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Hepatitis B Virus (HBV) Infection among Alcoholic Consumers at a Local Community, North-East Nigeria.

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Abstract
Alcohol remains the single most significant cause of liver disease throughout the Western world; which is responsible for about 40 – 80% cause of cirrhosis in different countries. This study was therefore carried out to investigate the sero-prevalence of HBV infection among alcoholics. One hundred and thirty eight (138) alcoholic consumers and fifty (50) control subjects at Billiri Community in Billiri Local Government Area of Gombe State were screened for HBsAg using Clinotech Diagnostic Third Generation ELISA Kit. Structured questionnaire was employed to obtain demographic data of study subjects.The result obtained showed a positivity of 10 (5.3%) among the subjects screened. Considering gender 7 (3.7%) seropositivity was recorded among the alcoholic males compared to 3 (2.1%) in females. Age consideration showed that subjects within 21 – 30 years recorded 4 (2.1%) prevalence. Equally control subjects had a prevalence of 4 (2.1%). Considering the serum amino transferase (ALT) among positive subjects screened 8 (4.3%) recorded an elevated ALT.The data obtained in this study calls for drastic measures at curtailing the spread of this virus, because of its attendant effects on the liver. Also, immunization of individuals in this community is highly recommended.
Keywords: Hepatitis B virus, Infection, Alcoholic consumers.

1. Introduction

Hepatitis B virus infects the liver of the hominidae including humans and causes an inflammation called hepatitis. It is a DNA virus and one of the unrelated viruses that cause viral hepatitis. The disease was originally known as "serum" hepatitis (Barker *et al.,* 1996) and has caused epidemics in parts of Asia and Africa. Hepatitis B is endemic in China and various other parts of Asia (Williams, 2006). The proportion of the world's population currently affected with the estimated at 3% - 6%. Symptoms of the acute illness caused by the virus include liver inflammation, vomiting, jaundice and rarely death. Chronic hepatitis B may eventually cause liver cirrhosis and liver cancer, a fatal disease with very poor response to current chemotherapy (Chang, 2007). The infection is prevented by vaccination (Pungpapong *et al.,* 2007).

Hepatitis B virus infection is estimated to be the cause of 30% of cirrhosis and 53% of liver cancer in the world,(Perz,2008).Approximately 15-40% of patients with chronic HBV will develop cirrhosis, end-stage liver failure or hepatocellular carcinoma (HCC) in their lifetime,(Lok 2002).Most of the deaths (94%) were attributed to complications. Chronic infection, such as cirrhosis and HCC, and only 6% were attributed directly to acute Hepatitis B, (Goldstien,*et al*,2002).Hepatocellular carcinoma is the sixth most common cancer and the third most common cause of cancer death in the world,(Ferly,et al 2010).Chronic HBV infection is the most common cause of HCC, accounting for 50% of HCC cases worldwide and up to 80% of cases in high HBV endemic regions,(Bosch,et al 2004). The risk of the world's population live in areas of low endemicity, developing HCC is greatly increased with the development of cirrhosis. Thus, the ideal way to decrease HBV-related deaths is to first prevent the infection through vaccination and strategies to reduce transmission and second, to prevent progression to cirrhosis and HCC in those already infected.

Hepatitis B virus infection may either be acute (self-limiting) or chronic (long standing), persons with self-limiting infection clear the infection, more than 95% of people who become infected as acute or older children will stage a full recovery and develop protective immunity to the virus. However only 5% new born that acquire the infection from their mother at birth will clear the infection. Those infected between the age of 1 – 6 years, 70% will clear the infection (Kerkar, 2005).

The liver which is the largest visceral organ, the most versatile organ in the body and any condition that severally damages the liver represent a serious threat to life as it affects almost every other system of the body. Liver has many functions which are vital to survival, they include: - Transformation of food into usable body chemicals, filtration of waste bacteria, poison from the blood, haematologic regulation, synthesis and secretion of bile and drug inactivation (detoxification). The liver also function as a store house for various minerals, vitamins and sugar that the body uses for energy (AIE, 2002). As a result of these functions, the liver is very vital to survival. A normal liver is smooth and firm to touch but progressive liver damage can lead to fibrosis, shrinkage and hardening and formation of nodules (NATAP, 2002). Liver injury and damages such as hepatitis,

fibrosis, cirrhosis, portal hypertension, hepatocellular failure and hepatocellular carcinoma are caused by various factors such as toxins (e.g. drugs, alcohol, poison and chemicals) and infective agents (e.g. some viruses, bacteria, parasite) (Abdalla, 2001; Martin *et al.,* 2000).

