



## Association of Glycemic Control with Platelet Indices Among Patients with Type 2 Diabetes Mellitus

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**Abstract:** Diabetes mellitus, a chronic metabolic disease affects various organs of the body on a long-term basis. Diabetes results in haematological changes that lead to development of complications such as hypercoagulability, anemia and cardiovascular disease (CVD). Hematological parameters play an important role in the treatment and follow up of diabetic patients. Hence, the objective of the study is to compare the mean levels of hematological parameters namely Platelet Distribution Width (PDW), Mean Platelet Volume (MPV) and Plateletcrit (PCT) between the type 2 diabetic patients with  $\text{HbA1c} \geq 6.5$  with the non-diabetic controls ( $\text{HbA1c} < 5.4$ ) and to correlate the  $\text{HbA1c}$  values with the haematological parameters among type 2 diabetes patients. The case-control study was conducted for 6 months on 50 participants between the age group of 25-50 years. Case group includes 25 patients diagnosed with type 2 diabetic patients with  $\text{HbA1c} \geq 6.5$  and controls were healthy participants with  $\text{HbA1c} < 5.4$ . The serum samples were analysed for the haematological parameters namely PCT, PDW and MPV by electrical impedance method and  $\text{HbA1c}$  by immunoturbidimetric method. Increased levels of PCT, PDW, MPV were found among cases with  $\text{HbA1c} \geq 6.5$  when compared with the controls with  $\text{HbA1c} < 5.4$ . There was a significant association between platelet PCT, PDW and MPV with  $\text{HbA1c}$  among type 2 diabetes mellitus patients. Increased mean levels of platelet indices (PCT, PDW and MPV) were found to be significantly associated with glycemic control in type 2 diabetes mellitus. Hence, diabetic patients during their routine biochemical investigation, hematological investigation can also be done which helps in easy recognition of increased platelet indices that helps in treatment and prevention of disease progression among type 2 diabetes patients.

**Key Words:** Diabetes mellitus, PCT, PDW, MPV, glycated haemoglobin

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## I. INTRODUCTION

The chronic metabolic disorder with an increasing prevalence rate all over the world is type 2 diabetes mellitus (DM). It is expected that the number of people affected will double in the next decade due to an increasing population of aging which will soon become an epidemic in most of the countries especially in poor and developing countries<sup>1</sup>. In year 2020, according to the International Diabetes Federation (IDF), worldwide above 463 million people have diabetes and 88 million people in the Southeast Asia region. Of this 88 million people, 77 million belong to India<sup>2</sup>. According to the World Health Organization, 2% of all deaths in India is due to diabetes<sup>3</sup>. Diabetes results in various complications which may be broadly classified into microvascular and macrovascular. The microvascular complications include neuropathy, nephropathy and retinopathy, while macrovascular complications are cardiovascular disease, stroke, and peripheral artery disease (PAD)<sup>4</sup>. Diabetes is a universal community health problem which is associated with cellular, metabolic and blood disturbances. Various haematological changes have been reported among type 2 diabetes individuals which may play a major role in diabetes-associated complications<sup>5</sup>. Increase in the formation of advanced glycation end products (AGEs) and production of reactive oxygen species (ROS) are the common factors seen in the diabetic patients as a result of persistent hyperglycaemic status which may lead to changes in the haematological parameters<sup>6</sup>. The common haematological changes include platelet hyperactivity, endothelial and RBC dysfunction as a result of oxidative stress due to increased ROS production, which is implicated in tissue damage<sup>7</sup>. Thus, changes in the haematological parameters in diabetic patients result in the complications such as hypercoagulability, anaemia and cardiovascular disease (CVD)<sup>8</sup>. Several hematologic anomalies have been defined among patients with diabetes mellitus. Studies have documented the reaction model of diabetes by post synthetic protein modification and glycemic status which is provided by the erythrocyte and the formation of hemoglobin A1c<sup>9</sup>. Hyperglycaemic individuals show increase in red blood cell viscosity with increased glycemic status<sup>10</sup>. Studies have also shown that diabetes mellitus is also associated with certain metabolic abnormalities. Abnormalities in the polymorphonuclear leukocyte involve the properties of adherence, random migration, chemotaxis, phagocytosis and killing<sup>11</sup>. Recent studies have developed interest on haematological parameters especially on platelet indices such as mean platelet volume (MPV), platelet distribution width, and platelet count as predictors of endothelial dysfunction and inflammation in T2DM<sup>12</sup>. Platelets play an important role in maintaining the integrity of normal homeostasis where MPV acts as a marker for its function. MPV levels are increased in case of nephropathy, retinopathy or in CVD<sup>13</sup>. On the other hand, mean platelet volume changes reflect on the rate of platelet production or stimulation<sup>14</sup>. Generally, haematological changes have been observed in T2DM patients. Therefore, analysis of these parameters could contribute to follow-up of diabetic patients to reduce the development of further complications like inflammatory and degenerative conditions<sup>15</sup>. Hence, the aim of the study is to analyse and compare the levels of haematological parameters with the glycaemic status among type 2 diabetes mellitus patients, which would help in implicating the same for the

