Full blood count values in adolescents and its comparison by gender and ethnicity in Seremban district, Malaysia

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ABSTRACT

Background: Adolescence is when an individual undergoes development and growth. Many studies suggest variations in the number and size of blood cells during this period in various individuals. The full blood count (FBC) is often the starting point of medical investigations, which help diagnose a wide range of illnesses, infections, and diseases. This study aimed to report the mean FBC values and compare them by gender and ethnicity, using blood results from the thalassemia screening programme in Seremban District, Malaysia.

Materials and Methods: This cross-sectional study used secondary data from the thalassemia screening programme on Form 4 students aged 15-16 years from January 2018 to October 2018 by the Seremban District Health Office, Malaysia. These students participated in the thalassemia screening programme in which their blood samples were taken for FBC analysis. The data were extracted for this study.

Results: There were statistically significant gender-based differences for total white blood cell (WBC) count, neutrophils, lymphocytes, mixed WBC, and platelets. It was also observed that ethnic-specific differences were statistically significant for RBC count, platelets, platelet distribution width and mean platelet volume.

Conclusion: This study was able to report the mean FBC values among Malaysian adolescents with respect to their gender and ethnicity, of which there is a lack of published data.

KEYWORDS:
RBC indices, full blood count, Adolescent

INTRODUCTION

Adolescence is a period in which an individual undergoes development and growth. Many studies suggest variations in the number and size of blood cells during this period in various individuals.[1-3] These differences are attributed to accelerated growth due to hormonal and body changes during puberty, such as increasing haemoglobin levels.[1]

A few studies have been conducted in Malaysia to derive the normal reference values in adults.[4,5] For example, Ambayya et al.,[4] reported differences in ethnic and gender-specific full blood count (FBC) values in the Malaysian population. They included adolescents as part of their data. However, the data were not stratified for this age group. Hence, the normal values for this age group were not published. It would be clinically beneficial to distinguish the range of values for common laboratory investigations to help diagnose disease more precisely, with regard to age, gender, ethnicity, genetic differences, and environmental factors.[6]

FBC consists of red blood cell (RBC) indices, which include RBC count, haemoglobin (Hb), haematocrit (HCT), mean corpuscular volume (MCV), mean corpuscular Hb (MCH), mean corpuscular Hb concentration (MCHC), red cell distribution width (RDW); and white blood cells (WBC), and platelet indices such as platelet count, platelet distribution width (PDW), and mean platelet volume (MPV). MCV measures the average size of red blood cells, and MCH and MCHC measure the amount and percentage of Hb within the RBC. RDW measures the variation in size of RBC. Similarly, PDW measures platelet size variability and MPV, the average size of platelets.

This study aimed to determine the range of FBC values and compare them by gender and ethnicity based on the thalassemia screening programme results in Seremban District, Malaysia.

MATERIALS AND METHODS

Study Design

This cross-sectional study was conducted using secondary data (FBC results) from the Thalassemia Screening Programme of Form 4 students in the Seremban District, which is situated to the south of Kuala Lumpur, the capital city. Between January and October 2018, these students participated in the screening programme, and their blood samples were drawn for FBC by School Health Teams under Seremban District Health Office. Blood samples were analysed by automated FBC analysers in the health clinic laboratories. The HydroDynamic focusing (DC detection) method was used for RBC indices and platelet count. At the

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Table I: Comparison of haematological parameters and RBC indices between male and female adolescents from Seremban. (n=1534)

