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Hemostatic Disorder in Chronic Liver Disease

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Abstract **Original Research Article**

Background*:** Liver diseases have varieties of clinical complications and manifestations of which some could be life threatening. Multiple interaction often opposing variables converge to produce net hemostasis in the patient with liver disease and derangements in haemostatic parameter which are associated with increased risk of complications such as bleeding and thrombosis. These abnormalities add morbidity to the primary pathology hence, increases the mortality. It is therefore imperative to study the hemostatic derangements to decrease it associated complication. ***Aim & Objective: To assess the haemostatic profile of patients with chronic liver disease visiting the University of Calabar Teaching Hospital assessing the haematological and hemostatic abnormalities in order to reduce the morbidity. ***Materials & Methods:*** A cross-sectional descriptive study involving consecutive chronic liver disease patients referred to the Gastroenterology unit of the University of Calabar Teaching Hospital. Over a 9 months period, a total of one hundred and six patients seen were recruited into the study. The CLD patients who met the eligibility criteria for chronic hepatitis (CH), liver cirrhosis (LC) and primary liver cell carcinoma (PLCC) were recruited for the study. ***Result:*** One hundred and six patients were selected for this study. 73 (69%) male and 33 (31%) female giving a male: female ratio of 2.2:1. The mean age of the subjects is 40.22 ± 14.31 years. 7 (6.60%) had elevated platelet count, 52 (49.06%) had normal platelet count while low platelet count was observed in 47 (44.34%). Normal INR was observed in 33 (31.10%) while elevated international normalized ratio (INR) was observed in 20 (18.87%) of the patients. ***Conclusion:*** Chronic liver disease is commoner in males with marked variation in platelet count and INR with predominantly thrombocytopaenia and elevated INR. This derangement is said to contribute to the risk of bleeding in chronic liver disease patient.

Keywords: Hemostasis, Chronic Liver Disease, Platelet Count, INR, and Calabar.

INTRODUCTION

Chronic liver disease (CLD) is characterized by a defective hepatic synthesis of clotting factors and thrombocytopenia, largely caused by portal hypertension and by hyperfibrinolysis that may further contribute to alterations in hemostasis [1]. CLD involves a progressive destruction and the regeneration of the liver parenchyma which may lead to fibrosis and cirrhosis [2]. CLD is associated with a wide range of liver pathologies which includes: inflammation (chronic hepatitis), liver cirrhosis and hepatocellular carcinoma [3].

Liver diseases have varieties of clinical complications and manifestations of which some could be life threatening. For example, patients diagnosed with liver cirrhosis have varying degrees of compensated liver function and it is imperative for clinicians to distinguish between patients that are stable, those with compensated cirrhosis and those with decompensated cirrhosis. Derangements in haemostatic indices are associated with increased risk of complications such as bleeding and thrombosis.

Normal hemostasis depends on the complex interaction of several variables which includes coagulation factors, cellular tissue factor and platelet functions [1]. Multiple interacting and often opposing variables converge to produce net hemostasis in the patient with liver disease [2]. Hemostatic derangements are one of the main challenges associated with liver transplantation [4].

International normalized ratio (INR) and platelet count are used to evaluate the bleeding risk in patients undergoing liver biopsy [5]. INR this is ratio of prothrombin test over prothrombin control raised to the power of international sensitive index (ISI) These

laboratory investigations are also used for the prediction of bleeding during laparoscopic procedures in patients with liver cirrhosis [6]. This study aims to assess the haemostatic indices of patient visiting or admitted into the Gastroenterology unit of UCTH Calabar and also to assess the severity of complications in the patients thereby reducing the possibility of future complications that could be prevented through early detection, proper intervention and management.

Aim of the Study

- To detect platelet abnormalities in patient with chronic liver disease
- To detect changes in INR in patient with chronic liver disease

MATERIALS AND METHODS

A total of one hundred and six patients were selected for this study. A referred to the Gastroenterology unit of the University of Calabar Teaching Hospital and were evaluated for chronic liver disease and the hematological abnormalities. Oral consent for the clinical examination and for the laboratory investigations were obtained from all patients. All the patients were interrogated regarding their symptoms, duration of illness, bleeding tendencies, abdominal distension, jaundice, oliguria. Past history regarding previous treatment of diabetes, hypertension, tuberculosis, coronary heart disease, trauma, blood transfusion, and contact with blood products. Personal history regarding alcoholism, smoking, high risk behavior was obtained. Family history of any liver disease was also noted. The CLD patients who met the eligibility criteria for chronic hepatitis (CH), liver cirrhosis (LC) and primary liver cell carcinoma (PLCC) were recruited for the study. Patients were submitted to blood investigations, haematologic work up was done for blood count estimation and international normalized ratio (INR). The methods for the diagnosis of CLD were based on a combination of clinical, biochemical, ultrasonographic and histological features. These methods have been previously described in another study [7].

The data obtained were collated using Microsoft excel 2016 and the data were analyzed using Statistical package for Social Sciences SPSS Version 22. The data were presented in tables and charts.

