ISSN: 2230-9926

Available online at http://www.journalijdr.com

IJDR

International Journal of Development Research
Vol. 6, Issue, 02, pp. 6713-6715, February, 2016

International Journal of
DEVELOPMENT RESEARCH

Full Length Research Article

PREVALENCE OF PROTEINURIA IN HIV NAIVE PATIENTS: A PILOT STUDY

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ARTICLE INFO

Article History:
Received 13th November, 2015
Received in revised form
26th December, 2015
Accepted 12th January, 2016
Published online 17th February, 2016

Key Words:
Proteinuria,
HIV naive Patients,
Dipstick,
uP/Cr ratio.

ABSTRACT

Background: Evaluation of proteinuria in HIV naive infected patients is important, as it is often an early indicator of underlying kidney dysfunction, a common sequel of HIV infection.
Objective: This study aimed to evaluate the prevalence of proteinuria in HIV positive naïve patients.
Method: This is a cross-sectional study involving hundred (100) newly diagnosed HIV positive patients which were randomly selected and recruited for the study. Patients were screened for proteinuria using urine dipstick to exclude subject with asymptomatic urinary tract infection and those without protein in their urine. Those patients found with protein in their urine, the proteinuria was quantified using uP/Cr ratio.
Result: The age range of the subjects was between 16 and 78 years and the mean age was 34.41 ±10.59 yrs. Proteinuria by dipstick analysis was present in 76 HIV positive patients (76%), with female 44(57.9%) and male 32 (42.1%), with female: male ratio of 1.7:1. The female HIV positive patients had 1+ protein in the urine of 36(81.8%) and 2+ proteins in the urine of 8(18.2%), while the male HIV positive patients had 1+ protein in urine of 27 (84.4%) and 2+proteins in the urine of 5(15.6%). The prevalence of proteinuria by urine protein: creatinine ratio was estimated to be 13%, with females 12% and males, 1%.
Conclusion: This study shows high prevalence of proteinuria in HIV positive naïve patients with female preponderance distribution.

INTRODUCTION

About 34.2 million people worldwide have been estimated to be infected with the human immunodeficient virus (HIV) (Vijay *et al.,* 2013). In Nigeria over the last decade, there has been an exponential increase in the prevalence of HIV, from less than 1% to 5.8% as reported by the Federal Ministry of Health (National AIDS/HIV/STD Control Programme, 1997, 1999, 2000, 2002 and 2003). The HIV infection affects multiple organs in the body including kidney (Han *et al.,* 2006). Therefore person infected with HIV may develop renal disorders during the course of the infection (Vijay *et al.,* 2013; Farrukh *et al.,* 2012). In a study conducted in Ile Ife and Port-Harcourt, southern part of Nigeria, a prevalence of 38% renal disease in HIV/AIDS was reported (Emem *et al.,* 2008). The spectrum of kidney diseases associated with HIV infection is broad with an estimated prevalence in sub-Saharan Africa ranging from 6% to 48.5% (Francois Folefackkaze *et al.,* 2013). The cause of renal disease in HIV infected patients are multi factorial and include HIV infection itself, co-infections, co-morbidities, and their treatments (Oche *et al.,* 2011). These renal disorders could be acute renal insufficiency or chronic renal insufficiency as seen in HIV associated nephropathy (HIVAN) (Han *et al.,* 2006). HIVAN is the commonest cause of end stage renal disease (ESRD) in these patients (Oche *et al.,* 2011) and is commonly found in blacks than the whites (Vijay *et al.,* 2013; Oche *et al.,* 2011; Han *et al.,* 2006). In healthy individual, small amounts of plasma albumin are filtered by the glomerulus, and negligible amount appears in the urine while most are reabsorbed by the tubules, if protein filtration exceeds the tubular cell reabsorptive capacity, a measurable quantity will appear in the urine (Samarawickrama *et al.,* 2012). In glomerular lesions e.g. HIVAN and HIV immune complex Kidney disease (HIVICK), the structure and charge barrier to filtration are altered, and more albumin and other proteins are filtered, resulting in a higher level of protein in the urine (proteinuria) (Samarawickrama *et al.,* 2012). In

