ORIGINAL ARTICLE

Serum alpha-fetoprotein level is higher in hepatitis C than hepatitis B infected chronic liver disease patients

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ABSTRACT

Background: The frequency of raised serum alpha-fetoprotein may vary in relation to hepatitis B or C infection in chronic liver disease (CLD). The study evaluated the frequency of hepatitis B and C in patients with chronic liver disease and correlated the levels of serum alpha-fetoprotein with hepatitis B and C infection in the patients. **Materials and Methods:** Eighty-six patients with CLD were recruited for the study. Fifty subjects, with no CLD were used as control. Hepatitis B surface Antigen (HBsAg) and hepatitis C antibody were determined using enzyme-linked immunosorbent assay (ELISA) technique (Human diagnostics, Germany and HCV Murex 4o Anhet laboratories, USA) while liver function tests were evaluated using express plus chemistry auto analyzer. Alpha-fetoprotein was assayed using ELECSYS 1010 auto analyser. **Results:** There were 60 males and 26 females, with a mean age of 46 + 6.5 years, while the controls were 25 males and 25 females with a mean age of 41 ± 2.5 years. Thirty-six subjects (41.7%) were seropositive for HBsAg while 24 (27.9%) were seropositive for Hepatitis C Virus (HCV) antibody. The mean alpha fetoprotein level was 359 ± 9.9 ng/mL while mean control value was 1.93 ± 0.24 ng/mL. Liver function test parameters were elevated compared with control subjects ($P < 0.001$). The increase in serum alpha-fetoprotein was higher ($P < 0.001$) in HCV than HBsAg positive patients. **Conclusion:** Serum alpha-fetoprotein level was highest in HCV compared to HBsAg positive and hepatitis negative patients with CLD.

Key words: Alpha fetoprotein, chronic liver disease, HBsAg, HCV antibody

INTRODUCTION

Even though hepatitis B virus (HBV) is the most common cause of hepatitis, hepatitis C virus (HCV) is rapidly emerging as an infection requiring attention.[1] HCV is a major cause of acute and chronic liver diseases. Several authors have reported the prevalence of these viruses among chronic liver disease (CLD) patients in various centres.[1-6] These studies have shown wide variations in the prevalence rates of these viruses among CLD and hepatocellular carcinoma (HCC) patients. Although there is no accurate record of yearly incidence of infection in this environment, an estimated 150,000-450,000 persons are infected yearly in United States of America.[7] An increasing trend of HBV antigenaemia was previously reported among general patients in Aminu Kano Teaching Hospital, Kano.[8] Serum Alpha-fetoprotein (AFP) is routinely used as marker of HCC in patients with CLD. Serum AFP is also elevated in some non-hepatic malignancies and in conditions such as acute and chronic hepatitis.[9,10] Serum AFP may also be elevated in patients with CLD due to hepatitis B and C infection. The frequency of elevated serum AFP in CLD patients may vary according to the hepatitis genotype infection.[11] The objective of this study was to evaluate the frequency of hepatitis B and C in patients with CLD and to correlate the levels of elevated serum AFP with hepatitis B and C infection in patients with CLD.

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MATERIALS AND METHODS

This study was based on a retrospective analysis of clinical and laboratory data collected between 2004 and 2007, as part of the routine management of patients with CLD in our Hospital. Records of 86 consecutive subjects, 62 males and 24 females were analysed. They were patients with biopsy proven CLD referred to the laboratory departments of the hospital for serum

AFP, liver function tests, Hepatitis B surface Antigen (HBsAg) and hepatitis C antibody investigations. Their health records were searched for diagnosis, age, sex and other medical history of the patients at the time of presentation. A specific laboratory code was assigned for each patient so that no name or identifier other than age, sex appears in our record. Neither informed consent nor ethics approval was requested for the analysis, since it was exclusively retrospective and did not require additional testing. Five milliliter of venous blood was collected aseptically and serum was separated, aliquoted and stored at –20°C until tested. AFP level was assayed using ELECSYS 1010 auto-analyser by Roche diagnostics, Switzerland. The principle of the technique is based on Electrochemiluminescence immunoassay. HBsAg and HCV antibody were assayed using enzyme-linked immunosorbent assay (ELISA) technique (Human diagnostics, Germany, and HCV Murex 40, Anhet laboratories, USA) while the liver function tests were evaluated using Express plus auto-analyser by Chiron diagnostics, USA.

