Original Article

Sonographic Characterization of Renal Pathologies in Hiv/aids in Plateau State, Nigeria

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ABSTRACT

BACKGROUND: The prevalence of HIV/AIDS in Jos is about 7% according to Idoko et al. Many deaths from infection occur from the complications involving vital organs. The effects of this complication on the kidneys being one of the vital organs are yet to be determined in the locality. The kidneys are prone to impairment due to direct viral attack, opportunistic infections and nephrotoxic drugs. Though renal sonographic features are well characterized in literature, there is no documentation of correlation between renal sonographic features in HIV/AIDS and healthy population in Nigeria. The objectives of the study are to determine the commonly occurring renal sonographic features in HIV/AIDS in terms of echogenicity and size, and correlate these features with measured CD4 cell count.

METHODS: 302 subjects were studied prospectively over a period of twenty two months. In order to determine renal sizes, several bilateral longitudinal and transverse scans of the subjects' kidneys in a supine position were done. In order to clarify renal echogenicity, a-four point scoring method was devised to measure the severity of sonographic changes in the kidneys. Subjects' CD4 cell counts were collected from the APIN laboratory and Faith Alive Foundation both in Jos. Pearson's correlation and regression were used for correlation between CD4 cell count and renal length, and between renal length and age, and Z-test was used to compare mean renal dimension of male and female of subjects and HIV sero negative subjects.

RESULTS: The subjects consisted of 123 males and 179 females with a mean age of 34.4 years, between the ages of 4 and 80 years. Results indicated that 77.7%of subjects had increased renal echogenicity reflecting the prevalence of renal disease in HIV/AIDS in the locality, 76.7% of the subjects were in their reproductive and sexually active ages(21-40years).There was significant negative correlation between renal length and measured CD4 cell count($p<0.01$) and also between renal length and age of subjects($p<0.05$).No significant correlation between renal echogenicity and CD4 cell count was noted. Result also indicate that renal length is related to CD4 cell count by the equation=0.0029CD4+11.1423

CONCLUSION: It is concluded that sonographic features of the kidneys in HIV infection in this locality is characterized by increased renal length with decreasing CD4 cell count amongst sexually active age group. And also a generally high incidence of renal involvement (disease) in HIV/AIDS is seen, similar to those reported in literatures.

KEYWORDS: HIV/AIDS, Ultrasound, CD4 cell count, renal sizes, Echogenicity.

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INTRODUCTION.

HIV was identified in 1981 and isolated in July 1983 from the lymph nodes of an AIDS patient and was referred to as lymphadenopathy associated virus[1]. In 1984, it was shown to be the cause of the Acquired Immunodeficiency Syndrome (AIDS). The first case in Nigeria was identified in 1986.And recent epidemiological fact-sheet shows that HIV infects six people every minute and forty million individuals are thought to have been infected with HIV throughout the world, with about 3.9% of Nigerians infected[2-6].

The prevalence of HIV/AIDS in Jos is about 7%according to Idoko et.al[7].Renal disease in HIV/AIDS has been described as late 'syndrome' in patients with AIDS[8].

The pathophysiology of HIV infection of various renal cells that lack CD4 cell receptors is poorly understood. Many deaths occur from complications involving vital organs. The kidney being one of the vital organs is prone to impairment due to direct viral attack, opportunistic infections, and nephrotoxic drugs. These involvement manifests clinically as nephrotic syndromes consisting of proteinuria greater than 3.5g/day ,hypoalbuminia and general edema[9-13]

Klotman, (2001)[14] in his study noted that HIV-associated nephropathy has become the most common single diagnosis in HIV-infected patients with renal insufficiency. He showed that the presence of active viral replication in renal tissues suggests that the kidneys could be reservoir for HIV, and is characterized by significant proteinuria and rapid progression to end stage renal disease, normal to enlarged kidneys on gross appearance.

In another study renal disease was identified as a common complication in patients with HIV disease and pentad of findings were outlined as characterizing renal involvement. These included proteinuria, azotemia, and normal to enlarged kidneys on ultrasound images, normal blood pressure and focal segmental glomerulosclerosis on renal biopsy.[15]

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In one study, renal insufficiency was present in 41% of hospitalized AIDS patients. A high percentage of these patients (12 out of 13) had associated proteinuria[16]

Kawamura (1997)[17] noted that the renal sonographic appearance in HIV/AIDS varies from normal size early in the disease process to enlargement with markedly increased echogenicity equal to that of the central echo of the renal sinus: on follow up examination the kidney progressively shrinks with reversal of azotemia, renal echogenicity may become normal.

