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Correlation of hematological parameters with ECG changes in type II diabetes mellitus

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Background*:-Diabetes mellitus results in abnormal metabolism that affects many systems of the body. It is necessary to understand the hematological & electrocardiographic changes that can occur in patients with type 2 diabetes.****Materials & method:-****Present cross sectional study carried out in tertiary care hospital from May 2015 to May 2017. 100 diabetic subjects (study group), 100 non-diabetic subjects (control group) were selected for study randomly from various departments of tertiary care hospital. In all study, subject's blood was tested for HbA1c; MPV & ECG changes were recorded.****Results****: - There was significant difference between cases and controls for mean blood sugar level & mean HbA1c (p<0.01). Mean Platelet Volume of study group is significantly more than that of control group (p < 0.0001**).ST segment changes, T wave inversion & Q-QS pattern were more among diabetic patient as compared to controls (p<0.01).****Conclusion****:-Mean HbA1c of study group is significantly more than that of control group.Mean Platelet Volume of study group is significantly more than that of control group .ECG changes suggestive of myocardial ischemia or myocardial infarction in the form of ST segment changes, T wave changes and Q-QS pattern were significantly more in the study as compared to control group. HbA1c levels and MPV values were higher in subjects with abnormal ECG than in subjects with normal ECG. Increased MPV is associated with increased risk of myocardial infarction,stroke and TIA.*

Keywords*: ECG,MPV, HbA1c, Type II Diabetes*

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I. Introduction

Diabetes Mellitus is very popular among the common man, everyone is acquainted with it.It occurs when there is a defect in insulin secretion from endocrine pancreas, or defect in action of insulin or both, resulting in chronic hyperglycemia and consequent increased risk of cardiovascular disease. It is a chronic metabolic disease. Majority of people are suffering from diabetes. Previously it was seen only in adults but now increasingly seen in children. Type II DM is caused due to interplay between genetic and metabolic factors, but obesity, family history of diabetes, old age, ethnicity, unhealthy diet and physical inactivity increase the risk. (1,2,3)

Objective:

1. To study HbA1c , mean platelet volume **(**MPV **)**and ECG changes in asymptomatic type II DM patients
2. To study correlation between HbA1c values, MPV and ECG changes in asymptomatic type II DM patients as compared to non-diabetic subjects **(**control group**).**

II. Material and Methods

Present cross sectional study carried out in tertiary care hospital from May 2015 to May 2017. 100 diabetic subjects (study group), 100 non diabetic subjects (control group) were selected for study randomly from various departments of tertiary care hospital.

Sample cases: Type II DM patients attending the Tertiary care hospital. Near relatives and other persons attending along with the patients were encouraged for blood glucose testing and those with fasting blood glucose values less than 126mg%were taken as control group.

Inclusion criteria:

1. Known cases of type II DM without any cardiovascular manifestations.
2. Duration of DM less than 10years.
3. Non-diabetic asymptomatic cases as sample control.

All the subjects were studied between 10am to12 noon.

Exclusion criteria:

1. Known cases of type II DM with cardiovascular disease.
2. Subjects with acute illness, chronic renal disease, stroke and peripheral vascular disease and stroke.
3. Who have not given written informed consent.

III. Methodology

Approval from institutional ethics committee was taken. 3ml of blood samples were collected in vials containing EDTA for HbA1c. HbA1c estimation was done by direct enzymatic assay (Diazyme) on Selectraautoanalyzer. It is IFCC standardized method of HbA1c estimation.

The resting ECGs of all the subjects were recorded. The procedure was explained to all subjects. They were allowed to relax for half an hour in lying down position on an examination table. 12 lead ECG was recorded in supine position. The recommendations of the manufacturer of BPL 108 ECG machine were followed. The ambient temperature during recording was between 27to 30 degree. On the basis on Minnesota code criteria, the ECGS were read and interpreted.

ECG abnormalities	Minnesota code
Q/QS pattern	1-1, 1-2,1-3
ST segment changes	4-1,4-2,4-4
T wave changes	5-1,5-2,5-3

All the data were recorded, documented and subjected for statistical analysis. Data analysis is carried out by using GrappadInstat Software. All the quantitative variables are compared using unpaired T test and Wilcoxon Signed Rank test. Qualitative variables are compared by using Z test for proportion. P<0.05is considered statistically significant at 5% level of significance.

