Original Article

To Study Platelet Indices in Alcoholic Liver Disease (ALD) Patients and to Correlate MPV to Platelet Count Ratio with Child Pugh Score to Predict the Severity

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Background : Several Non-invasive methods for predecting cirrhosis have been reported, but liver biopsy is only method for definitive diagnosis. However, liver biopsy is invasive and non invasive methods are more desirable. Platelet indices and Mean platelet volume to platelet count ratio can be determined by routine CBC data of blood sample. In the recent years these markers has attracted attention in liver cirrhosis specially due to alcohol.

Objectives : The purpose of this study was to determine platelet indices in alcoholic liver disease patients and to correlate MPV to platelet count ratio with Child-Turcotte-Pugh score.

Methods : This prospective observational case-control study was conducted on 100 patients with alcoholic liver disease. 100 healthy age-matched and sex-matched individuals were taken as controls. The patient and control groups were subjected to detailed history taking, examination and CBC, LFT and PT/INR assessment. Clinical and laboratory examination using the Child-Turcotte-Pugh score was carried out. MPV and platelet count was evaluated within the first 24 hours of admission.

Results : Maximum subjects in our study were in the age range of 40-49 years with 100% males. Mean platelet count of study group was 1.11±0.74 lakh/uL lower than the mean platelets count of control group ie, 3.36±0.87 lakh/uL and the difference between two was statistically significant (p<0.0001). Mean±SD MPV of control was 8.85±0.817 fL and Mean±SD MPV of study subjects was 10.9±0.9 fL and the difference between two was statistically significant with the p value of <0.0001. Mean PDW of study subject 14.88±2.35 fL was higher than mean PDW of control12.08±1.98 fL and the difference between two was statistically significant (p<0.0001).

Mean MPV to platelet count ratio of study subject 16.09±15.17fL/lakh was higher than the control 2.85±0.96 and the difference between two was statistically significant (p<0.0001). The value of MPV to platelet count ratio was also lowest in Child-Pugh class A(6.53±2.74) which gradually increased in Child-Pugh Class B(9.72±4.75) group and Child-Pugh Class C (22.69±17.80) with the highest MPV to platelet count ratio in Child-Pugh Class C group. In this study there was a positive correlation between MPV to platelet count ratio and Child-Turcotte-Pugh Score (r value=0.5241) and p-value was statistically significant (p<0.0001).

Conclusion : MPV to platelet count ratio were significantly higher in patients with Alcoholic Liver Disease than in controls. MPV to PC ratio increased with increasing severity of ALD.

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Key words **: Alcoholic Liver Disease, Platelet Indices, Mean Platelet Volume.**

Liver injury caused by the alcohol abuse is called Alcoholic Liver Disease (ALD) and it is classified into alcoholic steatosis (fatty liver), alcoholic hepatitis, and alcoholic liver cirrhosis. Alcohol can cause a significant alteration of cells, tissues, and organs. In particular, ethanol exposure induces cell membrane remodeling in different cells and lipid vesicles including membrane fluidization[1].

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Editor's Comment :

- Increased MPV is the predictor of liver injury in alcoholics.
- Decreased platelet count is indicator of liver injury with portal hypertension in alcoholics.
- Increased MPV to platelet count ratio is the strong indicator of liver injury in alcoholics.

Thrombocytopenia is the most common hematological abnormality encountered in patients with Chronic Liver Disease (CLD),[2] occurring in 64%-84% of patients with cirrhosis or fibrosis[3]. Among patients undergoing bone marrow biopsies for thrombocytopenia of unknown etiology, the prevalence of cirrhosis is as high as 35%[4]. In addition to being an indicator of advanced disease[5], thrombocytopenia is associated with a poorer prognosis and it frequently prevents patients from receiving crucial interventions

such as medications, as well as invasive diagnostic or therapeutic procedures[6].

