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Determination of a Mean andReference Range for Platelet volume indices inKashmiri Population (A Study at Tertiary Care Hospital)

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Abstract: ***Background;-*** *Platelet volume indices (PVI), andreference intervals (RIs) are associated in clinical practice with hematological and non-hematological diseases, i.e., cardiovascular and cerebrovascular diseases.The activity of the platelet effected is reflected in PVI i.e. platelet counts, MPV (mean platelet volume) and P-LCR (platelet large cell ratio) in these conditions, hence PVI provide a simple and easy method of indirect assessment of platelet function routinely generated by automated cell counters, both represents changes in their level of stimulation or rate of destruction. It isstill not clearly fully resolved yet.Several studies showed highly variable references due to heritable, [1] genetic,gender,altitudefactors both in healthy and diseasedindividuals [2-3].Similarly, ethnicity- related differences had been reported in Western studies i.e.USA, Italy [3] and various African countries [4], in addition other risk factors like hypertension, Diabetes mellitus, renal failure, atrial fibrillation, elderly people, obese, and smokers had also been associated.*

Aims*;-Asthe methodology has changed from manual to the modern automated analyzer, this study was conducted to document the significance of platelet large cell ratio (P-LCR), MPV (mean platelet volume) and their relation to total platelet count as very less literature is available on the subject.*

Method and Material*; -A study todetermine the reference range of PLCR, MPV (mean platelet volume) was conduct in government medical college and associated tertiary care Hospital. The studywas conducted on randomized 2084subjectsof original Kashmiri population aged 10-75yrs.Theblood collected was processed inan automated analyzer.*

Conclusion;- ***P****latelet counts variation does not reveal the underlying cause, as physiological, demographic,genetic,ethical, and pathological factors,with the emergence of new factors that had surfaced recently their correlation will preventinhabitants in different areas, who are at risk of receiving wrong diagnosisand treatment.*

Keywords*: Mean platelet volume; Platelets; Reference range, Thrombocytopenia*

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I. Introduction

After Max Schultz and Giulio Bizzozero identified platelets at the end of the 19th century[5], the proposed reference total count ranged from 130–350 to 500–900×10^9/L of whole blood.[6]The development of the Coulter Principle in 1953[7], revolutionized platelet counting and resulted in the development of the modern electronic instruments currently in use,as counts vary according to age, sex ethnicity and demographically, hence it is, questionable whether a single reference interval for all people is still valid or whether new normal ranges taking into account these variables have to be used in clinical practice. At the developmental stage of precursor cells (megakaryocytes) the activity of cytokines (especially interleukin 3 and interleukin 6) plays a significant role in the regulation of platelet pool and leads to the production of larger platelets that are more reactive [6–8].P-LCR, conveys the ratio of newly produced platelets with the largest volume, due to TNFα, vascular growth factors (VEGF), and synthesis of platelet activation factors. Platelet-large cell ratio (P-LCR) is percentage of platelet that exceed the normal value of mean platelet volume (MPV) of 12 fl (the norm for P-LCR is < 30% in the total platelet count) while mean platelet volume (MPV), the most commonly used index of platelet size, is a surrogate marker of platelet activation, itreflects the average size of platelets (7.5 fL to 10.5 fL). Increased MPV value is associated, among others, with hypertension [9], diabetes mellitus [10–11], renal

failure [12] and atrial fibrillation [13]. Higher MPV values were also observed in the elderly [14], obese patients [15], and smokers [4,16–17].P-LCR was inversely related to platelet count and directly related to PDW and MPV.A high number of large platelets (high MPV) in a person with a low platelet count suggests the bone marrow is producing platelets and releasing them into circulation rapidly,larger platelets are usually relatively young and contain more intracellular granules, greaterthrombogenic potential [18],an important link between inflammation and thrombotic complications in atherosclerosis [19]and coronary artery disease (CAD), septic disorders. In the clinical laboratory, reference interval (RI) arethe most widely used medical decision-making tool that separates healthy from diseased individuals. Clinicians compare the values of laboratory reports with the given RIs to make a decision regarding the health status of a given individual in clinical diagnosis, treatment, and therapeutic monitoring.[20–25].

