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HEMATOLOGICAL REFERENCE VALUES FOR HEALTHY ADULTS IN EGYPT

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Abstract

Hematological reference values are essential for the interpretation of the Result of laboratory tests and treatment decisions. The full blood count reference intervals in Egypt are generally derived from non-Egyptian subjects. This study aimed to establish hematological reference intervals for healthy adults in Egypt. From January 2018 to January 2020, 5620 volunteers were recruited for this study. A total of 5620 was divided into 1846 (32.8 %) males and 2926 (52.1 %) Females. but 848 (15.1 %) volunteers were excluded because of positive laboratory screening results. Males had higher median of hemoglobin (14 g/dL versus 12.3 g/dL), median of RBC (4.96 × 10^6/ µL versus 4.35 × 10^6/ µL), and hematocrit (41% versus 36.2%) than females. The difference in hemoglobin, RBC, and hematocrit by gender was statistically significantly different ($p < 0.05$). Males had lower median white blood cell (6.7× 10^3/ µL versus 6.9× 10^3/ µL) and median of Platelets (230 × 10^3/ µL versus 252.5 × 10^3/ µL) than Females ($p < 0.05$). in comparison to reference values that are commonly used in Egypt, the hemoglobin levels, RBC, and hematocrit from this study were lower.

Keywords: Hematological reference- Healthy adults-environment.

Introduction:

Laboratory Reference Range is used for the interpretation of laboratory tests Results and the proper management of Patients in clinical and research settings. These are established from a result of a sample of the reference population which was selected based on criteria such as gender, age, ethnicity, and the environment (**Wu et al., 2015).** Hematological reference values are essential for effectively screening blood donors, diagnosing diseases, and assessing overall health. and The use of different methods, instruments, and populations can lead to a significant difference in Hematological parameters, such as Red Blood Cells Hemoglobin, hematocrit, Platelets, and White Blood Cells (**Samaneka et al., 2016)**. The advances in standardizing methods, laboratory techniques, and instruments have minimized the effects of site-to-site differences in many analytical methods. The effect of Population instead is one of the key

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remaining variables which can influence reference values (**Samaneka et al., 2016; Wu et al., 2015).**

In most African countries, including Egypt, normal reference ranges for hematology are obtained from European and North American populations. However, there are marked differences in values of hematological variables between the normal African population and those of North America and Europe **(Mugisha et al., 2016)**. Many factors have been suggested for those differences, including genetic variation, the higher prevalence of pathogens (like Malaria, HIV, HBV, and HCV) **(Ambayya et al., 2014; Dosoo et al., 2012),** many constitutional hemoglobin abnormalities (sickle cell disease, thalassemia, and hemoglobin C) **Ambayya et al., 2014**, dietary, geographic, attitude and lifestyle differences **(Dosoo et al., 2012)**. Therefore, there is an urgent need to establish accurate hematological reference intervals for the Egyptian people. The present study aimed to establish the 95 % reference interval for hematological parameters from healthy Egyptian adults.

Material and methods:

Healthy males and non-pregnant Female range between 18 and 55 years of age were screened from different regions of Egypt. All Participants were examined, and a questionnaire was administered to confirm their condition and health history. And after prescreening, potentially eligible subjects with positive laboratory screening results were excluded based on the following criteria:

1- Diagnosed diseases include tumors, acute or chronic infections, renal failure, hepatic disorders, diabetes, thyroid disorder, and ischemic heart disease.
2- Surgery within 6 months.
3- Blood donation or transfusion within 3 months.
4- Hypertension
5- Pregnancy.
6- Hemoglobin concentration which less than 10 g/dL.
7- White blood cells less than 3×10^3/ µL or more than 12.5×10^3/ µL.
8- A positive test of malaria.

From January 2018 to January 2020, 5620 volunteers were recruited for this study. A total of 5020 was divided into 1846 (32.8 %) males and 2926 (52.1 %) Females. but 848 (15.1 %) volunteers were excluded because of positive laboratory screening results. Table (1).

