ORIGINAL RESEARCH

Mean platelet volume to lymphocyte ratio as a novel marker for diabetic nephropathy

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ABSTRACT

Aims: The present study was designed to compare Mean platelet Volume to Lymphocyte ratio (MPVLR) as predictor of inflammatory marker in patients with Diabetic nephropathy and diabetics without nephropathy.

Materials & methods: The study was conducted on 50 diabetic patients with nephropathy and 50 diabetics without nephropathy that presented to Medicine department (indoor/ outdoor department) of Guru Nanak Dev Hospital, Amritsar. The subjects were divided into two groups i.e. Group A and Group B. Group A comprised of 50 Diabetic patients with Nephropathy and Group B comprised of Diabetic patients without Nephropathy. Detailed history was taken and all patients underwent a detailed clinical evaluation including measurement of vitals. Plasma glucose, Blood urea, Serum creatinine were estimated by standard protocols. Urine complete examination was done microscopically. Albuminuria, which is the hallmark of diabetic nephropathy, was estimated using spot Urinary Albumin-creatinine ratio (UACR). The quantitative determination of microalbuminuria was done by Nephelometry method procuring commercially available kits. Mean Platelet Volume (MPV) and Absolute Lymphocyte Count (ALC) were calculated using cell counter (ABX Pentra 80) and then ratio was calculated by dividing MPV to ALC.

Results: In Group A, mean MPV was 10.46 fL while in Group B, it was 8.60 fL. The mean MPV in Group A was significantly higher as compared to Group B (p = 0.001). Mean Absolute Lymphocyte count (ALC) in Group A was 2.03x10^3/µL, while in Group B was 2.80x 10^3/µL. The mean MPVLR was 5.27 and 3.08 in Group A and Group B respectively and the difference was found to be statistically significant (p=0.001).

Conclusion: MPVLR values are higher in patients with diabetic nephropathy and this difference is statistically significant. MPVLR is easily available; cost effective and routinely done, hence, it can be considered as a novel marker for Diabetic nephropathy (DN)in diabetic patients.

Key words: Diabetic nephropathy, Mean Platelet volume, Mean platelet volume to lymphocytic ratio

INTRODUCTION

Diabetes mellitus (DM) refers to a group of metabolic disorders that share the common phenotype of hyperglycemia.[1] Diabetes can be classified into type 1 diabetes, type 2 diabetes, Gestational Diabetes Mellitus (GDM) and specific types of diabetes due to other causes.[2]

The prevalence of diabetes is increasing globally and has reached epidemic proportions in many developing countries. Currently, India and China are the largest contributors to the world's diabetes burden. As per International Diabetes Federation (IDF) 2019 data, the prevalence of diabetes between 20-79 year of age in India is 8.9%. This corresponds to total diabetes cases in adults as 77,005,600 and it is expected to reach 100 million by 2030.[3]

In micro and macro-vascular complications of diabetes, platelets may be involved in the pathogenesis owing to their altered morphology and function. DM is characterized by persistent hyperglycemia and insulin resistance which leads to injury to pericytes and endothelium. The increased platelet activity is also believed to play a vital role in the development of vascular complications of this metabolic disease.[4, 5]

DN, a major micro-angiopathic complication of diabetes, is a clinical syndrome characterized by persistent albuminuria (>300 mg/24 hours or urine albumin to creatinine ratio (UACR) > 300 mg/g of creatinine, a progressive decline in glomerular filtration rate (GFR), arterial hypertension, increased cardiovascular morbidity and mortality and end-stage renal disease (ESRD). The increasing number of people with diabetes has a major impact on the prevalence of DN, which occurs in 20% to 40% of all patients with type 2 DM.[6, 7]

Microalbuminuria is a potent risk factor for cardiovascular events and deaths in patients with type 2 DM. Many patients with type 2 DM and microalbuminuria succumb to cardiovascular event before they progress to overt proteinuria or renal failure.[8, 9]

Circulating platelets are heterogeneous with respect to their size, density, and reactivity. [10]Platelet hyperactivity and its increased baseline activation in patients with diabetes are multifactorial. It is associated with biochemical factors such as hyperglycemia, hyperlipidemia, insulin resistance, inflammatory and oxidative state and also with increased expression of glycoprotein receptors and growth factors. [11, 12]

Platelet size (MPV) is a marker and possibly determinant of platelet function. Large platelets are potentially more reactive and contain more dense granules, undergo greater in vitro aggregation in response to agonists such as ADP and collagen and release more serotonin and β-thromboglobulin (β-TG). It is found that hyperglycemia causes increase in platelet size.[13]

The peripheral total White Blood Cells, monocyte and neutrophil counts increase in parallel with advancement of DN. In contrast, Absolute Lymphocyte Count (ALC) have a tendency to decrease. Lymphocytes are essential for complete inflammatory response and a decrease in ALC due to induced apoptosis is also a marker of inflammatory damage.[14]