Twenty-five males and 25 females of similar ages were used as controls. They were recruited in 2007 from among apparently healthy staff and students of the hospital, who had no evidence of CLD based on history and normal laboratory findings. Students-*t*-test for parametric data was used for statistical comparison of the results.

RESULTS

There were 62 males and 24 females with age ranged from 40 years to 71 years with a mean of 46 ± 6.5 years. Thirty-six (41.7%) out of 86 subjects were seropositive for HBsAg, while 24 (27.9%) were seropositive for HCV antibody. The control subjects were seronegative for both HBsAg and HCV antibody. The mean AFP level of the study patients was 359 ± 9.9 ng/mL, while the mean of the controls was 1.93 ± 0.24 ng/mL.

The mean aspartate amino transferase activity was 145 ± 1.8 u/L, while the mean control value was 10.8 ± 1.2 u/L. The means alanine amino transferase and alkaline phosphatase activities were 75 ± 5.1 u/L and 176 ± 1.6 u/L, respectively, while the means activities in control subjects were 8.6 ± 1.2 u/L and 29±4.2u/L, respectively. The means total bilirubin and direct bilirubin were 68.7 ± 6.8 µmol/L and 26.0 ± 4.1 µmol/L, while the means of the control subjects were 10.6 ± 1.2 µmol/L and 4.2 ± 1.0 µmol/L, respectively. The means total protein, albumin and globulin were 50.6 ± 3.6 g/l, 29.6 ± 1.9g/L and 20.6 ± 2.8 g/L, respectively, their mean control values were 65.2 ± 1.1 g/L, 42.1 ± 1.1 g/L and 21.9 ± 1.2 g/L. Statistically significant differences were observed in all the parameters ($P < 0.001$) except for globulins [Table 1].

Table 2 shows clinical characteristics of chronic liver disease patients by status of hepatitis B and C infection. The mean AFP level in the 36 subjects, who were seropositive for HBsAg, was 279 ± 20, while the mean level of AFP in CLD patients that were seropositive for HCV antibody was 849 ± 23 ng/mL and in those without hepatitis infection was 16.3 ± 3.6 ng/mL. The mean AFP level was highest ($P < 0.001$) in HCV positive CLD patients followed by HBsAg positive and those without hepatitis infections.

DISCUSSION

The result indicated that 27.9% of the study patients were seropositive for HCV antibody. Although HCV has been implicated in non A non B hepatitis in CLD development in parts of Asia, the incidence of this virus was previously reported to be low in Kano, Nigeria.[1] The rate observed in this study is, however, consistent with 28% reported from Lagos,[12] but higher than 20.6% from Somalia[13] and 24.1% from Bangladesh,[14] and lower than that reported by

Table 1: Serum alpha fetoprotein, HBsAg, HCV antibody and liver function tests in patients with chronic liver disease and control subjects (Mean ± SEM)

Variables	Patients with CLD	Controls	*P*-value
Age (Years)	46±6.5	41±2.5	
Number of subjects	86	50	
No positive for HBsAg	36 (41.7%)	so (o%)	
No positive for HCV antibody	24 (27.9%)	o (o%)	
No negative for HBsAg and HCV	26 (18.6%)	o (o%)	
AFP (ng/mL)	359±9.9	1.93±0.24	*P*<0.001
AST (u/L)	145±1.8	10.8±1.2	*P*<0.001
Alk. Phosphatase (u/L)	75±5.1	8.6±1.2	*P*<0.001
Total Bilirubin (µmol/L)	68.7±6.8	10.6±1.2	*P*<0.001
Direct Bilirubin (µmol/L)	26±4.1	4.2±1.0	*P*<0.001
Total Protein (g/L)	50.6±3.6	65.2±1.1	*P*<0.001
Albumin (g/L)	29.6±1.9	42.1±1.1	*P*<0.001
Globulin (g/L)	20.6±2.8	21.9±1.2	*P*>0.001

Table 2: Laboratory parameters of chronic liver disease patients by status of Hepatitis B and Hepatitis C infection (mean ± SEM)