Case definition of AIDS on the interpretation of epidemiological trends includes any adolescent or adult with HIV infection and CD4+ lymphocytes count less than 200/mm^3 or a percentage less than 14[17].

Though renal sonographic features in HIV/AIDS are well are well characterized in literature, no documentation of correlation between renal sonographic features in HIV/AIDS with measured cluster designation cell count in Nigeria has been done. The objectives of the study were to determine the commonly occurring renal sonographic features in HIV/AIDS in terms of size and echogenicity and correlate these features with measured cluster designation (CD4) cell count. Features identified will serve as guide in characterizing renal disease in HIV/AIDS and may be useful as possible marker to predict progression of HIV infection.

MATERIALS AND METHODS

The study was carried out at the Jos University Teaching Hospital, a tertiary institution situated at the North central Nigeria.302 confirmed HIV seropositve subjects consisting of 123 males and 197 females between the ages of 4 and 80years were randomly selected and studied prospectively over a period of twenty two months. The aims were to identify the commonly occurring sonographic features (in terms of renal length, parenchymal echogenicity) in the kidney and to correlate these features with CD4 cell count, and to correlate renal length with age of subjects.

Subjects were included in the study with proven cases of HIV by Enzyme-linked immunosorbent assay (ELISA) confirmed by Western blot assay and referred from AIDS project in Nigeria Laboratory (APIN) and Faith Alive Foundation, Jos, Plateau State. Excluded from the study were subjects with the following conditions: patients with solitary kidney (there is usually compensatory renal hypertrophy associated with a solitary kidney), patients with clinical or biochemical evidence of renal impairment (known diseases of the kidneys or transplantation that could influence the result) and pregnant women.

Also one hundred randomly selected patients of all age groups consisting of 61 males and 39 females were recruited as control group and they were non pregnant showing no evidence of background retroviral infection sonographically Excluded from the group were patients with solitary kidney, evidence of clinical or biochemical impairment and pregnancy.

All subjects were on antiretroviral therapy at the time of the study; and each subject's CD4 cell count was assayed either from the AIDS Project in Nigeria laboratory or Faith Alive foundation both in Jos. All scans were carried out using sonoline 1500,770350 model ultrasound machine, manufactured by Hewlett Packard of America. All measurements were made with a curvilinear, 3.5 MHz probe using the on- screen electronic calipers calibrated for assumed speed of 1540m/s in soft tissues. The renal size, echogenicity and corticomedullary differentiation formed basis for the categorization of the sonographic features while the renal size was estimated by the longest bipolar length measured at right angles to each other.

A four point scoring system devised by Platt et al, 1998, was used to characterize the echogenicity of the kidneys[18].

The following grading was adopted:

Grade 0–Normal kidney, where the renal parenchymal echo is slightly less than that of the liver or spleen, with good corticomedullary differentiation.

Grade 1–Slightly increased renal parenchymal echogenicity approximately the same with the liver/spleen with good corticomedullary differentiation

Grade 2–Moderately increased renal parenchymal echogenicity greater than the liver/spleen with good corticomedullary differentiation.

Grade 3– severely increased renal parenchymal echogenicity greater than the liver/spleen with loss of corticomedullary differentiation.

Pearson's correlation and regressions were used to correlate the CD4 cell count with renal length and age. Renal parenchymal echogenicity was correlated with renal length using packages for social sciences (SPSS) 11 version for windows.[19]

Z-test was used to compare the mean renal length of males and females of subjects studied and those of control group.[20,21]

Ethical clearance

The study was approved by the Ethical clearance Committee of Jos University Teaching Hospital, directors of the Faith Alive foundation and APIN clinic. Participation by subjects was voluntary and informed consent was obtained from each subject.

RESULTS

TABLE 1: AGE AND SEX DISTRIBUTION OF PARTICIPANTS

Age(yrs)	Male	Female	Percentage
10-20	4	7	3.6
21-30	77	31	35.6
31-40	73	51	41.1
41-50	21	25	15.2
51-60	5	6	3.6
61-70	1	1	0.6

Table 1 show the age and sex distribution of subjects. Of the 302 subjects for the study 76.7% of them were within the age range of 18 and40 years.179 (59.3%) of subjects were females and 123(40.7%) were males showing a near one to one distribution.

