# TROPICAL JOURNAL OF NEPHROLOGY

*The Official Journal of the Nigerian Association of Nephrology*

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The aims and scope include the following:

1. *To provide a medium of exchange of ideas and knowledge of nephrology in the tropics through publication of research works, clinical experiences and relevant articles.*

2. *To promote nephrology education, clinical practice and research through publication of original research works, innovative clinical experience and authoritative review articles on topical issues.*

3. *To provide an avenue for global dissemination of consensus positions on issues of concern in tropical nephrology through publication of proceedings of consensus meetings, dedicated conferences and commissioned reviews.*

4. *To serve as a scientific link between the Nigerian Association of Nephrology and other such International Organizations all over the world.*

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# HIV and the Kidney

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**ABSTRACT**

There is a wide clinical spectrum of renal disease in the course of HIV infection which includes acute kidney injury, electrolyte and acid-base disturbances, HIV-associated glomerular disease, acute-on-chronic renal disease and side effects related to treatment of HIV. Studies from Africa have reported a variable prevalence of renal disease in HIV: 6% in South Africa, 38% in Nigeria, 26% in Cote d'Ivoire, 28% in Tanzania, 25% in Kenya, 20- 48.5% in Uganda and 33.5% in Zambia, depending on the populations studied and the criteria for diagnosis of kidney disease. Therapeutic strategies for HIV renal disease should include screening urinalysis and measurement of kidney function of all HIV+ individuals at presentation to facilitate early diagnosis of renal disease and initiation of treatment in an effort to prevent or slow progression to end stage renal disease, as well as renal replacement in the form of dialysis and transplantation as and when appropriate. Adequate support of those patients with acute kidney injury has resulted in recovery of renal function in the majority of patients

## Epidemiology of Human Immunodeficiency Virus Infection

The human immunodeficiency virus (HIV) is a retrovirus with viral genetic material stored as ribonucleic acid (RNA). Two strains of HIV are known to infect humans, HIV-1 and HIV-2 [1, 2].. HIV-1 is by far the most common and pathogenic worldwide.

Statistical data released by the Joint United Nations Programme on HIV/AIDS (UNAIDS) for 2007 (Figure 1) revealed the following:

- The number of people living with HIV worldwide is estimated to be 33.2 million
- The majority of people (61%) living with HIV in sub-Saharan Africa are women
- More than two-thirds (68%) of all people infected with HIV live in sub-Saharan Africa where more than three quarters (76%) of all AIDS-related deaths occurred in 2007
- Within the region, Southern Africa is the worst-affected with the national adult HIV prevalence exceeding 15% in eight Southern African countries from 2005 [3]

The majority of those who require antiretroviral therapy (ART) in sub-Saharan Africa continue to live without access to treatment. In South Africa only 33% of those requiring ART received it in 2006 [4].

## Spectrum of Kidney Disease with HIV Infection

HIV infection and its devastating consequences have placed an enormous strain on healthcare resources and those living both with/without HIV. In addition to the broad, multi-dimensional impact of this infection, when considering kidney disease, HIV has unleashed a new burden of both acute and chronic kidney disease. There is a wide clinical spectrum of renal disease in the course of HIV infection which includes:

- Acute kidney injury (AKI)
- Electrolyte and acid-base disturbances
- Intrinsic co-morbid renal disease unrelated to HIV itself (e.g. diabetes mellitus and hypertension)
- HIV-associated glomerulonephropathies (Table 1): these may present as either acute on chronic or chronic renal failure and it is this group that is primarily implicated in the burden of chronic kidney disease (CKD)
- Side effects related to treatment of HIV which include ART and drugs used to treat complications of HIV

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- Potential long term metabolic side-effects of ART

**Acute Kidney Injury in HIV**

The causes of acute kidney injury (AKI) in hospitalised HIV infected patients may be community or hospital acquired, the latter being 5-10 times more common than the former, with a worse outcome in hospital acquired AKI [5]. The known causes of AKI are similar in the HIV and non-HIV group with the most common being acute tubular necrosis (ATN) secondary to sepsis, hypotension, dehydration and nephrotoxins [5, 6, 7, 8]. Although potentially reversible with appropriate medical treatment and, if indicated, dialysis support, AKI carries a high mortality in this population [6].. Biopsy studies have confirmed a wide range of aetiologies [6, 9, 10]. In one study of hospitalised patients with HIV infection, AKI occurred in up to 20% of cases [11]. In another study, the short-term prognosis in this group of patients showed mortality of 18% at 2 months, with 80% of patients diagnosed with AIDS at the time of hospital admission [12]. Since the advent of ART, a recent prospective study on AKI in ambulatory HIV infected outpatients with access to ART concluded that more severe immunosuppression (CD4 <200 cells/$mm^3$ and/or HIV RNA level >10000 copies/ml) is still the predominant risk factor for AKI [13] .

**Electrolyte and Acid-Base Disturbances in HIV**

Numerous electrolyte and acid-base abnormalities have been documented with HIV infection (Table 2). Abnormalities may arise either from HIV infection itself, opportunistic infections and malignancies associated with advanced immunosuppression or with medication used to treat HIV and its complications.

**Glomerular Disease in HIV**

Initial autopsy reports of renal disease in HIV infected patients with advanced disease showed a broad spectrum of lesions that include ATN, interstitial nephritis, nephrocalcinosis, minimal change, mesangial proliferation/hyperplasia and focal glomerulosclerosis (FGS) [14-17]. Reports then began to appear in the literature describing various glomerulopathies, the most common of which was FGS. The distinguishing feature about the "classic" glomerular lesion in HIV was collapse of the glomerular tuft, so-called "collapsing glomerulopathy" [6, 9, 14, 18]. European and American-based biopsy studies reveal varying frequencies of the different histological patterns [7, 11, 19]. HIV-associated nephropathy (HIVAN) is the most common (up to 60%), with the other lesions accounting for one quarter to one third of the total.

**HIV- associated nephropathy (HIVAN)**

An association between HIV and renal disease was first reported in 1984 describing HIV infected individuals with nephrotic range proteinuria and progression to end stage renal disease (ESRD) within 8-16 weeks [15, 20, 21]. Mortality in these patients approached 100% within six months of diagnosis. The existence of a specific HIV-associated nephropathy (HIVAN) has been confirmed as a distinct clinicopathological entity [16, 22, 23, 24]. HIVAN was initially thought to be associated with advanced immunosuppression but it was later recognised that the lesion can occur at any stage of HIV infection, even prior to antibody seroconversion [25]. Most patients with HIVAN present late with advanced renal failure. This late detection of HIVAN could be due to a lack of screening for proteinuria and/ or renal dysfunction. The relative absence of overt symptoms and signs such as peripheral oedema and hypertension in those with HIVAN may also delay diagnosis. Outcome of patients with HIVAN has been correlated with the clinical stage of their disease, suggesting that survival improves with earlier detection [26]. There is an increased relative risk of 2.5 – 3.0 for overall mortality with proteinuria, after correcting for other risk factors [27, 28]. In one study 77% of renal abnormalities developed with CD4 counts above 200 cells/$mm^3$ [28]. This was also seen in the study from Durban where the mean CD4 count of those with biopsy-proven HIVAN was 232 cells/ $mm^3$ [29]. HIVAN was not previously an AIDS-defining illness, but criteria have recently been revised by the WHO and symptomatic HIVAN is considered clinical stage 4 disease [30].

**Epidemiology and Racial Predilection of HIVAN**

There is a marked racial predilection for the development of HIVAN - over 90% of patients are black [14, 26, 31-34]. This has been confirmed in paediatric studies [24]. Studies from African countries regarding the susceptibility of Africans to HIVAN are scanty. The reasons for the racial predilection of HIVAN are unexplained. Some have postulated a genetic predisposition, but candidate genes have not been identified [14, 32]. One study has shown that there appears to be a strong familial clustering of ESRD among blacks commencing renal replacement

therapy due to HIVAN, independent of HIV status [34]. In most cases, the affected relatives had ESRD due to hypertension or diabetes. HIVAN also appears to follow a more severe clinical course in black patients [35]. Studies in black patients have shown a higher prevalence of both severe glomerular lesions (FGS) and nephrotic range proteinuria with renal dysfunction in the presence of normo/hypotension [31, 33, 35].

In the 1980s HIVAN was an uncommon cause of ESRD in the USA [36]. This was in part, due to the high mortality in this group and the absence of ART. With improved survival after the introduction of ART, HIVAN became the most rapidly increasing cause of ESRD, being the third leading cause of ESRD after diabetes and hypertension in African Americans aged 20 - 64 years in the USA by 1990 [36]. While the rate of new cases of ESRD due to AIDS has fallen slightly since the beginning of the decade (HIVAN was the 7th leading cause of ESRD in the African American population in 2004): reaching 2.7 per million population in the 2004 - 2005 period, prevalence in the USA has grown steadily, reaching 8.9 in 2004–2005, indicating that people are living longer with the disease [37]. Statistics in the USA estimate the incidence of HIVAN to be 3.5 - 12% [36]. If this were to be extrapolated to Sub-Saharan Africa, with an estimated 22.5 million infected with HIV, between 788 000 – 2.7 million people would be predicted to have HIVAN. With the advent of unrestricted access to ART, the epidemiological pattern of HIVAN that evolved in the USA over the last 14 years may predict what will happen in sub-Saharan Africa. This presents a potentially unprecedented burden of chronic kidney disease, given the current resources available for managing renal disease in this region.

**HIV Renal Disease in Africa**

Very little data exists on screening asymptomatic HIV infected patients for early renal disease, especially in Africa. In a US study by Luke *et al.* 72 ambulatory HIV infected outpatients were prospectively screened for microalbuminuria (3 asymptomatic, 32 AIDS-related complex, 37 AIDS). Fourteen (14) patients (19.4%) had microalbuminuria. Microalbumin levels were not correlated with race, sex, risk factors of AIDS, disease history, or concurrent drug therapy. In contrast, urinary microalbumin levels were correlated with CD 4 T-cell and white blood cell, tumour necrosis factor alpha (TNF-á) and beta 2-microglobulin levels, suggesting an association between AIDS progression and microalbuminuria [38].

A urine dipstick screening study in Boston showed proteinuria in 16.6%, haematuria in 15.5% and leucocyturia in 11% of HIV infected outpatients, there was no HIV negative control group (39).The HERS study (HIV Epidemiology Research Study) found dipstick leucocyturia in 10.1% of HIV infected and 9.9% of HIV negative women; bacteriuria (from urine culture) was seen in 6.3% of HIV infected and 6.5% of HIV negative women. Within the HIV infected group there was no difference in prevalence based on CD4 count or whether co-trimoxazole was taken [40].

**South Africa**: A study of 99 inpatients biopsied at Chris Hani Baragwanath Hospital, Johannesburg showed that HIVAN was present in 27%, HIV-ICD (HIV- immune complex disease) in 21%, membranous nephropathy in 13%, other non-glomerulonephritic renal disease 10%, other glomerulonephritides 9%, post infectious glomerulonephritis 8%, mesangioproliferative glomerulonephritis 6% and IgA nephropathy 5% (41).

A screening study was conducted at King Edward Hospital in Durban in 615 HIV infected patients looking for proteinuria, including microalbuminuria [29]. This is one of few studies that have evaluated the prevalence and potential significance of microalbuminuria in the HIV infected population, as a marker of early renal disease. Two percent were hospitalised patients; 98% were asymptomatic (from a renal perspective) outpatients attending an HIV clinic. Black patients accounted for 98% of those screened. Six % had persistent proteinuria and 30 renal biopsies were done, of which 7 were for persistent microalbuminuria and 23 for overt proteinuria. Histology showed the following: HIVAN 25/30 (83.3%); HIVAN + membranous glomerulonephritis (GN) 4/30 (13.3%) - included in initial HIVAN group; membrano-proliferative GN 2/30 (6.7%); interstitial nephritis 3/30 (10%). This cross-sectional study specifically screening for renal disease found a prevalence of HIVAN of just over 4%.

The data from the Chris Hani Baragwanath and King Edward hospital cohorts are contradictory. Possible explanations may be population demographics - the studies were done in different

provinces of South Africa which serve varying black ethnic groups.

**Nigeria**: Emem *et al* [42] in a study of 400 consecutive HIV positive patients found evidence of renal disease as manifest by either proteinuria or abnormal serum creatinine in 38% of their patients. Of the 10 patients biopsied, the majority had collapsing FSGS.

**Cote D'Ivoire**: A few studies revealed that on screening for proteinuria, additional abnormalities in particular, leucocyturia and microscopic haematuria were found – the significance of which has not been investigated, nor is it understood. In a study comparing HIV infected patients in an industrialized setting (Paris) with a sub-Saharan setting (Abidjan), the respective prevalence of leucocyturia and albuminuria was higher in the cohort from Abidjan (16 versus 1% for leucocyturia and 26 versus 5% for albuminuria, both achieving statistical significance). Erythrocyturia was also more prevalent in the Abidjan group, but did not achieve statistical significance [43]. An explanation for this finding was not given, but the group from Abidjan had significantly lower CD4 counts with fewer patients on ART (34% versus 66%). Leucocyturia and albuminuria may therefore reflect more advanced or untreated HIV disease, but may also reflect host genetic factors.

**Tanzania**: A study on police officers in Tanzania found albuminuria, leucocyturia and erythrocyturia to be more frequent in an HIV infected cohort, when compared with a non HIV infected cohort (albuminuria 28.4 versus 16.8%; leucocyturia 14.2 versus 11.6%; erythrocyturia 1.6 versus 0.2% respectively) [44].

**Kenya**: In a Kenyan study, 216 antiretroviral-naïve patients with an average CD4 count of 383 cells/ $mm^3$ were screened for renal disease [45]. Those with known risk factors for renal disease were excluded. 25% of the remaining patients had creatinine clearance (Cr Cl) < 90ml/min (normal e•90ml/min), 2% had Cr Cl <60ml/min and 8% had proteinuria of >1gram/day. Although not statistically significant, there was a trend to more severe renal insufficiency and heavier proteinuria in those with a CD4 count <200 cells/$mm^3$ [45].

**Uganda**: A Ugandan study of 229 patients with World Health Organisation (WHO) clinical stage 3 disease showed a high prevalence of renal disease, with a Cr Cl of <80ml/min in 48.5% of patients; 20% had proteinuria >100mg/dl. Leucocyturia was present in 132/299 patients (44.1%) but confirmatory urine cultures were not done [46]. In the above studies, no renal biopsies were performed, nor was there further investigation into the causes of leucocyturia and microscopic haematuria.

