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Original Research Article

Profile of estimated glomerular filtration rate of children with Human Immunodeficiency Virus/ Acquired Immune Deficiency Syndrome

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ABSTRACT

Background: Kidney disease is more common in people of African descent in developed countries. Studies reporting estimate Glomerular Filtration Rate (eGFR) in African populations and people living with HIV have been carried more frequently on adults than children. The study aimed to assess eGFR by use of the SCHWARTZ formula in HIV infected children seen at tertiary hospital.
Methods: A descriptive, prospective and cross sectional study of 221 children with HIV infection. Schwartz formula was used to determine eGFR. The main outcome measures were eGFR. The study population comprised HIV infected children attending Paediatric out-patients' clinic and those admitted into the Paediatric wards, aged between 6 months and 15 years. Data was analysed using SPSS version 20 and results presented in tables and figures.
Results: The age range of the study subjects was 12 months to 15 years with the mean age and SD of 8.21±3.61 years. There were 129 (58.4%) male and 92 (41.6%) female children with male to female ratio 1: 0.7. The mean age for males was 7.87±3.49 years while that for females was 8.70±3.71 years. The eGFR for the study as determined by Schwartz formula had a range of 49.21 to 463.67 ml/ min/ 1.73m2 with the mean of 159.56±59.04 ml/min. The mean eGFR for the males and females were 166.39±63.54ml/ min and 149.99±45.01 ml/ min respectively.
Conclusion: The study, in comparison with other studies, observed a lower prevalence of CKD in HIV infected children. Detection of CKD in HIV infection children may be more optimal if combined methods are employed.

Keywords: Acquired immune deficiency syndrome, Children, Chronic kidney disease, Human immunodeficiency virus infection, Glomerular filtration rate, Renal function

INTRODUCTION

Chronic kidney disease (CKD) is a common complication of HIV infection in this modern era of antiretroviral therapy (ART) and more common in people of African descent in developed countries.[1,2] Studies reporting estimated glomerular filtration rate (eGFR) in African populations and people living with HIV have been carried more frequently on adults than children.[3-5] The various reports from different studies showed that the prevalence of CKD as defined by an estimated GFR of less than 60ml/min/1.73m2 ranges from 3.5 to 32.6%. It varies from one country to another and is dependent on estimation equation/ formula used and characteristics of the study population as well as the criteria used to define CKD.[6,7]

The serum creatinine (Scr) based equations and serum cystatin C based Filler's equation have been used in several studies in HIV infected population.[3,5,8-12] These estimates are particularly biased in the HIV infected individuals as a result of abnormalities in muscle mass, nutrition, liver diseases and medications that alter renal function.[10] In a multicentre AIDS cohort study (MACS) eGFR in a population of HIV infected and uninfected men, the proportion of HIV infected men with CKD was higher by eGFRcyst compared with eGFRscr of 7% versus 5% respectively.[13] The Eurosida study and US veteran affairs using Cockcroft-Gault (C-G) equation for estimation of GFR for HIV positive patients, found prevalence of CKD of 3.5% and 7.1% respectively while CKD prevalence of 15.5% using modification of diet in Renal Disease (MDRD) equation was observed in adults with HIV.[7,14,15] These studies were based on different eGFR equations, and this may have contributed to the varying prevalence obtained.

The Sub-Saharan African countries have high prevalence of chronic kidney diseases as documented in different studies done on people living with HIV/AIDS.[5,9,11,12.] In Zambian adult HIV infected patients the prevalence of CKD was 28% and 25.3% using C-G and MDRD equations respectively while in Kenya prevalence of 11.5% using MDRD in a small population of adults was reported. In a Scr based eGFR in children in Benin, Nigeria, a prevalence of 5.1% was obtained.[16]

In Southern Nigeria using cystatin C based evaluation of kidney function reported prevalence of CKD of 13.3% and 10% respectively. The differences in the prevalence may be traced to the dependence of serum creatinine based equations on age, gender and bias introduced by extremes of body weight.[8,13]

The use of the Schwartz formula to estimate GFR in asymptomatic HIV infected children is cheap, simple non-invasive and more likely to detect early stages of CKD than the use of serum creatinine alone.[17] Authors therefore aim to determine eGFR using SCHWARTZ formula in HIV infected children and to determine relationships (if any) between eGFR and sociodemographic variables (age, and gender) in HIV-infected children seen at the National Hospital, Abuja.

METHODS

The study was conducted at the National Hospital Abuja, a 220 bed tertiary hospital which is located in the Central Business District of the Abuja Municipal Area Council (AMAC). The National Hospital benefits from PEPFAR (the United States President's Emergency Plan for AIDS Relief) programme which provides care and support for both adults and children with HIV infection. Management including clinical evaluation, diagnosis (ELISA and HIV DNA PCR), investigations and drugs - (ARVs and certain medications for treatment and prevention of OIs) are all provided free of charge within the programme. The care of HIV infected children is overseen at the weekly Paediatric Haematology Clinic.

