SRYAHWA PUBLICATIONS

Archives of Hematology and Blood Diseases
ISSN: 2639-3581 | Volume 6, Issue 1, 2024
https://doi.org/10.22259/2639-3581.0601001

RESEARCH ARTICLE

Expression of Rh-C, Rh-c Antigens and Platelets Indices in an Undergraduate Student's Population in Port Harcourt Nigeria

Evelyn Mgbeoma Eze[1], Ransom Baribefii Jacob[1]*, Patricia Ibitein Anga[1], Legborsi Robinson-Mbato[2], Nelyn Akunna Okoye[3]

[1]Faculty of Medical Laboratory Science, Department of Haematology and Transfusion Science, Rivers State University, Port Harcourt, Nigeria.

[2]Faculty of Basic Medical Science, Department of Nursing, Rivers State University, Port Harcourt, Nigeria.

[3]Rivers State University Hospital Services Department Port Harcourt, Nigeria.

Received: 22 February 2024 Accepted: 29 February 2024 Published: 13 March 2024

Corresponding Author: Jacob, Ransom Baribefii, Faculty of Medical Laboratory Science, Department of Haematology and Transfusion Science, Rivers State University, Port Harcourt, Nigeria.

Abstract

The Rhesus blood group system remains the second most clinically significant blood group system after the ABO blood group system in transfusion medicine with high prevalence of its antigens clinically implicated in transfusion reactions and haemolytic disease of the new born. Platelets indices and Platelet/lymphocyte ratio is an inexpensive biomarker for accessing platelets activation, novel inflammatory marker for predicting inflammation. This cross-sectional study was carried out to determine Rh-C, Rh-c antigens, platelets indices and platelets/lymphocyte ratio amongst apparently healthy undergraduate student's population in Port Harcourt Nigeria. A total of one hundred and fifty (150) students comprising of 76 males and 74 females aged between 17-30 years were recruited for the study. A well-structured questionnaire was used to obtain the demographic information of each participant. Five millilitres (5 ml) of blood was collected from each participants using standard venipuncture techniques. Rh-C and Rh-c blood group antigens was determined using the Micro-titre agglutination technique; Platelet indices was assayed using Mindray automated analyzer and platelet/lymphocyte ratio calculated from the full blood count results. Data obtained was statistically analysed using Statistical Package for Social Science (SPSS) version 23. Amongst the 150 participants studied, 123 (82%) expressed the Rh-c while 31 (20.6%) expressed Rh-C antigens indicating that the Rh-c is more prevalent in the population. Mean±SD of Platelets count, Mean Platelets Volume (MPV), Platelets Distribution Width (PDW) and Plateletcrits (PCTs) in male and females were (210.9±6.94 versus 239.8±9.22fl); (9.74±0.77% versus 10.51±1.38%); (15.99±0.44 versus 15.8±0.45fl) and (0.21±0.06%, versus 0.25±0.07%) in the same order. This study has successfully provided prevalence rate for Rh-C and Rh-c antigens; baseline data/reference interval for Platelet Indices and Platelet/Lymphocyte ratio amongst undergraduate students of Rivers State University. It is therefore recommended that screening for Rh-C and Rh-c antigens be carried out on students prior to transfusion and Platelet indices and Platelet/Lymphocyte Ratio be accessed in cases of coagulation and inflammatory disorders in order to guide therapy.

Keywords: Rhesus Antigens, Platelets Indices, Platelets/Lymphocyte Ratio.

Citation: Evelyn Mgbeoma Eze, Ransom Baribefii Jacob, Patricia Ibitein Anga *et al*. Expression of Rh-C, Rh-c Antigens and Platelets Indices in an Undergraduate Student's Population in Port Harcourt Nigeria. Archives of Hematology and Blood Diseases. 2024; 6(1): 1-7.

1. Introduction

The Rhesus (Rh) blood group system remains the second most clinically significant blood group system after the ABO blood group system in transfusion medicine with high prevalence of its antigens clinically implicated in transfusion reactions and haemolytic disease of the new born. Platelets indices and Platelet/lymphocyte ratio is an inexpensive biomarker for accessing platelets activation, novel inflammatory marker for predicting inflammation.

Rhesus antigen is clinically importance in Rhesus D negative individuals in subsequent transfusions once they develop Rhesus antibodies and thus its incompatibilities have the potential of causing a major problem in some pregnancies when the mother is Rhesus negative and the foetus is Rhesus positive (1).

