

Serum Hepatitis C virus and hepatitis B surface antigenaemia in Nigerian patients with acute Icteric hepatitis

*S. O. Ola, J. A. Otegbayo, G. N. Odaibo, O. D. Olaleye and O. I. Olubuyide
Department of Medicine* and Department of Virology,
College of Medicine, University College Hospital,
Ibadan, Nigeria.

Summary

Acute hepatitis is common in Nigeria and hepatitis B virus (HBV) infection has been a major aetiological factor. However, the role of Hepatitis C Virus (HCV) infection is yet undetermined. Forty-five consecutive Nigerian patients with Acute Icteric hepatitis (AIH) attending the Medical Clinic of the University College Hospital, Ibadan, Nigeria and 45 healthy adult Nigerians (controls) were studied for evidence of infection with both viruses. Questionnaire on risk procedures which predispose to acquisition of both HBV and HCV infections were administered to the patients. Blood samples were collected from all the subjects and tested for antibody to HCV (Anti-HCV) and Hepatitis B surface Antigen (HBsAg) using the second generation Enzyme Linked Immunoassay (Monolisa -R, Sansofi, Pasteur; France). Anti-HCV was detected in 21(47%) and 17(38%) of the patients and controls respectively. The corresponding prevalences of HBsAg were 38(84%) and 11(24%), $p < 0.001$. Hepatitis B virus infection was found to occur more than HCV infection in the patients with AIH but similar among the controls. Combined HBV and HCV infection occurred more frequently among the patients (42.1%) than in the control (11%) ($p < 0.001$). Although there was no significant difference in the HCV infection between the two groups, isolated HCV infection is commoner in the control than in the patients with AIH, ($p < 0.001$). Similarly, single HCV infection is commoner than lone HBV infection among the control, $p < 0.05$. In summary, this study shows that while both HBV and HCV infections are common in Nigeria, AIH may be more associated with HBV than HCV in the country.

Key words: *Hepatitis B and C viruses, Anti-HCV, Hepatitis B Surface Antigen, Acute Icteric hepatitis, Nigeria.*

Résumé

La fréquence de l'hépatite aigue est notée au Nigéria, et l'infection du virus Hépatite B (VBH) reste toujours menaçant comme la trait étiologique principal. Cependant, on n'arrive pas à délimiter le rôle que joue l'infection du virus Hépatite C (VCH).

Quarante cinq malades consecutives Nigériens avec icteric Hépatite aigue (AIH) se sont présentés à la Clinique Médicale de Collège Hospitalier Universitaire d'Ibadan au nigéria, d'autre part, on avait étudié 45 adultes nigériens bien portant, (comme cas de témoins) comme signe de l'infection des deux virus. Questionnaire sur les dispositions des risques qui précèdent l'attaque d'infections des deux VBH et VCH était donné aux malades. On avait passer par la prise de sang de tous les malades et examiné afin de signaler les anticorps par rapport au VCH (Anti-VCH) et le Hépatite B surface Antigen (Hbs Ag) avec la méthode de la deuxième génération. On avait pu dépister la enzyme lié.

Immunoassay (monolisa - R sansofi, Pasteur, France). Anti-VCH dans 21 soit 47% et 17 soit 38% chez les malades et les cas de témoins respectivement. Les fréquences correspondentes de Hbs Ag étaient 38, soit 84% et 11 soit 24%, $P < 0,001$. On avait remarqué la fréquence de l'infection de Virus B Hépatite était plus élevée que l'infection VCH chez des malades avec AIH mais similaire chez les cas de témoins.

La fréquence de la combinaison des deux infections VEH et VCH était élevée chez les malades 42,1% plus que chez les cas de témoins (11%) ($P < 0,001$). Quoiqu'il n'y ait pas de différence remarquable dans l'infection VCH de deux groupes, on avait remarqué que quelques traits de l'infection VHS existaient normalement chez les cas de témoins plus que chez les malades avec AIH, $P < 0,001$. De plus l'infection VHC est plus fréquente plus que l'infection VBH chez les cas de témoins, $P < 0,05$.

En conclusion, à travers cette étude, on peut dégager que quoique les deux infections VBH et VCH soient fréquentes au Nigéria, le AIH peut-être bien lié avec le VBH plus qu'avec le VCH dans ce pays.

