International Journal of Science and Research (IJSR)
ISSN (Online): 2319-7064
Index Copernicus Value (2013): 6.14 | Impact Factor (2013): 4.438

Platelet Count and Mean Platelet Volume- Key Hematological Indices in Determination of Various Clinical Perspectives - A Review

Nasreen Sultan[1], S K Sharma[2]

[1]INSPIRE Fellow, Department of Science & Technology, Regional Medical Research Centre, N E Region (ICMR), Post Box # 105, Dibrugarh – 786001, Assam, India

[2]Regional Medical Research Centre, N E Region (ICMR), Post Box # 105, Dibrugarh – 786001, Assam, India

Abstract: ***The key role of Platelet is well known and studied in both physiological and clinical point of view in presumption of numerous aberrances. Moreover, it is the most indispensable and constitutional component of blood whose participation and activity is needed for the normal regulation of human physiology. The building mechanism of haemostatic plug at the site of injury is a quite interesting phenomenon, executed by these small platelets to stop blood shedding. Considering this event of bleeding arrestment, several works have been put forwarded to demonstrate the role of platelets and platelet related parameters. This review focuses on Platelet count and Mean Platelet Volume (MPV), which are found to be the most significant and extraordinary components of blood in assumption of various atypical facets interlinked with these hematological indices. A number of platelet defects have been recognized by many researchers to expose the various atherosclerotic complications, arises due to increased platelet activity. Instead, the size and morphology of platelet, the receptors provided on its surface unlocks many mysteries behind the diseases that can be categorizes as; immune deficiencies, inborn and acquired anomalies. Hence, it provides an obvious identification in correlating both the genotypic and phenotypic constitutions of an individual, associated with variable bleeding abnormalities. Platelet deformities also exists heterogenetically in some other diseased conditions like Beta-thalassemia and sickle cell anemia. These are the most common hemoglobinopathies prevailed in northeast India due to its diversified ethnic horizon. This in turn amplifies the bleeding manifestations and resulting into extreme critical events for survival. Therefore, any qualitative or quantitative etiologies behind platelet defects require deep analysis and investigation to discover the various responsible upshots.***

Keywords: Platelet, Mean Platelet Volume, Hemoglobinopathies, Thalassemia, Atherosclerosis

1. Introduction

Human physiology is crucially driven by the extraordinary role of platelet.[1]These multifunctional anucleated tiny cells are 2 to 4 µm in diameter and 0.5 to 1.0 µm in thickness. In normal healthy conditions, platelet count in peripheral blood ranges from 1.5 lakhs to 4.5 lakhs per microliter.[2,3,4] The precursor cells of platelets known as Megakaryocytes, originated from hematopoietic stem cells and undergo successive commitment steps to produce circulating platelets.[5] The inducer in development of Megakaryocyte is thrombopoietin, also called hematopoietic growth factor which drives the production of platelet and act as a primary growth regulator.[6] The arrestment of blood flow at the site of damage and building of haemostatic plug, incorporates a set of different physiological events, performed by these platelets. The procedure of thrombus formation includes adherence of platelet to the damaged endothelium, expansion and degranulation of containments. Deganulation recruit several other micro particles and procoagulants which enable huge platelet aggregation to stop bleeding. Hence, any malformation or functional break down in platelet conclusively affects hemostasis and maximizes the risk of bleeding. Instead, a pronounced rise in platelet count and activity evokes inappropriate thrombus formation, consequences several atherosclerotic conditions.[5,7] In platelet related aberrances, another essentially prominent hematologic parameter is the size of the platelet. Mean platelet volume (MPV) elucidates the average dimension of the platelets, ranges from 7.0-11.0 fl in apparently healthy individuals.[8] Moreover, the range of MPV may vacillates in a number of adverse circumstances and sometimes passes inherently to the next generation.[9] An elevated value for MPV results into uneventful platelet aggregation, as the surface of platelet is provided with receptors for numerous adhesive molecules.[10] Hence, in determination of various micro and macro vascular complications, this MPV works as an indicator, uncovering wide range of platelet activity.[11]