FBC Indices	Mean (SD)			Mean difference (95% CI)	t-stat (df)	p-value[a]
	Combined (n=1534)	Male (n=771)	Female (n=763)			
RBC count (million/m^3)	5.16 (0.55)	5.47 (0.48)	4.85 (0.43)	0.62 (0.57, 0.67)	26.46 (1516)	<0.001
Hb (gm/dL)	14.05 (1.42)	15.02 (1.11)	13.06 (0.94)	1.96 (1.86, 2.06)	37.13 (1500)	<0.001
Hct (%)	42.53 (3.92)	45.12 (2.89)	39.89 (2.95)	5.22 (4.93, 5.52)	35.03 (1531)	<0.001
MCV (fL)	83.25 (20.00)	82.85 (6.09)	83.66 (27.69)	-0.81 (-2.81, 1.20)	-0.79 (1532)	0.430
MCH (pg/dL)	27.41 (2.55)	27.64 (2.51)	27.17 (2.57)	0.47 (0.21, 0.72)	3.60 (1532)	<0.001
MCHC (g/dL)	33.00 (1.52)	33.31 (1.35)	32.70 (1.62)	0.61 (0.46, 0.76)	8.03 (1531)	<0.001
Total WBC count (mm^3)	8.23 (1.98)	7.85 (1.86)	8.61 (2.01)	-0.77 (-0.96, -0,57)	-7.75 (1531)	<0.001
Neutrophils (%)	53.67 (10.30)	51.63 (10.09)	55.83 (10.08)	-4.20 (-5.24, -3.17)	-7.99 (1468)	<0.001
Lymphocyte (%)	38.70 (106.70)	36.99 (8.38)	34.02 (7.41)	2.98 (2.17, 3.79)	7.25 (1469)	<0.001
Mixed (%)	10.61 (15.55)	10.79 (3.69)	9.58 (4.13)	1.21 (0.81, 1.61)	5.94 (1469)	<0.001
RDW_CV	13.53 (1.64)	13.42 (1.70)	13.64 (1.57)	-0.06 (-0.38, 0.05)	-2.55 (1524)	0.011
Platelet (mm^3)	314.49 (75.68)	302.33 (70.01)	326.79 (79.19)	-24.46 (-31.95, -16.97)	-6.40 (1504)	<0.001
PDW (%)	12.34 (1.91)	12.37 (1.83)	12.31 (2.00)	0.06 (-0.17, 0.29)	0.49 (1057)	0.622
MPV (%)	9.99 (0.99)	9.97 (0.94)	10.05 (1.04)	-0.03 (-0.15, 0.08)	-0.54 (1106)	0.593

[a] Independent t-test

Table II: Comparison of mean haematological parameters and RBC indices among ethnicity (n=1534)

FBC Indices	Mean (SD)			F-stat (df)	p-value[a]
	Malay (n=1228)	Chinese (n=138)	Indian (n=161)		
RBC count (million/m^3)	5.14 (0.52)	5.31 (0.78)	5.16 (0.55)	5.91 (2)	0.003
Hb (gm/dL)	14.04 (1.40)	14.14 (1.45)	14.02 (1.59)	0.36 (2)	0.698
Hct (%)	42.47 (3.88)	42.92 (3.86)	42.59 (4.27)	0.82 (2)	0.443
MCV (fL)	83.61 (21.92)	81.21 (11.00)	82.38 (6.20)	1.06 (2)	0.345
MCH (pg/dL)	27.45 (2.37)	27.11 (4.03)	27.32 (2.25)	1.26 (2)	0.283
MCHC (g/dL)	33.01 (1.54)	32.95 (1.61)	33.00 (1.36)	0.07 (2)	0.931
Total WBC count (mm^3)	8.26 (2.02)	7.95 (1.74)	8.19 (1.83)	1.62 (2)	0.198
Neutrophils (%)	53.64 (10.48)	55.40 (9.63)	52.49 (9.35)	2.82 (2)	0.060
Lymphocyte (%)	35.48 (7.99)	34.77 (8.50)	36.66 (8.15)	2.08 (2)	0.126
Mixed (%)	10.16 (3.95)	9.91 (3.15)	10.78 (4.59)	2.01 (2)	0.134
RDW_CV	13.51 (1.64)	13.68 (2.06)	13.50 (1.14)	0.68 (2)	0.509
Platelet (mm^3)	317.29 (76.95)	313.79 (76.87)	294.74 (61.97)	6.32 (2)	0.002
PDW (%)	12.22 (1.84)	12.37 (1.95)	13.08 (2.13)	11.06 (2)	<0.001
MPV (%)	9.91 (0.98)	10.14 (0.89)	10.38 (1.05)	14.56 (2)	<0.001

[a]One-way ANOVA

same time, the fluorescence flow cytometry method was utilised for WBC counts.