Table 1: No of samples

Volunteers	Count
Total	5620
Male	1846
Female	2926
Excluded	848

Sample Collection: All Samples were Collected using standard phlebotomy procedures by a clinician. Blood was collected as follows: 5 ml of venous blood into Plain vacutainer tubes or serum separator tubes to be used for renal function and liver function tests and 3 ml of venous blood into purple EDTA tube and mixed 4-6 times to mix with EDTA anticoagulant to prevent clotting and used for full blood counts. Prepared thick and thin films on clean slides and stained by Giemsa stain for malaria microscopy (thin films only fixed with absolute methanol).

Laboratory Testing: Samples were tested within 6 hours after collection. All laboratory investigations were carried out with standard operating procedures (SOPs) and good laboratory practices (GLP). Screening tests are done to exclude samples with positive results. Its included blood urea, serum creatinine, AST, and ALT The biochemical tests were analyzed using mindray BA-88A and Biosystems BTS-350.

Full blood count analyzes on Sysmex KXN 21 analyzer, mindray 5300, and Biote HL-3125 plus. the biochemical tests were analyzed using mindray BA-88A and Biosystems BTS-350 semi-

automatic analyzer. The following analytes were investigated: hemoglobin, hematocrit, mean corpuscular hemoglobin (MCH), mean corpuscular volume (MCV), Mean corpuscular hemoglobin concentration (MCHC), erythrocytes Count (RBC), leukocytes count (WBC), Platelets count, relative neutrophils, lymphocytes, monocytes, basophils, and eosinophils.

Quality control: The protocols for sample collection and investigation according to CLSI. Samples were analyzed within 6 hours from collection. Use both internal and external quality control protocols. Calibration of the automated analyzer according to the manufacturer's instructions. Use three levels of controls (High, Medium, and Low). the samples were run only when the controls were within range.

Statistical analysis: Data were fed to the computer and analyzed using IBM SPSS software package version 20.0**. (**Armonk, NY: IBM Corp**)** Qualitative data were described using numbers and percentages. **The Kolmogorov-Smirnov test** was used to verify the normality of distribution Quantitative data was described using mean, standard deviation, Median, and Reference values. The significance of the obtained results was judged at the 5% level.

The used test was; the Student t-test. for normally distributed quantitative variables, to compare two studied groups

Results:

Among the 4772 blood donor volunteers with a range of age from 18 to 55 years and different regions of Egypt (Alexandria, Al Beherah, Luxor, and Marsa Matrouh) were included in this study. 1846 (38.7 %)males and 2926 (61.3 %)Females. The median, mean ± S.D. (Standard deviation), and 95% reference intervals (2.5–97.5th percentiles) for hematological parameters in this study are presented in (Table, 2)

Males had higher mean of RBC (4.9 × 10^6/ µL) than females (4.4 ×10^6/ µL) with statistical significant different ($p < 0.001$), higher mean of hemoglobin (14 g/dL) than females (12.3 g/dL) with statistical significant different ($p < 0.001$), higher mean of hematocrit (41.4%) than females (36.4) with statistical significant different ($p < 0.001$) and higher mean of MCHC (34.2 g/dL) than in females(33.9 g/dL) with statistical significant different ($p < 0.001$) . but the mean of MCV (83.4 fl) in males, (83.7 fl) in females with ($p = 0.136$) and MCH were 28.4 pg in males and females with($p = 0.469$). MCV and MCH No gender difference were observed ($p > 0.05$).

The mean of total WBC in males (6.8× 10^3/ µL) was lower than in females (7× 10^3/ µL) with a statistically significantly different ($p < 0.001$). on the other hand in the similar mean of platelets in males (239.1× 10^3/ µL) was lower than in females (255.3× 10^3/ µL) with a significantly different ($p < 0.001$).

The differential of WBC show that males had higher mean relative lymphocyte (37 %) than females (35.1) with significant different ($p < 0.001$), the higher mean of relative monocyte (5.5 %) than females (5.0 %) with statistical significant different ($p < 0.001$) and mean of relative basophile (0.3 %) than in females (0.2 %) with significant different ($p < 0.001$). on the other hand, the mean of relative neutrophile in males (55.5 %) was lower than in females (57.6 %) with a statistically significantly different ($p < 0.001$), mean of relative Eosinophil are similar in males and females (2.1 %).

