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Hepatitis C virus infection in Nigerians with diabetes mellitus**¹Olokoba A.B., ²Badung L.H., ³Abdulrahman M.B., ²Salawu F.K., ²Danburam A.,****⁴Aderibigbe S., ²Midala J., ²Tidi S.K.**¹Department of Medicine, ³Department of ChemicalPathology, ⁴Department of Epidemiology & Community Health, University of Ilorin Teaching Hospital, Ilorin, Nigeria.²Federal Medical Centre, Yola, Nigeria.**ABSTRACT**

It has been reported from several Caucasian studies that there is an epidemiological association between hepatitis c virus infection and diabetes mellitus. The objective of this study was to determine whether any such relationship exists in a black African population. To determine the prevalence of Hepatitis C virus infection in Nigerians with diabetes mellitus in North-Eastern Nigeria. Hospital –based cross-sectional study. Medical out- patient clinic and the Blood bank of the Federal Medical Centre, Yola. Nigeria. From June, 2008 to December 2009, Two hundred and eighty consecutively recruited diabetes mellitus patients comprising 108 males and 172 females were screened for HCV infection. These were compared with five hundred and ninety-five voluntary blood donors who were screened during the same period. Serological testing for HCV infection was carried out with anti-HCV using Enzyme Linked Immuno-sorbent Assay (ELISA) method. The bio-data of the patients, history and duration of diabetes mellitus, history of jaundice, blood transfusion were recorded on a proforma. Out of the 280 diabetes mellitus patients tested, twenty-six were positive for anti-HCV antibodies giving an infection rate of 9.3% compared with fourteen subjects out of 595 voluntary blood donors 2.4% (p=0.0000105). History of blood transfusion, and jaundice was positively correlated with presence of HCV infection in diabetic patients. Hepatitis C virus is more common in Nigerian patients with diabetes mellitus than in non-diabetic control subjects. It may be necessary to screen patients with diabetes mellitus for hepatitis c virus infection particularly those with history of blood transfusion and jaundice.

Keywords: Hepatitis C virus, diabetes mellitus, anti-HCV, Nigeria**INTRODUCTION**

Diabetes mellitus (DM) is a metabolic syndrome of multiple aetiologies characterised by chronic hyperglycaemia with disturbances of carbohydrates, fat and protein metabolism resulting from defects in insulin secretion, insulin action or both (Olokoba *et al*, 2007). DM may result from the destruction of the beta cells of the pancreas with consequent insulin deficiency or resistance to insulin action at the receptor site (Olokoba *et al*, 2007). DM can be broadly classified into type 1DM, type 2 DM, gestational DM, and other specific types of DM (Olokoba *et al*, 2007).

Type 2 DM accounts for over 90% of all cases of DM (Alberti *et al*, 1990). Over 100 million people are diabetic worldwide and probably as many are not diagnosed (Alberti *et al*, 1990). A national survey in

Nigeria showed a prevalence rate of 2.7% among Nigerians (Akinkugbe, 1997).

At present, there are an estimated 170 million Hepatitis C virus (HCV) carriers worldwide, most of who are thought to be in the developing countries (Maddava *et al*, 2002). HCV plays an important role in the causation of chronic liver disease (CLD) (Lesi *et al*, 2002), and has become the leading cause of liver cirrhosis and primary liver cell carcinoma (PLCC) in North America, Southern Europe and Japan (Colquhon, 1996; Cheng, 1995).

Infection with HCV affects not only the liver but also other extra-hepatic tissues as well (Ali *et al*, 2007). A number of extra-hepatic manifestations have been recognised including DM (Sene *et al*, 2004; Mason, 2001). Although it remains to be determined whether HCV leads to DM or vice versa, but it is argued that patients with DM have an increased risk of exposure

to HCV owing to the nature of the disease and its inherent complications or frequent parenteral exposure (Ali *et al*, 2007).

It has been reported from several Caucasian studies that there is an epidemiological association between HCV infection and DM. The objective of this study was to determine whether any such relationship exists in a black African population. We therefore determined the prevalence of HCV infection in Nigerians with DM in North-Eastern Nigeria.