Sample Size Calculation

For sample size calculation, Openepi sample size calculator was used. The haemoglobin of <12 in males was 9%7 and in females was 14%, two-sided 95% Confidence Intervals (95%CI), power 80% and sample size calculated was 1342. An additional 20% (n=268) was added to compensate for missing data. Thus, the total required sample size of 1610 was determined.

Participants

Data for the study were sourced from the FBC results of 15-16 years old Form 4 secondary schools' students who participated in the National Thalassemia Screening Program. This programme commenced in Malaysia in 2016. In the Seremban district, there were a total of 54 secondary schools. In 2018, a total of 7903 students from these 54 schools had their FBC taken for screening by 14 school health teams (SHTs). Based on this screening, SHTs were able to identify cases with low haemoglobin levels and follow them up either for anaemia or proceed with further thalassemia investigation (haemoglobin analysis or DNA analysis).

Sample size calculated for this study was 1610. Estimating that at least 200 records could be retrieved from each SHTs, 9 SHTs were randomly selected (expecting at least 1800 samples). Unfortunately, only 1352 samples were retrieved. To complete the sample size, an additional two SHTs were selected using simple random sampling from the remaining five SHTs. This gave an additional 258 samples to complete the required 1610, from a total of 11 participating SHTs (Figure 1). Demographic data such as gender and ethnicity, as well as FBC parameters such as RBC indices, WBC, and platelet indices, were collected.

Inclusion and exclusion criteria

The inclusion criteria were Form 4 students from government secondary schools who participated in the thalassemia screening program in 2018. Non-Malaysian citizens were excluded from the sample.

Furthermore, students with anaemia were excluded. A Hb level of <11g/dL for females and <12g/dL for males4 were taken as the cutoff point for anaemia. Based on these criteria, 76 students (2 males and 74 females) were excluded from 1610, and the final data of 1534 students were analysed for this study.

Table III: Comparison of the obtained mean haematological values of adolescents in various populations

Parameter	Gender	Current study (n=1534)	Malaysian study[10] (n=199)	Ethiopian study[11] (n=249)	Japanese study[12] (n=12023)	Spain study[13] (n=581)	Kenya study[14] (n=298)	Saudi study[2] (n=1526)	Brazil study[15] (n=362)
RBC	Male	5.4	5.1	5.2	5.1	5.1	4.9	5.1	
(million/mm^3)	Female	4.8	4.7	4.9	4.6	4.4	4.7	4.9	
HGB	Male	15.0	13.9	14.8	15.2	14.8	13.1	14.2	
(gm/dL)	Female	13.0	12.4	14	13.3	13.3	12.2	13.8	
HT	Male	45.1		44.8	45.6	43.2	38.8	41.8	
(%)	Female	39.8		43.3	40.9	39.1	35.6	39.4	
MCV	Male	82.8	80.6	86.7		86.5	79	81.0	
(fL)	Female	83.6	81.4	88		87.5	78	81.0	
MCH	Male	27.6	27.6			29.6		27.8	
(pg/cell)	Female	27.1	26.7			29.9		27.1	
MCHC	Male	33.3	34.2	32.5		34.2		34.0	
(g/dL)	Female	32.7	33.9	32.2		34.1		33.6	
RDW	Male	13.4		14.1		13.2			
(%)	Female	13.6		13.7		13.1			
Total WBC count (mm^3)	Male	7.8		5.4		6.8	5.6	7.9	5.6
	Female	8.6		5.9		6.5	5.2	7.1	6.4
Neutrophils (%)	Male	51.6		45.5		52.0	33.9		55.3
	Female	55.8		50.6		55.2	38.4		60.9
Lymphocytes %	Male	36.9		40.0		36.7	39.3		35.7
	Female	34.0		38.9		36.9	42.3		29.6
Mixed	Male	10.7		14.5		8.8	16.8		
(%))	Female	9.5		10.5		7.6	16.1		
Platelets	Male	302.3		261	253	258	224		239
(mm^3)	Female	326.7		288	265	261	233		258

