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Prevalence of hepatitis B and C viruses in pre-dialysis patients with chronic renal failure

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Summary
CRF affects people in their prime of live; they are often the Nation's workforces thereby leading to severe economic and social problems. Many patients with CRF who need dialysis, present for the first time in end stage renal failure. The commonest causes of CRF in Nigeria and other tropical countries have been reported to be hypertensive nephrosclerosis and chronic glomerulonephritis. Various studies in and outside Nigeria have documented an increased seroprevalence of anti-HCV and HBsAg in chronic renal failure patients on maintenance haemodialysis. Any association established between these viruses and CRF would suggest that the prevention and /or treatment of these viruses may likely lead to a reduction in the prevalence of CRF. Thus, forty-five (45) consecutive subjects with CRF and (45) age– and sex– matched control subjects who satisfied the eligibility criteria for the study were enrolled. Marker of HBV (HBsAg) was assayed using HUMAN Enzyme linked Immunosorbent Assay (ELISA) Test. Marker of HCV (anti-HCV) was determined using the HUMAN ELISA Test. The mean age of the subjects was 37 ± 14 years (range 17 to 62 years) while the mean age of the control subjects was 38 ± 14 years (range of 18 to 66 years). There were no statistically significant differences in the prevalence of HBsAg and anti- HCV in the CRF patients and controls P=0.74 and *P*=1.0 respectively. Although, the sample was small anti- HCV seropositive CRF patients were significantly younger than anti-HCV seropositive controls *P*<0.027. In conclusion, this study has shown that there were no significant differences in the prevalences of HBsAg and anti- HCV in the CRF patients and controls. A larger scale study may be more desirable in defining the role of these viruses in patients with chronic renal failure.

Keywords: *Prevalence: HBV/HCV: CRF*

Résumé
Le défici renal chronique affectent les gens dans leur jeunesse, qui representent la force de la nation ainsi condusant des serieux probléme economique et sociaux. Plusiuers patients ayant la defici Renal Chronique ont besion de la dialyse comme dermiere étape de difici renal. Les causes au Nigeria et dans d'autre pays tropicaux sont bien documentes. L'hypertension, la nephro - sclerose et la glomerulonephrotique chronique. Differents etudes a l intenieure et exterieure du Nigeria ont documentees une augmentation de la seroprevalence de de l'anti HCV et HBs Ag chez les patients ayant des defici renal chronique sur maintenace hemodialyse. Une association entre ces virus et le defici renal chronique suggerait que la prevention et le traitement de ces virus peut conduine a une reduction dans la prevalence de defici renal chronique quarante cinq patients consecutive ayant de defici renal chronique d'age et de sex controllés inclu dans cette etude. Le markeur de HCV (HBs Ag) etait analyse utilisant l'enzyme Human lie au analyse de l'immunosorbent (Elisa). La markeur HCV (anti-HCV) etait determine utilisant le test Elisa Human. La moyenne d'age chez test adults etait de 37+14 ans (marge 17 – 62 ans) et chez les groupes de controle etait de 38 ± 14 ans (entre 18.66 ans). Il n'y avait pas de différence statistique significant entre la prevalence du HbsAg et l'anti – HCV chez les CRF et subjects de controle p=0.74 et p=1.0 respectivement .Bien que l' échantillon etait reduite en date-HCV seropositif patients etaient significanment Jeune que l'ante-HCV séropositive chez les controles P< 0.027. In conclusion, cette etude a demontre qu ils n'avaient pas de différence significante entre la prevalence du HBs Ag et l'anti-HCV chez les patients et le controles. Une large étude peut etre désirable pour définir le role de ces virus chez ces maladies.

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Introduction

Chronic renal failure (CRF) is characterised usually by progressive and irreversible deterioration in renal function with most patients progressing to end stage renal failure (ESRF). CRF affects people in the prime of their lives thereby leading to severe economic and social problems with disruption of family life, work and social activities [1,2]. Many patients with CRF who need dialysis present for the first time in end stage renal failure making etiological diagnosis and treatment very difficult. The commonest causes of CRF in Nigeria and other tropical countries have been reported to be hypertensive nephrosclerosis and chronic glomerulonephritis (CGN) [1,3,4]. Worldwide, the prevalence of glomerulonephritis (GN) as a consequence of various infectious agents in developing countries makes it the commonest cause of end-stage renal failure (ESRF) [5].

Various studies in and outside Nigeria have documented an increased seroprevalence of anti-HCV and HBsAg in chronic renal failure patients on maintenance haemodialysis [6,7]. It has been suggested that this high prevalence is a consequence of both parent (blood transfusions) and intradialytic transmission [6]. Such association may therefore, suggests that HCV and HBV might be important etiological agents in the pathogenesis of glomerulonephritis and CRF. On the other hand, CRF patients may be more susceptible to HCV and HBV infections as a result of deterioration in their immunity.

