RESEARCH ARTICLE

Normal Value of Thrombocytes Indices in Indonesian Adults: Focus on Gender and Ages

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Abstract

BACKGROUND: Monitoring platelet count and related indices is crucial for managing hematological disorders. No studies are reporting normal platelet indices in the adult Indonesian population. Therefore, this study was conducted to establish normal reference values for platelet count and indices in a healthy population in Indonesia and investigate their association with platelet count and each parameter.

METHODS: This cross-sectional study included healthy adults from both sexes who underwent hematological testing in our laboratory. Two mL of venous blood was drawn and analyzed using an automated machine ADVIA 2120 to identify platelet count, mean platelet volume (MPV), platelet distribution width (PDW), plateletcrit (PCT), mean platelet component (MPC), platelet component distribution width (PCDW), mean platelet mass (MPM), platelet mass distribution width (PMDW), and large platelet count.

RESULTS: This study included 1037 subjects with median of 27 (18–58) years old. Normal reference range values for platelet indices in adult Indonesians was established, which was significantly different between males and females (p<0.05) in following parameters: platelet count (191.77–400.37 *vs.* 203.00–433.00 $\times 10^9$/L), MPV (7.30–9.91 *vs*. 7.20–10.00 fL), PDW (38.09–59.83 *vs.* 37.10–58.50%), PCT (0.17–0.33 *vs.* 0.17–0.35%), PMDW (0.68–1.06 *vs.* 0.67–1.04 pg) for males *vs.* females, respectively. However, other parameters such as MPC, PCDW, MPM, and large platelet, did not show any significant differences.

CONCLUSION: The reference intervals of platelet indices in the adult Indonesian population were different from previously established reference values, indicating the importance of dedicated reference interval determination with gender consideration.

KEYWORDS: thrombocyte indices, platelet count, hematology reference values, blood platelet analysis

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Introduction

Thrombocytes are fragments of megakaryocyte and circulate in blood vessels maintaining the hemostasis system.(1) Thrombocytes, also known as platelets, are small, colorless blood cells that play a crucial role in the clotting process, which is essential for preventing excessive bleeding.(2) As platelet is very essential in our body, there are many advances measurement for platelet, including the indices. Platelet indices provide additional information about the platelet population and their functionality.(3) Commonly used platelet indices include mean platelet volume (MPV), platelet distribution width (PDW), and plateletcrit (PCT). (4) MPV represents the average volume of platelets in the bloodstream. It serves as an indicator of platelet production

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and activation.(5,6) Deviations from the normal MPV range may suggest various platelet-related disorders or underlying systemic conditions.(3) PDW measures the variation in platelet size within a blood sample. Increased PDW values may indicate increased platelet activation and release, while decreased values may suggest a more uniform platelet population.(7) PDW is often used in conjunction with MPV to assess platelet size distribution.(8) PCT is the volume fraction of platelets in whole blood. It provides an estimation of the total platelet mass.(9) Abnormal PCT values may indicate abnormalities in platelet production or consumption.(10,11) Aside from common indices, ADVIA 2120 also generate another indices called extended platelet parameters.(12) It consist of mean platelet component (MPC), mean platelet mass (MPM), platelet component distribution width (PCDW) dan platelet mass distribution width (PMDW). MPC was represents the mean refractive index of the platelets and could showing platelet activation. MPM was calculated from the platelet dry mass histogram. PCDW is a result of measurement of the variation in platelet component meanwhile PMDW is a result of measurement of the standard deviation of the platelet dry mass distribution and a measure of the variability of platelet.(3,13) All the later indices MPM, PCDW, and PMDW not fully understood the clinical significance as their relatively new.

Monitoring platelet count and related indices is crucial in diagnosing and managing various hematological disorders. However, the interpretation of these indices requires reliable reference values specific to the population under study. Accurate reference values for platelet count and indices are essential for diagnosing and monitoring various hematological conditions.(14) These reference values act as a baseline against which abnormal values can be compared, aiding in the early detection of platelet-related disorders. The establishment of normal reference values for thrombocyte indices is a crucial aspect of hematologic diagnostics. While studies using the ADVIA hematology analyzer have been conducted in other countries, such as Korea, it remains imperative to determine these values specifically for the Indonesian population. Manufacturer company also release the reference value, but genetic diversity, environmental factors, and ethnic variability can significantly influence hematologic parameters. Additionally, gender and age are known to play pivotal roles in thrombopoiesis, the process of platelet production. Another study showed that ages enhanced platelet activity thus changes the platelet indices.(15) Proteomic activity also influenced by age and hormonal. Hormonal differences between males and females, as well as age-related changes in bone marrow activity, can result in variations in platelet counts and indices.(16) Therefore, using reference values derived from manufacturer or other populations may lead to misinterpretations and suboptimal patient care. This study was conducted to establish accurate thrombocyte index reference values for Indonesian adults, ensuring that clinical interpretations and subsequent healthcare decisions are precisely tailored to the local population's needs.(17) This research was conducted to establish normal reference values for platelet count and platelet indices in a healthy population in Indonesia and their correlation with platelet count and each parameter itself.