treatment, diagnosis and prevention of development of severe complications in diabetic individuals.

## 2. MATERIALS AND METHODS

The case-control study included 50 participants between the age group of 25-50 years. This study was started after getting institutional ethical clearance (ethical clearance number – 002/SBMC/IHEC/2021/1615) The participants were divided into two groups in which 25 clinically diagnosed patients with type 2 diabetes mellitus with HbA1c  $\geq 6.5$  between the age group of 25-50 years were taken in case group and 25 nondiabetic healthy participants with HbA1c  $< 5.4$  were included in control group. Patients with clinical conditions like anemia, inflammatory disease, repeated blood transfusion, post-surgical patients on recovery, smokers, patients with acute and chronic bleeding conditions and those on medications that affect the platelet concentrations were excluded from the study. The study was conducted in the department of Biochemistry, Sree Balaji Medical College and Hospital, Tamil Nadu, India. Institutional ethical clearance was obtained. Patients with biochemical blood glucose range of fasting  $\geq 125$  mg/dl and 2 hrs blood glucose level  $\geq 200$  mg/dl are said to be diabetic. The HbA1c which refers to the blood glucose level over a period 3 months with the level of  $\geq 6.5$  were included in the study. After obtaining informed and written consent, under strict aseptic conditions 3 ml of venous blood sample was collected from antecubital vein using EDTA vacutainer. The samples were analysed for HbA1c and haematological parameters which includes PCT, PDW, MPV. Analysis of haematological parameters was carried out in fully automated haematology analyser BC6800 Mindray by electrical impedance method and HbA1c in fully automated Biochemistry analyser BS 390 Mindray by immunoturbidimetric method.

## 3. STATISTICAL ANALYSIS

The means and standard deviations (SD) of all the parameters were calculated in case and control groups. Statistical analysis was performed with the Statistical Package for the Social Sciences (SPSS) version 22 software. Student 't' test was used to find the statistical significance between groups and Pearson's correlation was done to correlate Plateletcrit (PCT), Platelet Distribution Width (PDW) and Mean Platelet Volume (MPV) with HbA1c levels.  $P \leq 0.05$  was considered significant.

