



EVALUATION OF MEAN PLATELET VOLUME (MPV), AS AN ATHEROSCLEROTIC MARKER IN TYPE 2 DIABETES MELLITUS PATIENTS.

Pathology

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ABSTRACT

This was a prospective observational study of patients with type 2 Diabetes Mellitus attending Dept. of Endocrinology and tests done in the endocrinology dept and regional diagnostic center and department of Pathology of SCB Medical College Cuttack. A total number of 100 cases of type 2 Diabetes Mellitus patients and 100 non diabetes subjects with detailed clinical history including age, sex, height, weight, BMI, Blood pressure, duration of diabetes, associated complications, personal history (smoking, alcoholism), and family history were taken. Risk factors in diabetes cases were identified by history taking, and from lipid profile, hypertension, BMI and hematological tests. On all cases routine CBC (Hb, TPC, MPV), Bloodsugar (FBS, PPBS), Lipid Profile and HbA1c were evaluated. Hyperglycemia leads to platelet hyper reactivity and platelet plays a major role in the pathogenesis of atherosclerosis. So diabetes patients are more prone to develop vascular complications like atherosclerosis and coronary artery disease (CAD). In our study it was found that MPV has a significant association with raised FBS and PPBS and these were similar to the study by Kodiatte et al [1]. KT Ulutal et al [2] suggested an association between MPV and HbA1c and said that platelets of diabetic patients become more aggregable and reactive due to increased MPV.

KEYWORDS:

MPV, Atherosclerosis, Hb A1c, LDL

Introduction:

Diabetes mellitus (DM) has become a global concern with a huge increase in number of patients having the disease and India has become the diabetic capital of the world with more than 62 million diabetic individuals currently diagnosed with the disease. DM is a group of common metabolic disorders characterized by hyperglycemia. In type 2 DM there are variable degrees of insulin resistance, impaired insulin secretion and increased glucose production. This metabolic disorder affects multiple organ systems of our body. It is a burden for the family members, society, health care systems and to the national economy of the country. The associated complications like retinopathy, neuropathy, nephropathy, microangiopathy are accelerated form of atherosclerosis. Cardiovascular complications are the most frequent cause of morbidity and mortality among diabetic patients. Atherosclerosis, thickening of the arterial wall is a chronic inflammation and healing response of the arterial wall to endothelial injury. Endothelial injury followed by accumulation of LDL and its oxidized form along with monocytes and there is adhesion of platelets to the endothelium, release of factors from activated platelets, macrophage proliferation, extracellular matrix production, recruitment of T cells and accumulation of lipid both extra and intracellularly. All these leads to development of fatty streaks and plaques.

When plasma glucose is consistently elevated, there is an increase in non enzymatic glycosylation of hemoglobin (Hb A1c). HbA1c is measured primarily to identify the average plasma glucose concentration over a 2-3 months of time. In DM higher amounts of HbA1c indicates poor control of blood glucose levels, associated with complications. Long term exposure of elevated glucose alone can contribute to the endothelial dysfunction and increase platelet activation. Other factors like dyslipidemia and hypertension contribute towards the pathogenesis of vascular disease i.e. atherosclerosis in diabetes [4]. MPV is an indicator of the average size and activity of platelets. Larger platelets are younger, more reactive, aggregable and contribute towards high MPV.

So evaluation of Hb A1c, MPV, Lipid profile in diabetes are necessary and are indicators of atherosclerosis.

Materials and Methods:

This study was a prospective observational study conducted in the Out Patient department of Endocrinology and Regional diagnostic center and department of pathology SCB Medical College and Hospital, Cuttack, Odisha.

All patients of both sex, all age group with no difference of socio economic status, diagnosed with type 2 diabetes mellitus are included in this study. Diabetic patients with anemia, malignancy and with anti platelet therapy were excluded from this study.

All relevant information of the patients were collected from the records of patients attending the Endocrine OPD of SCB Medical College, Cuttack, Odisha. A thorough history including age, sex, height, weight, BMI, Blood pressure, duration of diabetes, associated complications, medical, surgical, drug history along with personal and family history were taken. All recent test reports of 100 type 2 DM patients under inclusion criteria i.e. FBS, PPBS, Lipid profile, HbA1c, CBC (Hb, TPC, MPV) were recorded and also from 100 cases of non diabetic cases reports were compared. FBS, PPBS, Lipid profile were done in an autoanalyser. Hb A1c was measured by HPLC. CBC was done by automated cell counter (5 part differential).

