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Research Article
Platelet Indices as Clinical Markers in Sudanese Patients Suffering from Chronic Liver Diseases: Critical Analysis

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Abstract

Background and Objective: Platelets play a central role in primary hemostasis. The liver play major role in thrombopoietin hormone production thus liver disease may affect the platelet production and maturation. This study was conducted to determine the influence of chronic liver diseases on platelet parameter among chronic liver disease patients. **Materials and Methods:** This descriptive cross-sectional study, conducted in AL-Gadarif Hospital state during the period from February to May, 2018. A total of 80 subjects were enrolled in this study. Complete blood count (including PLTs indices) was carried out in automated hematology analyzer (Sysmex-XP 300). **Results:** patients of this study have significantly reduced PLTs count ($p = 0.000$). The PDW was significantly increased among patients of chronic liver disease ($p = 0.000$). Regarding indices across gender, the platelet count was significantly lower in males compared with females ($p = 0.022$). The study revealed a significant reduction in platelets count in the 4 types of liver diseases ($p = 0.038$). **Conclusion:** Patients with chronic liver disease exhibit significant changes in platelet indices. That is varied according to the type and time duration of liver disease.

Key words: Liver cirrhosis, hepatitis B, hepatitis C, alcoholic liver disease, platelet indices

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Competing Interest: The authors have declared that no competing interest exists.

Data Availability: All relevant data are within the paper and its supporting information files.

INTRODUCTION

There are two kinds of liver sickness that are intense and ceaseless cases[1]. Chronic ailment alludes to ailment of the liver which endures for a half year or more[2]. It comprises of a wide scope of liver pathologies including irritation, for example, chronic hepatitis, liver cirrhosis, hepatocellular carcinoma and alcoholic disease[3]. Chronic liver ailment in the clinical setting is an ailment procedure of the liver that includes a procedure of dynamic annihilation and recovery of the liver parenchyma prompting fibrosis and cirrhosis[4].

The liver is the main source of thrombopoietin hormone that is responsible for controlling thrombopoiesis, therefore deterioration of liver function may influence the process of platelet production[5]. This effect could be evaluated by counting parameter called platelet indices. The normally utilized platelet records incorporate PLTs check, mean platelet volume (MPV), platelet distribution width (PDW), plateletcrit (PCT) and platelet large cell ratio (PLCR). The Mean platelet volume (MPV) is a machine-determined estimation of the normal size of platelets found in the blood and is commonly incorporated into blood tests as a component of the complete blood count (CBC). Since the normal platelet size is bigger when the body is delivering expanded quantities of platelets, the MPV test outcomes can be utilized to make derivations about platelet creation in bone marrow or platelet demolition issues. PDW is numerically equal to the coefficient of PLTs volume variation, which is used to describe the dispersion of PLTs volume. Plateletcrit (PCT) is the volume involved by platelet in the blood as a rate and figuring as indicated by the equation:

$$PCT = \text{Platelet check} \times MPV/10{,}000$$

Under physiological conditions, the measure of platelets in the blood is kept up in a harmony state by regeneration and elimination. Platelet large cell ratio (P-LCR) is an indicator of circulating large platelets (>12 fl), which is presented as a percentage, the normal range is 14-35%. It has also been used to monitor platelets activity[6].

Originally, these indices have been applied in the diagnosis of hematological system diseases. Recently, it has been discovered that these indices are related to the severity of illness and patients' prognosis. However, whether other PLT indices are associated with the severity of illness and patients' prognosis is still under exploring[7].

In Sudan, to the best of our knowledge, there is no published research regarding this concern. Therefore, the aim of this study was to evaluate platelet indices in Sudanese patients with chronic liver disease that may help in predicting and minimizing possible hemorrhagic defects.

MATERIALS AND METHODS

Methods: This is a hospital-based, descriptive cross-sectional study conducted at Al-Gadarif Hospital in Sudan during the period from February-May, 2018. A total of 80 patients who have been diagnosed with any type of liver disease including (hepatitis B virus, hepatitis C virus, alcoholic liver disease and liver cirrhosis) for more than 6 months were enrolled for the study. All patients gave informed consent for participation in the study. Demographic data, duration of disease and medications used were reported for all participants. Fifty individuals apparently healthy participated in this study as controls.

Venous blood sample (2.5 mL) was collected from each participant and placed into EDTA tube. Complete blood count was immediately analyzed by automated hematology analyzer (SYSMEX XP-300, Japan). When flagged as Suspicious for platelet aggregates, an additional blood sample was collected in sodium citrate tube[8]. Blood smears were prepared, stained with (BIO-DIFF RTU KIT) Croatia and microscopically inspection of PLTs was performed.