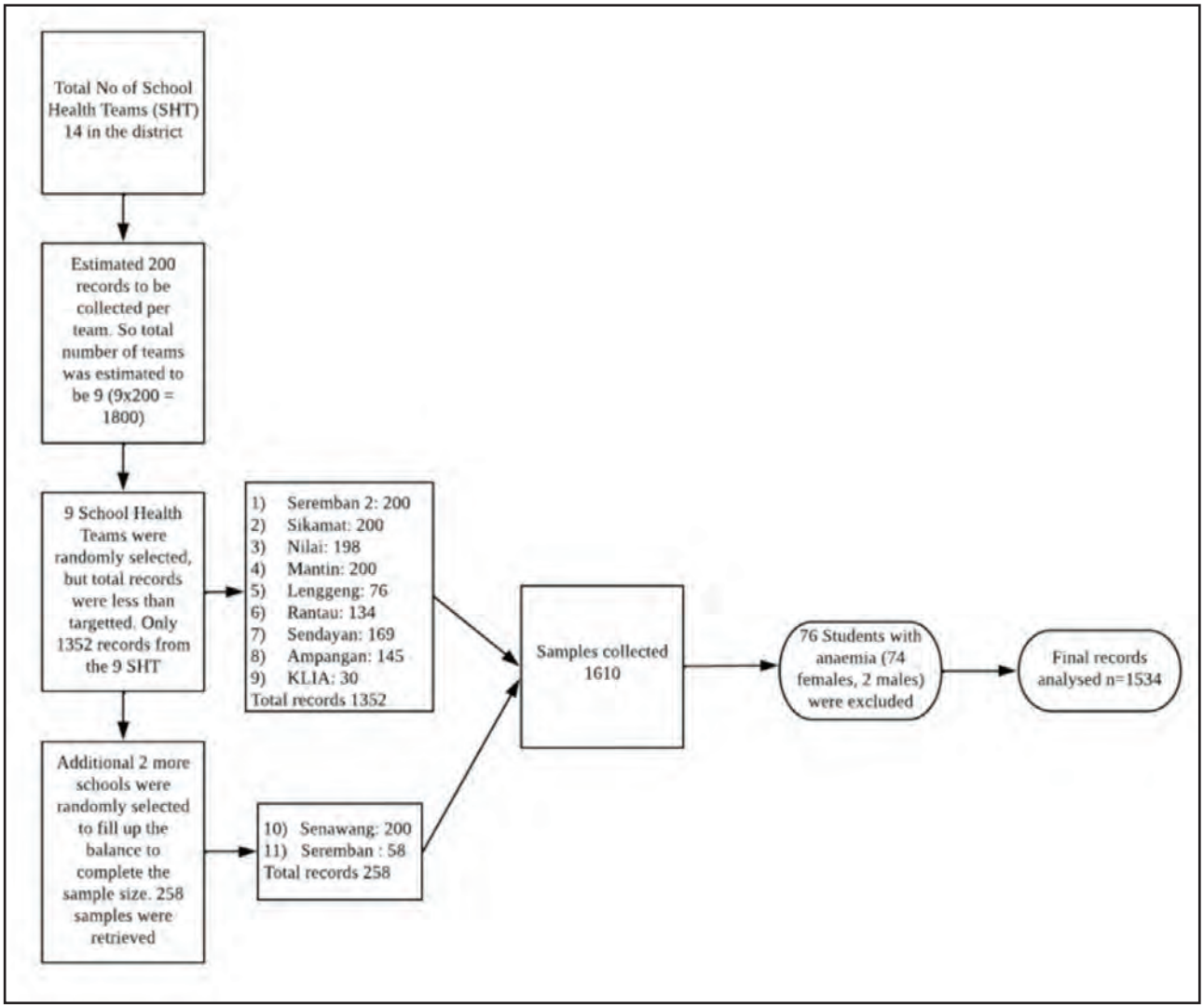

Fig. 1: Two stage sampling for record retrieval

Statistical Analysis

Data were anonymised and entered in Microsoft Excel for cleaning before importing into the Statistical Package for Social Sciences (SPSS) version 23.0 for analysis. Univariate analysis, namely independent t-test and one-way ANOVA was conducted in this study. The independent t-test was used to compare FBC indices between male and female adolescents. The level of significance was set at $p<0.05$. A one-way ANOVA analysis was further performed for comparison across the three ethnic groups (Malay, Chinese, and Indian). Post hoc test Dunnett-C was performed if Levene's test <0.05 and post hoc test Bonferroni was performed if Levene's test >0.05. A p value of <0.05 was considered statistically significant.

RESULTS

After excluding subjects with anaemia, a total of 1534 results were analysed for FBC values. There were 771 (50.3%) males and 763 (49.7%) females. By location, there were 1145 (74.6%) students in the urban areas compared to 389 (25.4%) in a rural setting. Malay ethnicity was the majority with 1228 (80.1%), followed by Indians 161 (10.5%), and Chinese 138 (9.0%). The mean FBC values for all parameters with the exception for MCV, PDW, and MPV showed a statistically significant difference between males and females (Table I).

FBC indices between the three ethnic groups (Malay, Chinese, and Indian) showed four variables to have a significant mean difference between groups for RBC, platelet, PDW, and MPV. Post hoc test Dunnett-C was performed for RBC and platelet (Levene's test <0.05) and post hoc test Bonferroni was performed for PDW and MPV (Levene's test >0.05) (Table II). Results of post hoc tests revealed that for RBC, there was a significant difference between Malay and Chinese [mean diff (95% CI): -0.17 (-0.33, -0.01) p=0.003]. Platelet mean differed significantly between the Malay and Indian groups [mean diff (95% CI): 22.54 (9.86, 35.23) p=0.002]. Mean of PDW differed significantly between Malay and Indian [mean diff (95% CI): -0.86 (-1.29, -0.42) p≤0.001] as well as Indian and Chinese [mean diff (95%CI): 0.71 (0.10, 1,32) p=0.017]. MPV