IV. Result

Table 1 Distribution of study subjects according to gender

SEX	STUDY	CONTROL
MALE	58	52
FEMALE	42	48
TOTAL	100	100

Table 2 Comparison of mean blood sugar level, mean HbA1c & MPV

Parameter	STUDY	CONTROL	P VALUE	TEST USED
	MEAN ± SD	MEAN ± SD		
BSL	236.63 ± 58.60	103.14 ± 15.94	P<0.0001**	Wilcoxon Signed Rank Test
HbA1c	9.31 ± 1.8	5.6 ± 0.45	P<0.0001**	Unpaired T Test
MPV	9.08 +/- .88	8.09 ± .46	P<0.0001**	WILCOXON SIGNED RANK TEST

1. Blood sugar levels : Blood sugar levels of study and control groups are compared by using Wilcoxon Signed Rank test and is statistically significant ($p < 0.0001^{**}$). Blood sugar levels of study group are significantly more than that of control group.
2. HbA1c :Mean HbA1c of study and control group are compared by using unpaired t test and is statistically significant ($p < 0.0001^{**}$) Mean HbA1c of study group is significantly more than that of control group.
3. MPV: Mean Platelet Volume of study and control group are compared by using Wilcoxon Signed Rank test and is statistically significant ($p < 0.0001^{**}$). Mean Platelet Volume of study group is significantly more than that of control group.

Table 3 Comparison of ECG changes among cases and control

ECG Changes	STUDY	CONTROL	P VALUE
ST segment changes	38	12	<0.0001**
T wave	42	25	0.010*
Q-QS pattern	12	0	0.0004**

Percentage of ST segment changes in study and control groups are compared by using Z test for proportion and is statistically highly significant (p<0.0001**), percentage is more in study group as compared to control group.

Percentage of T wave changes in study and control groups are compared by using Z test for proportion and is statistically highly significant (p<0.0001**), percentage is more in study group as compared to control group. Percentage of Q-QS pattern changes in study and control groups are compared by using Z test forproportion and is statistically highly significant (p<0.0001**), percentage is more in study group as compared to control group.

Table 4 Comparison of mean HbA1c , MPV& ECG findings.

	ECG NORMAL	ECG NOT NORMAL	P VALUE
HBA1C	8.56=/- 1.49	9.77 +/- 1.84	.0006**
MPV	8.88 +/- 1.028	9.19 +/- .79	.12 (NS)

Mean HbA1c in subjects with normal ECG are compared with subjects of abnormal ECG by using unpaired T test and it is statistically significant. There is significant difference between mean HbA1c in subjects with normal ECG and subjects with abnormal ECG (p<0.0006**).

Mean MPV in subjects with normal ECG are compared with subjects with abnormal ECG; by using unpaired t-test and it is statistically insignificant. But mean MPV in abnormal ECG group is more (9.19 ± 0.79) than MPV in normal ECG group (8.88 ± 1.028).

V. Discussion

The formation of HbA1c or glycohemoglobin occurs by non-enzymatic glycation of haemoglobin protein .In 2010; American Diabetes Association set the cut off limit of 6.5% for HbA1c. Thus HbA1c= or >6.5% can be diagnosed as type II DM. HbA1c assays are either immunoassays or enzymatic assays. IFCC (International Federation of Clinical Chemistry and Laboratory Medicine) has recommended the standardization of the assay.[4]

HbA1c gives a reliable measure of chronic glycaemia (As lifetime of RBCs is 120 days) and HbA1c levels give idea about average blood glucose levels in the preceding 3 months prior to the measurement. So HbA1c is used to diagnose and also to monitor glucose control as it is a reliable measure of chronic glycaemia. Cardiovascular diseases like Coronary Artery Disease (CAD), Myocardial Infarction (MI), and stroke are associated with increased HbA1c levels in subjects with type II DM.DM is associated with accelerated atherosclerosis which leads to IHD , a major complication of DM.[5]

In present study 100 type II DM patients (study group) out of which 58 were males and 42 were females, were compared with 100 non diabetic subjects(control group) which comprised of 52 males and 48 female (Ref. Table No.1). For age distribution mean and standard deviation of study and control group were 52.33± 8.19 years and 49.41± 11.15 years. As such, the study and control groups were matched for age and sex. As seen in Table 2, BSL and HbA1c were significantly elevated in study group as compared to that of control group. BSL 236.63 ± 58.60 mg%in study group and 103.14± 15.94 mg% in control group. HbA1c 9.31 ± 1.8 in study group and 5.6 ± .45 in control group. It shows high statistical significance.

Mean Platelet Volume of study group is significantly more than that of control group. It is seen in our study that increased MPV is associated with higher HbA1c levels and this coincides with results of Zuberi et al.[6,7,8]

Mean Platelet Volume (MPV) is a determinant of platelet functionality and activity. There is increased baseline activation in patients with DM. Hyperglycemia has a direct osmotic effect which increases MPV. Also hyperglycemia activates Protein Kinase C (PKC) and activates calcium sensitive PKC β isoenzyme, which is responsible for hyper reactive platelets in type II DM. Recurrent episodes of hyperglycemia leads through a cascade of reactions to the formation of Advanced Glycation End products (AGEs) which enhance thrombogenicity of platelets. Hyperglycemia causes glycation of proteins on the platelet surface which decreases membrane fluidity and increases platelet reactivity.