Methods

Study Design and Subject Recruitment

This was an observational retrospective study using a cross-sectional study design. The recruitment and analysis process follows the guidelines of Clinical and Laboratory Standards Institute number 28A3C (CLSI 28A3C).(17) As there is no strict guideline on CLSI 28A3C, the subjects were then categorized into three age groups: 18–24 years, 25–30 years, and >30 years, similar to another study.(18) This study enrolled 1037 healthy individuals attending the Department of Clinical Pathology, Faculty of Medicine, Public Health and Nursing, Universitas Gadjah Mada for hematological testing. Healthy subjects were the individuals with no physical or mental complaints, no relevant disease, such as diabetes, arterial hypertension, cardiopathy, renal disease, or hepatic disease, with normal hematology test results, and were not receiving any medications. Sample collection and test conduction were performed following the institutional standard operating procedures. The Medical and Health Research Ethics Committee Faculty of Medicine Public Health and Nursing, Universitas Gadjah Mada, Dr. Sardjito General Hospital had approved this study (No. KE/FK/1017/EC/2020).

Analysis of Blood Samples

Venous blood of 2 mL was aseptically collected from each enrolled subject into tripotassium ethylene diamine tetraacetate (K3-EDTA) vacutainer tubes. Samples were collected, mixed gently, and delivered for laboratory analysis. Samples were analyzed using an automated blood cell counter ADVIA 2120 (Bayer HealthCare, Diagnostics Division, Tarrytown, NY, USA) within 2 h of collection. Platelet count, including platelet indices, was performed as part of the full blood count by automated procedure. To

analyze blood samples, the whole blood mode was chosen to avoid predilution. Quality control measures, both internal and external, were strictly adhered to throughout the study to maintain high performance, with regular calibration of the instrument using standardized calibrators. The ADVIA 2120 calculated MPV from the platelet volume histogram, which ranges from 0 to 60 femtoliters (fL). PDW represented the distribution width of this histogram, while PCT indicated the percentage of blood volume occupied by platelets. MPC was derived from the platelet component histogram, which reflected platelet density within a range of 0 to 40 grams per deciliter (g/dL). MPM was calculated from the platelet dry mass histogram, ranging from 0 to 5 picograms (pg), and large platelet count refers to the number of platelets exceeding 20 fL in volume. PCDW was interpreted as the distribution width of the platelet component histogram, whereas PMDW was interpreted as the platelet mass histogram distribution width.(9)

Statistical Analysis

Microsoft Excel 2016 (Microsoft Corporation, Redmond, WA, USA) was used for data organization and analysis, while IBM SPSS Statistics version 23 (IBM Corporation, Armonk, NY, USA) was used for statistical data analysis. Qualitative data were presented as numbers and percentages [n(%)], while the quantitative data with non-normal distribution were demonstrated as medians, interquartile ranges, and percentiles. The two independent groups with quantitative data and not normal distribution were compared using the Mann–Whitney test, and the Spearman correlation analysis was used to determine the intercorrelations between parameters studied in this study. A p-value<0.05 was considered significant.

Results

Characteristics of Subjects

Of the 1037 healthy individuals, 497 (47.9%) were males and 540 (52.1%) were females. The subjects were from various provinces in Indonesia, indicating their heterogeneity. The ages ranged from 18 to 58 years, with a median of 27 years. The subjects were categorized into three age groups: 18–24 years, 25–30 years, and >30 years, with each group consisted of a similar number of participants, including 391 (37.7%), 364 (35.1%), and 282 (27.2%) participants, respectively, which already fulfil the minimum number of each subclasses that is 120. Each age group of 25–30 and >30 years consisted of more male participants, including 202 (55.5%) and 167 (59.2%), respectively. Only in the 18–24 years age group included more female participants at 263 (67.3%) individuals.

Platelet Count and Indices Profiles

The data were non-normally distributed platelet count and indices; therefore, the median was used rather than the mean. Reference intervals were defined as 95% confidence limits for values between the 2.5 and 97.5 percentiles. The medians, interquartile ranges, and reference intervals of platelet count and indices of the study population were presented. Statistically significant differences were observed upon comparing the median values of platelet count, MPV, PDW, PCT, and PMDW between males and females (p<0.05), where females presented slightly higher median and reference interval values in platelet count and PCT, whereas males demonstrated higher values in MPV, PDW, and PMDW (Table 1).

Table 1. Median, interquartile ranges and reference interval of platelet count and indices in males and females.

	Median (IQR)			Reference Interval[a]			p-value[b]
	All Subjects (n=1037)	Male (n=497)	Female (n=540)	All Subjects (n=1037)	Male (n=497)	Female (n=540)	
Platelet count ($\times 10^9$/L)	292 (249–332)	284 (239.7–320)	299 (259–345.5)	195.4–416.6	191.8–400.4	203–433	<0.001*
MPV (fL)	8.3 (7.8–8.8)	8.4 (7.9–8.9)	8.3 (7.8–8.7)	7.2–9.9	7.3–9.9	7.2–10	0.025*
PDW (%)	46.5 (43.1–50.8)	47.4 (43.8–52.1)	45.7 (42.4–49.7)	37.6–58.9	38.1–59.8	37.1–58.5	<0.001*
PCT (%)	0.24 (0.21–0.27)	0.23 (0.20–0.27)	0.25 (0.22–0.28)	0.17–0.34	0.17–0.33	0.17–0.35	<0.001*
MPC (g/dL)	26 (24.9–27)	25.9 (24.8–26.7)	26.1 (25.1–27.2)	22.9–28.6	23–28.6	22.8–28.6	0.060
PCDW (g/dL)	5.3 (5.1–5.6)	5.4 (5.1–5.6)	5.3 (5.1–5.6)	4.6–6.1	4.7–6.1	4.5–6.1	0.172
MPM (pg)	2.07 (1.96–2.19)	2.07 (1.96–2.19)	2.08 (1.95–2.19)	1.81–2.49	1.81–2.47	1.80–2.50	0.477
PMDW (pg)	0.84 (0.77–0.91)	0.85 (0.78–0.92)	0.83 (0.76–0.90)	0.67–1.06	0.68–1.06	0.67–1.04	0.002*
Large platelet (fL)	4 (3–6)	4 (3–6)	4 (3–6)	1–12	1–12	1–10.5	0.251

