TITLE: OBSTRUCTIVE NEPHROPATHY IN A KIDNEY HOSPITAL IN SOUTHWEST NIGERIA: THE NEED FOR EARLY SCREENING AND PREVENTION

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ABSTRACT

BACKGROUND: Most of the preventive efforts in Nephrology are focused on hypertension and diabetes mellitus. Obstructive Nephropathy (ON) which is a relatively common cause of CKD in Nigeria has not received adequate attention. This study reviewed the clinical profile of patients with ON at a Kidney hospital with the aim of identifying areas where preventive strategy should be targeted

METHODS: This was a 3 year retrospective study that reviewed records of patients managed for ON at Kidney Care Centre, Ondo, Southwest Nigeria.

RESULTS: Thirty-one out of 400 cases reviewed had ON with a prevalence of 7%. The mean age of the patients with OU was 63.20±12.02 years. Twenty-four (77.4%) were males and 7(22.6%) were females. The mean packed cell volume, creatinine and glomerular filtration rate at presentation were 25.17±7.84%, 893.47±649.54 micromol/l and 16.95±21.14mls/min/1.72m^2 respectively. Common aetiology of ON were prostate cancer in 13(41.9%), urolithiasis in 6(19.4%) and cervical cancer in 4(12.9%). Identified renal co-morbidities were hypertension 22(71%), diabetes mellitus 5(16.1%) and urinary tract infection in 15(30%). Anemia was present in 28(90.3%), hyperkalemia in 16(51.6%) and metabolic acidosis in 23(74.2%). Twenty-one (67.7%) had stage 5 CKD. Patients with malignancies were more likely to present in late stage of CKD (p= 0.001). Twenty-one (67.7%) were dialyzed.

CONCLUSION: Majority of patients with ON presented late and required hemodialysis. The common causes of ON were prostate cancer, stones and cervical cancers which are largely preventable or treatable. Screening for prostate and cervical cancer and human papilloma virus vaccination of at risk population is highly recommended.

INTRODUCTION

Chronic Kidney Disease (CKD) has become a major public health challenge due to its increasing incidence and prevalence globally, associated morbidity and mortality. According to the 2010 Global Burden of Disease study, CKD ranked amongst the top twenty causes of death.1 The global prevalence of CKD is estimated to be between11-13%. 2 In Nigeria, the reported prevalence of CKD according to both hospital and community based studies, vary between 6-12 %.3-6

The burden of chronic kidney disease is enormous especially in the developed countries due to late presentation, inaccessibility to continuous renal replacement therapy because of insufficient funds and or inadequate social security to meet these financial needs and high mortality. 7,8 The financial impact of CKD especially relating to RRT and cardiovascular complication is quite high even in countries like United Kingdom.9 Likewise, in other developed countries, 2-3% of their total health annual budget is expended on care of ESRD patients who account for only 0.02-0.03% of the total population.10 There is fear even in the developed countries of being unable to meet the financial requirements to cater for patients on renal replacement therapy in the near future if this evolving epidemic is not curbed.

Preventive nephrology is key to reducing the burden of CKD especially in developing countries where the budget allocated for the health sector is lean and cost of renal care is out of the reach of most patients. Most preventive efforts have been targeted at hypertension and diabetes mellitus and chronic glomerulonephritis which are the leading causes of CKD. However, obstructive uropathy which ranks as the 4^{th} or 5^{th} leading cause of CKD in Nigeria has not received adequate attention.

Previous reports showed that obstructive uropathy is the cause of CKD in between 4.4-11.0% of adult CKD patients.11-17. The most common common cause of CKD in pediatric Egyptian population is obstructive uropathy with a prevalence of 21.7%.18 Roth et al also reported that obstructive uropathy accounts for 16.5% of all paediatic renal transplantation.19 The burden of obstructive nephropathy has significantly reduced in North Africa, particularly in Egypt because of effective eradication and treatment of schistosomal infection which was identified to be largely responsible for its high prevalence. 20

The common causes of obstructive uropathy are benign prostatic hyperplasia, urolithiasis, prostatic cancer and cervical cancer. Obstructive uropathy as a cause of renal failure is preventable and potentially reversible if diagnosed early and there is timely institution of appropriate therapeutic intervention .

