Statistical Analysis of Diabetes Mellitus and Viral Hepatitis B and/or C among Asymptomatic Subjects in Taraba State Nigeria

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Abstract: **Hepatotropic viruses (HBV and HCV) and glucose metabolism disorder (Prediabetes Mellitus (Pre-DM) or Diabetes mellitus (DM)) are serious public health challenge. The triple are reported to be among the fastest growing diseases around the world. Little studies have been carried on the coinfections of these diseases. This study sought to determine the prevalence of hepatotropic viruses and glucose metabolism disorder and coinfections between the diseases.**

Methods**: This was a cross-sectional analysis performed among 138 randomly selected asymptomatic subjects in Taraba State using Cohcran's formular for determining sample size. Descriptive statistics, Chi-square test of association were used with the help of Microsoft excel 2016, SPSS version 25 and Minitab version 17. Specimen collection and laboratory analysis were carried out inline with WHO guidelines by well trained and qualified laboratory staff of CFID.**

Results**: The overall prevalence of HBV, HCV and glucose metabolism disorder recorded in the study were 8.7%, 15.2% and 4.3%. However, 9.4% of the subjects screened were prediabetic, 0.7% of the subjects were coinfected with HBV and DM, 0.7% were also coinfected with HCV and DM. None of the subjects were coinfected with the triple infections (HBV+HCV+DM). No statistically significant association was observed between glucose metabolism disorder and hepatotropic viruses. The demographic variables tested (gender and age) were not significantly associated with glucose metabolism disorder. However, age was statistically associated with one of the hepatotropic viruses (HCV).**

Conclusion**: This study recorded high prevalence of hepatotropic viruses (HBV = 8.7% and HCV = 15.2%) and glucose metabolism disorder (Pre-DM = 9.7% and DM = 4.3%).**

A bracket of 0.7% asymptomatic subjects were both coinfected with (HBV + DM) and (HCV+DM). None of the subjects had all the triple infections (HBV+HCV+DM) and no statistical association was observed between glucose metabolism disorder and hepatotropic viruses. Statistical association was observed between some demographic variables (age and HCV) but none of such association was observed between hepatotropic viruses and DM or demographic variables (Age and gender) and glucose metabolism disorder. Findings from this study indicates an immediate need for intervention due to the increase of the diseases (HBV,HCV and pre-DM).

Keywords**: glucose metabolism disorder, hepatotropic viruses and Coinfection**

I. INTRODUCTION

Diabetes can simply be defined as the impairment of glucose metabolism characterized by hyperglycemia which can either be due to insulin deficiency or insensitivity [1]. Diabetes mellitus (DM) and pre-diabetes mellitus (pre-DM) are two common glucose metabolism disorders that predominantly affect adults [2]. This condition is only manageable through nutrition and hormone supplements with constant monitoring of glucose levels. The disease has been reported to be one of the fastest growing diseases around the world and has been estimated by the International Diabetes Federation that there are now 425 million adults aged 20–79 with diabetes worldwide, including 212.4 million who are undiagnosed [3]. Diabetic patients are constantly exposed to invasive techniques in the course of monitoring and management of their glucose levels which places them at higher risk of contracting parenterally transmitted viruses HBV and HCV inclusive and vice versa [4, 5]. These viral infections poses health challenge globally as they may progress into chronic hepatitis, liver cirrhosis, and hepatocellular carcinoma (HCC) [5] and has been estimated that 257 million persons are chronically infected with HBV and 71 million of individuals are HCV chronic carriers [6, 5]. Hepatitis B and C viruses' rates are highly variable among the African countries with HBV and HCV prevalence rates ranging from 3–20% and 1–26%, respectively [7]. Infection of the liver with these viruses damages the liver which is a central organ for the metabolism of hormones and glucose [8]. About 90% of people infected with HBV evolve spontaneously towards healing, but 80-85% of those infected with hepatitis C virus (HCV) become chronic carriers with a risk of developing cirrhosis and hepatocellular carcinoma and