Introduction

Viral hepatitis is common in the tropics especially in a country like Nigeria where it accounts for a major cause of both acute and chronic liver diseases^{1,2}. Acute hepatitis is the commonest cause of acute liver diseases in Nigeria where viral aetiology seems to be predominating among other causes³. Hepatitis B virus (HBV) infection has been documented to be the commonest cause of hepatotropic viral agents of acute hepatitis^{1,3,5,6}. However, some patients were discovered to have hepatitis due to non A non B viral agents. Among these latter groups is the Hepatitis C Virus (HCV)^{1,8,9}. The HCV has been detected in both healthy adults¹⁰⁻¹³ and patients with chronic liver diseases,^{1,14-16} as well as acute hepatitis^{5,7} but its role in acute hepatitis has not been elucidated in Nigerians. Hence our study on the association of HCV and HBV in Nigerian adults patients with acute icteric hepatitis and healthy adult at the University College Hospital, Ibadan, Nigeria.

Materials and method

Forty-five consecutive adult Nigerian patients with AIH (Group I) attending the University College Hospital, Ibadan, were studied. In the selection of the patients, features such as hepatitis lasting more than 6 months, jaundice with ongoing fever, ingestion of icterogenic drugs within the preceding 6 months, presence of intrahepatic space occupying lesion and dilated biliary tree detected by hepatic ultrasonography and presence of mucoid bloody diarrhoea suggestive of amoebic disease were used as exclusion criteria.

Forty-five age- and sex- matched healthy Nigerian adults without a past history suggestive of hepatitis or chronic liver disease and drawn from relations of the patients were included in the study as control (Group II).

After informed consent were obtained from the subjects, questionnaires were administered to obtain information on possible routes of acquisition of HBV and HCV infections apart from the exclusion and inclusion clinical features.

The study protocol was approved by the Joint University College Hospital/University of Ibadan Ethical Committee.

About 10ml of blood was collected from each subject and the serum from each sample was separated after centrifugation and stored at -20°C until analysis was carried out.

Markers of HBV (HBsAg) and HCV (Anti-HCV) were analysed by Enzyme Linked Immunosorbent Assay (ELISA) using Monolisa^R, HBsAg and Anti-HCV second generation ELISA Kits, Sanofi, Pasteur; France.

*Correspondence

The data were analysed using students-t-test, Fisher's Z-test as well as computer analysis (EPI-Info) at a significant p-value < 0.05.

Results

Two groups of subjects were studied consisting of 45 Nigerian patients with AIH (group I), 45 healthy adult Nigerians as control (group II) aged 26 ± 9 years (Mean ± Standard Deviation) each. The groups were matched for age, sex, residence, tribe and occupation (Table 1). As shown in Table 2, HBV infection was detected in 38(84%) and 11(24%) of the patients with AIH and control respectively, p<0.001. Single HBV infection occurred in 19(42%) and 6(13%) of groups I and II respectively, p<0.001. The seroprevalences of anti-HCV in groups I and II were 21(47%) and 17(38%) respectively while single HCV infection was present in 2(5%) and 12(27%) of the respective groups I and II, p<0.001. Although there was no difference in the seroprevalences of HCV between the two groups, isolated HCV infection was commoner in the control than in the patients (p<0.001). Single HBV was more frequent than single HCV infection among the patients (p<0.001), with the converse for the control (p<0.05). Combined HCV and HBV infections were detected in 19(42%) and 5(11%) of groups I and II respectively (p<0.001).

Table 1 Biodata of all subjects studied

Parameter	Subjects	
	Acute Icteric hepatitis n = 45	Control n = 45
Male/Female	24/21	24/21
Age(mean±SD) years	26±9	26±9
14-20	12	11
21-40	29	29
41-60	4	5
State of residence		
Oyo	30	29
Others	15	16
Tribe		
Yoruba	37	36
Hausa	5	5
Igbo	3	4
Occupation		
Student	24	18
Civil Servant	21	27

SD = Standard Deviation

Table 2 Prevalence of HBV and HCV in patients with AIH and controls

HBV	AIH			HCV			Controls		
	+ve	-ve	Total	+ve	-ve	Total	+ve	-ve	Total
+ve	19(42)	19(42)	38(84)	5(11)	6(13)	11(24)			
-ve	2(5)	5(11)	7(16)	12(27)	22(49)	34(76)			
Total	21(47)	24(53)	45(100)	17(38)	28(62)	45(100)			

Parenthesis = Percentage

HBV = Hepatitis B Virus

AIH= Acute Icteric Hepatitis

HCV = Hepatitis C Virus

+ve = Positive

-ve = Negative

Table 3 Risk for AIH related to hepatitis B and C virus infections

Parameter	AIH n=45	Control n=45	Odd ratio
HBV			
Yes	38	11	16.7
No	7	34	
HCV			
Yes	21	17	1.44
No	24	28	

AIH - Acute icteric hepatitis HBV - Hepatitis B Virus

HCV - Hepatitis C Virus

Table 4 Probable risk factors for HBV and HCV infection in patients with acute icteric hepatitis