[a]95% reference interval (2.5 percentile–97.5 percentile). [b]Tested using Mann-Whitney to analyze the median difference between males and females; *significant if p<0.05.

Besides comparing the parameters by gender, we compared each parameter in the three age groups. Most of them demonstrated similar median and reference intervals despite their age group (Figure 1). Spearman correlation was used to determine the correlation between age and platelet indices. Age showed a weak significant positive correlation with MPV (r=0.281; $p<0.001$) (Figure 1A) and a very weak significant positive correlation with PDW (r=0.104; $p<0.001$) (Figure 1B), PCT (r=0.068; $p=0.029$) (Figure 1C), PMDW (r=0.077; $p=0.013$) (Figure 1G), and large platelet (r=0.153; $p<0.001$) (Figure 1H). A weak significant negative correlation was observed in MPC (r=−0.347; $p<0.001$) (Figure 1D) and PCDW (r=−0.277; $p<0.001$) (Figure 1E). There were no correlation between age and MPM ($p=0.285$) (Figure 1F).

Correlations between Platelet Indices

All platelet indices revealed significant correlations with platelet count. There was strong positive correlation between platelet counts and PCT (r=0.901; $p<0.001$) (Figure 2D)

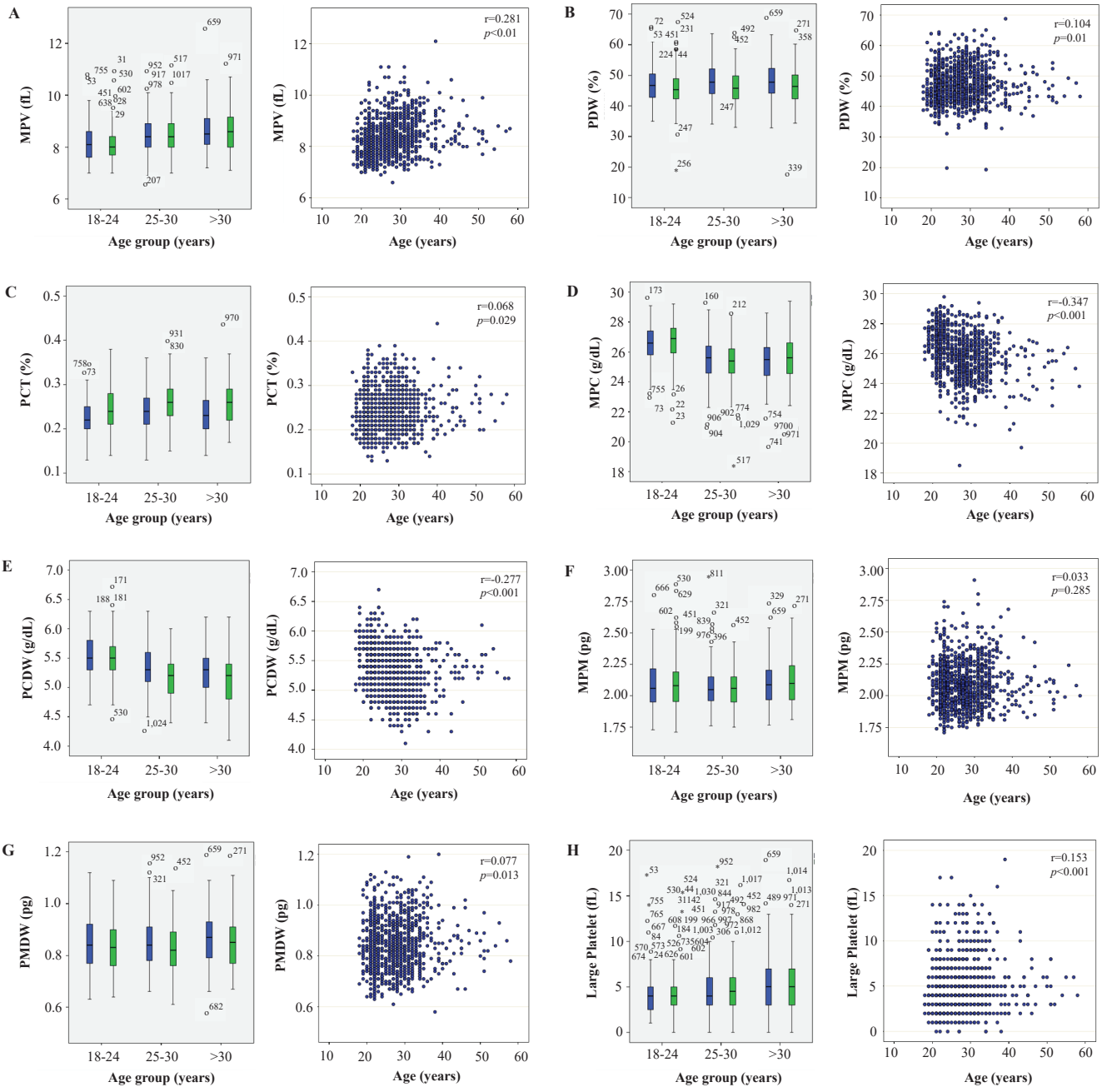

Figure 1. Data distribution of platelet indices divided by age group (left) and overall trend analysis of platelet indices and age (right). A: MPV; B: PDW; C: PCT; D; MPC; E: PCDW; F: MPM; G: PMDW; H: Large platelet.