Platelet to lymphocyte ratio (PLR) has been reported to exhibit hyperactive inflammatory response. However, the platelet size shows platelet activity more accurately than the platelet count. Mean platelet volume to lymphocyte ratio (MPVLR) is suggested to be more specific and sensitive than MPV and platelet-lymphocyte ratio (PLR) alone in selecting DN subjects.[15- 17]

As MPV and Lymphocyte count are simple and inexpensive to obtain, easy to interpret and routinely measured by automated cell counters, hence it becomes worthwhile to assess MPV to Lymphocyte ratio as a novel marker for DN.

MATERIALS & METHODS

The present study was conducted to assess the mean platelet volume to lymphocyte ratio as a novel marker for diabetic nephropathy. The study was conducted in the department of Medicine, Guru Nanak Dev Hospital attached to Govt. Medical College, Amritsar. This was Case-Control study which included100 diabetics that presented to Medicine department

(indoor/ outdoor department) of Guru Nanak Dev Hospital, Amritsar and fulfilled the inclusion criteria of the study. The subjects were divided into two groups as under: Group A: Diabetic patients with Nephropathy; and Group B: Diabetic patients without Nephropathy. Albuminuria, which is the hallmark of diabetic nephropathy, was examined using spot UACR. The quantitative determination of microalbumin in urine was done by Nephelometry method procuring commercially available kits. Patients with UACR of >30mg/g were taken as micro albuminuria positive, >300mg/g as macroalbuminuria positive and UACR <30mg/g were taken as controls. MPV and ALC were calculated using cell counter (ABX Pentra 80) and then ratio was calculated by dividing MPV to ALC. The data was collected systematically and comparison of demographic and laboratory characteristics were done between both the groups and appropriate significance tests were applied including Student's t test and Chi-square test. Analysis was done using Microsoft excel 2010 and SPSS 21.0 statistical package (SPSS, Chicago, IL).

RESULTS

The mean age in Group A was 56.10 years and mean age in Group B was 55.94 years. In Group A, 50% of the patients were males and 50% were females. In Group B, 56% of the patients were males and 44% were females. The mean duration of diabetes in Group A was significantly higher as compared to Group B (p= 0.001). The mean Hb in Group A was lower as compared to Group B but the difference was not significant statistically. The mean TLC in Group A was significantly higher as compared to Group B (p= 0.001).

Mean blood urea in Group A was 94.24 mg/dl while in Group B was 37.53 mg/dl. The mean urea in Group A was significantly higher as compared to Group B (p= 0.001). Mean creatinine in Group A was 2.70 mg/dl while in Group B was 0.96 mg/dl. The mean creatinine in Group A was significantly higher as compared to Group B (p= 0.001). Mean UACR in Group A was 258.87 mg/g, while in Group B was 19.80 mg/g. The mean UACR in Group A was significantly higher as compared to Group B (p = 0.001).

Mean MPV in Group A was 10.46 fL while in Group B was 8.60 fL. The mean MPV in Group A was significantly higher as compared to Group B (p = 0.001). Mean ALC in Group A was 2.03x10^3/µL, while in Group B was 2.80x 10^3/µL. The mean ALC in Group A was significantly lower as compared to Group B (p = 0.001). Mean MPVLR in Group A was 5.27; while in Group B were 3.08. The mean MPVLR in Group A was significantly higher as compared to Group B (p=0.001). Mean MPVLR in males in Group A was insignificantly lower as compared to females in Group A (p=0.95). Mean MPVLR in males in Group B was insignificantly higher as compared to females in Group B (p=0.83).

Table 1: Comparison Of Urine Albumin To Creatinine Ratio (Uacr) In Group A And Group B