Route	n	HBV ⁺	HCV ⁺	HBV ⁺ + HCV ⁺	HBV ^{-ve} + HCV ^{-ve}
Parenteral					
Scarifications	14	4	1	8	1
Surgery	10	2	1	6	1
Needle injection	7	3	-	3	1
Blood Transfusion	3	3	-	-	-
Contact with					
jaundiced patients	6	2	-	4	-
History of Jaundice	3	2	-	1	-

HBV = Hepatitis B Virus

HCV = Hepatitis C Virus

-ve = Negative

+ve = Positive

Single HBV and combined HCV and HBV infections occurred more in patients with AIH than the control (p<0.001 each). There was no difference in the mean age of the patients and control with either HBV or HCV infection. Similarly, the infections were not related to occupation, sex, tribe and residence of the subjects. Table 3 shows that AIH was more causally related to HBV than HCV. Scarification, surgery, needle injury, blood transfusion, contact with jaundiced patients and past history of jaundice were factors associated with acquisition of HBV, HCV and both infections in the patients with AIH. These factors favour acquisition of HBV more readily than that of HCV (p<0.0005, Table 4).

Discussion

Acute hepatitis is common worldwide. A previous study showed that it accounted for 30% of all hepato-biliary diseases in Nigerian². Among the various aetiological agents, HBV has accounted for 50-70% of acute viral hepatitis in Africa¹. The finding of 84.4% among our patients with AIH is relatively higher than previous works done in Africans^{1,5,7} but similar to previous report among American soldiers³. Similarly, the presence of HBV in 24% of our control subjects compared to 7-20% from previous reports shows a rising trend in the prevalence of the HBV infection among Nigerians. This further supports the fact that Nigeria is an endemic zone for HBV infection. However, some of our patients were seronegative for HBV infection which indicates the need for detection of other viruses or other causes of AIH.

The seroprevalence of HCV found in 47% of our patients with AIH is greater than the reports of 10%, 8% and 12% in Vietnam, Tunisia and Central Asia by Corwin et al¹⁷, Coursaget et al¹⁸ and Bajsakow et al¹⁹. The anti-HCV seroprevalence of 38% found among the control subjects in this study is also higher than previous reports in healthy populations world wide¹⁰⁻¹³. In spite of the small size of the subjects used for this study, it shows that HCV infection is very common among Nigerians.

Coinfection of HCV and HBV infections has been reported and the interaction of the viruses may determine the pattern of the clinical presentation of the patients. The presence of high rate of combined HBV and HCV infections in our patients compared to the controls and the higher rate of single HCV infection in latter group might be a reflection of the natural history of HCV infection which is often mild and asymptomatic in the acute form and indolent in the course to chronicity. The HBV unlike the HCV is able to generate a higher degree of immune response in the host by its polyvalent antigens and even integrate in the host DNA^{20,21}. This makes HBV infection to present symptomatically in a milieu of immuno-competence. Hence the higher prevalence of single HBV infection in AIH than the healthy subjects found in this study is not unexpected. This is further reflected by the results of this study which shows that AIH is causally related to HBV rather than HCV.

In spite of the higher prevalence of HBV infection than that of HCV in our study, the occurrence of the peak age group of either

infection among the young adults follows previous reports and this could be secondary to high reproductive activities including sex that are associated with the age group²².

This study has further re-affirmed that both HCV and HBV are efficiently transmitted by the parenteral route with HBV being more readily transmitted than HCV. This route is a *sine qua non* of the high sexual activities that characterise the peak age group of our study populations. Also, the similarity in the route of transmission of these viruses could justify the absence of any significant difference in the occupation, sex and residence of the subjects with either infection. The transmission of the infections could be secondary to the higher infectivity of blood, serum or body fluids associated with the route²¹.

It is pertinent to note that both HCV and HBV infections are absent in 11% of our patients with AIH. This calls for detection of other viral agents (Hepatitis Non B non C viruses) which could possibly be the yet unknown or the other yet undetermined aetiological factors of AIH.

In conclusion, our study has shown that both HCV and HBV are common causes of AIH in Nigerians but HBV may be more. Infection with HBV seems to be more symptomatic than that of HCV. Both infections are parenteral in transmission though HBV is more readily transmitted. Efforts should be made at preventing these infections by active immunisation against HBV infection, ensuring safe medical care, early diagnosis and treatment of infected persons.

Acknowledgement

This work was supported by Roche Nigeria Limited, Ikeja, Nigeria; Basir-Thomas Biomedical Foundation, Ibadan; and Senate Research Grant, University of Ibadan, Ibadan, Nigeria.

