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RESEARCH ARTICLE

ROLE OF MPV IN COMPLICATION OF DIABETES MELLITUS 2

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Abstract

Diabetes mellitus (DM) is a global health problem with increased risk of vascular disease. Platelets may contribute to the development of vascular complications in subjects with diabetes. Larger platelets are more reactive than smaller ones; therefore, mean platelet volume (MPV) can be used as a marker for platelet activity. Aim and Objectives: To determine the role of MPV in severity and complications of DM2 as compared to non diabetic patients and to determine the effect of glycemic control and duration of diabetes on platelet parameters. This is a cross-sectional prospective study to evaluate MPV in patients with diabetes mellitus 2 versus non-diabetic patients and to investigate the potential association between MPV and chronic diabetic complications. Our study revealed that MPV is increased in Diabetes mellitus (DM) and that platelets become more reactive and aggregable. The increased platelet size may be a risk factor for atherosclerosis associated with DM and its vascular complications. MPV was found to be higher in subjects with Type-2 diabetes and significantly increased in diabetics with poor glycemic control and In patient with complications. having a longer duration of diabetes. MPV can be used as a prognostic marker of vascular complications in patients with DM.

Introduction:-

According to International Diabetes Federation (IDF), in 2013, 382 million people in the world have diabetes. By 2035, this number will rise to 592 million. In fact, India ranked second in the world in diabetes prevalence, just behind China. Thus preventing vascular complications and monitoring of DM is important. Sustained hyperglycemia leads to a series of interrelated alterations that can cause evident endothelial dysfunction and vascular lesions in diabetic complications. Platelets in response to stimuli generated by the endothelium of blood vessels, changes shape, adhere to subendothelial surfaces; secrete the contents of intracellular organelles, and aggregate to form a thrombus leading to development of advanced atherosclerosis in diabetes. Mean Platelet Volume (MPV) is an indicator of the average size and activity of platelets. Larger platelets contain more dense granules and hence are more potent and thrombogenic. This suggests a relationship between the platelet function especially MPV and diabetic vascular complications thus indicating changes in MPV reflect the state of thrombogenesis. The data of MPV value in diabetics and their association with vascular complications are scarse in India.Diabetes mellitus (DM) is a major health problem worldwide and it's prevalence increased rapidly especially in developing countries[2]. In China it is estimated that DM prevalence increased to 11.6% (113.9 million adults)[1]. Studies indicated that the inflammation played an important role in the development of DM[2]. Systemic sub-clinical inflammation has been

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implicated in the development of type 2 diabetes[3]. Inflammatory biomarkers, such as white cell counts (WBC), C-reactive protein (CRP), tumor necrosis factor-α (TNF-α), and interleukin- 6 (IL-6), were showed to be correlated with prevalent and incident diabetes [6,7]. Studies showed that DM cases have increased platelet activity[4]. A latest meta-analysis[5] which included 30 case–control and cross-sectional studies found that MPV was significantly higher in T2DM cases than study participants without DM. The mean platelet volume (MPV) is a precise measurement of their dimension, calculated by hematological analyzers on the basis of volume distribution during routine blood morphology test. MPV ranges between 7.5 and 12.0 fl, whereas the percentage of large platelets should amount to 0.2-5.0% of the whole platelet population. In physiological conditions, MPV is inversely proportional to the platelet count, which is associated with hemostasis maintenance and preservation of constant platelet mass.[6] Although the underlying mechanism of higher MPV in diabetic subjects is incompletely understood, it has been suggested that increased MPV in diabetes may be due to osmotic swelling as a result of hyperglycemia[7]. In the National Health and Nutrition Examination Survey the researchers reported that MPV was strongly and independently associated with the presence and severity of diabetes in study participants with diabetes[4].

Aims & Objectives:-

Primary Objective-

To determine the role of mean platelet volume in severity and complication of diabetes mellitus 2.