Peters *et al* evaluated 508 patients with HIV infection: 8% had serum creatinine>133ìmol/l and 20% had creatinine clearance 25-50ml/min [47].

**Zambia:** Mulenga *et al* studied 25799 patients treated with ART from April 2004-September 2007; 33.5% had renal dysfunction: 3.1% had eGFR<30ml/min; 23.4% had eGFR of 30-59ml/min and 73.5% had eGFR of 60-89ml/min. Renal dysfunction was associated with increased mortality after 90 days (48).

**Aetiopathogenesis of HIVAN**

HIVAN is just one of many pathological manifestations of HIV-related renal disease. The protean manifestations of kidney disease may be the result of a complex interplay between the particular pheno- and/or genotypic variants of HIV, the genetic make-up of the host and environmental factors. The evidence in support of potential mechanisms for the development of HIVAN has been summarised as follows [49]:

- Cytopathic effects of HIV gene products
- Apoptosis mediated by HIV infection
- Elaboration of chemokines and cytokines as a result of viral or host protein synthesis in patients with a genetic susceptibility to nephropathy
- Subversion of the host metabolic and synthetic machinery by the virus may allow for rapidly progressive disease

**Treatment of HIV-associated Renal Disease**

There have been no prospective randomised controlled studies with any form of therapy for HIVAN to date, let alone other forms of HIV-associated related renal disease. Evidence from small studies and case reports have shown that pharmacological interventions for HIVAN (less so for other glomerular lesions) delay the progression or may reverse even renal disease in isolated cases [29, 50-52]. Therapies used in the treatment of HIVAN include corticosteroids, angiotensin converting enzyme inhibitors (ACE-I), cyclosporine and ART. Treatment options for patients who have reached ESRD include haemodialysis, peritoneal dialysis and renal transplantation.

**Corticosteroids**

Patients with HIVAN treated with prednisone experienced an improvement in renal function and reduction of proteinuria but complications such as relapse after steroid withdrawal, opportunistic infections, psychosis and gastrointestinal bleeding were relatively common [50, 53]. In addition, there were no controls in the analysis for the beneficial effects of ACE-I and ART [50]. An isolated case report showed response to corticosteroids and relapse after steroid withdrawal in a patient with HIVAN on zidovudine (AZT) monotherapy [54]. Because these studies have no long term follow up, are small in size and not randomised, no clear conclusions can be made regarding their use in HIVAN.

**Angiotensin Converting Enzyme Inhibitors (ACE-I)**

Captopril has been shown to delay progression of renal failure in a retrospective cohort of nine patients with HIVAN, when compared with controls [55]. Fosinopril was shown, in patients with biopsy-proven HIVAN who had both nephrotic and sub-nephrotic range proteinuria, to stabilise renal function and proteinuria [56]. This was compared to a control group who had declined the option of ACE-I and within 24 weeks of follow up had significant deterioration in renal function and proteinuria [56]. Both studies were conducted prior to availability of ART. In a larger prospective study to determine the long-term effects of ACE-I on renal survival in HIVAN patients, those on ACE-I showed a median renal survival of 479.5 days, with one patient progressing to ESRD, compared to a median renal survival of 146.5 days in untreated patients who all developed ESRD [57]. The potentially beneficial effects of ACE-I may be related to improved renal haemodynamics, reduced proteinuria or cytokine modulation [58]. The effects of angiotensin-2 receptor blockers (ARB) in the treatment of HIVAN is unknown, just as the effects of ACE-I or ARB in the treatment of HIV-associated renal disease other than HIVAN are unknown.

**Cyclosporine**

The effectiveness of cyclosporine in inducing remission of proteinuria was reported in children with HIVAN [59]. There are no studies evaluating the role of cyclosporine in adults.

**Highly active anti-retroviral therapy**

Because HIV itself appears to be the cause of HIVAN (and possibly other manifestations of HIV-associated renal disease), ART appears to be a logical choice in disease management. In one study with AZT monotherapy for HIVAN, at 20 months follow up, those on treatment had stable renal function and all those who were non-compliant progressed to ESRD [60]. Another study with AZT monotherapy in 11 patients showed a beneficial effect on renal function only if the AZT was initiated before advanced renal failure was present [61]. There appears to be a more beneficial effect of ART over AZT monotherapy in the management of HIVAN [62, 63, 64]. Regimens containing protease inhibitors were associated with significant slowing of the decline in creatinine clearance [65]. In addition to being effective in treating established HIVAN, ART may decrease the actual incidence of *de-novo* HIVAN [66, 67]. Peters et al. reported improvement in renal function with ART, with a 21% improvement in median creatinine clearance and a decline in serum creatinine by 16% (Peters *et al.* 2008).

**ESRD due to HIV renal disease**

The estimated burden of ESRD in HIV remains largely unknown, especially in view of the fact that the largest burden of HIV is found in the developing world where very poor epidemiological data exist. With increasing survival of HIV patients on treatment and the declining cost of ART, the magnitude of this problem will increase.

During 1985 to 1999, the percentage of haemodialysis centres providing care to patients with HIV in the United States increased from 11% to 39%, and the percentage of dialysis patients with HIV infection increased from 0.3% to 1.4% [68]. Similarly, a study in France documented an increase in the number of HIV patients on dialysis programs since 1997. Similarly, a study in France documented an increase in the number of HIV patients on dialysis programs since 1997 [69][68](Vigneau CE, 2005).The increasing numbers of patients receiving RRT is due to the advent of ART [70, 71][69, 70](Ahuja *et al.*, 2002, Ahuja TS, 2000).

**Antiretroviral therapy in ESRD**

For improved survival on dialysis the key is for early initiation of ART. Patients on dialysis appear to respond well to ART and in one study, 58.3% of treated patients had an undetectable viral load in contrast to only 29.6% in the untreated group [72].

It is important to remember that dosing requirements change with declining GFR and that dosing recommendations for patients with CKD should be followed (Table 3). In ESRD despite reduced dosing of several antiretrovirals, there is still little clinical evidence that this prevents the development of toxicity [58]. Importantly HIV, when treated with anti-retroviral agents, can behave like any chronic disease.

**Dialysis and Transplantation in HIV Patients**

Prior to the advent of ART, life expectancy on dialysis was approximately 10 months. Life expectancy has now increased to 10-20 years in developed countries, so that many of these patients are now dying from the consequences of ESRD rather than opportunistic infections. HIV-infected subjects requiring either haemodialysis or peritoneal dialysis and stable on ART are achieving survival rates comparable to those of dialysis patients without HIV infection. Thus more programmes are including these patients, who have the same complications as HIV negative dialysis patients.

**Haemodialysis and Peritoneal Dialysis**

The choice of dialysis modality between haemodialysis and peritoneal dialysis is not a factor in predicting survival among HIV-infected patients with ESRD (73). However, as would be expected, considering that most patients with HIV on dialysis are in the USA, 88% to 94% were on maintenance haemodialysis, and 6% to 12% on peritoneal dialysis (74) (73). Literature review shows that both maintenance HD and PD are effective modes of RRT in HIV patients with ESRD, although there are some points of concern with both modalities (58) (75). Overall, given the fact that outcome does not seem to depend on modality of dialysis the choice of RRT in HIV-infected patients should be based on an individual patient's lifestyle, preferences and availability of family and other support, and not on HIV seropositivity.

**Haemodialysis**

Haemodialysis exposes the dialysis staff to blood products and contaminated needles. The risk of HIV seroconversion after a needle stick injury from an infected patient is estimated to be about 0.3%. In addition, the larger the blood inoculum and the later the stage of HIV infection, the greater the risk of seroconversion. The use of universal precautions is the best form of prevention of nosocomial infection. HIV transmission in a dialysis unit has been documented via inadequate sterilization of re-used needles [76]. Other infections have been caused by breaks in universal precautions and infection control procedures. Guidelines for infection control and machine disinfection set by the Association for the Advancement of Medical Instrumentation and CDC should be adhered to at all times.

**Peritoneal dialysis (CAPD*)***

Theoretically there is less exposure of staff to HIV with PD than with HD because peritoneal fluid is much less infectious than blood, there is less likelihood of needle stick, and the nature of staff to-patient contact is different. HIV was shown to survive in PD effluents at room temperature for up to seven days and in PD exchange tubings for up to 48h. Both sodium hypochloride 50% (Amukin), and household bleach 10% solutions, in dilutions of 1:512, are effective in killing HIV in dialysate. HIV has been identified in the peritoneal dialysate, which should be handled as a contaminated body fluid (77). Patients need to be educated on the need to properly dispose of these fluids. Peritoneal dialysis patients should be instructed to pour dialysate into the home toilet and to dispose of dialysate bags and lines by tying them in plastic bags and disposing of the plastic bags in conventional home garbage (58) (78).

CAPD may aggravate the malnutrition and hypoalbuminemia in HIV patients with severe wasting syndrome. The rate of peritonitis has also been higher in patients with low CD4 counts in the pre-HAART era. Both gram positive infections and Pseudomonas infection as well as fungal infections have been reported as being more common (78).There appears to be a higher risk of infection in patients on peritoneal dialysis, especially when CD4 count is<200 cells/ $mm^3$, The largest series studied looked at 39 HIV-infected patients receiving peritoneal dialysis and found a higher overall risk of peritonitis and more cases of peritonitis attributed to pseudomonas species and fungi than in other patients with ESRD (79) (80). The higher peritonitis rates in the study could also have been attributed to HIV infection, a low socioeconomic status, and or intravenous drug abuse.

**Vascular access**

Considering that dialysis is being considered a viable option in HIV patients it is only prudent to recommend that the placement of arteriovenous fistulae (AVF) should not be withheld for patients solely because of HIV infection. Native arteriovenous fistulae are the preferred types of access because of excellent patency once established and lower complication

rates, compared with those associated with other access options [81, 82, 83].

**Anaemia Management**

The problem of anemia in patients with CKD due to insufficient production of erythropoietin is further compounded if patients are infected with HIV. In both CKD and HIV infection, the presence of anemia is independently associated with shorter survival (84) (85). Recombinant human erythropoietin therapy is an appropriate treatment option for patients with symptomatic mild anemia or moderate anemia. The target range for haemoglobin level recommended for patients with CKD is 11–12 g/dL. Shrivastava *et al.* [86] found that the response to recombinant erythropoietin in HIV-infected patients with ESRD, despite the presence of coexisting opportunistic infections and the use of the antiretroviral agent zidovudine, was similar to that in HIV negative patients.

Iron is also essential for hemoglobin formation. Measurements of iron indices are complicated in HIV-infected patients, especially because levels of ferritin, which is an acute-phase protein, are often elevated in patients with HIV infection. To achieve K/DOQI goals, administration of intravenous iron is required in the majority of patients receiving dialysis, although the safety of this form of therapy in terms of immune activation is unknown.

**Prevention of Transmission of HIV in Dialysis Units**

HIV-infected patients do not have to be isolated from other patients or dialyzed separately on separate machines. HIV is not transmitted efficiently through occupational exposures. Reprocessing dialyzers from HIV-positive patients should not place staff members at increased risk of infection if necessary sterile precautions are undertaken.

**Vaccination**

Vaccination schedules (Table 4) are the same as non-HIV dialysis patients and should include vaccinations for *Streptococcus pneumoniae*, Influenza virus, Hepatitis A and Hepatitis B. HIV-infected patients requiring hemodialysis should have anti-HBs titers checked after receiving a standard primary series of 3 hepatitis B vaccinations and should receive a fourth injection if these titers are <10 IU/L (B-II) [58].

Unfortunately this schedule may not be possible in developing countries and in those circumstances one should vaccinate for whatever is possible.

**Transplantation**

Transplantation has been performed with success in HIV infected patients in the USA. Follow up in these recipients remains fairly short term, but initial results would appear encouraging. HIV CKD Guidelines in the USA suggest that renal transplantation may be a viable treatment option for patients with ESRD and should be considered if provided in a supervised clinical trial or at centers with adequate experience in this area (58).

Transplantation in HIV positive patients is very challenging; whilst anti- rejection medication is being used on the one hand to try and suppress the immune system, ART is needed to try and boost immunity. There are also a number of interactions between the anti rejection medications and ART (Table 3).

Preliminary short-term data in liver, kidney, and heart transplant recipients suggest that patient survival rates may be similar to those in HIV-uninfected transplant recipients, implying that immunosuppression may not be uniquely dangerous in the context of HIV infection [87, 88] . However, surprisingly high rates of acute and chronic rejection have been observed among HIV-infected kidney transplant recipients [88, 89]. A National Institutes of Health– funded, multicenter study of the safety and efficacy of kidney and liver transplantation in HIV-infected patients is currently underway.

Because solid-organ transplantation in HIV infected patients is complicated by drug interactions and a complex set of infectious, metabolic, and neoplastic complications related to each condition, clinical management must be provided by a multidisciplinary team of providers who are able to communicate rapidly about evolving signs, symptoms, and laboratory abnormalities.

**Screening for Renal Disease in HIV**

Currently, there are no guidelines in South Africa for screening of HIV-infected individuals for chronic kidney disease. Screening of new / or “at risk” patients for the presence of renal disease in ART clinics in South Africa is not considered standard of care. The Infectious Diseases Society of America (IDSA) published guidelines to this effect in 2005 (58). Their recommendation is that all individuals be assessed for kidney disease at the time of diagnosis of HIV infection with a screening urinanalysis for proteinuria and a estimation of renal function. This allows for detection of renal disease and dose adjustment of ART and other commonly used drugs

in HIV infection, such as acyclovir, trimethoprim-sulphamethoxazole, anti-TB medication. The IDSA criteria for those at "high risk" for development of proteinuric renal disease are: African Americans, CD4 counts <200cells/$mm^3$, HIV RNA levels>4000 copies/ml, those with diabetes mellitus, hypertension or hepatitis C co-infection.

If there is no evidence of proteinuria at initial evaluation, patients at high risk (susceptible) for the development of proteinuria and renal disease should undergo annual screening (Figure 2). Patients with persistent proteinuria of grade >1+ by dipstick analysis, microalbuminuria between 30 and 300 mg/24 h or reduced renal function (GFR, <60mL/min per 1.73m2) should be referred to an internist or nephrologist and undergo additional evaluation, including quantification of proteinuria, renal ultrasound, and potentially renal biopsy.

It is important that this proteinuria is *persistent* as false positives are common in patients who may have infections, or heart failure, which occur commonly in HIV patients. Failing to confirm persistence of proteinuria can significantly impact on the number of referrals in high HIV burden populations. Therefore any patient with persistent proteinuria, persistent haematuria or a GFR <60mL/min per 1.73$m^2$ should be referred to an institution where a specialist can evaluate this patient for further investigations.

