Original Article

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Determination of Reference Intervals for Platelet Parameters using Sysmex XN-1000 among South Indian Population

Pathology Section

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ABSTRACT

Introduction: Reference intervals are important for interpretation of clinical laboratory tests. The platelet parameters are recently reported newer haematological parameters and serve as clinically valuable biomarkers. It provides further information on platelet morphology and proliferation kinetics. The lack of information from manufacturers about the geographical reference ranges for the Complete Blood Count (CBC) parameters highlights the need for laboratories to establish reference intervals.

Aim: To determine the reference interval for platelet parameters using Sysmex XN-1000 haematology analyser in South Indian population.

Materials and Methods: This retrospective record-based study was carried out from July 2021 to September 2021 and the data was retrieved from a continuous 12-month period (November 2018-October 2019) in the Haematology Laboratory at a tertiary care dental hospital, Chennai, Tamil Nadu, India. The data of CBC parameters were retrieved from the Sysmex XN-1000 analyser and a total of 1,883 reports labelled as negative/unflagged were included in the study. The reference intervals for platelet parameters which include Mean Platelet Volume (MPV), Platelet Distribution Width (PDW), Platelet Large Cell Ratio (P-LCR) and Plateletcrit (PCT) for male and female subjects were compared using the Mann-Whitney U-test. Kruskal-Wallis test was used to compare between the different age groups using Statistical Package for the Social Sciences (SPSS) version 24.0 software.

Results: The data for the platelet parameters are shown as median, with statistically significant difference in the reference interval for all the parameters with gender ($p<0.001$). There was no significant difference in age divided reference intervals, except for PCT (p-value=0.04). PDW was found to be 9-16.4 fL for males and 9.1-16.6 fL for females (p-value<0.001). Similarly, MPV was 9-12.3 fL for males and 9-12.6 fL for females (p-value <0.001); P-LCR was 16-42.1% for males and 16.6-43% for females (p-value <0.001); and PCT was 0.15-0.36% for males and 0.14-0.41% for females (p-value <0.001).

Conclusion: The study has determined the reference interval for platelet parameters with respect to age and gender in area specific population and these results can be utilised for other laboratories using the same analyser system for South Indian population.

Keywords: Mean platelet volume, Platelet indices, Platelet distribution width, Platelet larger cell ratio, Plateletcrit

INTRODUCTION

Automated cell counter was introduced in 1953 to overcome the disadvantages encountered in manual methods as it provides rapid, accurate, and precise CBC results [1,2]. Modern blood counting instruments are able to provide both quantitative and qualitative measurements of the cellular components of the blood. The Sysmex XN-1000 (Sysmex Corporation XN-series, Kobe Japan) is an advanced fully automatic haematology analyser which can determine many novel parameters together with CBC. Platelet parameters obtained as a part of automatic CBC has gained importance in the field of medicine owing to their potentialities in various diseases and disorders.

Concept of the reference interval was introduced by Grasbeck R and Saris NE in 1969 [3]. Reference interval is defined as the interval between and including two reference limits [4]. Reference intervals established by different manufactures may not be suitable across laboratories. According to the recommendations of International Federation of Clinical Chemistry and Laboratory Medicine (IFCC) and Clinical and Laboratory Standard Institute (CLSI), each laboratory has to establish its own reference interval [5]. Therefore, it is important to establish local reference interval for any blood parameter based on the type of haematology analyser, technique employed and the local population. MPV, PDW, P-LCR and PCT are a group of derived platelet parameters acquired as a part of the automatic CBC along with total platelet count [6]. However, various factors like age, gender, geographic locations, season etc., can influence the platelet parameters and hence it is important to define the precise reference intervals.

The lack of information from manufacturers about the geographical reference ranges for the CBC parameters highlights the need for laboratories to establish reference intervals for the CBC, using their own equipment and routines. The importance of this study relies on the usefulness of these results for other laboratories using this analyser system for South Indian population.

