

## A comparative study of platelet to lymphocyte ratio in diabetic and non-diabetic subjects

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### Abstract

**Background:** Type 2 diabetes mellitus is the most common non-communicable disease worldwide. It is known as a progressive metabolic disease which arises because of insulin resistance and impaired insulin secretion. The hallmark of type 2 diabetes mellitus is its microangiopathic complications. Oxidative stress is a key factor in pathological processes which are observed in type 2 diabetes mellitus. Platelet to lymphocyte ratio might be increased in type 2 diabetes mellitus due to chronic inflammation. **Aim:** To compare the platelet-to-lymphocyte ratio in the Type 2 diabetic group and the control group. **Materials and methods:** A cross sectional analytical study was conducted with 30 healthy volunteers as the control group and 30 type 2 diabetic individuals as the study group. The complete blood count was done and the platelet to lymphocyte ratio was calculated as the ratio of the platelet count to absolute lymphocyte count. **Results:** The data obtained were analyzed using Statistical Package for Social Sciences (SPSS) version 20. The mean platelet to lymphocyte ratio in control group was  $105.919 \pm 39.34$  versus  $132.192 \pm 42.01$  in type 2 diabetic group and was found to be statistically significant ( $p$ -value  $< 0.05$ ). **Conclusion:** The present study found that platelet to lymphocyte ratio was high in diabetic subjects than in control subjects which is statistically significant ( $p$ -value  $< 0.05$ ). Hence, during routine checkup the platelet to lymphocyte ratio should be checked for assessing the disease severity and to prevent atherosclerotic complications in type 2 diabetes mellitus.

**Key words:** inflammation, platelet to lymphocyte ratio, type 2 diabetes mellitus

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### Introduction

Type 2 diabetes mellitus is the most common non-communicable disease worldwide. It is known as a progressive metabolic disease which is due to insulin resistance and impaired insulin secretion. The hallmark of progressive form of type 2 diabetes mellitus is its microangiopathic complications. The clinical presentations of such microvascular complications include

diabetic nephropathy, diabetic neuropathy and coronary artery disease which are associated with chronic low grade systemic inflammation<sup>1</sup>. Oxidative stress is a key factor in pathological processes which are observed in type 2 diabetes mellitus<sup>2,3,4</sup>.

The level of oxidative stress in type 2 diabetes mellitus can be assessed by measuring circulating inflammatory biomarkers.

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The level of diabetes control can also be assessed by measuring various circulating inflammatory markers<sup>5</sup>. The platelet to lymphocyte ratio (PLR) is an important novel inflammatory biomarker. The PLR level can be assessed by routine hemogram. It is commonly employed in many diseases for assessing inflammation and prognosis. High platelet and low lymphocyte count are associated with adverse cardiovascular outcomes<sup>6</sup>.

Platelet to lymphocyte ratio is defined as the ratio of platelet count to absolute lymphocyte count<sup>7</sup>. Platelets release proinflammatory mediators such as chemokines and cytokines. Hence platelet to lymphocyte ratio might be increased in type 2 diabetes mellitus due to chronic inflammation. This increases the risk of cardiovascular events in type 2 diabetes mellitus<sup>8,9</sup>.

Hence in this study, we have compared the level of platelet to lymphocyte ratio in diabetic and healthy subjects.

### Aim and objectives

1. To assess the platelet-to-lymphocyte ratio in the Type 2 diabetic group.
2. To compare the platelet-to-lymphocyte ratio in the Type 2 diabetic group and the control group.

### Materials and Methods

A cross sectional analytical study was conducted with 30 healthy volunteers as the control group and 30 type 2 diabetic individuals as the study group. The duration of study was 6 months.

### Inclusion criteria

Type 2 diabetic individuals who fit into the World Health Organization diagnostic criteria of type 2 diabetes mellitus with fasting blood sugar  $\geq 126$ mg/dl or postprandial blood glucose  $\geq 200$ mg/dl or HbA1c  $\geq 6.5\%$ .

