Estimated Glomerular Filtration Rate in Patients with Lower Urinary Tract Symptoms/Benign Prostatic Obstruction in an Emerging Tertiary Centre

Dada Samuel Ayokunle[1*], O. Areo Peter[2], T. Adegun Patrick[2]
and G. Akanbi Olusola[3]

[1]*Department of Medicine, Nephrology Unit, Ekiti State University Teaching Hospital, Ado Ekiti, Nigeria.*
[2]*Department of Surgery, Urology Unit, Ekiti State University Teaching Hospital, Ado Ekiti, Nigeria.*
[3]*Radiology Department, Ekiti State University Teaching Hospital, Ado Ekiti, Nigeria.*

Authors' contributions

This work was carried out in collaboration between all authors. Author DSA designed the study, wrote the protocol, and wrote the first draft of the manuscript. Authors DSA, OAP and TAP managed the literature searches, analyses of the study. Authors OAP and TAP performed the clinical evaluation and author GAO performed the ultrasound analysis for the patients. All authors read and approved the final manuscript.

Original Research Article

ABSTRACT

Background: The association of benign prostatic hypertrophy (BPH) and chronic kidney disease (CKD) has been a subject of controversies. Combinations of recurrent urinary tract infections, chronic retention with large residual urine volumes and decreased bladder compliance have been reported to be associated with chronic renal failure in patients with benign prostatic obstruction.
Aims: To determine the estimated glomerular filtration rate (eGFR) and find out its relationship with the International Prostate Symptom Score (IPSS).
Methodology: This is a cross-sectional study involving 129 new patients with benign prostatic hypertrophy. The severity and the degree of bother associated with patient's lower urinary tract

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Corresponding author: Email: ayokunledada@yahoo.com, areolafemoris@yahoo.co.uk;

symptoms (LUTS) were assessed using the IPSS while the eGFR was determine using the modified Modification of Diets in Renal Disease.

Results: Majority (38.8%) were in stage 2 CKD with eGFR of 60-89 ml/min/1.73 m^2 and only 6(4.7%) patients were in stage 5 CKD with eGFR <15 ml/min/1.73 m^2. Overall 55(42.7%) were found to have CKD at presentation. There was no statistically significant difference between the severity of lower urinary tract symptoms (LUTS) and eGFR. The most observed symptom was urinary frequency followed by urgency which were present in 95 (73.6%) and 82 (63.6%) respectively. There was a significant difference in the quality of life among patient with eGFR less than or greater than 60 ml/min/1.73m^2 p = .005.

Conclusion: This study demonstrated an association between BPH and CKD in men whose symptoms were bothersome (those with poor QoL). The degree of bothersomeness (QoL) could be used as the determinant for requesting serum creatinine to assess the renal status of patient with BPH. Estimation of GFR among these patients with BPH will offer a rapid method of renal function assessment at presentation and thus facilitate the application of clinical practice guidelines and clinical performance measures to improve the outlook of possible renal complication.

1. INTRODUCTION

Chronic kidney disease (CKD) can develop at any age [1,2]. This is worrisome among the ageing population due to various causes notably among them is bladder outlet obstruction as a result of benign prostatic hypertrophy (BPH) [3,4]. CKD is a known complication of benign prostatic hyperplasia [5]. Both have been described as common medical conditions as well as important public health problem in older men [4,6].

Studies have demonstrated the relationship between CKD and bladder outlet obstruction. Hill et al reported that 8% of men had renal failure at presentation for prostate surgery [7]. Similarly, in a meta-analysis of men presenting for BPH treatment, McConnell and his colleagues showed that an average of 13.6% had renal failure [8]. The poor health seeking attitude of patients coupled with late presentation especially in sub-Saharan Africa, could ultimately lead to development of avoidable complications.

Because the prevalence of CKD increases with age, the diagnosis and management of obstructive nephropathy is particularly relevant to the elderly (geriatric) population [9] and the working class.

The most valuable tests in detecting abnormalities of kidney function are those that measure glomerular filtration rate (GFR) [10-13]. Glomerular filtration rate is useful for providing a consistent measure of kidney function, monitoring progression of the disease as well as response to treatment. It is also useful in forecasting the need for renal replacement therapy (RRT) and determining the appropriate drug dosing in patients with impaired renal function [13].

The GFR is the basis for the definition and classification of CKD employed by the National Kidney Foundation (NKF) in its current guideline thereby giving it a central role in its stage-specific recommendation [10-12,14].

The International prostate symptom score (IPSS), which was originally developed by the American Urological Association for a treatment outcome measure for benign prostatic hyperplasia, has now become a popular indicator of the severity of lower urinary tract symptom (LUTS) [15].

The main objective of the study was to determine the estimated glomerular filtration rate and its relationship with IPSS among patients with LUTS / BPO.