This was a prospective cross-sectional study of children with HIV infection who were consecutively enrolled into the study until the required sample size was achieved.

The study population comprised HIV infected children attending Paediatric Haematology Clinic, Out-patients' clinic and those admitted into the Paediatric wards, aged between 6 months and 15 years. The age 6 months was chosen because by this age all HIV exposed infants would be expected to have had a definitive diagnosis by HIV DNA PCR, according to Nigerian National guidelines on Paediatric HIV and AIDS.[18] Fifteen years is the upper limit for Paediatric age range according to the National Hospital policy. The study was carried out period of 6 months (from December 2012 to May 2013).

Ethical approval was obtained from the institution ethics and research committee. Assent was obtained from children 10 years and above after informed consents were obtained from their parents/caregivers.

Biodata of subjects such as name, age, gender, tribe, address, religion (demographic characteristics) were obtained from the patients/ parents/guardians. Also the parent's marital status, educational status and occupation were obtained. Also WHO clinical staging was done at initial presentation/enrolment as well as samples taken for serum creatinine for estimation of GFR.

The subjects were weighed in order to categorize them objectively as underweight, normal weight or obese during clinical evaluation. The weight was measured to the nearest 0.1 kg and the scale was checked for zero error before every weighing session. Each patient was weighed twice and the average weight was used for the patient. Infantometer was used for infants and children yet to walk. The length/height was measured to the nearest 0.1cm and each patient had two measurements thereafter the average was taken as the length.

To determine serum creatinine, 3mls of blood in lithium heparin bottle was analysed using the Jaffe's method on Corning colorimeter reading at 520 nanometers. The glomerular filtration rate (GFR) based on creatinine clearance was calculated using the Schwartz formula.[19]

$$\text{GFR} = \frac{KL}{\text{Pcr}}$$

Where K = a proportional constant
L = body length in cm
Pcr = plasma creatinine in mg/dl
GFR = glomerular filtratin rate in ml/min/1.73m2
The value of K in children is 0.55

Data analysis was done using the Statistical Package for Social Sciences (SPSS) version 20. Descriptive statistics were used like simple proportions and frequency tables as

well as Bar chart for age, gender, clinical staging and mean eGFR. Also mean, standard deviations and ranges of variables were computed.

Means of continuous variables were compared using Student's t test. Association between parameters were analyzed with appropriate statistical package which included Pearson Chi square test. The level of statistical significance was set at p less than 0.05.

RESULTS

The age range of the study subjects was 12 months to 15 years with the mean±SD age of 8.21±3.61 years. There were 129 (58.4%) male and 92 (41.6%) female children with male to female ratio 1: 0.7. The mean±SD age for males was 7.87±3.49 years while that for females was 8.70±3.71 years.

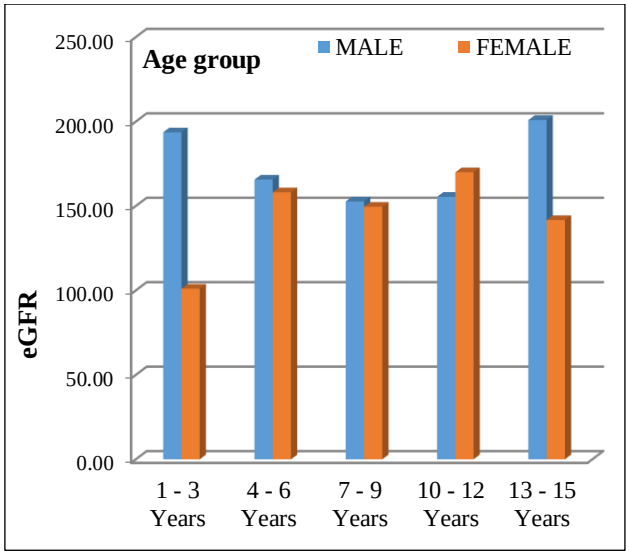

Figure 1: Age group and gender distribution of eGFR.

Table 1: Participants General characteristics.