Background

The worldwide prevalence of DM has risen dramatically over the past two decades, from an estimated 30 million cases in 1985 to 415 million in 2017. Based on current trends, the IDF (International diabetes federation) projects that 642 million individuals will have diabetes by the year 2040. Although the prevalence of both type 1 and type 2 DM is increasing worldwide, the prevalence of type 2 DM is rising much more rapidly, presumably because of increasing obesity, reduced activity levels as countries become more industrialized, and the aging of the population. The incidence of type 1 diabetes has been increasing at a rate of 3–5% per year worldwide. The ages. In 2015, the prevalence of diabetes in individuals aged 20–79 ranged from 7.2–11.4%. The countries with the greatest number of individuals with diabetes in 2015 are China (109.6 million), India (73 million), the United States (30.3 million), Brazil (14 million), and the Russian Federation (9 million). In the most recent estimate for the United States (2017), the Centers for Disease Control and Prevention (CDC) estimated that 9.4% of the population had diabetes, and as many as 34% of U.S. adults had prediabetes. Approximately 25% of the individuals with diabetes in the United States were undiagnosed; globally, it is estimated that as many of 50% of individuals with diabetes may be undiagnosed.

Genetic Factors:

There is a 70 - 90% concordance of type 2 DM in between identical twins. Increased risk of type 2 DM is observed among individuals with a parent with type 2 DM. The risk approaches 40% if both the parents have type 2 DM. It is interesting to note that the in utero environment also plays a significant role in the development of this disease. Either increased or reduced birth weight can increase the risk of type 2 DM in adult life.

Environmental Factors:

Well recognised environmental factors leading to development of type 2 diabetes are physical inactivity and excessive caloric intake. These factors can either independently produce the disease in a genetically susceptible person, or can do so via production of obesity and metabolic syndrome. Visceral or central obesity (as evidenced by the waist- hip ratio), is very common in type 2 DM (≥80% are obese).

Metabolic Abnormalities:

Abnormal muscle and fat metabolism: The reduced ability of insulin to act effectively on target tissues (especially fat, liver and muscle); insulin resistance, is the prominent feature of type 2 DM. The combination of obesity and genetic susceptibility results in development of insulin resistance. This leads to impaired glucose utilization by insulin-sensitive tissues and increased hepatic glucose output. Both effects lead to the hyperglycemia.

Impaired insulin secretion:

Initially insulin secretion increases in response to insulin resistance in type 2 DM to maintain normal glucose tolerance. Hence, the insulin secretory defect is initially mild and involves glucose stimulated insulin secretion only, including a great reduction in the first secretory phase. The decrease in Beta cell mass in individuals with long-standing type 2 DM is by approximately 50%.

Increased hepatic glucose and lipid production:
In the liver, insulin resistance reflects the failure of hyperinsulinemia to suppress gluconeogenesis, which results in decreased glycogen storage by the liver in the postprandial state and in fasting hyperglycemia. Insulin resistance in adipose tissue leads to increase in lipolysis as well as free fatty acid flux from adipocytes, which in turn leads to increased lipid (triglyceride and very-low-density lipoprotein[VLDL]) synthesis in hepatocytes.

Other Risk Factors:
Hypertension causes dysfunction of endothelium, impaired availability of NO, renal vasoconstriction, decrease in glomerular filtration, impairment in tubuloglomerular feedback, decrease in medullary flow and worsened pressure natriuresis and progressive proteinuria. This causes rise in intraglomerular pressure and leads to a series of changes in matrix. Thus hypertension is an important determinant of macroangiopathy and microangiopathy in diabetes. Along with glycemic control, strict lowering of blood pressure with angiotensin receptor blockers (ARBs) or ACE-inhibitors (ACE-I) causes reduction in intraglomerular pressure and blockage of the RAS. This has been shown to result in reduced incidence of nephropathy.

Diabetic Kidney Disease (DKD):
It took more than three millennia from the first description of diabetes in 1552 BC to the recognition of an association between diabetes and kidney disease, but it took only several decades for diabetic kidney disease (DKD) to become the leading cause of ESRD(end stage renal disease) in the United States[8]. This microvascular complication develops in approximately 30% of patients with type 1 diabetes mellitus (DM1) and approximately 40% of patients with type 2 diabetes mellitus [9].