There are many analysers that are available across the globe extending its support to physicians and the people throughout the world. Coulter counter, Technicon Instruments Corporation, Ortho Diagnostics, Instrumentation Laboratories and Toa Medical Electronics, (presently Sysmex Corporation) were the pioneer manufactures of haematology analysers [7]. The analysers manufactured by Sysmex Corporation includes XN series (XN-1000, XN-2000, 3000, XN- Vet), XN SERIES systemisation (XN-1500, XN-3000, XN-3200, XN-9000, XN-9100, DI-60) XN-L series (XN-330, XN-350, XN-450, XN550), XP series (XP-100, 300) [8].

To avoid instrument bias (the principle used, reagents and calibrations) the study compared the reference intervals with studies done using Sysmex XN-1000 only. Hence, this study aimed to determine the reference interval for platelet parameters using Sysmex XN-1000 haematology analyser in South Indian population. The objectives of the study include: (i) To determine the reference intervals for platelet parameters (MPV, PDW, P-LCR and PCT) in South Indian population. (ii) To compare the reference intervals between the different age groups. (iii) To compare the reference intervals between males and females.

MATERIALS AND METHODS

This retrospective record-based study was carried out from July 2021 to September 2021 and the data was retrieved from a continuous 12-month period (November 2018-October 2019) in the Haematology laboratory, at a tertiary care Government Dental Hospital, Chennai, Tamil Nadu, India. The Institutional Ethics and Review Board had approved the study protocol (NO: 5/IRB/2019).

Inclusion criteria: The study included subjects who were ≥18 years (18-85 years), of both genders were included. The age groups were stratified as recommended by World Health Organisation (WHO) for population surveys [9]. In addition, this study also includes subjects older than 74 years (middle-old and oldest-old) [10]. The data of CBC parameters from the Sysmex XN-1000 analyser were analysed and only the reports within the normal reference interval were also included in the study.

Exclusion criteria: The reports of study subjects labelled "positive/flagged" were excluded, and also, the repeat results were excluded, so that each patient contributes only one result to the dataset.

Procedure

Haematology analysers generate suspect flags in the presence of abnormal cells. The abnormal cells differ in the following aspects such as cell and nuclear size, altered granular content and abnormal cell count. In the presence of abnormal cells, most instruments generate an "abnormal" cell or "suspect" flag. By combining the pattern abnormalities from four different channels {White cell Nucleated Channel (WNR), White cell Differentiated Channel (WDF), Platelet count-Fluorescent channel (PLT-F) and White cell Precursor Channel (WPC)} the flags are generated by the XN analysers. WNR channels detect platelet clumps, abnormal White Blood Cells (WBC) and nucleated Red Blood Cells (RBC). Atypical lymphocytes and blast are detected by WDF channels while platelet and platelet clumps are identified by PLT-F channel. WPC is used only when abnormal lymphocyte or blast was detected [11].

Out of 6,650 subjects only 1,883, satisfied the inclusion criteria. The data of the platelet parameters, which include PDW (fL), MPV (fL), P-LCR (%), and PCT (%), were retrieved from the Sysmex XN-1000 automated haematology analyser. The samples from all the consecutive subjects included 2 mL of venous blood collected in Ethylene Diaminetetraacetic Acid K2 (EDTA K2) tubes in the haematology laboratory, were uniformly processed within 3 hours of collection and analysed on Sysmex XN-1000. XN-trilevel quality control check was done before processing the samples.

SYSMEX XN-1000: The Sysmex XN-1000 (Corporation XN-series, Kobe Japan) is an advanced fully automatic haematology analyser which can determine many novel parameters together with CBC [12]. Sysmex XN-series device, a quantitative multiparameter automated analyser with the test principle of hydrodynamic focusing (DC detection), flow cytometry method (using a semi-conductor laser), and Sodium Lauryl Sulphate (SLS) haemoglobin method. More preferably, Sysmex XN-1000 is a low volume six-part analyser (5-part differential and nucleated red blood cell count) used for quantitative analysis of haematological parameters [13].

The quality control check was done by XN check trilevel before the start of the machine. XN calibrator was used once in a year. The blood is collected by venepuncture in K2 EDTA tube. The tubes are arranged in racks and the number of samples that can be processed is minimum of 100/hour. Two modes are available namely the manual and semi-automatic modes. In the manual mode, a single sample can be studied in case of emergency. Racks loaded with the sample test tubes are either placed on automated racks or inserted directly into the analyser.