and a very weak positive correlation between platelet count and PCDW (r=0.199; p<0.001) (Figure 2G). While other correlation analysis showed negative correlations between platelet count and other platelet indices component. Moderate negative correlations were observed with MPM (r=−0.500; p<0.001) (Figure 2A) and PMDW (r=−0.523; p<0.001) (Figure 2C), and weak negative correlations were observed between platelet count and MPV (r=−0.347; p< 0.001) (Figure 2E), PDW (r=−0.473; p<0.001) (Figure 2H), and MPC (r=−0.262; p<0.001) (Figure 2F). Large platelets demonstrated a very weak negative correlation (r=−0.179; p<0.001) (Figure 2B) with platelet count.

We also examined the correlations between platelet indices. We found a strong positive correlation between MPV and PDW (r=0.605) (Figure 3A), MPV and MPM (r=0.723) (Figure 3C), and PDW and MPM (r=0.685) (Figure 3E). Additionally, there was a moderate positive correlation between PDW and MPC (r=0.206) (Figure 3D), as well as between MPC and MPM (r=0.385) (Figure 3F). Conversely, a moderate negative correlation was observed between MPV and MPC (r=-0.293) (Figure 3B). All correlations were statistically significant (p<0.001).

Discussion

The results of this study showed the correlation of gender and ages to some thrombocyte indices as mentioned previously.(13,18-20) However, it did not significantly deviate from other established reference ranges. Specifically, the reference values for thrombocyte indices in our study are consistent with those reported in the Korean population.(21) Despite the similarities observed in Asian populations, our study underscores the importance of establishing localized reference values specific to the Indonesian population. In this study we found the platelet count reference range

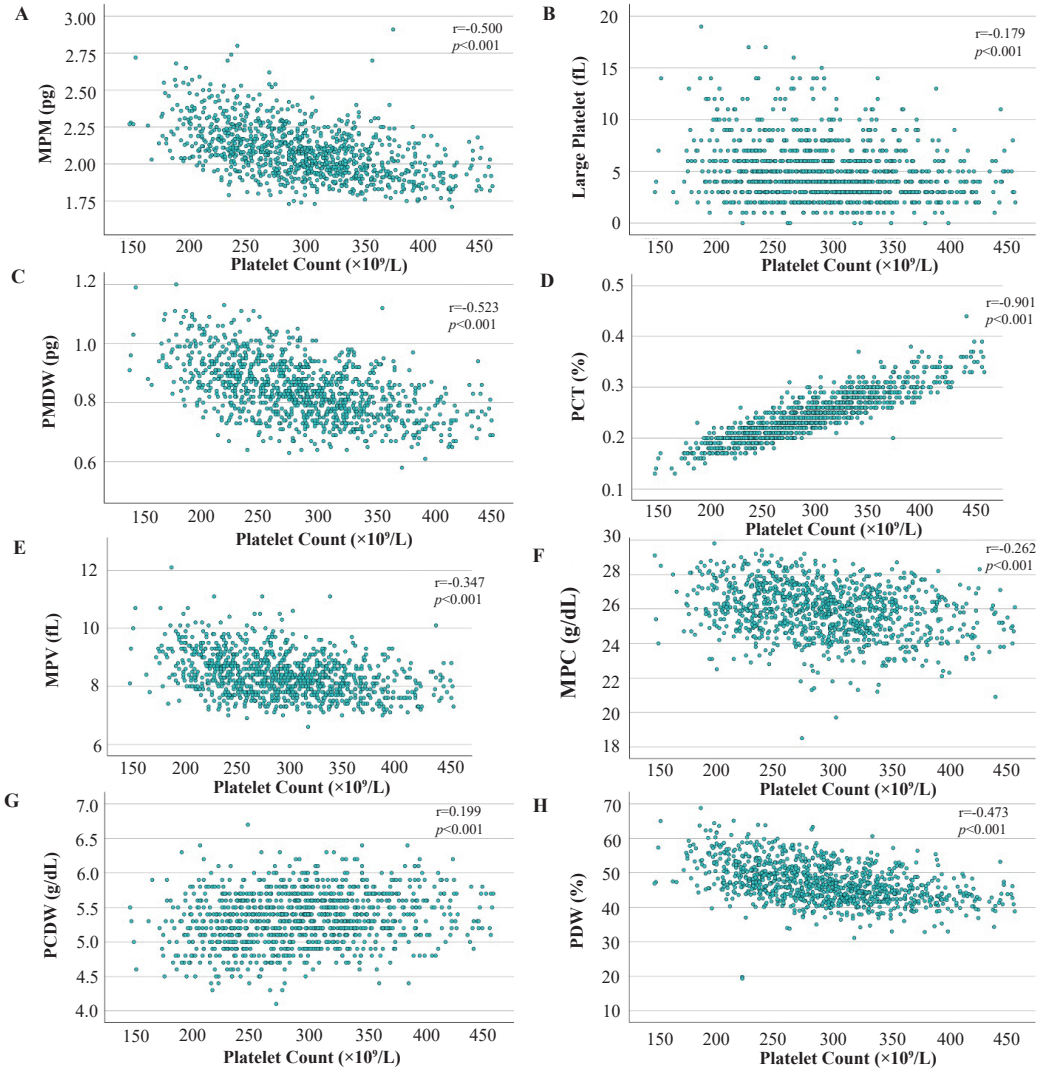

Figure 2. Correlation between platelet count and the other platelet indices components.