between Malay and Indian differed [mean diff (95% CI): -0.47 (-0.69, -0.25) p≤0.001].

DISCUSSION

Summary of the Main Findings

The current study observed statistically significant gender-based differences amongst the study population of 15-16 years old adolescents for RBC indices such as RBC count, Hb, HCT, MCH, MCHC, and RDW. In addition, for haematological parameters, the present study also found statistically significant gender-based differences for total WBC count, neutrophils, lymphocytes, mixed WBC, and platelets. However, ethnic-specific differences were statistically significant only for RBC count, platelets, PDW, and MPV.

Findings in Comparison to Previous Studies

Britannica encyclopedia defines adolescence as the intermediary phase of physical and psychological changes between childhood and adulthood.[8] On the other hand, the World Health Organization (WHO) age group defined adolescents as anyone between the ages 10 and 19.[9]

There is a lack of published haematological parameters reference data in adolescents in Malaysia. The present study will discuss the most significant gender-based differences compared to other studies. Our findings show statistically significant differences between males and females for FBC parameters. The differences were observed for the mean values of RBC count, Hb, HCT, MCH, MCHC, RDW, total WBC count, neutrophils, lymphocytes, mixed WBC, platelets, PDW, and MPV (Table I). These findings are consistent with the study by Menard,[10] who reported gender-based differences. The gender-based differences have been reported in various countries. The factors contributing to these differences could be menstruation, hormonal influences of androgen, estrogens, and testosterone on erythropoiesis, and the relatively high prevalence of iron deficiency anaemia in women.[10]