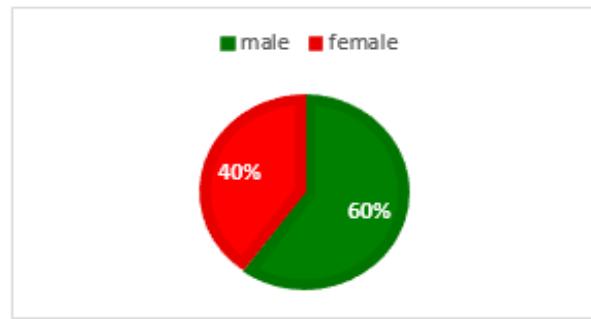
## 4. RESULTS

### 4.1 Demographic features

A total of 50 subjects were studied in which 25 subjects diagnosed with type 2 diabetes mellitus with HbA1c  $\geq 6.5$  were included in the case group and 25 healthy subjects with HbA1c  $< 5.4$  were in the control group between the age group of 25-50 years (Table 1). Both male and female were included in the study in which the number of male cases were higher compared to controls (figure 1) in the case group which shows that males are more prone to develop diabetes mellitus than females (Table 1). The mean of cases and controls were  $38.8 \pm 8.2$  and  $33.1 \pm 8.6$  years, respectively. Among 50 subjects about 60% case and 56% control were males and 40% case and 44% control were females.

**Table 1 Demographic features of the study group**

Parameters	CASE (n= 25)	CONTROL (n = 25)
<b>Mean age (years, mean <math>\pm</math> SD)</b>	38.8 $\pm$ 8.2	33.1 $\pm$ 8.6
<b>Male %</b>	60 %	56 %
<b>Female%</b>	40 %	44 %

**Fig 1: The % of males and females among case groups**

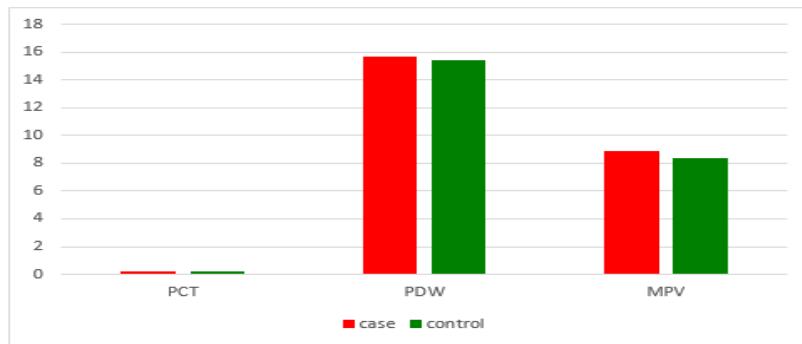
In this study, we observed that the mean and SD of HbA1c for case and control group was  $8.9 \pm 2.4$  and  $5.1 \pm 0.2$ , respectively. The mean values of haematological parameters PCT, PDW and MPV were compared between two groups

(Table 2). The platelet indices were significantly elevated in the case group when compared to the healthy participants of the control group. This shows that the platelet indices increase in diabetic patients with  $\text{HbA1c} \geq 6.5$  (Figure 2).

**Table 2 Comparison of Mean  $\pm$  SD of the Measured Biochemical and Haematological Parameters between the Case and Control groups.**

PARAMETERS	CASE (n = 25)	CONTROL (n = 25)	p VALUE
<b>HbA1c</b>	$8.9 \pm 2.4$	$5.1 \pm 0.2$	<0.0001***
<b>PCT</b>	$0.24 \pm 0.07$	$0.21 \pm 0.04$	<0.0001***
<b>PDW</b>	$15.7 \pm 0.4$	$15.4 \pm 0.2$	<0.0001***
<b>MPV</b>	$8.88 \pm 1.6$	$8.4 \pm 0.6$	0.03*

The values are statistically significant based on the p value. \*p value < .05, \*\* p value < .01, \*\*\* p value < .001, NS-Not Significant.

**Fig 2: Comparison of mean levels of platelet indices between groups**

Pearson correlation analysis among the type 2 diabetic individuals with HbA1C showed a strong positive correlation with PCT, PDW and MPV (Table 2). The results show that there is a significant association of increased glycaemic status

