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Research Article

HOW MUCH IT MATTERS: A PREDICTIVE ROLE OF PLATELETS IN LIVER INJURY

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Abstract:

Platelets or Thrombocytes are cells without a nucleus with various morphological shapes (Oval, round and biconvex discs) containing granules of physiological, pathological and clinical importance. The plug forming cells have diameter ranging from 2-4 μm derived from megakaryocytes from bone marrow. Platelets (Thrombocytes) perform numerous functions for hemostasis maintenance, response to vascular injury, tissue repair etc. The functions of platelet can be assessed by various parameters like MPV (mean platelet volume) that depicts the size variation (8to12fl) megakaryocyte dependent, PWD (platelet distribution width) and platelet large cell ratio etc. Hepatitis C is an issue of prime concern globally, the virus destroys the liver architecture resulting into hepatic failure and carcinoma. It is a hidden disease and often diagnosed accidentally or at a stage of no return with maximum damage occurred. We tried to search into the predictive role of platelets in hepatocellular injury as it is a routine investigation usually done for various purposes. For this purpose we selected 32 patients diagnosed as Cirrhosis and their platelets finding were compared with 32 non-cirrhotic volunteers of age and sex match from LUMHS, and Isra University. We found significant difference between the two groups on various platelet related parameters.

Conclusion:

It is concluded that higher MPV, Platelet Distribution Width along with low platelet count have a predictive role in advanced liver fibrosis.

Key Words: *Platelets, Megakaryocytes, MPV, Hepatitis.*

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INTRODUCTION:

Hepatitis C as the name indicates is an infection of the liver caused by hepatitis C virus leading chronic hepatitis (65-80%), hepatic cirrhosis (20%) and hepatocellular carcinoma (25%). Who reports 3% of the world population (170 millions) suffering from hepatitis globally at an annual occurrence rate of 3-4 million. Consequently, it is estimated to be the leading cause of mortality and morbidity worldwide [1]. The prevalence chronic hepatitis infections ranges from less than 1% to more than 10% while it is 4.8% in Pakistan, 22% in Egypt and 3.2% in China as reported by the WHO in 2012 resulting into >350,000 deaths as a complication. The practice of unsafe injections, surgeries, transfusion and barbers are responsible for transmitting the HCV from one patient to another patient or person. An individual receives 13 injection / year on average in Pakistan placing the country on list of high endemic area for the disease [2,3]. HCV is found 6 genotypes(1-6) differing in RNA sequence by 35% and about 50 sub-genotypes subtypes(represented by a, b, c etc) ,genotype 2 and 3 are more prevalent in Pakistan(OSZTOVIST, J. 2011). Long term infection causes an irreversible parenchymal damage due hepatocytes necrosis, fibrosis formation of nodule termed as cirrhosis. There is blood flow compromise that results in portal hypertension and hepatic insufficiency [4-6]. There are two types of platelets granules 1. Dense (δ) granules containing serotonin, ADP, calcium and ATP while 2. Alpha (α) granules containing plasminogen activator inhibitor, high molecular weight kininogens (HMWK), clotting factors V, XI, and XIII, PDGF, TGF, vWF, thrombospondin, vitronectin and platelet factor-4 (PF-4) [7]. With development in hematology many additional parameters are determined automatically by analyzer with prime clinical significance. In normal physiological conditions, the mass of platelets is regulated within normal limits but megakaryocytes get stimulated via cytokines e.g thrombopoietin which possess more DNA with multi-lobulated nuclei which produce larger PVI platelets by fragmentation. The relationship between PVI and diseases is reported for many diseases like heart diseases, vasculitis, diabetic nephropathy, leukemia and lymphomas [8].

METHODOLOGY:

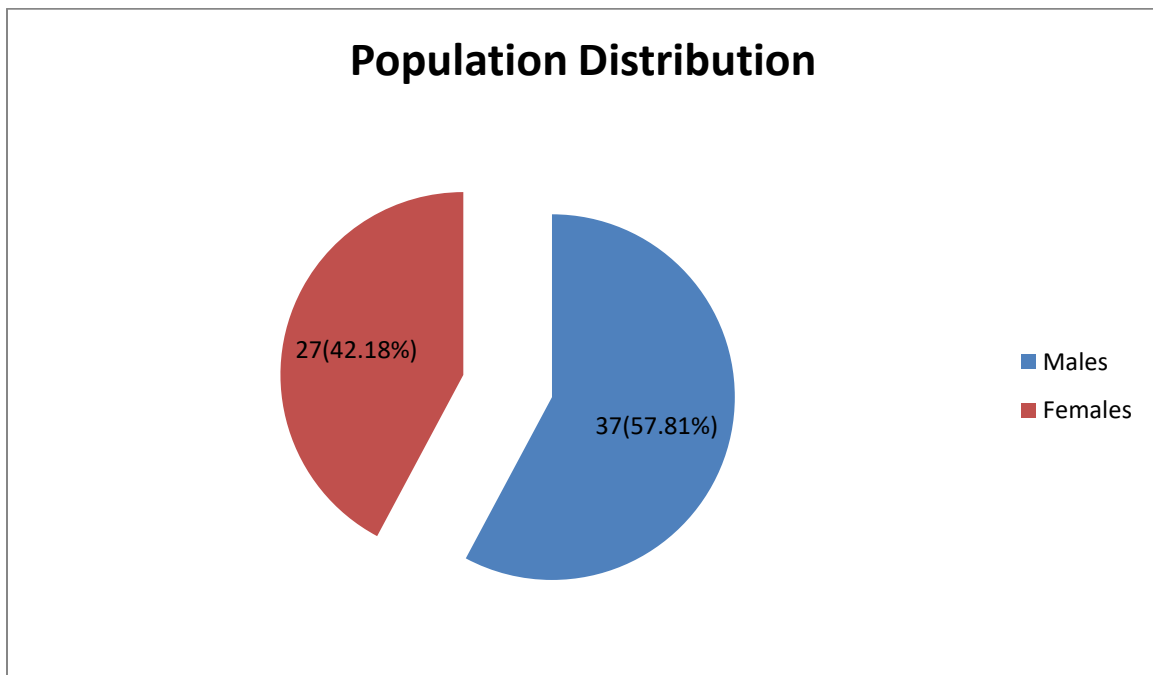
Study Design was Comparative and case control which took place at Gastroenterology unit of Isra University Hospital along with AIMS (Asian Institute of Medical Sciences) Hyderabad on 64 subjects (32control+32cases) over 6 months. The only Inclusion criteria was diagnosed patients of chronic hepatitis C whereas exclusion criteria was much lengthy like patients of hepatitis B, patients of hepatitis B & C co-infected, patients of decompensate Liver cirrhosis, patients with bleeding disorders, systemic diseases, hypertension, diabetes mellitus, Ischemic heart disease. Platelet count as well as volume indices for platelets were calculated by automatic analyzer, (Sysmex KX 21), whereas Hitachi analyzer was used to measure Alanine aminotransferase (ALT). The Data was analyzed using SPSS version 16.0 (Chicago, Illinois, USA). The quantitative variables were analyzed comparing mean \pm SD using t-test. Frequency and percentages were presented by pie charts.

