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Erythrocyte/ Reticulocyte Parameters Cut-off Values of Egyptian Adults in Fayoum University Hospital, Egypt

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Abstract:

Introduction: Establishing reference values for erythrocyte and reticulocyte parameters is critical for diagnosing and managing hematologic red cell disorders.

Aim of the study: To establish the normal cut-off values of erythrocyte/ reticulocyte parameters in Egyptian adults attending the Fayoum University Hospital.

Subjects and Methods: This cross-sectional research enrolled 114 apparently healthy Egyptian adults to measure erythrocyte indices and reticulocyte counts using Sysmex XN 1000 automated hematology analyzers. Statistical analysis was performed to define reference ranges and assess sex and age-related variations.

Results: The normal cut-off reference values of the factors have been computed with 95% confidence intervals. Gender specific values have been calculated for hemoglobin concentration with a significant difference ($p<0.001$) (male: 13.50–15.50 gm/dl, female: 12.13–14.7 gm/dl); however, there was no significant difference between the gender reference range of Ret-He ($p =0.41$). The normal cut-off value of RET-He for discriminating Egyptian adults with functional hemoglobin abnormalities was 30.9 ±2.5 pg.

Conclusions: The findings provide a foundation for improved clinical decision-making in diagnosing anemia, bone marrow disorders, and other hematological conditions in the Fayoum Governorate. Further, larger multicentric studies are recommended.

Keywords: Egyptian; Hematologic; Parameters; Reference; Ret-He.

1. Introduction

Erythrocyte and reticulocyte parameters are fundamental components of hematological assessments, providing critical insights into the status of red blood cell [RBC] production, destruction, and overall bone marrow activity. These hematological parameters are vital for diagnosing a wide range of red cell disorders [1].

Erythrocyte indices, such as hematocrit [Hct], hemoglobin (Hb), mean corpuscular hemoglobin (MCH), and mean corpuscular volume (MCV) indices that serve as primary markers for assessing RBC status are crucial for differentiating types of anemia (e.g., microcytic, macrocytic, normocytic) and identifying underlying causes such as nutritional deficiencies, bone marrow dysfunction, or chronic diseases [2].

Reticulocytes, the immature form of RBCs, are indicative of bone marrow activity and the body's response to blood loss or anemia [3]. Reticulocyte parameters, including absolute count, percentage, and reticulocyte hemoglobin equivalent (Ret-He), offer additional insights into erythropoiesis [4]. Ret-He, in particular, has emerged as a reliable marker for assessing functional iron availability, providing an early indication of iron deficiency before anemia manifests [5].

Reference intervals for hematological parameters vary significantly across populations due to genetic, environmental, dietary, and lifestyle factors [6]. Despite the global utility of erythrocyte and reticulocyte indices, reliance on reference ranges derived from other populations may lead to diagnostic inaccuracies [7]. Studies have shown significant differences in hematological parameters between African, Asian, and Western populations, underscoring the importance of developing population-specific reference intervals [6,8,9]. In Egypt, with its unique demographic and environmental characteristics, limited data are available on hematological parameters, particularly reticulocyte indices in adult populations. This knowledge gap can hinder the accurate diagnosis and management of hematological disorders in local clinical settings. Hence, this research seeks to define the cut-off values for erythrocyte and reticulocyte indices among Egyptian adults in the Fayoum Governorate, providing a foundation for improved clinical decision-making.

2. Subjects and Methods

2.1 Subjects

This cross-sectional study enrolled 114 apparently healthy Egyptian adults undergoing routine checkups, recruited over a period of 7 months, from July 1, 2023, to January 31, 2024, after obtaining the approval of the Institutional Ethical Committee.

Apparently healthy Egyptian adults above 18 years of age with normal complete blood count (CBC), serum ferritin levels, and iron profiles were included in the study after obtaining informed consent. Participants were carefully screened to ensure their eligibility, and those with acute or chronic illnesses, pregnancy, or on any form of medication were excluded to minimize confounding factors.

A full history taking, a thorough general examination, and laboratory testing were conducted for all the participants. A detailed history-taking to identify any potential risk factors or underlying conditions. This included inquiries about medical history, lifestyle habits, and family history of any inherited disorders or chronic diseases. Special attention was given to identifying any symptoms suggestive of subclinical conditions that might not be immediately apparent. A thorough general examination was performed for each participant, focusing on detecting overt or subtle signs of illness. This included an assessment of vital signs such as blood pressure, heart rate, respiratory rate, and temperature. Anthropometric measurements, including weight and height, were taken with precision to calculate the body mass index (BMI) using the formula: weight (kg) / height (m) [²].