II. Aims and objectives;-

1. Determination of the mean values of P-LCR ,MPV, and total platelet counts
2. Determination of a reference range ofP-LCR ,MPV,and total platelet counts
3. To evaluate percentage of different platelet morphology
4. To evaluate relation between platelet counts and P-LCR, MPV.

III. Method and Material

A study of2084 blood samples from subjectsof Kashmiri origin who attend OPD or were admitted indoor,in tertiary care Hospital ofGovernment Medical College Baramulla.

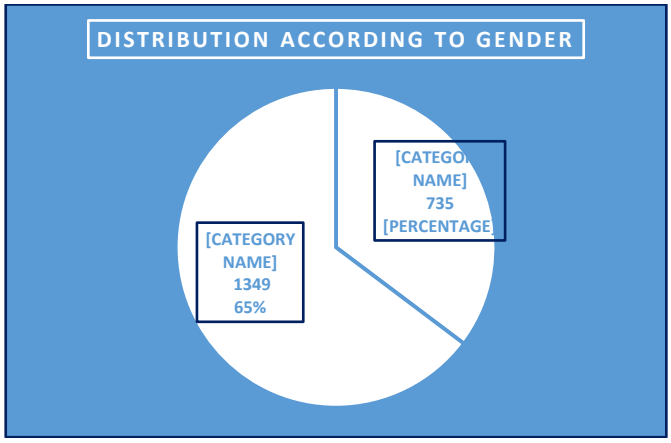
Exclusion criteria: included subjects receiving drugs like aspirin, anticoagulants, recent platelet transfusion, and malignancy.

Collection of Blood samples;- 5ml of a venous blood was obtained through venous puncture in an EDTA coated (0.5M, pH8.0) sterilized plastic vials. The vials were properly labeled according to a specially designed coding system, to prevent possible mixing of the sample vials and for easy retrieval. All blood samples were analyzed within 2hours after phlebotomy as P-LCR and MPV increases if the sample is collected in EDTA is left for more than 2-hours.Informed consent was taken. Total complete blood count and differential counts were done on IRIS-I count 5 Hematology Analyzer an advanced instrument using the latest principle ofimpedances improved by hydrodynamic focusing. (i.e.centered stream principle will 'jacket' the stream of particles by a sheath flow so that the particles are passing centrally and one after the other through the measuring capillary) excluding interference factors such as double passages by coincidence, recirculation, etc. Hence cells were counted with greater precision, parameters included P-LCR, MPV, PLT count, and WBC. Calculation by the software usedthe formula:P-LCR = P-LCC/PLT. (PLT = Total Platelets Count -LCC = platelets larger than 12 fl and smaller than 30fl= femtoliter)

IV. Results

Platelets play a key role in both homeostasis thrombosisand tissue healing.It is important to measure platelets accurately for identifying patients with either platelet dysfunction or monitoring modern antiplatelet therapy. Microsoft office 2016 was used for statistical analysis. Descriptive statistics like mean and percentage were used for data interpretation.

GRAPH NO. 1



In the present study,2084samples of blood were collected from rural Kashmiriorigin population of Baramulla district. The difference insample of gender is shown in graph no.1.

1. The mean value of platelet count for both the sexes was estimated by automated analyzer was found to be 193.1/10^3/µl (RANGE:16.0-652 x 10^3/µl,STDEV± 82.2) Similarly, the mean value of platelet count estimated by automated analyzer in males and females was found to be192.3x10^3/µl (RANGE: 29- 608 x10^3/µl) STDEV (±87.3)and193.9x10^3/µl (RANGE: (16-652x10^3/µl)STDEV (±81.07)respectively, and was to be found statistically insignificant 0.8796 (p>0.05).