Platelets:
Platelets, the smallest of the human blood cells (3.6 x 0.7μm), are central players in processes of hemostasis and thrombosis. In addition, platelets are specialized cells of the innate immune defence, modulators of the inflammatory response, and involved in wound healing as well as in hematogenic metastasis. They are released from megakaryocytes in the bone marrow as anucleated fragments into the circulation.[10]

Platelet Granules[11]:
Two major storage granules are present in platelets, namely, α and dense granules. Their function is to store biologically active molecules which are involved in initiation of coagulation and recruitment of other cells during inflammation.

Alpha granules: contain platelet specific proteins like PF-4, thromboglobulin, PDGF, thrombospondin, homologs of plasma proteins like fibrinogen, fibronectin, albumin, GPIIbIIIa, fibrinogen, vWf and also P-selectin (CD62P) and CD36.

Platelet Metabolic Alterations:
Hyperglycemia is an established causal factor for platelet hyperactivity and in vivo activation of platelet in patients with diabetes mellitus. Glucose concentration inside the platelet parallel the extra cellular concentration as glucose entry into the platelets is insulin-independent.[12] Increased sensitivity of platelets to agonists are due to metabolic alterations which include impaired calcium homeostasis, decreased platelet-derived nitric acid production, activation of PKC and increased of superoxide anion formation. In addition, reduced levels of glutathione levels and nitric oxide synthase activity are observed in the platelets of diabetic patients.[13]

Material and Methods:-
The present study is carrying out in Department of Medicine, Netaji Subhash Chandra Bose Medical College & Hospital-Jabalpur (M.P.).

Sample size :
100 cases and 100 control were taken.

Study design:
Case Control Study.

Study period:
January 2018 to August 2019

Inclusion criteria:
Case .OPD / IPD patients in NSCB MCH Jabalpur, Age Between 14 Years To 80 Years, Diagnosed and newly diagnosed cases of diabetes mellitus, Availability Of Patient/ Caregiver To Give Inform Consent To Involve Voluntary In My Study, Control—Nondiabetic Individual

Exclusion criteria:
Diabetics on antiplatelet drugs such as aspirin and clopidogrel, Subjects with any diagnosed malignancy, Infections affecting platelets, Subjects with primary disease of liver and kidney, disease of bone marrow and reticuloendothelial system, Subjects with liver failure ,Subjects with anaemia.

Laboratory Methods:
Complete Blood Counts, Random Blood Sugar, Fasting Blood Sugar, ECG, Fundus Examination, Renal Function Test, Urine Routine And Microscopy, HbA1c, 2D Echo

Sampling method :With All aseptic precaution 6 ml blood is taken from anticubital vein, 2 ml for CBC in EDTA vial and 4 ml in non EDTA vial for RBS ,FLP,RFT and FBS.Various platelet indices is measured by automated analyser. Mean Platelet Volume was estimated and correlated with blood sugar level.

Result:-

Table1:- Age Wise Distribution.

Age Group	Case		Control	
	n	%	N	%
31-40 yrs	15	15.00%	27	27.00%
41-50 yrs	26	26.00%	29	29.00%
51-60 yrs	26	26.00%	26	26.00%
61-70 yrs	27	27.00%	13	13.00%
71-80 yrs	6	6.00%	5	5.00%
71-80 yrs	0	0.00%	0	0.00%
Chi square=8.2 ,P=0.072				

Age	cases	Control	T test
mean	54.42	50.02	2.80
SD	11.25	10.95	P=0.0056

Table showed the distribution of age groups between case and control group. Most of the study participants were belonging between 41 – 70 years of the age. Percent distribution of the age group between case and control was not found significant statistically (P=0.072). However, the participants of the control group were significantly younger than participants of the case group (P=0.0056).

Table 2:- Sex Wise Distribution.

Sex	Case		Control	
	n	%	N	%
F	50	50.00%	43	43.00%
M	50	50.00%	57	57.00%
Chi square=0.92, P=0.321				

Table showed the distribution of gender in case and control group. Female and male ratio in case group was 50:50 and among control group the female and male ratio was 43:57. The difference in female and male ratio among case and control group was not found significant statistically (P=0.321).

Table 3:- FBS V/S HbA1C.