This study determined the profile of patients presenting with obstructive nephropathy at Kidney Care Centre, Ondo, Southwest, Nigeria with the aim of identifying areas where preventive strategy should be targeted.

METHODOLOGY

This study was a descriptive retrospective study carried out at Kidney Care Centre, a tertiary health institution located in Ondo City Southwest Nigeria that receives referral within and outside Ondo State.

Adult patients with CKD from obstructive nephropathy who presented to the centre over 3 year period between May 2014 to April 2017 were recruited for the study. Out of 400 adult patients managed for CKD, only 31 had obstructive nephropathy. Patients below the age of 18 years and those who had acute kidney injury were excluded. The case records of the adult patients with obstructive nephropathy were retrieved and the following information extracted using a proforma: socio-demographic data, clinical characteristics at presentation, co-morbidities like hypertension and diabetes mellitus, mode of referral to the nephrologist, investigation results and outcome of management

Operational Definitions

Obstructive nephropathy was defined based on unilateral or bilateral uretero-pelvic dilatation confirmed on ultrasound by a radiologist and presence of impaired renal function.

The Modification of Diet in Renal Disease (MDRD) equation was used to estimate GFR. CKD staging was done using estimated GFR (eGFR) as follows: stage 1 (GFR of $\geq$ 90 mls/min with evidence of kidney damage), stage 2 (GFR of 60-89 mls/min with evidence of kidney damage), stage 3 (GFR of 59-30 mls/min with or without evidence of kidney damage), stage 4 (GFR of 15-29 mls/ min with or without evidence of kidney damage) and stage 5 (GFR < 15mls/min with or without evidence of kidney damage)21

Anaemia was defined as haematocrit < 36% in females and < 39 % in males. 22 Hyperkalemia was defined as serum potassium than 5.0 mmol/l while metabolic acidosis was defined as serum bicarbonate <18.0 mmol/l

Data Analysis

Data generated were analyzed using the statistical package for social sciences (SPSS) version 17.0 by Chicago Inc. Results were presented in tabular form. Discrete variables were presented

as frequency and percentages. Continuous variables were presented as mean and standard deviation. Chi-square was used to determine association between categorical variables. $P < 0.05$ was taken as significant

RESULTS

This study showed that 31 patients out of 400 adult patients with CKD had obstructive nephropathy over the study duration. The prevalence of obstructive nephropathy was 7%. Amongst the patients with obstructive nephropathy 24(77.4%) were males and 7(22.6%) were females.

The mean age, systolic BP, diastolic BP and packed cell volume were 63.20±12.02 years, 146.13±38.24 mmHg, 83.74±22.47mmHg and 25.17±7.84% respectively. The mean serum urea, creatinine, sodium, potassium, chloride and bicarbonate were 25.29±15.75mg/dl, 893.47±649.54 micromol/l, 128.75±10.4mmol/l,5.32±1.45mmol/l,17.35±7.26mmol/l and 104.64±10.03mmol/l respectively.

The mean session of HD among those dialyzed was 7.2(6.4) while the mean duration of hospital stay among those admitted was15.9±6.71 days. Only 8(25.8%) of the patient presented on account of self-referral while others were referred from other health facilities.

Anemia was present in 28(90.3%), hyperkalemia in 16(51.6%) and metabolic acidosis in 23(74.2%). Twenty-one (67.7%) had stage 5 CKD, 6(19.4%) had stage 4 CKD and 3(9.7%) had stage 3 CKD at presentation

The aetiology of obstructive nephropathy were prostate cancer in 13(41.9%), urolithiasis in 6(19.4%), cervical cancer in 4(12.9%), BPH in 3(9.7%), Pelvi-ureteral junction obstruction in 1(3.2%) while aetiology was unknown in 3(9.7%)

The identified renal co-morbidities were hypertension in 22(71%), diabetes mellitus in 5(16.1%) and urinary tract infection in 15(50%) . Twenty (64.5%) had blood transfusion and 21(67.7%) were managed with dialytic therapy.

