

## Study of platelet indices in hyperlipidemia

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### Abstract

**Introduction:** Atherosclerosis is a chronic inflammatory condition resulting from hyperlipidemia and involves platelet mediated recruitment of white blood cells to arteries. The platelet activation is measured indirectly through several platelet indices routinely available without any additional cost in newer fully automated haematology analysers. These indices include platelet count, mean platelet volume(MPV), platelet distribution width(PDW), plateletcrit(PCT), mean platelet(component) concentration (MPC), mean platelet dry mass (MPM), platelet large cell count and platelet large cell ratio (PLCR).. The present study was undertaken in the pathology department of our diagnostic centre to find an association between platelet indices reported by Advia 2120(Siemens) fully automated haematology analyser and hyperlipidemia.

**Materials and Methods:** This was a prospective study carried out in our diagnostic centre from April to July 2018. 100 patients with hyperlipidemia without any associated diseases and 100 controls with normal lipid profile were included in the study. Statistical analysis was done using Pearson's correlation test and data was expressed as mean  $\pm$ SD for each parameter. A *p* value of  $< 0.05$  was considered to be significant.

**Results:** Maximum number of patients were in 41-60 years of age (65%). The male to female ratio was 1.7: 1 with 63% males and 37% females. The mean cholesterol, mean triglyceride and mean HDL cholesterol level in study group was  $218.6 \pm 36.3$ ,  $244.3 \pm 154.38$ ,  $7 \pm 9.6$  respectively and  $158 \pm 26.8$ ,  $94.1 \pm 34.8$ , and  $42.1 \pm 9.3$  in control group respectively. Mean LDL cholesterol was  $131.1 \pm 39.4$  in study group and  $97.1 \pm 25.2$  in control group. There was a significant difference in platelet counts in both groups with a *p* value of 0.01. PCT and MPC also showed a *p* value of 0.004. The mean platelet mass (MPM) was  $2.17 \pm 0.2$  in study group as compared to  $2.13 \pm 0.21$  in control group. Large platelet count was  $7.09 \pm 4.9$  in study group while it was  $5.95 \pm 3.81$  in control group which was also significantly different.

**Conclusion:** Our study indicates that PCT, MPM large platelets and platelet count are significantly higher in hyperlipidemia patients. These indices are available without any additional cost to clinicians, pathologists and patients and can be used to assess the risk associated with hyperlipidemia.

**Keywords:** Hyperlipidemia, MPV, Plateletcrit, MPC, MPM, PLC-R.

### Introduction

The role of hyperlipidemia as a major risk for coronary heart disease, stroke and myocardial infarction has been known since long and several studies have been conducted all over the world linking the role of increased lipids with diabetes, coronary artery disease, hypertension and obesity.<sup>1-5</sup> However, hyperlipidemia is mostly diagnosed during a regular health checkup and often goes unnoticed in the absence of any specific symptoms.

Platelets and their role in haemostasis and thrombosis has been studied in great details worldwide but now the focus is on studies correlating the role of platelets in immunity and inflammation in healthy subjects as well as in diseased individuals.<sup>6-8</sup>

Atherosclerosis is a chronic inflammatory condition resulting from hyperlipidemia and involves platelet mediated recruitment of white blood cells to arteries.<sup>9-11</sup> When the arteries are inflamed due to atherosclerosis, platelets are activated and interact with endothelial cells and deposit platelet derived cytokines on the surface of the endothelial cells, thereby facilitating deposition of leucocytes on the surface of these lesions.<sup>12</sup> Hypercholesterolemia and hyperlipidemia in general is known to cause platelet

activation and thrombotic events.<sup>13-15</sup> Large platelets are known to be more active metabolically, enzymatically and functionally as compared to smaller platelets.<sup>16</sup> They are considered to produce more Thromboxane A<sub>2</sub> leading to a potentially increased thrombogenic tendency.<sup>17,18</sup> The platelet activation is measured indirectly through several platelet indices routinely available without any additional cost in newer fully automated haematology analysers. These indices include platelet count, mean platelet volume(MPV), platelet distribution width(PDW), plateletcrit(PCT), mean platelet(component) concentration (MPC), mean platelet dry mass (MPM), platelet large cell count and platelet large cell ratio (PLC-R). Several studies have shown a positive correlation between MPV and hyperlipidemic states, coronary artery disease, cerebral stroke and Diabetes mellitus.

The present study was undertaken in the pathology department of our diagnostic centre to find an association between platelet indices reported by Advia 2120(Siemens) fully automated haematology analyser and hyperlipidemia.