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tubular disease (e.g. cART-related tubular toxicity), urinary proteins are derived from a failure to reabsorb filtered protein and other proteins that originate from damaged tubular cells, and may not be picked up by the assay for albumin(particularly dipstick analysis), but will be picked up by a total protein assay (e.g. uP/CR) (Samarawickrama *et al.,* 2012). Renal disease can also be caused by combination antiretroviral therapy (cART) (Samarawickrama *et al.,* 2012). It is therefore necessary to assess the status of the kidney in these patients before commencing antiretroviral therapy. Screening for proteinuria in HIV naive infected patients is therefore important, as it is often an early indicator of underlying kidney dysfunction (Samarawickrama *et al.,* 2012), and there is paucity of information to this regard in this environment. It is generally accepted that measurement of the urine protein/creatinine ratio (uP/CR) is a relatively effective way to screen for renal disease (Samarawickrama *et al.,* 2012).

MATERIALS AND METHODS

This prospectus cross sectional study was carried out at University of Maiduguri Teaching Hospital between January and June 2013. Ethical approval for the study was obtained from the Research and Ethical committee of the Hospital. Being a pilot study in this part of the country, the initial sample size was not calculated and subjects were taken as a sample of convenience. Written informed consent was obtained from all the patients. Hundred (100) newly diagnosed HIV positive patients were consecutively recruited for the study. Subjects were screen for HIV status using Determine strip and Uni-gold cassettes and confirmed using Westernn-Blod. Patients with pre-existing chronic diseases such as chronic renal disease, hypertension, diabetes mellitus and cardiovascular disease or having proteinuria due to other confounding factors such as uncontrolled HTN,DM, cardiac failure, acute illness, heavy exercise and urinary tract infection were excluded from this study. Subjects with serum creatinine >132.6µmol/L were also excluded. Only newly diagnosed HIV positive subjects not yet on antiretroviral drugs were included.

Ten (10) ml of freshly voided spot urine were collected by mid-stream clean catch urine sample collection method and five (5) ml of blood were collected aseptically, allowed to clot and serum was separated. The samples were frozen until analysis. Demographic variables such as age, sex, blood pressure were taken. Standard urine dipstick test was carried out using ComboStik 12MAC in all patients on fresh urine sample. Those with positive test for proteinuria were then used for urinary protein quantitation. Urine protein was determined by turbidometric method using SSA (Samarawickrama *et al.,* 2012), Urine creatinine was determined using Jafee slot method (Greenwald, 1928). Serum urea and creatinine was analyzed to exclude Subjects with renal disease

Statistical Analysis

All analysis was done using Statistical Package for Social Science (SPSS) version 17. Continuous variables were described as mean ± SD and Categorical data were described as proportions.

RESULTS

A total of 100 freshly diagnosed HIV positive naive patients were recruited for the study. The gender distribution of the HIV positive patients was 64 females and 36 males, and female: male ratio of 1.7:1. The age range of the subjects was between 16 and 78 years and the mean age was 34.41 ±10.59yrs. Proteinuria by dipstick analysis was present in 76 HIV positive patients (76%), with female 44(57.9%) and male 32 (42.1%). Grading of proteinuria is as summarized in Table 1. The female HIV positive patients had 1+ protein in the urine of 36(81.8%) and 2+ proteins in the urine of 8(18.2%), while the male HIV positive patients had 1+ protein in urine of 27 (84.4%) and 2+proteins in the urine of 5(15.6%) table1.No patient was found with proteinuria >2+. Table 2 shows the distribution of urinary protein by dipstick among HIV positive patients according to age. This shows that 16-24 years age group had 5, negative for protein; 10,1+ protein; and 0, 2+ protein; the age group of 25-50 years had 18, negative; 48,1+ protein; and 11, 2+ proteins; the group 51-75 years had 1,negative; 5, 1+ protein; and 1, 2+ proteins; the group 76-78 years had 1, 2+ protein in urine only. This indicates that proteinuria decreases in older ages. The prevalence of proteinuria by urine protein: creatinine ratio was 13%, Table 3, with females had 12% and males had 1%.