Patients with malignancies were more likely to present in late stages of CKD compared to other more benign aetiolgies.(p= 0.001)

DISCUSSION

This study showed that the prevalence of obstructive nephropathy among CKD patients managed in Kidney Care Centre, Southwest Nigeria is 7%. This is similar to report by Arogundade et al who reported a prevalence of 6.7% in a study done in Ile-Ife, Southwest Nigeria.13 This is lower than 4.4% and 5.6% reported by Amoaka et al and Okaka et al in studies done in Southern Nigeria and Ghana respectively.11,12 Roth et al and Setouh et al reported a higher prevalence of obstructive uropathy: 16.5% and 21.7% of their respective CKD study population had obstructive uropathy.18,19 However, they studied pediatric population unlike our study that involved only adults.

Majority of the affected patients were middle aged and elderly with a mean age of 63.20±12.02 years. The mean age in this study is higher than 50±18 years reported by Halle et al.23 This implies that we may have more cases of obstructive nephropathy in Nigeria as the life expectancy increases due to improvement in health care services and delivery if preventive measures are not put in place. Obstructive uropathy largely affected males more than females which agrees with previous studies. 23,24,25

The common etiologies associated with obstructive uropathy in this study are prostate cancer, urolithiasis and cervical cancers which is similar to reports by Halle et al and Soyebi et al. 24,25 These are largely preventable or treatable if diagnosis is promptly made. Surprisingly, some of these patients were firstly diagnosed of cancer during the course of evaluation for renal disease, showing ignorance on awareness of common symptoms of prostate and cervical cancer among our population. This agrees with the findings of Ajape et al who reported poor awareness of prostate cancer among men in a Nigerian urban population.26 Various reports have also shown poor awareness and low utilization of cervical screening methods among Nigerian women.27-29 This underscores the need to continuously educate our at risk population on early symptoms and screen them for BPH, prostate and cervical cancer.

Vaccination of young females against human papilloma virus is an effective way of reducing the incidence of cervical cancer and attendant complications such as obstructive uropathy, however the high cost has severely limited its utilization among Nigerians despite high acceptance.27,28 Government could improve the utilization of this vaccine by incorporating it into the national immunization scheme or subsidizing its cost to make if affordable and accessible

This study shows that patients with malignancies were more likely to present in late stage of CKD compared to other etiologies like BPH and stones. This may be due to the fact that severe pain is a common feature of renal stones, hence they are likely present earlier compared to those with malignancies.

Majority of our patient had anaemia at presentation with about 64.5% requiring transfusion during the course of treatment. This may be due to the fact that most of them presented very late with advanced stage of renal impairment and malignancies. About two-third of our patients were managed as in-patient with an average hospital stay of about 2 weeks. Hyperkalemia and metabolic acidosis were present in about 50% and 75% of the patients which may be partly related to defective bicarbonate absorption in proximal tubules and or defect in hydrogen ATPase activity of the alpha intercalated cells that commonly occurs in obstructive nephropathy.

Hypertension, diabetes mellitus and urinary tract infection were common co-morbidities present in these patients. These conditions could contribute to loss of renal function in these patients hence blood pressure and glycemic control must be carefully achieved in hypertensive and or diabetic patients with obstructive uropathy in order to reduce their renal risk. Recurrent urinary tract infection which is common in patients with obstructive uropathy due to urinary stasis may also contribute to deterioration in renal function. Therefore, patients with obstructive nephropathy should be regularly screened for urinary tract infection and adequately treated if indicated with appropriate antibiotics with consideration of renal safety.

Majority of the patients presented late with about 68% presenting in end stage renal disease and requiring dialysis at first contact with a nephrologist. This is higher than 41 % and 23% reported by Halle et al and Imam et al respectively.23,30 The higher proportion of our patients requiring urgent dialysis compared to these latter studies may be related to the fact that we studied patients with obstructive nephropathy unlike the other studies that involved patients with obstructive uropathy.