Table No. 1 Mean Values in Our Study

S.No.	Name	♂	♀	MEANFOR BOTH
1	WBC	8.58 x 10^3/µl	8.57 x 10^3/µl	8.575 x 10^3/µl
2	TOTAL PL COUNT	192.3 x 10^3/µl	193.9 x 10^3/µl	193.1 x 10^3/µl
3	MVP	5.75 fl	5.99 fl	5.87 fl
4	P-LCR	32.83%	34.76%	33.79%

2.The mean platelet volume (MPV) for both the sexes was estimated by automated analyzer was found to be 5.87 fl(RANGE: 2.9-165fl) similarly, the mean platelet volume estimated by automated analyzer in males and females was found to be 5.799 fl(RANGE: 3-16.5fl, STDEV (±8) and 5.996 fl(Range:2.9-11.9flSTDEV (±1.46)) respectively, and was to be found statisticallysignificant 0.0152 (p<0.05).

Table No. 2 Range and STDEV of Values in Our Study

S.NO	NAME	♂	♀
1	Total subjects	735	1349
2	WBC	(1.4- 45.6 10^3/µl) (±4.42)	(1.2- 44.6 10^3/µl) (±3.93)
3	Total PL count	(29- 608 10^3/µl) (±87.3)	(16- 652 10^3/µl) (±81.07)
4	MVP	(3- 16.5 fl) (±1.51)	(2.9- 11.9 fl) (±1.46)
5	P-LCR	(4.53-53.3 %) (±8.2)	(2.8- 59.4 %) (±3.93)

3.The platelet large cell ratio (P-LCR) for boththe sexes was estimated by automated analyzer was found to be 33.63% (RANGE: 2.8- 59.4% STDEV ±8.26).Similarly, the platelet large cell ratio (P-LCR) estimated by automated analyzer in males andfemales was found to be 32.832 (RANGE: 4.35-53.3%STDEV (±8.258)

Table No. 3 Comparison with International and National Studies

S NO.	Author	Auto-analyzer	MPV fL	P-LCR %
1	Pekelharing[26],	SYSMEX XE - 2100	9.1-12.1	29.6-35.8
2	J. Botma[27],	SYSMEX XE - 2000	8.8-12.	34-43
3	Kaito[28],	SMEX XE - 2001	8.7-13.1	31-37
4	Karnataka, India [29],	SYSMEX XE – 2000i	9.3-13.8	30.4-36.3
5	Turkey.[23],		8.9 ± 1.4	
6	Other study in Kashmir done for counts only[31],		♂	♀
			125.64 x 10^3/µl	152.93 x 10^3/µl
7	Present study	IRIS-I count 5	5.87	33.79

and34.76% (RANGE: 2.8-59.4% STDEV (±3.935))respectively, andwas foundstatisticallysignificant 0.00112 (p<0.05).
4. Platelet large cell ratio (PLCR), mean platelet volumeshowed a significant role in the discrimination of having inverse relationship with platelet count.

V. Discussion

Evidence-based laboratory medicine is an essential part of modern laboratory medicinepractices [30]. It is estimated that clinical laboratory data influence 70% of clinical decisions; Platelets are the smallest blood corpuscles with a diameter of 1–4µm and a cell volume of 2 to 20fL, with younger platelets being largerthan the older ones. They have no cell nucleus but residual mRNAoriginating from the megakaryocytes. Size reflects activity; therefore platelet volume indices especially MPV and P-LCR are a simple and easy method of an indirect assessment of platelet stimulation. People who live at low altitudes (below sea level) may have higher than average platelet counts, while those who live at high altitudes mayhave a high MPV, disease. Smoking, high blood pressure, and high glucoselevels (without a diagnosis of diabetes) have all been associated with a high MPV in men, while menstruation and oral contraceptives are associated with high MPV in women. Strenuous exercise has also been associated with an increase in platelet count if it is severe enough to cause tissue damage. Platelet-large cell ratio (P-LCR) is defined as the percentage of platelets that exceed the normal