The Rh blood group system consist of 49 defined blood group antigens, among which the five antigens D, C, c, E, e, are the most important (2,3,4,5). Report in literature shows that the Rh antigens C, c, E, and e are not so immunogenic but are highly important in patient care upon the development of the corresponding antibody (6). Research by Yazer and Triulzi (7) shows that detection of anti-E suggests the presence of anti-c due to combine genetic inheritance, implying that E and c antigens are likely to be inherited together, based on Rh haplotypes.

Also detecting anti-E raises suspicion for formation of anti-c, as seen in most cases that patients sometimes form both. Anti-c antibodies arise through previous exposure through fetomaternal haemorrhage or previous transfusion and are capable of producing acute or delayed haemolytic reactions (2, 8).

Platelets is a universal indicator of haemostasis in a clinical setting and is utilized as a sensitive biomarker for a range of diseases. They are mainly seen as small cell fragments that clumped together at an injured blood vessel site, and circulate as anucleate dynamic specialized cells, formed in an elaborate style from its precursor cell, the megakaryocyte (9, 10). They contain granules that are generally secretory in nature and can release their contents either to the platelet surface or to extracellular fluid by endocytosis (11). The granules are capable of storing high concentrations of non-protein molecules such as adenosine diphosphate (ADP), adenosine triphosphate (ATP), calcium, histamine, polyphosphate and serotonin that potentiate platelet activation (12, 13).

Normal platelet counts ranges between 150-450 × 10^3 per microliter of blood, constituting the second most abundant cell type in blood after red blood cells. The size of a mature platelet is approximately 2–4 μm, making them the smallest cells in circulation, while their average thickness is 0.5 μm and their volume about 7 μm^3 (14).

Platelet indices are useful as inexpensive non-invasive biomarkers for assessing platelet activation (15). Platelet indices are straightforwardly measured by semi-automated counters in complete blood counts (CBC) and usually include four factors; platelet count (PLT), mean platelet volume (MPV), platelet distribution width (PDW), plateletcrit (PCT), and depending on the analyser, platelet large cell ratio (PLCR). The indices MPV, PDW and PLCR are quantitative measures of the variability in platelet size. MPV reflects the average platelet size while PDW reflects the volume variability in platelet size (16, 17, 18).

Platelet/Lymphocyte ratio is a novel inflammatory marker that can be used in many diseases for predicting inflammation and mortality. It can be calculated by platelets count divided by absolute lymphocyte count (19). Platelets lymphocyte ratio is found to be a useful index to evaluate rheumatoid arthritis (RA) disease activity and response to biologic therapy (20), It is useful in evaluating deep venous thrombosis (21). Research of Asahina et al., (19) suggest that Platelets lymphocyte ratio may be useful markers to evaluate systemic inflammation in psoriatic patients and serve as simple, convenient and cost-effective biomarkers to monitor the disease course after systemic therapy.

Rhesus antigen is a major threat during blood transfusion if unknown can lead to transfusion reactions. Abnormality in Platelets count, Platelet indices and Platelet Lymphocyte ratio is a pointer to clotting defect, predictor of inflammation and mortality. However, the Rh-C antigen status, Platelet indices and Platelet Lymphocyte ratio of undergraduate students of Rivers State University are yet to be accessed and documented. This study is thus aimed at synthesizing scientific information on the Rh-C, Rh-c antigen status, Platelets and Platelet indices values as well as Platelet/Lymphocyte ratio of undergraduate students of Rivers State University Port Harcourt Nigeria with the view of enhancing better treatment and management in case of blood transfusion.

2. Materials and Methods

2.1 Study Design/Population

This cross-sectional study aimed at determining Rh-C, Rh-c Antigens and Platelets Indices in an

Undergraduate Student's Population in Port Harcourt Nigeria was carried out within August-November, 2022 with a total of one hundred and fifty (150) apparently healthy male and female participants aged between 17 to 30 years recruited through well-structured questionnaire.

2.2 Sample Collection, Transportation, Processing and Preservation

Five (5) millilitres (ml) of venous blood sample were collected from each participants through venepuncture techniques and three (3) millilitres (ml) dispensed into ethylene diamine tetraacetic acid (EDTA) vacutainer bottle while two (2) millilitres (ml) was dispensed into plain bottle and transported under recommended condition to the laboratory for determination of platelets indices and Rh-antigens.