Exclusion criteria: Patients with chronic liver disease that lasts over a period of 6 months, patient with dysplastic bone marrow, malignancies including hematologic malignancies, splenectomy, massive splenomegaly, immune disease, heart disease, vascular disease, thrombosis, bleeding, pregnancy women, renal failure, HIV, any drugs interaction with platelet, infection and inflammation were excluded.

Ethical consideration: All patients had agreed to be involved in this study, received full explanation details of the project and have signed the informed consent form through their referral physician following the Ministry of Health-Al- Gadarif hospital. All specimens used in this study are anonymous and no name will be link to their finding. Thus, all information will be remained confidential and not for public use. Furthermore, all reported results will be delivered back to each patient's through their referral physician.

Statistical analysis: Laboratory results and patients' data were entered into excel sheet by using Microsoft Excel version 2015. All data were analysed using (SPSS software version 23.0). Descriptive statistics, frequency tables were used to summarize patient characteristics. The study population was divided into four groups according to the type of liver disease by using frequency tables. Numerical data were summarized by using range, mean and standard deviation (SD). One sample t-test was used to compare mean values PLTs indices of study participants with the reference values. Independent

sample t-test was applied to compare mean PLTs indices across genders. Analysis of variance ANOVA) was applied to compare mean PLTs indices across study groups according to the type of liver disease. Pearson's correlation was applied to find out the correlation between duration of liver disease with values of PLTs indices. For all tests, $p<0.05$ were considered a statistically significant.

RESULTS

Patients' characteristics according to the gender in liver diseases: A total of 80 (59 male/21 female) subjects with chronic liver disease were enrolled for this study. All participants were diagnosed as a chronic liver disease before at least 6 months. The majority (68.8%) of patients have HBV. Patients' characteristics are shown in (Table 1).

Summaries of PLTs indices results are shown in (Table 2). Comparison of mean PLTs indices with the reference values showed significant changes in all parameters. PLTs count, MPV and PDW are significantly decreased (p-values<0.05), while PLCR is significantly increased when compared with reference values (Table 3).

Comparison of mean PLTs indices across gender showed that, a significant difference between males and females exists in the PLTs count only ($p = 0.022$), where the MPV ($p = 0.490$), PDW ($p = 0.486$) and PLCR ($p = 0.834$) were not affected by gender (Table 4).

Platelets indices in liver diseases: Comparison of mean PLTs indices across types of liver disease showed that the PLTs level was significantly decreased in patients with HBV, Liver cirrhosis, HCV and alcoholic liver disease ($p = 0.038$) in comparison with normal values, MPV also affected in HBV, liver cirrhosis. While alcoholic liver disease was not affected ($p = 0.012$) and PDW also affected on HBV, liver cirrhosis, HCV and alcoholic liver disease ($p = 0.000$) while the PLCR insignificantly affected in HBV, liver cirrhosis, HCV and alcoholic liver disease ($p = 0.835$) in comparison with normal values Table 5.

Statistically significant negative correlations between duration of liver disease and PLTs count ($R = -0406$, $p = 0.000$) and PLCR ($R = -0.343$, $p = 0.011$) had been observed Table 6.

Table 1: Frequency of patient's characteristics

Variables	Frequency	Percentage
Gender		
Male	59	73.8
Female	21	26.3
Disease		
HBV	55	68.8
Liver cirrhosis	12	15.0
Alcoholic liver disease	7	8.8
HCV	6	7.5
Total	80	100.0

Table 2: Descriptive statistics of the study population

Parameters	Minimum	Maximum	Mean±SD
Duration	0.50	6.0	2.2±1.3
PLTs	26.00	400.0	134.5±74.8
MPV	7.00	17.5	10.8±1.9
PDW	8.90	18.2	13.6±2.3
PLCR	10.50	46.6	23.6±7.1

SD: Standard deviation

Table 3: Comparison of mean platelets indices of study patients with controls

Parameters	Mean±SD	Mean (RV)	p-value
PLTs	134.5±74.8	319.3± 80.3	0.000
MPV	10.8±1.9	13.0± 2.7	0.000
PDW	13.6±2.3	28.0±4.6	0.000
PLCR	23.6±7.1	11.0±2.2	0.000