The patient information was fed in the machine and the samples were arranged in racks for processing. Racks containing blood samples enter the analyser from the right, and exit from the left side. The racks can hold about 10 tubes of 2.5 mL, and have a notch so they can move along in one direction. As the tubes goes through the machine, a single tube was picked up and inverted five times to mix before sampling. Further, the tubes were compactly capped all along the process and a piercer take the sample through the rubber centre. In either case, closed tube sampling is advocated to ensure safety of workers from the direct exposure to samples. Automated cell counters employ both the electrical and optical techniques to quantify the cell populations present in the sample. The diluted blood sample passes between two electrodes through a narrow aperture [14]. As each cell passes through the aperture there is a change in the impedance which is proportional to the cell volume. This is based on Coulter principle. Due to their lower cell volume platelets produce smaller impedance spikes when compared to WBC's. Resistance pulse caused by each cell enables cell counting [6].

Sampled blood is diluted, and moved through a thin tube such that cell pass one at a time. Characteristics about the cell are measured using lasers (fluorescence flow cytometry) or electrical impedance. Blood is separated into a number of channels. Before the sample was passed through the second detector, lyser will be added to the blood sample to selectively lyse the RBC. This enables counting RBCs, WBCs, and platelets. The platelet count is easily separated from the WBC count by the smaller impedance spikes [15]. In optical detection method the diluted blood sample is streamlined through a flow cell and the cells are hydrodynamically oriented. A laser or halogen light beam when allowed to pass through the stream and scattering of light results, depending upon the refractive index of the cell, which in turn relies on cell form and volume. The photo-detectors convert these signals into an electrical impulse and transmit to a computer for further analysis using advanced software algorithms [16].

STATISTICAL ANALYSIS

For determination of reference intervals of non parametric continuous variables, the interquartile range was used based on the CLSI guidelines [5]. The reference intervals were determined as 95% confidence intervals of the population. The reference interval for platelet parameters which includes MPV, PDW, P-LCR and PCT for male and female subjects were compared using the Mann-Whitney U-test. Kruskal-Wallis test was used to find the difference between age groups using SPSS version 24.0 software. However, p-values of ≤0.05 were considered significant for both the tests.

RESULTS

The platelet parameters of 1,883 subjects (1185 males and 698 females; age range from 18-85 years), were retrieved from the Sysmex XN-1000 analyser. The data for the platelet parameters of all the subjects are shown as mean, standard deviation, standard error of mean and 95% confidence interval with upper and lower limits [Table/Fig-1].

Platelet parameter	Mean	Standard deviation	Standard error of mean	95% CI for Mean	
				Lower limit	Upper limit
PDW	11.65	1.506	0.035	11.58	11.71
MPV	10.28	0.720	0.017	10.25	10.32
P-LCR	27.00	5.949	0.137	26.73	27.27
PCT	0.27	0.043	0.001	0.27	0.27

[Table/Fig-1]: Mean, standard deviation, standard error of mean and 95% confidence interval for mean of the platelet parameters.
PDW: Platelet distribution width; MPV: Mean platelet volume; P-LCR: Platelet large cell ratio; PCT: Plateletcrit

As the data was non normal in distribution between age groups and gender therefore, non parametric Mann-Whitney U-test method was used. The data are shown as median between age groups

and gender, with statistically significant difference in the reference interval for the all the parameters (p-value <0.001) with respect to gender [Table/Fig-2]. PDW was found to be 9-16.4 fL for males and 9.1-16.6 fL for females. Similarly, MPV was 9-12.3 fL for males and 9-12.6 fL for females; P-LCR was 16-42.1% for males and 16.6-43% for females; and PCT was 0.15-0.36% for males and 0.14-0.41% for females. The study population was stratified into five groups according to age as follows; group I (≤34 years) n=887, group II (35-44 years) n=420, group III (45-64 years) n=495, group IV (65-74 years) n=63, and group V (≥75 years) n=18. There was no significant difference observed in PDW (p-value=0.988), MPV (p-value=0.953), and P-LCR (p-value=0.985), whereas a statistically significant difference was in PCT (p-value=0.043) [Table/Fig-2].