2.3 Methodology

Estimation of Platelets Count and Lymphocyte count was carried using BC 5000 Mindray Hematology Auto-Analyzer and Platelets/lymphocyte ratio calculated and Rh-antigens was carried out using Micro-titre agglutination technique.

2.3.1 Determination of Rh-C and Rh-c Antigen Using Micro-Titre Agglutination Technique

Phenotyping of red cells was done using Micro-titre Agglutination technique as described by Lorne laboratory Ltd. A 5% suspension of red blood cell was prepared using normal saline. 20 µl of anti-Rh-C antibodies were added unto separate micro-titre plate, and 20 µl washed red cell was added into the micro-titre plate containing the anti-Rh-C antibodies. The sample was incubated for 15 minutes with intermittent rocking and observation for agglutination every 30 seconds. If no agglutination was found after 30 minutes, 20 µl of AHG antibody was added and observed for 15-30 minutes. Confirmation of agglutination and no agglutination was done by placing the sample on a slide and viewed microscopically. Presence of agglutination indicates a positive result and absence of agglutination indicates a negative result.

2.3.2 Calculation of Platelet/Lymphocyte Ratio

Platelets/lymphocyte ratio was calculated by dividing absolutes values of platelets count and lymphocyte count estimation from full blood count haematology autoanalysers. This was done by respective calculation and multiplying lymphocyte values by white blood cell count and dividing by 100 and then dividing the results of platelet count by lymphocytes.

2.4 Data Analysis

Data was statistically analyzed using Statistical package for Social Sciences (SPSS) version 23 and results presented as mean ± SD with statistical significance set at $P<0.05$.

3. Results

3.1 Demographic Data of Studied Participants

Table 1 shows a total of one hundred and fifty (150) subjects were enrolled for the study, comprising of seventy-six (76) male and seventy-four (74) female participants aged between 17-30years.

Table 1. *Demographic Data of Studied Participants*

Parameters	Frequency (%)
Age range in years	17-30
Male	76(50.7%)
Female	74(49.3%)
Total	150

3.2 Percentage Expression of Rhesus Factor

Among the 150 participants in the study, 31 (20.7%) [11 (35.5% female and 20 (64.5%) male] were positive for Rh-C antigen, while 119 (79.3%) [were negative and did not express Rh-C on their red cell. 123 (82%) were positive for Rh-c antigen and 27 (18%) were negative for Rh-c antigens and did not express Rh-c on their red cell as shown in Table 2.

Table 2. *Percentage Expression of Rhesus Factors*

Rhesus Antigen	Male (n=76)	Female (n=74)	Frequency (%)
Rh-C Positive	11	20	31 (20.7)
Rh-C Negative	65	54	119 (79.3)
Rh-c Positive	64	59	123 (82)
Rh-c Negative	12	15	27 (18)

Key. *Rh-C= Rh-C antigen, Rh-c= Rh-c antigen, n= Number of participants.*

3.3 Platelets Count, Platelets Indices and Platelets/Lymphocytes Ratio in Study Population Based on Sex

Table 3 shows a comparison of Platelets Count, Platelets Indices and Platelets/Lymphocytes Ratio in study population based on Sex. There was a statistically significant difference in the mean ± STD of Platelet Count for males (239.8 ± 9.22) and females (210.9 ± 6.94) (p= 0.0129), MPV for males (10.51 ± 1.38fl) and females (9.74 ± 0.77fl) (p<0.0001). PDW for males (15.8 ± 0.45%) and females (15.99 ± 0.44%) (p=0.0115). PCT for males (0.25 ± 0.07%) and females (0.21 ± 0.06%) (p=0.005) respectively. Platelet Lymphocyte Ratio (PLR) for males (102.8 ± 4.23) and females (96.69 ± 4.05) showed no statistically significant difference (p=0.2971) respectively as shown in Table 3.

Table 3. *Platelets Count, Platelets Indices and Platelets/Lymphocytes Ratio in Study Population Based on Sex*

Parameter	Female (n=74)	Male (n=76)	p-value	Remark
PLT (x10^9)	239.8 ± 9.22	210.9 ± 6.94	0.0129	S
MPV(fl)	10.51 ± 1.38	9.74 ± 0.77	<0.0001	S
PDW%	15.8 ± 0.45	15.99 ± 0.44	0.0115	S
PCT%	0.25 ± 0.07	0.21 ± 0.06	0.0005	S
PLR	102.8 ± 4.23	96.69 ± 4.05	0.2971	N

