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Normal Blood Cells Reference Intervals of Healthy Adults at the Gaza Strip—Palestine

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Hematological parameters are affected by different factors that include age, sex, smoking, ethnicity, and environmental altitude. It has been justified that each population must establish its own normal reference intervals to be used in clinical assessments and interpretations. Hematological reference intervals for adults from the Gaza Strip—Palestine have never been addressed. Therefore, this study was designed and aimed at the establishment of normal blood cells reference intervals for healthy adults at the Gaza Strip—Palestine. This study involved 89,491 apparently healthy individuals (*from both sexes and from the different governorates of the Gaza Strip*) who were referred to the Thalassemia Central Laboratory during the period from September 2000 until February 2008. Complete blood counts were performed. Subjects were categorized into subgroups according to gender, smoking habit, and age (15–18, 19–45, and >45 years old). For each subgroup, descriptive and comparative statistical analysis was performed for hematological parameters. The results showed substantial differences between males and females, between smokers and nonsmokers, and between the different age groups. Moreover, reference intervals derived from our population are markedly shifted downward as compared with Western European and American populations. It was concluded that separate and region-specific reference intervals based on gender, smoking, and age for the Palestinian population at the Gaza Strip should be generalized for clinical laboratories and clinical practitioners, which could help in interpreting laboratory hematological tests more specifically, and potentially develop the quality of medical care provided to patients. J. Clin. Lab. Anal. 22:353–361, 2008.

Key words: reference intervals; blood cells; percentiles; hematological parameters; smoking; age-related changes; sex-related changes

INTRODUCTION

Establishing normal reference intervals for the hematological parameters is an important step in interpreting the laboratory investigations in health and disease cases. Even for healthy populations, the values of the hematological parameters are affected by different factors that include age, sex, ethnicity, and environmental altitude (1–8). Different studies have been performed and significant differences have been reported in different populations. Consequently, different populations and ethnic groups had reported their own normal reference intervals for the hematological parameters at least for the different age and gender subgroups (9–13). More detailed investigations reported also significant differences in these parameters with respect to other confounding factors such as smoking and nutritional status (14,15). For these reasons, it has been justified that each population must establish its own normal reference interval values, not only for hematological parameters but also for all laboratory tests, to be used in clinical assessments and interpretations (2,16). Hematological reference intervals for adults from the Gaza Strip—Palestine have never been established. The values that are currently used in the

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Gaza Strip are adopted from hematology textbooks that were mainly used in Western European or American populations.

This study, therefore, aims to establish normal reference intervals for the blood cells parameters in adult healthy Palestinian population of the Gaza Strip and compare the results between age, gender, smoking, and governorates subgroups.

MATERIAL AND METHODS

Area of the Study

The Gaza Strip (geographic coordinates 31°25′N, 34°20′E) of Palestine is a narrow piece (365 km^2) of land along the Mediterranean coast, just 40 km long and 10 km wide. Altitude and elevation extreme measurements of the Gaza Strip showed the lowest point at the Mediterranean sea level (0 m), whereas the highest point is only 105 m above sea level. The Gaza Strip is divided into five governorates: Gaza, Khan Younis, Rafah, Deirelbalah, and North governorate. Gaza Strip is considered as one of the most populated areas in the world (3,890/km^2) with an estimated population of about 1.42 million according to February 2008 records (17).

Subjects

During the period from September 2000 until February 2008, more than 94,811 individuals have been referred to the Thalassemia Central Laboratory to be screened for the premarital tests (18). Of the total screened, complete blood count (CBC) results of 89,491 apparently healthy individuals (from both sexes and from the different governorates of the Gaza Strip) were involved aiming at the establishment of normal reference intervals for the blood cells parameters.

For each governorate, the subjects were categorized into subgroups according to gender (male and female), smoking habit (smokers and nonsmokers), and age (15–18, 19–45, and >45 years old). Age groups were chosen based on the published literature about age-related changes in laboratory values (19,20).

Preanalytical Conditions

The premarital tests are performed according to a definite protocol in accordance with the 1975 Helsinki Declaration. For all subjects involved, 2.5 ml of venous blood samples were collected in 12 × 56 mm K_3-EDTA polypropylene tubes (Meus, Piove Di Sacco, Italy). The daily collection of the blood samples is performed in the morning (8:00 a.m.–12:00 a.m.), whereas the blood samples are subjected to CBC analysis within 1–2 hr of collection, usually during the first hour. Withdrawal of venous blood samples and CBC analysis are carried out by four well-trained and experienced technicians who are holding university degrees in laboratory medicine or laboratory sciences.