The etiological perspective behind the quantitative defect in platelet may either be acquired or inheritable. In medical terminology, lowing in platelet count is also designated as thrombocytopenia and intended as one of the common hematologic problem observed in people of all age groups upon infections. A neonatal study revealed that thrombocytopenia is the prime diagnosed condition which includes three observable issues viz. immune deficiencies, congenital and adaptive disorders.[12] Along with low platelet count, the value for MPV also deviates in different level of hemorrhagic incidents in severe to mild thrombocytopenia.[13] It has already stated that larger platelets display more receptors on their surface and hence turned as more functional and reactive.[10] A study revealed that, patients affected with severe thrombocytopenia, suffers recurrent hemorrhagic episodes accompanied with a high MPV value.[14] However, this provision is not so intense for those having mild or lower thrombocytopenic conditions. High value for MPV is also discovered and radically perceived in patients with Diabetes mellitus Type 2 and in patients with paroxysmal atrial fibrillation (PAF).[15,16,17]Thus it acts as marker in suspection of both these two diseased condition.

In numerous clinical assumptions, these two hematological parameters appeared non-linearly, relative to each other. The condition is well assayed in patients with leukemic blast fragmentation where an unusual low MPV has discovered with high platelet count comparative to the patients with erythrocytic fragmentation along with high MPV.[18] Furthermore, a prescribed connection in between inflammatory reactions and platelet parameters are firmly documented in patients with rheumatoid arthritis.[19] Hemoglobinopathies related thrombocytic defect is also a matter of concern.[20] The effective rate of hemoglobinopathies is 5% of the world's population; majority includes Sickle cell anemia and Thalassemia. Although, India reported 2.78% prevalence for β-thalassemia trait (BTT) and the country rich in ethnic diversity residing in different geographical locations.[22,23] Simultaneously, the frequencies for hemoglobinopathies also vary. In both circumstances, a mild thrombocytic deficiency is experienced and the values for platelet count and MPV varies depending upon severity of infection.[21]

In both acute and chronically afflicted provisions, platelet count and MPV are taken as the most striking means for diagnosis, in reference to cardiovascular and cerebral infarction.[24] In Western population, the prime reason for morbidity and mortality is linked with increased platelet number and reactivity which explicit unfortunate thrombus deposition and causes atherosclerotic lesions.[24] This believed to be the foremost reason for strokes and myocardial infarctions.[25]A prominently high value for MPV with low platelet count is also confirmed in a study carried out specifically on patients with unstable angina pectoris and intense myocardial infarction.[26] Moreover, its brutal consequences are also monitored in individuals with acute ischemic cardiovascular events and in ischaemic cerebral infraction.[27]