## CONCLUSION

The extent of the HIV epidemic, its associated burden of chronic kidney disease in sub-Saharan Africa, coupled with the cost of RRT in a resource-limited setting, makes this a challenging problem. The stark reality at present in South Africa and many developing countries is that most people with ESRD and HIV die; some have limited access to dialysis. Currently, most clinicians deal with advanced stages of CKD in HIV and prevention or early detection of renal disease in this population is neglected. Primary health care practitioners need a working system in place for screening, early detection and referral. Referral centres require resources for appropriate investigation and treatment of those with confirmed CKD.

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# Markers of Chronic Kidney Disease in a Rural Community of Kwara State: Outcome of a screening programme

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**ABSTRACT**

The actual prevalence and aetiological factors of chronic kidney disease (CKD) within a community are difficult to evaluate as majority of individuals are asymptomatic in the early stages of the disease. Some renal abnormalities with potentially serious long term implications may evolve insidiously until they become major life threatening health problems. The most cost effective process to unravel the existence of CKD is through periodic clinical evaluation and simple screening tests. Hence this study was designed to screen for markers of CKD amongst people living in a rural community of Kwara State, Nigeria.

The Ilorin renal study group carried out screening campaign for renal diseases at Afon, in ASA Local Government Area (LGA) of Kwara State as part of activities to mark the 2007 World Kidney Day. The colourful ceremony was declared open by the chairman of the LGA with participants drawn from all the wards that constitute the LGA. All the consenting participants were screened with specific reference to anthropometric and blood pressure measurements, urine analysis and urine microscopy after a promotional health talk.

The mean age of the study population was 27.2 years. Obesity and hypertension were found in 6 (3.6%) and 8 (4.6%) respectively. There was no remarkable urine abnormality among the hypertensives in the study. Crystalluria, Pyuria, Proteinuria, Haematuria, Casturia and Glycosuria were detected in 17.9%, 18.5%, 15.0%, 6.9%, 6.4% and 1.2% respectively.

Obesity and systemic hypertension occurred in a small percentage of the study population, although the prevalence of isolated elevation of systolic blood pressure was appreciable and worthy of note. Crystalluria, pyuria and proteinuria were the commonest urinary abnormalities followed by haematuria and casturia while glycosuria was rare.

## INTRODUCTION

Chronic kidney disease (CKD) refers to progressive and irreversible loss of renal function. The kidney diseases outcome quality initiative (K/DOQ1) guideline has classified CKD into five stages[1]. The magnitude of CKD within a community is difficult to assess because the early stages of the disease are largely asymptomatic. This is because of the inherent functional reserve which makes it possible for features of malfunction to manifest only when the diseased kidneys have lost more than 50% of the functional mass [2, 3, 4]. The implication of adequate compensation for progressive loss of function is that many people do not realize that they are sick of kidney disease until it is advanced or they are rushed to hospital for salvage dialysis.

Since early CKD has no symptom, routine or periodic screening tests are necessary for the detection of the disease. This would rely on screening for risk factors such as obesity, hypertension, diabetes mellitus, urinary sediments, haematuria, proteinuria and pyuria. A population study by Iseki *et al*[5] revealed that proteinuria and haematuria increased with age. It has also been found that obesity, hypertension, type II diabetes and dyslipidemia have a complex

relationship with each being an independent risk factor for chronic kidney disease. [6,9,8,9, 10]

In the light of foregoing, the Ilorin renal study group carried out renal disease screening campaign in Afon, headquarters of Asa LGA in Kwara State as part of activities to mark 2007 world kidney day which formed a template for community health promotion program.

## METHODOLOGY

It was a descriptive cross-sectional study in which the participants were drawn from all the 12 wards of the local government with the assistance of the Councilors. Health promotion talk was organized for participants before the commencement of the screening exercise which involved children and adults. All the consenting participants went through a diagnostic screen which included weight, height, waist and hip circumference, waist/hip ratio, body mass index and blood pressure measurements at the health centre of the local Government . The urine samples of the participants were also collected and taken to our Hospital laboratory for analysis and microscopy. A dip stick method, using an Ames-Multistix reagent strips were utilized for urine analysis with specific reference to proteinuria, haematuria, glycosuria, and nitrite. Both low and high power objective lens of light microscopes were used to examine for casts, white blood cells, red blood cells, epithelial cells and crystals.

The results were entered into Microsoft excel spread sheet before the age range, mean, percentages and standard deviations were computed.

## RESULTS

A total of 207 participants consented to the screening exercise in which satisfactory analysable data were obtained from 176 (96 male and 80 females) with a male to female ratio of 1.2:1. The age range of the participants was 8 to 75 years with a mean of 27.2 $\pm$ 15.4 years.

The mean of the weight, height and BMI were 53.84 $\pm$ 16.09kg, 158 $\pm$ 12.8cm and 21.1$\pm$5.3$m^2$ respectively. The mean waist and hip circumferences were 28.9 $\pm$4.61cm and 34$\pm$6.2cm. Only 6 (3.5%) were found to be obese with waist/hip ratio being abnormal (>1) in 5 of them (Table1). Table 2 depicts the pattern of urinary abnormalities. The overall percentage with abnormal urinary sediments was 65% with crystalluria, pyuria, proteinuria, haematuria, casturia and glycosuria observed in 31(17.9%), 32 (18.5%) 26 (15.1%), 12 (6.9%), 11 (6.4%) and 2 (1.2%) respectively. The crystalluria consisted mainly of calcium oxalate crystals which occurred in 23(74.2%) participants, while triple phosphate crystals were obtained in 8(25.8%) participants. The male/ female distribution of the various urinary abnormalities is shown in Table 3. The systolic and diastolic blood pressure was elevated in 8 (4.6%) while isolated systolic and diastolic blood pressure elevation was observed in 23 (13%) and 9 (5%) respectively (Table 4). Mean systolic and diastolic blood pressure in the eight hypertensive participants was 165 and 106 mmg.

## DISCUSSION

The screening for renal disease is now recommended World wide as an effective preventive strategy for renal disorders. The screening campaign at Afon was quite informative as morbidities such as obesity, hypertension, proteinuria, haematuria, pyuria, casturia and crystalluria were detected using simple, accessible and affordable tools. The age range of the participants was 8 to75years with a mean of 27.2 $\pm$ 15.4years. The mean age in this study is in accord with 27.03$\pm$10.75 years reported by the National Kidney Disease Awareness and Sensitization implementation committees of the Nigerian Association of Nephrology in Abuja which is an urban setting[11]. It is however lower than the 36.6years observed in the non-communicable disease survey by the Federal Ministery of health in 1997[12]. The possible reason for the difference is that the Ministry focused on non-communicable disease in contrast to this study which was an unselected population. Obesity and hypertension were uncommon and accounted for 3.5% and 4.6% of the studied population respectively. These figures are lower than the 10% and 13.6% from Abuja study [11]. The findings also contrast with the report by Ugo[13] in 1997 , who noted 10% prevalence of obesity in Enugu. The implication is that the prevalence of obesity and hypertension are high in urban areas as opposed to rural communities. This may be related to stressful conditions, westernized diet and sedentary life style that are characteristic of most Nigerian cities. However, the finding of elevated body mass index (BMI) and waist/ hip ratio in some of the hypertensive participants is instructive as obese individuals have three-fold

increased prevalence of hypertension and weight reduction is an effective means of controlling hypertension.[14] Studies have shown that obesity, type II diabetes and hypertension are independent risk factors for developing cardiovascular and renal disease. Their co-existence have a synergistic effect in progression of renal disease.[15-16] Obesity has been linked with faster rate of progression of CRF in a study in which hypertension-free survival was shorter in obese when compared with those with normal weight.[17] Obesity is also positively correlated with severity of hypertension and good control of hypertension slows down the progression of renal disease.[9,18] It was observed that 85% of participant had normal BMI of less than 25kg/$m^2$ which is higher than 70% noted among urban dwellers.[11] Despite the disparity between the urban and rural findings, obesity seems not to be a major health problem in Nigeria when compared with developed countries.[19,20] It has been reported that the average BMI in Africa and Asia was between 20 -23kg/$m^2$ which corresponds to the finding in this study.[19]

The significance of pyuria obtained in 18.5% of the participants could not be adequately explained as nitrite was negative in them and urine culture was not done. The presence of pyuria also prompts a search for tubercule bacilli in urine as the signs and symptoms of renal tuberculosis mimic those of other infections of the kidney.[21] Proteinuria as observed in 15% of the studied population usually evokes a suspicion of renal damage. The nature and severity of renal involvement in a particular patient are suggested by the clinical picture and the amount/ pattern of proteinuria. The prevalence of proteinuria in this study is comparable to 19% found in an urban area[11]. This suggests that the aetiological factors for glomerular disease may be similar in urban and rural areas of Nigeria. These figures contrast sharply with the results from other parts of the world which range from 0.3 to 3.2%. [22,23,24] The observation in this study is in accord with reports from other tropical and temperate countries which showed primary glomerular disease as the leading cause of end stage renal disease in the tropics. [25-28] A variety of infective agents implicated in the aetiology of chronic glomerular disease which are more prevalent in the tropics may account for the differences in proteinuria.[29-32] The presence of haematuria in approximately 7% of the participants of a rural community that depend on moving streams for their source of water supply prompts a search for parasitic infestations like schistosomiasis. There is need to include it in future exercise since schistosoma haematobium infection is capable of causing obstructive uropathy.[33,34] Haematuria in the screened population also merit evaluation for renal parenchymal disease. An accurate determination of red cell morphology with use of phase contrast microscopy distinguishes between glomerular and non glomerular bleeding.[35] The alternative is to assess urinary red cell size by counter analysis as dysmorphic red cells are smaller than normal red cell.[36]

The presence of crystalluria in 18% of the participants is noteworthy as they were numerous and consisted mainly of calcium oxalate crystals. It is possible that the cystalluria may have been related to dehydration from hot weather and/ or hard drinking water from wells and moving streams. This calls for further study as calcium oxalate renal stone disease may develop in some of them. Calcium containing kidney stones may result from excessive excretion of calcium, oxalate or uric acid, renal tubular acidosis and congenital anomalies of the urinary tract.[37,38] The predisposition to calcium stone formation may result from excessive intestinal calcium absorption or decreased tubular reabsorption which has been linked to excessive number of receptors for vitamin D[39].

Although a far reaching conclusion could not be drawn from this screening exercise designed to unravel markers of CKD in the Afon community, periodic renal screening is capable of identifying persons at risk of CKD. This will help in planning intervention strategies in the early asymptomatic stages of CKD so as to reduce the prevalence of end stage renal disease.

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# Abstracts of Papers Presented at NANCONF 2008

## CHEMICAL QUALITY OF DAILYSIS WATER

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**Introduction:** Water used in dialysis must fulfill more stringent quality criteria than drinking water, contamination of water with chemicals ormicroorganism is fact in many clinics worldwide. Unprocessed water contains particles e.g. clay, iron and silical-colloid, which are responsible for water turbidity as well as dissolved inorganic and organic substances.Inorganic salt e.g. calcium, iron, zinc and organic compounds represent chemical contamination.

**How to Determine Contermination of Dialysis Water:** The water treatment, storage and distribution system must be constructed and serviced to meet a certain standard. Deionization, reverse osmosis, or a combination of both, allows a good purification of water from chemical contamination except from certain chemicals such as chloramines and chlorine. Therefore, for deionizer audible and visual alarm must be activated. When the resistivity of reverse osmosis water falls below a such limit i.e. (IM /cm at 25oC) and the product water must be rejected. Reverse Osmosis devices should be equipped with online monitors which allows determination of product. Water and rejected water resistivities or conductivities as well as waste water. Audible and visual alarm are activated when the production/rejection ratio falls below a define value. Monitor which measure total dissolved solid (TDS) may be used in place of resistivity or conductivity monitor and it must be temperature compensated. Apart from this important online conductivity, resistivity or TDS monitoring, a regular chemical analysis of both incoming and product water is mandatory at least twice a year. The frequency of testing must be increased upon any indication of contamination. In the chemical analysis of incoming water, special attention should be paid to aluminum, calcium, magnesium, pH, total and free chlorine, chloramine and heavy metals contents.The chemical analysis of the contaminants must be conducted using sample of raw water and of treated water used to prepare dialysis fluid. In addition, sample water used to process dialyzers or for any other clinical applications must also be analyzed. During sampling and testing, appropriate container should be used. In order to protect patient from disinfectant-related chemical poisoning, exact disinfection and rinsing procedure for the water treatment system must be defined and tested.

**Conclusion:** The following must be standardized and documented in order to be assured of correct chemicals testing.

1. Sample technique
2. Sample time (e.g. twice a year and after any alterations in the water treatment system)
3. Sample storage and transport
4. Method for laboratory analysis
5. Data interpretation and action protocol

## THE REACTION TIME IN HAEMODIALYSIS

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**Background:** Haemodialysis therapy is often delayed for several reasons ranging from logistics to personnel issues. This on the long run affects mortality. *Reaction time* is defined as the time taken to initiate dialysis right from presentation at the emergency/casualty unit to the commencement of the first dialysis session. We sought to determine the causes of delay in initiating haemodialysis and its effect on morbidity and mortality.

**Materials and methods:** A total of 120 case notes of patients offered HD over a 3 year period by our unit were randomly selected. There were 66 males and 54 females. 100 patients had CRF while 20 patients had ARF. Identified causes of delay in our patients were Haematological factors in 45 (37.5%), financial in 40(33.33%), machine error (at onset) in 20(16.67%), reluctance in accepting dialysis 5 (4.17%) and access problems in 10 (8.33%). *reaction time* at our centre ranged from 6 hours to 100 days, mean of 1200 hours. There was no correlation between outcome/survival and *reaction time* in cases of (CKD). However, there was a strong correlation in those with acute renal failure (esp referral cases from non-medical units) as those with shorter *reaction times* survived.

**Conclusion:** There is a need to incorporate blood banking services and pre-dialysis serology screening facilities into dialysis units. Also flexibility/adequate staffing in terms of working hours should be encouraged in individual units.

## SHOULD ANTIHYPERTENSIVE DRUGS BE PRESCRIBED PRE-DIALYSIS TO MAINTENANCE HAEMODIALYSIS PATIENTS?

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**Background:** Haemodialysis induced hypotension is quite common with acetate dialysis on account of which antihypertensive administration pre dialysis is usually discouraged. Hypertension on the other hand used to be rare on acetate dialysis and complicates only 3% of HD sessions in our series. Since commencement of bicarbonate dialysis in our centre 6 years ago the prevalence of dialysis induced hypertension had steadily increased.