Personal, demographic, and further required information were collected through a specific questionnaire that was filled by each subject involved in the study. In addition, the questionnaire includes a consent statement that was signed by each subject about her/his approval for the blood withdrawal, blood sample testing, and also the publication of the results without specific identification of the subject. All individuals who accepted to participate and signed the consent statement are eligible subjects and were involved in this study.

CBCs were performed [white blood cell (WBC), red blood cell (RBC), hemoglobin (Hb), hematocrit (Hct), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), red cell distribution width (RDW), and platelets (PLT)] on the collected blood samples using a Cell Dyne 1700 electronic counter (Sequoia-Turner Corporation, Santa Clara, CA). Two Cell Dyne 1700 electronic counters were involved; both were purchased together and were working at the same laboratory room under same conditions and room temperature. Blood samples for CBC analysis are withdrawn and analyzed at the same floor of the Thalassemia Central Laboratory building; neither transportation nor storage of blood samples is needed.

Quality Control

The Thalassemia Central Laboratory, where this work was carried out, is accrediting and running a definite working protocol that includes quality control (QC) measures and procedures, which were approved by the scientific committee of the Palestinian Avenir Foundation. The QC procedure includes daily measurements, testing (in duplicates or triplicates), comparisons, and evaluation for the relevant qualitative and quantitative commercially available control samples prior to the hematological tests that include CBC, serum ferritin, Hb electrophoresis, and HbA2 quantitation by microcolumn chromatography. The QC measures include CBC control (Cell-Dyn 16 tri-level control, reference number 99109-01, Abbott Laboratories, Abbott Park, IL); AFSA2 hemo control for cellulose acetate electrophoresis (AFSA2, catalogue number 5330, Helena Laboratories, Beaumont, TX); normal and elevated hemolysate for HbA2 quantitation (HbA2 controls, code numbers 10000 and 10011, Biosystems, Barcelona, Spain); and three levels of ferritin controls (reference number 9C01-10, Abbott Laboratories). Additionally to the daily control measurements and calibrations, the two

Cell-Dyn analyzers are checked weekly for comparability using 20–30 blood samples and each CBC parameter is analyzed using the paired samples *t*-test.

Statistics and Presentation

All hematological parameters of this study were tested for normality using the Kolmogorov–Smirnov test. Parameters that are not deviated from Gaussian distribution, $P>0.05$, were statistically analyzed using the independent samples *t*-test and analysis of variance (ANOVA), whereas in the case of those that are deviated from the Gaussian distribution, the Mann–Whitney *U* and Kruskal–Wallis tests were used.

For each governorate and subgroups, descriptive [mean, standard deviation (SD), 2.5th; 50th (median); 97.5th percentile values, and reference interval (mean $\pm$2SD)] and comparative statistical analyses were performed using SPSS® (version 13, SPSS Inc., Chicago, IL) program; significance results were reported at $P<0.05$.

RESULTS

During the period of the study, about 94,811 individuals have been referred to the Thalassemia Central Laboratory to be screened for the premarital tests. According to the hematological and biochemical tests performed (CBC, serum ferritin concentrations, Hb electrophoresis, and HbA2 quantitation by microcolumn chromatography), CBC results of 89,491 individuals were involved. The excluded 5,279 CBC results were confirmed as β-thalassemia carriers [2285 (2.4%)] with HbA2 $>3.5\%$ and as iron deficient [2994 (3.2%)] with decreased serum ferritin $\leq 12\,\mu g/L$. Subjects who reported iron or other treatment regimen are also excluded from early stages of the study.

Numbers, distribution, and subcategorization of the subjects according to the study criteria (locality, sex, smoking habit, and age groups) are mentioned in Table 1. The Gaza Strip is a part of the Middle East where oriental conservative traditions and regulations govern the majority of the population. Among these tradition and regulations is the tendency for cigarette smoking, which is very dominant among males and very limited or prohibited among females (17). Therefore, it is worthwhile to mention that all females of this study are nonsmokers; data of smoker females (41/7,987) were excluded from the statistical treatment stages of the results. Furthermore, the females included in this study are nonpregnant and unmarried.