The importance of screening patients with risk factor for CKD such as bladder outlet obstruction cannot be overemphasized. This measure will lead to early diagnosis of renal involvement and early referral for nephrologist care. This becomes very important in our environment where there are scarce resources to manage CKD.

To our knowledge, research in this area is very few in our environment. The poor health seeking attitude of our people coupled with late presentation can ultimately lead to the development of avoidable complications. This underscores the importance of carrying out this

study to highlight the need to anticipate and investigate patients with BPH for kidney disease and if necessary early referral for nephrologist care.

2. MATERIALS AND METHODS

This was a prospective, purposeful, cross-sectional study conducted at the Urology clinic of Ekiti State University Teaching Hospital Ado-Ekiti, Nigeria. The study period was between January 1 and December 31, 2014.

The study was conducted at the Urology clinic of Ekiti State University Teaching Hospital Ado-Ekiti, Nigeria. Ethical approval was obtained from the ethical and research committee of the hospital.

One hundred and twenty-nine new patients were recruited during the study period. Patients who were 45 years old with lower urinary tract symptoms secondary to BPH and who have been histologically confirmed were recruited into the study. However, patients with co-morbid conditions such as uncontrolled hypertension, diabetes mellitus and patients who were already diagnosed as CKD and on any form of renal replacement therapy were excluded. Also excluded were patients with prostate cancer, urethral stricture and LUTS / BPH who have been on treatment.

Patient's bio-data, history and anthropometric measurements were entered into a proforma.

The severity and the degree of bother associated with patient's lower urinary tract symptoms (LUTS) were assessed using the International Prostate Symptoms Score (IPSS). Findings on physical examination particularly digital rectal examination (DRE) of the prostate gland were recorded. Abdominopelvic ultrasound scan of the kidneys, bladder and prostate was done.

Blood sample analysis for electrolytes, urea, creatinine and complete blood count were performed in the laboratory.

A urine sample was collected for analysis and microscopy to detect among other finding, any subclinical urinary tract infection. Dipstick proteinuria of at least 2+ was taken as significant and represents markers of kidney injury. Serum creatinine was measured using Jaffe's reaction and the value obtained was used to calculate the glomerular filtration rate (GFR) of each subject using the modified Modification of Diets in Renal Disease [MDRD] [16] formula.

$$GFR = 186 \times (Cr)^{-1.154} \times (Age)^{-0.203} \times 0.742 \text{ (if female)} \times 1.210 \text{ (if black)}.$$

According to the National kidney foundation using the Kidney Disease Outcomes Quality Initiative (K / DOQI) guidelines [10], patients were classified into five stages based on eGFR as follows; Stage 1 (Normal or increased eGFR) = ≥90 ml/min/1.73 m^2; Stage 2 (Mildly decreased eGFR) = 60–89 ml/min/1.73 m^2; Stage 3 (Moderately decreased eGFR) = 30–59 ml/min/1.73 m^2; Stage 4 (Severely decreased eGFR) = 15–29 ml/min/1.73 m^2 and Stage 5 (Kidney failure) = <15 ml/min/1.73 m^2.

CKD was defined in this study as eGFR ≤ 30–59 ml/min/1.73 m^2 and /or ≥2+ dipstick proteinuria.

Ethical approval was obtained from the ethical and research committee of the Ekiti State University Teaching Hospital. Informed consent was obtained from all participants. Vernacular was used to obtain informed consent from participants who do not speak English.

2.1 Data Analysis

The data was analyzed using SPSS® version 16(SPSS Inc., Chicago Il.) computer software package. The mean ± SD was computed for the quantitative variables such as age and chi-square for categorical variables. Student t-test was used to determine differences in means of the numerical variable. Non-normal data were expressed as median (interquartile range) and differences were evaluated using the Mann–Whitney test. Partial correlation statistic was used to determine the association between eGFR and IPSS after adjusting for the effect of age, prostate volume and PSA. The QoL score was dichotomized to poor (0-3) and good (4-6) for the purpose of analysis. A p-value of ≤ 0.05 was taken as statistically significant.

3. RESULTS

There were one hundred and twenty-nine participants with the mean age of 69.72±9.32 and a range of 48-95 years. Most of the participants (70.5%) were in the age range 45-65 years while 38 (29.5%) were in the age range 66-95 years.