MATERIALS AND METHODS

The serum samples of all consecutively recruited patients with confirmed DM were screened for HCV using rapid test ELISA kits (ACON Laboratories, Inc San Diego CA 92121 USA) to detect antibodies to hepatitis C virus (anti-HCV). Similarly, the serum samples of all consecutively recruited voluntary blood donors (VBD) were screened for HCV infection. All positive serum samples were re-tested to eliminate false positives.

Their bio data was obtained. Written informed consent was obtained from each patient.

The study was approved by the Ethics and Research committee of the Federal Medical Centre, Yola, Nigeria.

Analysis: The data obtained were analysed using the statistical package for social sciences (SPSS, version 11.0) statistical software.

RESULTS

At the conclusion of the study, out of the 280 DM patients tested, twenty-six were positive for anti-HCV antibodies giving an infection rate of 9.3% compared with fourteen subjects out of 595 VBD.

History of blood transfusion and jaundice is positively correlated with presence of HCV infection in diabetic patients.

Age

The age of the DM patients studied ranged from 26-85years with a mean of 51.5+/-12.0years. There was a steady increase in the age of the DM patients until a plateau at 5th decade (i.e. 40-49years). Thereafter there was a decline. Majority of the DM patients were in the 40-59 year age bracket (57.5%). The age range of the VBD was from 18-61 years with a mean of 31.3+/-7.9 years. Majority of the VBD were in the 20-39 year age bracket (83.3%). See table 1.

Gender: Out of the 280 DM patients screened, 108 patients (38.6%) were males while 172 patients (61.4%) were females, giving a male to female ratio of 1:1.59. while out of the 595 VBD screened, 571 were males (96.0%) while 24 were females (4.0%) giving a male to female ratio 23.8:1. There is no gender predilection in the occurrence of HCV infection in DM patients. See table 2.

table 1. Age distribution of diabetes mellitus patients and voluntary blood donors

Age groups (Years)	DM patients	voluntary blood donors
	frequency (n) (%)	frequency (n) (%)
<20	0 (0)	15(2.5)
20-29	7(2.5)	265(44.5)
30-39	35(12.5)	231(38.8)
40-49	87(31.1)	66(11.1)
50-59	74(26.4)	15(2.5)
60-69	46(16.4)	3(0.5)
70-79	27(9.6)	0(0)
80-89	4(1.4)	0(0)
Total	280(100.0)	595(100.0)

Table 2. Gender distribution of diabetes mellitus patients and voluntary blood donors

Gender	DM patients	voluntary blood donors
	frequency (n) (%)	frequency (n) (%)
Male	108(38.6)	571(96.0)
Female	172(61.4)	24(4.0)
Total	280(100.0)	595(100.0)

Duration of diabetes mellitus: The duration of DM ranged from 0.1 to 27 years with a mean of 5.67+/-5.08 years

Blood sugar control: The range of fasting blood sugar control was 3.6 to 31.6 mmol/L with a mean of 8.97+/-4.27 years. The range of glycosylated

haemoglobin was 5.0 and 14.6 with a mean of 7.76+/-1.49 %.

Frequency of HCV infection: Out of the 280 DM patients screened, 26 of them (9.3%) were seropositive for anti-HCV antibodies while 14(2.4%) of the 595 VBD were seropositive. There was a statistically significant increase in the sero-positivity for anti-HCV in DM patients compared with non-diabetic VBD (p<0.05) See table 3.

Risk factors to HCV infection

Table 3. Frequency of HCV infection

Variable	DM patients frequency (n)	voluntary blood donors frequency (n) (%)	χ^2	p-value
Anti-HCV positive	26 (9.3)	14(2.4)	19.42	0.0000105
Anti-HCV negative	254(90.7)	581(97.6)		
Total	280(100.0)	595(100.0)		

Out of the 26 DM patients who were sero-positive for anti-HCV antibodies, 18 of them (69.2%) had a history of jaundice compared with 8(30.8%) who did not. This difference is statistically significant (p=0.00). Similarly, out of the 26 DM patients who were sero-positive for anti-HCV antibodies, 18 of them(69.2%) had a history of blood transfusion compared with 8(30.8%) who did not. This is also statistically significant (P=0.00). Therefore, a history of blood transfusion and jaundice is positively correlated with presence of HCV infection in DM patients. See table 4.