Normality of the CBC Parameters

All the hematological parameters of this study were tested for normality using the Kolmogorov–Smirnov test. All, except for the WBC and PLT, are not deviated from Gaussian distribution, $P>0.05$. Therefore, the statistical analysis for the normally distributed variables (RBC, Hb, Hct, MCV, MCH, MCHC, and RDW) was performed using the *t*-test and ANOVA, whereas for those that are deviated from the Gaussian distribution, WBC and PLT, the Mann–Whitney *U* and Kruskal–-Wallis tests were used. When there are relatively unequal sample sizes, as in males and females of the different governorates, the authors used the ANOVA Tamhane's T2 test, which is considered more appropriate than the least significant difference test or Tukey's honestly significant difference test where cell sizes are unequal (21,22).

Grouping According to Sex and Smoking Habit

The descriptive and statistical analysis of the hematological parameters and indices for the overall males (smokers and nonsmokers) and females (nonsmokers only) of this study are presented in Table 2. The results from this group showed significant increases in RBC, Hb, Hct, MCV, MCH, and MCHC hematological parameters of the nonsmoker males as compared with nonsmoker females. However, for WBC count, PLT count, and RDW, nonsmoker females showed significantly higher values than nonsmoker males.

With respect to grouping according to smoking habit (Table 2), the statistical comparisons (*smoker males vs. nonsmoker males*) showed that smokers exhibited significantly higher hematological parameters (RBC,

TABLE 1. Distribution of Subjects According to Locality, Sex, Smoking Habit, and Age Group

						Age (yr)		
Governorate	Overall	Males	Females	Smokers	Nonsmokers	15–18	19–45	>45
Gaza	38,219	35,112	3,107	16,823	21,396	3,162	33,893	1,164
Khan Younis	15,943	14,356	1,587	6,909	9,034	957	14,498	488
Rafah	9,781	8,852	929	4,436	5,345	630	8,860	291
Middle	11,439	10,470	969	5,487	5,952	499	10,585	355
North	14,109	12,755	1,354	5,709	8,400	1,935	11,851	323
Total	89,491	81,545	7,946	39,364	50,127	7,183	79,687	2,621

TABLE 2. Mean and SD, Reference Interval (Mean ± 2SD), and 2.5th, 50th (Median), 97.5th Percentiles of the Hematological Parameters and Related Indices According to Sex and Smoking Habit

	Sex														
	Males										Females				
	Smokers ($N = 39{,}364$)					Nonsmokers ($N = 42{,}181$)					Nonsmokers ($N = 7{,}946$)				
			Percentile					Percentile					Percentile		
Hematological parameters[a]	Mean (SD)	Reference interval	2.5	50 (median)	97.5	Mean (SD)	Reference interval	2.5	50 (median)	97.5	Mean (SD)	Reference interval	2.5	50 (median)	97.5
RBC $\times 10^{12}$/L	5.11 (0.44)[a]	4.23–5.99	4.30	5.10	6.00	5.09 (0.43)[b]	4.23–5.95	4.30	5.10	6.00	4.50 (0.42)	3.66–5.34	3.80	4.47	5.50
Hb (g/dL)	15.09 (1.09)[a]	12.91–17.27	12.90	15.10	17.20	14.75 (1.09)[b]	12.57–16.93	12.5	14.80	16.80	12.36 (1.18)	10.00–14.72	9.70	12.50	14.30
Hct (%)	45.26 (3.22)[a]	38.82–51.70	38.70	45.30	51.50	44.32 (3.20)[b]	37.92–50.72	37.70	44.40	50.30	37.73 (3.39)	30.95–44.51	30.30	37.90	43.70
MCV (fL)	88.40 (5.69)[a]	77.02–99.78	75.30	88.90	97.70	86.79 (5.52)[b]	75.75- 97.83	72.20	87.30	95.70	83.83 (7.65)	68.53–99.13	62.67	85.20	95.00
MCH (pg)	29.51 (2.38)[a]	24.75–34.27	24.10	29.70	33.70	28.93 (2.32)[b]	24.29–33.57	23.00	29.10	32.90	27.50 (3.03)	21.44–33.56	19.50	28.00	32.00
MCHC (g/dL)	33.36 (1.32)	30.72–36.00	30.80	33.30	36.40	33.30 (1.32)[b]	30.66–35.94	30.70	33.30	36.20	32.75 (1.30)	30.15–35.35	30.10	32.80	35.30
WBC $\times 10^{9}$/L	7.40 (2.15)	3.10–11.70	3.80	7.2[a]	12.20	6.89 (1.87)	3.15–10.63	3.70	6.70	11.00	7.07 (2.05)	2.97–11.17	3.80	6.90[c]	11.40
PLT $\times 10^{9}$/L	262.77 (62.20)	138.37–387.17	154.00	258.00	397.00	270.93 (64.20)	142.53–399.33	161.00	266.00[d]	412.00	304.98 (73.85)	157.28–452.68	176.00	299.00[c]	470.00
RDW (%)	14.25 (1.08)	12.09–16.41	12.60	14.10	16.80	14.21 (1.07)	12.07–16.35	12.60	14.10	16.80	14.91 (1.92)[c]	11.07–18.75	12.60	14.40	20.10