The majority of the participants were retiree 55 (39.9%), closely followed by farmers 31 (22.5%). Others included civil servants (13.8%) and traders (11.6%). The mean systolic and diastolic systemic blood pressure were 136.90±18.50 mmHg and 84.51±11.88 mmHg respectively. There was a statistical significant difference in the mean value of pack cell volume (PCV) (p= 0.026) and systolic blood pressure (p=0.023) among patient who had eGFR greater and less than 60 ml/min/1.73 m^2. The mean weight and body mass index of the participants were 63.76±9.98 kg and 23.50±3.41 kg/m^2 respectively. One hundred and four (80.6%) had palpably enlarge prostate while 24 (18.6) were observed to have loss of median sulcus on digital rectal examination

Majority of the patients 50 (38.8%) had eGFR of 60-89 ml/min/1.73 m^2 which classified these patients in stage 2 CKD. Six patients (4.7%) were in stage 5 CKD with eGFR <15 ml/min/1.73 m^2 (Table 1).

Table 1. Distribution of eGFR categories among the participants

eGFR in ml/min/1.73 m^2	Frequency	Percentage
≥90	24	18.6
60–89	50	38.8
30–59	34	26.4
15–29	15	11.6
<15	6	4.7

eGFR = estimated glomerular filtration rate

LUTS identified were as shown in Table 2. There was no statistically significant difference between the LUTS and eGFR. Forty-three (33.4%) of the patients had at least 2+ of dipstick proteinuria. 12 (9.4%) had hydronephrosis while the renal corticomedullary differentiation was observed to be loss in 37 (28.7%) patients. Overall 55 (42.7%) were found to have CKD at presentation. Eighteen (13.95%) had open surgery, 35

(27.13%) were managed medically with drug and 75 (58.14%) were on catheter awaiting surgery while 1 (0.78%) with chronic renal failure had dialysis.

Among the participant, 47 (36.4%) who were more than 65years old had eGFR <60 ml/min/1.73 m^2 (Table 3).

There is a significant difference in the quality of life among patient with eGFR less than or greater than 60 ml/min/1.73 m^2 p = 0.005. The prostate volume was observed to be high with a median value +IQR of 83.96 (64.50 -105.00) ml while the median value of PSA was 11.30 (6.00-11.30) ng/ml, with a p-value of 0.456. After controlling for age, prostate volume and serum PSA, there is a weak negative correlation between the eGFR and total IPPS score (r= -0.03, p=0.97) and between eGFR and QoL scores (r= -0.046, p= 0.666).

4. DISCUSSION

Benign prostatic hyperplasia (BPH) has been found to be the commonest aetiology of bladder obstruction (BOO) in men above the fifth decade of life [17]. The prostate gland enlarges as men grow old starting from the age of 45 years. This may or may not be symptomatic. The prevalence of BPH in Nigeria is 25.35% according to Ikuerowo et al. [18].

Benign prostatic hypertrophy has static and dynamic components. Static component as a result of the enlarged lobes of the gland due to cellular increase and the dynamic component due to the contractile elements of the gland [19]. Both components cause impedance to antegrade flow of urine out of the bladder. Increasing residual urine volume in the bladder in the presence of prostatic obstruction leads to reflux of infected urine back to the kidneys which

Table 2. Distribution of LUTS and eGFR

LUTS	Pt with eGFR <60 N (%)	Pt with eGFR >60 N (%)	P value
Irritative symptoms			
Urgency	34(41.5)	48(58.5)	0.853
Frequency	37(38.9)	58(61.1)	0.165
Nocturia	39(47.0)	44(53.0)	0.198
Obstructive symptoms			
Straining	29(43.9)	37(56.1)	0.859
Hesitancy	26(43.3)	34(56.7)	0.100
Intermittency	18(52.9)	16(47.1)	0.165
Incomplete emptying	37(46.8)	42(53.5)	0.274

LUTS= lower urinary symptoms, eGFR =estimated glomerular filtration rate, Pt= patient

Table 3. Comparison of variables among patient with eGFR less and greater than 60 ml/min/1.73 m^2

	All patient No (%)	Pt with eGFR <60ml/min/1.73 m^2. n=55	Pt with eGFR > 60ml/min/1.73 m^2. n=74	P value
IPSS Scores				
Mildly symptomatic	18(14)	6(4.7)	12(9.3)	
Moderately symptomatic	77(59.7)	31(24.0)	46(35.7)	0.507[b]
Severely symptomatic	34(26.4)	18(14.0)	16(12.4)	
QoL				
Poor	98(76.0)	49(38.0)	49(38.0)	
Good	31(24.0)	6(5.0)	25(19.4)	0.005[a]
Age group				
<65 years	38(29.5)	8(6.2)	30(23.3)	0.001[a]
>65 years	91(70.5)	47(36.4)	44(34.1)	
SPB (mean±SD)	136.90±18.50	141±21.494	133.72±15.31	0.023
DBP(mean±SD)	84.51±11.88	86.91±13.281	82.73±10.50	0.056
PCV(mean±SD)	36.69±5.78	35.38±6.16	37.66±5.53	0.026
PSA(median+IOR)*[φ]	11.30(1.0-211)	8.9(6.3-40)	12.20(6-73)	0.459[#]
PV (median+IOR)*	83.96(19.7-302)	86.37(65-108)	82.35(64-103)	0.462[#]