The study participants belong to the age group of 30-50yrs and duration of diabetes mellitus  $\leq 5$  years.

### Exclusion criteria

- Age  $< 30$ yrs or  $> 50$ yrs.
- H/O Chronic inflammatory disorder
- H/O smoking or tobacco chewing
- H/O hypertension
- BMI  $> 30$ .
- Pregnancy

Institutional Ethical Committee clearance was obtained. After giving complete information about the study, informed and written consent was obtained from the participants who were selected from Out Patient department of Diabetology. The participants were assured of the confidentiality. Using a validated semi structured proforma, a detailed history was obtained. A detailed clinical examination was done.

Under sterile precautions, 2ml of venous blood sample was collected for complete blood count assessment. The complete blood count was done using SYSMEX automated complete blood count analyzer. The platelet to lymphocyte ratio was calculated as the ratio of the platelet count to absolute lymphocyte count.

### Statistical analysis

The data obtained were analyzed by using Statistical Package for Social Sciences (SPSS) version 20. The comparisons of the variables among the study groups were done using student 't'-test.

### Results

The data were analyzed and Mean and standard deviation was calculated for parameters like age, BMI, biochemical parameters and platelet

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to lymphocyte ratio for the control group and type 2 diabetic group. Comparison of the parameters among the study groups was done using student 't'test.

Table 1: Depicts the comparison of age, BMI, biochemical parameters and Platelet to Lymphocyte Ratio among the study groups. The mean age in the control group was  $44 \pm 4.44$  versus  $44 \pm 5.13$  in type 2 diabetic group. The

mean BMI in the control group was  $22 \pm 2.69$  versus  $22 \pm 2.25$  in type 2 diabetic group. The p-value of age and BMI was not statistically significant. This shows that the study groups were age and BMI matched. The mean Platelet count in control group was  $2.9631 \pm 0.81$  versus  $2.9631 \pm 0.814645$  in type 2 diabetic group and was found to statistically significant (p-value  $< 0.05$ ).

**Table 1: Comparison of age, BMI and biochemical parameters among the study groups**

Variables	Control group (Mean $\pm$ SD) (n=30)	Type 2 diabetes mellitus group (Mean $\pm$ SD) (n=30)	*p-value
AGE (yrs)	$44 \pm 4.44$	$44 \pm 5.13$	0.1546
HEIGHT (cm)	$157 \pm 4.98$	$157 \pm 3.87$	0.2584
WEIGHT (Kg)	$63 \pm 6.98$	$65 \pm 5.36$	0.1565
BMI	$22 \pm 2.69$	$22 \pm 2.25$	0.2124
HbA1C (%)	$4.3 \pm 0.49$	$6.2 \pm 0.36$	0.0354*
FBS (mg/dl)	$92 \pm 8.88$	$172 \pm 37.13$	0.0006**
PPBS (mg/dl)	$117 \pm 8.96$	$216 \pm 80.54$	0.0008**
RBS (mg/dl)	$115 \pm 6.53$	$210 \pm 69.25$	0.0006**
Platelet Count (Lakhs/mm <sup>3</sup> )	$2.9631 \pm 0.81$	$3.1355 \pm 0.69$	0.0412*
Absolute Lymphocyte Count (cells/mm <sup>3</sup> )	$3014 \pm 948.15$	$2469 \pm 632.69$	0.0486*
Platelet to Lymphocyte Ratio	$105.919 \pm 39.34$	$132.192 \pm 42.01$	0.0124*