The limitation of this study is that it is a single-centre study with relatively small sample size, hence the findings cannot be generalized. However, the study has been able to show that the common causes of obstructive nephropathy in our patients were prostate cancer, stones, cervical cancers and BPH which are largely preventable or treatable. Also, majority of these patients with obstructive nephropathy presented late and required hemodialysis. We therefore propose the following recommendations in order to reduce the burden of obstructive nephropathy:

1. Regular screening for prostate and cervical cancer among middle and elderly population
2. Incorporation of HPV vaccination into the national immunization scheme or government should make the vaccine easily available and affordable by subsidizing its cost
3. Education of at risk group on early symptoms of prostate and cervical cancer and the importance of screening.
4. Regular assessment of renal function in patients with obstructive uropathy in urological clinics.

   The above recommendation will reduce the incidence of prostate and cervical cancer as well their attendant complications such as obstructive nephropathy. These will also ensure that patients with obstructive uropathy present early before irreversible renal damage occurs.

Table 1: Characteristics of Study Population

Parameters	Mean(sd)/ n(%)
Age	63.20± 12.02
<40 years	1(3.2%)
40-64 years	14(45.2%)
≥65 years	16(51.6%)
Systolic Blood Pressure	146.13±38.24
Diastolic Blood Pressure	83.74±222.47
Dialyzed	
Yes	21(67.7%)
No	10(33.3%)
Num of HD sessions	7.2±6.4
Required In-patient Care	
Yes	20(64.5%)
No	11(35.5%)
Duration of Hospital stay	15.8±6.7
ANEMIA	
Present	28(90.3%)
Present	3(9.7%)
TRANSFUSED	
Yes	20(64.5%)
No	11(35.5%)
REFERRAL PATTERN	
Self Presentation	8(25.8%)
Secondary level of Care	14 (45.2%)
Tertiary level of Care	8(25.8%)

Table 2: Laboratory Parameters of Study Population

Parameters	Mean (SD)
Packed Cell Volume (%)	25.17±7.84
Serum Urea (mg/dl)	25.29±15.75
Serum Creatinine (microl/l)	893.47± 649.54
Serum Sodium (mmol/l)	128.75±10.4
Serum Potassium (mmol/l)	5.32±1.45
Serum Chloride (mmol/l)	104.64±10.03
Serum Bicarbonate (mmol/)	17.35±7.26
Estimated GFR(mls/min/1.73m^2)	16.95±21.14