Table 1. Gender distribution of hiv positive subjects by degree of dipstick urinary proteinuria

SEX	NEG	1+	2+	Proteinuria(≥1+)
Female n=64, (%)	20(83.3%)	36(81.8%)	8(18.2%)	44(68.8)
Male n=36, (%)	4(16.7%)	27(84.4%)	5(15.6%)	32(88.9)
Total n=100 (%)	24%	63%	13%	76%

Table2. Age distribution by degree of dipstick urinary proteinuria among hiv positive subjects

Age(in years)	Neg	Positive 1+	Positive 2+
16-24	5	10	0
25-50	18	48	11
51-75	1	5	1
76-78	0	0	1
Total	24	63	13

Table3. Prevalence of proteinuria by UP/CR ratio of HIV positive subjects

uPCR	Female n=64	Male n=36	Total n=100
<30mg/mmol	52(59.8%)	35(40.2%)	87%
≥30mg/mmol*	12(92.3%)	1(7.7%)	13%

uPCR = Urinary Protein to Creatinine Ratio.
*A Cut-off point for diagnosis of Nephrotic Proteinuria
(Anne-Marie Cote *et al.,* ?) & (Lamontague *et al.,* 2014)

DISCUSSION

Kidney disease is an increasingly important cause of death in HIV positive patients (Lamontague *et al.,* 2014). HIV associated nephropathy (HIVAN) has been found to be the commonest form of renal involvement in HIV positive black patients (Lesi *et al.,* 2014). As with other causes, proteinuria which is also associated with HIV infection is not only a

marker of kidney disease, but also a progression factor in CKD, heralding a further deterioration in renal function (Greenwald, 1928). The mean age of the patients of 34.41± 10.59yrs which falls within the age group of 25-50yrs are the most affected. This is comparable with report of Emem *et al.,* (2008) in a study done in Ile Ife in southwestern part of Nigeria (34.6±9.4 yrs). It is also similar to report of Lesi from Lagos, Nigeria (36.7± 9.14 yrs) (Lesi *et al.,* 2014). This is so because sexual activity is high at this age group (Farrukh *et al.,* 2012). In this study, we examined the prevalence of proteinuria in newly diagnosed HIV positive naive patients. Mild proteinuria with dipstick 1+ was higher(63%) than those with moderate proteinuria dipstick 2+ (13%) which is similar to report of Lesi(+1, 66% and +2, 24.7%) (Lesi *et al.,* 2014).Prevalence of dipstick proteinuria ≥1+ was found to be 76% which is consistent with prevalence of 80.2% reported from north India by (Vijay *et al.,* 2013). However, prevalence of proteinuria by dipstick as low as 42.5% was also reported by (Lesi *et al.,* 2014) and 38-48% reported by (Okafor *et al.,* 2011). Such difference may be related to the clinical and immunological stage of patients at presentation and methodology of protein evaluation or Urine collection. The high proportion of proteinuria by dipstick may also be attributed to observer's error. Our study also showed that prevalence of proteinuria by uP/CR was 13% with female preponderance of 12% and male 1%. This may not be explained by proportional gender representation in subjects recruited but may also be due to the fact that the health seeking behavior between sexes varies with males more like to seek for medical care earlier than females. This may be due to sociocultural, religion and socioeconomic factors which may affect females more than males which consequently affect female presentation to the hospital. Since this study shows high prevalence of proteinuria in HIV positive naïve patients, all HIV positive naïve patients should be screen for proteinuria for early treatment and management to retard possible progression of nephropathy and other associated complications.

Conclusion

This study shows high prevalence of proteinuria in HIV positive naïve patients with female preponderance distribution. Since proteinuria and HIV infection are risk factors for renal dysfunction, there is the need for routine check up to monitor both serum and urine chemistries in HIV infected patients to detect and proffer early effective management

Limitation

This study design involved sample of convenience rather than random sample. Also the glomerular filtration rate (GFR) for the determination of the patients renal clearance could not be done.

Recommendations

Since this study showed high prevalence of proteinuria in HIV-naïve newly diagnosed patients, it is therefore recommended that detailed renal investigation and nephrology review including renal biopsy be done on all subjects with nephritic proteinuria which will help in the early diagnosis and treatment of renal lesion

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