A few studies on mean RBC indices across several studies conducted in Malaysia, Ethiopia, Japan, Spain, Kenya, and Saudi Arabia are compared with current study results in Table 3. However, the causes of these differences still need to be studied in detail. The highest values for RBC count for adolescents were reported in both males and females. However, in the current study, the RBC values in males were higher compared with other studies (Table III). There is a lack of accurate correlation between these differences in various populations. However, on average, RBC count is seen lower in females than males, attributed to the effects of oestrogen and androgens on erythropoiesis.[11]

Regarding RBC indices, Foo et al.,[7] in their study involving adolescents aged 12-19 years (94 males and 105 females), reported the median reference intervals (RI) of Hb, HCT, and MCV values for a healthy adolescent population from Sabah, Malaysia.[7] In our study, the values for MCH in males were in agreement; however, Hb and MCV values for males and females showed higher mean values, and MCHC (both genders) were lower than those reported for adolescents in Sabah, Malaysia. In the study from Spain,[12] the MCV, MCH, and MCHC values reported are higher than in the current study (Table III).

Furthermore, our study reports higher MCV values in Malaysian male and female adolescents than those reported by El-Hazmi and Warsy.[2] They studied 1526 children aged 13–15 years from the Central Province of Saudi Arabia. These differences could be explained by covariates that can influence the values, such as nutritional status or using different laboratory methods in these populations.

In this study, females showed significantly lower RBC count, Hb, and HCT values compared to males (Table I). This is contrary to findings by Foo et al.[7] and El-Hazmi and Warsy,[2] in which no significant differences in RBC count were noted between males and females. This outcome could be due to nutritional status, menarche age, or may be due to ethnic differences between Malaysian and Saudi adolescent populations. This issue needs to be further explored. Nevertheless, the current findings concur with those reported from the National Health and Nutrition Examination Survey (NHANES) study on adolescents from the USA and data from Spain[12], revealing that males show significantly higher RBC indices than females. These differences could be due to the influence of the endocrine disruption during puberty, hormone androgen on erythropoiesis, and menstrual losses.[13]

The values of total WBC count for males and females showed statistically significant variation. The current study observed significant differences in WBC differentials percentages between males and females. However, there is minimal literature on WBC value ranges for adolescents. Regarding WBC count, the current study showed higher mean values for males and females than those reported for Ethiopia, Kenya, and Brazil[14–16] adolescents. However, in Saudi Arabia,[2] the WBC values reported in males are higher than in the current study (Table III). These findings are supported by previous studies implying that haematological values are affected by several factors such as ethnic background and incidence of infections and parasitosis.[1,17]

Moreover, there was a statistically significant difference in platelet count between the two sexes in this study. The platelet count reported in Japanese, Kenya, Spain, and Brazil studies in adolescents is lower than in the present study.[12,15,16,18] The present study observed higher platelet counts in females than in other studies (Table III). A few studies have demonstrated gender-dependent differences in platelet count.[19,20] In women, the platelet count is higher than in men, reflecting different hormonal profiles or a compensatory mechanism associated with menstrual blood loss.[20]

Higher WBC and platelet count were observed in the present study compared to other population ranges for adolescence. The exact cause is unknown; however, the influence of environmental, genetic factors or undetected subclinical illness cannot be ruled out. Gender-based differences in the total WBC, neutrophil, and platelet counts have been reported in all ethnic groups and could be related to biological differences.[19] For ethnic groups, reference values for common haematological investigations are usually not

established separately. However, various studies have shown that racial/ethnic differences in reference values of various laboratory tests were mainly between blacks and whites[19,21] Whites show significantly higher values than blacks for total WBC, neutrophil counts,[22] platelet counts,[19] HCT, MCHC, MCH, and Hb,[22] and significantly lower mononuclear and lymphocyte percentages. In the current study, the RBC count, platelet count, PDW, and MPV showed a statistically significant difference between the Malays, Chinese, and Indians (Table II). These differences could be associated with genetic variations in these ethnicities.