Key. *PLT= Platelets, MPV= Mean Platelets volume, PDW= Platelets distribution width, PCT= Plateletcrits, PLR= Platelets/lymphocytes ratio and n= No of participant, S= Significant at p<0.05, N= Not Significant at p<0.05*

3.4 Reference Values of Measured Parameters in the Study.

The Mean ± STD of Platelets (225.20 ± 5.85 x10^9) Reference Values (213.50 - 263.90 x10^9), Mean Platelet Volume (MPV) (10.12 ± 1.17fl) Reference Values of (7.78 - 12.46 fl), Platelet Distribution Width (PDW) (15.90 ± 0.46%) Reference Values (14.98 - 16.82%), Plateletcrit (PCT) (0.23 ± 0.07%) Reference Values (0.09 - 0.37%) and Platelet Lymphocyte Ratio (PLR) (99.71 ± 2.93) Reference Values (93.85 - 105. 57) in the same order were obtained as shown in Table 4.

Table 4. *Reference Values of Measured Parameters*

Parameter	Mean ± STD	Reference Values
PLT (x10^9)	225.20 ± 5.85	213.50 – 263.90
MPV (fl)	10.12 ± 1.17	7.78 – 12.46
PDW (%)	15.90 ± 0.46	14.98 – 16.82
PCT (%)	0.23 ± 0.07	0.09 – 0.37
PLR	99.71 ± 2.93	93.85 – 105.57

Key. *PLT= Platelets, MPV= Mean Platelets volume, PDW= Platelets distribution width, PCT= Plateletcrits, PLR= Platelets/lymphocytes ratio and n= 150*

4. Discussion

This study evaluated the percentage expression of Rhesus antigen (Rh-C and Rh-c), Platelets and Platelets Indices and platelet/Lymphocyte ratio in an undergraduate student's population in Port Harcourt Nigeria.

In the study, a percentage positivity for Rh-C and Rh-c was 20.7% and 82% respectively while 119 (79.3%) and 27 (18%) were negative and did not express Rh-C and Rh-c on their red cell. This indicates that the Rh-c is most prevalent amongst the study population. The high percentage expression in this study is not unconnected with the non-inclusion of these antigen in pre-screening processes prior to transfusion and this could be responsible for the increased exposure to the antibodies among the study population. Also, there is a relatively low awareness campaign and sensitization for other Rh-antigens other than Rh-D. Awareness on the clinical relevance of Rh-C, Rh-c in haemolytic reactions and transfusion medicine is low and thus little or no attention is given to it in routine screening thus the antigens freely circulates in the population unscreened and undetected. Also the high cost of the antisera used for this analysis is another limiting factor for pre-screening for these Rh-antigens thus their continuous circulation in the population accounting for the high prevalence observed in this study.

Results from this study is a further indication that Rh-c is predominant in descent of Port Harcourt and in agreement with the research of Jacob et al. (2), who evaluated the percentage expression of Rhesus antigen among multiparous women in Port Harcourt Nigeria. The percentage positivity of Rh-c recorded in this study is lower than the 93.3% observed by Jacob et al. (4) in their study population. Adedoyin et al. (22) who reported percentage positivity of 97% in their study and Erhabor et al. (23) who reported 92% for Rh-c antigens in their study population.

Comparison of the values of platelets and platelets indices based on sex shows significant difference in the study population. However, there was no significant difference in the values of platelets/lymphocytes ratio indicating that sex does have significant effect on platelets count, mean platelets volume, platelets distribution width and plateletcrit but not on the platelets lymphocytes ratio.

The observation in this study is in tandem with the findings of Zuo and Yang, (24), who in their study observed a similar changes in the PLT, MPV, PDW and PCT in their study population. However, finding in this study is discordant with another study by Krenn-Pilko et al. (25) and You et al. (26), who in their independent studies observed and recorded a non-significant difference in PDW and PCT but a significance in other platelet parameters. This variation could be as a result of sample size used in their study, ethnicity and environmental related conditions such as altitude capable of causing derangement in haematological parameters. Findings in this study showed that reference values for measured parameters were within normal established reference ranges. This is indicative of the fact that the study participants have normal haematological reference values and are devoid of any haematological related blood disorders. This finding is in agreement with previous study carried out by Giacomini et al. (27) and Adibi et al. (28) on the reference ranges of Platelets and Platelets indices.