Several epidemiologic studies suggest that chronic alcoholics are at risk of viral infections. Clinical and basic research has demonstrated that alcohol not only worsens the natural history of chronic viral hepatitis, like hepatitis B virus (HBV) but also seems to interact with the viral replication cycle leading to an unusual serum virologic profile and/or modification in the serum concentration of viral particles (Nalpas et al., 1998). Several studies have shown that patients with alcoholic cirrhosis showed evidence of past or current infection with HBV more commonly than did healthy nonalcoholic subjects (Bassendine et al., 1983, Goudeau et al., 1981, Inoue, 1977 and Mills et al., 1981).

An alcoholic has been defined as one who consumes more of alcohol i.e. 5 fluid oz of wine or 1.5 fluid ounce (oz) of distilled spirits and contain approximately 0.5 oz (14 grams) of pure alcohol and these level represents heavy alcohol intake and typically alcohol abuse (Lieber, 2001; Peters *et al.,* 2002) chronic alcohol intake is the most frequent cause of liver disease and accounts for majority estimated 100,000 alcohol related deaths each year (NIAAA, 1998; Abdalla, 2001). Alcohol affects many organ including the liver (AIE, 2002). Any one who consumes excessive amount of alcohol will have liver damage, but may not always develop into cirrhosis.

Several vaccines have been developed for the prevention of hepatitis B virus infection. These rely on the use of one of the viral enveloped protein (hepatitis B surface antigen). The vaccine was originally prepared from plasma obtained from patients who had long-standing hepatitis B virus infection. However, recombinant DNA technology through plasma derived vaccines is equally effective and safe (Zuckerman, 2006). Hepatitis B surface antigen may be detected in serum for several days; this is known as vaccine antigenaemia (Martin-Abcel, *et al.,* 2004).Prevention of the transmission of viral hepatitis should focus on public enlightenment campaign to prevent transmission to others and protection of those at risk group against the virus. (De Palma, 2002).

2. Methodology:

2.1. Study Design: Alcoholic consumers in a local community North- eastern Nigeria were recruited for this study. The study ensured that only volunteers who agreed to alcoholic consumption at various stages of life were recruited for the study.

2.2. Enrolment and Data Collection: After obtaining in- formed consent, volunteer subjects completed a questionnaire which was based mainly on the knowledge of risk of exposure. These questionnaires were distributed and filled by subjects through the help of guides where ever necessary. Ethical clearance was then obtained from relevant ethical committee before sampling commenced.

2.3 Sample collection: 3ml of venous blood was collected, duly labeled and allowed to clot and sera carefully separated into cryovials and stored at -20^{o}C prior use.

2.4 Sample assay/Analytical process: This was carried out using the HBsAg EIA, which is a solid –phase simultaneous sandwich immune assay, which employs monoclonal antibodies specific for HBsAg. Microtiter well is coated with monoclonal antibodies specific for HBsAg. A serum specimen is added to the antibody coated microtiters wells together with enzyme conjugated polyclonal antibodies.

2.5 **HBsAg Testing:**

Clinotech Diagnostics HBsAg EIA 3RD Generation was used for the detection of HBsAg in serum.(Procedures employed in the Assay were based on manufacturers instructions).

Principles:

The HBsAg EIA is a solid –phase simultaneous sandwich immune assay, which employs monoclonal antibodies specific for HBsAg. Microtiter well are coated with monoclonal antibodies specific for HBsAg. A serum specimen is added to the antibody coated microtiters wells together with enzyme conjugated polyclonal antibodies. HBsAg, if present, will form a antibody-HBsAg-antibody-enzymes complex. The plate is then washed to remove unbound materials. Finally, a solution of HRP enzyme substrate (TMB) is added to the wells and incubated. A blue colour will develop in proportion to the amount of HBsAg present in the specimen. The enzyme substrate reaction can stopped and the result is visualized by naked eye or read by EIA plate reader for absorbance at the wavelength of 450nm.

Preparation:

Test sample, control, conjugate, distilled water, substrate aluminum bag containing tetramethyl benzidine (TMB) were allowed to stand to ambient temperature before used.

Assay:

It was strongly advised to analyze each specimen and control in duplicate. All the reagents should equilibrate to room temperature before used.

1. 50ul was dispensed on positive as well as negative control in duplicate into respective wells. Blank was set as a background control, and 50ul of serum or plasma samples into

the respective wells.

2. 50ul Enzyme conjugate was added to each well-mixed gently by swirling the microtiter plate on the bench for 2 minutes. DO NOT ADD ENZYME CONJUGATE TO THE BLANK WELL.
3. Incubate at 37^{o}C for 1 hour (60 minutes).
4. Each well was washed 5 times by filling each well with diluted wash buffer, then inverting the plate vigorously to get all water out and blocking the rim of the wells on absorbent paper for a few seconds.
5. 100ul substrate solution(TMB) was added to each well, then incubated at 37^{o}C for 15 minutes.
6. 50ul stop solution was added to each well to stop the color reaction. Read O.D at 450nm and 630nm with an EIA plate reader within 10 minutes.