Inclusion Criteria

Apparently healthy Egyptian adult above 18 years old with normal complete blood count [CBC], normal ferritin level, and normal iron profile.

Exclusion Criteria

Any participant with acute or chronic illness, pregnancy, or under any medication.

2.2 Study Design

Cross-sectional study.

2.3 Statistical Methods

Software version 22 of Statistical Package for Social Sciences [SPSS] on Windows 7 [SPSS Inc., Chicago, Illinois, United States of America] was utilized for computing the study data analysis. Simple descriptive analysis for qualitative data was presented as numbers and percentages. Arithmetic means and standard deviations were used for presenting quantitative parametric data. The One-Sample Kolmogorov-Smirnov test was applied for testing normality of quantitative data in each study group, followed by the selection of inferential statistical tests. Sensitivity and specificity tests were conducted using the ROC curve (Receiver Operating Characteristic). A *p*-value of less than 0.05 was considered statistically significant.

3. Results

The mean age of apparently healthy adults with normal ferritin levels was 40.5 ±14.9 years. Sociodemographic data are illustrated in **Table 1.**

Table 1: Demographic and Clinical Data of Study Adults.

Variables		Frequency (N=114)
Age (years)		40.5 ±14.9
BMI (Kg/m^2)		24.03 ±2.9
Gender	Male	47 (41.2%)
	Female	67 (58.8%)
Smoking	Yes	34 (29.8%)
	No	80 (70.2%)

BMI: Body mass index.

The normal reference values of the erythrocyte and reticulocyte parameters for assessing hematological disorders among Egyptian adults were estimated with 95% confidence intervals **(Table 2)**.

Though 29.8% of the study population were smokers, all of them were male gender. In comparing the reference intervals of hematological parameters between smokers and non-smokers, there was a statistically significantly higher level

of HB, MCV, MCH, MCHC, and serum ferritin with *p* <0.05 among smokers. On the other hand, there was no statistically significant difference with *p*>0.05 regarding other blood indices, including the reticulocyte parameters (RET-He).

Table 2: Normal Reference Range of Hematological Parameters in Egyptian Adults Study Population.

Variables	Gender	Frequency (N=114)			*P*-value
		Mean	SD	Range	
RBCs (10^{12}/L)	M	5.20	0.48	4.72 – 5.68	<0.001*
	F	4.80	0.53	4.27 – 5.33	
Hb (gm/dl)	M	14.50	1.00	13.50 – 15.50	<0.001*
	F	13.10	0.97	12.13 – 14.07	
MCV (fl)	M/F	81.70	5.20	76.50 - 86.90	--
MCH (pg)	M/F	27.40	2.20	25.20 - 29.60	--
MCHC (g/dl)	M/F	33.50	1.20	32.30 - 34.70	--
Ret (%)	M/F	1.50	0.53	0.97 - 2.03	--
RET-He (pg)	M	31.10	2.30	28.80 - 33.40	0.41
	F	30.70	2.70	28.00 -33.40	
IRF (%)	M/F	12.60	5.50	7.10 - 18.10	--
LFR (%)	M/F	87.10	5.60	81.50 - 92.70	--
MFR (%)	M/F	9.70	2.70	7.00 -12.40	--
HFR (%)	M/F	2.80	3.20	0.40 – 6.00	--
RDW-SD (fl)	M/F	39.30	4.70	34.60 – 44.00	--
RDW-CV (%)	M/F	13.50	1.90	11.60 - 15.40	--
TLC (10^9/L)	M/F	7.10	2.60	4.50 – 9.70	--
PLT (10^9/L)	M/F	264.40	72.70	191.70– 337.10	--
S. Ferritin (ng/mL)	M	89.70	49.90	39.80 -139.60	0.53
	F	83.20	63.60	19.70 - 146.8	

RBCs: red cell count; Hb: hemoglobin concentration; MCV: mean corpuscular volume; MCH: mean corpuscular hemoglobin; MCHC: mean corpuscular hemoglobin concentration; Ret: retics; IRF: Immature reticulocyte fraction; LFR: low-fluorescence ratio; MFR: medium-fluorescence ratio; HFR: high-fluorescence ratio; RDW-SD: red cell distribution width - standard deviation; RDW-CV: red cell distribution width - coefficient of variation.　***** Statistically significant at *p* <0.05.