is particularly high with more rapid progression when the infection occurs in a diabetic subject [9]. Studies have also reported that diabetic patients have abnormal liver function tests, hepatomegaly, hepatic steatosis, and steatohepatitis [10] which are predisposing factors to viral hepatitis. It has also been reported that diabetic patients, particularly those with a long duration and poor glycemic control have a reduced immunity; hence they are more prone to develop chronic HBV infection whilst most literatures reported prominent correlation of HCV with diabetes mellitus; hence, noting a higher prevalence of HCV among diabetic patients [11, 5] and people with HCV infection were also reported to be at risk populations to DM [1]. Given the pivotal role of the liver in glucose metabolism, the presence of severe hepatic diseases, such as liver cirrhosis and hepatocellular carcinoma, leads to dysregulation in glucose homeostasis [11]. Mechanism underlying the development of diabetes in chronic HCV infection has been attributed to direct disturbance of the insulin signaling cascade in infected hepatocytes [12]. While information regarding the mechanism in chronic HBV remains unclear, it has been mostly attributed to HBV-related cirrhosis [13]. However, the mechanisms underlying the disruption in glucose metabolism in the context of viral hepatitis without cirrhosis remains to be understood [11]. Diabetes is a disease with dilapidating consequences, hence co-infection with hepatotropic viruses can turn it more devastating. Despite the high prevalence of both hepatitis and diabetes in Nigeria, information regarding their comorbidity remains scanty in the country. This study aimed at determining the comorbidity rate among asymptomatic subjects so as to provide information that will be useful in increasing awareness of the populace and health practitioners on the dangers of such co-infectious or comorbidity status of this virus and diabetes thence, reducing comorbidity and mortality due to co-infection.

II. MATERIALS AND METHODS

Study Area

This study was conducted at the secretariat complex in Jalingo Taraba State in commemoration of World Hepatitis Day. Frequency of Hepatitis positivity and diabetes Mellitus statuses were compared among asymptomatic subjects in Jalingo Taraba State using Pearson Chi-square test. The level of significance was set at 0.05.

Study Population

The study population comprised all asymptomatic adult subjects in Jalingo metropolis of Taraba State who were present at the time of the study and gave written consent to participate in the study.

Sample Size

In order to determine a representative sample for this study, Cochran's formula for determining sample size was used. The formula is given as follows:

$$n = \frac{z^2 pq}{e^2}$$

Where: n = *the required sample size*

p = *the estimated population proportion (0.10) is based on the recent studies conducted by [25]*

q = *1-p (0.90)*

e = *the desired level of precision (0.05)*

Therefore,

$$n = \frac{(1.96)^2 \; x \; 0.10 \; x \; 0.90}{(0.05)^2} = 138$$

Sampling Technique

All subjects were recruited using simple random sampling technique in which asymptomatic subjects were randomly selected and enrolled. Demographic data of the subjects were obtained via oral interview in December, 2021.

Specimen Collection and Analysis

Serological testing for HBV and HCV were performed at CFID Diagnostic Centre in Jalingo Taraba State. HBsAg in patients' serum were detected using test strip which was immersed vertically in the serum for at least 10 – 15 seconds, the test strip was later placed on a non-absorbent flat surface, while waiting for the red line(s) to appear, the timer started, then the result was read at 15 minutes in accordance with the manufacturers' guide in December, 2021.

Laboratory Analysis and Screening for Random Blood Sugar Test

There exist different varieties of glucometer each of which depends on the manufacturer's instruction. The tests generally involved pricking of finger and dropping blood on a strip which is subsequently inserted into the glucometer. Chemical reaction usually takes place during this process after which the device gives the output of the result in approximately 20 seconds. The interpretation of random blood glucose test results was in line with WHO guidelines as given by Mayo Foundation for Medical Education and Research [MFMER](2020).

i. A blood glucose level less than 140mg/dL (7.8mmol/L) is considered normal
ii. A blood glucose level from 140 – 199mg/dL (7.8 – 11.0mmol/L) is considered prediabetes.
This is sometimes referred to as impaired glucose tolerance.
iii. A blood glucose level of 200mg/dL (11.1mmol/L) or higher indicates type 2 diabetes.

Statistical Analysis

The statistical tools used for data analyses were Pearson Chi-square and Fisher exact tests for test of association between categorical variables. Descriptive statistics such as cross

tabulations, frequency, percentages and charts were also performed with the help of Statistical Package for Social Sciences (SPSS) version 25, R and Microsoft Excel 2016. Data was extracted from Microsoft Excel and transferred into statistical packages for cleaning and hypothesis testing. A conventional p-value of less than 0.05 was considered statistically significant.

Limitation

This study made use of Random Blood glucose test to check for diabetes mellitus (type 2) ssamong asymptomatic patients in Jalingo Metropolis. Sample size considered for this study is 138. The study of Hepatotropic viruses and diabetes are vast, however, this study is limited to HBV and/or HCV and Diabetes mellitus (type 2).