FBS Category	HbA1C Category			
	<7		>7	
	n	%	N	%
≤100 mg/dl	9	22.50%	3	5.00%
101-120 mg/dl	3	7.50%	4	6.70%
121-140 mg/dl	5	12.50%	6	10.00%
>140 mg/dl	23	57.50%	47	78.30%
Chi square = 7.77, P = 0.05				

FBS distribution	Good glycemic control (GROUP A)	Poor glycemic control (GROUP B)	Unpaired t test
Mean	157	227	3.59
SD	64.69	113.48	P value = 0.0006

While analyzing FBS distribution, it was observed that, majority in good glycemic control group belonged to >140 mg/dl FBS class interval (57.50%) with a mean FBS of 157+64.69 mg/dl and majority in poor glycemic control group also belonged to > 140 mg/dl FBS class interval (78.30%) with a mean FBS of 277+113.48 mg/dl .The mean difference of FBS among glycemic control group was found statistically significant (P=0.0006).

Table 4:- MPV V/S HbA1C.

MPV Category	HbA1C Category			
	<7		>7	
	n	%	N	%
≤8 fl	3	7.50%	0	0.00%
8.01-10.00 fl	35	87.50%	11	18.30%
>10.0 fl	2	5.00%	49	81.70%
Chi square=57.12,P<0.0001				

MPV Distribution	Good glycemic control(Group A)	Poor glycemic control(GroupB)	Unpaired t test
Mean	9.11	11.05	9.58
SD	0.68	1.15	P<0.0001

While analyzing MPV distribution, it was observed that, majority in good glycemic control group belonged to 8.00-10.00 fL MPV class interval (87.50%) with a mean MPV of 9.11 fL and majority in poor glycemic control group belonged to >10.01 fL MPV class interval (81.70%) with a mean MPV of 11.05 fL . This significance is exhibited by the increased mean MPV levels in poor glycemic control group compared to good glycemic control group . The data subjected to statistical unpaired t test reveals the existence of statistically significant association between MPV distribution and glycemic control based on HbA1c levels. (P < 0.0001)

Table 5:- MPV VS Proteinuria.

MPV Category	PROTEIN (Yes/No)			
	N		Y	
	n	%	N	%
<=8	1	2.00%	2	4.10%
8.01-10.00	25	49.00%	21	42.90%
>10.00	25	49.00%	26	53.10%

MPV Vs Protinuria	Proteinuria -	Proteinuria +	Unpaired t test
Mean	10.12	10.44	1.14
SD	1.27	1.46	P=0.259

While analyzing MPV distribution, it was observed that, majority in proteinuria -ve group belonged to 8.01-10 AND10.01 fL MPV class interval (49 %) with a mean MPV of 10.12 fL and majority in proteinuria +ve group belonged to >10.01 fL MPV class interval (53.10%) with a mean MPV of 10.44 fL . there is no statistical significance.(P=0.259)

Table 6:- Comparison Between Cases and Control.

	group	N	Group Statistics		SE	T test	P value
			Mean	SD			
AGE	Case	100	54.42	11.25	1.13		
	Control	100	50.02	10.95	1.10	2.80	0.006
MPV	Case	100	10.28	1.37	0.14		
	Control	100	9.51	0.92	0.09	4.63	<0.0001
FBS	Case	100	199.21	102.57	10.26		
	Control	100	102.35	5.56	0.56	9.43	<0.0001
PPBS	Case	100	213.17	72.09	7.21		
	Control	100	122.12	7.79	0.78	12.56	<0.0001

There is a strong positive correlation between HbA1c levels and MPV levels. This is indicated by the Pearson's Correlation coefficient value r= 0.65with a P value of <0.0001. By conventional criteria the relationship between the HbA1c levels and MPV levels is considered to be statistically significant since P< 0.0001. This means as HbA1c levels increases MPV levels also increases in a direct fashion in our study subjects. This proves that increased platelet volume and activity results from hyperglycaemic states. In simple terms, for every 1% increase in HbA1c level there is a 2.28 fl increase in MPV among the study subjects. There is a positive correlation between RBS levels and MPV levels. This is indicated by the Pearson's r Correlation value of 0.42 with a P-value of < 0.0001. This means as RBS increases MPV levels also increases in a direct and linear fashion in our study subjects. In simple terms, for every 100mg/dl increase in RBS there is a 2.96 fl increase in MPV among the study subjects.