Table 2: Age Variation Of Renal Length In Hiv/aids And Healthy Subjects.

Age (yrs)	HIV Subjects	Number of subj.	Normal subjects
10-20	9.31-13.10	11	9.21-11.19
21-30	9.14-12.70	108	11.41-12.39
31-40	6.83-16.50	124	10.7-10.8
41-50	7.20-13.31	46	9.8-10.2
51-60	10.2-12.90	11	9.6-10.8
61-70	11.5-11.6	2	9.6-9.5
Mean=147.57	10.68		

Table 2 shows the variation of renal dimension of subjects and control group with age. The longest bipolar length and width were 16.5cm and 7,49cm dimensions respectively, and were noted in the 31-40 age groups and accounted for about 41% of the subjects. A bipolar renal length of 10.8cm was recorded among the age group of 31-40 years of the control group. The subjects' increase in dimension is significant compared to the normal subjects in the locality ($p<0.5$).

TABLE 3: Variation of renal parenchymal echogenicity WITH CD4 CELL COUNT

Range of CD4 count	Grading of renal echogenicity			
	0	1	2	3
30-60	7	7	27	5
61-90	3	3	7	
91-120	3	1	5	
121-150	5	7	7	
151-180	4	2	1	2
181-210	2	5	6	
211-240	1	1	2	
241-270	2	1	5	
271-300	1	2	1	
301-330				1
331- 360				
361 - 390				
391-420		1		
421-450	1	2	2	
451-480				2
481-510		1		
511-540	1	1		
541-570				
571-600				
601-630				
631-660				
661-690	1			

Table 3 shows the variation of renal parenchymal echogenicity with CD4 cell count of subjects. 77.7.% of subjects had abnormal renal parenchymal echogenicity. 22.3% had normal renal parenchymal echogenicity, 30.1% of the subjects had CD4 cell count less than 200 cells/cm^3

No significant correlation between renal echogenicity and CD4 cell count was noted. But significant difference in mean renal size was seen between the subjects and control group<0.05

A significant negative correlation was noted between renal length and values of the CD4 cell count r=-0.23) and a regression analysis on this relationship is expressed by the equation Renal length =-0.0029CD4+11.1423.(Figure 1).

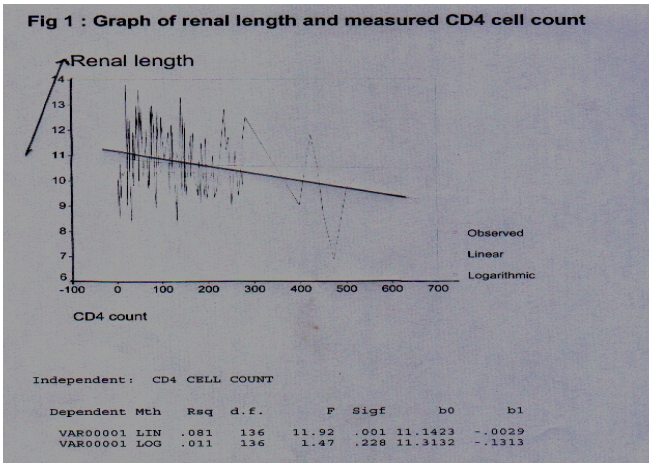

Table 4: Z-tests Comparison of Mean Renal Length of Subjects Vs Normal Subjects.

	N	Renal length (cm)	Standard deviation	Calculated Z	Critical value of Z
Subjects	302	10.68	1.26	4.84	1.96
Control group	100	10.00	1.00		

Table 4 shows the Z-test comparison of mean renal length of subjects with normal subjects. The calculated value of Z= 4.84, was greater than the critical value of Z=1.96; P<0.05. Hence, there was a significant difference in mean renal length of subjects with the mean renal length of the control group.

DISCUSSION

HIV/AIDS is a multi-organ infection and the kidneys are prone to impairment due to infection by microorganisms found in the urinary tract, direct viral attack on the kidneys and the use of variety of therapeutic agents employed in the management of the infection.