Age in years	N = 221	Male = 129	Female = 92
Range	1–15	1–15	1–15
Mean (SD)	8.21(3.60)	7.87 (3.49)	8.70 (3.71)
Height (cm)	N=221	Male=129	Female=92
Range	67.00–174.00	72.00–174.00	67.00–170.00
Mean (SD)	126.48 (21.32)	125.10 (20.75)	128.42 (22.07)
< 90% of EHA	14 (6.3%)	7 (5.4%)	7 (7.6%)
≥90% of EHA	207 (93.7%)	122 (94.6%)	85 (92.4%)
Weight (kg)	N=221	Male=129	Female=92
Range	7.10-59.90	7.20 - 59.90	7.10 - 58.00
Mean (SD)	27.15(11.23)	26.50 (10.65)	28.06 (12.00)
<80% of EWA	30(13.6%)	16 (12.4%)	14 (15.2%)
80% - 100% "	109(49.3%)	60 (46.5%)	49 (53.2%)
>100 - 120%"	63(28.5%)	38 (29.5%)	25 (27.2%)
>120% of EWA	19(8.6%)	15 (11.6%)	4 (4.4%)
eGFR (ml/min/1.73m^2)	N=221	Male=129	Female=92
Range	49.21- 463.67	49.21- 463.50	51.24-265.00
Mean (SD)	159.56(57.04)	166.39 (63.54)	149.99 (45.01)
WHO clinical Staging	N=221	Male=129	Female=92
Stage I	37(16.7%)	24 (18.6%)	13(14.1%)
Stage II	98(44.3%)	61(47.3%)	37(40.2%)
Stage III	70(31.7%)	35 (27.1%)	35(38.0%)
Stage IV	16(7.2%)	9 (7.0%)	7(7.6%)

Table 2: Classification of eGFR as determined by Schwartz formula.

eGFR ml/min/1.73m^2 Categories	CKD Stages	Sex		N (%)	Mean eGFR ± SD
		Male	Female		
≥ 90	I	125	86	211(95.4)	163.95±54.51
60–89	II	3	2	5 (2.3)	78.44±6.49
30–59	III	1	4	5 (2.3)	55.29±4.50
Total		129	92	221(100.0)	159.56±59.04

Table 3: Relationship between eGFR and age groups of subjects with HIV/AIDS.

Age in years	N	eGFR Mean±SD ml/ min/ 1.73m^2
1–3	22	155.74±67.54
4–6	52	163.02±68.27
7–9	68	151.46±44.33
10–12	48	162.09±47.95
13–15	31	170.33±66.63
Total	221	159.56±57.04

F = 0.712 df = 4 P value = 0.585

Table 4: Intra age – group gender comparison of EGFR.

Age in Years	Mean±SD eGFR (ml/ min/ 1.73m^2) Male	Female	t	p value
1–3	193.62±56.60	101.03±38.34	4.262	0.000
4–6	165.64±77.43	158.09±47.98	0.376	0.708
7–9	152.60±47.89	149.57±39.12	0.282	0.779
10–12	155.42±53.79	169.97±39.77	–1.048	0.300
13–15	200.90±74.71	141.66±43.09	2.727	0.011

Table 5: Association between eGFR and WHO clinical staging of subjects with HIV/AIDS.

WHO Clinical Staging	eGFR Stages (ml/ min/1.73m^2) ≥ 90 (stage I)	60–89 (stage II)	30–59 (stage III)	Total
Stage I	33	2	2	37
Stage II	97	0	1	98
Stage III	67	2	1	70
Stage IV	14	1	1	16
Total	211	5	5	221

χ^2 = 9.076 df = 6 p value = 0.169

Figure 1 demonstrates bar chart reflecting age group and gender distribution of estimated GFR. The weight of the children ranged from 7.10 to 59.90 kilograms (kg) with the mean±SD weight of 27.20±11.20 kg (Table 1). Thirty (13.6%) children were underweight (weight less than 80% of expected weight for age, EWA), while 109 (49.3%) had normal weight (weight of 80-100% of EWA). Sixty three (28.5%) children were overweight (>100-120% EWA) while 19 (8.6%) were obese (weight >120% EWA). Out of the 221 HIV infected children 14 (6.3%) were stunted (height <90% of expected for height, EHA) while 207 (93.6%) had normal height (height ≥ 90% of EHA).

The estimated glomerular filtration rate (eGFR) for the study as determined by Schwartz formula had a range of 49.21 to 463.67 ml/ min/ 1.73m2 with the mean±SD of 159.56±59.04 ml/min. The mean eGFR for the males and females were 166.39±63.54ml/ min and 149.99±45.01 ml/ min respectively (Table 1).

Stage I, the category of normal eGFR (≥ 90 ml/ min /1.73m2) had the highest number of children, 211(95.4%) among the study subjects with 125 (59.2%) of them being males and 86 (40.8%) females. The mean±SD eGFR for the stage was 163.95±54.51 ml/min/ 1.73m2. Stage II eGFR of 60–89 ml/ min/ 1.73m2 had 5 children with mean±SD eGFR of 78.44±6.49 ml/ min/1.73m2. Stage III (eGFR of 30-59 ml/min/1.73m2) had 5 children, 1 male and 4 females with mean±SD of 55.29±4.50ml/ min/1.73m2. No child was in the categories of 15-29 ml/min (stage IV) and less than 15 ml/ min (stage V).