Alcohol's adverse effects on the blood building, or hematopoietic system are both direct and indirect. The direct consequences of excessive alcohol consumption include toxic effects on the bone marrow; the blood cell precursors; and the mature Red Blood Cells (RBC's), White Blood Cells (WBC's), and Platelets. Alcohol's indirect effects include nutritional deficiencies that impair the production and function of various blood cells. These direct and indirect effects of alcohol can result in serious medical problems for the drinker. For example, anemia resulting from diminished RBC production and impaired RBC metabolism and function can cause fatigue, shortness of breath, lightheadedness, and even reduced mental capacity and abnormal heartbeats. A decrease in the number and function of WBC's increases the drinker's risk of serious infection and impaired platelet production and function interfere with blood clotting, leading to symptoms ranging from a simple nosebleed to bleeding in the brain (ie, hemorrhagic stroke).

Aims and Objectives

The aim of this study was to determine MPV to platelet count ratio in alcoholic liver disease patients and its correlation with Child-Turcotte-Pugh score.

Materials and Methods

After obtaining approval from Institutional Ethical Committee, a hospital based prospective and observational study was conducted on 100 patients of alcoholic liver disease admitted in Department of Medicine, Government Medical College and Associated MBS Hospital, Kota from 2021 to 2022 and compared with 100 equal number of age and gender matched controls. All Patients of Age >18 years diagnosed with liver disease with history of excessive alcohol intake with exclusion of other etiologies such as viral hepatitis and non-alcoholic steato-hepatitis and had given written informed consent to participate were included in our study whereas Patients of Age <18 years, Viral hepatitis, Non-alcoholic steato-hepatitis, Renal disease, Known thyroid disease, Hematological malignancy, History of drug intake that alter hematological profile, Immuno-suppressed individual, Systemic acute or chronic inflammatory or autoimmune or infectious disease, connective tissue diseases or prior myocardial infarction, Pregnant patient, History of recent blood transfusion, History of recent gastro-intestinal bleeding, History of vitamin supplementation, hematinics or drugs known to interfere with folate metabolism and patient refusing to give informed consent for the study were excluded. The study conducted in patients presented to us with features of Liver disease, Medical history and Ultrasound imaging done to recognize the liver injury and physical examination used in order to determine the definitive diagnosis of Alcoholic Liver Disease. Blood sample was collected from the antecubital vein using a 21-gauge sterile syringe in laboratory. Severity of Alcolic Liver Disease was determined with the Child -Turcotte-Pugh score in all patients at initial presentation. Severity of ALD was grouped in Child-Pugh Class A (5-6), Child-Pugh Class B (7-9), and Child-Pugh Class C (10-15).

Statistical Analysis :

Continuous variables were presented as Mean±SD, categorical variables were expressed in frequency and percentages. Demographic, haematological and clinical parameters were compared between cases and controls by performing independent t- test. Categorical variables were compared by performing chi- square test. Statistical method used was unpaired Student's t-test and chi-square test between MPV to platelet count ratio and severity of ALD including other variables using Graph pad in Stat Version 3. A value of $p>0.05$ was considered as not significant and $p<0.05$ as statistically significant. Correlation coefficient was also assessed between MPV to platelet count ratio and Child-turcotte-pugh Score (Tables 1-3).

Observation and Results

In our study, cases had mean age of 40.46±6.63 years which was comparable with the mean age of control group ie, 39.31±6.71 years and both groups had maximum subjects in the range of 40-49 years ie, 48 and 46 respectively. Out of 100 subjects in the study

Table 1 — *Age distribution of subjects in Case and Control group*

Age	Control Group	Study Group
20-29	10	7
30-39	38	34
40-49	48	46
>49	4	13
Mean age±SD	39.31±6.71	40.46±6.63

Table 2 — *Hematological profile of Case and Control group*

Parameters	Study group (Mean±SD)	Control group (Mean±SD)	P value
Hb	11.27±2.21	13.86±1.15	<0.0001
TRBC	3.51±.0.85	4.39±0.5	<0.0001
MCV	107.86±11.88	87.9±8.35	<0.0001
Platelet Counts	1.11±0.74	3.36±0.87	<0.0001
MPV	10.9±0.9	8.85±0.817	<0.0001
PDW	14.08±2.35	12.08±1.98	<0.0001
MPV to PC ratio	16.09±15.17	2.85±0.96	<0.0001