Variables	Patients with HBsAg	Patients with HCV infection	Patients without Hepatitis infection
Numbers of subjects	36	24	26
AFP (ng/mL)	279±20	849±23	16.3±3.6
AST (u/L)	131±2.6	142±2.0	109±5.6
ALT (u/L)	74±6.2	73±5.6	68±4.8
Alk. Phosphatase (u/L)	168±6.2	176±5.2	146±8.6
Total Bilirubin (µmol/L)	69±5.1	66±4.1	65±6.0
Direct Bilirubin (µmol/L)	28±6.1	26±3.6	25±4.1
Total protein (g/L)	51±4.1	50.2±2.1	50.7±3.1
Albumin (g/L)	29.1±1.2	28.5±2.1	29.1±2.0
Globulin (g/L)	20.1±2.8	21±3.1	20.4±1.4

Singh *et al*., in India.[15] This result also showed that about 41.7% of patients with CLD tested positive to HBsAg, higher percentage than ours was reported by some authors elsewhere. HBsAg seropositivity of 55% was reported in patients with CLD in Ethiopia[16] and Pakistan,[17] 60.6% in India,[6] while lower percentages than ours were also observed: 28% in Lagos,[12] and 30.3% in Hazara division, Pakistan.[18] The reason for the relatively higher incidence of HBV and HCV infections among the study patients is not known, however, it may be due to the fact that the study was conducted in CLD patients and not in general population.

Although co-infection with both HBV and HCV was not observed in this study, it was reported that co-infection with HBV and HCV seems to result in more severe liver disease than mono infection with a risk of liver cancer.[19,20] Imoru *et al*.,[21] previously reported a HCV prevalence of 0.4% among blood donors in Kano. In a similar study carried out in Vietnam, CLD due to HBV was 47% while 23% of these cases were HCV seropositive.[22] In Africa, it was reported that the third most common cause of death in medical wards is due to liver diseases, where hepatitis B was commonest cause of these liver diseases.[23] The relative importance of HBV and HCV infections in liver diseases aetiology is known to vary from one region to another and can change over time.

The AFP levels in the study patients were expectedly high and were statistically different when compared with the control subjects ($P < 0.001$). Serum AFP is an important tumour marker of liver disease and its determination is of high value in making the diagnosis and follow up after treatment. It also serves as predictive marker for the development of hepatocellular carcinoma during follow up of patients with cirrhosis.[20] Serum AFP level was highest in CLD patients with HCV antibody positive compared to HBsAg positive and those without hepatitis infection. This result is consistent with findings from other study.[11] In a previous study by Abdoul *et al.,*[10] they showed an association between serum AFP level and sustained virological response in HCV infected patients. This is an indication that HCV infection causes more severe liver disease than hepatitis B and CLD of other aetiologies. HCV gene products, which include core, NS3, NS4B and NS5A, are capable of malignant transformation of hepatocytes in cell model system which are capable of causing hepatocellular carcinoma in some individuals.[24] In addition, the expression of HCV protein has been shown to alter several potentially oncogenic pathway via cell signaling transcription modulation, apoptosis, transformation, translational regulation and through interaction with the translational machinery and post translational modification system.[24,25] Apart from possible direct effects exerted by HCV virus on the host genome, carcinoma may result in cycle of inflammation, necrosis and regeneration due to chronic hepatitis C-induced liver cell injury in the liver. Increased cell turnover in this setting of inflammation and oxidative deoxyribonucleic acid (DNA) damage may facilitate the accumulation of genetic and epigenetic alterations that include the activation of cellular oncogenes and proliferative signaling pathways, telomerase activation and the inactivation of tumour suppressor genes and the over-expression of growth and angiogenic factors.[25] The high levels of AFP observed in these patients may be due to false positive results often observed in patients with chronic hepatitis. It was reported that AFP test has a high false positive rate of 20% among patients with chronic hepatitis and 20-50% among those with liver cirrhosis.[26]

All the liver function test parameters were higher as expected in the study patients than in the control subjects ($P < 0.001$).

CONCLUSION

Serum AFP level was highest in CLD patients with HCV antibody positive compared to HBsAg positive CLD and hepatitis negative patients. Clinicians should maintain high level of suspicion of HCV infection when high levels of AFP was recorded in patients with CLD.

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