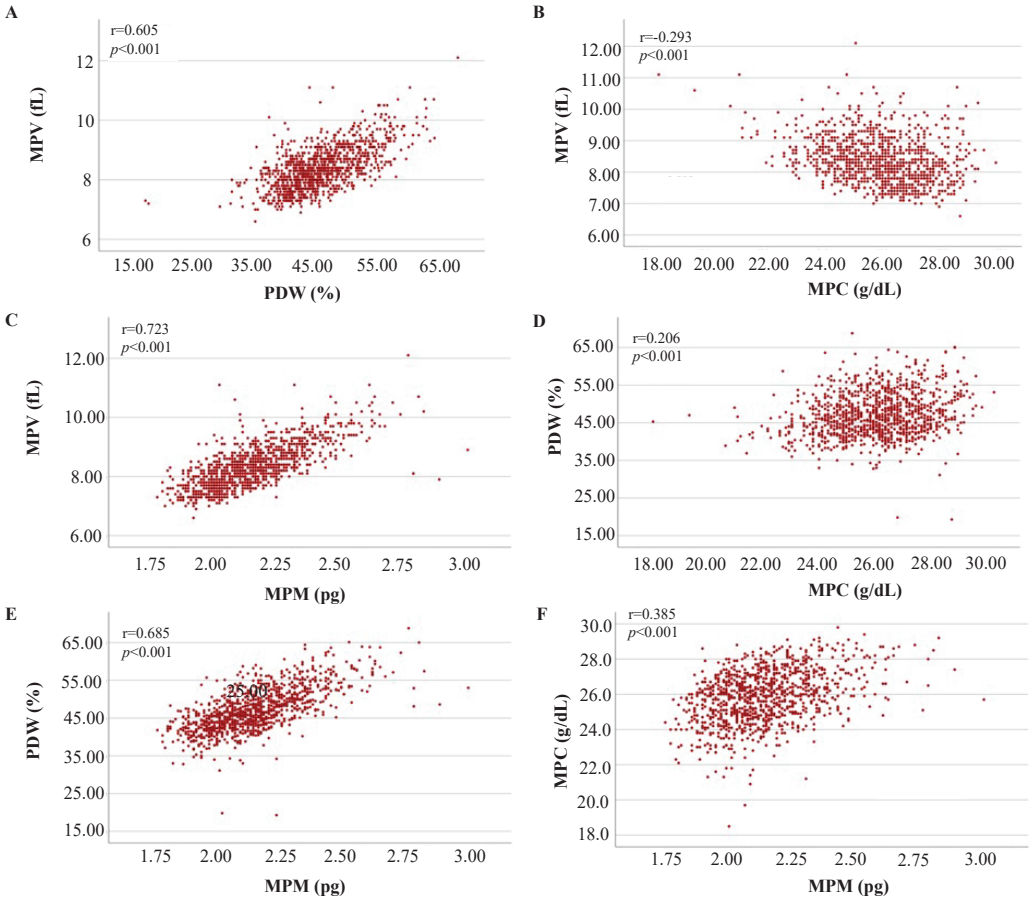

Figure 3. Platelet indices intra-correlations.

(195–416 $\times 10^9$/L) was little bit different than international reference range (150–450 $\times 10^9$/L) (22), although still in its normal range. MPV reference range in present study (7.20–9.96 fL) showed identic results with Iran study (7.4–10.7 fL) (23) as well study in India (24) and South Korea (21), meanwhile other study showed slightly higher reference range. PDW has different units depending on the analyzer used, that we can't compared with every study. This study used percentage as the unit, as well as Korean and Iranian studies. South Korean PDW reference range (39.3–64.7%) showed more similar with our reference range (37.64–58.86%) than Iranian (40.2–57.4%). In PCT reference range, resemblance was found in most of other studies. Other parameters such as MPC, MPM and Large Platelet could only be compared with Korean study as both studies used same analyzer and other study didn't analyze these parameters. A study by National Health and Nutrition Examination Survey of United States, found that differences in platelet counts among different ethnic groups in the United States were likely to be real and not caused just by environmental differences.(25) As a study in China compared platelet count and other parameters reference range from six different cities and a significant result was found in one region.(26) Table 2 shows the comparison between the reference value obtained from other studies from various country and the current study.