Discussion:-

Diabetes is one of the largest global health emergencies of the 21st century.MPV is a determinant of platelet function and platelet size. It reflects changes either platelet stimulation or rate of platelet production.Large platelets are hemostatically more active and a risk factor for vascular complications.In our study,we have selected 100 patients who have fulfilled the criteria for the diagnosis of diabetes mellitus according to international diabetes federation and 100 control. In our study,the mean of age of cases are 54.42+11.25Years while mean of control is 50.02+10.95 Years. Similar studies done by[14]a total of 87 patients fulfilling the selection criteria includes 37 female and 50 male.study carried out by[15] ,total 211 subjects are taken,105 with diabetes and 106 healthy individuals, where 55 were male and 50 female in diabetic and 49 males and 47 females in the non diabetic group.In our study 40 % diabetic cases have HbA1c <7 and 60 % diabetic cases have HbA1≥ 7. Study done by[16]10 % pt had HbA1c < 7% while 90% pt had HbA1c≥7%.In our study mean of MPV in proteinuria group was 10.44+1.46fl and without protienuria was 10.12+1.27fl . Similar study done by[17]mean of MPV in microalbuminuria was 11.61+2.29fl and without microalbuminuria was 10.65+2.32fl.In our study mean of MPV in retinopathy group was 10.91+1.37fl and without retinopathy is 9.69+1.09fl. Similar study done by[17]mean of MPV in retinopathy was 11.71+2.28fl and without retinopathy was 10.74+2.31fl. One more study done by[18]mean of MPV in retinopathy was 11.40+1.96fl .Our study mean of MPV in cases and control are 10.28+1.37fl and 9.51+0.92 fl respectively. Study carried out by[19]mean of MPV in diabetic and non diabetics are 9.89+1.27fl and 8.82+1.14fl respectively . Similar study by[20]says mean of MPV in diabetic was 8.83+0.72 fl while in nondiabetic was 7.62+0.42fl.In our study mean of triglyceride in group A was 135.98+61.76mg/dl and in groub B was169.06+66.23mg/dl.Our study was consistent with study of [15]with sr TG in HbA1c<6.5 was 133.19+46.30mg/dl and in HbA1c≥6.5 was 176.96+88.54mg/dl .

Conclusion:-

Age and gender status had no statistically significant role to play on mean platelet volume while correlating it with HbA1c and studying its association with microvascular complications in type 2 diabetes mellitus . On comparison between good and poor glycemic control patient higher fasting blood sugar levels was found in poor glycemic control patients ,and higher post prandial blood sugar levels is found in poor glycemic control patients. There was higher incidence of triglyceridemia in poor glycemic control patients. There was higher incidence of retinopathy in poor glycemic control patients.There was higher mean platelet volume levels in poor glycemic control patients.On

comparison between proteinuria based patient groups higher mean platelet volume levels in patients with proteinuria, but no significance was found. On comparison between retinopathy based patient groups higher mean platelet volume levels was found in pt with retinopathy. For every 1% increase in HbA1c level there is a 2.5 fl increase in MPV For every 100mg/dl increase in RBS there is a 2.96 fl increase in MPV. Our study shows MPV is increased in subjects with diabetic complication when compared with non-diabetics and that an increase in HbA1c concentration, which indicates poor glycemic control, was accompanied by increased MPV and PDW values. Longer duration of diabetes also increases the MPV. MPV is found to be higher in patients with complications of DM2 as compared to non diabetic patients. As the diabetic subjects have higher baseline platelet reactivity, assessment of MPV, a simple and cost-effective laboratory test would be a useful prognostic marker of cardiovascular complications in diabetes and thereby help hold the morbidity and mortality.