**Objective:** To determine the pattern of occurrence of hypertension as well as its variations during the course of HD.

**Methods:** The data retrieved from patients dialysed between 1st January 2007 to 31st December 2007 were reviewed. Patients that had HD for longer than 3 months were selected and pattern of blood pressure changes in them studied.

**Results:** A total 105 patients had 664 sessions of HD during the period. Twelve of them had dialysis sessions for longer than 3 months accounting for 11.43%. Ten of these patients were recruited and the pattern of blood pressure changes during dialysis studied. Nine of them had a rise of between 10 - 30mmHg in systolic BP while the rise in diastolic BP ranged between 5 - 15mmHg. Two of the patients had parenteral antihypertensive for symptomatic hypertensive encephalopathy. One patient reverted back to normotension without therapy.

**Conclusion:** Dialysis induced hypertension is common in maintenance HD patients on bicarbonate dialysis. Routine administration of antihypertensives should be encouraged in such patients.

## SPECTRUM OF PATIENTS PRESENTING FOR DIALYSIS IN A NEW DIALYSIS FACILITY AT UPTH PORTHARCOURT (JAN. – DEC. 2007)

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University of Port Harcourt Teaching Hospital, Port Harcourt.

**Objective:** To describe the spectrum of patients presenting for dialysis.

**Methods:** Over a period of one (1st January o 31st December 2007) the medical records of patients dialysed at the renal unit of UPTH were reviewed. The biodata, type and cause of renal disease, the clinical and

laboratory data, duration/frequency of haemodialysis and outcome were recorded and analyzed using SPSS 13.0.

**Results:** A total of 91 patients received haemodialysis during the period under study. Forty-three patients (56.5%) were males, mean age was 43±19 years. The Ibo tribe was most represented. The most common diagnosis was hypertensive nephropathy 20 (22.4%) closely followed by CGN and DN each with 18(19.7%) respondents. Most patients had chronic kidney disease with 72.4% in ESRD, 14.5% in ARF and others had acute on chronic renal failure. Most patients were hypertensive, about 90% of patients were anaemic and only 32.9% presented in stable clinical condition. The mean urea and creatinine were 28.7±27.9mmo/l and 1213.2±1090.0umol/l respectively. The mean total dialysis obtained by patients was 3.5±3.9 times with a range of 1 to 21 times. Only 5.3% were still dialyzing, only 2.6% had renal transplant, but most patients were lost to follow up or died. There was no significant difference in outcome among the various sexes, age, occupation but patients with ESRD and higher azotaemia had worse outcome. Patients that died were more anaemic and younger.

**Conclusion:** Kidney disease is still more common among the young adult. Patients present late and in poor clinical condition. Patients were unable to maintain adequate/consistent dialysis. Outcome is very poor.

## DIALYSER REUSE AT LAUTECH TEACHING HOSPITAL, OSOGBO – A 2 YEAR PRELIM REPORT

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**Background:** Dialyser reuse system is a safe and effective practice in most developed countries for reprocessing dialysers. In view of the current economic and fiscal challenges in our environment, we carried out a 2-year retrospective study of the automated reuse system on our patients between October 2005 to October 2007

**Methodolgy:** During the study period, 30 hollow fibre dialyzers were used for a total of 100 sessions of haemodialysis. After each use, dialyzer membrane clearance was tested by measuring the fibre volume of blood compartment and the efficacy of the dialyzer was determined by measuring the Urea Reduction Ratio (URR).

**Results:** The URR was maintained between 45±5% at first use and 40% at the third use. Dialyser volume was averagely maintained between 70mls and 66mls at the first and third use. Total cost savings of 25% was achieved at our centre with the dialyser reuse. Not much difference in side effects was observed as compared with a control of single use and no clinically significant adverse event was attributed to reuse.

**Conclusion:** Automated dialyzer reuse is an effective way of reducing the cost of haemodialysis in our practice on the long run and is quite safe provided the standard specifications and guidelines are maintained

## *TRANSPLANTATION*

## RISK FACTORS ASSOCIATED WITH CMV INFECTION IN RENAL TRANSPLANT RECIPIENTS AND THEIR DONORS IN LAGOS

***Menakaya C, Mabayoje MO and Bamgboye EL***

**Background:** Renal transplantation started in Nigeria in the year 2000 and the transplant population is increasing steadily. Cytomegalovirus (CMV) infection is the most important infection in renal transplant recipients and has significant impact on long-term recipient and graft survival. Although prior studies have indicated high rates of CMV seropositivity in Nigerians, no research has been done on renal transplant

recipients and their donor population. The aim of this study was to assess the risk factors important in its transmission and evaluate the benefits of CMV prophylaxis.

**Method:** This study was a cross-sectional, case-controlled sero-epidemiologic study. The study subjects were 40 renal transplant recipients aged 16 to 58 years, and 22 kidney graft donors recruited from three post transplant follow-up renal clinics in Lagos during the period October 2004 to July 2005. One hundred subjects from the general population and 36 patients with stage 4 or 5 chronic kidney disease (CKD) served as controls. The prevalence of CMV infection was determined using Enzyme Linked Immunosorbent Assay (ELISA) to detect CMV IgG and IgM antibodies. Risk factors associated with CMV infection in both subjects and controls were assessed by means of a structured self-administered pre-tested questionnaire. Conditional logistic regression and multiple logistic regression analyses were applied to identify significant risk factors associated with CMV infection in the study subjects and controls. Data on the use of CMV prophylaxis in the transplant recipients were obtained from their hospital case records, and the effect of CMV prophylaxis on the prevalence of recent CMV infection (CMV-IgM seropositivity) in the recipients was assessed by Chi-square and Fisher exact tests as appropriate. All statistical analyses were done using EPI-INFO 2002.

**Results:** Exposure to multiple sexual partners was the only independent risk factor associated with recent CMV infection after multiple logistic regression analysis (odds ratio= 3.05, 95% confidence interval=1.02-9.12, p = 0.045). The use of CMV prophylaxis (acyclovir) was not associated with a reduction in the prevalence of recent CMV infection in recipients (Fisher exact p=0.45).

**CONCLUSIONS:** Indiscriminate sexual practice is an independent risk factor for CMV infection.

## PERCEPTION OF ORGAN TRANSPLANTATION AMONG DOCTORS AND PATIENTS' RELATIVES AT THE UNIVERSITY COLLEGE HOSPITAL, IBADAN: A PRELIMINARY REPORT

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**Background:** Organ transplantation remains the definitive treatment for most end stage medical conditions. However the practice of organ donation and transplantation is still evolving in Nigeria. A significant problem is the dearth of ready and willing organ donors.

**Aim:** The study aimed at evaluating the perception of organ transplantation among doctors and patients' relatives and the factors that may influence such perceptions.

**Methodolgy:** A structured pretested questionnaire was administered on doctors and patient' relatives at the University College Hospital. Socio-demographic information was collected. Medical school attended, number of years in practice and specialty were the additional information sought from the doctors. Information on knowledge of and training in organ donation, contact with donors and/or recipients, support and willingness to donate and barriers to organ donation was collected from respondents.

**Results:** A total of 122 respondents including 102 doctors and 20 patients' relatives were interviewed. Among doctors, nearly 90% were aged 25-35 years; about 70% were males while 30% were females. Fifty percent admitted having had formal lectures in organ donation/transplantation in medical school while another 50% have had some contact with an organ donor/recipient. About 40% were willing to donate an organ while alive while a greater majority, over 60%, would only donate after death. Various barriers identified included inadequate knowledge, ethical, religious and fears about future medical problems and the competence of clinical staff in managing donor/recipient clinical problems.

**Conclusion:** There appears to be willingness on the part of doctors to donate organs both while alive and dead. However, patients' relatives need more information in this regard. There is the need for doctors to educate their patients and their relatives while ensuring the training of staff to ensure a sustainable organ transplant programme.

## WILLINGNESS OF NIGERIAN HEALTHCARE WORKERS TO DONATE KIDNEYS: A SINGLE CENTER SURVEY

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**Background:**The attitude of healthcare workers (HCW) towards organ donation is cardinal to the successful implementation and sustainability of transplant programs. We present the outcome of a survey among HCW in a single tertiary institution in Nigeria about willingness to be living related kidney donors.

**Methods:** Self-administered questionnaires were randomly distributed to HCW evaluating their attitude towards living related kidney donation.

**Results:**Of the 650 questionnaires distributed only 502 responded (clinical medical students 51%, physicians 31.7% and nurses 17.3%). 75.6% of respondents were willing to be living donors while 5.8% were against it and 18.5% were undecided. Multivariate analysis identified willingness to receive, perceived risk associated with kidney donation and attitude towards cadaveric donation as independent predictors of willingness of HCW to be living donors.

**Conclusion:** Nigerian HCWs have a positive attitude toward kidney donation.

## CARE OF THE KIDNEY TRANSPLANT RECIPIENT: ESTABLISHING CLINICAL PRACTICE GUIDELINES FOR NIGERIA.

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Renal transplantation offers the best quality of life for those in end-stage renal disease undergoing renal replacement therapy. However this option is not readily available and accessible to most patients worldwide. This situation is even more glaring in Nigeria whose renal replacement program is still very poor in terms of available facilities and personnel. The renal transplantation program in Nigeria is still very small, slow in expansion and at infancy stage in comparison to the well developed centers in North America, Europe and Asia –Pacific world. The reasons for the stunted growth in renal transplantation in most countries may be due to well known factors such as organ shortage, poor facilities, poorly trained personnel and lack of necessary guidelines to start or even improve on the program.

To examine these and other factors that may hinder care of the kidney transplant recipients, the National Kidney Foundation (USA), convened a meeting of experts and persons in Lisbon, Portugal in February 2006. This is to discuss an acceptable guideline that will assist clinicians, policy makers and health care industry in the field of renal transplantation. It was hoped that the guidelines will assist further development of National guidelines suitable for their environment. The overall aim was to have minimum criteria applicable worldwide for renal transplant program.

A summary of the report will be discussed and hopefully useful discussions thereafter should lead to recommendations for establishment of a future renal transplant program and better care for the renal transplant recipients.

## *CLINICAL NEPHROLOGY*

### EVALUATION OF C-REACTIVE PROTEIN LEVELS IN NIGERIAN DIALYSIS PATIENTS

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**Introduction:** Cardiovascular diseases have been shown to be very prevalent in patients with end stage renal disease (ESRD). It is estimated to be responsible for 43.6% of all deaths in patients with end stage renal disease. Atherosclerotic outcomes including those from coronary artery disease, peripheral vascular disease and cerebrovascular disease have been shown by earlier studies to contribute significantly to these cardiovascular morbidity and mortality. Therefore, assessment of C-reactive protein values in patients with chronic kidney disease (CKD) becomes important due to the high prevalence of cardiovascular diseases in these patients and the known role of high levels of CRP in the pathogenesis of atherothrombosis.

**Aim:** To evaluate the levels of C-reactive protein in Nigerian patients undergoing dialysis.

**Patients and methods:** Fifty-seven (57) patients undergoing dialysis at our centre were recruited into the study. Their CRP was assessed using commercially available clinotec –R diagnostic kit.

**Results:** In the 57 dialysis patients studied, the mean CRP value was 222.19± 96.39mg/L. (Range 46mg/L to 567mg/L) compared with 8.7± 9.6mg/L (range 6mg/L to 48mg/L), $p<0.05$ in the control group. Our values are also much higher than the average values seen in the developed countries. This could be attributed to the higher incidence of infection related tropical nephropathies as the underlying aetiology of renal failure in our patients. Also, patients with acute renal failure had significantly higher CRP levels compared with patients with chronic renal failure 267.91± 46.39mg/L Vs 209.92± 102.86mg/L, $p<0.05$. This observation is due to the fact that active sepsis was present in 90% of the acute renal failure patients dialyzed.

**Conclusion:** It was concluded that baseline C-reactive protein levels in our dialysis patients are much higher than values documented by other investigators in the developed countries, due to higher aetiological contributions of infection related tropical nephropathies in our dialysis patients. Practicing nephrologists in Nigeria need to be aware of the potential heavy burden that cardiovascular diseases may pose on the clinical outcomes of CKD treatment.

### CARDIOVASCULAR DISEASE IN CKD; ARE OUR PATIENTS PREDISPOSED?

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**Background:** Cardiovascular disease is common in patients with CKD and contributes significantly to morbidity and mortality. It's now recognized that patients with CKD are more likely to die of cardiovascular diseases than progress to end stage renal disease.

**Aim:** We therefore set out to determine the prevalence and pattern of the established risk factors and events in our CKD population.

**Methods:** 52 subjects with CKD were recruited as well as 50 age and sex-matched controls. They were taken through a questionnaire, had clinical examination and laboratory investigations which included echocardiography, lipid profile, CBC, serum chemistry, uric acid as well as ca2+ & po4.

**Results:**The prevalence of anaemia, hypertension, proteinuria, and LVH were found to be 88.46%, 80.7%, 98.07%, and 88.6% respectively. Prevalence of CCF and PVD were 61.5% and 30.8% respectively.

Dyslipidaemia, obesity, smoking, and CaP04 product were not found to be significantly deranged in our CKD population. But CVD prevalence was not different from the controls. CHD was not found in any of the study population and controls.

**Conclusion:** We therefore concluded that management of our patients with CKD in this environment should be directed at preventing or controlling anaemia, hypertension, proteinuria and LVH.

## PATTERN OF IRON STATUS IN ANAEMIC PREDIALYTIC CHRONIC KIDNEY DISEASE PATIENTS

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**Background:** Anaemia is known to develop in the course of chronic renal disease and has been associated with increased mortality. Iron deficiency is also common particularly in chronic kidney disease on dialysis.

**Objectives:** To determine the pattern of iron status in the predialytic CKD patients.

**Methods:** A total of 60 consecutive stage 2-4 predialytic CKD patients attending the out patient clinic of were screened. The cut off for anaemia was PCV<33% (Hb<11g/l). Their iron status was assessed using MCV, MCH, MCHC and Serum iron concentration. Total iron Binding Capacity and Transferrin saturation were also assessed.