There were a lot of previous studies compared the difference of reference range in female and male. This study showed significant difference in platelet count, MPV, PDW, PCT and PMDW reference range. Platelet count reference range was higher in female than male (p<0.001). This finding is in agreement with the previously published literature in Sudan, Iran, and China.(27,23,26) Although the exact cause of this difference is uncertain and debated, it may be due to hormone-related differences or a compensatory mechanism related to blood loss during menstruation.(27) The MPV reference intervals for males and females were 7.3–9.91 fL and 7.2–10.0 fL, only slightly different with statistical significance (p=0.025). This result is in accordance with at least three previous studies.(7,21,27) Conversely, some researchers have found that females exhibit higher MPV than males.(23,28) In this study a significant difference of PDW was also found between male reference range is slightly higher than female. This was similar as previous studies.(23,24,26-28) However, another study in Brazil population showed no significant different between males and females in platelet count and all indices.(29) This resembles the importance of localized reference values.

Table 2. Comparison reference range with previous studies.

Author	Abass[27]	Adibi[23]	Alexander[28]	Hong[26]	Kim[21]	Maluf[29]	Sachdev[9]	This study
Population	Sudanese	Iranian	Nigerian	Chinese	Korean	Brazilian	Indian	Indonesian
Instruments	Sysmex KX-21	Technocon H*2	Sysmex KX 21N	Sysmex XE-2100	ADVIA 2120	Sysmex XE-2100	Sysmex XE-2100	ADVIA 2120
Sample size	300	19993	500	4642	480	580	945	1037
Platelet count (x10^9/L)	146–378	145–356		115–323			247–254	195–416
MPV (fL)	8.2–11.6	7.4–10.7	9.7–11.5	9.27–13.22	6.7–9.6	8.9–11.8	11.6–11.78	7.20–9.96
PDW	8.3–15.9 fL	40.2–57.4%		9.13–18.33 fL	39.3–64.7%	9.6–15.3 fL	14.33–14.72 fL	37.64–58.86%
PCT (%)	0.13–0.34	0.13–0.32		0.14–0.36	F : 0.15–0.31; M : 0.14–0.28		0.28–0.29	0.17–0.34
MPC (g/dL)					22.8–28.0			22.90–28.60
PCDW (g/dL)								4.60–6.10
MPM (pg)					1.67–2.29			1.81–2.49
PMDW (pg)								0.67–1.06
Large Plt (fL)					1.00–11.00			1.00–12.00

Clinical and Laboratory Standards Institute suggest sub analysis to determine whether the normal value should or not stratified based on age.(17) This study divides the reference range into three age groups; 18–24 years old, 25–30 years old and more than 30 years old. However our study showed that there is no difference. We couldn't compare this result to previous studies as there is no such similar age categories and indices analyzed. As a note, there is a previous study from China showed that age is influencing almost all platelet indices in subjects ranging from 18 years old to more than 81 years old.(30) As this study have narrowed range, the differences not significant.

Strong positive correlations between MPV and PDW (r=0.605), MPV and MPM (r=0.723), and PDW and MPM (r=0.685) were observed. These relationships suggest that as the MPV increases, both the PDW and MPM also tend to increase. This could indicate that larger platelets, which are typically more reactive, exhibit greater variability in size and mass, reflecting heightened platelet production or activation states.(31) The strong positive correlation between MPV and PDW highlights important aspects of platelet physiology. MPV represents the average size of platelets in the blood, with larger values indicating larger platelets. PDW, on the other hand, reflects the variation in platelet size, with higher values suggesting greater variability. This strong positive correlation is well-documented in the literature, indicating that as MPV increases, PDW tends to increase as well.(32,33) The correlation between MPV and PDW has significant implications for platelet activation and function. Larger platelets, indicated by higher MPV, are generally more reactive and prone to activation. Increased PDW suggests greater variability in platelet size, which can impact platelet function. Together, elevated MPV and PDW may lead to enhanced platelet activation, potentially influencing the body's response to vascular injury and other hemostatic processes.(32,34) The strong positive correlation between MPV and MPM further emphasizes the interconnected nature of platelet indices. MPV reflects the average size of platelets in the blood, with larger values indicating larger platelets.(35) MPM represents the total mass of platelets in a given blood sample. Studies have consistently shown that as MPV increases, MPM tends to increase as well.(36) This relationship underscores the role of larger platelets in hemostasis.(37)

A moderate positive correlation between MPC and MPM (r=0.385) were also found. The positive correlation suggests that larger platelets (higher MPM) may contribute to a higher overall platelet count (MPC). This could be due to larger platelets being more metabolically active, leading to increased production or reduced clearance.(38) Enhanced thrombopoiesis, or platelet production, could result in both larger and more numerous platelets, thus elevating both MPC and MPM.(39,40) Interestingly, a moderate negative correlation was found between MPV and MPC (r=-0.293). MPV represents the average size of platelets, and the negative correlation suggests that larger platelets (higher MPV) may be associated with a lower platelet count. This inverse relationship could be explained by altered platelet production pathways, where conditions affecting megakaryocytes (platelet precursors) might lead

to the production of larger platelets but a reduced overall count.(39) Additionally, larger platelets could be more prone to activation and subsequent removal from circulation which may also contribute to the observed negative correlation.(38)

These findings underscore the necessity of establishing gender-specific reference intervals for certain platelet indices to ensure precise clinical interpretation while confirming that some parameters remain consistent across sexes. The divergence of our population's reference values from those reported in other studies highlights the critical need for localized reference ranges tailored to the Indonesian population to optimize patient care. The established reference values and the interrelationships among platelet indices in the Indonesian adult population provide a valuable reference for clinicians and researchers, aiding in the diagnosis and monitoring of various hematological disorders where deviations from normal platelet indices may serve as diagnostic or prognostic markers.