Assay validity:

Using the O.D value of the blank well to correct all the O.D reading from the wells, OD value of positive control should be more than 1.0 and of negative control less than 0.1. Otherwise, the test is invalid.

Interpretation of result:

Positive (p)

The ration of $\frac{\text{OD value of sample}}{\text{OD value of negative control}} > 2.1$

Negative (N)

The ration of $\frac{\text{OD value of sample}}{\text{OD value of Negative control}} < 2.1$

Where

N= The mean absorbance of the negative controls.

P= The mean absorbance of the positive controls.

S= The absorbance of the test sample.

If the OD value of the Negative control is less than 0.05, it should be reported as 0.05. If it is more than 0.05, it should be reported that as the actual OD value measured.

Calculation of cut-off value:

The cut-off value is 2.1xNegative (N)

Test result:

A Test is positive if S > cut off value

A Test is Negative if S < cut off value.

2.6 Statistical Analysis. Data from all questionnaires obtained were entered into SPSS, version 16, and analyzed. While level of significance was set at $P<0.05$.

3. Results

Table 1: Show the distribution of HBV among alcoholics and non-alcoholic subjects. Highest prevalence of 10 (5.3%) was recorded, out of a total of 138 alcoholic subjects screened while 4 (2.1%) among the non-alcoholic (control) subjects.

Table 2: The age distribution among alcoholic showed subject aged 21 – 30 years recording the highest seroprevalence with 4 (2.9%) while the lowest prevalence of 1 (0.7%) was recorded among those aged 51 – 60 years.

Table 3: show the prevalence of HBV based on gender among alcoholic subjects. The highest prevalence of HBV among alcoholics was recorded among male subjects with 7 (5.1%) while the female subjects 3 (2.1%).

Table 4: Risk factors put into consideration among alcoholic subjects showed that subjects with history of blood transfusion recorded 3 (1.6%) prevalence. Similarly risk factors based on subjects with history of surgery showed a record of 1 (2.5%), with P-value of $P<0.05$ or $P>0.05$.

Table 5: showed risk factor among control (Non-alcoholic) subjects those with history of blood transfusion recorded 3 (25.0%) positivity.

Table 6: The serum aninotransferase level recorded were based on the 14 (7.4%) HBsAg positive samples, 10 (5.4%) showed a slight elevation of liver enzyme while 4(1.4%) recorded normal level.

Table 1: Total Number of Subjects screened.

Status of subjects screened	Total No of subjects screened (%)	Total No of Positive Subjects (%)	Total of Negative Subjects (%)
Alcoholics	138 (73.4)	10 (5.3)	128 (68.1)
Non-alcoholics (Control group)	50 (26.6)	4 (2.1)	46 (24.5)
Total	188 (100)	14 (7.4)	174 (92.6)

X^2 = 0.305, df = 1, P =0.823, P-value < 0.05

Table 2: Age distribution of HBV infection among alcoholic subjects screened

Age range	Total No of subjects screened (%)	Total No of Positive Subjects (%)	Total of Negative Subjects (%)
21 – 30	50 (36.2)	4 (2.9)	46 (33.3)
31 – 40	35 (25.4)	2 (1.5)	33 (23.9)
41 – 50	26 (18.8)	2 (2.14)	25 (18.2)
51 – 60	20 (14.5)	1 (0.7)	18 (13.0)
61 – 70	7 (5.1)	1 (0.7)	6 (4.3)
Total	138 (100)	10 (7.3)	128 (92.7)

X^2 = 0.459, df = 2, P values = 0.795, P-value > 0.05

Table 3: Distribution of HBV Prevalence based on gender among (Alcoholic) subjects.

Gender	Total No of subjects screened (%)	Total No of Positive Subjects (%)	Total of Negative Subjects (%)
Males	88 (63.8)	7 (5.1)	81 (58.7)
Females	50 (36.2)	3 (2.1)	47 (34.1)
Total	138 (100)	10 (7.2)	128 (92.8)

X^2 = 0.128, df = 1, P –values = 0.720, P-value > 0.05

Table 4: Risk factors based on clinical history of Alcoholic subjects

Risk Factors	Total No of subjects screened (%)	Total No of Positive Subjects (%)	Total of Negative Subjects (%)
History of Blood transfusion	35 (18.6)	3 (1.6)	32 (17.0)
History of Surgical Operation	15 (8.0)	1 (0.5)	14 (7.5)
Total	50 (26.6)	4 (2.1)	46 (24.5)

X^2 = 0.052, df = 1, P value = 0.820, P-value <0.05

Table 5: Risk factors based on clinical history of control (Non-alcoholic) subjects

Risk Factors	Total No of subjects screened (%)	Total No of Positive Subjects (5)	Total of Negative Subjects (%)
History of Blood transfusion	8 (16.0)	3 (6.0)	5 (10.0)
History of Surgical Operation	4 (8.0)	1 (2.0)	3 (6.0)
Total	12 (24.0)	4 (8.0)	8 (16.0)

X^2 = 0.188 , df = 1, P value = 0.665, P-value > 0.05

Table 6: Determination based on total subject of serum transaminase level on positive subjects.