**Results:** Of the 60 patients selected 41(68.3%) of them were found to be anaemic. The mean age of the patients was 36.66±16.17yrs while the mean creatinine clearance was 37.90±12.17. PCV ranged from 18%to 32% with a mean of 25.46±4.3 in females and 26.0±3.14 in males. The mean ± SD values for MCV, MCH, and MCHC were 72.37±15.65fl, 26.59±3.20pg and 29.75±2.81pg/ml respectively while the mean serum ferritin, Transferrin Saturation (TSAT) and serum iron were 303.93±162.75ng/ml, 21.44±12.28% and 65.52±25.25µg respectively. 43.9% of the patients had normal iron status defined as TSAT >25% and serum ferritin >300ng/ml, 56.1% of the patients had iron deficiency (TSAT<25% and serum ferritin <300ng/ml). 7.3% of the anaemic patients had absolute iron deficiency (serum ferritin <100ng.ml)

**Conclusion:** Anaemia is common in our predialytic CKD Population and the prevalence of iron deficiency is high. This calls for a more aggressive iron repletion therapy in CKD patients.

## RENAL DISEASE IN HIV INFECTED PATIENT: WHAT RELATIONSHIP WITH LEVEL OF CD4 CELL COUNT

*Okafor UH, Unuigbe EI, Ojogwu LI and Oviasu E.*

**Objectives:** To determine the relationship between level of renal functions and CD4 cell count in HIV/AIDS patients.

**Methods:** HIV infected patients presenting at UBTH Benin City were screened for renal function impairment. Their biodata, CD4 cell count, serum urea, serum creatinine, serum albumin, urine protein and creatinine were assessed. Their GFR using the 6 equation of MDRD and protein excretion using protein creatinine ratio were calculated. Patients were stratified according to their renal functions into normal renal function, mild, moderate and severe renal impairment using GFR ≥60ml/min and PCR $\underline{\geq}$ 200, GFR ≥60ml/min but PCR<200, GFR 30 – 59ml/min, GFR<30ml/min respectively. The data was analyzed using SPSS 13.0. The relationship between CD4 cell count and renal functions were assessed using Pearson's correlation. P value <. 05 were considered significant.

**Results:** A total of 383 patients were screened 204(53.3%) patients had renal function impairment, 40.2% had mild, 37.7% had moderate and 22.2% had severe impairment in their renal functions respectively. Their mean age was about 35.6±8.3 years, no sex difference. The distribution of CD4 cell count showed that patients with impaired renal function had lower CD4 cell count than those with normal renal functions. Further analysis showed that patients with mild renal functions had CD4 cell count comparable to those with normal renal functions (>300 cells/ul) but patients with moderate and severe impaired renal functions had lower CD4 cell count (<200 cells/ul). There was a positive correlation between CD4 cell count and degree of renal function impairment using GFR as a marker of renal function.

**Conclusion:** Impairment of renal function is a common occurrence in patients with HIV infection. CD4 cell count is a better assessor of severity than onset of impaired renal function. Proper assessment of renal functions in all patients with HIV infection is imperative.

## ARF IN TYPHOID PERFORATION: CASE REPORTS

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Typhoid is an important cause of ARF especially in developing countries where it is endemic. The morbidity and mortality increase in the presence of perforation which occurs in about 3% of cases. Worse still, this could be very high after surgical treatment. Treatments for these conditions with regards to the timing of renal replacement in the treatment of ARF have not yet been assessed in randomized controlled trials.
We therefore present two cases of typhoid perforation complicated by ARF which were managed with Renal Replacement Therapy post operatively. The two patients survived.

**Conclusion:** Considering the incidence and high mortality that is often associated with typhoid perforation and the economic status of majority of patients with this conditions; we suggest that surgery should not be delayed for renal replacement therapy (RRT) as more patients survive with prompt surgery before haemodialysis.

## ASYMPTOMATIC PROTEINURIA AND RENAL SONOGRAPHIC FINDINGS IN PRE-SCHOOL CHILDREN IN ENUGU SOUTH-EAST NIGERIA.

***Odetunde IO, Okafor HU, Odetunde OA, Ani CO and Njeze NR***
*University of Nigeria Teaching Hospital, Enugu.*

**Background:** Asymptomatic Proteinuria with or without haematuria and or hypertension deserve special emphasis because they are hallmark of possible significant renal disorder. Among the plethora of indications for imaging of the renal tract, the guiding principle in paediatrics should be to choose the least invasive technique with the lowest radiation dose and work up only as necessary to the most invasive technique and higher radiation burden.

**Objectives:** The study was conducted to study the usefulness of symptomatic proteinuria and renal ultrasonic findings in the early detection of renal disorder in Pre– School Children.

**Methods:** Multi – staged random sampling method was used to select subjects from registered nursery school within Enugu Town. The Study involved collection of early morning urine for urinalysis and physical examination. Subjects with abnormal urinalysis findings (significant proteinuria etc) with or without elevated blood were re-evaluated by repeating the urinalysis two weeks after the first urinalysis. Subjects with persistent abnormal urinalysis findings were further evaluated by conducting renal ultrasound.

**Results:** The result showed a prevalence of 2.7% for asymptomatic proteinuria. Proteinuria was found to be independent of age, sex and social class with P. value >0.05. The prevalence of persistent proteinuria was found to be 1.6 %. On further investigation of pupils with persistent proteinuria, the renal Ultrasonography revealed abnormal finding in 30% of the pupils with persistent proteinuria.

**Conclusion and Recommendation:** Asymptomatic and persistent proteinuria, haematuria with or without hypertension could be a presumptive evidence of an underlying renal parenchymal disease and they should be properly investigated and followed – up. Inevitably all children with asymptomatic presumptive evidence of renal disease should start with a renal ultrasound examination.

## SONOGRAPHIC DETERMINATION OF RENAL SIZES IN NIGERIAN ADULTS WITHOUT KNOWN RENAL DISEASE: CORRELATIONS WITH DEMOGRAPHIC PARAMETERS.

***Adebayo SB, Alebiosu CO, Awosanya GO and Adebayo P***

**Background:** Renal dimensions are important for the diagnosis and the prognosis of nephropathies. Information on renal dimensions among normal Africans is scanty. This study aimed to define sonographically measured renal sizes and their relations to age, sex, height and weight among Nigerian in a hospital setting.

**Methods:** A total number of consecutive 132 subjects, mean age 37.8 $\pm$ 12.8 years (range 18-76years), were studied. Mean renal dimensions were obtained for both kidneys. The relationships of renal dimensions to age, height, weight and sex were determined. Renal dimensions were correlated with these parameters. Data were presented as mean ± SD and analyzed using SPSS 14.0 software. A p-value < 0.05 was considered as statistically significant.

**Results:**Mean Renal Dimensions
Mean renal lengths were 10.2$\pm$0.7cm (left side) and 10.0$\pm$0.8 cm (right side), p< 0.0001. Median renal volumes were 125.5$\pm$35.1 cm3 and 118.7$\pm$33.3 cm3 respectively.
*Correlations*
There were statistically significant correlations between the patients' weight, height, renal length and renal volume and Body Surface Area, but not with Body Mass Index. A simple linear regression equation obtained predicted renal lengths based on height: renal length = 6.1078 + 0.0248 (height) cm, p< 0.001. Another equation obtained predicted renal length based on body surface area (BSA): renal length = 0.8839BSA+ 8.6260, p< 0.001. Thus, patient average renal lengths increased by 0.24cm for each cm of height and 0.88cm for each unit of BSA.

**Conclusion:** This study shows the values of renal sizes in Nigerians, which may be helpful in clinical settings.

## OUTCOME OF SCREENING FOR RENAL ABNORMALITIES IN A RURAL COMMUNNIITY IN KWARA STATE, NIGERIA.

*(By Ilorin Renal study group-Aderibigbe A et al.)*

**Background:** Some renal abnormalities with serious long term implications are asymptomatic and evolve gradually until they become a major life threatening health problem. They can only be detected by routine or periodic screening.

**Objective:** To screen for renal abnormalities amongst people living in a rural community in Kwara state, Nigeria.

**Methodology:** As part of activities to mark the World Kidney Day 2007, the Ilorin Renal study group carried out screening campaign for renal diseases at Afon, Asa LGA, Kwara State. The participants were drawn from all the wards in the Local Government. After a successful health promotional talks, consenting participants were screened. The colourful ceremony was declared opened by the Chairman of the LGA. The screening exercise carried out comprised of anthropometric and blood pressure measurements, urinalysis including urine microscopy, culture and sensitivity and renal ultrasonography.

**Result:** The mean age of the participants was 27.2 years. Haematuria was detected in 12/207 (5.8%), proteinuria in 26/172 (15.1%), glucosuria 2/172 (1.2%), pyuria in 32/207 (15.5%), casturia in 11/207 (5.3%), crystalluria in 31/207(15%) and hypertension in 8/207(3.9%). Among the 8 people with hypertension, there was no remarkable associated urinary abnormality except the presence of calcium oxalate crystals, pyuria and mild proteinuria in each of 3 of them respectively. Appropriate intervention measures have been instituted in those in whom abnormalities were found.

**Conclusion:** There is a low prevalence of urinary abnormalities in Afon, Asa LGA of Kwara State.

## HEPATORENAL SYNDROME: STILL A GLOOMY OUTCOME?

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**Background:** Hepatorenal syndrome (HRS) is defined as the development of acute onset of renal insufficiency and /or failure in patients with established chronic liver disease (CLD). It's a common cause of intensive care admission in patients with CLD.

**Objective:** To assess magnitude and outcome of HRS in our setting and determine if possible factors contributing to mortality.

**Methods:** The case records of patients managed with chronic liver disease over a five year period were retrieved. Information on socio-demographic data, clinical evaluation, investigation results, duration of admission, treatment and outcome were retrieved and collated.

**Results:** A total 22 patients with established CLD (Liver Cirrhosis and/or primary liver cell carcinoma) had HRS during the period which comprised of 17 males and 5 females with a M:F ratio of 3.4:1. Their ages ranged between 12 and 67 years (mean ± SD; 45.5 ± 15.76years). 11 (50%) were admitted with hepatic encephalopathy and 13 (59%) had clinical ascites which was massive in 10(45.5%) patients. Majority had type 1 HRS while only 2 had type 2. Mean values of serum urea and creatinine were 25.18 ± 15.7mmol/L and 608 ± 420.9 umol/L respectively. 15 (68.2%) had hyponatraemia while only 2 (0.9%) had hypokalaemia. 16 (72.7%) patients died between 1 and 67 days of admission while 2 patients were discharged after 21-34 days of admission. The last 4 discharged against medical advice. The mean (± SD) duration of admission for all patients was 13.55 (± 16.6) days.

**Conclusion:** The outcome of hepatorenal syndrome is still very poor. There is the need to explore use of octreotide, midodrine and continuous haemofilteration on a short term as a bridge to liver transplantation which is the definitive treatment.

## EFFECT OF PROLONGED USE OF ANGIOTENSIN CONVERTING ENZYME INHIBITOR (ACEI) IN 7 CHILDREN WITH STEROID RESISTANT OR FREQUENTLY RELAPSING NEPHROTIC SYNDROME (NS)

***Adedoyin OT, Mark F, Ajetomobi A and Adeniyi A.***

**Background:** Steroid has remained the mainstay of treatment in NS, even though resistance to it is well documented. Steroid resistant NS has continued to pose therapeutic challenge. Many alternative drugs including ACEI have therefore been tried under these circumstances.

**Objective:** To determine the effect of prolonged use of ACEI in 7 children with steroid resistant or frequently relapsing nephrotic syndrome.

**Methodology:** An observational study using ACEI over periods ranging from 3-51 months was carried out. Inclusion criteria were steroid resistance, administration of oral cyclophosphamide, refusal of renal biopsy and frequently relapsing NS. All steroid responsive patients were excluded. They were commenced on either lisinopril or captopril. Outcome variable sought was number of relapses during the administration of the drug.

**Results:**A total of 5 males and 2 females met the inclusion criteria. There were a total of 5 relapses in all the patients. Four of these relapses occurred among the three patients who received the drug for 3-12 months. Among those who received it for 16-51 months, one relapse was recorded. There was no hypotension and no side effect of the drug was observed.

**Conclusion:** ACEI may be useful in the treatment of steroid resistant and frequently relapsing NS.

# Minimal Change Nephrotic Syndrome and Graves' Disease in a Nigerian Child

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**ABSTRACT**

We report a 12 year old Nigerian boy with steroid sensitive nephrotic syndrome who developed Graves' disease 12 months after the diagnosis of nephrotic syndrome. He had two relapses of the nephrotic syndrome with early response to steroids on both occasions. Renal biopsy showed normal findings on light microscopy. Graves' disease is rare among black African children, minimal change nephrotic syndrome is also not commonly reported among them. The coexistence of these two disorders in our patient underscores possible similar immunologic mechanisms in the aetiology of both diseases.

**KEYWORDS:** *nephrotic syndrome, minimal change nephrotic syndrome, hyperthyroidism, Graves' disease, steroids*

## INTRODUCTION

Hyperthyroidism has rarely been reported in association with Nephrotic Syndrome (NS)[1-5]. Nephrotic syndrome in African children, is relatively common, [6, 7] while hyperthyroidism is rare[8].We report a 12 year old Nigerian boy with steroid sensitive NS who developed hyperthyroidism in the course of the nephrotic syndrome.

## CASE REPORT

A 12 year old boy presented at the University College Hospital Ibadan, Nigeria with facial oedema of 2 weeks and two day history of scrotal swelling and pedal oedema. He weighed 36kg ($25^{TH}$ centile for age), and height was156cm ($75^{th}$ centile for age), Blood pressure was 100/70mmHg and heart rate was 120/min. Laboratory data showed serum protein 6.2g/dL; serum albumin1.6g/dl, serum cholesterol 384mg/dL, Serum urea 39mg/dL and serum Creatinine 0.8mg/dl. Serum electrolytes were normal. HIV screening and HBsAg were negative. Dipstick urinalysis showed proteinuria of 4+ and trace of blood. Urine microscopy was normal and urinary protein excretion was 1 gram in 24 hours.

He was commenced on oral prednisolone at 50mg/day and went into remission 11 days after commencement of steroids. He had 17 days of daily steroid therapy and then 7months of alternate day steroids. At the end of steroid therapy serum protein was 7.5g/dL; serum albumin, 4.3g/dL and 24 hour urinary protein, 0.1g in 24 hours.