Table 3 — *Distribution of ALD patients in different Child-Turcotte-Pughscore group*

Child-Turcotte-Pugh class	No of study subjects
A	17
B	27
C	56

group all were males because females were not consuming alcohol in HADOTI region and this is why 100 males control were considered for study. Maximum number of patients was in Child-Pugh class C (56%) followed by 27% in Child-Pugh class B and 17% in Child-Pugh class A. In study population 43% had hepatic encephalopathy, 69% had ascites and out of which 21% had significant ascites, 36% of the patients had jaundice. Anaemia was present in 58% of the cases, haematocrit was low in 58% of the cases, Total RBC count was low in 48% of the cases, Macrocytosis was present in 74% of the cases, Thrombocytopenia was present in 76% of the cases, MPV was raised in 54% of the cases and PDW was raised in 13% of the cases in study (Tables 4-6).

When MPV of the study subjects compared with controls we found that among the study subjects 54% had MPV more than 11 fL and among the control 3% had MPV more than 11 fL. Mean±SD MPV of control was 8.85±0.817 fL and Mean±SD MPV of study subjects was 10.9±0.9 fL, and the difference between two was statistically significant with the p-value of <0.0001. In the study group the value of MPV was lowest ie, 10.14±0.47fL in cases with Child-Turcotte-Pugh score group 5-6 (Child Pugh Class A) which increased to 10.38±0.56fL in Child-Turcotte-Pugh Score group 7-9 (Child Pugh Class B) and 11.32±0.85fL in Child-Turcotte-Pugh Score group 10-15 (Child Pugh Class C). In this study there was a positive correlation between MPV and Child-Turcotte-Pugh Score (r-value=0.7316) and p-value was statistically significant (p<0.0001).

Table 4 — *MPV and Child-Turcotte-Pugh score*

Child-Turcotte-Pugh Class	MPV in Study Group	
	Mean	Standard Deviation
A	10.14	0.47
B	10.38	0.56
C	11.32	0.85
P value	<0.0001 (ANOVA test)	
R (linear regression)	0.7316	

Table 5 — *Platelet Count and Child-Turcotte-Pugh Score*

Child-Turcotte-Pugh Class	Platelet Count in Study Group	
	Mean (lakh/Ul)	Standard Deviation
A	1.78	0.65
B	1.40	0.81
C	0.77	0.51
P value	<0.0001(ANOVA test)	
R (linear regression)	0.4351	

Table 6 — *MPV to Platelet Count Ratio and Child-Turcotte-Pugh Score*

Child-Turcotte-Pugh Class	MPV to platelet Count Ratio in Study Group	
	Mean	Standard Deviation
A	6.53	2.74
B	9.72	4.75
C	22.69	17.80
P value	<0.0001(ANOVA test)	
R(linear regression)	0.5241	

Among the study subjects three fourth (76%) had platelets less than 1.5 lakh/uL, out of which 15% had platelets less than 50,000/uL, 42% had platelets 50,000-100,000/uL and 19% had platelets 1-1.5 lakh/uL and 24% have >1.5 lakh/uL. In control group 1% had 1-1.5 lakh/uL and 99% had >1.5 lakh/uL. When compared Mean±SD values, mean platelet count of study group was 1.11±0.74 lakh/uL lower than the mean platelets count of control group ie, 3.36±0.87 lakh/uL and the difference between two was statistically significant with the p-value of <0.0001. Among the study population, platelet count was lowest ie, 1.78±0.65 lakh/uL in cases with Child-Turcotte-Pugh Score group 5-6 (Child Pugh Class A) which increased to 1.40±0.81 lakh/uL in Child-Turcotte-Pugh Score group 7-9 (Child Pugh Class B) and 0.77±0.51 lakh/uL in Child-Turcotte-Pugh Score group 10-15 (Child Pugh Class C). In this study there was a positive correlation between platelet count and Child-Turcotte-Pughscore (r value=0.4351) and p-value was statistically significant(p<0.0001).