\*-Significant

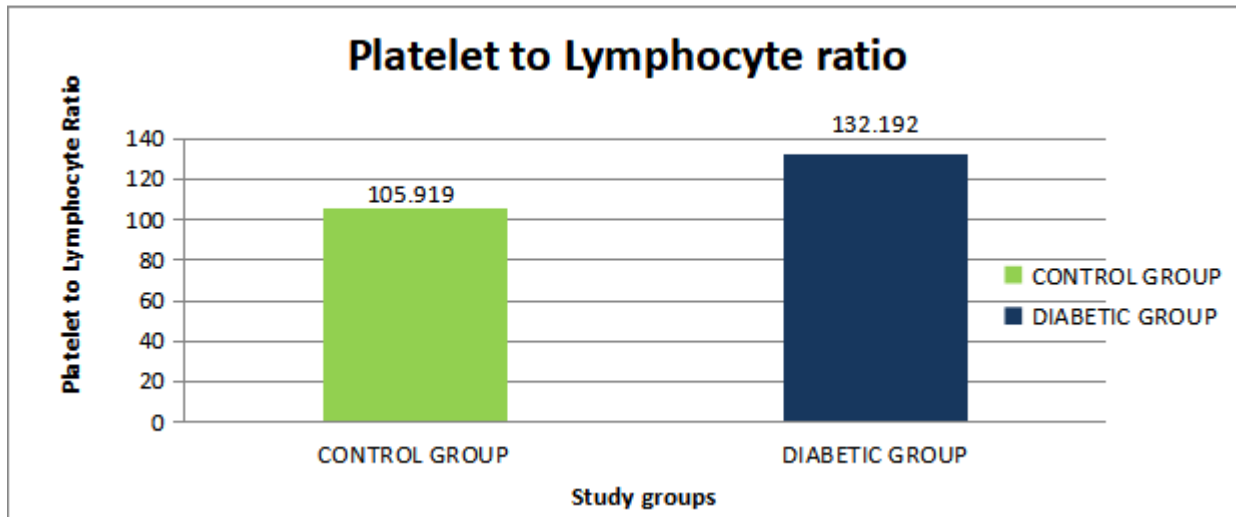
\*\*-Highly significant

The mean absolute lymphocyte count in control group was  $3014 \pm 948.15$  versus  $2469 \pm 632.69$  in type 2 diabetic group and was found to statistically significant (p-value  $< 0.05$ ). The mean platelet to lymphocyte ratio in control group was  $105.919 \pm 39.34$  versus  $132.192 \pm 42.01$  in type 2 diabetic group and

was found to be statistically significant (p-value  $< 0.05$ ). Figure 1 depicts the comparison of platelet to lymphocyte ratio between control group and diabetic group It shows that platelet to lymphocyte ratio was high in diabetic subjects than in control subjects.

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**Figure 1: Comparison of Platelet to Lymphocyte ratio between control group and diabetic group**



### Discussion

The present study was undertaken to compare the platelet to lymphocyte ratio between diabetic and healthy subjects. In type 2 diabetes mellitus, the pathogenesis is an inflammatory process<sup>10</sup>. Type 2 diabetes mellitus is a chronic inflammatory disease which gets aggravated with poor diabetic control. Pradhan et al in their study found that rise in inflammatory markers such as IL-6 and CRP predicts the occurrence of type 2 diabetes mellitus<sup>11</sup>. It was also found that chronic inflammation was associated with high mortality risk in type 2 diabetes mellitus<sup>12</sup>. Navarro et al in their study found that inflammatory markers such as CRP and TNF alpha was closely associated with albuminuria in type 2 diabetes mellitus<sup>13</sup>.

Platelet to lymphocyte ratio (PLR) was studied as an inflammatory marker in various diseases. The role of platelets in inflammation was found to be due to its interaction with various cell types such as T-lymphocytes, dendritic cells, neutrophils, endothelial cells and phagocytes<sup>14</sup>. Akboga et al in their study found that platelet to lymphocyte ratio was associated with disease severity in coronary artery disease<sup>15</sup>.

