and relevant reported medical history are shown in **Table 1**. Tobacco and alcohol use within the preceding 4 weeks were 37 (14.2%) and 172 (65.6%) and significantly more prevalent in males, p < 0.01 respectively (**Table 1**).

3.2. Proteinuria

Trace amounts of protein were detected in urine samples of 225 (85.9%) individuals (**Figure 1**). One or more pulses of protein (significant proteinuria) was detected in 3.8% of the samples. The distribution of significant proteinuria is shown in **Table 2**. It was more prevalent in 40 - 49-year-olds (6%) and tobacco user. Individuals with significant proteinuria also had lower mean diastolic blood pressure. Significant correlates of proteinuria (0 =no/trace proteinuria, 1 =

significant proteinuria) were lower diastolic blood pressure and current tobacco use, p = 0.02 and 0.02 respectively. Lower body mass index weakly correlated with proteinuria, p = 0.07 (Table 3).

Table 1. Characteristics of participants.

Characteristic	Female	Male	Total	p-value
N (%)	165 (63)	97 (37)	262 (100)	<0.01
Age, Years (mean, sd)	40.4 (13.5)	49.5 (16.9)	43.7 (15.5)	<0.01
Body Mass Index, kg/m^2 (sd)	26.9 (5.7)	23.8 (4.1)	25.8 (5.4)	<0.01
Age Group, N (%)				
20 - 29	42 (25.5)	19 (19.6)	61 (23.3)	
30 - 39	40 (24.2)	10 (10.3)	50 (19.1)	
40 - 49	35 (21.2)	15 (15.5)	50 (19.1)	
50 - 59	23 (13.9)	18 (18.6)	41 (15.6)	
60 - 69	18 (10.9)	20 (20.6)	38 (14.5)	
≥70	7 (4.2)	15 (15.5)	22 (8.4)	<0.01
Level of Education				
None/Primary, N (%)	68 (41.2)	52 (53.6)	293 (45.8)	
Secondary and Above, N (%)	97 (58.8)	45 (46.4)	142 (54.2)	0.05
Occupation				
Business*	80 (48.5)	16 (16.5)	96 (36.6)	
Artisans	10 (6.1)	29 (29.9)	39 (14.9)	
Office Workers	15 (9.1)	15 (15.5)	30 (11.5)	
Students	16 (9.7)	10 (10.3)	26 (9.9)	
Unemployed	19 (11.5)	8 (8.2)	27 (10.3)	
Retired and Others	25 (15.2)	19 (19.6)	44 (16.8)	<0.01
Blood Pressure				
Systolic Pressure, mm/Hg (mean sd)	132.3 (24.7)	136.6 (23.8)	133.9 (24.3)	0.16
Diastolic Pressure, mm/Hg (mean sd)	82.4 (16.4)	82.4 (14.7)	82.4 (15.7)	0.96
Glucose, mg/dL (mean sd)	92.7 (23.8)	95.9 (30.7)	93.4 (26.5)	0.37
Lifestyle				
Current Tobacco Use, N (%)	10 (6.1)	27 (28.1)	37 (14.2)	<0.01
Current Alcohol Use, N (%)	96 (58.2)	76 (78.2)	172 (65.6)	<0.01
Medical History				
Hypertension, N (%)	35 (21.2)	23 (23.7)	58 (22.1)	0.64
Diabetes, N (%)	5 (3)	11 (11.3)	16 (6.1)	0.65
Stroke, N (%)	2 (1.2)	3 (3.1)	5 (1.9)	0.28
Arthritis, N (%)	25 (15.2)	25 (25.8)	50 (19.1)	0.04
Primary Sources of Medications				
Hospital or Pharmacy	132 (80)	79 (81.4)	211 (80.5)	-
Open Market	33 (20)	18 (18.6)	51 (19.5)	0.78

p-values are for the sex differences.

Table 2. Distribution of significant proteinuria.

Characteristic**	None/Trace	One-Two Pluses	p-value
N	252 (96.2)	10 (3.8)	-
Males	93 (95.9)	4 (4.1)	-
Females	159 (96.4)	6 (3.6)	0.84
Age (Mean, sd)	43.7 (15.5)	44.2 (15.3)	0.93
Age Group, N (%)			
20 - 29	59 (96.7)	2 (3.3)	-
30 - 39	48 (96)	2 (4)	-
40 - 49	47 (94)	3 (6)	-
50 - 59	41 (100)	-	-
60 - 69	36 (94.7)	2 (5.3)	-
≥70	21 (95.5)	1 (4.5)	0.77*
BMI (mean, sd)	25.9 (5.4)	22.8 (3.3)	0.07
SBP (mean, sd)	134.1 (24.5)	128.6 (21.2)	0.49
DBP (mean, sd)	82.8 (15.8)	71.3 (9.2)	0.02
FBS (mean sd)	94.2 (26.9)	86.7 (12)	0.38
Medical History, N (%)			
Diabetes	10 (4.1)	-	0.41*
Hypertension	8 (3.9)	2 (3.4)	0.87*
Stroke	10 (3.9)	-	0.65*
Substance Use, N (%)			
Alcohol Use	2 (2.2)	8 (4.7)	0.33
Tobacco Use	6 (2.7)	4 (10.8)	0.02
Primary Source of Drugs, N (%)			
Open Market	49 (96.1)	2 (3.9)	-
Hospital/Pharmacy	203 (96.2)	8 (3.8)	0.95

*Fisher's Exact Test.