## Materials and Methods

This was a prospective study carried out in our diagnostic centre from April to July 2018. The study included all patients of both sexes above 20 years of age coming to our diagnostic centre for routine health checkup. These patients underwent lipid profile testing after 12-14 hours of overnight fasting and a complete blood count as a part of their routine health checkup. 100 patients with hyperlipidemia without any associated diseases and 100 controls with normal lipid profile were included in the study. We excluded patients with any other associated disease such as known history of coronary heart disease, diabetes mellitus or hypertension or patients receiving medications for any of these conditions as they may affect the lipid levels and platelet indices. Patients with Haemoglobin below 12.0 gm% in males and 11.0 gm% in females were also excluded from the study as anaemia is known to cause reactive thrombocytosis and may affect the platelet indices. All patients with cholesterol  $\geq 200$  mg%, triglycerides  $\geq 150$  mg% and HDL cholesterol  $\leq 35$  mg% were included in the study group according to the third report of the national cholesterol education programme (NCEP) and expert panel on detection, evaluation and treatment of high blood cholesterol in adults (adult treatment panel III) 2002.

Blood was collected in plain red top tubes for lipid profile and in K2 EDTA for complete blood count by standard protocol and were analysed within one hour of collection to avoid any changes in platelet indices due to prolonged storage which might affect the results. Lipid profile testing was done on Dade Dimension RxL Max (Siemens) and CBC was performed on Advia 2120 (Siemens) 5 part fully automated haematology analyser. In addition to routine CBC parameters Advia 2120 also gives platelet indices which include mean platelet volume (MPV), platelet distribution width (PDW), plateletcrit (PCT), mean platelet (component) concentration (MPC), mean platelet (dry) mass (MPM), platelet large cell count. The platelet large cell ratio (PLC-R) was calculated from the platelet count and large platelet count. Statistical analysis was done using Pearson's correlation test and data was expressed as mean  $\pm$  SD for each parameter. A  $p$  value of  $< 0.05$  was considered to be significant.

**Table 2: Comparison of Patients in study and control groups**

Parameter	Total	Study group	Normal Controls	R Value	P value
		Mean $\pm$ SD	Mean $\pm$ SD		
Total cases (Male+Female)	200				
Male(%)	60.0%				
Female (%)	40.0%				
Age (in years)	200	48.1 $\pm$ 11.9	49.4 $\pm$ 13.7		
Cholesterol	200	218.6 $\pm$ 36.3	158 $\pm$ 26.8	0.0187	0.79

## Results

A total of 100 patients with hyperlipidemia above 20 years of age were included in the study group with 100 age matched controls with normal lipid profile results. The patients were divided into 21-40, 41-60, 61-80 and  $> 80$  years of age in both the sexes. Maximum number of patients were in 41-60 years of age (65%) followed by 26% in 21-40 years of age, 8% in 61-80 years age group and one patient above 80 years of age. The male to female ratio was 1.7: 1 with 63% males and 37% females. (Table 1). The mean age was 48.1 $\pm$ 11.9 in study group and 49.4 $\pm$ 13.7 in the control group. The mean cholesterol, mean triglyceride and mean HDL cholesterol level in study group was 218.6 $\pm$ 36.3, 244.3 $\pm$ 154, 38.7 $\pm$ 9.6 respectively and 158 $\pm$ 26.8, 94.1 $\pm$ 34.8, and 42.1 $\pm$ 9.3 in control group respectively. Mean LDL cholesterol was 131.1 $\pm$ 39.4 in study group and 97.1 $\pm$ 25.2 in control group (Table 2). There was significant difference in cholesterol, triglyceride and LDL cholesterol levels in both the groups. When platelet parameters were compared in both the groups, it was observed that the mean platelet count was 320 $\pm$ 78.8 in study group as compared to 306 $\pm$ 76.8 in control group. There was a significant difference in platelet counts in both groups with a  $p$  value of 0.01. PCT and MPC also showed a  $p$  value of 0.004. The mean platelet mass (MPM) was 2.17 $\pm$ 0.2 in study group as compared to 2.13 $\pm$ 0.21 in control group. Large platelet count was 7.09 $\pm$ 4.9 in study group while it was 5.95 $\pm$ 3.81 in control group which was also significantly different. However, the PLC-R did not show a significant difference in both groups. (Table 3). However, PLC-R was above the normal range in both the groups. (Table 4)

**Table 1: Demographic data of patients in study group**

Age	Male	Female	Total	%
21-40	21	5	26	26.0%
41-60	36	29	65	65.0%
61-80	5	3	8	8.0%
$>80$	1	0	1	1.00%
Total	63	37	100	

Triglycerides	200	244.3 ± 154	94.1 ± 34.8	0.1892	0.01
HDL	200	38.7 ± 9.6	42.1 ± 9.3	0.013	0.86
LDL	200	131.1 ± 39.4	97.1 ± 25.2	0.1359	0.06

**Table 3: Comparison of Platelets Parameters in study and control groups**

Parameter	Total	Study group	Normal Controls	R Value	P value
		Mean ± SD	Mean ± SD		
Platelets	200	320.6 ± 78.8	306 ± 76.8	0.1962	0.01
MPV	200	8.5 ± 1.2	8.4 ± 0.76	-0.0265	0.71
PDW	200	49.7 ± 8.3	49.4 ± 8.3	-0.0778	0.28
PCT	200	0.28 ± 0.1	0.26 ± .07	0.2476	0.0004
MPC	200	26.9 ± 1.7	26.2 ± 3.01	-0.2467	0.0004
MPM	200	2.17 ± 0.2	2.13 ± 0.21	-0.0203	0.78
Large Platelet	200	7.09 ± 4.9	5.95 ± 3.81	0.0159	0.82
PLCR	200	72.9 ± 59.9	74.82 ± 67.5	0.0358	0.61