Platelet parameters	Variables		Median	IQR	p-value
PDW	Gender	Male (n=1185)	11.30	2.1	<0.001
		Female (n=698)	11.60	2.2	
	Age	≤34 (n=887)	11.50	2	0.988
		35-44 ((n=420)	11.40	2	
		45-64 (n=495)	11.40	2	
		65-74 (n=63)	11.50	2	
		≥75 (n=18)	11.10	2	
MPV	Gender	Male	10.10	1.07	<0.001
		Female	10.40	1.1	
	Age	≤34	10.20	1	0.953
		35-44	10.20	1	
		45-64	10.20	1	
		65-74	10.20	1	
		≥75	10.30	1	
P-LCR	Gender	Male	25.70	8.5	<0.001
		Female	27.40	8.85	
	Age	≤34	26.40	9	0.985
		35-44	26.15	9	
		45-64	26.40	9	
		65-74	26.40	8	
		≥75	26.60	8	
PCT	Gender	Male	0.26	0.06	<0.001
		Female	0.28	0.07	
	Age	≤34	0.27	0	0.043
		35-44	0.27	0	
		45-64	0.27	0	
		65-74	0.26	0	
		≥75	0.25	0	

[Table/Fig-2]: Comparison of platelet parameters within gender and age groups.
The reference intervals for male and female were compared using Mann-Whitney U test and between the different groups by Kruskal–Wallis test.
PDW: Platelet distribution width; MPV: Mean platelet volume; P:LCR: Platelet large cell ratio; PCT: Plateletcrit; p-value <0.05 considered significant

DISCUSSION

Scientific literature gives immense and improved knowledge of various diseases and disease conditions when the information of an automated blood count is combined with other parameters. The clinical usefulness of the analyser derived haematological parameters such as the platelet parameters have been explored in recent years. Its utility in various fields have set a new milestone. The reference interval of platelet parameters were compared with the Clinical Reference Range XN-series provided by the manufacturer [17] and studies done on the same Sysmex XN-series [18,19] [Table/Fig-3].

In contemplation of this, a study to determine the reference intervals of the platelet parameters and the difference of age and gender was carried out. There was no significant difference in age divided reference intervals, except for PCT (p-value=0.043). A statistically significant difference in reference ranges between the gender for the PDW, MPV, P-LCR, and PCT was observed. Although it can be seen that the earlier studies focused on reference intervals of various platelet parameters using the XE-5000, KX-21, XE-2100, and XT-1800i, the present study aimed to analyse in Sysmex XN 1000 analyser [20-23].

Compared with the previously reported reference intervals done in Sysmex XN series, the present study showed comparable reference intervals for platelet parameters in South Indian population [17-19]. Reference interval can rightly be defined as the interval between and including two reference limits (e.g., the 95% apparently healthy men between 18 and 65 years) [24].

While the use of reference intervals defined in other populations may not mirror the same characteristics of the population evaluated, a satisfactory interpretation of the laboratory results depends on the evaluation of local reference values. The present study was done by indirect sampling technique. There are two methods for determining reference intervals which includes direct and indirect sampling techniques. In the traditional/ direct approach to determine reference intervals the sample populations are selected based on defined criteria from the reference population and specimens are collected from these individuals for analysis. In the indirect method the data collected from the routine clinical pathological testing are utilised to determine the reference intervals and this process of data mining is facilitated by the modern laboratory database [25].

Indirect sampling techniques make use of results in a database where the results from routine clinical pathology testing are stored in laboratory databases are most often used. Advantages of indirect approach are cost-effectiveness, less time-consuming, reflect routine laboratory operating conditions and overcome ethical issues since the participants are not subjected to venesection solely for a reference interval study like less time-consuming and cost-effective, reflect routine laboratory operating conditions and have ethical advantages since the participants are not subjected to venesection solely for a reference interval study.