Additionally, gender gender-specific reference ranges of RBCs, Hb, and RET-He were determined, in which there was a statistically significant lower level of HB, and RBC counts among females (P <0.001) **[Figure 1].** Conversely, there was a statistically insignificant distinction regarding serum ferritin and RET-He levels between genders, with $p = 0.53$ and 0.41, respectively**.**

In comparison with different racial populations from various countries**,** our results also revealed that RET-He cut-off value in apparently healthy Egyptian adults with normal ferritin levels was 30.9 ±2.5 pg **(Table 3)**.
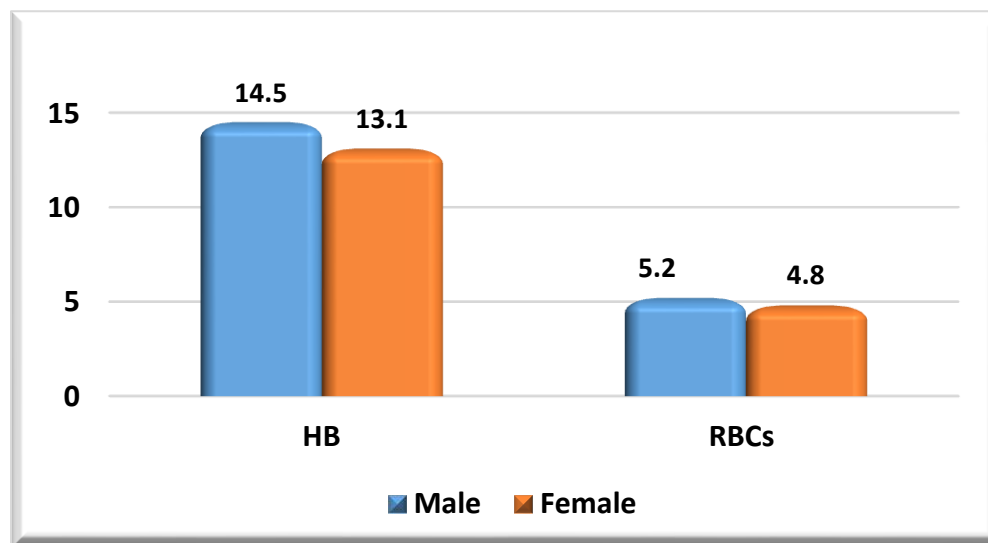

Figure 1: Comparisons of Hemoglobin (HB) and Red Cell Counts (RBCs) in different genders of the Study Population.

Table 3: Comparison of Estimated Reference Range of Erythrocyte/ Reticulocyte Parameters between Various Published Adult Populations.

Study	Current study	Mustafa et al.	Omuse et al.	Al-Mawali et al.	Bakr et al.	Oğuz et al.	Sherzay et al.	Shin et al.	Hoffmann et al.	Cheng et al.	Dacie
Year		2024	2018	2018	2024	2022	2024	2003	2012	2004	2006
Location	Egypt	Sudan	Kenya	Oman	Saudi	Tukey	Afghanistan	Korea	Netherlands	American	High income
RBCs (10^{12}/L)	M: 4.72-5.68 F: 4.27-5.33	M: 4.6-6.3 F: 4.1-5.6	M: 4.9-6.5 F: 4.3-5.7	M: 4.5–5.8 F: 4.1–5.4	M: 5.2 – 5.7 F: 4.5 – 5	--	M: 4.54-6.70 F: 4.08-6.00	M: 4.22-5.46 F: 3.92-4.96	--	M: 4.5-5.9 F: 4.0-5.2	M: 4.5-6 F: 4.1-5.1
Hb (gm/dl)	M: 13.5-15.5 F: 12.13-14.07	M: 12.7-18.6 F: 10.4-16.2	M: 14.5-18.7 F: 12-16.5	M: 11.5 – 15.5 F: 11–14.5	M: 12.9–17.9 F: 11.4-15.4	--	M: 13.75-17.77 F: 10.6-17.33	M: 13.7-16.6 F: 12.1-14.4	--	M: 13.5-17.4 F: 12-16	M: 14-18 F: 12-15
MCV (fl)	76.50-86.90	75.9-102	76.5-95.5	78–95	77.4-94.6	--	59.8-97.4	84.7-98.5	80 -101	--	--
MCH (pg)	25.20 -29.60	21.9-33	73.4-95.8	26–33	24.7–32.7	25.2-30.5	19.9-34.6	27.4-32.9	25.3 – 34.3	--	--
MCHC (g/dl)	32.30 -34.70	28.7-33	32.0-34.5	31–35	30.4–34.4	--	31.6-41.8	31.6-34.3	30.4 – 35.6	--	--