RV: Random variable

Table 4: Comparison of mean platelets indices across genders

Parameters	Male (Mean±SD)	Female (Mean±SD)	p-value
PLTs	131.9±66.8	142.0±75.2	0.022
MPV	10.8±2.0	11.1±1.8	0.490
PDW	13.5±2.2	13.9±2.3	0.486
PLCR	23.6±7.5	23.9±6.0	0.834

SD: Standard deviation

Table 5: Comparison of mean platelets indices across types of liver disease

	Mean±SD				
Parameters	HBV	Liver cirrhosis	HCV	Alcoholic liver disease	p-value
PLTs	148.7±78.9*	91.5±43.2*	140.5±77.2*	92.1±39.4*	0.038
MPV	10.7±1.8*	12.3±2.0*	9.4±0.5*	10.9±2.5	0.012
PDW	13.3±2.1*	15.4±1.6*	11.5±2.0*	11.5±2.0*	0.000
PLCR	24.1±2.3^{Ns}	22.8±7.6^{Ns}	22.3±5.2^{Ns}	22.4±6.4^{Ns}	0.836

*$p \leq 0.05$, Ns: Not significant

Table 6: Correlation between duration of disease and values of platelets indices

Parameters	r-value	p-value
PLTs	-0.406**	0.000
MPV	0.177	0.116
PDW	0.172	0.126
PLCR	-0.343*	0.011

*$p \leq 0.05$, **$p \leq 0.01$

DISCUSSION

Abnormalities in hematological indices are frequently encountered in chronic liver disease. Multiple causes contribute to the occurrence of these abnormalities. Recent studies suggest that the presence of hematological cytopenias is associated with poor prognosis in chronic liver disease[9].

With the availability of newer high performance designed automated blood cells analyzers, platelet indices are also being estimated with better standardization and thus have greater clinical utility. Most importantly is Platelet count, (MPV), (PDW) and (PLCR). In this study, we studied platelet indices in patients with chronic liver diseases including (HBV, HCV, alcoholic liver disease and liver cirrhosis).

Findings of this study showed that mean platelet count in chronic liver diseases was significantly reduced in comparison with reference values (134.5±74.8, p = 0.000). This in agreement with Portugal study reported by Costa *et al.*[10] which showed a significant reduction in PLTs count among patients of liver disease (74.36±34.76, p = 0.001). In this study, PDW was significantly increased among patients of chronic liver disease (13.6±2.3, p = 0.000). This also is in agreement with the same Portugal study which showed a significant elevation of PDW (19.01±1.78, p = 0.002)[10].

Regarding indices across gender, the platelet count was significantly lower in males (131.9±66.8) compared with females (142.0±75.2) (p = 0.022). The predominance of males in this study sample (59 males versus 21 females) could explain the greater contribution of male subjects on the overall result. Physiological differences between males and females could provide an explanation for the discrepancy of PLTs count value across genders.

The study revealed a significant reduction in platelets count in the four types of liver diseases (p = 0.038). Previous studies showed that significant reduction in PLTs count among patients of liver cirrhosis (p = 0.0001, 0.038)[11,12]. At the other hand, findings of the later study showed that no significant difference between mean platelets count in patients with HB virus-related liver disease (p = 0.4655)[12]. This difference of results could be related to differences in severity and time duration of HB in that study compared with our study population.

Another study conducted in India agreed with our study, MPV and PDW were significantly higher in cirrhosis compared to control population. Platelet counts (PLTs) and PCT were significantly lower in cirrhosis compared to control population. Sepsis in cirrhosis was associated with a significant decrease in platelet count and PCT but caused a significant increase in PDW compared to cirrhosis without sepsis[13].

In this study, the platelets count showed significant negative correlation with the duration of chronic liver disease (R = -0.406, p = 0.000). This in agreement with the study conducted by Pan *et al.*[14] (R = -0.396, p = 0.001). The PLCR also has a negative correlation with chronic liver disease (R = -0.343, p = 0.011), while others parameter has no significant correlation with chronic liver diseases.

Limited data on clinical remarks and patients disease history represent one limitation of this study. Moreover, no diagnostic markers for the severity of the liver were carried out. These limitations are due to the poor documentation system in the study area, limited financial and technical resources available for this study.

CONCLUSION

This study discovers that patients with chronic liver disease exhibit important changes and differences in platelet indices, being the most important change during chronic liver disease. In addition, the changes in platelets indices can be beneficial for give an indication of the severity of disease and the appropriate therapeutic intervention in addition to the patients' response to treatments.

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