Quantitative and qualitative measurements of the components of blood are done truly to the best by modern blood counting

S. No.	Clinical reference range XN-series provided by the manufacturer 2011 [17]		Ali U et al., United Kingdom population (XN-1000) 2017 [18]		Pelt van JL et al., Dutch population (XN analysers) 2022 [19]*	Current study, South Indian population (XN-1000) 2022	
Gender	Male	Female	Male	Female	Males and females	Male	Female
Sample size	415	794	791	1565	18,484	1185	698
PDW (fL)	9.8-15.2	9.6-15.2	9.3-17	9.3-17.3	10-17.4	9-16.4	9.1-16.6
MPV (fL)	9.1-12	9.2-12.1	9.1-13	9.2-12.8	9.3-12.7	9-12.3	9-12.6
P-LCR (%)	19.5-41.9	19.6-42.6	17.6-47	17.8-47.8	19.3-47.1	16-42.1	16.6-43
PCT (%)	0.19-0.36	0.19-0.40	0.16-0.35	0.18-0.37	0.002-0.004	0.15-0.36	0.14-0.41

[Table/Fig-3]: Comparison of platelet parameters with other studies done in XN-series [17-19].
*The SDRsex is less than 0.4 for all parameters. Hence, the results are given for males and females together; PDW: Platelet distribution width; MPV: Mean platelet volume; P-LCR: Platelet large cell ratio; PCT: Plateletcrit

instruments. Across the globe authors come across various automated analysers from different manufactures with each one having their own advantages and disadvantages. Platelet parameters obtained as a part of automatic CBC uses the principle of analysis of hydrodynamic focusing detection. This detection mechanism offers the advantage of cell count accuracy and repeatability.

The MPV (fL) is an analyser-calculated measure of thrombocyte volume and usually increases when platelet production is decreased [26]. MPV reference ranges vary between different analysers. The contributing factors are the technology (impedence/optical) used in a particular analyser and the method employed to calculate MPV. This implies that the reference range is to be calculated for different analysers [27]. The PDW (fL) is an indicator of volume dispersion in platelet size, a more specific indicator of platelet activation, increases when platelet anisocytosis is present [28]. The P-LCR (%) is an indicator of circulating platelets that are larger than 12 fL, and has been used to monitor the activity of platelets [28]. The PCT (%) is the platelet-occupied volume reflecting platelet mass and is calculated using the formula PCT=Platelet count×MPV/10,000 [28].

The reference interval of platelet parameters were compared with the Clinical Reference Range XN-series provided by the manufacturer [17], and studies done on the same Sysmex XN-series on Western population by Ali U et al., [18] and in Dutch population by Pelt van JL et al., [19] [Table/Fig-3]. Ali U et al., have analysed the platelet parameters in UK population using Sysmex XN-1000 automated haematology analyser [18]. In this, males represented 34% and females 66%, whereas in present study the males comprised of 63% and females 37%. The PDW in present study was 9-16.4 fL and 9.1-16.6 fL in males and females, respectively, with a statistically significant difference (p-value<0.001), whereas in their study, a total reference interval was calculated without gender bias as it was of no statistical significance. The MPV is similar in both studies.

According to Arbiol-Roca A et al., the reference intervals for CBC parameters evaluated in Sysmex XN-2000 the MPV reference interval was 9.7-13.2 fL without any gender specifications [26]. However, in this study male and female participants showed a statistical significance (p-value <0.001) in reference intervals for P-LCR of about 16-42.1% and 16.6-43%, respectively, and there was a difference when compared with the previous study which showed higher values of 17.6-47% and 17.8-47.8% in males and females, respectively [26]. The PCT reference intervals for males and females were 0.15-0.36% and 0.14-0.41%, respectively, with a statistically significant difference, which was closer to those that have been previously reported [18]. The evaluated parameters were not affected by age with the exception of PCT.

Alterations in platelet parameters are associated with various diseases such as inflammatory, autoimmune, cardiovascular, and malignancy [3-6]. As markers of platelet activation, these parameters have involved attention with several studies assessing their diverse potentialities. Some studies have demonstrated the value of these parameters were significantly higher in cancers of colon, stomach, liver and thyroid than healthy subjects or significantly lower in breast, lung carcinoma [29-34]. These parameters are simple readily available biomarker for screening and monitoring the healthy people for such malignancies and might help physicians to arrive at an early diagnosis.