5. Conclusion

This study has successfully provided prevalence rate for Rh-C and Rh-c antigens and baseline data/ reference range for Platelet Indices and Platelet/ Lymphocyte ratio amongst undergraduate students of Rivers State University. Also reference values for measured parameters were within normal established reference ranges. This is indicative of the fact that the study participants have normal haematological reference values and are devoid of any haematological related blood disorders.

6. Recommendation

Based on the findings in this study, it is recommended that screening for Rh-C and Rh-c antigens be carried out on students prior to blood donation and transfusion and that the Platelet, Platelet indices and Platelet/ Lymphocyte ratio be assessed in cases of coagulation and inflammatory disorders in order to guide therapy for the benefit of the students. Strong advocacy for pre-transfusion screening for those population that tested negative to these blood group antigens is recommended since they have the potential to be alloimmunized during blood transfusion and can develop antibodies, some of which can be responsible for transfusion reaction and haemolytic disease of the new born when not screen for.

Competing Interests

The authors declare that there are no competing interests regarding the publication of this paper.

Funding Statement

There was no funding for this case report.

Acknowledgements

We thank the technical staff of Haematology and Blood Transfusion Science Department, Rivers State University Port Harcourt, Nigeria.

7. References

1. Egesie, U.G., Egesie, O. J., Usar, I. & Johnbull, T. O. (2008). Distribution of ABO, Rhesus Blood Groups and Haemoglobin Electrophoresis among the Undergraduate Students Of Niger Delta University Nigeria. Nigerian Journal of Physiological Sciences, 23 (1-2), 5 - 8.
2. Jacob, R. B., Eboh, C., ThankGod, S.D. & Moore-Igwe, B.W. (2023). Rhesus (Rh) Blood Group Antigens in Multiparous Women Attending Antenatal Clinic in Tertiary Hospital, Port Harcourt Nigeria. Haematology and Transfusion International Journal, 11(1),16-20.
3. Dean, L. (2005). Blood Groups and Red Cell Antigens. National Center for Biotechnology Information.
4. Jacob, R.B., Azia,M.G., Christian, S.G., Robinson-Mbato, L. & Eze, E.M. (2021). Prevalence of Lewis A, Rh-c, M and ABO/Rh-D Antigens in Bonny Kingdom Rivers State Nigeria.Journal of Medical and Dental Science Research, 8(6), 15-21. www.questjournals.org.