Parameter	Group	Mean± SD	p VALUE
UACR (mg/g)	A	258.87±15.53	0.001
	B	19.80±7.13	

Table 2: Comparison Of Mean Platelet Volume (Mpv, Fl) In Group A And Group B

Group	Mean± SD	p VALUE
A	10.46±1.95	0.001
B	8.60±1.12	

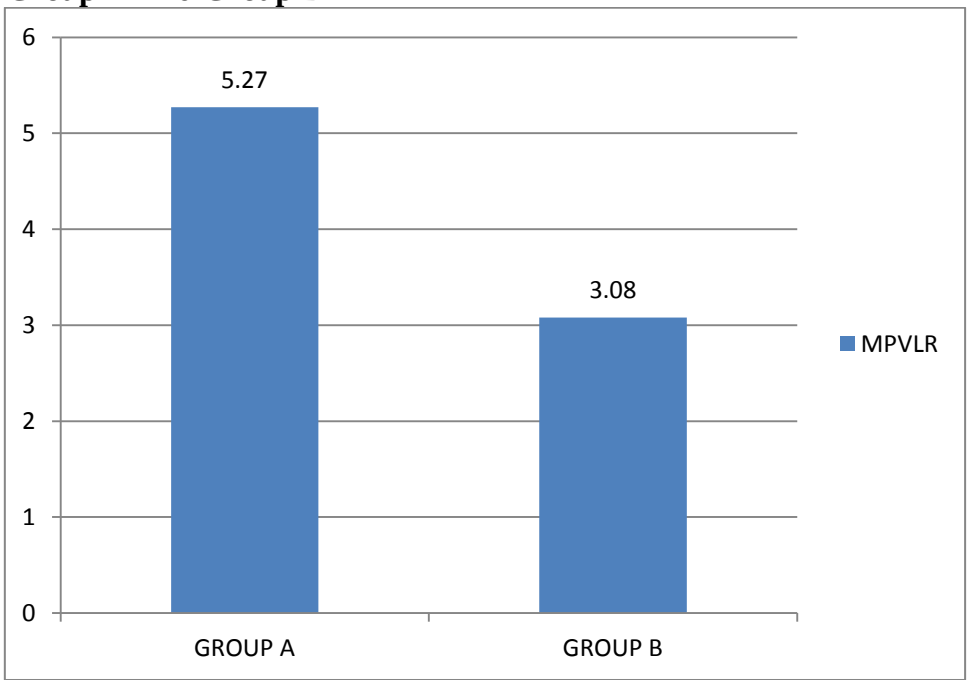
Table 3: Comparison Of Mean Absolute Lymphocyte Count (ALC × 10^3/µL) In Group A And Group B

Group	Mean± SD	p VALUE
A	2.03±0.38	0.001
B	2.80±0.49	

Table 4: Comparison Of Mean Platelet Volume To Lymphocyte Ratio (MPVLR) Between Group A And Group B

Group	MPVLR Mean± SD	p VALUE
A	5.27±0.89	0.001
B	3.08±0.46	

Figure 1: Comparison Of Mean Platelet Volume To Lymphocyte Ratio (MPVLR) Between Group A And Group B



DISCUSSION

Hyperglycaemia is a characteristic feature of diabetes which causes an array of long-term systemic complications.[18] Diabetic nephropathy, a major micro-angiopathic complication of diabetes, is a clinical syndrome characterized by persistent albuminuria.

The pathophysiology leading to the development of DN is the generation and circulation of advanced glycation end products, elaboration of growth factors, and hemodynamic as well as hormonal changes.

Platelet hyperactivity and its increased baseline activation in patients with diabetes are multifactorial. It is associated with biochemical factors such as hyperglycaemia, hyperlipidaemia, insulin resistance, inflammatory and oxidative state.[19,20]

MPV is a marker of platelet function as large platelets are potentially more reactive and contain dense granules, undergo greater in vitro aggregation in response to agonists such as ADP and collagen and release more serotonin and β-thromboglobulin (β-TG). It has been found that hyperglycaemia causes increase in platelet size. In diabetic patients, MPV has been considered as an emerging risk factor for diabetes related microvascular and

macrovascular complications because hyperglycaemia can increase platelet reactivity by inducing non-enzymatic glycation of proteins on the surface of the platelet. [21]Several studies have indicated a reduction in peripheral blood lymphocytes in patients with diabetic renal disease. The dysfunctional immune system has a substantial clinical impact in progression of renal dysfunction in diabetics.

Current study examined the relationship between MPV to lymphocyte ratio in diabetic patients with and without nephropathy. We found that patients with diabetic nephropathy tend to have significant higher MPVLR than the control group. The study by Kocak MZ et al showed consistent findings with our study, where they compared MPVLR of DN subjects to those diabetics without nephropathy.[17]Similar study by Papanas N et al found that mean MPV was significantly higher in patients with microalbuminuria (15.6±1.2 fL) than in patients without microalbuminuria (10.1±1.2 fL).[22] Another study by Buch A. et al found that MPV was significantly increased in diabetic patients with complications as compared to diabetics without complications.[23] In the present study we demonstrate that MPVLR is better predictor of diabetic nephropathy compared to MPV alone.

The study has several limitations, such as the follow up of the patients was not possible to examine the prognostic value of our findings and to examine correlation between high MPVLR and mortality rate.

However, Platelet indices and ALC are an inexpensive marker and a part of routine evaluation. Their assessment can be used for early risk stratification.

CONCLUSION

MPVLR values are higher in patients with DN in comparison to diabetics without nephropathy and this difference is statistically significant. MPVLR is easily calculated and cost effective, hence it can be useful adjunct to standard tests in diagnosis of diabetic nephropathy in patients with diabetes mellitus.

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