Status of subjects	Total No of Subject (%)	AST Abnormal (%)	AST Normal (%)	ALT Abnormal (%)	ALT Normal (%)
Alcoholic	10 (5.3)	8 (4.3)	2 (1.0)	8 (4.3)	2 (1.0)
Non-Alcoholic	4 (2.1)	2 (1.1)	2 (1.0)	0 (0.0)	4 (2.1)
Total	14 (7.4)	10 (5.4)	4 (2.0)	8 (4.3)	6 (3.1)

5. Discussion

The result obtained showed that the frequency of HBV infection in alcoholics in the community is higher than in non-alcoholics. However, active infection (HBsAg positive) was higher in the individuals with history of alcoholism than in those without such case history or control subjects. Highest prevalence rate of 10 (5.3%) out of 138 subjects screened was recorded among the alcoholics while 4 (2.1%) was recorded among the non-alcoholic subjects screened (Table I). Statistical analysis showed an insignificant value in both groups (P-

value = 0.823). These findings agrees with the work of Jerrells *et al.,* (2002) that alcoholism has a part to play in viral hepatitis, since prevalence was higher in key subjects than in controls,the reason may be from the different substances such as alcohol (Dunn *et al.,* 2005; Jennifer, 2006), which can cause viral hepatitis.According to Bedogni, *et al.,* 2008HBV infection in alcoholic is associated with faster progression in liver injury with an elevated isk of developing cirrhosis in another study conducted by Laskus, . *et al.,* 1992 among alcoholics it was found that prevalence of HBV is estimated to be four fold higher than in controls.

Considering age group, the highest prevalence of 4 (2.9%) was recorded among the age 21 – 30 years, while the lowest 1 (0.7%) was recorded among those age 51 – 60 years (Table II).Statistical analysis between the age groups indicated no significant differences with P-value 0.795 (i.e. P-value<0.05),The age group considered to have the highest prevalence in this study, agrees with the work of Ndako et al 2009 in a similar studies conducted among alcoholics, this could also be attributed to youthful exuberance and hyperactivity among this age group.

Considering gender, a higher prevalent was observed among males with 7 (5.1%) while female 3 (2.1%) prevalent rate. This result corresponds to the work of Kradjen *et al.,* (2005) who report that the prevalence of HBsAg depending on the cause is found higher in males than in females; also it in agreement with the report of Ndako *et al.,* 2009, where a higher prevalence was recorded among male subjects screened. This might also be attributed to that fact that men in this locality consumed the local brew as stimulants before embarking on several activities such as farming and others social functions. Hepatitis B infection might influence the development of liver disease in heavy drinkers in several ways. Firstly, persistent infection with HBV might potentiate alcohol-induced liver damage, and there is evidence that this may occur at fairly low alcohol intakes (Villa et al., 1982). Secondly, chronic active hepatitis associated with HBsAg may coexist with alcoholic liver disease, and the two disease processes would probably result in more rapid progression to cirrhosis.

The serum amino transferase levels recorded were based on the 14 (7.4%) HBsAg positive samples screened, controls inclusive of these 10 (5.4%) showed a slight elevation of liver enzyme; Bellentani *et al.,* (1997) reported similar findings which shows a sporadic alteration of liver enzymes level among the positive subjects screened. However, according to Gamen *et al.,* (2004) persistent elevation of serum ALT for more than six months indicates progression to chronic hepatitis.

Conclusion:

In conclusion, Hepatitis B infection might influence the development of liver disease in heavy drinkers in several ways, this could be due to the fact that persistent infection with HBV might potentiate alcohol-induced liver damage, and there is evidence that this may occur at fairly low alcohol intakes (Villa et al., 1982).Equally chronic active hepatitis associated with HBsAg may coexist with alcoholic liver disease, and the two disease processes would probably result in more rapid progression to cirrhosis.From our studies,vaccination of subjects is strongly advocated in this community,while enlightenment on the dangers of this infectious agent be given considerable attention so as to reduce the consequences of this viral infection among the populace.

Disclosure

The authors report no conflicts of interests and did not request or receive any form of financial support for this project.

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