value of platelet volume of 12fL Thus, platelet volume indices in association with other predictive parameters may be utilized as important elements of various risk scores to assess outcome in coronary heart disease. Also Rechciński et al. have demonstrated values remain related to greater long-term mortality in patients with STEMI undergoing percutaneous coronary interventioncomplexity according to the Gensini and SYNTAX scores. A number of observations in different populations unequivocally demonstrated that age, sex and genetic background modulate platelet count in healthy people. The effect of aging is much higher than those of sex, and ethnicity. A correlation between platelet count and age was also found by a larger study that evaluated 12,142 adult inhabitants of the United States and found statistically significant differences between young and old individuals [32]. Finally, a recent study put together all data of subjects in Italy, enrolled in the three different population-based studies referenced age-related changes were actually very large: platelet count in old age was reduced by 35% in men and by 25% in women with respect to early infancy. [33], There is no proven explanation for these age-related changes, during infancy reflects the decline of thrombopoietin levels occurring from birth to adulthood. Similarly, an association had been established between MPV and some nutritional deficiencies such as vitamin D and vitamin B_{12}. In individuals with MPV $\geq$ 11.7 fL long-term mortality was nearly three times higher in comparison with patients with MPV < 11.7 fL. In cases of P-LCR values equal or over 38.1% mortality was also significantly higher compared to individuals with lower values. A low platelet count along with low MPV (older) points toward bone marrow disorders that slow down or decrease the production of platelets, such as aplastic anemia. A highplatelet count along with low MPV often signifies an infection, inflammation, or cancer. Some studies suggest that should be considered along with your overall health status and your other lab result.Platelet indexes were studied in 779 patients with normal platelet counts, 74 patients with high platelet counts and 41 cases with low platelet counts. P-LCR was significantly decreased in patients with thrombocytosis than in normal while it was increased in thrombocytopenia it can be precisely used to differentiate hyperdestructive type (ITP) from hypoproliferative type (acute leukemia's, aplastic anemia In patients with high counts, P-LCR was significantly decreased in reactive thrombocytosis than neoplastic thrombocytosis. P-LCR was increased in destructive thrombocytopenia than those with hypoproliferative thrombocytopenia though it was not statistically significant. P-LCR was inversely related to platelet count and directly related to PDW and MPV. Even so, this area of hematology still needed deep researches in various prospects to demonstrate the role of every constituent of platelet responsible for any cause. During our study females were more in number than males and the mean value of platelet volume indices including platelet counts was found same by automated platelet counting analysis.

The result demonstrated slight statistical insignificant variation in platelet count between the genders in the same population through an automated analyzer. Platelet large cell ratio (PLCR), mean platelet volume showed a significant role in the discrimination of having inverse relationship with platelet count as they are increased in hyper-destructive type and shows a linear relationship in hypoproliferative type. However,the variation in P-LCR was statistically significant, which can be speculated due to the reduction in body iron in females, which occurs in menstruating women and persists in the elderly [34]stimulates platelet production, [35], however the hormonal differences between men and women after puberty could also play a role. In particular, the observation that estrogens favor platelet formation in mouse supports our hypothesis,[36], although no data in humans are available.The difference in the platelet counts from previous Kashmiri studywasonly the platelet counts were done results were 126.40 by analyzer while manually139.06 that were found to be statistically significant ($p<0.0001$)[31]. Higher platelet count by the manual method may be because of large platelet size which analyzers are not able to count correctly, in our study with the latest hematological analyzer which usesthe latest impedance measurement principles making a difference.

VI. Conclusion

In conclusion, there is little doubt that a new reference range taking into account these variables would be desirable to identify more accurately, subjects with platelet disorders. Indeed, such a tool has been recently developed for the USA, Italian, some of Africans countries[37], and are similar to those observed in other Caucasian populations suggests that their use could be verified for other populations with ethnic, genetic, demographic, diseases set up.

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