Mean (SD) = value of mean with standard deviation in parentheses. (1) Independent *t*-test for normally distributed parameters and Mann–Whitney *U*-test for nonnormally distributed parameters were done between nonsmoker males and nonsmoker females. (2) Independent *t*-test for normally distributed parameters and Mann–Whitney *U*-test for nonnormally distributed parameters were done between smoker males and nonsmoker males. SD, standard deviation; WBC, white blood cell; RBC, red blood cell; Hb, hemoglobin; Hct, hematocrit; MCV, mean corpuscular volume; MCH, mean corpuscular hemoglobin; MCHC, mean corpuscular hemoglobin concentration; RDW, red cell distribution width; PLT, platelets.

[a]Smoker males showed significantly ($P < 0.001$) higher values than nonsmoker males.

[b]Nonsmoker males showed significantly ($P < 0.001$) higher values than nonsmoker females.

[c]Nonsmoker females showed significantly ($P < 0.001$) higher values than nonsmoker males.

[d]Nonsmoker males showed significantly ($P < 0.001$) higher values than smoker males.

Hb, Hct, MCV, MCH, and WBC) except for PLT where nonsmokers exhibited significantly higher values. MCHC and RDW did not show any significant differences between smokers and nonsmokers.

Grouping According to Age

According to the age groups [group I (15–18), group II (19–45), group III (>45)], the ANOVA and Kruskal–Wallis statistical treatments showed (Table 3) significant differences in all examined hematological parameters between the three groups. Moreover, in males, group II (19–45) showed significantly better values regarding the RBC mass (RBC count, Hb, Hct), whereas in females group III (>45) showed significantly better values regarding the RBC mass.

It is worthwhile to mention that for each age group, significant increases in RBC, Hb, Hct, MCV, MCH, and MCHC hematological parameters were reported in males as compared with females. However, for PLT count and RDW, females reported significantly higher values than males.

Grouping According to Locality

The overall subjects were categorized according to governorates and for each governorate subjects were subcategorized according to sex and smoking habit. Tables 4 and 5 present the means and SDs of the involved hematological parameters. For each governorate, statistical comparisons (independent *t*-test and Mann–Whitney *U*-test) were done between nonsmoker males and nonsmoker females and between smoker males and nonsmoker males. Results showed that for RBC, Hb, Hct, MCV, and MCH, males and smokers exhibited significantly higher values than females and nonsmokers, respectively, whereas for PLT females and nonsmokers showed significantly higher values than males and smokers, respectively.

Moreover, statistical comparison (one-way ANOVA and Kruskal–Wallis tests) was done between the five governorates for RBC, Hb, Hct, MCV, MCH, MCHC, WBC, PLT, and RDW. All hematological parameters examined except MCHC showed significant differences between different governorates.

DISCUSSION

Hematological reference intervals for healthy adults from the Gaza Strip—Palestine have never been established. The values that are currently used in the Gaza Strip are adopted from hematology textbooks, which were mainly derived from studies on Western European or American populations (23,24). In the Middle East and Arab world, only one study was performed in this regard on adults and it included 804 apparently healthy Saudi Arabian students 20–29 years old (2). Therefore, this study could be considered as the first ever study that addresses the hematological reference intervals for healthy adults in the Arab world and that covers such huge number of subjects (89,491) from both sexes, smokers and nonsmokers, and at a wide age range of 15–65 years.