RESULTS

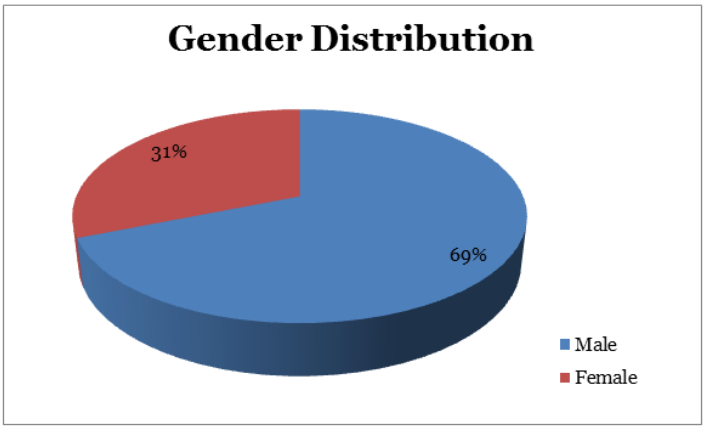

Fig-1: Showing the gender distribution of the participants

Male: Female = 2.2:1

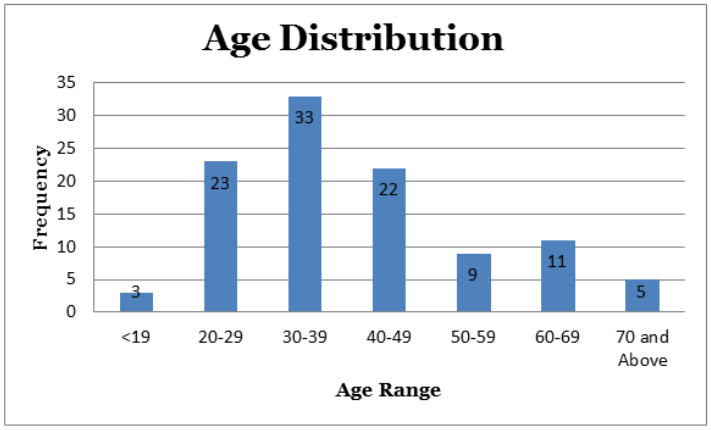

Fig-2: Showing the age distribution of the participants

The mean age was 40.22 years with standard deviation of 14.31. CLD was observed to be more within the age range 30-39 years with continuous declination.

Table-1: Showing the participants' platelet count

PLATELET COUNT RANGE	FREQEUNCY	PERCENTAGE
<150x10^9/L (Low platelet count)	47	44.34
150-400x10^9/L (Normal platelet count)	52	49.06
>400x10^9/L (High platelet count)	7	6.60
Total	106	100.00

Total of 7 (6.60%) had elevated platelet count while majority of the participants (52, 49.06%) had normal platelet count

Table-2: Showing the participants' INR distribution

INR RANGE	FREQUENCY	PERCENTAGE
0.8-1.2 (Normal human range)	33	31.1
1.2-2 (Undefined range)	53	50.0
2-3 (STTR)*	13	12.3
2.5-3.5 (More intense target range)	4	3.8
3-4.5 (High clot risk target range)	3	2.8
Total	106	100

*(STTR) - Standard therapeutic target range. Elevated international normalized ratio was observed in 20 (18.87%) of the patients

DISCUSSION

The index study showed that chronic liver disease is more in males than female in a ratio of 2.2:1 with mean age of 40.22 years this was similar to the study conducted in Enugu South South Nigeria by Nwokediuko *et al.* [8] reported male preponderance with ratio of 2.2:1 and mean age of 46±18 years furthermore this was somewhat similar to the study conducted by Scalone *et al.* [9] on the societal burden of chronic liver disease but varies in term of mean age which was higher in their study. This variation can be attributed to the difference in study design. However, a study by Setiawan Veronica *et al.* [10] gave a contradicting report of female preponderance with a ratio of 1.1:1 in a study to determine the prevalence of chronic liver disease and cirrhosis the underlying cause in understudied ethnic group in a multiethnic cohort.

This study also shows inconsistency in platelet count with 49.06% having normal platelet, followed by 44.34% with thrombocytopaenia and 6.60% with thrombocytosis this was similar to the report by Nwokediuko *et al.* [8] on quantitative platelet abnormalities in patient with hepatitis B virus liver disease. Another study by Bashour [11] reported a prevalence of 49-64% of thrombocytopaenia in patient with non-alcoholic liver disease. Similarly, Afdhal *et al.* [12] reported thrombocytopaenia with higher prevalence, in like manner Witter *et al.* [13] also reported similar finding. Furthermore, Hancox *et al.* [14] also reported a prevalence of 58% thrombocytopaenia. However, despite the inconsistency in most of the available study the commonest finding among them is predominantly thrombocytopaenia which is attributed to decrease production of thrombopoietin in damaged liver, increase destruction of platelet by enlarge spleen or immune thrombocytopaenia purpura and loss of haempoietic function in the bone marrow while the rare thrombocytosis can be attributed to paraneoplastic manifestation.

There was also inconsistency in the INR level in the index study with majority greater than 1.2 and about 33% were within normal range, this is similar to the finding by Fisher [15] in a study on the central venous cannulation in patient with liver disease and coagulopathy. In like manner similar finding was reported by Mallory *et al.* [16]. Furthermore, Patel *et al.* [17] also reported similar finding in a study on Consensus guidelines for periprocedural management of coagulation status and hemostasis risk in percutaneous image-guided interventions.

Due to this variations, INR is consider a contraindication for procedural intervention including liver biopsy paracentesis thoracentesis and lumbar puncture. This variation in INR level can be attributed to difference in thromboplastin reagent preparation. The pitfall of INR as a predictor for risk of bleeding in patient with chronic liver disease is due to the obsolete model of coagulation cascade which is now been replaced by cell model theory. Also, the benefit of assessing platelet count and function using bleeding time is inclusion of the entire in vivo coagulation cascade rather than the incomplete in vitro coagulation cascade commonly assessed by PT and INR.

CONCLUSION

Chronic liver disease is commoner in males with marked variation in platelet count and INR with predominantly thrombocytopaenia and elevated INR.

This derangement is said to contribute to the risk of bleeding in chronic liver disease patient with platelet concentration and function is a more concerning factor in influencing bleeding risk in CLD patient than INR.

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