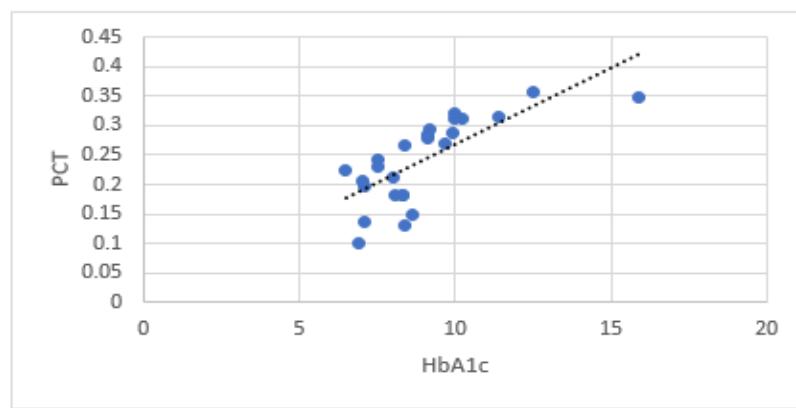
among type 2 diabetes mellitus individuals with increased PCT, PDW and MPV (Figure 3, 4 and 5). Hence, based on the results obtained it shows that glycemic status of diabetic patients is associated with increased platelet indices.

**Table 3: Pearson correlation analysis of HbA1c with haematological parameters in case group.**

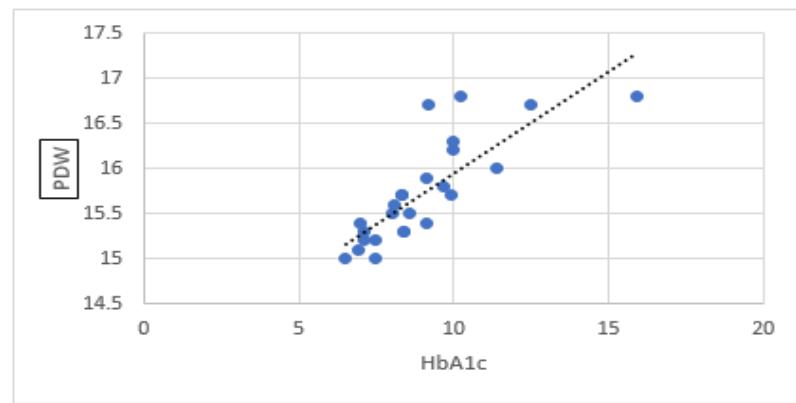
Parameters	HbA1cr	p value
<b>PCT</b>	0.3 <sup>a</sup>	0.03*
<b>PDW</b>	0.5 <sup>a</sup>	0.0002***
<b>MPV</b>	0.9 <sup>a</sup>	0.0001***

The values are statistically significant based on the p value. \*p value < .05, \*\* p value < .01, \*\*\* p value < .001, NS-Not Significant.

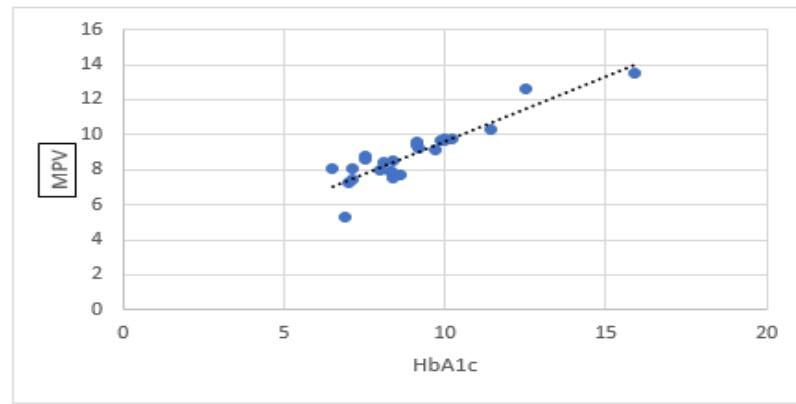
<sup>a</sup>Positive Correlation and <sup>b</sup>Negative Correlation.