Malaysia has a multiracial population. A study from Malaysia[4] compared haematological intervals in multiethnic adult subjects; however, they concluded that there were no ethnic-specific differences. Haniff et al.,[22] from their multicentre analysis of pregnant females, found that the average Hb level of the Malays was significantly lower than the Chinese. However, in the current study, the RBC indices showed no statistically significant ethnic difference for Hb, MCV, MCH, and MCHC values (Table II).

The RBC count was significantly higher in Chinese than in Malays and Indians. However, the magnitude of the differences was small. The high RBC count in Chinese could be due to obesity, lifestyle behaviour, or a sign of underlying illness; however, it does not always show a medical condition.[24] We did not record the BMI of subjects in this study; therefore, the correlation of high RBC count with BMI is lacking in this study. We also observed a significantly lower platelet count in Indians compared to Malays. The exact reason for low platelet count is not well studied, but the influence of genetic, dietary, and environmental factors can be speculated as reported in other studies.[25,26] Researchers from India in 2014 reported regional differences in platelet count and observed low platelet count in Chennai compared to other regions of India.[27] Indians in Malaysia have ancestors who migrated mainly from regions in South India,[28] such as Chennai. This genetic influence may account for the lower platelet count. Nevertheless, this study proposes that all these ethnicity-based differences are not clinically significant as the values are still within the normal range for RBC and platelet count.

The comparative published data on racially based differences in platelet count is sparse. The differences in mean platelet count related to ethnicity, gender, and age are not clearly explained by variables known to impact platelet count. Instead, these differences could be explained by genetic influences on the platelet count.[23] Compared with Caucasian ranges, lower platelet counts have been confirmed for Africans and Afro-Caribbean women.[18,24] These differences are sufficient to be of practical importance in interpreting counts around the lower end of the reference range. In this study, platelet count was higher in Malays than in Chinese and Indians. Mean platelet count showed statistically significant differences among ethnicities. Malays showed lower MPV than the other two ethnicities (Table III).

Strengths and Limitations

This study is one of the few studies for this age group reporting the laboratory values for haematological parameters and RBC indices in adolescents in Malaysia. It remains the key strength of this study. Ambayya e al4 included this age group as part of their data; however, data were not stratified for this age group. Therefore, the normal or expected values for this age group were not known. These findings of the normal haematological values could contribute to the body of knowledge and help physicians provide greater precision in diagnosis to offer the right intervention and treatment of related diseases in adolescents.

Another limitation was that this study was confined only to the three major ethnic groups (Malay, Chinese, and Indian) and did not include the other ethnicities in the country. The data captured FBC values for adolescents aged 15-16 years old and not the entire adolescent population age group.

CONCLUSION

There were statistically significant gender-based differences for total WBC count, neutrophils, lymphocytes, mixed WBC, and platelets. Gender, independently or interactively, can determine differentials in disease burden, and their blood parameter values may influence early diagnoses and interventions. It was also observed that ethnic-specific differences were statistically significant for RBC count, platelets, PDW, and MPV. This study could be an impetus for further follow-through studies to develop a home-based Malaysian Reference Interval standard that can be used nationwide.

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INSTITUTIONAL REVIEW BOARD STATEMENT

The study was conducted in compliance with ethical principles outlined in the Declaration of Helsinki as revised in 2013. Also, ethical approval was obtained from Medical Research & Ethics Committee (MREC # KKM/NIHSEC/ P20-2406 (4) dated 01-Dec-2020). All information collected was strictly confidential, and anonymity was ensured.

INFORMED CONSENT STATEMENT

Permission was obtained from Seremban District Health Office to use this secondary data. However, individual consent from parents was not taken as this data was collected in 2018. However, steps have been taken to anonymise the data for this study.

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CONFLICTS OF INTEREST

The authors declare no conflict of interest.

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