Table 4. Anti-HCV status versus variables in diabetic patients

Variable	History of Jaundice		History of BT		Gender	
	Yes	No	Yes	No	Yes	No
Anti-HCV positive	18(69.2)	8(30.8)	18(69.2)	8(30.8)	18(69.2)	8(30.8)
Anti-HCV negative	62(24.4)	192(75.6)	50(19.7)	204(80.3)	154(60.6)	100(39.4)

$\chi^2 = 21.17$ p-value=0.00, $\chi^2 = 28.85$ p-value=0.00, $\chi^2 = 0.42$ p-value=0.52

Key

BT= Blood transfusion

DISCUSSION

A review of the literature shows that controversy exists in the relationship between HCV infection and DM (Nwokediuko and Oli, 2008; Adegoke *et al*, 2008; Balogun *et al*, 2006). Our study shows a significant increase in HCV infection in patients with DM compared with non-diabetic controls as 9.3% of our diabetic patients were found to have HCV infection compared with 2.4% of non-diabetic VBD. A review of the local literature shows that there are few Nigerian studies with which to compare. Nwokediuko and Oli (2008) in Enugu, South-eastern, Nigeria found that HCV infection is more common in DM patients compared with their non-diabetic controls (14.1% versus 3.7%). However, Adegoke *et al* (2008) in Ile-ife, South-west, Nigeria found a low prevalence of HCV infection (0.01%) among DM patients. Similarly, Balogun *et al* (2006) found a low prevalence of HCV infection in their DM patients in Ibadan, South-west, Nigeria.

Ali *et al* (2007) in their study amongst Pakistanis found that HCV infection occurred more in DM

patients. Similarly, Bahtiyar *et al* (2004) found a higher prevalence of HCV seropositivity in DM patients than in the general population in the United States of America. Furthermore, Knobler and Schattner (2001) found a positive association between HCV infection and DM among their Israeli patients. Manson *et al* (1999) and Ryu *et al* (2001) working separately, found a positive association between HCV infection and DM among American and Korean patients respectively. Conversely, Mangia *et al* (1998) found a negative association between HCV infection and DM among their Italian patients. Various reasons have been adduced for the increased occurrence of HCV infection in DM patients. These are frequent parenteral injections and exposure due to frequent insulin administration, extra-hepatic manifestations of HCV infection which includes DM, and the fact that patients with liver diseases are known to have a higher prevalence of glucose intolerance. A higher prevalence of DM in HCV related liver cirrhosis in comparison with cirrhosis secondary to other causes has also been postulated (Chen *et al*, 2003). There is scant evidence for

infection of pancreas by HCV and destruction of beta cells either directly by HCV or by an immune response, although HCV ribonucleic acid has been found in pancreatic tissue (Everhart, 1999).

In this study, only anti-HCV antibodies were used to screen for HCV infection. HCV RNA was not assayed for. If HCV RNA was assayed for, the actual HCV infection rate would probably be higher than the present reported figure of 9.3%. We also observed that a history of blood transfusion and a past history of jaundice are positive predictors of HCV infection in patients with DM. From this study, we did not find any relationship between gender and the presence of HCV seropositivity in DM patients. This is similar to the findings of Ali *et al* (2007) who did not find any relationship between gender and the risk of HCV infection. In contrast to this, Cacoub *et al* (1999) found female gender as a frequent factor in the extrahepatic manifestation of HCV infection. In conclusion, HCV infection is more common in Nigerians with DM. A past history of blood transfusion and a past history of jaundice are independent predictors of HCV infection in DM patients. There is no relationship between gender and the occurrence of seropositivity to HCV infection in DM patients.

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