**Fig 3: Association between glycemic status and Plateletcrit (PCT)**



**Fig 4: Association between glycemic status and Platelet Distribution Width (PDW)**



**Fig 5: Association between glycemic status and Mean Platelet Volume (MPV)**

## 5. DISCUSSION

Diabetes mellitus is a group of metabolic diseases that shares the common features of hyperglycemia. Uncontrolled hyperglycemia with metabolic dysregulation is associated with multiple organ failure damage especially the blood vessels, eye and kidney<sup>16</sup>. It is seen that type 2 diabetes mellitus patients are found to have platelet indices associated with increased reactivity and baseline activation plays a key role in development of vascular complications<sup>17</sup>. Sustained hyperglycemia results in a series of interrelated changes that lead to platelet, endothelial and vascular dysfunctions<sup>18</sup>. In this study, the mean levels of age group were  $38.8 \pm 8.2$  among cases and  $33.1 \pm 8.6$  among controls. A study by Wenjun Zou

et al, found that the age group between 31-45 years who develop diabetes mellitus are at higher risk of developing complications<sup>19</sup>. It was found that males were found to have a higher chance of developing diabetes mellitus as the % of males in the case group was 60% and in females was 40%. This is similar to the study conducted by Anna Nordstrom et al, shows that males are more prone to developing diabetes mellitus than females<sup>20</sup>. Controversy to our findings, a study by Hongyan Zhang et al, found that females are more likely to develop type 2 diabetes mellitus than males and have higher risk of developing complications<sup>21</sup>. In this study the mean levels of platelet indices namely PCT, PDW and MPV levels were found to be significantly higher in type 2 diabetes mellitus patients with  $\text{HbA1c} \geq 6.5$  when compared to the

healthy individuals with HbA1c < 5.7. This shows that diabetic patients are likely to develop endothelial and vascular complications. This is similar to the study of Ravindra *et al*, where the mean levels of fasting glucose and platelet indices were found to be increased among diabetic individuals which is associated with microvascular complications<sup>22</sup>. Another study by Karthikeyan *et al*, has observed that elevated MPV and PDW were seen in diabetic patients with complications<sup>23</sup>. Diabetic patients are significantly associated with development of microvascular complications<sup>24-25</sup>. Another study by Sonali Jindal *et al*, also found that there is an increase in MPV and PDW among the diabetics in which PDW was higher in those with complications as compared to those without complication<sup>26</sup>. In this study there was a positive correlation between HbA1c values with platelet indices such as PDW, MPV and PCT. This correlated with the study of Aparajita Sharma *et al*<sup>27</sup>. A study by Kamilla R. Alhadas *et al*, showed that study on patients with microvascular complications showed positive correlation with HbA1c which is similar to our study<sup>28</sup>. Study by Archana Buch *et al*, found an MPV is significantly associated with the diabetic complication of diabetes mellitus<sup>29</sup>. The current study was conducted in South-India with a similar study done in North- Indian population<sup>30</sup>.

## 6. CONCLUSION

Increased levels of PCT, PDW, MPV were found among type 2 diabetes patients when compared with the controls. The platelet indices (PCT, PDW and MPV) were found to be significantly associated positively with glycemic status among type 2 diabetes mellitus. Hence, diabetic patients during their routine biochemical investigation, hematological investigation can also be done which helps in easy recognition of increased

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platelet indices that helps in treatment and prevention of disease progression among type 2 diabetes patients.

## 7. AUTHORS CONTRIBUTION STATEMENT

This study was done by Dr. Jainulavudeen Mohamed Rabeek under the guidance of Dr. B. Shanthi. Dr. Mary Chandrika Anton and Dr.V.S.Kalai Selvi, contributed to literature review and discussion.

## 8. ACKNOWLEDGEMENT

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## 9. ETHICAL STANDARDS

The study involved human participants following the ethical standards of the tertiary health care institution where the study was conducted.

## 10. LIMITATIONS OF THE STUDY

The study population shall be enlarged as it was relatively less.

## 11. FUNDING

The principal investigator did not get funds from any agencies for carrying out this project.

## 12. CONFLICT OF INTEREST

Conflict of interest declared none.

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