In order to diminish any possible effects on the reliability of the percentiles and reference intervals calculated in this study, we excluded all the CBC data of the confirmed β-thalassemia carriers and iron-deficient individuals. Moreover, subjects who reported iron or other treatment regimen are also excluded from early stages of the study. Another confusing factor in establishing population-based hematological reference intervals could be the iron-fortified food. In the Gaza Strip—Palestine, iron-fortified foods are not yet considered to correct the iron status of the population, even that in our previous publications (18,25) we recommended nationwide programs to correct the iron status in the Gaza Strip, specially in school children and women of the child bearing age.

In this study we categorized the subjects into the different subgroups aiming at neutralizing potential confounding factors so that the reference interval represents the group itself.

With regard to the gender effect, the results mentioned in Tables 2 and 3 revealed that maleness is characterized by significantly higher RBC mass values and indices than femaleness along the different age groups, whereas feminineness is characterized by significantly higher WBC and PLT counts. Although of the exclusion of all iron-deficient CBC results, however, the higher PLT count in females could be attributed to early stages of iron depletion (normal or borderline serum ferritin) owing to physiological menstruation. The sex-related changes are concomitant with what have been published for other populations except for the WBC in female subjects (3,9,12,26,27). Smoking in this study (Table 2) was among the potential factors that significantly affected blood cells values and indices and must be considered well while interpreting the hematological values of smokers. Significantly higher levels were reported in RBC, Hb, Hct, MCV, MCH, and WBC of smokers, whereas smokers showed significantly lower PLT count. The significantly higher levels of RBC, Hb, Hct, MCV, MCH, and WBC in smokers were reported also by other scientific studies and, consequently, different international health parties and centers developed smoking-specific hematological adjustments to define the cutoff values in smokers (28,29).

The changes in hematological values are not only affected by gender and smoking but also significantly by

TABLE 3. Mean and SD, Reference Interval (Mean ± 2SD), and 2.5th, 50th (Median), 97.5th Percentiles of the Hematological Parameters and Related Indices of Nonsmokers According to Age Groups and Sex

	Age groups ($N = 50{,}127$)														
	15–18 years old ($N = 5{,}924$)					19–45 years old ($N = 42{,}772$)					>45 years old ($N = 1{,}431$)				
			Percentile					Percentile					Percentile		
Hematological parameters[a]	Mean (SD)	Reference interval	2.5	50 (median)	97.5	Mean (SD)	Reference interval	2.5	50 (median)	97.5	Mean (SD)	Reference interval	2.5	50 (median)	97.5
RBC × 10^{12}/L[a]															
M	5.02 (0.46)	4.10–5.94	4.16	5.00	6.00	5.10 (0.43)	4.24–5.96	4.30	5.10	6.00	4.99 (0.50)	3.99–5.99	4.00	4.99	5.95
F	4.51 (0.43)	3.65-5.37	3.80	4.47	5.60	4.48 (0.41)	3.66–5.30	3.80	4.47	5.50	4.71 (0.42)	3.87–5.55	4.00	4.71	5.72
Hb (g/dL)[a]															
M	14.24 (1.24)	11.76–16.72	11.50	14.30	16.50	14.79 (1.06)	12.67–16.91	12.60	14.80	16.80	14.52 (1.22)	12.08–16.96	11.90	14.50	16.70
F	12.31 (1.15)	10.01–14.61	9.70	12.40	14.20	12.39 (1.20)	9.99–14.79	9.70	12.50	14.40	12.48 (1.28)	9.92–15.04	9.68	12.50	14.80
Hct (%)[a]															
M	42.92 (3.53)	35.86–49.98	35.30	43.20	49.20	44.43 (3.14)	38.15–50.71	38.10	44.50	50.40	43.81 (3.63)	36.55–51.07	36.55	43.90	50.60
F	37.56 (3.27)	31.02–44.10	30.40	37.80	43.39	37.84 (3.44)	30.96–44.72	30.10	38.10	44.10	38.84 (5.13)	28.58–49.10	29.74	38.30	58.10
MCV (fL)[a]															
M	85.32 (6.50)	72.32–98.32	65.61	86.10	95.20	86.86 (5.41)	76.04–97.68	73.11	87.40	95.60	87.80 (6.20)	75.40–100.20	73.70	88.20	100.00
F	83.23 (7.91)	67.41–99.05	61.80	84.70	94.70	84.30 (7.42)	69.46–99.14	63.43	85.60	95.20	80.69 (7.82)	65.05–96.33	60.50	82.70	90.90
MCH (pg)[a]															
M	28.36 (2.67)	23.02–33.70	20.40	28.70	32.60	28.96 (2.28)	24.40–33.52	23.30	29.20	32.80	29.11 (2.51)	24.09–34.13	23.68	29.10	34.30
F	27.31 (3.10)	21.11–33.51	19.30	27.90	32.00	27.66 (2.98)	21.70–33.62	19.80	28.20	32.10	26.44 (3.01)	20.42–32.46	19.00	26.85	31.90
MCHC (g/dL)[a]															
M	33.19(1.34)	30.51–35.87	30.60	33.20	36.20	33.32 (1.32)	30.68–35.96	30.80	33.30	36.20	33.15 (1.36)	30.43–35.87	30.70	33.10	36.30
F	32.76 (1.24)	30.28–35.24	30.40	32.80	35.30	32.74 (1.35)	30.04–35.44	30.00	32.80	35.38	32.72 (0.94)	30.84–34.60	31.18	32.55	35.10
WBC × 10^{9}/L[a]															
M	6.97 (2.01)	2.95–10.99	3.80	6.80	11.50	6.85 (1.84)	3.17–10.53	3.70	6.70	11.00	7.61 (2.05)	3.51–11.71	4.10	7.40	12.10
F	7.15 (2.12)	2.91–11.39	3.90	7.00	11.40	7.01 (1.99)	3.03–10.99	3.70	6.80	11.38	7.58 (1.75)	4.08–11.08	4.50	7.70	11.40
PLT × 10^{9}/L[a]															
M	279.29 (67.61)	144.07–414.51	158.00	275.00	421.95	270.28 (63.53)	143.22–397.34	161.00	265.00	411.00	273.14 (74.09)	124.96–421.32	155.45	266.00	423.00
F	306.49 (71.67)	163.15–449.83	179.00	300.00	469.00	303.73 (75.22)	153.29–454.17	175.00	298.00	471.00	318.13 (86.86)	144.41–491.85	144.38	311.50	588.00
RDW (%)[a]															
M	14.47 (1.20)	12.07–16.87	12.80	14.20	17.50	14.18 (1.05)	12.08–16.28	12.60	14.00	16.70	14.51 (1.16)	12.19–16.83	12.80	14.30	17.50
F	14.97 (1.87)	11.23–18.71	12.60	14.50	20.38	14.86 (1.96)	10.94–18.78	12.50	14.40	20.08	15.12 (1.60)	11.92–18.32	12.90	14.70	20.50