Table 3. Correlates of proteinuria and significant proteinuria.

Characteristic	Proteinuria r (p-value)
Age	0.01 (0.88)
Gender	0.01 (0.84)
Body Mass Index	−0.12 (0.06)
Systolic Pressure	−0.04 (0.56)
Diastolic Pressure	−0.17 (0.01)
Glucose, mg/dL	−0.00 (0.97)
Current Tobacco Use	0.15 (0.02)
Current Alcohol Use	0.06 (0.33)
Source of Drugs (1 Market, 2 Pharmacy/Hospital)	−0.00 (0.97)

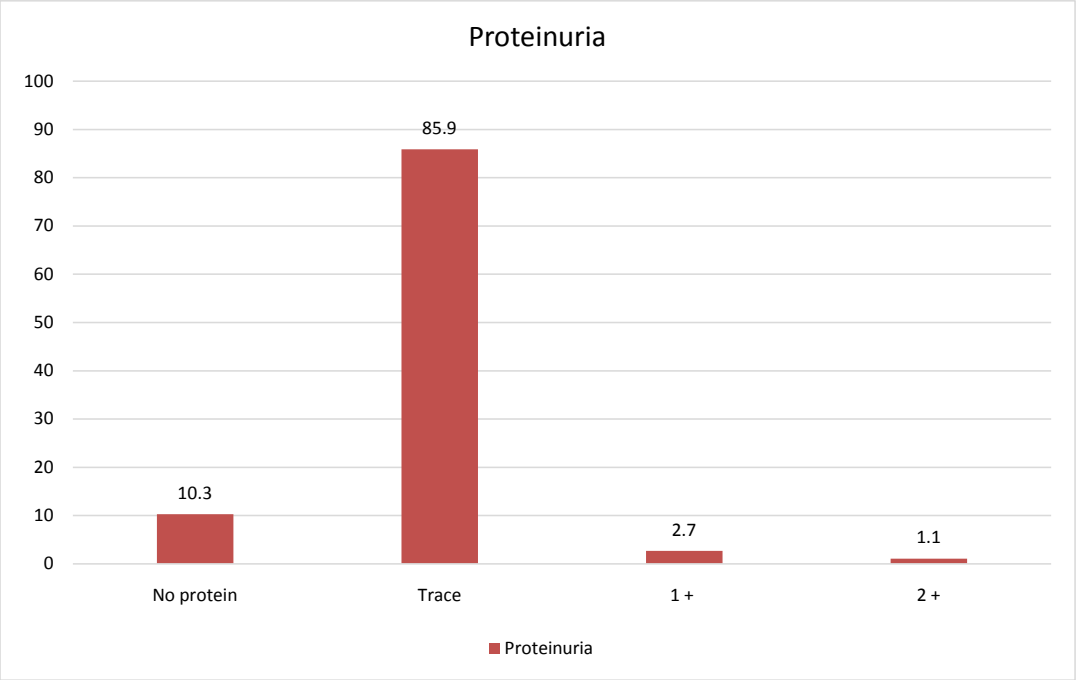

Figure 1. Distribution of proteinuria in the population studied.

4. Discussions

Proteinuria is one of the most potent predictors of renal injury and chronic renal impairment [1] [2]. The index study explored the frequency of early morning proteinuria defined as one or more pluses of protein in dipstick testing in the community. The prevalence of significant proteinuria was 3.8%. It peaked at 40 - 49 years and positively correlated with tobacco use and lower diastolic blood pressure.

The prevalence of significant proteinuria in this study is similar to a prevalence of 4.3%, 6.6% and 6.3% reported by previous studies. [5] [27] [28]. Generally, it has been estimated that about 5% of the general population would develop proteinuria, 15% of whom who may develop renal disease [15]. Though dipstick testing for proteinuria has been considered a non-cost effective way of screening for renal disease in some studies it remains a cheap and cost effective approach to investigating renal disease in the tropics [11] [12]. One major drawback in screening for proteinuria in adults is the very high prevalence of possible causes [1] [2] [13]. These include common infections such as malaria as well as urinary tract infections in the elderly. Few studies have actually studied the prevalence and distribution of proteinuria in adults Nigerians, most of which were conducted on a mixed population of adolescents and adults. In one study conducted among undergraduates in northern Nigeria, the prevalence of proteinuria was as high as 20.2% [19]. Other Nigerian studies have reported high rates of 19% to 29.7% also [16] [17] [29] [30]. In Argentina, a prevalence of 21.8% was reported among Toba aborigines [31] while a total of 1.07% was reported in a multiracial Asian Southeast Asian Community in Singapore [22]. Reasons for

wide ranges reported in these studies may be attributed to the prevalence of risk factors, age of the population studied as well as methodological differences considering the numerous possible causes of proteinuria. Ulasi *et al.* [16] did not find any correlation between proteinuria and blood pressure and body mass in dex. Similar to a study from China proteinuria was significantly higher in smokers [5].

