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Coagulation Parameters among Individuals with Hepatitis B Infections in Okada, Edo State, Nigeria

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Hepatitis B Viral (HBV) infection is a condition of inflammation of the liver. The Liver plays a vital role in the body which includes filtration of the blood, production of coagulation proteins and also as a storage organ. In this study, alteration of some coagulation parameters which include, Prothrombin time (PT), activated partial thromboplastin time (APTT), Platelets counts (PLATS) were

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determined in sixty (60) known seropositive individuals using standard haemostatic techniques. There was a significant reduction in the mean value (mean values) on platelet counts in the seropositive individuals (p- value) compared to the control group (mean value), also revealed in this study is an increase in the mean-time which was significant of PT among test individuals compared to seronegative controls individuals, there was an increase prothrombin time as well as Activated partial prothrombin time with both having p- values < 0.001. The average PT and APTT were 25.53 and 48.89 respectively. Individuals with Hepatitis B infection are thus liable to thrombocytopenia if not managed.

Keywords: Coagulation parameters; hepatitis b; thrombocytopenia, fibronolysis.

1. INTRODUCTION

Hepatitis B virus (HBV) is one of the key etiological agents for liver diseases, including chronic hepatitis, liver cirrhosis and liver cancer [1]. It is the second commonest human carcinogen after tobacco [2], the virus is highly contagious and extremely resilience to environmental conditions [3]. The liver plays a pivotal role in the hemostatic system as it provides the framework for the coagulation factors and proteins involved in fibrinolysis [4]. Consequently, chronic or acute liver diseases frequently have a profound effect on the hemostatic system [5] Routine laboratory investigation for coagulation profile such as the platelet count, prothrombin time (PT), and the activated partial thromboplastin time (APTT) are frequently abnormal in patients with liver disease [6].The combination of thrombocytopenia in association with prolonged PT and APTT is suggestive of a bleeding diathesis and is traditionally assumed that patients with liver disease are at a risk for bleeding as a results of these changes in the hemostatic framework.

In apparently normal healthy individuals, the hemostatic framework is in a fragile harmony between excessive bleeding state and clotting. Notwithstanding, irregularities in the framework cause either hemorrhagic or coagulating disorder [7]. There are various elements that influence the ordinary hemostatic framework, of which HBV disease is known to have been one of the primary drivers of hemostatic anomaly [8]. HBV contamination causes serious haemostatic difficulty particularly in the late phase of HBV, as resistant concealment, and the presence of simultaneous contamination or neoplastic sicknesses compounds the condition [9].

Coagulation abnormalities in HBV patients can be as a result of the impact of the infection which causes various anomalies that incline the patients toward the events of coagulation. The aim of this study was to determine changes in the coagulation parameters which are Activated Partial Thromboplastin Time (APTT), Prothrombin Time (PT) and Platelet count among Hepatitis B seropositive individuals in Okada Metropolis.

2. MATERIALS AND METHODS

2.1 Study Area

The study was carried out at Haematology Laboratory of Igbinedion University Teaching Hospital, Okada town, Edo state, Nigeria.

2.2 Study Subjects

Individuals recruited for the study were confirmed seropositive individuals to HBV and without any other underlying disease.

2.3 Study Design

This is a descriptive case – controlled study intended to determine the quantitative values of APTT, PT and platelets using seropositive Hepatitis B individuals as the test group and Hepatitis B seronegative individuals as control.

2.4 Sample Size

A total of 60 subjects took part in this study utilizing the equation

N=(Z^2 PQ)/D^2

Where n is the base example size

Z standard deviation which is normally 1.96 which relates to 95% certainty level
D represents level of accuracy (taken as 0.05)
P commonness level of 0.5%
Q is elective extent (1-p) which is 1-0.5=0.5

2.5 Sample Collection

Eight milliliters (8ml) of venous blood test was collected and dispensed trisodium citrate specimen bottle and spun to obtain plasma to be used for PT and APTT investigation, while the remaining 3.0 ml was dispensed into EDTA specimen container for platelet counts.

2.6 Prothrombin Time Assay

PT was determined using the manual instructions as follows. The expected volume of PT reagent to be utilized was eliminated from the vial and incubated for 10 min at 37°C. 100µl microliters of the test plasma was added into a cuvette and incubated at 37°C for 3 min. 200µl of the pre incubated PT reagent was quickly added and the clock was started. The time taken for cluster to shape was recorded as the prothrombin time.

2.7 Activated Partial Thromboplastin Time (Modified with Kaolin) Assay

The anti- coagulated blood was centrifuged at 2500RPM for 15 minutes and the test procedure was done within two hours at room temperature. Plasma samples were stored frozen at -20℃ for up to a month, for tests not completed same day [10].

Procedure:

The sample mixture was brought to 37℃ and placed in test tubes. 100µl of plasma citrate was added, and 100µl of reagent added. Mixture was incubated for 3-5 minutes at 37℃.

100µl of calcium chloride was added and the time for clot formation was recorded by the coaglometer.

2.8 Platelet Count Assay

This was assayed using the Mythic 18 auto analyzer.

2.9 Data Analysis

The data obtained from this study research was subjected to statistical analysis using Chi-square and SPSS 23.0 (Statistical Package for Social Sciences), Frequency dispersion, Bivariate Correlation (Pearson and Spearman's rho Correlation Coefficients). Results were communicated as mean ± standard deviation, and correlations among gatherings and among bunches were broke down utilizing the autonomous t-test and the examination of difference, individually. The degree of significance was set at $P < 0.05$.