Mean (SD) = value of mean with standard deviation in parentheses. Statistical comparison (ANOVA for normally distributed and Kruskal–Wallis test for nonnormally distributed) was done between the three age groups of the nonsmokers. SD, standard deviation; ANOVA, analysis of variance; WBC, white blood cell; RBC, red blood cell; Hb, hemoglobin; Hct, hematocrit; MCV, mean corpuscular volume; MCH, mean corpuscular hemoglobin; MCHC, mean corpuscular hemoglobin concentration; RDW, red cell distribution width; PLT, platelets.
[a]Hematological parameters investigated showed significant differences between the three groups.

TABLE 4. Mean and SD of RBC Parameters and Related Indices in the Different Governorates

	RBC[ab]			Hb[ab]			Hct[ab]			MCV[ab]			MCH[a,b]			MCHC		
	M		F	M		F	M		F	M		F	M		F	M		F
Governorate	S	N	N	S	N	N	S	N	N	S	N	N	S	N	N	S	N	N
Gaza	5.12	5.10	4.52	15.13	14.79	12.37	45.37	44.39	37.75	88.27	86.66	83.41	29.47	28.91	27.40	33.35	33.32	32.77
(N = 38,219)	(0.42)	(0.42)	(0.41)	(1.09)	(1.08)	(1.20)	(3.12)	(3.11)	(3.33)	(5.50)	(5.35)	(7.77)	(2.29)	(2.24)	(3.14)	(1.17)	(1.18)	(1.24)
Khan Younis	5.11	5.10	4.51	15.12	14.79	12.46	45.33	44.54	38.16	88.60	87.14	84.62	29.59	28.98	27.69	33.39	33.26	32.69
(N = 15,943)	(0.47)	(0.45)	(0.43)	(1.08)	(1.09)	(1.21)	(3.40)	(3.39)	(3.69)	(5.83)	(5.39)	(7.43)	(2.50)	(2.34)	(2.85)	(1.61)	(1.63)	(1.42)
Rafah	5.07	5.06	4.44	14.95	14.65	12.21	44.87	44.07	37.31	88.46	86.95	84.06	29.53	28.96	27.55	33.37	33.28	32.72
(N = 9,781)	(0.45)	(0.46)	(0.40)	(1.05)	(1.09)	(1.14)	(3.42)	(3.46)	(3.40)	(5.65)	(5.43)	(7.77)	(2.43)	(2.29)	(3.07)	(1.61)	(1.60)	(1.58)
Middle	5.11	5.09	4.51	15.17	14.82	12.35	45.49	44.47	37.70	88.69	86.95	83.49	29.62	29.00	27.37	33.36	33.33	32.75
(N = 11,439)	(0.44)	(0.42)	(0.45)	(1.11)	(1.05)	(1.19)	(3.15)	(3.02)	(3.31)	(5.65)	(5.60)	(7.87)	(2.35)	(2.33)	(3.08)	(1.26)	(1.19)	(1.16)
North	5.08	5.06	4.46	14.98	14.62	12.31	44.94	43.93	37.49	88.20	86.58	83.94	29.42	28.85	27.56	33.33	33.29	32.80
(N = 14,109)	(0.43)	(0.45)	(0.41)	(1.12)	(1.12)	(1.13)	(3.16)	(3.18)	(3.13)	(6.10)	(6.07)	(7.35)	(2.48)	(2.52)	(2.94)	(1.14)	(1.19)	(1.16)