Hyperglycemia leads to release of larger platelets with more GPIb and GPIIb/IIIa receptors and higher thromboxane forming capacity.As membrane fluidity of platelets is altered in type 2 DM ,other platelet receptors like P2Y12 are also present in more numbers in DM platelets. Increase in P2Y12 enhances platelet activation and aggregation. Platelets in diabetic patients have lower level of cAMP and higher intracellular calcium level which make them more active and aggregable. Younger platelets are larger,contain more granules and produce more amount of vasoactive and prothrombotic factors such as thromboxane A2 and Serotonin.[9]

This study shows (Table No.3) that ECG changes in the form of ST Segment changes in study group (38) compared with control group (12) which is statistically significant (p < 0.0001**). T Wave changes(T

inversion) are more in the study group (42) as compared to control group, which is statistically significant.(p = 0.010*). Presence of Q wave or QS pattern is seen more in study group (12) as against nil in control group, which is again statistically significant.

Our studies are similar with the studies conducted by SharolAshma Menezes et al. They found ECG changes like Q Waves, ST-T changes and poor progression of R waves in T2DM patients. Overall ECG changes were more common in cases of T2DM as compared to controls (non-diabetics)[(10)].The most frequent ECG abnormality found in persons with T2DM in Kaduna, Northern Nigeria reported by Fatima Bello-Sani et al in their study , were ST-T segment depression and LVH. The prevalence of IHD by ECG criteria in T2DM in their study was 20%.None of the patients with suggestive ECG findings of IHD presented with typical angina pain.[(11)]

M.S.Draman et al. illustrates a case of silent myocardial infarction in a 62 yrs. old man attending diabetes OPD clinic. Routine ECG showed changes of myocardial infarction but he was asymptomatic.[(8)]American Diabetes Association (ADA) recommends screening for occult myocardial ischemia to be performed in DM subjects with abnormal resting ECG. Silent Myocardial Infarction (SMI) is more common in T2DM and occurs in greater than 1 in 5 clinically asymptomatic patients[(10)]. The ECG changes reported in T2DM in our study may represent myocardial ischemia or infarction. Silent ischemia or infarction may be due to cardiac autonomic neuropathy.

Even early in the course of diabetes ECG alterations such as ST-T changes may be observed. These changes help detect signs of myocardial ischemia even in asymptomatic patients. This helps to assess prognosis and predict mortality. V.Mohan et al .observed overall prevalence of IHD to be 17.9 % in NIDDM patients [(12)]

We observed in our study (Table 4) there is significant difference between mean HbA1c in subjects with normal ECG compared with mean HbA1c in subjects with ECG changes (r = 0.33, p = 0.0006**). Thus higher HbA1c levels indicating poor glycaemic control in T2DM resulting more number of patients with ECG changes suggestive of IHD. Ramchandra Rao et al. in their study of ECG changes in asymptomatic T2DM (without any symptom of cardiac disease), found that 24% of patients had ischemia (ST-T changes) and 62% had ischemia plus LVH and only 12% patients had normal ECGs[(13)].Thus majority of the time diabetic patients present with MI and heart failure, being the end stages of cardiovascular disease. They are due to macro and micro vascular complications.Table 4 also shows that the subjects with higher MPV values have more ECG changes suggestive of IHD, though correlation between MPV and ECG changes is not statistically significant.(r = 0.18 , p = 0.0593).

VI. Conclusion

In our study HbA1c, mean platelet volume and ECG changes were found to be more in T2DM patients. Increased HbA1c &MPV was associated with more abnormal ECG changes in T2DM patients.

ECG is inexpensive, painless and reproducible investigation.

MPV is a simple, inexpensive test that can be carried out on diabetic patients.It is easy to interpret it and automated cell counters can routinely measure it.

Our studies suggest that T2DM patients, even if they have no cardiovascular symptoms like angina and breathlessness on exertion, should be screened early in their disease and regularly before the appearance of cardiovascular symptoms so that the complications like myocardial infarction can be delayed and mortality can be reduced.

Primary prevention of cardiovascular disease is an established component of medical practice. With early diagnosis, preventive therapies can be offered for those at risk.MPV and ECG are relatively inexpensive tests and can be carried out at rural setup. Those at risk can be referred for further noninvasive/invasive evaluation.We also conclude that MPV might be used as a simple cost effective laboratory test in the follow up of DM along with HbA1c and thereby reduce morbidity and mortality.

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