The magnitude of the existing burden of illness caused by renal failure, the projection for increasing incidence of ESRD and the limitations of our existing treatments for renal failure all point to the need for clinical and population based interventions aimed at prevention of ESRD. We therefore assessed the prevalence of HCV and HBV viruses among predialysis CRF subjects in UCH in an attempt to establish a relationship between these viruses and CRF.

Materials and methods

The study was carried out in the Renal Unit of the Department of Medicine, University College Hospital, Ibadan. Forty-five (45) consecutive subjects with CRF and (45) age– and sex–matched control subjects who satisfied the eligibility criteria for the study were enrolled. CRF was defined by persistent

elevation of plasma creatinine above 2mg/dL (176.8 μmol/L), bilateral shrunken kidneys on ultrasound except in diabetic nephropathy, autosomal dominant polycystic kidney disease, obstructive uropathy, where renal size may be normal/increased with loss of corticomedullary differentiation and increased parenchymal echogenicity and presence of clinical features of uraemia such as body weakness, anorexia, nausea and vomiting. Other features that suggest CRF included anaemia, hypertension and bone disease. Patients who satisfied the above definition of CRF and requiring first dialysis were recruited into the study if they gave written/oral informed consent. Patients were excluded from the study if they had features of acute renal failure with acute deterioration in renal function and normal sized kidneys and echogenicity on ultrasound or patients with history of hepatitis B vaccination and patients with history of blood transfusion and scarification marks. Control subjects were healthy adults most of whom were patient's relations, they were recruited if they had normal blood pressure with no urinary abnormalities such as proteinuria, microscopic haematuria, cellular / granular casts and no history of hepatitis B vaccination, blood transfusion and scarification marks. Any subjects recruited as control with any of the above features were excluded from the study.

Ethical approval for the study was sought and obtained from the Joint University College Hospital/University of Ibadan Ethical Committee. History was taken from the patients and/or relatives and a complete physical examination was performed on each patient. These were tailored towards determining the underlying aetiology of CRF. Investigations carried out on the patients include 12 lead Electrocardiography, renal ultrasound, serum electrolytes and urea, creatinine, total protein and albumin, full blood count and fasting blood sugar. Fresh urine was collected from subjects and controls, centrifuged and the deposit viewed under the microscope. 24-hour urine sample was collected. Ten milliliters (10mL) of venous blood was collected from the antecubital vein of each patient and control subject. Sera were separated by centrifugation at 4000rpm and stored at – 20°C till seroanalysis. Marker of HBV (HBsAg) was assayed using HUMAN Enzyme linked Immunosorbent Assay (ELISA) Test. Marker of HCV (anti-HCV) was determined using the HUMAN ELISA Test, which is a 3rd generation kit.

Creatinine clearance was calculated using the formula:

$$\text{Creatinine clearance (ml/min.)} = \frac{UV}{P}$$

Where,

U is the urinary creatinine concentration

V is the volume of urine collected over 24 hours

P is the plasma creatinine level.

Patients with detectable proteinuria equal to or greater than 2+, age less than 35years, history of previous body swelling, presence of haematuria, red cell, and granular casts were classified as having chronic glomerulonephritis. Patients with previous history of hypertension, presence of trace or 1+proteinuria and no cast were classified as having hypertensive nephrosclerosis. Patients with markedly elevated blood pressure and presence of retinal exudates; hemorrhages and/or papilloedema were classified as having malignant hypertension. Patients with history of diabetes mellitus, proteinuria, diabetic retinopathy and normal or increased renal sizes on ultrasound were classified as having diabetic nephropathy. Patients with history of significant urinary obstruction were classified as having obstructive uropathy.

The statistical computer package EPI-Info version 6.0 was used for data analysis. For comparing prevalence (frequency) data between different population (subjects and controls) and different sub groups of the same population (seronegative and seropositive subjects), chi-square test was used with Yates continuity correction applied as appropriate. Student t test was used to compare mean values of two separate groups. A p-value < 0.05 was considered significant. All p-values were calculated as two-tailed.