**Table 4: Normal Range for Platelet Parameters**

Parameter	Range	Units
Platelets	140 – 360	x10 <sup>3</sup> /uL
Mean Platelet Volume (MPV)	7.0 – 9.0	fl
Platelet Distribution Width (PDW)	41.9 – 65.1	%
Plateletcrit (PCT)	0.108-0.282	%
Mean Platelet (Component) Concentration (MPC)	26.4-28.8	g/dL
Mean Platelet (dry) Mass (MPM)	1.76-2.52	pg
Platelet Large Cell Ratio (PLC-R)	11.0-45.0	

**Table 5: Normal Range for Lipid Parameters**

Parameter	Range	Units
Cholesterol	Desirable: <200 Borderline: 200 – 239 High Risk: 240	mg/dL
HDL Cholesterol	Desirable: 60 Borderline: 35 - 45 High Risk: <35	mg/dL
Triglycerides	Desirable: <150 Borderline: 150 - 199 High Risk: 200 - 499	mg/dL
LDL Cholesterol	Desirable: 60 – 130 Borderline: 130 - 159 High Risk: 160 - 189	mg/dL

## Discussion

Coronary artery disease is one of the major causes of morbidity and mortality in the world as well as in the Indian population. Atherosclerosis is a major causative pathological factor for CHD and usually starts in the second decade of life due to hyperlipidemia and by the fourth decade of life manifests as CHD. Platelets are known to convert chronic atherosclerotic plaques into a thrombus causing occlusion of the arteries.<sup>19</sup> The platelet count is a parameter which reflects the functioning, production and ageing of the platelets.<sup>20</sup> MPV is used to assess the size and function of the platelets. PDW, on the other hand, is an indicator of the size distribution of the platelets and an increased PDW is considered to be an indicator of increased thrombotic tendency in individuals.<sup>21</sup> Large platelets have a high metabolic activity and contain more dense granules and are thus have a potential to cause platelet aggregation as compared to smaller platelets.<sup>21,22</sup> MPC or the mean

platelet component concentration, a parameter reported by Advia 2120, when reduced, indicates platelet activation, reflecting a decrease in platelet density.

In our study, we found a male to female ratio of 1.7:1 which correlates with the study of Khemka R et al. In their study, maximum patients were in 51-70 years age group.<sup>23</sup> In their study, they found a significant difference between MPV, PDW and PLC-R in study and control group. However, in our study, we found a significant difference in platelet counts, PCT, MPC and large platelet count in study and control groups while no significant difference was observed in MPV, PDW and PLC-R. In a study by Grotto et al, MPV, PDW and PLC-R were significantly higher in the hyperlipidemia patients as compared to normal controls.<sup>24</sup> Chih Hao Tseng et al in their study observed a significant difference in MPV, PDW and PLC-R between study and control groups and a positive correlation with LDL/HDL ratio.<sup>25</sup> Our study correlates

with the study of Dogru et al who did not find a significant correlation between MPV and hyperlipidemia.<sup>26</sup> The study by Ravindran et al did not show any significant correlation between platelet count and hypercholesterolemia.<sup>27</sup>

The difference in the observation between different studies may be due to the fact that we included the patients without any associated clinical disease while others may have included patients with associated CHD, Diabetes and hypertension with hyperlipidemia which may have affected the platelet indices. The novel platelet parameters like MPM, MPC and PCT reported by Advia 2120 have not been studied so far in published studies and probably this is the first study to find an association between hyperlipidemia and these novel parameters. We found a significant correlation between MPC and PCT in our study.

It is suggested that hypercholesterolemia leads to priming of platelets and increases the platelet activity by increasing platelet production. As the platelets are activated, the risk of CAD increases. The accumulation of cholesterol particles in platelets or defective cholesterol efflux pathways leads to increased platelet production and increased activity of platelets thereby causing atherosclerosis and increased possibility of a thrombotic event.

In a study by Khandekar et al it was observed that all platelet indices are significantly raised in patients with acute MI as compared to those with stable CAD.<sup>28</sup> Damodar et al observed that raised MPV is not a risk factor for development of acute coronary syndrome.<sup>29</sup>

Our study has few limitations. The sample size is small which may have created a potential bias in the observations. Additional multicentric studies involving large population groups and all ethnic groups would be required to confirm and validate the role of different platelet indices in the pathogenesis of hyperlipidemia and subsequent atherosclerosis.

## Conclusion

Hyperlipidemia may cause a variety of thromboembolic complications and platelet indices reported by modern day automated haematology analysers are used to assess the risk of such events in hyperlipidemic patients. Our study indicates that PCT, MPM, large platelets and platelet count are significantly higher in hyperlipidemia patients. These indices are available without any additional cost to clinicians, pathologists and patients and can be used to assess the risk associated with hyperlipidemia.

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