Conflict of Interest: None

III. RESULTS

Table 1. Demographic Data

Variables	Categories	Frequency	Percentage (%)
Gender	Male	76	55.1
	Female	62	44.9
Age Category	<=33years	90	65.2
	>33years	48	34.8

Table 2. Gender and Age Distributions of HBV Status and Pearson Chi-square Asymptotic Significance value

Variables	Categories	Positive	Negative	P-value
Gender	Male	7(5.1%)	69(50%)	0.812
	Female	5(3.6%)	57(41.3%)	
	Total	**12(8.6)**	**126(91.3%)**	
Age Category	<=33years	7(5.1)	83(60.1%)	0.600
	>33years	5(3.6)	43(31.2%)	
	Total	**12(8.7%)**	**126(91.3%)**	

Table 3. Gender and Age Distributions of HCV Status and Pearson Chi-square Asymptotic Significance value

Variables	Categories	Positive	Negative	P-value
Gender	Male	10(7.2%)	66(47.8%)	0.456
	Female	11(8%)	51(37%)	
	Total	**21(15.2%)**	**117(84.8%)**	
Age Category	<=33years	8(5.8%)	82(59.4%)	0.005
	>33years	13(9.4%)	35(25.4%)	
	Total	**21(15.2%)**	**117(84.8%)**	

Table 4. Gender and Age Distributions of Diabetes Mellitus and Pearson Chi-square Asymptotic Significance value

Variables	Categories	Diabetic	Prediabetic	Normal	P-value
Gender	Male	3(2.2%)	6(4.3%)	67(48.6%)	0.456
	Female	3(2.2%)	7(5.1%)	52(37.7%)	
	Total	6(4.3%)	13(9.4%)	119(86.2%)	
Age Category	<=33years	4(2.9%)	8(5.8%)	78(56.5%)	0.758
	>33years	2(1.4%)	5(3.6%)	41(29.7%)	
	Total	6(4.3%)	13(9.4%)	119(86.2%)	

Table 5. Distribution of Co-morbidity of HBV and Diabetes Mellitus and Pearson Chi-square Asymptotic Significance value

HBV Status of Participants			Diabetes Mellitus Status			Total	P-value
			Normal	Prediabetic	Diabetic		
HBV	Negative	Count	110	11	5	126	0.495
		% of Total	79.7 %	8.0%	3.6%	91.3 %	
	Positive	Count	9	2	1	12	
		% of Total	6.5%	1.4%	0.7%	8.7%	
Total		Count	119	13	6	138	
		% of Total	86.2 %	9.4%	4.3%	100. 0%	

Table 6. Distribution of Co-morbidity of HCV and Diabetes Mellitus and Pearson Chi-square Asymptotic Significance value

HCV Status of Participants			Diabetes Mellitus Status			Total	P-value
			Normal	Prediabetic	Diabetic		
HCV	Negative	Count	102	10	5	117	0.700
		% of Total	73.9 %	7.2%	3.6%	84.8 %	
	Positive	Count	17	3	1	21	
		% of Total	12.3 %	2.2%	0.7%	15.2 %	
Total		Count	119	13	6	138	
		% of Total	86.2 %	9.4%	4.3%	100. 0	