The age group 13-15 years had the highest mean eGFR± SD value of 170.33±66.63 ml/min/1.73m2 (Table 3). The relationship between age of subjects and eGFR, within groups and between groups was not statistically significant (F=0.712, p value=0.585). There was significant relationship observed between intra age-group of 1-3 and 13-15yrs with gender comparison of eGFR (Table 4). The severity of the clinical staging of the disease had no significant relationship with the occurrence of CKD as p value=0.295 (Table 5).

DISCUSSION

The prevalence of chronic kidney disease (defined as eGFR of <60ml/min /1.73m2) in the study was 2.3%

which is lower than figures previously reported from Nigeria 5.1% and 10.7% both from Benin in 2013 and 2010 respectively, as well 13.3% from Lagos in 2010.[7,8,10] 2010 reviewed published literatures and reported prevalence of CKD in HIV infected patients of 3.5-4.7% in 31 European countries, Israel and Argentina, 1.1-5.6% in Brazil, 18% in Switzerland, 27% in India, 12.3% in Iran and 6-48.5% in Sub-Saharan Africa using different criteria for defining renal diseases in the various studies.[20] The CKD prevalence from Nigeria of 5.1% was from serum creatinine (Scr) based study on HIV infected children on HAART while the 13.3% and 10% prevalence were from serum cystatin C based studies on HIV infected children yet to start antiretroviral drugs (ARVs).[8,10,16] The differing CKD prevalence obtained from these studies may be related to the different methods of estimation of glomerular filtration rate (eGFR), different endogenous substances studied and ARVs use by the HIV infected children during the study.

The serum cystatin C (Scyst) based eGFR, has been argued to be more accurate than Scr based estimation of GFR. This is because serum cystatin C is less affected by lean muscle mass, diet, not affected by tubular secretion but dependent on age, sex and race like serum creatinine. However, the increase in cystatin C level during systemic inflammatory process cast doubts on the (accurate) specificity of such substance as being ideal for measuring eGFR.[13]

The higher prevalence of CKD found in the Scyst based studies may also be attributed to the lack of use of HAART by the subjects in these studies. HAART has been found to slow down or halt the rate of progression of renal diseases to ESRD.[21-24] The HIV infected children in the quoted studies were not on ARVs, while 97.7% of the children in our present study were on HAART. The low prevalence from our study which is similar to that may be related to sample size since the same number of children were found to have CKD from the different studies.

The use of only eGFR estimation to detect CKD may not be as effective as combined methods of identifying those with renal dysfunction and as such may not give true prevalence of renal diseases in HIV infected children. This is because proteinuria which is a marker of glomerular disease can present with normal GFR and reduced GFR (an indicator of nephron loss) can occur in the absence of proteinuria.[16]

This study identified 5 children with chronic kidney disease. The male to female ratio of the children with CKD was 1:4, in spite of the study subjects being predominantly males. This observation is in contrast to the findings in majority of other studies in which there were predominantly male children with CKD.[10,16,25-27] The reason for this observation is not clear (or apparent) and may be a chance finding.

Though not statistically significant the study revealed a trend of increasing eGFR with increasing age of the children except at the age group of 7-9 years. The increase in eGFR with age had been noted in other studies where it was also found that at each age group males had higher eGFR than females.[28-30] This is similar to the findings in the current study except for the age group 10-12 years. However, the highest mean eGFR recorded at age group (13-15 years) could be explained by increase muscular activity, hormonal interference and pubertal growth spurt. Gender distribution in the study showed male preponderance with significantly higher eGFR in males than females. This observation is similar to the reports of other studies on relationship between gender and glomerular filtration rate where gender specific values of eGFR were found to be higher in males than females.[29-31] This is because of a higher average muscle mass and generation rate of creatinine in males.[32] The eGFR was lower in males in the age group of 10-12 years. This may be dependent on nephron damage, immunological compromise, viraemia or low CD4 + cell count in the age group.

In the study, there was no significant association between eGFR and clinical stages of HIV disease. The eGFR was found to be increasing with worsening clinical stage of the infection. There are similar reports from other studies that found that eGFR was independently associated with increased risk of HIV disease progression.[8,26,33] This may be connected to the different times acute insult occurred to the kidney, immunity of the individual, associated opportunistic infections and HIV viraemia. Renal impairment in HIV antiretroviral naïve patients in Western Kenya was independent of several parameters for clinical staging of HIV infection.[34]

The use of single measurement of glomerular filtration rate without repeating it in 3 or more months later to exclude transient reduction in glomerular filtration rate limits its relevance in the determination of CKD. The serum creatinine (Scr) derived formula/equation has not been validated in HIV infected people especially children.

CONCLUSION

The study, in comparison with other studies, observed a lower prevalence of CKD in HIV infected children. Detection of CKD in HIV infected children may be more optimal if combined methods are employed. There is need for determining the renal status of HIV infected children as early detection and management retards diseases progression to end stage.

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