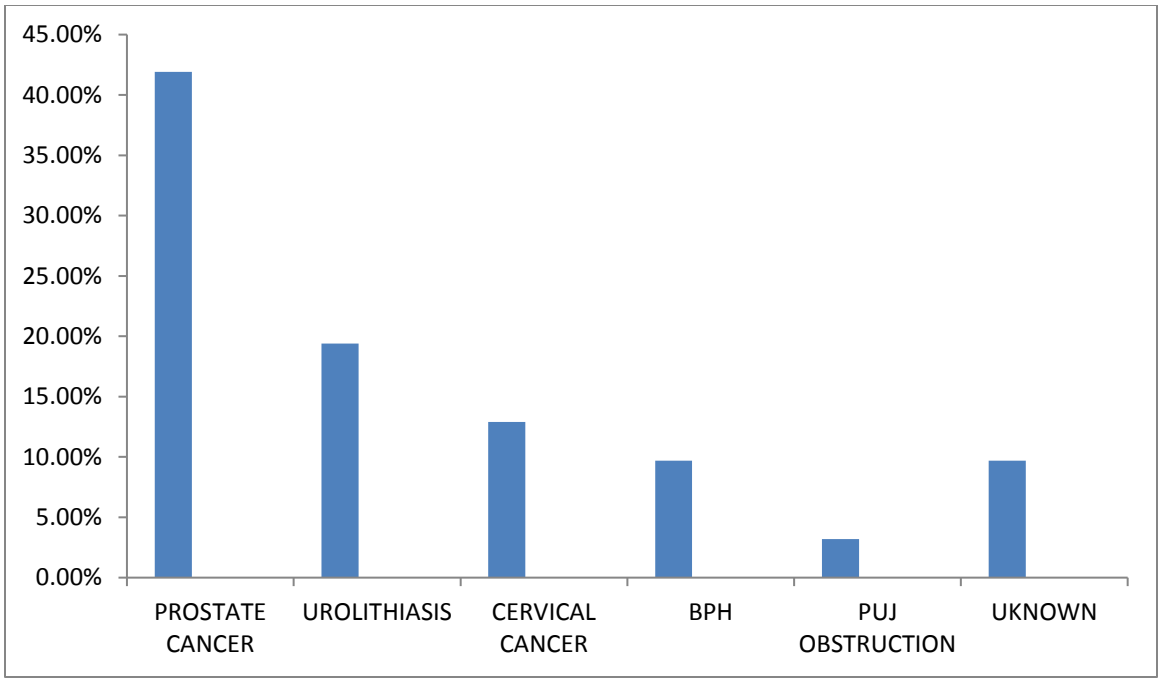

Fig 1: Aetiology of Obstructive Nephropathy

Table 3: Association between aetiology of obstructive nephropathy and stage of presentation

	Benign Causes	Malignant Causes	p-value
CKD Stage			
1	0(0%)	1(100%)	
3	0(0%)	4(100%)	0.001
4	1(25%)	4(80%)	
5	4(19%)	17(81%)	

REFERENCES

1. Jha V, Garcia-Garcia G, Iseki K, Li Z, Naicker S, Plattner B, et al. Chronic kidney disease: global dimension and perspectives. Lancet. 2013;382(9888):260–72.
2. Fatoba ST,Oke JL, Hirst JA, O'Callaghan CA, Lesserson DS, Hobbs FDR. Global prevalence of chronic kidney disease- a systematic review and meta-analysis. PloS ONE 2016;11(7): e0158765.doi:10.371/journal.pone.0158765
3. Kadiri S, Arije A. Temporal variations and meteorological factors in hospital admissions of chronic renal failure in south west Nigeria. West Afr J Med. 1999;18(1):49–51.
4. Akinsola W, Odesanmi WO, Ogunniyi JO, Ladipo GO. Diseases causing chronic renal failure in Nigerians--a prospective study of 100 cases. Afr J Med Med Sci. 1989;18(2):131–7.
5. Ulasi II, Ijoma CK. The enormity of chronic kidney disease in Nigeria: the situation in a teaching hospital in South-East Nigeria. J Trop Med 2010;2010:1–6.
6. Ulasi II, Ijoma CK, Onodugo OD, Arodiwe EB, Ifebunandu NA, Okoye JU. Towards prevention of chronic kidney disease in Nigeria: a community-based study in Southeast Nigeria. Kidney Int Suppl. 2013;3(2):195–201.
7. Adejumo OA, Akinbodewa AA, Okaka EI, Alli OE, Ibukun IF. Chronic kidney disease in Nigeria; Late presentation is still the norm. Niger Med J 2016;57:185-189
8. Odubanjo MO,Oluwasola AO, Kadiri S. The epidemiology of end stage renal disease in Nigeria: way forward. Int Urol Nephrol 2011;43(3):785-92
9. Kerr M, Bray B, Medcalf J, O'Donoghue DJ, Matthews B. Estimating the financial cost of chronic kidney disease to the NHS in England. Nephrol Dial Transplant 2012;27(Suppl 3):73-80
10. Levy AS, Atkins R, Coresh J, Cohen EP, Collins AJ, Eckardt K et al. Chronic kdney disease as a global public health problem: approaches and initiatives position from- a position from Kidney Disease Improving Global Outcomes. Kid Int 2007;27(3):247-259
11. Amoaka YA, Laryea DO, Bedu-Addo G, Andoh H, Awuku YA. Clinical and demographic characteristics of chronic kidney disease patients in a tertiary facility in Ghana. Pan Afri Med J 2014:18;274 doi:10.11604/pamj 2014.18.274.4192
12. Okaka EI, Enuigbe EI. Eight year review of hemodialysis treated patients in a tertiary centre in Southern Nigeria. Ann Afr Med 2014;13:221-225