Unfortunately, the sampling method used in this study was not a stratified random sampling although the subjects were heterogeneous and represented a presentation from the Indonesian population, which may have influenced the results. Other than age and gender, thrombocyte indices values are also influenced by various factors including ethnic differences, preanalytical variables (such as venipuncture method, accuracy in filling and mixing sample tubes, temperature, delay between sampling and analysis, and the type of anticoagulant used), and the measurement technique of the automated cell counter, therefore further study analyzing those factors might be beneficial.

Conclusion

This study established normal reference ranges for platelet indices in adult Indonesians, revealing significant sex-based differences in several key parameters, including platelet count, MPV, PDW, PCT, and PMDW. In contrast, other indices such as MPC, PCDW, MPM, and large platelet count did not show significant differences between sexes.

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Authors Contribution

US conceived and designed the study, conducted data analysis, interpreted the results, performed data collection and processing, and wrote the manuscript. AZA assisted with study design and contributed to the interpretation of the data and manuscript revision. TR and RDS provided statistical guidance and critically reviewed and revised the manuscript for important intellectual content.

References

1. Holinstat M. Normal platelet function. Cancer Metastasis Rev. 2017; 36(2): 195–8.
2. Gibbins JM. Platelet adhesion signalling and the regulation of thrombus formation. J Cell Sci. 2004; 117(Pt 16): 3415–25.
3. Budak YU, Polat M, Huysal K. The use of platelet indices, plateletcrit, mean platelet volume and platelet distribution width in emergency non-traumatic abdominal surgery: a systematic review. Biochem Med (Zagreb). 2016; 26(2): 178–93.
4. Wiwanitkit V. Plateletcrit, mean platelet volume, platelet distribution width: its expected values and correlation with parallel red blood cell parameters. Clin Appl Thromb Hemost. 2004; 10(2): 175–8.
5. Lippi G, Pavesi F, Pipitone S. Evaluation of mean platelet volume with four hematological analyzers: harmonization is still an unresolved issue. Blood Coagul Fibrinolysis. 2015; 26(2): 235–7.
6. Kemuning AR, Wulanjani HA, Limijadi IEKS, Samsuria IK, Rachmawati B. Transthyretin, immature platelet fraction, and mean platelet volume in normotensive and preeclampsia pregnancy. Indones Biomed J. 2022; 14(2): 193–8.
7. Giacomini A, Legovini P, Gessoni G, Antico F, Valverde S, Salvadego MM, *et al.* Platelet count and parameters determined by the Bayer ADVIA 120 in reference subjects and patients. Clin Lab Haematol. 2001; 23(3): 181–6.
8. Golwala ZM, Shah H, Gupta N, Sreenivas V, Puliyel JM. Mean platelet volume (MPV), platelet distribution width (PDW), platelet count and plateletcrit (PCT) as predictors of in-hospital paediatric mortality: A case-control Study. Afr Health Sci. 2016; 16(2): 356–62.
9. Sachdev R, Tiwari AK, Goel S, Raina V, Sethi M. Establishing biological reference intervals for novel platelet parameters (immature platelet fraction, high immature platelet fraction, platelet distribution width, platelet large cell ratio, platelet-X, plateletcrit, and platelet distribution width) and their correlations among each other. Indian J Pathol Microbiol. 2014; 57(2): 231–5.
10. Ergelen M, Uyarel H. Plateletcrit: A novel prognostic marker for acute coronary syndrome. Int J Cardiol. 2014; 177(1): 161. doi: 10.1016/j.ijcard.2014.09.
11. Akpinar I, Sayin MR, Gursoy YC, Aktop Z, Karabag T, Kucuk E, *et al.* Plateletcrit and red cell distribution width are independent predictors of the slow coronary flow phenomenon. J Cardiol. 2014; 63(2): 112–8.
12. Diaz-Ricart M, Brunso L, Pino M, Navalon F, Jou JM, Heras M, *et al.* Preanalytical treatment of EDTA-anticoagulated blood to ensure stabilization of the mean platelet volume and component measured with the ADVIA counters. Thromb Res. 2010; 126(1): e30–5.
13. Boos CJ, Beevers GD, Lip GYH. Assessment of platelet activation

