Determination of a Mean and Reference Range for Platelet volume indices in Kashmiri Population (A Study at Tertiary Care Hospital)

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Abstract: Background:- Platelet volume indices (PVI), and reference 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 is still not clearly resolved yet. Several studies showed highly variable references due to heritable, genetic, gender, altitude factors both in healthy and diseased individuals. Similarly, ethnicity-related differences had been reported in Western studies i.e. USA, Italy and various African countries, in addition other risk factors like hypertension, Diabetes mellitus, renal failure, atrial fibrillation, elderly people, obese, and smokers had also been associated.

Aims: - As the 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 to determine the reference range of P-LCR, MPV (mean platelet volume) was conducted in government medical college and associated tertiary care Hospital. The study was conducted on 2084 subjects of original Kashmiri population aged 10-75yrs. The blood collected was processed in an automated analyzer.

Conclusion: - Platelet counts variation does not reveal the underlying cause, as physiological, demographic, genetic, ethnic, and pathological factors, with the emergence of new factors that had surfaced recently their correlation will prevent inhabitants in different areas, who are at risk of receiving wrong diagnosis and treatment.

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

Date of Submission: 26-04-2019 Date of acceptance: 11-05-2019

I. Introduction

After Max Schultz and Giulio Bizzozero identified platelets at the end of the 19th century, the proposed reference total count ranged from 130–350 to 500–900×10^9/L of whole blood. The development of the Coulter Principle in 1953, 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. 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, affects the average size of platelets (7.5 fl to 10.5 fl). Increased MPV value is associated, among others, with hypertension, diabetes mellitus, renal function.

DOI: 10.9790/0853-1805033237
Committee. A study of 2084 blood samples from subjects of Kashmiri origin who attend OPD or were admitted to the tertiary care Hospital of Government Medical College Baramulla. Exclusion criteria: included subjects receiving drugs like aspirin, anticoagulants, recent platelet transfusion, and malignancy.

Collection of Blood samples:- 5 ml 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 2 hours 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-1 count 5 Hematology Analyzer an advanced instrument using the latest principle of impedances 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 use the 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 thrombosis and 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.

In the present study, 2084 samples of blood were collected from rural Kashmiri origin population of Baramulla district. The difference in sample 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 193.1/10^9/µl (RANGE:16.0-652 x 10^9/µl,STDEV: ±82.2) Similarly, the mean value of platelet count estimated by automated analyzer in males and females was found to be192.3/10^9/µl (RANGE: 29-608 x10^9/µl) STDEV (±87.3)and193.9/10^9/µl (RANGE: 16-652x10^9/µl)STDEV (±81.07)respectively, and was to be found statistically insignificant 0.8796 (p<0.05).

<table>
<thead>
<tr>
<th>S.No.</th>
<th>Name</th>
<th>Ø</th>
<th>Ø</th>
<th>MEAN FOR BOTH</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>WBC</td>
<td>8.58 x 10^9/µl</td>
<td>8.57 x 10^9/µl</td>
<td>8.575 x 10^9/µl</td>
</tr>
<tr>
<td>2</td>
<td>TOTAL PL COUNT</td>
<td>192.3 x 10^9/µl</td>
<td>193.9 x 10^9/µl</td>
<td>193.1 x 10^9/µl</td>
</tr>
<tr>
<td>3</td>
<td>MVP</td>
<td>5.75 fl</td>
<td>5.99 fl</td>
<td>5.87 fl</td>
</tr>
<tr>
<td>4</td>
<td>P-LCR</td>
<td>32.83%</td>
<td>34.76%</td>
<td>33.79%</td>
</tr>
</tbody>
</table>

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:2.9-11.9fl)STDEV (±1.46)) respectively, and was to be found statistically significant 0.0152 (p<0.05).

<table>
<thead>
<tr>
<th>S.NO</th>
<th>NAME</th>
<th>Ø</th>
<th>Ø</th>
<th>MEAN FOR BOTH</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Total subjects</td>
<td>735</td>
<td>1349</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>WBC</td>
<td>(1.4-45.6 x 10^9/µl) (±4.42)</td>
<td>(1.2-44.6 x 10^9/µl) (±3.93)</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Total PL count</td>
<td>(29-608 x10^9/µl) (±87.3)</td>
<td>(16-652 x10^9/µl) (±81.07)</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>MVP</td>
<td>(3-16.5 fl) (±1.51)</td>
<td>(2.9-11.9 fl) (±1.46)</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>P-LCR</td>
<td>(4.53-55.3 %) (±8.2)</td>
<td>(2.8-59.4 %) (±3.93)</td>
<td></td>
</tr>
</tbody>
</table>

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 ±3.26).Similarly, the platelet large cell ratio (P-LCR) estimated by automated analyzer in males and females was found to be 32.832 (RANGE: 4.35-53.3%STDEV (±8.25))

<table>
<thead>
<tr>
<th>S.NO</th>
<th>Author</th>
<th>Auto-analyzer</th>
<th>MPV fl</th>
<th>P-LCR %</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Pekelharum[28]</td>
<td>SYMEX XE - 2100</td>
<td>9.1-12.1</td>
<td>29.6-35.8</td>
</tr>
<tr>
<td>2</td>
<td>J. Botma[29]</td>
<td>SYMEX XE - 2000</td>
<td>8.8-12.</td>
<td>34-43</td>
</tr>
<tr>
<td>4</td>
<td>Karnataka, India [29]</td>
<td>SYMEX XE ~ 2000</td>
<td>9.3-13.8</td>
<td>30.4-36.3</td>
</tr>
<tr>
<td>5</td>
<td>Turkey[30]</td>
<td></td>
<td>8.9 ± 1.4</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>Other study in Kashmir done for counts only[29]</td>
<td></td>
<td>125.64 x 10^9/µl</td>
<td>608 x 10^9/µl</td>
</tr>
<tr>
<td>7</td>
<td>Present study IRIS-I count 5</td>
<td></td>
<td>5.87</td>
<td>33.79</td>
</tr>
</tbody>
</table>

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 volume showed 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. 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 201L, with younger platelets being larger than 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 may have 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 Rechcitski 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. 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. 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 \text{ fL} long-term mortality was nearly three times higher in comparison with patients with MPV < 11.7 \text{ 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 \cite{34}, stimulates platelet production, 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, although no data in humans are available. The difference in the platelet counts from previous Kashmiri study was only the platelet counts were done results were 126.40 by analyzer while manually 139.06 that were found to be statistically significant (p<0.0001)\cite{35}. 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 uses the 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 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.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

DOI: 10.9790/0853-1805032337 www.iosrjournals.org
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