Mean±SD MPV to platelet count ratio of control was 2.85±0.96 and study subjects was 16.09±15.17, and the difference between two was statistically significant with the p-value of <0.0001. On comparing MPV to platelet count ratio it was found to be lowest ie, 6.53±2.74 in Child-Turcotte-Pugh score group 5-6 (Child Pugh Class A) which increased to 9.72±0.4.75 in Child-Turcotte-Pugh Score group 7-9 (Child Pugh Class B) and 22.69±17.80 in Child-Turcotte-Pugh Score group 10-15 (Child Pugh Class C). The highest MPV to PC ratio was present in Child Pugh Class C. In this study there was a positive correlation between MPV to platelet count ratio and Child-Turcotte-Pughscore (r-value=0.5241) and p-value was statistically significant (p<0.0001). When we correlate MPV to platelet count ratio as a predictor of severity of Alcoholic Liver Disease it is more powerful indicator and prognostic tool as compare to individual MPV and platelet count.

Discussion

Our study included 100 patients of Alcoholic Liver Disease and 100 age and sex matched control

subjects. The control subjects were free from alcohol intake. In our study all the cases were males because in *HADOTI* region the females are not consuming alcohol. Studies conducted by 2003 E Giannini, *et al*[7] and 2010 Demriel, *et al*[8] included 29% and 32% females respectively but geographical region was different. In our study, maximum no. of cases (46%) and control (48%) were in the age group of 40-49 years and the mean age was 40.46±6.63 and 39.31±6.71 respectively. In a study conducted by Etesar H Fshaqawy, *et al*[9], it had been observed that mean age in Alcoholic Liver Disease was 49.84±7.28. Also a study by Mona, *et al*[10] had mean age of 45 years with similar results. In the present study, the mean age of cases and controls were comparable with 40.46±6.63 years and 39.31±6.71 years respectively. This confirms that younger age group are more to develop Alcoholic Liver Disease.

In our study MPV of control was 8.85±0.817 fL and MPV of study subjects was 10.9±0.9 fL, Thus MPV in cases were significantly higher (p<0.0001). In study conducted by Das SK, Mukherjee S, *et al*[11] found that MPV in ALD patients was ALD 8.9 ± 1.46 fL (n=40) and in non-alcoholic was Control 8.5 ± 0.97 (n=77) (p<0.001), result was similar to the present study. In our study we noticed that when Child-Turcotte-Pugh score increased, the value of MPV also increased proportionately. The value of MPV was lowest ie, 10.14±0.47 fL in cases with Child-Turcotte-Pugh Score group 5-6 (Child Pugh Class A) which increased to 10.38±0.56 fL in Child-Turcotte-Pugh Score group 7-9 (Child Pugh Class B) and 11.32±0.85 fL in Child-Turcotte-Pugh score group 10-15 (Child Pugh Class C). Our study highlighted that there was a positive correlation between MPV and Child-Turcotte-Pugh score (r value=0.7316) and p value was statistically significant (p<0.0001). Study conducted by Edoardo G Giannini, *et al*[7] showed a similar finding such that the groups of Alcoholic Liver Disease with low Child-Turcotte-Pugh score had low MPV and those with high Child-Turcotte-Pugh score had high MPV values which were statistically significant. Mohamed S Mohamed, *et al*[12] study in 2018 also demonstrated the positive correlation between MPV values and PT/INR, serum bilirubin, lower serum albumin in ALD patients. Also, the MPV values were significantly higher in patients with more severe liver disease according to the model for end-stage liver disease (r=+0.424, P=0.008) and CTP scores (r=+0.353, P=0.03).