Table (2): Comparison between Males and Females according to different parameters

		Males (n=1846)			**Females (n=2926)**				
	Unit	**Mean ± SD.**	**Median**	**Reference values**	**Mean ± SD.**	**Median**	**Reference values**	**T**	**p**
Age	**years**	36.7± 11.1	36.0	18.0 – 55.0	33.5 ± 11.6	32.0	18.0 – 55.0	9.685*	<0.001*
Hemoglobin	**g/dL**	14.0 ± 1.0	14.0	12.40 – 16.30	12.3 ± 0.9	12.30	11.0 – 14.10	58.929*	<0.001*
RBCs	**10^6/ µL**	4.9 ± 0.5	4.95	4.16 – 5.90	4.4 ± 0.4	4.36	3.66 – 5.21	41.041*	<0.001*
HCT	**%**	41.4 ± 4.5	41.0	33.70 – 49.40	36.4 ± 3.3	36.20	30.50 – 43.0	40.702*	<0.001*
MCV	**fL**	83.4 ± 7.7	84.35	66.10 – 96.10	83.7 ± 7.4	84.0	69.10 – 96.20	1.491	0.136
MCH	**Pg**	28.4 ± 2.3	28.70	23.30 – 32.30	28.4 ± 2.5	28.70	21.90 – 32.68	0.725	0.469
MCHC	**g/dL**	34.2 ± 2.3	33.90	30.0 – 38.50	33.9 ± 2.0	33.40	30.92 – 37.80	4.439*	<0.001*
Platelet	**10^3/ µL**	239.1±56 .6	230.0	158.0 – 376.0	255.3±62.0	252.50	153.0 – 398.0	9.240*	<0.001*
WBCs	**10^3/ µL**	6.8 ± 1.8	6.70	3.90 – 10.70	7.0 ± 1.9	6.90	3.90 – 11.20	3.960*	<0.001*
Neutrophils	**%**	55.5 ± 11.0	57.0	33.0 – 74.0	57.6 ±10.6	58.0	38.0 – 75.0	6.422*	<0.001*
Lymphocytes	**%**	37.0 ±10.3	36.0	20.0 – 59.0	35.1 ± 10.0	34.0	18.0 – 54.0	6.191*	<0.001*
Monocytes	**%**	5.5 ± 1.4	5.0	3.0 – 8.0	5.0 ± 1.3	5.0	3.0 – 8.0	12.508*	<0.001*
Eosinophils	**µ%**	2.1 ± 1.1	2.0	1.0 – 5.0	2.1 ± 1.0	2.0	0.0 – 4.0	0.001	0.999
Basophils	**%**	0.3 ± 0.4	0.0	0.0 – 1.0	0.2 ± 0.4	0.0	0.0 – 1.0	9.917*	<0.001*

SD: Standard deviation Reference values (2.5 – 97.5)
t: Student t-test
p: p-value for comparing Males and Females
*: Statistically significant at $p \leq 0.05$

Table 3: Comparison of median and 95% reference range between our study and other countries:

		OUR STUDY		Ghana		USA		Brazil
		Median	Reference range	Median	Reference range	Median	Reference range	Reference range
Hemoglobin g/dl	Male Female	14.0 12.3	12.40 – 16.30 11.0 – 14.10	15.2 12.5	10.69-18.7 8.19-16.17	12.30	13.5 – 17.5 12 – 16	13.1 – 16.9 11.5 – 14.6
RBCs 10^6/ µL	Male Female	4.95 4.36	4.16 – 5.90 3.66 – 5.21	5.19 4.38	3.61-6.97 3.08-5.88	4.36	4.5 – 5.9 4.0 – 5.2	4.4 – 5.8 3.9 – 5.1
HCT %	Male Female	41.0 36.20	33.70 – 49.40 30.50 – 43.0	45.20 37.40	31.8-61.83 26.76-50.44	36.20	36 – 46 41 – 53	39.9 – 52.1 35.4 – 45.9
MCV (fL)	Male Female	84.35 84.0	66.10 – 96.10 69.10 – 96.20	87.05 86.8	69.71-103.23 64.44-103.53	84.0	80 – 100	81.5 – 100.2 81.0 – 100.1
MCH (Pg)	Male Female	28.70 28.7	23.30 – 32.30 21.90 – 32.68	29.4 28.7	23.30-34.16 19.54-33.73	28.70	26.0–34.0	26.9 – 32.5 26.3 – 32.3
MCHC (g/dl)	Male Female	33.90 33.40	30.0 – 38.50 30.92 – 37.80	33.7 33.1	29.74-37.16 26.81-37.13	33.40	31.0–37.0	30.6 – 34.6 30.5 – 34.5
Platelet 10^3/ µL	Male Female	230.0 252.5	158.0 – 376.0 153.0 – 398.0	186 214	85.93-348.20 110.95-416.30	252.50	150 – 350	128.4 – 302.2 137.9 – 344.7
WBCs 10^3/ µL	Male Female	6.70 6.90	3.90 – 10.70 3.90 – 11.20	5.47 5.62	3.28-11.23 3.25-10.64	6.90	4.5 – 11.0	2.844 – 9.403 2.908 – 10.047
Neutrophil (%)	Male Female	57.0 58.0	33.0 – 74.0 38.0 – 75.0	39.55 44.75	17.57-67.46 20.93-	58.0	40–70	NA