Results

Forty-five (45) patients (29 males, 16 females) with chronic renal failure and 45 age- and sex-matched control subjects were studied. The mean age of the subjects was 37 ± 14 years (range 17 to 62 years) while the mean age of the control subjects was 38 ± 14 years (range of 18 to 66 years). The mean (S.D) of the laboratory parameters of both subjects and controls are shown in table 1. Using the criteria in the methodology, the presumptive etiological classification is show in Table 2. Table 3 shows the intra/inter group comparison of the distribution of HbsAg status in subjects and control. In both cases, more males than females were HBsAg positive. The difference in the frequency of positive HbsAg did not reach statistical significance (x^2 = 0.1, P = 0.74). The mean age of patients who were HBsAg positive was (34 (14) years while the mean age (S.D) of patients who were HBsAg negative was (38 (14) years. This difference did not reach statistical significance (P = 0.7). The mean age (S.D) of the control group who were seropositive for HBsAg was 46 (15) years while in those who were seronegative, it was 36 (14) years. There was a statistical significance difference between the ages (P =0.0016). When patients and control subjects who were HBsAg positive were compared, there were no statistically significant differences in their mean ages (P = 0.18).

Table 1: Laboratory indices of patients and control

Parameters	Mean Values (*S.D.)	
	Subjects	Controls
Na^+ (mmol.L)	130 (6)	133 (25)
K^+ (mmol/L)	5 (1)	4 (1)
Cl- (mmol/L)	99 (1)	99 (20)
HCO_3^- (mmol/L)	18 (3)	22 (4)
Urea (mg/DL)	239 (69)	34 (15)
Creatinine (mg/dL)	15 (7)	1.2 (0.4)
Ca^{2+} (mg/dL)	8 (1)	9.1 (2)
Uric acid (mg/dL)	11 (4)	5 (2)
Phosphate (mg/dL)	7 (3)	3.7 (1)
PCV (%)	21 (5)	39 (10)
Creatinine clearance (ml/min)	5 (4)	98 (6)

*S.D - Standard deviation

Four (9%) of the patients with CRF and four (9%) of the control were anti-HCV positive. There was no statistically significant difference in the frequency of occurrence of anti-HCV (P = 1.0). The mean (S.D) age of patients with CRF who were anti-HCV positive was 34 (7) years. This did not differ significantly from the mean age of patients (38 (14) years who were seronegative (P = 0.55). The mean age of control subjects who were anti-HCV positive was significantly higher than the mean age of anti-HCV seronegative controls (52 (7) years; vs (36 (14) years, (P= 0.027) (Table 4).

Table 2: Presumptive aetiology and gender distribution of subjects with CRF

Aetiology	No. of patients %	Male	Females	Mean Age (yrs)
Chronic glomerulonephritis	21 (47)	13	8	31.5
Malignant hypertension	6 (13)	5	1	38.7
Hypertensive nephrosclerosis	9 (20)	6	3	57
Obstructive uropathy	1 (2)	1	0	43
Diabetic nephropathy	2 (5)	1	1	58.5
Unknown aetiology	6 (13)	3	3	28.8

Table 3: Comparison of Hbs Ag status in subjects and controls

	HBs Ag Status (subjects with) CRF		HBsAg Status of controls	
	Negative (%)	Positive (%)	Negative (%)	Positive (%)
Mean age (S.D) Years	38 (14)	34 (14)	36 (14)	46 (15)
Gender				
Female	15 (38.5)	1 (16.7)	14 (35)	2 (40)
Male	24 (61.5)	5 (83.3)	26 (65)	3 (60)
Total Number	39 (86.7)	6 (13.3)	40 (89)	5 (11)

HBs Ag positive: Age- subjects vs control, P = 0.00016
Proportion - subjects vs control, P = 0.074

Table 4: Comparison of Anti-HCV status in subjects and controls

Parameters	Anti-HCV Status of Subjects with CRF		Anti-HCV Status of Controls	
	Negative (%)	Positive (%)	Negative (%)	Positive (%)
Mean age (S.D) Years	38 (14)	34 (7)	36 (14)	52 (7)
Gender				
Female	16 (39)	0 (0)	15 (37)	1 (25)
Male	25 (61)	4 (100)	26 (63)	3 (75)
Total	41 (91)	4 (9)	41 (91)	4 (9)

Anti-HCV positive- Age- subjects vs control, P = 0.0093
-Proportion- subject vs control, P = 1.0

All the four anti-HCV seropositive patients were males. Three (3) males and one female in the control group were anti-HCV seropositive. When CRF patients and controls who were anti-HCV positive were compared, there was a statistically significant difference in the mean age of patients who were seropositive (34 (7) years, compared with controls that were seropositive (52(7) years, $P = 0.0093$.

Discussion

In this study, a male preponderance was found amongst patients with chronic renal failure giving a male to female ratio of 1.8:1. Also the mean age (S.D) of patients studied was 38 (14) years. The findings were similar to that reported by previous workers [1,2] This lends support to the fact that CRF affects people in their productive years in Nigeria leading to severe economic and manpower wastage. The trend here contrasts with what obtains in the Western countries where the incidence of end-stage renal failure has been found to increase with age [7,8]..