indices using the ADVIATM 120 amongst 'high-risk' patients with hypertension. Ann Med. 2007; 39(1): 72–8.
14. Balandina AN, Koltsova EM, Shibeko AM, Kuprash AD, Budkova VA, Demina IA, *et al.* Platelets provide robustness of spatial blood coagulation to the variation of initial conditions. Thromb Res. 2023; 230: 133–43.
15. Le Blanc J, Lordkipanidzé M. Platelet function in aging. Front Cardiovasc Med. 2019; 6: 109. doi: 10.3389/fcvm.2019.00109.
16. Campbell RA, Franks Z, Bhatnagar A, Rowley JW, Manne BK, Supiano MA, *et al.* Granzyme a in human platelets regulates the synthesis of proinflammatory cytokines by monocytes in aging. J Immunol. 2018; 200(1): 295–304.
17. Horowitz GL, Altaie S, Boyd JC, Ceriotti F, Garg U, Horn P, *et al.* EP28-A3c Defining, Establishing, and Verifying Reference Intervals in the Clinical Laboratory; Approved Guideline-Third Edition. Wayne, PA: Clinical and Laboratory Standards Institute; 2008.
18. Ken-Ezihuo SU, Bartimaeus EAS. Reference ranges of platelet variables amongst apparently healthy adults in Port Harcourt, Rivers State, Nigeria. Eur J Biomed Pharm Sci. 2017; 4(7): 49–54.
19. Adhane YB, Sardar MA, Chettiankandy TJ, Sachdev SS, Tupkari JV. Reference intervals and gender variation in establishing blood parameters in dental institution: A retrospective study. Indian J Clin Anat Physiol. 2022; 9(1): 16–21.
20. Nunes MN, Santos D. Hematology, transfusion and cell therapy scientific comment does gender influence reference values of platelet indices? Hematol Transfus Cell Ther. 2019; 41(2): 104–5.
21. Kim MJ, Park PW, Seo YH, Kim KH, Seo JY, Jeong JH, *et al.* Reference intervals for platelet parameters in Korean adults using ADVIA 2120. Ann Lab Med. 2013; 33(5): 364–6.
22. Bain BJ, Bates I, Laffan MA, Lewis SM. Dacie and Lewis Practical Haematology. 11th Ed. Amsterdam: Elsevier Health Sciences; 2012.
23. Adibi P, Faghih Imani E, Talaei M, Ghanei M. Population-based platelet reference values for an Iranian population. Int J Lab Hematol. 2007; 29(3): 195–9.
24. Subhashree AR, Parameaswari PJ, Shanthi B, Carnagarin R, Parijatham BO. The reference intervals for the haematological parameters in healthy adult population of Chennai, Southern India. J Clin Diagn Res. 2012; 6(10): 1675–80.
25. Segal JB, Moliterno AR. Platelet counts differ by sex, ethnicity, and age in the United States. Ann Epidemiol. 2006; 16(2): 123–30.
26. Hong J, Min Z, Bai-shen P, Jie Z, Ming-ting P, Xian-zhang H, *et al.* Investigation on reference intervals and regional differences of platelet indices in healthy Chinese Han adults. J Clin Lab Anal. 2015; 29(1): 21–7.
27. Abass AE, Ismail I, Ali E, Mohammed R, Mohammed S, Alamin H, *et al.* Reference value of platelets count and indices in Sudanese using Sysmex KX-21. Int J Health Sci. 2015; 3: 120–5.
28. Alexander NI. Reference values of neutrophil-lymphocyte ratio, platelet-lymphocyte ratio and mean platelet volume in healthy adults in North Central Nigeria. J Blood Lymph. 2016, 6: 1 doi: 10.4172/2165-7831.1000143.
29. Maluf CB, Barreto SM, Vidigal PG. Standardization and reference intervals of platelet volume indices: Insight from the Brazilian longitudinal study of adult health (ELSA-BRASIL). Platelets. 2015; 26(5): 413–20.
30. Zhang J, Li M, He Y. Large population study for age- and gender-related variations of platelet indices in Southwest China healthy adults. Hematol Transfus Int J. 2015;V 1(4):108–114.
31. Xu Y, Guo Y. Platelet indices and blood pressure: A multivariable mendelian randomization study. Thromb J. 2023; 21(1): 1–9. doi: 10.1186/s12959-023-00475-6.
32. Zheng Y ying, Wang L, Shi Q. Mean platelet volume (MPV) and platelet distribution width (PDW) predict clinical outcome of acute ischemic stroke: A systematic review and meta-analysis. J Clin Neurosci. 2022; 101: 221–7.
33. van der Meijden PEJ, Heemskerk JWM. Platelet biology and functions: New concepts and clinical perspectives. Nat Rev Cardiol. 2019; 16(3): 166–79.
34. Mappangara I, Mappahya AA, Witjaksono S. The comparative and usefulness of platelet distribution width in acute coronary syndrome. Indones Biomed J. 2016; 8(3): 173–8.
35. Kazemi N, Bordbar A, Bavarsad SS, Ghasemi P, Bakhshi M, Rezaeeyan H. Molecular insights into the relationship between platelet activation and endothelial dysfunction: Molecular approaches and clinical practice. Mol Biotechnol. 2024; 66(5): 932–47.
36. Wang J, Ma X, Si X, Wu M, Han W. Mean platelet volume and the association with all-cause mortality and cardiovascular mortality among incident peritoneal dialysis patients. BMC Cardiovasc Disord. 2023; 23(1): 1–9. doi: 10.1186/s12872-023-03551-x.
37. Meiliana A, Dewi NM, Wijaya A. Mitochondria: Master regulator of metabolism, homeostasis, stress, aging and epigenetics. Indones Biomed J. 2021; 13(3): 221–41.
38. Cay N, Ipek A, Gumus M, Birkan Z, Ozmen E. Platelet activity indices in patients with deep vein thrombosis. Clin Appl Thromb Hemost. 2012; 18(2): 206–10.
39. Zareifar S, Farahmand Far MR, Golfeshan F, Cohan N. Changes in platelet count and mean platelet volume during infectious and inflammatory disease and their correlation with ESR and CRP. J Clin Lab Anal. 2014; 28(3): 245–8.
40. Saran K, Vidya K, Seema K, Prasad A, Prakash J. Study of platelet indices and their role in evaluation of thrombocytopenia. J Family Med Prim Care. 2022; 11(10): 6236–42.