The prevalence of HIV/AIDS in Jos is about 7% Idoko et al,[7]. Many deaths from the infection occur as a result of complications involving vital organs. The effects of this complication on the kidneys, being one of the vital

organs is yet to be determined in the locality. The objective of this study was to characterize these features in the kidneys such that data generated may be useful as a possible marker to predict progression of HIV infection and would be useful in the management of HIV/AIDS in the locality.

The study consisted of 302 subjects; aged between 10 and 80 years with a mean age of 34.4years. High prevalence (76.7%) of HIV infection was noted in the age range of 21 and 40 years. This corroborated the fact that HIV infection is more common in people in their reproductive and sexually active age group. 123 of subjects were male constituting 40.7% while 179 were female constituting 59.3%, thus a near one to one male-female ratio, this differs with a report among Africa-Americans which observed that renal disease in HIV/AIDS is more often in men than women with a male- to- female ratio of 10:1, where 50% of the subjects were black male drug addicts[15]

The hallmark of parenchymal disease, as in HIV infections, is a diffuse increase in echogenicity throughout the parenchyma of the kidneys. This study showed that 77.7% of subjects had increased renal parenchymal echogenicity. Although other renal medical diseases such as acute and chronic glomerulonephritis,acute tubular necrosis, hypertensive nephrosclerosis, acute interstitial nephritis etc lead to increase in renal parenchyma echogenicity, HIV infections also cause such increase in parenchymal echogenicity due to profound tubulo-insterstitial scarring and atrophy in response to the infection. This feature is well documented in literatures [14,9,22]

The study showed a renal length ranged of 6.83cm 16.5cm, the upper limit representing a remarkable abnormal increase in renal dimension when compared to as the upper limit of renal length in healthy individuals in the locality -13cm[23,24] .This may have resulted from prominent interstitial expansion by cellular infiltrate resulting from the viral infection. This feature also well characterized HIV infection and is consistent with reports of other workers [14,15].

There was significant negative correlation of renal length with measured CD4 cell count at 0.01 levels (2-tailed). With the depletion of CD4 cell count, which play significant role in the immune mechanism of the body there is greater risk of opportunistic infection of the kidneys. The effect is reflected in the increase in renal length (due to the microscopic dilatation of renal tubules with the lumen being filled with pale-staining cast). This finding agrees with reports of other published works[9,12].

And from the regression curve equation it is possible to predict renal length from CD4 cell count using the regression curve equation, renal length = -.0029CD4 + 11.1423.

Though increased parenchymal echogenicity, nephromegaly and the depletion of the CD4 cell count in the peripheral blood are the hallmark of HIV infection, this study showed negative correlation though weak, r= -0.107@0.210 level, between measured CD4 cell count and renal parenchymal echogenicity, this also corroborated the fact that parenchymal renal sonographic changes may not completely reflect the functional status of the kidneys. Renal length correlated positively with renal parenchymal echogenicity at 0.05 levels (2-tailed). Regression curve yielded a relationship between renal length and parenchymal echogenicity; echogeenicity=-0.1179, renal lenght =+0.0687. No documented report was seen by the researcher on the correlation between renal length and parenchymal echogenicity by other researchers. However, with increase in renal length as a result of interstitial expansion by cellular infiltrate, there is a likelihood of tubointerstitial scarring and atrophy leading to increase in parenchymal echogenicity in the HIV infected individuals.

Z-test comparison of mean renal length of subjects with a control group showed significant difference, as calculated Z value (4.84) was higher than the critical value of Z (1.96), $P<0.05$. This difference is expected as it may be reflecting the combined effect of HIV infection and drugs on the kidneys of HIV/AID subjects among other renal medical disease conditions [16,25]

CONCLUSION

Results showed high incidence of increased kidney echogenicity consistent with nephropathy in HIV/AIDS in the locality especially among subjects in their reproductive and sexually active ages(18-40years).CD4 cell count significantly correlated negatively with renal length; there was also significant increase in renal bipolar length compared to the normal subjects in the locality. These features could be useful as predictor to monitor progression of HIV infection in subjects, among other indices. However, no significant relationship was seen to exist between subjects' immune status (CD4) and the development of cysts, calcification and hydronephrosis .

This study recommends ultrasound screening of HIV seropositive patients for HIV-associated nephropathy to provide better management.

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