In the index study, significant proteinuria was not significantly higher among individuals with disorders that are traditionally regarded as risk factors for proteinuria. The reason for this may not be so clear considering the limitations of the present survey but one possible reason may be the inclusion of all reported cases irrespective of the duration of the illness and treatment status. However, it is interesting to note that when trace proteinuria is taken into consideration, the prevalence of proteinuria in these individuals exceeded the average 89.7% obtained for the whole population (**Figure 2**). The relationship between some of the diseases listed in **Figure 2** (arthritis and abdominal pains) and proteinuria may lie in the frequent use of non-steroidal anti-inflammatory agents. The use of skin lightening creams has also been implicated in the cause of proteinuria in the tropics [31] is similar to the index study.

The only significant correlates for proteinuria in this study were smoking and lower DBP. The relationship between smoking and proteinuria in both people with or without diabetes has been well documented [4] [32] [33] [34] [35]. Cigarette smoke-induced renal damage is due, at least in part, to activation of the sympathetic nervous system resulting in an elevation in blood pressure [3]. Other factors such as renal elimination of nicotine and the presence of heavy metals in tobacco have been suggested [34] [35] [36] [37]. The relationship between proteinuria lower diastolic blood pressure in the index study might be an indirect reflection of the strong negative correlation between DBP and smoking

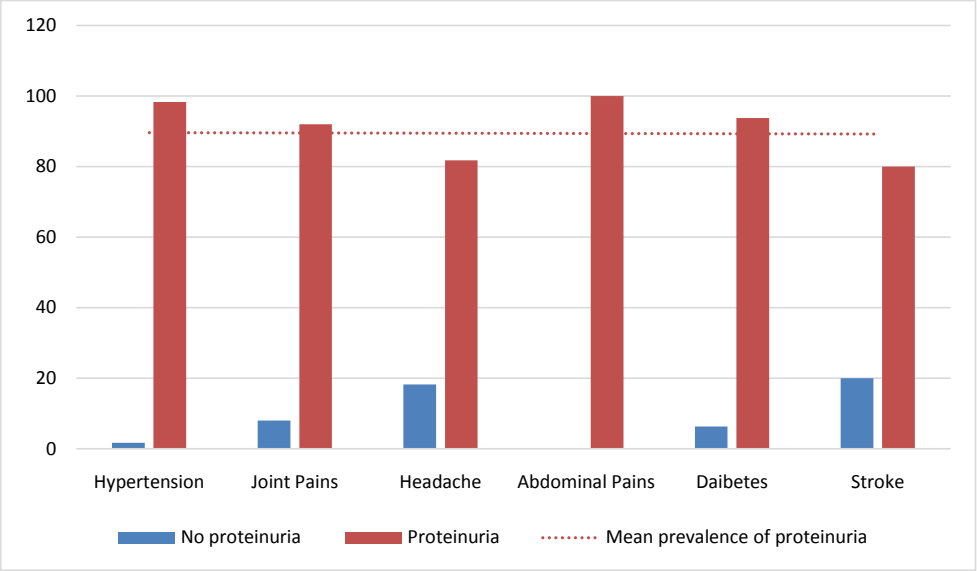

Figure 2. Prevalence of proteinuria among individuals with common medical diseases.

($r = -0.196$, $p = 0.001$). Smokers are more prone to alcohol abuse and possibly not eat well especially if one takes into consideration thesocioeconomic environment where our study was carried out.

5. Limitations

This study has some limitations. Firstly, causes of proteinuria are likely to be many, transient and unrelated to kidney disease in community-based studies like ours. Urine samples were collected at home without supervision. It is possible that some of the participants may not have followed previously outlined instructions. Although the study sought to differentiate common medical cases that may cause proteinuria, most of these cases were self-reported and were not confirmed using previous medical notes. Dip-stick testing only provides qualitative and not quantitative estimates of proteinuria. Notwithstanding these shortcomings, this study is one of the few community-based surveys of the prevalence of proteinuria among adults in Nigeria. The results may well be representative in poor neighborhoods of Enugu and can be reasonably used as base for further studies.

6. Conclusion

The prevalence of significant early morning proteinuria in a community-based study in Enugu was 3.8%. Significant correlates of proteinuria included low diastolic blood pressure and tobacco use. Community based awareness programs targeted at prevention of chronic renal diseases should be incorporated in public health programs.

Acknowledgements

The project described was supported by the Medical Education Partnership Initiative in Nigeria (MEPIN) project funded by Fogarty International Center, the Office of AIDS Research, and the National Human Genome Research Institute of the National Institute of Health, the Health Resources and Services Administration (HRSA) and the Office of the U.S. Global AIDS Coordinator under Award Number R24TW008878. The content is solely the responsibility of the authors and does not necessarily represent the official views of the funding organizations.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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