The present study holds a large sample size from indirect approach with the advantages of indirect over direct. The study has determined the reference interval for platelet parameters for the subjects older than 74 years (middle-old and oldest-old). It is a cost-effective and versatile method used for screening and monitoring various infectious, inflammatory and neoplastic medical conditions.

Limitation(s)

The study included subjects who reported to a tertiary care Government Dental Hospital, which constraints generalisation. So, further multicentre prospective studies in general population are recommended to authenticate the usage of these platelet parameters in day-to-day clinical practice.

CONCLUSION(S)

This study determines the reference interval for platelet parameters with respect to age and gender and these results can be utilised by other laboratories using this analyser system for South Indian population. This study establishes normal values of platelet parameters and these can serve to be used as a comparison in various infectious, inflammatory and neoplastic medical conditions.

REFERENCES

[1] Brummitt DR, Barker HF. The determination of a reference range for new platelet parameters produced by the Bayer ADVIA (TM) 120 full blood count analyser. Clin Lab Haematol. 2000;22:103-07.
[2] Kaito K, Otsubo H, Usui N, Yoshida M, Tanno J, Kurihara E, et al. Platelet size deviation width, platelet large cell ratio, and mean platelet volume have sufficient sensitivity and specificity in the diagnosis of immune thrombocytopenia. Br J Haematol. 2005;128:698-02.
[3] Grasbeck R, Saris NE. Establishment and use of normal values. Scand J Clin Lab Invest. 1969;26(Suppl 110):62-63.
[4] Higgins C. An introduction to reference intervals (1)- some theoretical considerations. 2009. www.bloodgas.org. Assesed date: 16th February 2022.
[5] Clinical and Laboratory Standards Institute. How to define and determine reference intervals in the clinical laboratory; Approved guideline, NCCLS document. C28-A2. Wayne, PA: Clinical and Laboratory Standards Institute, 2000.
[6] Buoro S, Seghezzi M, Manenti B, Pacioni A, Carobene A, Ceriotti F, et al. Biological variation of platelet parameters determined by the Sysmex XN haematology analyser. Clin Chim Acta. 2017;470:125.
[7] Green R, Wachsmann-Hogiu S. Development, history, and future of automated cell counters. Clin Lab Med. 2015;35(1):01-10.
[8] https://www.sysmex-p.com/products/haematlogy/. Assesed date: 11th July 2022.
[9] Petersen, Poul Erik, Baez, Ramon J & World Health Organization. (2013). Oral health surveys: Basic methods, 5th ed. World Health Organization. https://apps.who.int/iris/handle/10665/97035.
[10] Alterovitz SS, Mendelsohn GA. Relationship goals of middle-aged, young-old, and old-old Internet daters: An analysis of online personal ads. J Aging Stud. 2013;27:159-65.
[11] Briggs C, Longair I, Kumar P, Singh D, Machin SJ. Performance evaluation of the Sysmex haematology XN modular system. J Clin Pathol. 2012;65(11):1024-30.
[12] https://www.sysmex.co.jp/en/products_solutions/library/journal/vol30_no1/summary02/vol30_1_02.pdf. Assesed date: 7th June 2022.
[13] Briggs CJ, Linssen J, Longair I, Machin SJ. Improved flagging rates on the Sysmex XE-5000 compared with the XE-2100 reduce the number of manual film reviews and increase laboratory productivity. Am J Clin Pathol. 2011;136:309-16.
[14] Vembadi A, Menachery A, Qasaimeh MA. Cell cytometry: Review and perspective on biotechnological advances. Front Bioeng Biotechnol. 2019;7:147.
[15] Thomas ETA, Bhagya S, Majeed A. Clinical utility of blood cell histogram interpretation. J Clin Diagn Res. 2017;11(9):OE01-04.
[16] https://www.technologynetworks.com/diagnostics/articles/optimizing-optical-technology-for-automated-hematology-analyzers-322252. Assesed date: 7th June 2022.
[17] Clinical Reference Ranges Sysmex XN series at Kochi Medical School Hospital, India. 2011. Assesed date: 11th June 2022.
[18] Ali U, Gibbs R, Knight G, Tsitsikasa D. Sex-divided reference intervals for mean platelet volume, platelet large cell ratio and plateletcrit using the Sysmex XN-10 automated haematology analyser in a UK population. Hematol Transfus Cell Ther. 2019;41:153-57.
[19] Pelt van JL, Klatte S, Hwandih T, Barcaru A, Riphagen I, Linssen J, et al. Reference intervals for Sysmex XN hematological parameters as assessed in the Dutch Lifelines cohort. Clin Chem Lab Med. 2022;60(6):s907-20.
[20] Joergensen M, Bathum L. Reference intervals for mean platelet volume and immature platelet fraction determined on a sysmex XE5000 hematology analyzer. Scandinavian J Clin Lab Investigation. 2016;76:01-05.
[21] Awad-Elkareem A, Israa I, Razaz Y, Eman A, Reem M, Sara M, et al. Reference value of platelets count and indices in sudanese using Sysmex KX-21. Int J Health Sci. 2015;3:2348-5728120.
[22] Sehgal KK, Tina D, Choksey U, Dalal RJ, Shanaz KJ. Reference range evaluation of CBC parameters with emphasis on newer research parameters on the CBC analyzer Sysmex XE-2100. Indian J Pathol Microbiol. 2013;56:120-24.
[23] Boshnak NH. Reference intervals for platelet indices using Sysmex XT-1800i in Egyptian population. Int J Med Health Res. 2017;3(2):04-11
[24] Jones G, Barker A. Reference intervals. Clin Biochem Rev. 2008;29(Suppl 1):S93-97.
[25] Jones GRD, Haeckel R, Loh TP, Sikaris K, Streichert T, Katayev A, et al. IFCC Committee on Reference Intervals and Decision Limits. Indirect methods for reference interval determination- Review and recommendations. Clin Chem Lab Med. 2018;57(1):20-29.
[26] Arbiol-Roca A, Imperiali CE, Montserrat MM, Cerro AS, Bosch de Basea AC, Navarro LS, et al. Reference intervals for a complete blood count on an automated haematology analyser Sysmex XN in healthy adults from the southern metropolitan area of Barcelona. EJIFCC. 2018;29(1):48-54.
[27] Hoffmann JJ. Reference range of mean platelet volume. Thromb Res. 2012;129(4):534-35.