Values represent the mean with standard deviation in parentheses. SD, standard deviation; ANOVA, analysis of variance; RBC, red blood cell; Hb, hemoglobin; Hct, hematocrit; MCV, mean corpuscular volume; MCH, mean corpuscular hemoglobin; MCHC, mean corpuscular hemoglobin concentration; M, males; F, females; S, smokers; N, nonsmokers. (1) For each governorate, statistical comparisons (independent t-test) were done between nonsmoker males and nonsmoker females and between smoker males and nonsmoker males. (2) Statistical comparison (ANOVA) was done between the five governorates for RBC, Hb, Hct, MCV, MCH, and MCHC.

[a]Males and smokers showed significantly ($P < 0.01$) higher values than females and nonsmokers, respectively.

[b]All hematological parameters except MCHC showed significant differences between different governorates.

TABLE 5. Mean, SD, and Median of WBC, PLT, and RDW in the Different Governorates

	WBC[a]			PLT[ab]			RDW[ac]		
	M		F	M		F	M		F
Governorate	S	N	N	S	N	N	S	N	N
Gaza	7.63 (2.17)	7.04 (1.84)	7.16 (2.01)	266.40 (62.18)	272.13 (63.84)	310.67 (75.53)	14.31 (1.05)	14.29 (1.08)	15.11 (2.07)
(N = 38,219)	*7.4*	*6.9*	*7.0*	*261*	*268*	*305*	*14.2*	*14.1*	*14.6*
Khan Younis	7.02 (2.02)	6.61 (1.81)	6.96 (1.95)	258.78 (64.54)	270.68 (66.06)	304.29 (73.93)	14.07 (1.12)	14.00 (1.04)	14.60 (1.76)
(N = 15,943)	*6.9*	*6.5*	*6.8*	*252*	*265*	*302*	*13.9*	*13.9*	*14.2*
Rafah	6.93 (2.08)	6.45 (1.88)	6.78 (2.02)	259.14 (61.66)	266.30 (64.21)	296.06 (75.13)	14.04 (1.02)	14.01 (1.01)	14.82 (1.91)
(N = 9,781)	*6.7*	*6.2*	*6.5*	*253*	*262*	*289*	*13.9*	*13.9*	*14.4*
Middle	7.44 (2.21)	6.87 (1.92)	6.88 (2.06)	260.81 (60.69)	271.18 (64.60)	300.12 (69.55)	14.37 (1.15)	14.29 (1.06)	15.01 (1.87)
(N = 11,439)	*7.2*	*6.7*	*6.7*	*256*	*266*	*291*	*14.2*	*14.1*	*14.6*
North	7.51 (2.09)	7.08 (1.86)	7.34 (2.21)	261.59 (60.66)	270.78 (62.72)	302.35 (70.99)	14.34 (1.10)	14.27 (1.08)	14.77 (1.73)
(N = 14,109)	*7.3*	*6.9*	*7.2*	*258*	*265*	*295*	*14.2*	*14.1*	*14.3*

Values represent the mean with standard deviation in parentheses. For WBC, PLT the median values are indicated as *underlineditalic*. SD, standard deviation; ANOVA, analysis of variance; WBC, white blood cell; RDW, red cell distribution width; PLT, platelets; M, males; F, females; S, smokers; N, nonsmokers. (1) For each governorate, independent t-test for normally distributed parameters and Mann–Whitney U-test for nonnormally distributed parameters were done between nonsmoker males and nonsmoker females and between smoker males. (2) Statistical comparisons (ANOVA for normally distributed and Kruskal–Wallis test for nonnormally distributed) were done between the five governorates for WBC, PLT, and RDW and nonsmoker males.