Reference:-

1. Xu Y, Wang L, He J, Bi Y, Li M, Wang T, et al. Prevalence and control ofdiabetes in Chinese adults. JAMA. 2013;310:948–59.
2. Marques-Vidal P, Schmid R, Bochud M, Bastardot F, von Känel R, PaccaudF, et al. Adipocytokines, hepatic and inflammatory biomarkers and incidenceof type 2 diabetes. The CoLaus study. PLoS ONE. 2012;7:e51768.
3. Kolb H, Mandrup-Poulsen T. An immune origin of type 2 diabetes? Diabetologia.2005;48:1038–50.
4. Winocour PD. Platelet abnormalities in diabetes mellitus. Diabetes.1992;41(Suppl 2):26–31.
5. Zaccardi F, Rocca B, Pitocco D, Tanese L, Rizzi A, Ghirlanda G. Plateletmean volume, distribution width, and count in type 2 diabetes, impairedfasting glucose, and metabolic syndrome: a meta-analysis. DiabetesMetab Res Rev. 2015;31:402–10.
6. J. Sikora and B. Kostka, "Blood platelets as pharmacological model," Postępy Biologii Komórki, vol. 3, no. 32, pp. 561– 569, 2005. Thompson and J. A. Jakubowski, "The pathophysiology and clinical relevance of platelet heterogeneity," Blood, vol. 72, no. 1, pp. 1–8, 1988.
7. . Martyn CN, Matthews DM, Popp-Snijders C, Tucker J, Ewing DJ, Clarke BF. Effects of sorbinil treatment on erythrocytes and platelets of persons with diabetes. Diabetes Care 1986;9:36–39
8. Cameron JS: The discovery of diabetic nephropathy: From smallprint to centre stage. J Nephrol 19[Suppl 10]: S75–S87, 2006
9. Reutens AT: Epidemiology of diabetic kidney disease. Med ClinNorth Am 97: 1–18, 2013
10. Bhatt DL, Topol EJ. Scientific and therapeutic advances inantiplatelet therapy. Nat Rev Drug Discov 2003;2:15–28
11. Comprehensive Textbook of Medical Physiology G.K. Pal Pg 187-189
12. Davi G, Gresele P, Violi F, Basili S, Catalano M, Giammarresi C,et al. Diabetes mellitus, hypercholesterolemia, and hypertensionbut not vascular disease per se are associated with persistentplatelet activation in vivo. Evidence derived from the study ofperipheral arterial disease. Circulation 1997;96:69–75
13. Li Y, Woo W, Bose R. Platelet hyperactivity and abnormal Ca(2+) homeostasis in diabetes mellitus. Am J Physiol Heart CircPhysiol 2001;280:H1480–9.
14. Sadikuj Jaman1, 2,*, Sawgat Rezwan2 , Sakibul Alam3, Rayhanul Islam2,4 , Asma Ul Husna5 and Md. Abu Sayeed6,7 Association of Mean Platelet Volume and Platelet DistributionWidth with Hba1c.
15. Anupama Dayal, sadhana Kothari, Rupal J Shah and S.M Patel Mean Platelet volume in diabetes mellitus type IIannals of pathology and laboratory medicine, vol 03, No 03 (Suppl) December 2016.
16. Ishan Dubey*, Bindu Singh Gaur, Roma Singh A study to find correlation of platelet indices with HbA1c in diabetic patients with absence/presence of vascular complications International Journal of Research in Medical Sciences Dubey I et al. Int J Res Med Sci. 2017 Mar;5(3):1042-1047.
17. Madhavan K, Priyadarshini V2 Sivaprakash V, Bharath Kumaran M Study on mean platelet Volume in Type 2 Diabetes Mellitus Patients vs Non Diabetic Patients JMSCR Volume 05 Issue 03 March 2017.
18. Archana Buch, Supreet Kaur, Rahul Nair, Ambuj Jain Platelet volume indices as predictive biomarkers for diabetic complications in Type 2 diabetic patients 2017 Journal of Laboratory Physicians | Published by Wolters Kluwer – Medknow Tuesday, September 3, 2019, IP: 157.34.151.10.
19. Shilalipi Pradhan1, Aurobinda Chinara1, Bimal Kumar Sahoo2 Use of mean platelet volume as a tool to assess the progression of type 2diabetes mellitus2019 | Vol 9 | Issue 3
20. Navya B. N., Dhanalakshmi D.P., Vivek T.G., Kariappa T.M. Evaluation of Mean platelet volume as a prognostic marker in type II diabetes mellitus 1 of evolution of med and Dent Sci / eIssN – 2278-4802, pISSN – 2278-4748/Vol.4/Issue 19/ March 05,2015.