Twelve months after initial presentation and two months after discontinuation of alternate day prednisolone, he was noted to have a goiter, associated with proptosis and excessive sweating. Blood pressure was 120/ 70 mmHg and heart rate was 120/ minute. Thyroid gland ultrasound showed homogenous parenchymal echoes. The volume of the right lobe of the thyroid was at the upper limit of normal, while volume of the left lobe of the thyroid was normal. Total T3 was 8.3nmol/L (normal= 1.0-3.25), Total T4 was 244nmol/L (normal= 65-175) and TSH 0.1miu/L (normal=0.5-6.5). Three months later, he had a relapse of the nephrotic syndrome. Serum protein was 5.4g/dL, serum albumin 1.6g/dL, 24 hour urinary protein 4.1g and creatinine clearance 147ml/min. Serum urea was 33mg/dL, serum creatinine was 0.3mg/dl and the serum electrolytes were normal. The weight of 36kg at initial presentation had increased to 45 kg, while his height remained essentially unchanged at 158cm. He was recommenced on oral prednisolone. He went into remission on the $9^{th}$ day of steroid therapy. He had

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14 days of daily prednisolone therapy and he was then changed to alternate day prednisolone.

The goiter however persisted with bilateral hand tremors, exophthalmos, warm moist palms and increased aggression. Repeat Thyroid function test, after 4 months of alternate day steroids, showed Total T3 5.4ng/ml (0.8-2ng/ml); Total T4 190ng/ml (45-115ng/ml);TSH <0.3µIU/ml(0.54-3.7 µIU/mL). He was then started on oral Carbimazole 10mg tds.

He had 9 months of alternate day steroids; 20 days after discontinuation of steroids he had a second relapse of nephrotic syndrome. He had a recurrence of oedema and dipstick urinalysis showed 4+ proteinuria, while the 24 hour urinary protein excretion was 4.8g in 24 hours. His serum urea was 34 mg/dL, while serum creatinine was 0.6mg/dl, his serum electrolytes remained normal. Renal biopsy, revealed normal findings on light microscopy. He was recommenced on daily prednisolone and achieved remission after the 6$^{th}$ day of daily steroids. Clinical and biochemical features of Graves' disease resolved with p.o carbimazole therapy.

## DISCUSSION

Autoimmune thyroid disorders have rarely been associated with nephrotic syndrome[1-5, 9-11]. Nephrotic syndrome has been associated with both hyperthyroidism[1-5]and hypothyroidism[12]. Initial reports were of membranous glomerulonephritis secondary to immune complex deposition of thyroid antigens[1, 12, 13]. More recently few reports of association of autoimmune thyroid disorders with minimal change nephrotic syndrome have been documented [2-5, 9, 11], with Graves' disease occurring in association with minimal change nephrotic syndrome[2-5]. Three of the reports of Graves' disease were in adults. In the only case reported in the paediatric age group the patient developed Graves' disease about 9 years after the diagnosis of minimal change nephrotic syndrome[5]. Our patient developed Graves' disease about 1 year after the development of minimal change nephrotic syndrome.

Minimal change nephrotic syndrome is suspected to be secondary to an abnormality in T Cell immunity[14]. The association of minimal change nephrotic syndrome with lymphoma, particularly the T cell disease 'mycosis fungoides', is well recognized[3]. Remission of minimal change nephrotic syndrome may coincide with measles infection[15]. Minimal change nephrotic syndrome largely responds to steroids and calcineurin inhibitors which modulate T cell immunity. A glomerular permeability factor (VPF) isolated from T cell hybridomas has been implicated in the pathogenesis of minimal change disease (MCD)[16]. Cytokine stimulation and inhibition of VPF production by T lymphocytes has been described in *in vitro* studies[17]. T cell subset changes and high IL 2R expression on peripheral lymphocytes may indicate the presence of stimulated T cells populations in MCD[18]. There are reports of reduction in VPF production in lymphocytes from patients with MCD who were treated with tacrolimus or cyclosporine[19].

Thyroid stimulating antibodies play a major role in Graves' disease and the extracellular domain of the thyrotropin receptor is the autoantigen. They are mainly produced by lymphocytes infiltrating the thyroid gland and their production is T cell dependent. Infiltrating T lymphocytes secrete interferon γ which stimulate the thyroid cells to express HLA class II molecules allowing the thyroid cells to present antigens such as the thyrotropin receptor to activated T cells[20, 21].

Autoimmune disorders tend to cluster together; either appearing simultaneously or consecutively in the same patient. Graves' disease has been documented in association with other autoimmune disorders such as Addisons disease, vitiligo and pernicious anaemia, which further emphasizes the autoimmune basis of Graves' disease[20].The association of Graves' disease with minimal change nephrotic syndrome suggests a common aetiology

Grave's disease occurs 5-10 times more frequently in women than in men, and is unusual in children. The prevalence of Graves' disease is similar among whites and Asians, and it is lower among blacks[20]. In a European study Graves' disease had an estimated incidence of 3 per 100,000 at puberty[22]. In Sub-Saharan Africa Graves' disease is rare in childhood, Laditan documented 3 cases of hyperthyroidism associated with exophthalmos over a 5 year period, accounting for 0.02 % of paediatric cases seen at at our centre between 1972 and 1976[8]. Minimal change nephrotic syndrome is also less common among Africans than among Caucasians. Among Americans, Asians and in Europe minimal change nephrotic syndrome accounted for 76.6% of cases of idiopathic nephrotic syndrome[23]. In a standard Paediatric nephrology text it was noted that 90% of children with idiopathic nephrotic syndrome may be steroid responsive[24]. In Nigeria

minimal change nephrotic syndrome occurred in 9.8% of 41 children with nephrotic syndrome. In Northern Africa, the histopathology of nephrotic syndrome shows a profile that is similar to the pattern in Europeans, however in other parts of Africa minimal change disease accounted for 18-56% of cases of nephrotic syndrome[6]. In Nigeria 25.5-60% of nephrotic syndrome patients are steroid sensitive[7, 25, 26]. The coexistence of these two relatively rare conditions in our patient further supports an immunologic link in the aetiology of both diseases rather than coincidence.

Features of nephrotic syndrome preceded those of hyperthyroidism in our patient. This association is probably secondary to some dysregulation in the T cell Lymphocyte population possibly producing vasoactive peptide and then thyroid stimulating antibodies[3]. Association of minimal change nephrotic syndrome and Graves' disease should perhaps be considered a syndrome.

The renal biopsy in our patient was analysed by light microscopy only and it showed normal findings. Immunofluorescence or electron microscopy was not carried out, but the frequent relapses of the nephrotic syndrome without impairment of renal function, and complete remission following steroid therapy together with normal findings on light microscopy of the kidney biopsy are in keeping with minimal change nephrotic syndrome[27].

Free T3, free T4, and anti thyroid antibodies were not estimated in our patient but with the clinical features of hyperthyroidism, the features of mild ophthalmopathy, a diffuse goitre, the elevated total T4 and T3, and depressed TSH which remained so over a 6 month period we made a diagnosis of Graves disease.

Though the development of Grave's disease in the course of nephrotic syndrome is not common, Graves' disease should be considered in patients with nephrotic syndrome with careful clinical evaluation for features of Grave's disease such as ophthalmopathy and goitre.

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# *Chronic Kidney Disease in HIV Infected Patients in North Western Nigeria*

**ABSTRACT**

Renal disease increase the morbidity and mortality in patients infected with HIV. Reports on the prevalence of renal disease in HIV infected patients vary widely. In the USA and Europe, prevalence of between 3 – 10 % is reported. In Africa, the true prevalence is unknown, but prevalence of between 6 -51.8% in screened cohorts has been reported. The objective of the study was to provide data on the occurrence of, and factors associated with, renal disease in HIV infected persons in our environment. Four hundred consenting HIV infected patients were screened for evidence of renal disease using simple urinalysis for proteinuria on spot urine sample and estimated glomerular filtration rate from serum creatinine levels. These were repeated at every monthly visit for three months. Renal disease was defined by persistent proteinuria 1+ and above or estimated glomerular filtration rate of less than 60mls/min. for not less than three months. There were more males than females. Mean age was 37.5 ± 10.3 years with 76% aged 30 – 49 years. 31.8% had evidence of renal disease as defined and 71.8% of these were between the ages of 30 and 49 years. 81.1% were on anti retroviral drugs with no case of ESRD reported. The major symptoms were nocturia and reduced urine output while body swelling was rare. Weight loss and pallor were predominant signs but oedema was rare. 46.5% had CD4 count within the range 100 – 200cells/ul. 37% had nephrotic range proteinuria, 33.1% had microalbuminuria and 58.3% had hypoalbuminaemia. Those with microalbuminuria had higher estimated GFR than those with overt proteinuria. We conclude that renal disease is highly prevalent among HIV infected Nigerians and associated with anaemia, low CD4 count. Hypoalbuminaemia is common but peripheral oedema was rare.

**Keywords:** *Chronic kidney disease, Estimated Glomerular Filtration rate, HIV infection, North Western Nigeria, Proteinuria*

## INTRODUCTION

Renal disease contributes significantly to the morbidity and mortality in patients infected with Human Immunodeficiency Virus (HIV)[1-3]. There is a wide variability in the prevalence of renal disease in people living with HIV reported from various regions of the world. In the USA a prevalence of 3 – 10 % is reported with more than 50% being intravenous drug abusers [4-7]. In Europe, the data is scanty but Nochy *et al* reported a prevalence of 5.3% in 206 patients, 83% of whom were Africans and Afro-Caribbean. Only 16% of those with renal disease in the European series were intravenous drug abusers compared to 50% reported from the United States [8]. HIV associated nephropathy (HIVAN) is the commonest manifestation of renal disease in HIV infected black patients[5,9]. Wools-Kaloustian *et al* in Western Kenya [10] found eGFR to be <60mls/min in 11.5% and proteinuria in only 6.2% of their screened cohort while Pepper et al in Uganda[11] reported 50%. In

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South Africa Gerntholtz *et al* in a retrospective review of renal biopsies done on HIV infected persons suspected to have chronic kidney disease, found HIVAN in 27% of the renal lesions reviewed[12]. Han et al in a cross sectional study found only 6% of their screened cohort with evidence of chronic renal disease but 83% of those with proteinuria who had renal biopsy were found to have HIVAN[13]. Other reports from Africa on screened cohorts of persons living with HIV gave wide variation in figures between 6 – 51.8%[14-17].

Nigeria has a population of over 140 million people and about 5% prevalence of HIV seropositivity. Only very few studies have looked at renal disease among Nigerians with HIV seropositive status. Though the prevalence of HIV seropositivity in North Western Nigeria (with 25% of the Nation's population) is 4.3%, we are not aware of any published study on the occurrence of renal disease in this group of people.

The objective of the study was to provide data on the occurrence of, and factors associated with, renal disease in HIV infected persons in our environment.

## MATERIALS AND METHODS

A cross-sectional descriptive study was designed to determine the prevalence of and risk factors associated with renal disease in a cohort of HIV-infected adults attending an HIV clinic in North western Nigeria. Patients presenting to the clinic were eligible for enrolment if they were e"18 years of age, HIV-infected (confirmed by double Elisa tests) and able to provide informed consent. At enrollment, participants underwent comprehensive health history and physical examination, blood pressure, weight (in Kg) and height (in meters) were documented and body mass index calculated using the formula;

BMI = Wt (Kg)/$Ht^2$ (m)

CD4+T-cell count was done using commercial Kits (Dynal$^R$ T4 quadrant kit – Dynal Biotech ASA, Oslo Norway). Haemoglobin and haematocrit were done using automated haematology analyzer while serum albumin, urea, creatinine, serum lipids and glucose were measured using Cole Spectrophotometer model 721. The same machine was used to estimate urine albumin and creatinine and the ratio was calculated from the results. The urine protein was screened for using the combi 2 dipstick. Screening for hepatitis B and C were done using Ortho Antibody to HBsAg ELISA test system 3 and Ortho HCV version 3.0 ELISA test system respectively. The glomerular filtration rate was estimated using the Cockroft and Gault equation [18]. The urine dipstick and albumin to creatinine ratio in urine (ACR) tests were repeated at every monthly visit for three months.

Renal disease was defined by persistent proteinuria e"1+ or estimated GFR < 60mls/min. e" 3 months[3 & 19].

*Exclusion:*

Pregnant women, patients with urinary tract infection (urine cultures were done) fever and/or congestive heart failure at presentation were excluded since conditions could be associated with proteinuria.

*Statistical analysis*

Statistical analysis was done using the statistical package for social science (SPSS) for windows version 11.5. Quantitative values were presented as mean ± standard deviation or median as appropriate and the Qualitative data were tested by cross tabulation. Student's t – test, Chi-squire and Pearson correlation test were used to assess significant differences and associations between groups and p value d" 0.05 taken as significant with 95% confidence interval.

## RESULTS

A total of four hundred HIV infected persons [234 (58.5%) males and 166 (41.5%) females] were studied. The mean age was 37.5 ± 10.3 years (range 20 – 70). The age group 40 – 49 years had the highest percentage of patients as seen in Table I. There were no intravenous drug users and 332 (83%) were on

**Table 1: Age Range of all Patients and Patients with Renal Disease**

| Age | All pts | RD pts |
|---|---|---|
| 20-29 | 62 (15.5%) | 29 (22.8%) |
| 30-39 | 148 (37%) | 38 (30.9%) |
| 40-49 | 156 (39%) | 52 (40.9%) |
| 50-59 | 29 (7.3%) | 4 (3.2%) |
| 60+ | 5 (1.2%) | 4 (3.2%) |
| Total | 400 | 127 |

anti- retroviral triple combination therapy comprising of Lamivudine, Stavudine and Nevirapine for a mean duration of 19.3 ± 18.1 (median 12 and range 0-48) months.

One hundred and twenty seven (31.8%) had evidence of renal disease as defined by persistent proteinuria, and/or estimated glomerular filtration rate < 60ml/min. One hundred and three patients (81.1%) were on triple therapy anti retroviral drugs with only 31 for longer than twelve months.