RESULTS:

The male proportion was (n=43) and the female proportion was (n=21) in the current study (Fig.1). The age in control group was 27-58 year with a mean and SD of 44.7 ± 9.3 years while in the cases group it was found 36-58 years with 46.4 ± 6.2 years as mean and standard deviation the difference was non-significant p-value 0.73. The difference in BMI of the two groups was non-significant as the mean and SD in group I was $26.7 \pm 3.45 \text{ kg/m}^2$ while in group II it was $25.2 \pm 4.66 \text{ kg/m}^2$ P-Value 0.90. The platelet count was found $290.2 \pm 86.1 (\times 10^6/\mu\text{L})$ in cases while it was $301.6 \pm 67.5 (\times 10^6/\mu\text{L})$ in controls the difference was significant at p-value 0.04. The mean platelet volume (MPV) in controls was $9.13 \pm 0.45 \text{ fl}$ where as it was increased in cases to $11.29 \pm 1.25 \text{ fl}$ with significant statistical difference, p-value 0.0001, the PDW was $10.38 \pm 0.53 \text{ fl}$ in controls and 16.23 ± 3.77 in cases p-value 0.0001, P-LCR in controls was 27.7 ± 6.25 while in cases it was 36.5 ± 2.99 with highly significant p-values 0.0001. The Alanine transaminase level was noted as $36.40 \pm 4.32 \text{ IU/L}$ in control group $88.96 \pm 41.52 \text{ IU/L}$ in cases group p-0.0001 that is highly significant (Table 1.).

Table1. Comparison of study variables on t-test

S. No.	Parameters	Cases (32)	Controls (32)	P-Value
1.	Age (Years)	46.4±6.2	44.7±9.3	0.73
2.	BMI (kg/m ²)	25.2±4.66	26.7±3.45	0.90
3.	Platelet Count (x10 ⁶ /μL)	290.2±86.1	301.6±67.5	0.04
4.	MPV (fl)	11.29±1.25	9.13 ±0.45	0.0001
5.	Platelet distribution width (fl)	16.23±3.77	10.38±0.53	0.0001
6.	Platelet large cell ratio (%)	36.5±2.99	27.7±6.25	0.0001
7.	Alanine transaminase (IU/L)	88.96±41.52	36.40±4.32	0.0001

**Fig.1 Gender distribution represented by pie chart****DISCUSSION:**

We found significant differences in various platelet indices between the normal individuals and patients of hepatitis C chronic infection so these are good predictive indicators for chronic liver injury. The consistent findings were reported by Zubcevic et al. (2010) giving MPV a reliable predictive value in determining the severity of Crohn's disease however it was not so supportive for clinical differentiation between various degrees of the disease [9]. Another consistency of results was published by Korkmaz et al. (2012) declaring higher MPV reflects to increased risk of development of cardiovascular disease (atherosclerotic heart diseases) [10]. Polinska, et al. (2011) reported that the reduction in MPV shows the activation of platelets in response to mucosal

inflammatory changes in colon indicating the active Ulcerative colitis lesion [11]. Yazici et al. (2011) reported prognostic value of MPV in metabolic syndrome and ST elevation MI [12]. Kosus, et al. (2012) also gave elevated MPV, a predictive role in the poor glycemic control for diabetics patients and an increased risk for cardiovascular events to occur [13]. Omran et al. (2011) in his study on 57 HCV patients concluded no significant role of PDW and P-LCR in determining the chronicity of the disease and the MPV was found reduced in his study that was in contradistinction to our results [14]. Comparable findings were given by Chen et al. (2013) as Platelet Count, Mean Platelet Volume, Platelet Distribution Width as well as RDW-Platelet ratio were suggested as non-invasive markers of liver fibrosis [15]. Another

recent work from Turkey by Aktas, et al. (2013) also concluded significant role of MPV and RDW in hepato-steatosis declaring these parameters as an inexpensive and non-invasive indicator for the condition [16].

CONCLUSION:

We found platelet count, MPV, PDW and P-LCR having a good predictive role in chronic hepatitis C infection

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