Type 2 diabetes mellitus has been linked with

platelet dysfunction<sup>16,17</sup>. The hormone insulin is a major antagonist of platelet hyperactivity. Insulin sensitizes the platelets to prostacyclins and also leads to increased generation of prostacyclins and nitric oxide from endothelium. This causes vasodilatation of smooth muscles and also prevents platelets adhesion and aggregation. Insulin also acts on monocytes and thereby exerts anti-inflammatory effects. It downregulates pro-aggregatory substances such as ADP, collagen and thrombin<sup>18</sup>. Impairment of several inflammatory pathways in type 2 diabetes mellitus leads to increased platelet reactivity<sup>19</sup>. In type 2 diabetes mellitus, platelets easily adhere and aggregate to endothelial cells<sup>16</sup>. The increase in platelet to lymphocyte ratio has been explained by increase in absolute platelet count in type 2 diabetes mellitus because of chronic systemic inflammation<sup>20</sup>.

Insulin resistance in type 2 diabetes mellitus is defined as a metabolic state in which for the apparently available insulin, the tissue response to insulin is less than the expected. Almer et al in their study found that elevated intravascular thrombin generation as well as decreased fibrinolytic potential in type 2 diabetes mellitus are the key contributors of atherosclerosis<sup>21</sup>.

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The low fibrinolytic activity in type 2 diabetes mellitus was found to be due to increased PAI-1 which prevents the formation of plasmin from plasminogen<sup>22</sup>. Festa et al in their study found that insulin resistance was associated with increased level of PAI-1 which acts as a link between coronary artery disease and insulin resistance<sup>23</sup>. Oxidative stress and inflammation in type 2 diabetes mellitus are associated with enhanced fibrinogen synthesis which promotes atherogenesis<sup>24</sup>. Increased fibrinogen levels in type 2 diabetes mellitus promotes platelet aggregation and fibrin clot formation<sup>25</sup>. Platelet to Lymphocyte ratio is said to be a major factor which emphasizes the interplay of two major components, thrombosis and inflammation in microangiopathy of type 2 diabetes mellitus<sup>26</sup>. Hence, Platelet to lymphocyte ratio predicts both inflammation and hyperactive coagulation in type 2 diabetes mellitus.

Our present study found that platelet to lymphocyte ratio was increased in type 2 diabetic individuals with duration of diabetes <5 years when compared to healthy individuals. This indicates that increased platelet to lymphocyte ratio is associated with increased systemic inflammation as well as disease severity. This shows that there is an increased risk of microangiopathy complications in early type 2 diabetes mellitus. Similar findings were observed in Burcin et al study<sup>5</sup>. Pickup and Jialal et al in their study showed that increased inflammation in type 2 diabetes mellitus was associated with development of complications<sup>27,28</sup>.

Ahmed et al in their study found that platelet to lymphocyte ratio was increased in diabetic nephropathy<sup>29</sup>. They found that endothelial dysfunction and inflammation in type 2 diabetes mellitus could be the underlying reason for diabetic nephropathy. Similar findings are present in our study. Demirtas et al in their study found that PLR levels were found to be independent predictor of diabetes and independent predictor of impaired glucose

regulation in type 2 diabetic patients<sup>30</sup>. Zhang in their study found that platelet to lymphocyte ratio was elevated in diabetic foot ulcer due to underlying inflammation<sup>31</sup>. Similar findings are present in our study.

### Conclusion

The present study found that platelet to lymphocyte ratio in type 2 diabetes mellitus was increased in type 2 diabetic group with duration of diabetes <5 years when compared to normal group which is statistically significant (p-value<0.05). This shows that platelet to lymphocyte ratio can be used as an inflammatory marker to find out the disease severity in early type 2 diabetes mellitus. Hence, during routine checkup the platelet to lymphocyte ratio should be checked for assessing the disease severity as well to prevent atherosclerotic complications in type 2 diabetes mellitus.

### Limitations

The present study has not assessed other inflammatory markers like CRP, Neutrophil to Lymphocyte ratio, Fibrinogen, Ferritin and TNF. Based on the findings from the current study, future studies on study of inflammation in type 2 diabetes mellitus can be done by assessing all the other inflammatory biomarkers.

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**Conflict of interest:** Nil

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