The major symptoms were nocturia 43 (33.8%) and oliguria 43 (33.8%). The frequency of symptoms is shown in Table 2. Weight loss and pallor were the predominant signs occurring in 80 (63%) and 43 (33.8) respectively. Thirteen patients (10.2%) had BMI less than 18.5kg/m2. The mean spot urine albumin to creatinine ratio (ACR) was 427.67 ± 267.66 (median 389.5 and range 29-1280) mg/g, 47 (37%) had nephrotic range proteinuria (ACR >500mg/g) and 42 (33.1%) had microalbuminuria (ACR of 30 – 299mg/g) [3, 19]. The degree of proteinuria among the patients studied is as presented in Table 3. Hypoalbuminaemia (serum albumin less than 35g/l) was seen in 74 persons (58.3%) with mean serum albumin of 32.66 ± 4.98g/l but the mean total serum proteins was 69.97 ± 7.9g/l and mean serum globulin was 37.31 ± 8.57g/l. Eighteen patients (14.2%) had hyperlipidaemia (serum cholesterol > 6.5mmol/l).The PCV ranged from 27.9 – 47.9% with a mean of 33.9 ± 6.7. Thirty four (34) or 26.8% had PCV less than 30%, another 34 (26.8%) between 30 – 35.9%. The mean total white blood cell count was 5492 ± 261 cells/$mm^3$, with neutrophils 52.16 ± 15.29%. The mean CD4 count was 219.57 ± 89.22cells/ul (range 100 – 464), with 59 (46.5%) within the range 100 – 200cells/ul. The mean serum creatinine was 113.77 ± 72.89umol/l, mean creatinine clearance 68.77 ± 21.22mls/min (range 15.2 – 100mls/min.) with 38 (30%) having creatinine clearance <60mls/min. Sixty seven (52.8%) had mild decrease in GFR (stage 2 CKD) but none of our subjects had stage 5 CKD. The mean serum potassium was 3.81± 0.47mmol/l and 17 patients (13.4%) had hypokalaemia (serum potassium less

**Table 2: Major Symptoms and Signs Among Patients with Renal Disease**

| Symptoms | | Signs | |
|---|---|---|---|
| Nocturia | 43 (33.8%) | Weight loss | 80 (63.0%) |
| Low urine | 43 (33.8%) | Pallor | 43 (33.8%) |
| Frothy urine | 38 (30.0%) | Hypertension | 13(10.2%) |
| Body itch | 29 (22.8%) | Periorbital oedema | 4(3.1%) |
| Leg swelling | 17 (13.4%) | Pedal oedema | 4(3.1%) |
| Vomiting | 17 (13.4%) | Ascites | 1 (0.8%) |
| Facial swelling | 13 (10.2%) | | |
| Hiccups | 13(10.2%) | | |
| High urine | 13(10.2%) | | |
| Abd. Swelling | 1 (0.8%) | | |

*Mean BMI 22.9±3.8kg/m2 (range 16.0-33.0). 13(10.2%) had BMI d"18.5kg/m2*

**Table 3: Distribution of Proteinuria Among Patients with Renal Disease**

| 127 out of 400 (31.8%) had proteinuria. | | | |
|---|---|---|---|
| Degree of proteinuria | | Albumin/creatinine ratio | |
| 1+ | 52 (40.9%) | >500mg/g | 47 (37%) |
| 2+ | 34 (26.8%) | 300 -500mg/g | 34 (26.8%) |
| 3+ | 26 (20.5%) | 30 – 299mg/g | 42 (33.1%) |
| 4+ | 15 (11.8%) | | |
| TOTAL | 127 (100%) | | |

*The mean urine albumin/creatinine ratio was 427.67 ± 267.66mg/g (range 29 – 1280)*

**Table 4: Stages of CKD among Subjects with Renal Disease**

| Stage | Description | GFR mls /min | Number (%) |
|---|---|---|---|
| 1. | Kidney damage with normal GFR | 90 | 22 (17.3%) |
| 2. | Kidney damage with mild decrease in GFR | 60 – 89 | 67 (52.8%) |
| 3. | Moderate decrease in GFR ± Kidney damage | 30 – 59 | 34 (26.8%) |
| 4. | Severe decrease in GFR ± Kidney damage | 15 – 29 | 4 (3.1%) |
| 5. | Kidney failure | <15 | 0 |
| | TOTAL | | 127 (100%) |

than 3.5mmol/l), no patient had hyperkalaemia. Hyponatraemia occurred in 8 persons (6.3%) while hypernatraemia was seen in 4 persons (3.2%). The Pearson correlation statistics showed significant association between occurrence of renal disease and anaemia ($p<0.01$) and low CD4+ T lymphocyte count ($p<0.01$). Also there was significant correlation between ACR and estimated GFR ($p<0.05$).

## DISCUSSION

Sub-Saharan Africa has less than one quarter of the world's population but carries about 70 % of the world's burden of HIV infection with about 2.8 million persons living with HIV/AIDS (PLWHA) in the region [20].

Our study found the prevalence of chronic kidney disease among people living with HIV/AIDS, attending the virology clinic in ABU teaching hospital, Zaria, to be 31.8%. This is lower than 51.8% reported by Agaba et al and 38% by Emem et al from Jos and Ile Ife respectively[14 & 16]. The lower prevalence in this study might be related to the use of highly active anti retroviral drugs in our own patients as opposed to other Nigerian studies quoted above where the patients were anti retroviral naïve (earlier studies have demonstrated improvement in renal function following highly active antiretroviral therapy) [21-23]. In our study, the young productive age group is most affected with a male preponderance. However all our patients were heterosexual and there were no intravenous drug users. Hypertension and peripheral oedema were rare among our patients with renal disease similar to some earlier reports[24]. However, some case control led studies have demonstrated no significant association between hypertension and immune status or antiretroviral therapy[25 - 27]. In some earlier reports, more than 30% of patients with HIVAN presented without peripheral oedema even when serum albumin was reduced to about 22g/l [24 & 28]. Some authors have

suggested that the absence of oedema despite the magnitude of proteinuria and hypoalbuminaemia could be due to increased oncotic pressure probably from hypergammaglobulinaemia which is also responsible for the near normal total serum proteins [24,28].

Our cohort had no intravenous drug users in contrast to the reports from US and Europe[8]. Also in contrast, the reports from America and Europe are based on large scale screening while the reports from Africa are based on small population cohort studies which may not be representative enough to be generalized.

Some earlier reports by Emem *et al* [16] and D'Agatti *et al* [29] found more than 50% of their subjects with BMI <19kg/m$^2$ but our study showed only 10.2%. This may be due to antiretroviral therapy with improved general well being and nutrition. Anaemia and very low CD4 counts were common findings in our study and is similar to earlier reports elsewhere [30 & 31]. Hyperlipidaemia was more common in our patients (14.2%) than in earlier reports (10%) [29 & 32]. This may also be due to the antiretroviral therapy.

End stage renal disease was rare in our study most likely due to the effect of on going therapy [21-23]. There was significant correlation between renal disease and low CD4+ count and anaemia and between estimated GFR and degree of proteinuria. This is similar to reports by Han et al [13] and Emem et al [16]. There was no significant correlation between renal disease and co infection with either hepatitis B or C.

We therefore conclude that renal disease is highly prevalent among HIV infected Nigerians but symptoms and signs of renal disease are uncommon. Anaemia, hypoalbuminaemia, and low CD4+ count are common among Nigerian patients infected with HIV who develop renal disease. Treatment with highly active anti retroviral drugs may prevent progression to end stage renal disease. Although we could not do viral load tests to ascertain the efficacy of the antiretroviral drugs on our patients, majority of those with kidney disease were on the drugs for less than one year. Lack of biopsy reports in this study makes classification of the type of kidney disease impossible.

We recommend that all patients with HIV/ AIDS should be screened for renal disease to ensure early diagnosis and commencement of antiretroviral therapy to prevent progression to end stage renal disease.

## DISCLOSURE

We wish to state that there is no interest to disclose by any of the authors.


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# The Availability of Paediatric Dialysis in Nigeria and Problems Associated with its Delivery

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**ABSTRACT**

Little information exists about the availability of paediatric dialysis in Nigeria. The aim of this study was to carry out a preliminary survey into the availability of paediatric dialysis and determine problems associated with its delivery. A convenience sample of health practitioners was taken using questionnaires distributed to participants at the Nigerian Association of Nephrology and Paediatric Association of Nigeria 2005 conferences. Questionnaires were also sent to health professionals of other identified dialysis centres whose staff were not at the conferences. Thirty–seven dialysis centres in 12 of 36 states and the Federal Capital Authority were identified (most located in commercial urban areas). Nineteen facilities (51.4%) were owned by private organizations, 18(48.6%) by Federal/state Governments. Responses from 26 centres, revealed only 6 dialyzed HIV positive and 13 hepatitis patients. Seventeen (65.4%) claimed to have facilities for dialyzing children (7 Haemodialysis (HD), 5 peritoneal dialysis (PD), 5 both HD and PD), situated where paediatricians were available. Problems included lack of appropriate equipment for HD (limiting it to children over 8 years), shortage of fluids for PD, and financial difficulties of patients. The numbers and spread of dialysis facilities are grossly inadequate. It is recommended that facilities for paediatric dialysis should be improved in established centres, more provision made for HIV/ hepatitis patients, and training in dialysis made compulsory for pediatric residents. A national register of dialysis centres and services they offer should be compiled. Research is needed into innovative ways of overcoming identified problems and funding patient care (including Public-Private Enterprise).

**Keywords:** *Paediatric, Dialysis, Haemodialysis, Peritoneal, Nigeria*

## INTRODUCTION

With the advent of renal transplantation in Nigeria, dialysis has taken on an added importance as dialysis prolongs the lives of people with renal failure while they await transplantation. However renal failure is still a cause of mortality in both adults and children. Rates as high as 46% are reported in children with acute renal failure and 58.3% in those with chronic renal failure [1, 2]. In children in developing countries renal failure occurs mainly as a result of a variety of acquired causes including dehydration from gastroenteritis, infections, and toxicity from traditional medications [1-5]. Prevention of these causes is an important strategy in dealing with paediatric renal disease but this approach is a long-term one. For children in established renal failure, early and appropriate management including the use of dialysis as indicated. However studies show that lack of dialysis facilities or inability to access them is a major factor contributing to the high mortality rate in patients with renal failure [1-7]. Information about dialysis in Nigeria comes mostly from reports of centres located in public facilities. Recently there have been increases in the number of dialysis centres (including private facilities) in the country. However, it is uncertain how many facilities offer paediatric dialysis. This study was a preliminary survey to investigate the

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availability of paediatric dialysis in Nigeria and the problems associated with the delivery of it.

## MATERIALS AND METHODS

A convenience sampling was taken from health practitioners most likely to be involved with patients needing dialysis. These were doctors and dialysis nurses attending the Annual General Meeting and Scientific Conferences of the Nigerian Association of Nephrology and the Paediatric Association of Nigeria 2005. Informed consent was obtained from the participants before the questionnaires were administered. The questionnaire was made up of open and closed questions and contained questions about the status of the respondent (doctor, nurse, paediatrician etc); the location and type of institution the respondent worked in: the management of patients with renal failure at the institution and the type of dialysis facilities (if any) present in the institution. Questions were asked about the type of dialysis facilities that were available for children, ages of children dialyzed, cost of dialysis and problems encountered.

Respondents were asked to name all other health facilities in their localities that they knew performed dialysis. In this way it was hoped to identify dialysis centres in various parts of the country whose personnel were not present at the conferences. Questionnaires were sent by mail or hand delivery together with self addressed stamped envelopes in order to enhance return of the questionnaires. Where no response was received from the dialysis facilities, follow up was done either through personal contact or by sending more questionnaires by mail. Where more than one questionnaire was filled in from individuals working in an institution, information from the questionnaires was collated into one proforma which was then entered into a computer. Variables analyzed included characteristics of the health practitioners, institutions and dialysis centres. Frequencies and cross-tabulations were done using EPIINFO version 6.04

## RESULTS

### Location of Dialysis Facilities (Table I)

Responses were obtained from 64 health personnel of 49 institutions (26 which had facilities for dialysis and 23 which did not). Of the 64 respondents, 23 were paediatricians, 20 adult physicians, 11 general practitioners and 10 dialysis nurses. Thirty-seven dialysis centres were identified by the respondents (Table I). The centres were situated in each of the 6 geopolitical zones of the country but the distribution was uneven as they were located in only 12 of the 36 states of the country and the Federal Capital Territory. Just one dialysis centre was situated in a rural area- the rest were in urban areas, mainly state capitals. More centres were situated in areas of high commercial activity (over a third of the centres were located in the city of Lagos). Nineteen dialysis centres (51.4%) were owned and run by private organizations while the other 18 facilities (48.6%) were run by Federal or State Governments.

### Types of Dialysis Available

Of the 37 identified dialysis centres, completed questionnaires were received from personnel of 26 (70.3%) institutions. Despite repeated attempts, no response was obtained from 11(29.7%) centers all of which were private health facilities situated in major cities. Of the 26 dialysis centres from which completed questionnaires were received, 12 (46.2%) were located in University Teaching hospitals, 5 (19.2%) in private hospitals, 4(15.4%) in State government hospitals, 2 (7.2%) in Military institutions, 2(7.2%) in health facilities of multinational Corporations and 1(3.6%) in a Federal tertiary hospital. Both haemodialysis (HD) and peritoneal dialysis (PD) were available in 13(50%) of the 26 centres; HD alone in 12 centres (46%) and PD alone in one centre. However only half (13) of the centres dialyzed hepatitis B positive patients, and 6 (23.1%) dialyzed HIV positive patients.

Haemodialysis was carried out for patients with chronic renal failure (87.5%) and acute renal failure (79.2%). The numbers of patients dialyzed varied greatly depending on the institution with most centres dialyzing between 11 to 50 patients a month (range 1 to 720) at a cost varying from N3,000 (US$30 at the time of the study) to N40,000(US$400) per session. Thirteen (50%) of the centres were open all day, while the rest operated for only for part of the day (usually 12 hours) and were closed at weekends. Peritoneal dialysis (83.3%) was done mainly for patients with acute renal failure. The numbers of patients dialyzed varied from 0 to 4 per month. The total cost varied from N3,500 (US$350) to N100,000(US$1,000). Only one institution carried out Continuous ambulatory peritoneal dialysis (CAPD) for patients with chronic renal failure. No

institution offered Continuous Cyclic Peritoneal Dialysis (CCPD).

**Availability of Paediatric Dialysis (Figure I)**

Seventeen (65.4%) out of the 26 dialysis centres reported that they could carry out paediatric dialysis. These were mainly government institutions (i.e. 12 University Teaching hospitals, 1 Federal tertiary hospital, 1 State government hospital) as well as 3 private hospitals. Dialysis was used mainly for children with acute renal failure. Five (19.2%) institutions could carry out both HD and PD, 7 (26.9%) only HD and 5 (19.2%) acute PD only. In all these hospitals the services of paediatricians were available either on a full time or part time basis. However no institution had special Haemodialysis units for children. Children needing HD were dialyzed in centres primarily set up for adults. Of the 10 institutions carrying out PD, 8(80%) did them only on children 2 years and older. No centre carried out Continuous Ambulatory Peritoneal Dialysis (CAPD), or Continuous Cyclic Peritoneal Dialysis (CCPD) for children.