Atypical platelet count and its activity are also influenced by some transmissible disorders. Inherited platelet disorders (IPDs) are a cluster of some extraordinary heritable defects, characterized by the existence of large volume platelet and thrombocytopenia which further distinguished by inconsistent bleeding symptoms.[28] These defects emphasized on the basis of platelet production, morphology, function and pattern of gene mutations and distributions. Macrothrombocytopenia or large platelet related thrombocytopenia is depicted by presence of huge platelet with terribly low platelet count.[29] This quantitative defect is recognized by mutation in receptors proteins located on platelet membrane. The type of conditions are more specifically prevailed in few somatic recessive gene disorders such as Bernard Soulier syndrome (BSS) and Glanzmann thrombasthenia (GT).[30,31,32] Both the drawbacks are observed with existence of mutated multiple protein complex, GP Ib-IX-V and GP IIb-IIIa respectively with persistence of considerably large size platelet.[33,35] BSS is very rarely occurred disorder, where incidental rate is 1 out of 1 million population.[29] In BSS, the protein complex binds to Von willebrand factor (vwf) and several other interlinking molecules to initiate the mechanism of plug formation.[34] On the other hand, absence or defective synthesis of surface protein in case of GT, prevents the binding of vwf and fibrinogen and ultimately affects the bleeding . The earlier studies reported that, in GT cases, the initial platelet aggregation at damaged endothelium is normal, but in later phases, the aggregation impeded due to absence or reduced synthesis of surface receptors. Another very renowned inherited macrothrombocytopanic disorder is Velocardiofacial syndrome (VS), which sometimes found heterogeneously in patients who are BSS carrier. The syndrome displays a decreased aggregation of platelet with ristocetin. It was genetically proved that microdeletion in chromosome number 22 at position q11.2, causes wrong production of GPIbβ receptor. Some other clinically manifested physiological abnormalities like heart diseases, craniofacial abnormalities, defects of palate and underdeveloped thymus together with a number of immune deficiencies observed in patients with VS.[36,37] Sebastian syndrome also lies in the same category of hereditarily transmitted thrombocytopenia. In general, there is no any clinical symptoms observed but patients having giant platelet in their blood smear when examined under microscope.[28]Macrothrombocytopenia is also associated with progressive onset of high-frequency sensorineural hearing loss, presenile cataract, and nephritis in case of MYH9-related disorders (MYH9RD).[38,39] Besides, Harris platelet syndrome (HPS) is found to be the most common inherited giant platelet disorder in Indian subcontinents, although relatively rare in occurrence. The analysis revealed that, this macrothrombocytopenia is more prevailed amongst the northeastern population of India due to the increased diversity of hemoglobinopathies and coexists heterogenetically.[40,41]

Some of the inherent disorder begins with faulty manufacture of Megakaryocytes which eventually affects platelet production. This rare stipulation is well understood and demonstrated in case of Congenital amegakaryocytic thrombocytopenia (CAMT) accompanied with severe hemorrhagic conditions observed in neonates and sometimes the worse consequences leads to death just after birth.[42,43] The volume and morphology of thrombocytes or platelets are normal in CAMT patients but they exhibit a considerably low megakaryocyte and platelet count that ultimately progresses to thrombocytopenia and aplastic anaemia. It is also reported that patients with CAMT have high risk for myelodysplastic syndrome and leukemia and untreated circumstances may cause life threatening events.[44]The biochemical and molecular analysis discloses a series of transcription factors associated in the developmental process of Megakaryocytes viz. GATA-1, FLI-1 and FOG-1.[45,46] Hence, mutation in the said genes will either produce false protein or absence of the protein and ultimately down regulate and arrest the developmental process. Bone defects are also seen associated with Amegakaryocytic thrombocytopenia. A few congenital thrombocytopenic disorders like- Amegakaryocytic thrombocytopenia with radioulnar synostosis (ATRUS) and Thrombocytopenia with absent radii syndrome (TAR), are considered as very exceptional bone abnormality.[47] In both criteria, patients are found with fused radius and ulna bone and absence of a radius in each forearm respectively.[47] Recent researches exposed that the reason for bone abnormalities in ATRUS was mutation in HOXA11 gene at transcription level.[48] However, the exact genetic makeup of TAR cases is yet to investigate but it has been observed that patients with TAR,

exhibit microdeletion on chromosome 1q21.1 which anticipates as the reason of occurrence of this syndrome.[49]

Inherited thrombocytopenia is not only confined to the mutations occurs in somatic cell line but also arises due to germ line gene mutations. Examples of some X-linked inherited thrombocytopenic disorders that occur due to gene mutation in X chromosome are Wiskott-Aldrich syndrome (WASp gene) and GATA-1 gene related thrombocytopenia. Likewise thrombopoeitin, GATA-1 genes are also engaged in developmental processes of erythroid and megakaryocytic cells.[50] Therefore, mutation in above said genes causes thrombocytopenia together with large and small platelets, dysmegakaryopoiesis and α-granule deficiency. In certain rare cases, β-thalassemia and GATA-1 gene related thrombocytopenia coexists together and discovered with persistence of Fetal hemoglobin (HbF) in their blood.[51,52] WAS indulged with immunodeficiency syndrome causes by mutation in WAS protein gene. Its activity influences the normal functioning of actin filament characterized primarily for controlling various cellular and organelles dimensions.[53] This gene houses on X chromosome at position q11.22-23 and an altered gene pattern manifests inconsistent blood shedding associated with thrombocytopenia and small size platelet.[54]

