INTRODUCTION
Diabetes mellitus is a clinical syndrome characterized chiefly by hyperglycemia resulting from absolute or relative deficiency of insulin [1]. The resultant metabolic dysfunction in diabetes leads to microvascular and macrovascular complications. These vascular complications in turn result in secondary damage to multiple organ systems [2].

The prevalence of diabetes has risen worldwide from 108 million cases in 1980 to 422 million cases in 2014. According to WHO, Diabetes was the seventh leading cause of death in 2016. A recent estimate in 2016 has suggested that diabetes causes almost 1.6 million deaths globally [3]. Type 2 diabetes mellitus is the predominant form of diabetes worldwide accounting for 90% of cases. India has the second-largest prevalence of diabetes accounting for 62.1 million cases in 2013 [2].

Type 2 Diabetes mellitus is considered as a prothrombotic state with enhanced platelet reactivity that increases the risk for microvascular complications like retinopathy [4]. Insulin antagonizes the effect of platelet agonists like collagen, adenosine diphosphate, epinephrine and platelet-activating factor. Hence insulin resistance leads to increased reactivity of platelets [5].

Platelet indices such as platelet count, mean platelet volume (MPV), platelet distribution width (PDW), plateletcrit (PCT) have been used to assess the platelet activity. MPV indicates the average size and activity of platelets. This in turn reflects either a change in platelet stimulation or a change in the rate of platelet production [6].

Increase in MPV has been demonstrated in metabolic syndrome and stroke, which are prothrombotic states [6]. Platelet distribution width (PDW) which indicates heterogeneity in platelet size and shape is a sign of active platelet release [7].

Investigations such as fibrinogen, prothrombin time (PT), activated partial thromboplastin time (aPTT) assesses the prothrombotic state. Many of these tests cannot be employed for screening prothrombotic conditions. Partial thromboplastin time (aPTT) assesses the prothrombotic state. Hence insulin resistance leads to increased reactivity of platelets [5].

Platelet indices especially MPV, PDW assesses the thrombogenic state and hence can be used to monitor treatment.

MATERIALS AND METHODS
This cross-sectional comparative study was conducted in the Department of Medicine, from May 2018 to April 2019 after getting Institutional Ethics Clearance. Sample size was calculated with Open Epi software version 3.01 using 80% power, 95% confidence interval and by substituting mean ± SD values of platelet indices obtained from a study conducted by Shilpi K, et al [4]. The calculated sample size was 60 with 30 subjects without diabetes mellitus in Group A and 30 subjects with type 2 diabetes mellitus in Group B.

Inclusion criteria
- Age of the subjects: 35-70 years
- Gender: Both males and females
- Subjects with type 2 diabetes mellitus on treatment. Diagnosis of type 2 diabetes mellitus was made using WHO criteria [11]

Exclusion criteria
- Subjects who were pregnant.
- Subjects with acute infections, trauma or recent myocardial infarction.
- Subjects with hematological disorders like anemia (hemoglobin values <12g/dl in females and <13g/dl in males), polycythemia, lymphoma, multiple myeloma or with bleeding disorders.
- Subjects with autoimmune disorders such as rheumatoid arthritis, systemic lupus erythematosus.
- Subjects with hypertension, thyroid disorders like hypothyroidism.
- Subjects with cardiac failure, hepatic failure, renal failure, malignancies or poor general conditions.
- Subjects on antplatelet medications like aspirin, clopidogrel.
- Subjects who were not willing to participate.

After getting informed and written consent, the data was collected using a data collection tool. Under sterile aseptic precautions, 2ml of venous blood was drawn from the antecubital veins of the subjects. The withdrawn blood was anticoagulated with EDTA. Platelet indices were computed using Beckman Coulter LH 780. Plasma glucose level was measured by the glucose oxidase method and HbA1c was measured by HPLC, if they have not been already done in the study population.

The data collected were analyzed using IBM SPSS software version 24. Normally distributed variables were presented as mean ± SD. Categorical variables were presented as frequencies and proportions. Independent t-test was used to compare the variables between the two groups. Karl Pearson’s correlation was used to compare the continuous variables which were normally distributed. p-value < 0.05 was considered to be statistically significant.

RESULTS
The mean age of the subjects in groups A (non-diabetic) and B...
A study conducted by Buch A, Kaur S, et al has showed an increase in lifespan of platelets in diabetic patients [10].

The mean duration of diabetes (years), fasting blood sugar (mg/dl), postprandial blood sugar (mg/dl) and glycated hemoglobin HbA1c (%) in diabetic subjects were 4.13 ± 0.39, 117.03 ± 4.39, 189.50 ± 5.77 and 8.49 ± 0.30 respectively.