**Problems Associated With Paediatric Dialysis**

The commonest problem which all (100%) units complained about was financial difficulties experienced by most of the patients needing dialysis. Difficulty in obtaining suitable equipment for dialyzing children was another major problem. . Ten (83.3 %) of the 12 HD centres had difficulty in obtaining the necessary equipment for HD (dialyzers and suitable blood lines) and 8 (66.5%) with the creation of arteriovenous shunts. The majority 10 (83.3%) of haemodialys centres were unable to dialyze children less than 8 years though 2 centres stated they could dialyze children as young as 4 years

All 10 centres which carried out peritoneal dialysis complained of having problems in obtaining peritoneal dialysis fluids and 9 (90%) in obtaining appropriately sized peritoneal catheters for access into the peritoneal cavity. One centre used nasogastric feeding tubes instead.

## DISCUSSION

In a country of over 120 million citizens, health professionals were only able to identify 37 institutions which performed dialysis. This is an indication that the number of dialysis facilities is grossly inadequate. Further the distribution of the centres was uneven as most of them were located in urban areas of high commercial activity. Generally in Africa (as in this study), most dialysis centres are situated in urban areas making access difficult for patients from rural areas[8]. Inadequate dialysis facilities or lack of access to them is reported to be a major problem for children with acute renal failure. In their study Anochie and Eke from Southeast Nigeria found that only 22% of children requiring acute peritoneal dialysis received it while Olowu in the Southwest got an even lower access rate of 10.9%[1,7]. Children with chronic renal failure are usually treated conservatively because there are no permanent facilities for chronic dialysis[2, 3,9] e.g. Michael and Gabriel in Benin, Midwest Nigeria reported that lack of dialysis facilities resulted in a mortality rate of over 50% in children with chronic failure over a five year period[2]. There is little information about paediatric dialysis in the North of the country[10].

Various factors appeared to affect the availability of paediatric dialysis. Lack of appropriate equipment and/or supplies was a major problem and affected paediatric dialysis e.g. haemodialysis (HD) was limited to older (and bigger) children because of difficulty in obtaining appropriate sized dialyzers. Shortage of dialysis fluids also adversely affected peritoneal dialysis (PD). Thus there is a need to improve facilities for dialysis of children in already existing centres. This includes providing more facilities to dialyze patients with HIV and hepatitis as the rising incidence of children with HIV and hepatitis makes it likely that there will be an increase in numbers of patients with these conditions requiring dialysis[11,12].

Paediatric dialysis was only carried out in centres where the services of paediatricians were available. This could simply reflect the fact that very sick children are usually referred to paediatricians but it is reasonable to infer that the presence of paediatricians affected availability of paediatric dialysis though further research is needed to determine whether this is actually the case.

More centres offered HD than PD and this may have been another factor affecting availability of paediatric dialysis as PD is the preferred mode of dialysis for children in both acute and chronic renal failure[13]. PD is generally cheaper, simpler to perform than HD, does not need extensive training and can be done without sophisticated expensive equipment[14] but despite a study that showed chronic PD is feasible in an African setting[15], only one centre carried out CAPD and this was just for adults. Surprisingly in

some centres the cost of performing PD was higher than that of HD but it was outside the scope of the study to determine the reason for this.

Availability of dialysis in Africa depends on funding and donors[8]. In this study about half of the dialysis facilities were privately funded which means the private sector cannot be ignored and the possibility of Public-Private Enterprise needs to be seriously considered. But it should be noted that paediatric dialysis was mainly carried out in government funded facilities. Thus it may be necessary to encourage more private facilities to consider providing facilities for paediatric dialysis. However whether dialysis is performed by private or public facilities, one issue to be addressed is finance as this was the commonest problem identified by all the centres who complained that their patients had financial difficulties. The source of patient funding could not be adequately investigated in a study of this nature but financial difficulties is a major problem which has resulted in patients discontinuing or receiving insufficient dialysis[1-3,6-9,16,17]. The government is the obvious candidate to subsidize patient care but in countries where the major or total cost of treatment is borne by them, rationing of dialysis is the inevitable result[18]. Other sources of funding to support patient care thus need to be explored. These include various types of insurance schemes (community, government and private), as well as donations from private individuals including celebrities and multinational corporations. But before seeking funding from them it will be necessary to create or increase public awareness about the need for paediatric dialysis.

The study was limited in that it was based on information given by participants and some responses were estimates e.g. the numbers of patients dialyzed and the amounts patients spent on dialysis. These responses may not reflect actual costs as other expenses e.g. cost of accommodation, drugs and travel expenses may not have been taken into account. The total cost of dialysis can only be verified by records of actual patient care from the various health facilities and interviews with patients. Further it is possible that some dialysis centres were not identified. This could have affected the information obtained about paediatric dialysis. However the need to increase the number and spread of dialysis centres for both adults and children and of improving facilities for paediatric dialysis in already established centres is highlighted.

It is recommended that a national register of all dialysis centres in the country and the services they offer should be compiled and updated regularly. Training in dialysis techniques should also be made compulsory for all pediatric residents. Innovative, sustainable ways of ways of overcoming the challenges identified in this study must be found. Research is of vital importance to assist in healthcare planning of children with renal disease. This includes compiling statistics Nationwide determining the need for paediatric dialysis as well as the acceptability or otherwise of dialysis and renal transplantation among parents. This is because in a world of economic realities it is observed that some caregivers feel that it is cheaper to have another child than struggle along with one with a chronic problem.

With passage of time, more dialysis facilities have been and will be set up. It is important that these centres be made aware of the need to provide facilities for paediatric dialysis. Situational analysis, advocacy and activities to increase awareness are best carried out by the Nigerian Association of Nephrology and would greatly improve the care of children with renal disease in Nigeria.

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# Effect of Prolonged use of Angiotensin Converting Enzyme Inhibitor in Children with Nephrotic Syndrome: A Preliminary Report


## ABSTRACT

We report 7 children with nephrotic syndrome (NS) in whom oral angiotensin converting enzyme inhibitor (ACEI) therapy was tried. Six of these children had steroid resistant nephrotic syndrome, while one of them had frequently relapsing nephrotic syndrome. Out of the 6 that were steroid resistant, 1 of them had minimal change lesion, 2 of them had focal and segmental glomerulosclerosis (FSGS) and had received cyclophosphamide for 8 weeks, yet developed relapse. Three of them refused renal biopsy. Amongst the 3 patients who received ACEI for 3months -1year, there were a total of 4 relapses. Among the 4 patients who received it for 2 - 5years, one relapse was recorded. It is postulated that ACEI may be a potent alternative therapy in the management of steroid resistant or frequently relapsing NS. This may be a plausible answer to the numerous side effects of cyclophosphamide and other drugs used in the management of steroid resistant NS.


## INTRODUCTION

Steroids has remained the mainstay of treatment in nephrotic syndrome (NS), even though resistance to it is well documented.[1] Steroid resistant NS continues to pose therapeutic problems and many alternative drugs such as cyclophosphamide, chlorambucil, levamisole, cyclosporin, and angiotensin converting enzyme inhibitors (ACEI) have been tried under these circumstances.[2, 3] The effect of these drugs have varied and many of them have several drawbacks and side effects. Cyclophosphamide has to be cautiously administered in children because of the side effect of sterility in later life. Cylosporin has been found to be effective for as long as it is administered but relapses occurs once it is discontinued. The effectiveness of levamisole still remains doubtful, even though it may be beneficial if it is administered over a long period. The implication of all these is that there is yet no cure for nephrotic syndrome, hence the search for a better drug continues. A decrease in proteinuria following administration of angiotensin converting enzyme inhibitor has been documented in animal models, patients on treatment for hypertension and diabetic patients with proteinuria. Most of these observations were made in adults with few trials in children. We therefore report our observations in 7 children with steroid resistant NS who have reduced number of relapses and more clinically stable since being on ACEI for between 3-51months.

## MATERIALS AND METHODS

Children attending the Paediatric nephrology clinic of the University of Ilorin Teaching hospital, Ilorin who fulfilled the following inclusion criteria were recruited for the study. The criteria included presence of proteinuria of 3+ and above, resistance to daily divided dose of prednisolone 60mg/m$^2$ given over a month, occurrence of relapse after administration of eight weeks of daily oral cyclophosphamide 3mg/kg, refusal of renal biopsy in patients who were steroid resistant and frequently relapsing NS (occurrence of relapse of more than thrice in a year). All steroid responsive patients were excluded. Children were diagnosed to have nephrotic syndrome based on standard criteria. They were commenced either on lisinopril 5mg daily for those less than 5 years and

10mg daily for those older than 5years. Where lisinopril was not available, they were commenced on captopril 0.5mg/kg/dose thrice daily, hence a few of the patients had a mixture of captopril and lisinopril based on which was readily available in the market. The children were managed over a period ranging from 3 months – 51months.

Outcome variables sought included number of relapses during the period of administration of the drug, remission of proteinuria, The latest biochemical results and observed or reported side effects were also recorded.

## RESULTS

A total of 5 males and 2 females met the inclusion criteria. Only one had frequently relapsing NS though steroid responsive, while the other 6 had steroid resistant NS. Out of the 6 that were steroid resistant, 1 had minimal change lesion, 2 had focal segmental glomerulosclerosis (FSGS) and those 2 had received cyclophosphamide for 8 weeks. (Table 1)

proteinuria in 5 patients, while the other 2 had traces of protein.

Amongst the 3 patients who received ACEI for 3months -1year, there were a total of 4 relapses. Among the 4 patients who received it for 2 - 5years there was one relapse in a patient (Figure I).

**Fig. 1:** Relationship between the duration of ACEI therapy and number of relapses in the study population

**Table 1: Characteristics of children in the study population**

| Patient No. | Age(yr.) | Steroid Status | Diagnosis | Side effects |
|---|---|---|---|---|
| 1 | 11 | SR | MCNS | Nil |
| 2 | 2 | SR | NS | Nil |
| 3 | 7 | SR | FSGS | Nil |
| 4 | 21 | FR | MCNS | Nil |
| 5 | 8 | SR | NS | Nil |
| 6 | 9 | SR | NS | Nil |
| 7 | 10 | SR | FSGS | Nil |

*SR-Steroid resistant, FR-Frequently relapsing NS,*

*NS- clinically diagnosed nephrotic syndrome*

As three parents refused renal biopsy, the histological characteristics of their lesions are not known. They were not commenced on cyclophosphamide, but were commenced on a trial of oral ACEI. There were a total of 5 relapses in all the patients, no side effect of the drug was reported in any of the children (Table 1). There was also no episode of hypotension observed and biochemical indices were normal (Table 2). There was no

The relapses occurred within 1-8 months after commencement of ACEI in the 4 affected patients (Table 2).

## DISCUSSION

Historically, a decrease in proteinuria following pharmacologic angiotensin converting enzyme inhibition has been documented in animal models and observed in patients receiving ACEI for treatment of

**Table 2: Duration of ACEI therapy, relapses and biochemical results in the study population**

| Pt No. | Duration of ACEI (months) | Relapses | Duration of ACEI before relapse (months) | Pre-ACEI Proteinuria | Post-ACEI Proteinuria | Sod. | Pot. | Urea | Creat. |
|---|---|---|---|---|---|---|---|---|---|
| 1 | 12 | 1 | 5 | 3+ | nil | 134 | 4.0 | 9.4 | 42 |
| 2 | 3 | 1 | 1 | 3+ | trace | 138 | 2.9 | 7.8 | 47 |
| 3 | 8 | 2 | 3.6 | 3+ | trace | 132 | 3.4 | 6.6 | 67 |
| 4 | 51 | - | | 3+ | nil | 134 | 4.7 | 7.6 | 70 |
| 5 | 3 | - | | 3+ | nil | 132 | 4.2 | 5.7 | 56 |
| 6 | 16 | 1 | 8 | 3+ | nil | 138 | 4.3 | 9.0 | 52 |
| 7 | 40 | - | | 3+ | nil | 128 | 4.5 | 8.0 | 56 |

*Sod- Serum Sodium, Pot- Serum Potassium, Urea- Serum urea, Creat. –Serum Creatinine.*

*Serum sodium, potassium, and urea are in mmol/l, while serum creatinine is in μmol/l.*

*Pre-ACEI proteinuria indicates proteinuria before commencement of ACEI.*

*Post-ACEI proteinuria indicates proteinuria at the expiration of the duration stated against each patient.*

hypertension, in diabetic patients with proteinuria and more recently in patients with other renal diseases.[4] Several works have since followed mostly in the adult population with a few done amongst children. Some of the studies in children used few patients like we did, hence the deduction from the studies could be inconclusive. Our finding of reduction in proteinuria agrees with their work, though our analyses were based on qualitative assessment of proteinuria.[5-11]

One of the studies in children examined the effect of combination of ACEI and angiotensin receptor blocker (ARB) on proteinuria, which we did not do. Glomerular hypertension, hyperfiltration and proteinuria contribute to the progression of renal insufficiency in Nephrotic syndrome[12, 13]. Furthermore, ACEI inhibit the angiotensin-II mediated synthesis of such local growth factors as transforming growth factor B and platelet derived growth factor and thus reduce glomerular sclerosis and extracellular matrix expansion.[14-16] ACEI not only reduced glomerular hypertension but also prevent the urinary protein losses and the development of glomerular sclerosis. Further postulated mechanisms by which ACEI preserve renal function in various proteinuric kidney diseases such as NS include a decrease in intraglomerular filtration pressure, improvement in glomerular size and charge selectivity [17, 18] Proteinuria is an independent risk factor for renal disease progression, most likely because of a toxic effect on the tubulointerstitial compartment leading to interstitial scarring [19, 20, 21, 22].

The patients in our small series have mostly received the drug for varying long periods with no untoward effect observed, the renal function stabilized and no hypotension reported. This is in agreement with the findings of Ravid [23], and Lebovitz [24] where reduction in proteinuria and stabilized renal function were achieved in patients with renal disease in Type 2 diabetes.

Our study is significant because it is carried out among black children living in Nigeria, Africa and remarkable response has been observed which can be translated to action.

Unanswered question however remains; What happens if the ACEI is stopped? How long does it

take for remission to be achieved? As the therapy advanced further, will there be side effects?

While we continue this investigation in more children in our center, we are recommending further studies on a larger population in other centres. If similar finding such as ours is found, ACEI may then be of beneficial effect in steroid resistant NS and Frequently relapsing minimal change NS.

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