[a]All hematological parameters showed significant differences between different governorates.

[b]Females and nonsmokers showed significantly ($P < 0.001$) higher values than males and smokers, respectively.

[c]Females showed significantly ($P < 0.001$) higher values than males.

the age group (Table 3). For RBC mass (RBC count, Hb, and Hct), age group II of males and age group III of females are characterized by the significantly better values. The age-related differences in hematological tests are to a large extent attributable to the normal development physiological changes. The age-related differences of this study are in agreement with the results of the second National Health and Nutrition Examination Survey (NHANES II) (12,19,20).

Although the governorate-related changes in the hematological parameters except for MCHC of this study were statistically significant, however, the increment or decrements in these parameters between the different governorates are not of a magnitude that justifies the necessity for establishing governorate-specific reference values. Therefore, in our study we treated our data and established our hematological reference intervals (Tables 2 and 3) based on sex, smoking, and age groups.

The hematological reference intervals of this study were established as mean $\pm$2SD (30). As compared with the already published and followed hematological reference intervals for nearly same age groups and sex, the RBC mass (RBC count, Hb, and Hct) and related indices (MCV, MCH, and MCHC) reference intervals of our population are markedly shifted downward for males and females and also for the different age groups. For example, the NHANES II study revealed that for age group 15–18, the male lower limits (mean$-$2SD) for Hb and Hct were 12.3 g/dL and 37.0%, respectively, whereas in our population the comparative values are 11.76 g/dL and 35.86%, respectively. Moreover, the female values of the same group in the NHANES II study were 11.70 g/dL and 34.0%, respectively; however, in our population female reference values are 10.01 g/dL and 31.02%, respectively. The same is applied for the other RBC parameters and indices in the different age groups and sexes (12,19,20).

Different factors are attributed positively to the importance of this study. Among these attributable factors are the large number of the subjects, the subcategorization of the subjects according to locality, gender, smoking, and age groups, which minimized or diminished any potential confounding factor. Other positively attributable factors include the limited and narrow range of altitude of the Gaza Strip (0–105 m above sea level), the uniformity and constancy in the blood sampling and CBC analysis, which were performed at the same laboratory and instruments for all the subjects; meanwhile, all blood samples were analyzed within 1–2 hr of collection.

This study is a large-scale population-based study that was designed in order for identifying the normal reference intervals for the blood cells parameters in adult healthy Palestinian population residing in Gaza Strip where geographical altitudes are very limited (0–105 m above sea level). Therefore, the hematological reference intervals were established based on sex, smoking, and age groups. These reference intervals could be evaluated, compared, and applied to other Palestinian and/or Arabic populations who are sharing similar geographical altitudes. However, for the Palestinian population residing at other cities and geographical localities, such as the Palestinian population of the West Bank where geographical altitudes vary from 400 m below sea level in Jericho to more than 1,100 m above sea level in Halhoul-Hebron (31), specific reference intervals should be established and compared with the values of this study. In addition, Arabic researchers and hematologists should start large-scale population-based studies at their countries aiming at establishing, if possible and applicable, Arabic-based reference intervals for the hematological parameters.

In conclusion, substantial differences in hematological values were reported between males and females, between smokers and nonsmokers, between the different age groups, and also between our population and the Western European and American populations. Consequently, separate and region-specific reference intervals based on gender, smoking, and age for the Palestinian population at the Gaza Strip should be declared and generalized for the clinical laboratories and clinical practitioners, which could help in interpreting the laboratory hematological tests more specifically, and potentially develop the quality of medical care provided to the patients. Moreover, for the Palestinian population living at the West Bank where altitudes range from 400 m below sea level and reach more than 1,100 m above sea level, it is highly recommended to establish altitude-based reference intervals in addition to gender, smoking, and age reference intervals.

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