References

1. Ayoola EA. Viral hepatitis in Africa in the 90s: Facing realities. In viral hepatitis and liver disease. Editor Nishiola K, Susuki H, Mishiro S, Oda T. Springer - Verlay, Tokyo, 1994; 381 - 4.
2. Olubuyide IO, Ayoola EA and Atoba MA. Hepatobiliary disease in tropical Africa - the Ibadan experience. *Trop. gastroenterol.* 1986; 7(2): 54-61.
3. Lemon SM, Lednar WM, Bancroft WH et al. Aetiology of viral hepatitis in American soldiers. *Amer. J. Epid.* 1982; 116(3): 438 - 50.
4. Greefield C, Karayiannis F, Wankya BM et al. Aetiology of acute hepatitis in adults in Kenya. *Med Virol.* 1984; 14(4): 357 - 62.
5. Crochiolo PR, Caredda F, Diarminio MA et al. The aetiology of acute hepatitis in Zimbabwe. *Trans. Roy. Soc. Trop. Med. Hyg.* 1984; 78(4): 514-8.
6. Ayoola EA. Non A, Non B hepatitis in Nigerians, *East Afr. Med. J.* 1983; 60: 88-91.
7. Zakaria S, Goldsmith RSS, Kamel MA et al. The aetiology of acute hepatitis in adults in Egypt. *Trop. Geog. med.* 1988, 40: 285-92.
8. Choo QL, Kuo G, Weiner AJ, Isolation of a cDNA fragment derived from a blood borne Non-A, Non-B Viral hepatitis agent *Sci.* 1989, 244; 59-67.
9. Van de Poel GL and Cuyper HW. Hepatitis C virus, six years on. *Lancet* 1994; 334: 1475 - 9.
10. Sulaiman HA, Julitasari, Sie A, Rustam M, Melini W et al. Prevalence of hepatitis B and C virus in healthy Indonesian blood donors. *Trans. Roy. Soc. Trop. Med. Hyg.* 1995, 89: 167-170.
11. Kowo MP, Goubau P, Mdam EN, Njoya A, Sasaki S, et al. Prevalence of hepatitis C virus and other blood borne viruses in Pygmies and neighbouring Bantus in Southern Cameroon. *Trans. Roy. Soc. Trop. Med. Hyg.* 1995, 484-6.
12. Neal KR, Dorman J, Irving WL. Prevalence of Hepatitis C (antibodies) among healthcare workers of two teaching hospitals. Who is at risk? *B.M.J.* Jan. 1997, 514; 179 - 180.
13. Olubuyide I O, Ola S O, Aliyu B, Dosumu OO, Arotiba JT et al. Hepatitis B and C in doctors in Nigeria. *Quart. J. Med.* 1997; 90: 417-422.
14. Tsega E, Nordenfelt E and Hansson BG. Hepatitis C virus infections and chronic liver disease in Ethiopia where hepatitis B infection is hyperendemic. *Trans. Roy. Soc. Trop. Med. Hyg.* 1995, 89; 171-4.
15. Ojo OS, Thursz HC, Thomas HC, Ndububa DA, Adeolu OO et al. Hepatitis B virus markers, Hepatitis D virus antigen and hepatitis C virus antibodies in Nigerian patients with chronic liver disease. *East Afr. Med. J.* 1995, 72(11); 719 - 721.
16. Olubuyide IO, Aliyu B, Olaleye OD, Ola SO, Olawayi F et al. Hepatitis B and C virus and hepatocellular carcinoma. *Trans. Roy. Soc. Trop. Med. Hyg.* 1997, 91; 38 - 41.
17. Corwin AL, Dai TC, Duc DD, Suu PI, Van NT et al. Acute hepatitis in Hanoi, Vietnam. *Trans. Roy. Soc. Trop. Med. Hyg.* 1996, 90: 647 - 8.
18. Coursaget P, Simpson B, El Goali N, Khalifa HB, Kestally R. Hepatitis B core Antibody detection in acute hepatitis and cirrhosis in patients from Tunisia. *Path. Biol. (Paris)* 1992; 40: 640-8.
19. Bajsakow S, Idrisowa RS, Frosner GG, Aetiology of viral hepatitis in Central Asia. Triennial International Symposium on viral hepatitis and liver diseases. Rome, Italy, Apr. 1996, Abstract B 301, 200.
20. Bhauderi BN and Wright TC, Hepatitis C an overview. *Ann. Rev. Med.* 1995; 46: 309 - 17.
21. Ola SO. The pathogenesis and natural history of Hepatitis B virus infection. *Dokita* 1996; 23(1): 11-16, 24-25.
22. Alter MJ. Epidemiology of hepatitis C (review) *Hepatology* 1996, 26(3) suppl 1; 625-656.