Continuous data were summarized as mean ± SD and non-normal data as median (IQR); the 25th-75th percentiles are specified. Categorical data were expressed as number (%). a= chi-square, b= Kruskal-Wallis Test, # Mann-Whitney U Test, incomplete data (73% available) φ. The proportion of data available for PSA was 72.87%. IPSS=International Prostate Score System, QoL= Quality of life, SBP=Systolic blood pressure, DBP=Diastolic blood pressure, PCV= Pack cell volume, PSA= prostatic specific antigen, PV= Prostate volume*

further impairs renal function. Chronic kidney disease have been reported to be a rare complication of BPH nonetheless, recent evidence have suggested a strong link between BPH and CKD [20].

In this study, 42.7% of patients with BPH were found to have CKD. Hill et al. [7] showed that 8% of men presenting for prostate surgery had renal failure compared to 3.7% in age-matched men presenting for non-prostate surgery. This figure is lower than our value though the renal failure was defined as plasma urea > 14 mmol/l or plasma creatinine > 200 µmol/l. A meta-analysis done by McConnell et al of men presenting to urologist for BPH treatment showed that an average of 13.6% (range 0.3% to 30%) had renal failure [8]. However, AK Eziyi et al. [21] in Oshogbo Southwest Nigeria, found a higher number (78%) of patients presenting with BPH had renal impairment. Sacks and his colleague in their analysis of 19 patients who presented with renal failure due to bladder outflow obstruction found that 16 patients received some form of dialysis during the course of the management [22].

According to American Urological Association guidelines on management of BPH, routine measurement of serum creation was not advocated based on the conclusion that renal involvement was not higher in patient with BPH compared with men of the same age group in the general population. However the EAU Guidelines

on BPH (2004) and the nephrology-focused NICE (National Institute for Health and Clinical Excellence) guidelines for the United Kingdom supported screening of BPH patients for renal involvement as it is cost effective as BOO due to BPH is a risk factor for CKD [5].

This study showed a weak negative correlation between the eGFR and IPSS score though the relationship did not reach a statistical significance. Findings of Kwon YM et al. [23] among Korean men demonstrated a negative association between total IPSS score and glomerular filtration rate (MDRD). Similarly, a prospective cohort study from Norway showed that IPSS was not significantly associated with future kidney failure [24]. However our findings is in contrast to American studies which demonstrated a significant relationship between signs and symptoms of BPH and CKD in their population-based sample of 476 white men [25].

However, there was statistical significance between the quality of life (QoL) and CKD. A Higher proportion of those with poor QoL (50%) had CKD compared with 19.4% in those with good QoL. This could be that patients with BPH with poor QoL following assessment are likely to have developed CKD irrespective of the severity of their symptoms. The degree of bothersomeness (QoL) of symptoms of BPH may be a risk factor for development of CKD. Patients with poor QoL following initial consultation should

have their renal function assessed albeit routine assessment of renal function has not been generally recommended for all patients with BPH.

Our study did not show any association between specific symptoms of BPH whether obstructive or irritative and eGFR. This is similar to the finding of Gerber et al. [26] where they found no link between serum creatinine levels and LUTS. Hong et al. [27] reported a significant association between individual obstructive symptoms such as hesitancy and / or weak stream and CKD but failed to show any significant association between overall symptoms (IPSS score) with CKD.

5. CONCLUSION

This study demonstrated an association between BPH and CKD in men whose symptoms were bothersome (those with poor QoL). The degree of bothersomeness (QoL) could be used as the determinant for requesting serum creatinine to assess the renal status of patients with BPH as men with LUTS often tolerate and disregard their symptoms and fail to seek medical care.

Estimating eGFR among these patients with BPH will offer a rapid method of renal function assessment at presentation and thus facilitate application of clinical practice guidelines and clinical performance measures to improve the outlook of possible renal complication.

6. LIMITATIONS

We acknowledge some limitations including the cross-sectional design of the study with a single measurement of serum creatinine which was used to categorize the patients. Serial measurement of the serum creatinine with at least 3 months apart would have been the best representation of the derangement in renal function according to KDQOI guidelines. The MDRD equation was used with the aim of improving the prediction of GFR from the plasma creatinine concentration. Though to our knowledge, MDRD equation has not been validated in people with obstructive nephropathy.

CONSENT

All authors declare that written informed consent was obtained from the patient (or other approved parties) for publication of this manuscript.

ETHICAL APPROVAL

All authors hereby declare that the work was approved by the ethical committee of the Ekiti State University Teaching Hospital.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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