5. Owaidah, A. Y., Naffaa, N. M., Alumran A. & Alzahrani F. (2020). Phenotype frequencies of major blood group systems (Rh, Kell, Kidd, Duffy, MNS, P, Lewis, and Lutheran) among blood donors in the eastern region of Saudi Arabia. Journal of Blood Medicine, 11, 59-65.
6. Jacob, R. B., Akan, M. N., Robinson-Mbato, L., Christian, S. G., Olusola, O. A. & Eze, E. M. (2022). Expression of Kidd, Rh-C, E and D Antigen among Indigenes of Bobby Kingdom, Nigeria. Journal of Blood Disorders and Transfusion, 13, 492.
7. Yazer, M. H., Triulzi,D. J.(2007).Detection of anti-D in D–recipients transfused with D+ red blood cells. Transfusion, 47(12), 2197-2201.
8. Wagner, F.F and Flegel, W.A. (2000). RHD gene deletion occurred in the rhesus box. Blood, 95(12), 3662–3668.
9. Thon, J.N., Peters, C.G., Machlus, K. R., Rowley, J. & Macleod, H. (2012). Granules in human platelets function in TLR9 organization and signaling. The Journal of Cell Biology, 198(4), 561-574.
10. Patel, S., Dhillon, M. S., Aggarwal, S., Marwaha, N., & Jain, A. (2013). Treatment with platelet-rich plasma is more effective than placebo for knee osteoarthritis: A prospective, double blind, randomized trial. The American Journal of Sports Medicine, 41(2), 356-364.
11. Blair, P. & Flaumenhaft, R. (2009). alpha-granules: Basic biology and clinical correlates. Blood Reviews, 23(4), 177-189.
12. Ruiz, F. A., Lea ,C. R., Oldfield, E. & Docampo, R. (2004). Human platelet dense granules contain polyphosphate and are similar to acidocalcisomes of bacteria and unicellular eukaryotes. The Journal of Biological Chemistry, 279(43), 44250-44257.
13. Morrell, C. N., Aggrey, A. A., Chapman, L. M. & Modjeski, K. L. (2014). Emerging roles for platelets as immune and inflammatory cells. Blood, 123(18), 2759-2767
14. Xu, X.R., Zhang, D., Oswald, B. E., Carrim, N., Wang, X. & Hou, Y. (2016). Platelets are versatile cells: New discoveries in hemostasis, thrombosis, immune responses, tumor metastasis and beyond. Critical Reviews in Clinical Laboratory Sciences, 53(6), 409-430.
15. Budak, Y. U., Polat, M. & Huysal, K. (2016). The use of platelet indices, plateletcrit, mean platelet volume and platelet distribution width in emergency non-traumatic abdominal surgery: A systematic review. Biochemia Medical, 26(2), 178-193.
16. Wiwanitkit, V. (2004). Plateletcrit, mean platelet volume, platelet distribution width: its expected values and correlation with parallel red blood cell parameters. Clinical Applied Thrombotic Haemostasis, 10, 175–178.
17. Khandekar, M. M., Khurana, A. S., Deshmukh, S. D., Kakrani, A. L., Katdare, A. D. & Inamdar A. K. (2006). Platelet volume indices in patients with coronary artery disease and acute myocardial infarction: An Indian scenario. Journal of Clinical Pathology, 59(2), 146-149.
18. Vagdatli, E., Gounari, E., Lazaridou, E., Katsibourlia, E., Tsikopoulou, F. & Labrianou, I. (2010). Platelet distribution width: A simple, practical and specific marker of activation of coagulation. Hippokratia, 14(1), 28-32.
19. Asahina, A., Kubo, N., Umezawa, Y., Honda, H., Yanaba, K. & Nakagawa, H. (2017). Neutrophillymphocyte ratio, platelet-lymphocyte ratio and mean platelet volume in Japanese patients with psoriasis and psoriatic arthritis: Response to therapy with biologics. Journal of Dermatology, 44(10), 1112–11121.
20. Sargin, G., Senturk, T., Yavasoglu, I. & Kose, R. (2018). Relationship between neutrophil-lymphocyte, platelet-lymphocyte ratio and disease activity in rheumatoid arthritis treated with rituximab. International Journal of Rheumatic Disease, 21(12), 2122–2127.
21. Velioglu, Y. & Yüksel, A. (2019). Utility of Platelet-to-Lymphocyte Ratio to Support the Diagnosis of Acute Deep Vein Thrombosis. Turk. Gogus Kalp Damar Cerrahisi Derg, 27, 493–498.
22. Adewoyin, A.S., Lee, G.M., Adeyemo, T.A, et al. (2018). Rh and Kell blood group antigen prevalence in a multi-ethnic cohort in Nigeria: implications for local transfusion service. Immunohematology, 34(2), 61–65.
23. Erhabor, O., Okwesili, A., Aliyu, B.S., et al. (2016). Prevalence of rhesus c and e phenotype among pregnant women attending antenatal clinic in Usmanu Danfodiyo University Teaching Hospital, Sokoto. Journal of Gynecology and Neonatal Biology, 2(1), 13–16.
24. Zuo, K. & Yang, X. (2020). Decreased Platelet-to-Lymphocyte Ratio as Predictor of Thrombogenesis in Nonvalvular Atrial Fibrillation. Herz , 45, 684–688.
25. Krenn-Pilko, S., Langsenlehner, U., Thurner, E. M., Stojakovic, T., Pichler, M., Gerger, A., Kapp, K.S. & Langsenlehner, T. (2014). The Elevated Preoperative Platelet-to-Lymphocyte Ratio Predicts Poor Prognosis in Breast Cancer Patients. Journal of Cancer, 110, 2524–2530.
26. You, J., Zhu, G. Q., Xie, L., Liu, W. Y., Shi, L., Wang, O. C., Huang, Z. H., Braddock, M., Guo, G. L. & Zheng, M. H. (2016). PreoperativePlatelet to

Lymphocyte Ratio Is a Valuable Prognostic Biomarker in Patients with Colorectal Cancer. Oncotarget, 7, 25516–25527.

27. Giacomini, A., Legovini, P., Gessoni, G., Antico, F., Valverde, S. & Salvadego, M.M. (2001). Platelet count and Parameters determined by the Bayer ADVIA 120 in reference subjects and patients. Clinical Laboratory of Haematology, 23, 181-186.
28. Adibi, P., Faghih, Imani, E., Talaei, M. & Ghanei, M. (2007). Population-based Platelet reference values for an Iranian Population. Journal of laboratory Haematology, 29, 195-199.