3. RESULTS

Table 1 is the average PT, PTTK INR and PLT of the HBV subject (Test) were 23.53, 48.89, 2.30, and 110.88 respectively with exception of the PLT, the values of theses variable were lesser in the control subject. The mean comparison by t-test showed that PT, PTTK and INR level of the HBV patient was statistically significantly higher than that of the control group ($p<0.05$). The mean PLT was significantly higher ($p<0.05$) in the control group than the test.

Table 2 indicates the Multivariate regression analysis. There was a significant correlation associated with HBV status while other variables are held constant. All the independent variables were enter into the model except INR because it has nearly a perfect correlation with PT and PTTK to avoid multi co-linearity. The model significantly predict HBV status $\chi^2(3) = 23.8$, $p<.001$. The model account for 32.8% (cox&snell R^2) of the variance in the HBV status. No variable was significantly independently associated with HBV status with other variable held constant.

Table 3 showed the output of the Pearson correlation coefficient (r). The association of the variables with each other in the control group was not significant. PT showed a very strong correlation with PTTK and INR. PTTK showed very strong to near perfect correlation with INR and PLT but not significant. This outcome may have resulted from a very small sample size. In the Test group PT showed statistically significant positive moderate and very strong correlation with PTTK and INR respectively. PTTK showed statistically significant positive and negative moderate correlation with INR and PLT respectively.

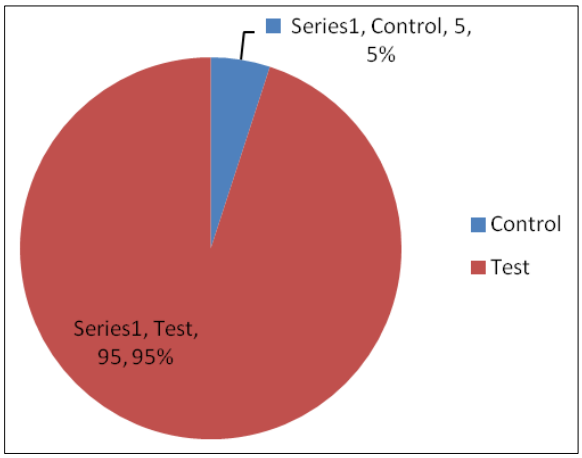

Fig. 1. Percentage distribution of the subject

Table 1. Mean comparison of the variables between groups

Variables	Control	Test	t-test	p-value
PT	13±1.00	23.53±3.87	4.67	<0.001
PTTK	37.00±4.36	48.89±4.54	4.43	<0.001
INR	1.05±0.08	2.30±0.56	3.85	<0.001
PLT	282.33±33.01	110.88±26.53	10.81	<0.001

Table 2. Logistics regression analysis

Variables	B	S.E.	p-value	Odd Ratio
PT	3.43	1007.94	0.99	31.006
PTTK	0.53	968.04	1	1.693
PLT	-0.13	87.42	0.99	0.881
Constant	-50.36	46245.429	0.99	0

Table 3. The Correlation of the variables in the control and the Test

Status	Variables	PT	PTTK	INR	PLT
Control	PT	1			
	PTTK	-0.803	1		
	INR	0.866	-0.993	1	
	PLT	-0.515	0.924	-0.875	
Test	PT	1			
	PTTK	.418**	1		
	INR	.969**	.375**	1	
	PLT	-0.07	-.397**	-0.075	1

4. DISCUSSION

Hepatitis B virus remains a major health problem worldwide, contributing considerably to cirrhosis and hepatocellular carcinoma- related mortality of 0.5 -1million per year [11]. It is well known that the liver plays a critical role in hemostasis as most of the coagulation factors; anticoagulant and components of the fibrinolytic system are synthesized by the liver parenchymal cells. Therefore, these liver functions can be impaired as a result of HBV infection.

The research findings showed that there is a marked thrombocytopenia (p- value < 0.001). This was in line with work done by [12-15], this reduced platelets count could be as a result of the disease progression, the individuals in this case are chronic hepatitis B seropositive carriers and also as a result of impaired hepatic synthesis

of thrombopoietin which is the principal physiological regulator of platelet production [16]. Nevertheless, the INR (International normalized ratio) value obtained were high, p- value < 0.001, an indication that the subjects are at risk for bleeding or clotting disorder.

Also there exists a statistical change in PT and APTT (using modified Kaolin). According to Yang-Mei et al., 2008, infection of the liver by virus especially those not self- limiting such as Hepatitis B causes virus induced tumor necrosis factor production which mediates a significant liver pathology. These changes can therefore be explained on the basis of the state of the diseased liver which is saddled with the responsibility of clotting factor synthesis [18] and most likely loss of hepatic function following HBV infection creating hepatic inflammation as a result of hepatitis B virus X protein which is pro-inflammatory cytokine mediating a Fas- mediated cell apoptosis [19].

5. CONCLUSION

Viral hepatitis B can be deduced to cause alterations in the coagulation factors as seen in this study. Hence, coagulation process backing, checking and evaluation ought to be important for routine operation in the management of patients with Hepatitis B infection.

CONSENT AND ETHICAL APPROVAL

Ethical approval was sought and obtained from the Institutional Ethics Committee of the Igbinedion University Teaching Hospital, Okada, Edo State. Informed written consent and verbal communication relating to the aims of the study were administered to participants. Each recruit was identified by means of serial numbers rather than names to ensure confidentiality.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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