13. Arogundade FA, Sanusi AA, Hassan MO, Akinsola A.The pattern, clinical characteristics and outcome of end stage renal disease in Ile-Ife, Nigeria. Afr Health Sci 2011;11(4):594-601
14. Barsoum RS. End stage renal disease in North Africa. Kid Int Suppl 2003;83:111-114
15. Salman M, Khan AH, Adnan AS, Sulaiman SAS, Hussai K, Shehzadi N et al. Attributable causes of chronic kidney disease in adults; a 5 year retrospective study in a tertiary hospital in northeast of Malaysian Peninsula. Sao Paulo Med J 2015;133(6) dx.doi.org/10.1590/1516-3180.2015.005
16. Amira OA, Lesi OA. Seroprevalence of hepatitis B and C infection among Nigerians with chronic kidney disease. J Clin Sci 2017; 14(2):58-61he
17. Banaga ASI, Mohammed EB, Siddig RM, Salama D, Elbashir SB, Khojali MO et al Causes of end stage renal disease among haemodialysis patients in Khartoum. BMC Res Notes 2015; 8:502 doi 10.1186/s 13104-015-1509-x
18. Safouh H, Fadel F, Essam R, Salah A, Bekhet A. Causes of chronic kidney disease in Egyptian children. Saudi J kidney Dis Transpl 2015; 26(4):806-809
19. Roth KS, Koo HP, Spotswood SE, Chan JC. Obstructive uropathy: an important cause of chronic renal failure in children. Clin Pediatr 2012;41(5):309-314
20. El-Arbagy AR, Yassin YS, Boshra BN. Study of prevalence of end stage renal disease in Assiut governote, upper Egypt. Menoufia Med J 2016;29(2):232-237
21. Kidney Disease Improving Global Outcome (KDIGO) 2012 Clinical Practice Guideline of evaluation and management of CKD. Kidney Int Supplements 2013;3:1-150
22. World Health Organization (WHO). Iron deficiency anaemia: Assessment, prevention and control. A guide for programme manager. Geneva Switzerland: WHO;2001
23. Halle MP, Toukep LN, Nzuobontane SE, Ebana HF, Ekane GH, Priso EB.Profile of obstructive uropathy in Cameroon: case of Douala General Hospital. Pan Afri Med J 2016;23:67 doi:10.11604/pamj.2016.23.67.8170
24. Soyebi KO, Awosanya GOG. Causes of obstructive uropathy at the Lagos University Teaching Hospital. Niger Q J Hosp Medicine 1996;6:173-177
25. Banaga ASI, Mohammed EB, Siddig RM, Salama DE, Elbashir SB, Khojali MO et al. Causes of end stage renal failure in haemodialysis patiensts in Khartoum State/Sudan. BMC Research Note 2015;8:502 doi: 10.1186/s13104-015-1509-x

26. Ajape AA, Babata A, Abiola OO. Knowledge of prostate cancer screening among native African urban population in Nigeria. Nig Q J Hosp Med 2010; 20(2):94-96
27. Eze JN, Umeora OU, Obuna JA, Egwuatu VE, E jikeme BN. Cervical cancer awareness and cervical screening uptake at the Mater Misericordiae Hospital, Afikpo, Southeast Nigeria. Ann Afr Med 2012;11(4):238-243
28. Hyacinth HI, Adekeye OA, Ibeh JN, Osoba T. Cervical cancer and Pap smear awareness and utilization of Pap smear test among federal civil servants in North central Nigeria. PLos ONE 7(10): e46583 doi: 10.1371/journal. Pone.0046583
29. Brown B, Folayan M. Barriers to uptake of human papilloma virus vaccine in Nigeria: A population in need. Niger Med J 2015;56(4):301
30. El Imam M, Omran M, Nugud F,Elsabiq M, Saad K, Taha O. Obstructive uropathy in Sudanese patients. Saudi J Kidney Dis Transpl 2006;17:415-419