In our study among the study subjects 76% had thrombocytopenia, out of which 15% have platelets less than 50,000/uL, 42% have platelets 50,000-100,000/uL and 19% have 1-1.5 lakh/uL and 24% have >1.5 lakh/uL. In control group 1% have 1-1.5 lakh/uL and 99% have >1.5 lakh/uL. When compared mean values, mean platelet count of study group is 1.11±0.74 lakh/uL that was lower than mean platelet count of control group ie, 3.36±0.87 lakh/uL, which was statistically significant (p=<0.0001). Dr G Balasubramanian, *et al* 2007[13] also found platelets less than 1.5lakh/uL in 73% patients of Alcoholic Liver Disease with sample size of 200 patients as compare to control and was significant with p(0.0001), result of this study was closely similar to present study. 2011 Das S K, Mukherjee S, Vasudevan D M, Balakrishnan, *et al* found that Platelet count in control was 237.9 ± 51.30k/uL and ALD patients was 142.2 ± 73.80k/uL and the result was in accordance with present study. Bibhu Prasad Behera, *et al*[14] study found that among the 69 ALD patients 47 patients had platelets less than 1.5lakh/uL, 21 patients had platelets 1.5-4.5lakh/uL and 1 patient had platelets >4.5lakh/uL. Deepak Jain, H K Aggarwal, *et al*[15] concluded that Median platelet count among the study subjects was 150×103/µl. Median platelet count in the individual MELD score groups was as follows; in group 1 it was 380×103/µl, in group 2 it was 315×103/µl, in group 3 it was 130×103/µl, in group 4 it was 105×103/µl and in group 5 it was 100×103/µl. Among 88 study subjects, 43 had thrombocytopenia. MELD score group 1 and 2 patients did not have thrombocytopenia. Of 27 patients in group 3, 20 (74.1%) patients had thrombocytopenia. All the patients in group 4 and 5 had thrombocytopenia. The variation of thrombocytopenia among different groups was statistically significant with p value of <0.01. In study done by 2021 E Halleys Kumar, A Radhakrishnan, *et al*[16] thrombocytopenia is seen in 38 males and 18 females with (22.9 percent) of the males and (22 percent) of the females has thrombocytopenia.

In our study MPV to Platelet Count (PC) ratio of control was 2.85±0.96 and study subjects was 16.81±15.17. Thus MPV to PC in cases were significantly higher (p<0.0001). In our study we noticed that when Child-Turcotte-Pugh Score increased, the value of MPV to platelet count ratio also increased proportionately. The value of MPV to PC ratio was lowest ie, 6.53±2.74 in cases with Child-Turcotte-Pugh score group 5-6 (Child Pugh Class A) which increased to 9.72±4.75 fL/lakh in Child-Turcotte-Pugh Score group 7-9 (Child Pugh Class B) and 22.69±17.80 in Child-Turcotte-Pugh Score group 10-15 (Child Pugh Class C). Our study highlighted that there was a positive correlation between MPV to platelet count ratio

and Child-Turcotte-Pugh Score (r value=0.5241) and p-value was statistically significant (p<0.0001).

When we correlate MPV to platelet count ratio as a predictor of severity of alcoholic liver disease it is more powerful indicator and prognostic tool as compare to individual MPV and platelet count.

Conclusion

MPV to platelet count ratio is a simple, cost-effective marker that may help in diagnosis of alcoholic liver disease, predicting the severity of disease and prognosis in terms of functional outcome as evidenced by its raised value in alcoholic liver disease patients as well as its linear positive correlation with Child-Turcotte-Pugh Score. Though, more studies are needed to validate our results.

Limitation of Study :

Despite our best efforts our studies had few limitations

(1) The sample size of our study was small involving only single centre patients of acute ischemic stroke.

(2) Owing to lack of long term follow up for our patients, we cannot comment whether platelet indicesarethe useful predictor of long-term prognostic outcome in Alcoholic Liver Disease patients or not.

(3) Our study was carried out in a tertiary centre where the cases are either serious or referred. Our study may thus be biased towards more serious cases.

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