	Sysmex XN 1000	Sysmex KX 21	Beckman Coulter ACT	Sysmex XS-1000i	Sysmex XN 10	Sysmex XN 1000	Medonic analyzer	Siemens ADVIA 120	Abbott CELL-DYN Sapphire	Coulter S-Plus Jr	---
Ret (%)	0.97- 2.03	--	--	--	--	--	--	0.9-2.5	0.5 – 3.2	--	--
RET-He (pg)	M: 28.8-33.4 F: 28 - 33.4	--	--	--	--	M: 25.4-33.8 F: 21.8-33.8	--	M: 28.5-33.1 F: 27.4-32.3	M: 25.6 – 35 F: 26 – 35.1	--	--
IRF (%)	7.1 - 18.1	--	--	--	--	2.8 – 17.8	--	1.5-10.6	--	--	--
LFR (%)	81.5- 92.7	--	--	--	--	82.2-97.2	--	--	--	--	--
MFR (%)	7 -12.4	--	--	--	--	2.5-16.3	--	1.3-9.8	--	--	--
HFR (%)	0.4 – 6	--	--	--	--	0.1-3.2	--	0-1.5	--	--	--
RDW-SD (fl)	34.6- 44	--	--	--	--	--	--	--	--	--	42.5
RDW-CV (%)	11.6-15.4	--	--	11.5 –16.5	--	--	--	12.1-14.4	10.8 – 16.9	--	<15
TLC (10^9/L)	4.5 – 9.7	2.5-9.1	2.8-7.7	2.2 –10	3.6-10.6	--	--	--	--	4.5-11	4-10
PLT (10^9/L)	191.7-337.1	85.4-485.5	133-443	140 – 400	219-303	--	--	--	--	150-350	150-410
Hematology Analyzer	Sysmex XN 1000	Sysmex KX 21	Beckman Coulter ACT	Sysmex XS-1000i	Sysmex XN 10	Sysmex XN 1000	Medonic analyzer	Siemens ADVIA 120	Abbott CELL-DYN Sapphire	Coulter S-Plus Jr	---

4. Discussion

The study establishes baseline normal reference intervals of CBC erythrocyte/ reticulocyte parameters in Egyptian adults of Fayoum Governorate, revealing significant sex-related variation. These findings highlight the importance of population-specific reference intervals for accurate diagnosis and management of hematological disorders.

Regarding smoking effects on erythrocyte/ reticulocyte indices, though there was no statistical significance difference of various reticulocyte parameters, including RET-He, a statistically significantly higher level of HB, MCV, MCH, MCHC, and serum ferritin with p <0.05 among smokers of the study population. Previous studies reported that smoking usually results in secondary polycythemia with an increase in RBC and reticulocyte counts [10]. The effect of smoking on reticulocyte parameters requires further study with a larger sample size.

Egyptian erythrocyte and reticulocyte values align with Korean populations [11], but differ from other African, Middle Eastern, Turkish, and Western references [6, 12-19], emphasizing genetic and environmental influences [6].

Unlike other populations from various countries [12,13], our results also revealed that RET-He cut-off value in apparently healthy Egyptian adults with normal ferritin levels was 30.9 ±2.5 pg. In fact, the normal reference values for automated hematological parameters, including immature reticulocytes, vary owing to the numerous instruments and methods utilized; each laboratory must determine its reference cut-off values [20].

In previous research evaluating reticulocyte parameters in patients with various types of microcytic anemia compared to healthy controls, the average Ret-He value in healthy controls ranged from 26.5 pg to 29.9 pg. Ret-He values were significantly lower in patients with β-thalassemia minor and iron deficiency anemia [12].

This study has several limitations. First, it was exclusive for the adult population, excluding the pediatric population. Second, the limited number of participants prevented the evaluation of

5. Conclusion

This study provides population-specific normal cut-off values for complete blood counts, particularly erythrocyte/reticulocyte parameters in Egyptian adults,

reference ranges based on age or decade. However, to the best of our knowledge, this is the 1st research to evaluate normal cut-off values of erythrocyte and reticulocyte parameters in the Egyptian population.

The provided reference interval for erythrocyte and reticulocyte indices in Egyptian adults will be a foundation for improved clinical decision-making in diagnosing anemia and monitoring response to treatment in the Fayoum population. This study is limited to a single center, and larger multi-center studies are recommended.

enhancing the diagnostic precision for hematological disorders in Fayoum and similar populations. Further larger multicentric studies are recommended for validating these research values.

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