Apart from all thrombocytic defects, another cellular defect is also documented in thrombocytopenia and categorized as granular deficiencies. The granular part of thrombocytes, preferably the α-granules are constituted of several micro particles such as P-selectin, fibrinogen, vwf, Platelet derived growth factor, fibronectin and thrombospodin.[55] All these components together diffused with the plasma membrane of platelet to increase its surface area and enable its spreading 2-4 fold more when needed. Examples of some granular defects are Quebec platelet disorder, Gray platelet and Paris-Trousseau syndrome and several more and all of them are assigned for contributing and sharing the common property for mild to moderate bleeding incidents with thrombocytopenia and large agranular platelets.[56,57]

2. Conclusion

Platelet count and Mean Platelet volume (MPV) are the utmost remarkable hematological indices, well noticed in a series of clinical evaluations that proportionately influences the bleeding physiology of human body. They also provide knowledge related to both acquired and congenital defects and the mutation patterns that co-associate various other diseases and sometimes coexist heterogenetically in clinical manifestations. Hence, in assessment of various symptomatic and asymptomatic features, platelet indices serve as an extraordinary mean, as well as marker in understanding and diagnosing the abnormality. Even so, this area of hematology is still needed deep researches in various prospects to demonstrate the role of every constituents of platelet responsible for any cause.

Reference

[1] Coller BS. Historical perspective and future directions in platelet research. J Thromb Haemost. 2011;1:374-95.
[2] Gazzaniga V, Ottini L. The discovery of platelets and their function. Vesalius. 2001; 7:22-26.
[3] Martina ED. Determinants of platelet count in humans. *Haematol*. 2011; 9:10-13.
[4] Erkurt MA, et al. Thrombocytopenia in Adults: Review Article. J Hematol. 2012; 1:44-53.
[5] Deutsch VR and Tomer A. Megakaryocyte development and platelet production. Br J Haematol. 2006; 134:453–466.
[6] Kaushansky K. Thrombopoietin. N Engl J Med. 1998; 339:746-754.
[7] Brewer DB. Max Schultze (1865), G. Bizzozero (1882) and the discovery of the platelet. Br J Haematol. 2006; 133:251–258.
[8] Koc S, Eyibilen A and Erdogan AS. Mean Platelet Volume as an Inflammatory Marker in Chronic Sinusitis. Eur J Gen Med. 2011; 8:314-317.
[9] Balduini CL, et al. Inherited thrombocytopenias: a proposed diagnostic algorithm from the Italian Group di Studio delle Piastrine. J Haematol. 2003; 88:582-592.
[10] Park Y, Schoene N and Harris W. Mean platelet volume as an indicator of platelet activation: methodological issues. Platelets. 2002; 13:301-306.
[11] Kodiatte TA, et al. Mean Platelet Volume in Type 2 Diabetes Mellitus. J Lab Physicians. 2012; 4:5–9.
[12] Fernandez KS, and Alarcon PD. Neonatal Thrombocytopenia. Neo. 2013; 14:74-82
[13] Martin JF, Trowbridge EA and Salmon G. The biological significance of platelet volume: Its relationship to bleeding time, platelet thromboxane B_2 production and megakaryocyte nuclear DNA concentration. Thromb Res. 1983; 32:443–460.
[14] Eldor A, Avitzour M, Or R, Hanna R, and Penchas S. Prediction of haemorrhagic diathesis in thrombocytopenia by mean platelet volume. Br Med J. 1982; 285:397–400.
[15] Vizioli L, Muscari S and Muscari A. The relationship of mean platelet volume with the risk and prognosis of cardiovascular diseases. Int J Clin Pract. 2009; 63:1509-1515.
[16] Hekimsoy Z, Payzinb B, Ornek T and Kandogan G. Mean platelet volume in Type 2 diabetic patients. J Diabetes Complicat. 2004; 18:173-176.
[17] Yucel C, et al. Mean platelet volume is elevated during paroxysmal atrial fibrillation: a marker of increased platelet activation? Blood Coag Fibrin. 2008; 19:411–414.
[18] Bessman JD, Williams LJ and Jr Gilmer PR . Mean platelet volume: The inverse relation of platelet size and count in normal subjects, and an artifact of other particles. Am J Clin Pathol.1981; 76:289-293.
[19] Yazici S, et al. The platelet indices in patients with rheumatoid arthritis: Mean platelet volume reflects disease activity. Platelets. 2010; 21:122-125.
[20] Patki V, et al. Study of Sickle cell Disease Phenotypes and Sickle Cell Gene Frequency in Some Tribals belonging to Tipeshwar Forest Region, Yavatmal District, Maharashtra, India. Int. Res. J. Biological Sci. 2013; 2:57-59.
[21] Horan JT, Liesveld JL, Fenton P, Blumberg N and Walters MC. Hematopoietic stem cell transplantation for multiply transfused patients with sickle cell disease and thalassemia after low-dose total body irradiation,