Attempts were made at classifying patients with CRF into different aetiological groups based on the clinical presentation, urinalysis, urine microscopy and renal ultrasound findings. However, the pathognomonic features are not always present which makes classification sometimes difficult. For example, the absence of cellular casts does not rule out CGN and extensive glomerulosclerosis may lead to reduction in urinary protein excretion. Also, most of the patients present in ESRD when differentiation by aetiology may be difficult even by renal biopsy.

The frequency of occurrence of HBsAg in the CRF patients did not differ significantly from that in the control subjects. Perhaps if the seroprevalence of antibody to HBsAg (anti-HBs) and antibody to core antigen (IgG anti-HBc), which are measures of past exposure to HBV, were determined the result might have been different. In some studies of hepatitis virus infection (HBV and HCV), prevalence rates of HBsAg, anti-HBs, anti-HBc were found to be 1.6%, 18% and 37% respectively [9]. However, this present study did not estimate the prevalence of anti-HBs in the patients and control group due to reason of cost.

The HBsAg seroprevalence of 11% obtained in the control group in this study is comparable to 6 – 12% obtained in blood donors in Nigeria and 8% in University freshmen at Ife [10,11]. . However, the prevalence of HBsAg in blood donors may not be representative of the population at large since most of the donors were below 40 years. The high prevalence of HBsAg in the control subjects shows that HBV is still prevalent in Nigeria and efforts should be made to prevent HBV infection by active immunization.

The prevalence of HCV infection in CRF patients varies according to geographical location and the diagnostic methods used. Reported prevalence rates of anti-HCV in CRF patients on chronic haemodialysis (HD) vary between 2-47% [6,12,13]. Agbaji in Jos reported a prevalence of 22.2% in CRF patients on chronic haemodialysis compared to 6.4% in the control [6]. This high prevalence of antibodies in chronic HD patients is thought to represent HCV infection by blood transfusion and/or intradialytic contamination. The prevalence is known to increase with the number of units of blood transfused and the duration on dialysis.

The frequency of occurrence of anti-HCV in predialytic CRF patients in this study was 9%. This finding was within the previously reported range of anti-HCV seroprevalence of 0 to 18% in predialytic CRF patients [14]. The frequency of occurrence of anti-HCV in the controls was also 9%. The equal frequency of occurrence of anti-HCV in the patients and controls may suggest that HCV has no significant aetiologic role in the patients that were studied. There is a likelihood that the ELISA method used in this study may underestimate the prevalence of HCV infection in CRF patients since patients may not be able to mount antibodies to the infection as a result of immune depression in CRF. In this setting, determination of the HCV-RNA level in the circulation will give a better indication of HCV infection in CRF patients. The frequency of occurrence of anti-HCV of 9% in the control group is greater than 6.4% reported by Agbaji [6] but lower than 12% and 11% reported

by Olubuyide *et al* in blood donors and health workers respectively [15].

The prevalence of anti-HCV is higher in males than females in the CRF group, this trend has been observed in some studies. However, the lifetime risk of HCV infection is generally considered to be the same for both sexes if all other risk factors and confounders are taken into account. In the CRF patients, the mean age of those who were positive for anti-HCV though lower did not differ significantly from the mean age of those who were negative. This is in contrast to what was reported by Garci-Valdecasas *et al* who documented a higher prevalence of anti-HCV in CRF patients older than 50 years when compared to the normal population [16]. The mean age of the control subjects who were positive was significantly higher than the mean age of seronegative controls, this might relate to a higher frequency of exposure to HCV infection over time or to deterioration in immunity associated with age. The mean age of patients who were anti-HCV positive was significantly lower than the mean age of the control subjects who were seropositive, the same trend was noticed in between subjects and controls who were positive for HBsAg. None of the patients with CRF or control subjects had combined HBsAg and anti-HCV positivity. This inverse relationship between HBV and HCV seropositivity has been demonstrated by in vitro work which indicates that the HCV structural proteins, in particular the core protein, may interfere with expression and replication of the HBV genome in the absence of host factors [17].

In conclusion, this comparative hospital-based study has shown that there were no statistically significant differences in the prevalences of HBsAg and anti- HCV in the CRF patients and controls. Also, none of the patients and controls was positive for both HBsAg and anti-HCV. In addition anti- HCV seropositive CRF patients were significantly younger than anti-HCV seropositive controls, it should however be noted that the sample in this study was small. A larger scale study may be more desirable in defining the role of these viruses in patients with chronic renal failure.

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