Observation:

Study conducted on 100 DM Patients and 100 non diabetic subjects. Of 100 DM 25 were females and 75 males while among 100 non diabetic subjects 67 were male and 33 female. The mean age of the diabetic population was 48.1 ± 8.14 years and that of non diabetic population was 47.88 ± 7.26 yrs. Of the 100 diabetes patients 15 had diabetes associated complications like nephropathy, neuropathy and retinopathy. 17 of 100 gave a positive family history of CAD. Of 100 cases 58 had their BMI > 24.9 kg/m² and of 100 non diabetic subjects, 40 had their BMI > 24.9 kg/m² (21 were over weight and 3 were moderately obese). Mean BMI of diabetic patients was 24.63 ± 4.22 kg/m² and of control was 23.56 ± 3.21 kg/m².

The mean FBS level of diabetic population was 127.5 ± 44.28 mg/dL and non diabetic population was 82.4 ± 26.37 mg/dL. ($p < 0.001$). The mean PPBS level of diabetic population was 217.06 ± 76.77 mg/dL and of non diabetic population was 135.35 ± 63.12 mg/dL ($p < 0.001$). The

mean HbA1C % of diabetic population was $6.16 \pm 1.39\%$ and non diabetic population was $5.07 \pm 0.23\%$ ($p < 0.001$). Out of 100 diabetic patients 24 were with HbA1C level $\geq 6.5\%$ and 76 were with HbA1C $< 6.5\%$.

The mean haemoglobin level of the diabetic patients was 13.6 ± 1.01 g/dL and of the non diabetic was 13.0 ± 0.84 g/dL ($p = 0.0964$ i.e. not quite significantly different). The mean total platelet count of the diabetic population was 2.31 ± 0.51 lakhs/ μ l and of the non-diabetic population was 2.53 ± 0.64 lakhs/ μ l ($p = 0.0326$ i.e. not quite significantly different). The mean platelet volume (MPV) of the diabetic population was 10.42 ± 1.39 fl and of the non-diabetic subjects was 10.07 ± 1.57 fl ($p = 0.1898$ i.e. not significantly different). In the diabetic group, the mean MPV in subjects with complications (10.44 ± 0.75 fl) were higher than that of subjects without complications (10.41 ± 0.86 fl) but independent student t-test did not show any statistical significance ($p = 0.9385$).

It was found that MPV has a strong positive statistical correlation with HbA1c $\geq 6.5\%$ ($p < 0.001$), FBS ($p < 0.001$) and weak positive correlation with PPBS ($p = 0.0036$ i.e. quite significant). There was no correlation of MPV with HbA1c $< 6.5\%$ ($p = 0.051$) and BMI ($P = 0.193$) and duration of diabetes ($P = 0.173$) (Table-2). There were 10 smokers and 17 hypertensive among the 100 diabetic patients.

The mean FBS, PPBS and HbA1c of diabetic patients with HbA1c level $\geq 6.5\%$ was significantly higher than the patients with HbA1c $< 6.5\%$ ($p = 0.003$, $p < 0.001$ respectively) which was significantly different statistically. But the mean MPV of diabetes with HbA1c $< 6.5\%$ was slightly higher than that of diabetes with HbA1c $\geq 6.5\%$ ($P = 0.733$) which was not significantly different. The mean BMI of diabetic patients with HbA1c level $\geq 6.5\%$ (25.12 ± 1.30 kg/m²) was more than diabetic patients with HbA1c $< 6.5\%$ (24.42 ± 2.46 kg/m²) but this was not significantly different ($P = 0.2413$). (Table-3)

Table -1 Comparison of various parameters between the diabetic and non diabetic subjects.

	Diabetics	Non-Diabetics	P value
No. of Samples	100	100	
Male, Female	75,25	67,33	0.2206
Age (years)	48.1 \pm 8.14	47.88 \pm 7.26	0.8816
Mean Duration of diabetes (yrs)	4.10 \pm 3.22		
BMI (kg/m ²)	24.63 \pm 4.22	23.56 \pm 3.21	0.1484
BP (SBP/DBP) mm of Hg	127.65 \pm 6.54/74.71 \pm 6.15	125.24 \pm 7.56/76.21 \pm 7.35	
Cholesterol (mg/dL)	165.54 \pm 26.63		
Triglyceride (mg/dL)	186.54 \pm 104.33		
FBS (mg/dL)	127.5 \pm 44.28		<0.001
PPBS (mg/dL)	217.06 \pm 76.77	135.35 \pm 63.12	<0.001
HbA1c(%)	6.16 \pm 1.39	5.07 \pm 0.23	<0.001
Hb(gm%)	13.6 \pm 1.01	13.0 \pm 0.84	0.0964
TPC (lakhs/ml)	2.31 \pm 0.51	2.53 \pm 0.64	0.0326
MPV (fl)	10.42 \pm 1.37	10.07 \pm 1.56	0.1898