fludarabine, and rabbit anti-thymocyte globulin. Bone Marrow Transpl. 2005; 35:171–177.
[22] Hamamy H and Alwan A. Hereditary disorders in the Eastern Mediterranean Region. Bull Worl Health Org. 1994; 72:145-154.
[23] Mohanty D, et al. Prevalence of β-thalassemia and other haemoglobinopathies in six cities in India: a multicentre study. J Commun Genet. 2013; 4:33-42.
[24] Ruggeri ZM. Platelets in atherothrombosis. Nat Med. 2002; 8:1227-1234.
[25] Mercan R, Demir C, Dilek I, Asker M and Atmaca M. Mean Platelet Volume In Acute Coronary Syndrome. Van Tıp Dergisi. 2010; 17:89-95.
[26] Greisenegger S, et al. Is Elevated Mean Platelet Volume Associated With a Worse Outcome in Patients With Acute Ischemic Cerebrovascular Events? Stroke. 2004; 35: 1688-1691.
[27] D'erasmo E, et al. Platelet count, mean platelet volume and their relation to prognosis in cerebral infarction. J Intern Med. 1990; 227:11–14.
[28] Mhawech P and Saleem. Inherited Giant Platelet Disorders. Am J Clin Pathol. 2000; 113:176-190.
[29] Diz-Kucukkaya R. Inherited platelet disorders including Glanzmann thrombosthenia and Bernard-Soulier syndrome. Hematol. 2013; 268-275.
[30] Berndt MC and Andrews RK. Bernard-Soulier syndrome. Haematologica. 2011; 96:355-359.
[31] Andrews RK and Berndt MC. Bernard–Soulier Syndrome: An Update. Semin Thromb Hemost. 2013; 39:656-662.
[32] Lo´pez JA, Andrews RK, Afshar-Kharghan V, and Berndt MC. Bernard-Soulier Syndrome. Blood. 1998; 91:4397-4418.
[33] Bennett JS, Berger BW and Billings PC. The structure and function of platelet integrins. J Thromb Haemost. 2009; 7:200-205.
[34] Coller BS and Shattil SJ. The GPIIb/IIIa (integrin αIIbβ3) odyssey: a technology-driven saga of a receptor with twists, turns, and evens a bend. Blood. 2008; 112:3011-3025.
[35] George JN, Caen JP and Nurden AT. Glanzmann's thrombasthenia: the spectrum of clinical disease. Blood. 1990; 75:1383-1395.
[36] Liang HP, et al. Heterozygous loss of platelet glycoprotein (GP) Ib-V-IX variably affects platelet function in velocardiofacial syndrome (VCFS) patients. Thromb Haemost. 2007; 98:1298-308.
[37] Kobrynski LJ and Sullivan KE. Velocardiofacial syndrome, DiGeorge syndrome: the chromosome 22q11.2 deletion syndromes. Lancet. 2007; 370:1443-1452.
[38] Althaus K and Greinacher A. MYH9-Related Platelet Disorders. Semin Thromb Hemost. 2009; 35:189-203.
[39] Chen Z and Shivdasani RA. Regulation of platelet biogenesis: insights from the May–Hegglin anomaly and other MYH9-related disorders. J Thromb Haemost. 2009; 7:272–276.
[40] Lorenzo FR. Inherited Giant Platelet Disorder, Kashmiri Thrombocytopenia, a Common Syndrome Found in Srinagar, India. Blood. 2014; 124.