**Figure 1: Comparison of MPV and PDW between non-diabetic and diabetic subjects**

![Comparison of MPV and PDW between non-diabetic and diabetic subjects](chart)

Table 1: Comparison of platelet indices between non-diabetic and diabetic subjects

<table>
<thead>
<tr>
<th>Variables</th>
<th>Non-diabetic (n=30) Group A Mean ± SD</th>
<th>Diabetic (n=30) Group B Mean ± SD</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>MPV (fL)</td>
<td>11.80 ± 0.53</td>
<td>10.34 ± 0.92</td>
<td>0.000*</td>
</tr>
<tr>
<td>Platelet count (x10^12/μL)</td>
<td>153.33 ± 31.59</td>
<td>135.03 ± 50.22</td>
<td>0.001*</td>
</tr>
<tr>
<td>PDW (%)</td>
<td>17.51 ± 2.00</td>
<td>17.64 ± 0.79</td>
<td>0.001*</td>
</tr>
</tbody>
</table>

Table 2: Correlation of platelet indices with HbA1c in the diabetic patients

<table>
<thead>
<tr>
<th>Platelet indices</th>
<th>Pearson's coefficient (r)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>MPV (fL)</td>
<td>0.382</td>
<td>0.037*</td>
</tr>
<tr>
<td>Platelet count (x10^12/μL)</td>
<td>0.513</td>
<td>0.004*</td>
</tr>
<tr>
<td>PDW (%)</td>
<td>0.164</td>
<td>0.387</td>
</tr>
<tr>
<td>Plateletcrit (%)</td>
<td>0.074</td>
<td>0.697</td>
</tr>
</tbody>
</table>

Correlation of platelet indices such as MPV, platelet count with HbA1c showed statistical significance. Other indices like PDW and plateletcrit showed a positive correlation with HbA1c, though significance was not produced.

**DISCUSSION**

Hyperglycemia associated with diabetes mellitus modifies the platelet reactivity by both direct and indirect ways. Hyperglycemia induced enhanced glycation of platelet proteins is the direct effect. This glycation causes the externalization of platelet membrane phosphatidylserine leading to the activation of surface clotting factors [17].

In addition to this, hyperglycemia activates protein kinase C, a transduction pathway mediator for many proaggregatory platelet agonists. Platelets of diabetic patients manifest with short term activation of calcium-sensitive PKCβ isoenzyme in the presence of hyperglycemia alone. This demonstrates the platelet dysfunction in diabetes [17]. As insulin inhibits platelet activation, diabetes mellitus resulting from either relative or absolute deficiencies of insulin presents with increased platelet reactivity. This is the indirect effect [7].

Platelet activation not only triggers thrombus formation but also induces micropapillary embolization and release of constructive, oxidative and mitogenic substances that accelerate the progression of local vascular lesions [17].

In the present study, platelet count and platelet distribution width (PDW) were increased in diabetic subjects compared to non diabetic subjects. A study conducted by Jindal S, et al showed a significant elevation in platelet indices such as platelet count, MPV and PDW in diabetic subjects when compared to non diabetic subjects. Within the diabetic subjects, PDW was elevated in diabetic subjects with complications than those without complications [6].

Both MPV and PDW increases during platelet activation. As seen earlier, the increase in MPV may be due to osmotic swelling in diabetes [10]; but PDW analyzed based on impedance technology describes more about the activation of platelets. For their activation, platelets change their shape from discoid to spherical forms along with pseudopodia formation. These changes during activation can be computed by impedance technology [8]. Hence PDW can be used to assess diabetic complications.

A study conducted by Levin J, et al has shown an inverse relationship between MPV and platelet count in normal subjects. It is postulated that with increased production of platelets, more immature cells with larger size enter the circulation and hence MPV increases with a decrease in platelet count [18].

But in studies conducted in diabetic patients [7, 9, 11, 13-16], platelet count showed an increase along with MPV and PDW. This could be due to variation in platelet shape during activation and not because of blast cells entering the circulation.

In the present study, a positive correlation of platelet indices with HbA1c was produced. Sustained hyperglycemia as denoted by glycated hemoglobin (HbA1c) leads to endothelial dysfunction and vascular complications. Endothelial dysfunction results from upregulation of platelet glycoproteins like GPIb, GPIIb/IIIa. Vascular complications result from disturbances in the polyol pathway, deposition of advanced glycated end products and activation of protein kinase C[19].

Anasul cordoid platelets play a major role in hemostasis. In response to endothelial injury, platelets alter their shape, adhere to subendothelium and get activated in turn releasing thromboxane A2, serotonin, thrombomodulin [10]. Thus platelets indices indicate the prothrombotic state in diabetes mellitus which leads to vascular complications.

The advantage of this study is that platelet indices were obtained by automated cell counters and hence the readings are less prone to error.

MPV in diabetic patients with complications compared to those without complications [12]. An increase in MPV has been documented in patients with metabolic syndrome, stroke, transient ischemic attacks and myocardial infarction [13].

Similar observations were made in studies conducted by Khandekar M.M, et al [14], Kilichi Camur N, et al [15] and O’ Malley T, et al [16]. The hypothesis that has been proposed is that larger platelets with more dense granules are more potent and thrombogenic [6]. Higher mean platelet volume (MPV) suggests augmented platelet activation and thrombosis [10].
The limitation of the study is that the bias of selection and information could not be avoided as the study participants were selected from a single center. The study size was small.

CONCLUSION
Platelet indices indicate the prothrombotic state in diabetic mellitus that lead to vascular complications resulting in morbidity and mortality. Hence prompt treatment of this condition can save numerous lives. HbA1c was positively correlated with platelet indices and hence strict glycemic control can prevent the prothrombotic state from manifesting clinically. In addition to MPV, PDW also needs special mention for being a marker of thrombogenic state.

Conflict of interest
There was no conflict of interest in the present study

REFERENCES