Table-2 Correlation of MPV to the various parameters studied

		p
MPV	Duration of diabetes	0.173
MPV	BMI	0.193
MPV	HbA1c	0.623
MPV	FBS	<0.001
MPV	PPBS	0.0036
MPV	Cholesterol	0.3240
MPV	Triglycerides	0.0515

Table -3 Comparison of various parameters among diabetic study population

	HbA1c<6.5%	HbA1c \geq 6.5%	P value
No. of samples	67	33	
BMI (kg/m ²)	24.42 \pm 2.46	25.12 \pm 1.30	0.2413
HbA1c (%)	5.17 \pm 0.46	7.36 \pm 1.18	<0.001
FBS(mg/dL)	106.52 \pm 21.88	136.4 \pm 31.84	0.003

PPBS (mg/dL)	170.5 \pm 23.55	268.2 \pm 59.36	<0.001
TPC (lakhs/ml)	2.26 \pm 0.50	2.44 \pm 0.4	0.4527
MPV (fl)	10.46 \pm 0.97	10.33 \pm 1.36	0.733
Correlation of MPV with HbA1c (P=0.051)			p<0.001

(P value calculated using t-test)

DISCUSSION:

Type 2 DM is a metabolic disorder and a major health problem for its high prevalence and morbidity. The metabolic syndrome comprising of hyperglycemia, dyslipidemia, hypertension and abdominal obesity which raises the risk for heart disease, stroke, diabetes. Mean platelet volume (MPV) is higher in diabetes as compared to non diabetes.[1] MPV is an indicator of the average size and activity of platelets. Younger platelets are larger, more reactive and aggregable and they contain denser granules, secrete more serotonin, β thromboglobulin, more thromboxane A2 as compared to smaller platelets. This platelet hyper reactivity leads to a pro-coagulant state and further vascular complications. It is proposed that hyperglycemia can increase platelet reactivity by inducing platelet and protein kinase C activation [5]. Platelets play an important role in the pathogenesis of atherosclerosis by adhering to endothelium and releasing factors that induce plaques and thrombus formation.

There are several risk factors for atherosclerosis. These risk factors have roughly multiplicative effect. Thus, two factors increase risk approximately four-fold, and three (i.e. hyperlipidemia, hypertension, and smoking), increase risk by a factor of seven[6]. In this study among 100 diabetes patients there were no smokers, alcoholics, hypertensive. The reason for this may be the small sample size.

Age and sex of the diabetes population and non-diabetes subjects were not significantly different. This means our findings were not influenced by age and sex.

16 out of 100 patients had their cholesterol in borderline high range, 40 of the 100 had low HDL level (i.e. < 40 mg/dL), 5 had high LDL level and 28 of the 100 had hypertriglyceridemia. 16 of the 100 had low HDL + high triglyceride, 52 of the 40 were overweight and 5 were moderately obese. As a result of insulin resistance in adipose tissue, lipolysis and free fatty acid flux from adipocytes are increased, leading to increased lipid [very low-density lipoprotein (VLDL) and triglyceride] synthesis in hepatocytes and decreased clearance of VLDL because of decreased activity of insulin sensitive lipoprotein lipase in muscle and fat. This is responsible for dyslipidemia found in type 2 DM [elevated triglycerides, reduced high density lipoprotein (HDL) and increased small dense low-density lipoprotein (LDL) particles]. Dyslipidemia is one of the key risk factors for cardiovascular disease (CVD) in diabetes mellitus. This can be well activity in the pathogenesis of vascular complications. Role of activated platelets in development of vascular complications in diabetes patients needs to be confirmed by larger studies. Hekimsoy et al.[6] and Demirtune et al[7]. found that MPV was not significantly different between those diabetic patients with complications and those without. Their possible explanation was centered on the rapid consumption of activated platelets in diabetes with complications. No association of MPV was seen with BMI and duration of diabetes. Similar findings were seen in other studies.

Conclusion:

This study was undertaken for 100 cases of type 2 DM patients and 100 non diabetic subjects with routine CBC (Hb., TPC, MPV), Blood sugar (FBS, PPBS), Lipid profile and Hb A1c. The purpose of this study was to evaluate various risk factors of atherosclerosis in type 2 DM patients attending Out patient department of Endocrinology of SCB Medical College, Cuttack. From various studies it was found that hyperglycemia leads to platelet hyper reactivity and it plays a major role in the pathogenesis of atherosclerosis. So diabetes patients are more prone to develop vascular complications like atherosclerosis and coronary artery disease.

In our study it was concluded that MPV has a significant association with Fasting blood sugar and Hb A1c $\geq 6.5\%$. Since the MPV is towards the higher side of the normal range and it is more in diabetes patients as compared to non diabetes cases.

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