Figure 1. Distribution of HBV Status among the Subjects

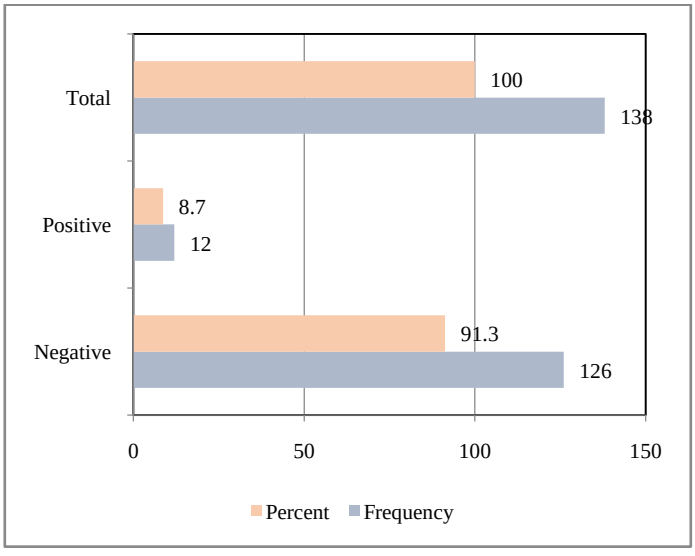


Figure 2. Distribution of HCV Status in the study Subjects

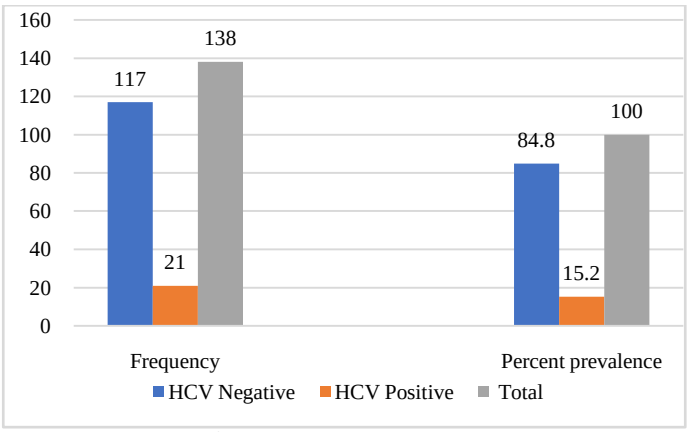
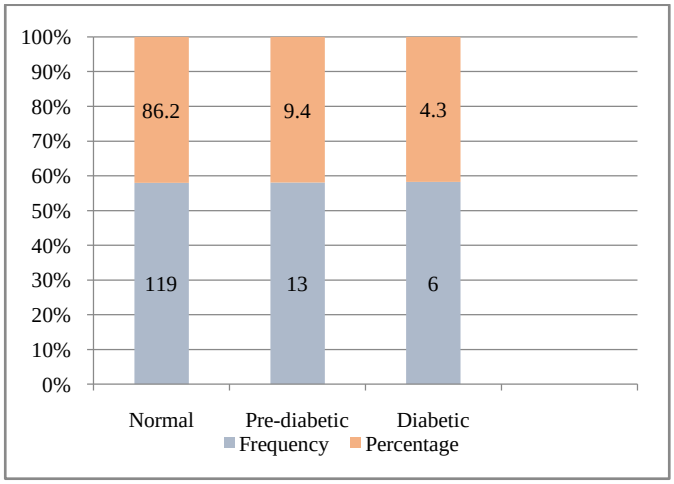


Figure 3. Distribution of Diabetes Mellitus Status Among the study Subjects



IV. RESULTS DESCRIPTION

A total of 138 asymptomatic subjects were enlisted for the study out of which 76(55.1%) were male while 62(44.9%) were females. The mean age of the subjects recruited was 32.6 with age specification of less than or equal to 33 years and above 33 years respectively **(Table 1)** this classification is based on the mean age and previous studies carried out [23,35].

Ninety asymptomatic subjects representing 65.2% were 33 years and below while 48 subjects representing 34.8% were more than 33 years of age **(Table 1)**.

The overall prevalence of HBV, HCV and diabetes mellitus in the study were 12, 21 and 6 representing 8.7%, 15.2% and 4.3% respectively however, 13(9.4%) of the subjects screened were prediabetic **(Table 2-4, Figure 1-3)**.

Table 2. Shows whether there exist statistical association between age/gender and HBV status. The P-values 0.812 and 0.600 clearly indicated no association. **Table 3.** Also shows no statistical association between gender and HCV (P-value = 0.456 > 0.05). Strong statistical association was observed between age and HCV (P-value = 0.005 < 0.05).

Table 4. Further indicated no statistical association between gender/age categories and diabetes mellitus status of participants as the P-values are greater than 0.05 (0.456 and 0.758). **Table 5.** Shows the co-morbidity of hepatitis B virus and diabetes mellitus among subjects. The table **(Table 4)** revealed that one subject representing 0.7% who was positive to HBV also had diabetes mellitus (co-infection). Also, 2 of the subjects representing 1.45 who were positive to HBV were also prediabetic. However, no statically significant association was observed between HBV and diabetes mellitus statuses (P-value = 0.495 > 0.05).

Finally, **Table 5.** Shows that 1 of the subjects representing 0.7% who was positive to HCV also had diabetes mellitus comorbidity. Three subjects representing 2.2% who were prediabetic were also found to have HCV. However, no statistically significant association was found between HCV and diabetes mellitus statuses of the asymptomatic subjects sampled (P-value = 0.70 > 0.05)