[28] Pereira KN, Carvalho JAM, Paniz C. Reference intervals of the platelet indexes in a healthy population in Santa Maria, Rio Grande doSul, Brazil. Hematol Transfus Cell Ther. 2019;41:187-89.
[29] Kemal Y, Demirag G, Ekiz K, Yücel I. Mean platelet volume could be a useful biomarker for monitoring epithelial ovarian cancer. J Obstet Gynaecol 2014;34:515-18.
[30] Yun ZY, Li N, Zhang X, Zhang H, Bu Y, Sun Y, et al. Mean platelet volume, platelet distribution width and carcinoembryonic antigen to discriminate gastric cancer from gastric ulcer. Oncotarget. 2017;8:62600-05.
[31] Karagoz B, Alacacioglu A, Bilgi O, Demirci H, Ozgun A, Ericki AA, et al. Platelet count and platelet distribution width increase in lung cancer patients. Anatol J Clin Investig. 2009;3:32-34.
[32] Okuturlar Y, Gunaldi M, Tiken EE, Oztosun B, Inan YO, Ercan T, et al. Utility of peripheral blood parameters in predicting breast cancer risk. Asian Pac J Cancer Prev. 2015;16:2409-12.
[33] Yaylaci S, Tosun O, Sahin O, Genc AB, Aydin E, Demiral G, et al. Lack of variation in inflammatory hematological parameters between benign nodular goiter and papillary thyroid cancer. Asian Pac J Cancer Prev. 2016;17:2321-23.
[34] Pogorzelska K, Krętowska A, Krawczuk-Rybak M, Sawicka-ukowska M. Characteristics of platelet indices and their prognostic significance in selected medical condition- A systematic review. Adv Med Sci. 2020;65(2):310-15.

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PLAGIARISM CHECKING METHODS: [Jain H et al.]
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