					74.47			
Lymphocyte (%)	**Male** **Female**	**36.0** **34.0**	**20.0 – 59.0** **18.0 – 54.0**	**45.70** **41.25**	**11.98-66.91** **14.59-62.25**	**34.0**	**22 – 44**	**NA**
Monocyte (%)	**Male** **Female**	**5.0** **5.0**	**3.0 – 8.0** **3.0 – 8.0**	**9.69** **8.80**	**4.30-15.17** **4.55 – 17.18**	**5.0**	**4 – 11**	**NA**
Eiosinophile (%)	**Male** **Female**	**2.0** **2.0**	**1.0 – 5.0** **0.0 – 4.0**	**3.0** **2.4**	**0.21-13.91** **0.33-14.30**	**2.0**	**0 – 8**	**NA**
Basophile (%)	**Male** **Female**	**0.0** **0.0**	**0.0 – 1.0** **0.0 – 1.0**	**0.6** **0.5**	**0.10-1.94** **0.10 – 2.14**	**0.0**	**0 – 3**	**NA**

Discussion:

In this study, there were significant gender-related differences in the hematological reference ranges (Table, 2**).** A similar observation was made when compared with the reference ranges in different countries**.**

Reference ranges for RBC count, hemoglobin, and HCT were higher among males compared to females (Table 2). This finding is consistent with most other studies in Africa **(Addai-Mensah et al., 2019; Bimerew et al., 2018; Ayemoba et al, 2019; Rosenfeld et al., 2019; B Kone et al., 2017).** as well as USA (**Kratz et al.,. 2004)**. These gender differences are due to menstrual blood loss in females and the androgenic hormonal effect in males **(Ayemoba et al., 2019**). mean of MCHC in males higher than in females with a significant difference. But there is no significant difference mean of MCV and MCH this is similar to some studies in Africa **(Addai-Mensah et al., 2019**; **Yalew et al., 2016)**.

In this study, the mean of total WBC in males was lower than in females with a statistically significant difference ($p < 0.001$). which is comparable with the studies done in Ghana, Mali, Nigeria, and the USA, but it is similar to the study in Brazil (**Rosenfeld et al., 2019**). The reference range of platelet count was higher in women than in men, consistent with studies by (**Addai-Mensah et al., 2019; Rosenfeld et al**., **2019; Kibaya et al., 2008).** These differences in reference range may be attributed to the variations in the types of hormones produced and their concentrations in the different sexes as the effect of erythropoietin release in response to regular menstruation and cross-stimulating megakaryopoiesis **(Addai-Mensah et al., 2019**).

The differential of WBC shows that males had a higher mean of relative lymphocyte, relative monocyte, and relative basophile than females with significant differences the differences were partly confirmed with the mean, but without any differences in the limits. on the other hand, the mean of relative neutrophils in males is lower than in females with a statistically significantly different, there is no significant difference in the mean of relative Eosinophil by gender.

Conclusion: This study established the first hematological Reference values for a larger population in Egypt, This study found that the Haematological reference values established from a

healthy adult of Egypt were different from other African countries, and the international reference values

Recommendation:

Recommended for Further studies on hematological reference values for all age groups to derive standard hematological reference.

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