V. DISCUSSIONS

Viral hepatitis B and/or C and diabetes mellitus (glucose metabolism disorder) are serious public health challenge worldwide [9]. There are scanty studies on association between diabetes mellitus, HBV and HCV [14, 15]. Several arguments have erupted in relation to the subject matter. It has been reported that HCV infected patients have higher risk of developing diabetes mellitus, essentially type 2 [4]. There are claims that someone who is diabetic is at high risk for HCV infection [16], despite all these, the mechanisms underlying this association is yet to be understood. Similar trend is applicable to HBV seroprevalence and glucose metabolism disorder (diabetes mellitus); controversies are said to be persistent. Most studies failed to observe differences in seroprevalence of HBV between diabetic and non-diabetic subjects [17, 18, 16, 4]. Only few studies indicated a higher risk of HBV infection in diabetics compared to non-diabetics [19, 20, 21, 22] and a high risk of diabetes mellitus in HBV infected patients (Cuixia, 2015). This study reported a percent prevalence of 8.7% for HBV, 15.2% for HCV, 4.3% for type 2 diabetes, 9.4% for prediabetics, 0.7% for co-infection of HBV and diabetes mellitus (HBV+DM), 1.4% for prediabetic subjects who were also positive to HBV, 0.7% for co-infection of HCV and diabetes mellitus (HCV+DM) and 2.2% for prediabetic subjects who were also positive to HCV. [23] classified the prevalence of HBV into three categories thus: low, intermediate, and high of which corresponds to < 2%, 2 to 8% and > 8% respectively. [23], further grouped HCV prevalence as ≥3%, 2 to 2.9%, 1 to 1.9% and < 1% which means high, moderate, low and very low prevalence in endemic regions. On the other hand, [24] also noted that nationally, there is an average prevalence of 2.2% of diabetes mellitus in Nigeria with an extrapolated prevalence of 4.99%. From the above groupings given by [24, 23], one can deduce from the findings of this study that there is high prevalence of both HBV and HCV among asymptomatic subjects in Taraba State. Also, 4.3% type 2 diabetes prevalence reported for this

study is higher than the national average percent given by [24] but slightly lower than the extrapolated national prevalence (4.99%). The findings for HBV and HCV prevalence reported for this study is high which also agrees with the fact that Taraba State has highest burden of viral hepatitis B & C in Nigeria. The prediabetic prevalence rate of 9.4% reported in this study is quite alarming and clearly suggests the need for immediate action.

The prevalence rate of HBV and HCV reported in this study is far more than some earlier studies carried out in Ethiopia where prevalence rates of HBsAg and HCV were reported to be 3.7% [4] and 9.3% in North Eastern Nigeria [25]. That of type 2 diabetes reported in this study is slightly higher than some studies carried out in Nigeria by [26, 27] in Sokoto and Abia States whose prevalence rates were 0.8% and 3.6%, but lower than some earlier studies carried out by [28, 29] in Oyo and Uyo whose prevalence rates were 11% and 10.5%. (Olokoba et al., 23) also reported a positive correlation between HCV infection and diabetes mellitus at Yola (9.3% versus 2.4%). On the contrary, [30, 31] found low prevalence of HCV among T2DM subjects at the South West region of Nigeria. Results from this current study show no significant association between glucose metabolism disorder and hepatotropic virus(es) infections. This study concurs with several other studies carried out across the globe who have equally reported that no detected association exists between DM and HBV or HCV infection [32, 33]. The study however, contradicts with the assertion given by [26, 27] who reported that DM can be triggered by hepatotropic viruses.

Several studies have shown that HCV infection significantly increases the prevalence of DM [35]. Results from this finding show no statistical association between HBV and DM or HCV and DM this agrees with the studies carried out by [31, 36] whose studies equally show no significant association between HCV infection and the prevalence of DM. Similar conflicting results have been found among studies of the association between DM and HBV infection [19]. Previous studies are said to have concentrated more comparison between the association of hepatotropic viruses (HBV or HCV) infections and DM; little or no studies have incorporated the association of HBV or HCV and pre-DM. In these studies, despite the high prevalence of pre-diabetes mellitus in the study area, yet, there exists no association between the triple infections. This study also compared the association gender/age and HBV or HCV and DM among asymptomatic subjects in Taraba State. Thus, our results had it that no significant association exists between gender/age and glucose metabolism disorder. These studies contradict with several studies and could be attributed to the low sample size used for this study. Age and weight have been reported in previous studies as an important factor that triggers glucose metabolism disorder however, in this study, age was only statistically associated with HCV. No statistical association was observed between gender/age and glucose metabolism disorder.

There is therefore need for further studies to be conducted with possibly larger sample in order to draw meaningful conclusions putting family history, gender, BMI, Age and hypertensive or not into consideration as this may give or deliver more reliable results.

VI. CONCLUSION

This study recorded high prevalence of hepatotropic viruses (8.7% and 15.2%) with 4.3% and 9.7% prevalence rates of DM and pre-DM among asymptomatic subjects in Taraba State (Jalingo). No statistical significant association was observed between DM or pre-DM and hepatotropic viruses (HBV or HCV) infection. The pragmatic evidence of high prevalence recorded from the findings of this study suggests necessary actions by researchers, policymakers, and public health stakeholders to derive health promoting policies, allocate resources, and set priorities for monitoring future trends of these diseases.

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