[41] Naina HVK and Harris S. Platelet and red blood cell indices in Harris platelet syndrome. Platelets. 2010; 21:303-306.
[42] Geddis AE. Inherited Thrombocytopenia: Congenital Amegakaryocytic Thrombocytopenia and Thrombocytopenia With Absent Radii. Elsevier. 2006; 43:196-203.
[43] Ballmaier M and Germeshausen M. Advances in the understanding of congenital amegakaryocytic thrombocytopenia. Br J Haematol. 2009; 146:3-16.
[44] King S, Germeshausen M, Strauss G, Welte K and Ballmaier M. Congenital amegakaryocytic thrombocytopenia: a retrospective clinical analysis of 20 patients. Br J Haematol. 2005; 131:636-644.
[45] de Graaf CA and Metcalf D. Thrombopoietin and hematopoietic stem cells. Cell Cycle. 2011; 10: 1582-1589.
[46] Wang X, et al. Control of megakaryocyte-specific gene expression by GATA-1 and FOG-1: role of Ets transcription factors. EMBO J . 2002; 21:5225–5234.
[47] Fiedler J, et al. Two Patterns Of Thrombopoietin Signaling Suggest No Coupling Between Platelet Production And Thrombopoietin Reactivity In Thrombocytopenia-Absent Radii Syndrome. Haematologica. 2012; 97:73-81.
[48] Horvat-Switzer RD, and Thompson AA. HOXA11 Mutation in Amegakaryocytic Thrombocytopenia with Radio-Ulnar Synostosis Syndrome Inhibits Megakaryocytic Differentiation In Vitro. Blood. 2005; 106:1751.
[49] Albers CA, Newbury-Ecob R, Ouwehand WH and Ghevaert C. New insights into the genetic basis of TAR (thrombocytopeniaabsent radii) syndrome. Curr Opin Genet Dev. 2013; 23:316–323.
[50] Mehaffey MG, Newton AL, Gandhi MJ, Crossley M, and Drachman JG. X-linked thrombocytopenia caused by a novel mutation of*GATA-1*. Blood. 2001; 98:2681-2688.
[51] Millikan PD, Balamohan SM, Raskind WH and Kacena MA. Inherited Thrombocytopenia Due to GATA-1 Mutations. Semin Thromb Hemost. 2011; 37:682-689.
[52] Phillips JD, Steensma DP, Pulsipher MA, Spangrude GJ anKushner JP. Congenital erythropoietic porphyria due to a mutation in GATA1: the first trans-acting mutation causative for a human porphyria. Blood. 2007; 109:2618-2621.
[53] Massaad MJ, Ramesh N and Geha RS. Wiskott-Aldrich syndrome: a comprehensive review. Ann N Y Acad Sci. 2013; 1285:26–43.
[54] Sharathkumar AA and Shapiro A. Platelet function disorders. Haemophilia. 1999; 19:1-22.
[55] Blair P and Flaumenhaft R. Platelet α–granules: Basic biology and clinical correlates. Blood Rev. 2009; 23:177–189.
[56] Bolton-Maggs PHB, et al. A review of inherited platelet disorders with guidelines for their management on behalf of the UKHCDO. Br J Haematol. 2006; 135:603-633.
[57] Sandrock K and Zieger B. Current Strategies in Diagnosis of Inherited Storage Pool Defects. Transfus Med Hemother. 2010; 37:248–258.