

Hematological indices reference intervals for a healthy Arab population in Qatar

Effect of age, gender, and geographic location

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Abstract

Hematologic reference intervals vary with gender, age, ethnicity, and geographic area. Therefore, local or national laboratory reference ranges are essential to enhance the accuracy when diagnosing health conditions. Still, no comprehensive list of reference ranges tailored to the Arab population living in Qatar. Accordingly, this study aims at establishing a hematology reference guide for Arabs in Qatar.

This is a retrospective study where 750 healthy volunteers (18–69 years) from 2015 to 2019 were included, analyzed by an automated hematology analyzer. Arab adults were divided into African (Egypt, Libya, Tunisia, Morocco) and Asian (Syria, Lebanon, Jordan, Palestine, Qatar). The Cell-Dyn and Sysmex were used for measuring hematological parameters.

The mean \pm 2SD were established for all the study groups. Arab males had significantly higher Hb, Hct, red cell distribution width, absolute neutrophil count, lymphocytes, and monocyte counts than females. Asian-Arab males had significantly higher Hb concentration and higher WBC, lymphocytes, and eosinophils than African Arabs. Asian-Arab young (>18: <40 years) males had significantly higher Hb and lymphocytes and lower monocytes than older males (>40 years). African-Arab young males had significantly higher lymphocytes and lower monocytes than older males. Asian-Arab young females had higher WBC and absolute neutrophil count than older Asian Arabs.

The findings of this study will help in establishing specific reference intervals in the Arab world. The differences in hematology reference intervals considering age, gender, and geographical location highlight the importance of establishing blood reference intervals in each country considering the ethnic diversity of each country.

Abbreviations: ANC = absolute neutrophil count, CBC = complete blood count, RDW = red cell distribution width, WBCs = White Blood Cells.

Keywords: African Arabs, Asian Arab, differential leucocytic count, hemoglobin, reference intervals, white cell count

This study has been funded by the medical research center (MRC) at Hamad Medical Corporation (HMC), grant (MRC-01-19-240).

Ethical approval for the study was obtained from the institutional review board (IRB) at the Medical Research Center (MRC), Hamad Medical Corporation, Doha, Qatar (MRC-01-19-240). The informed consent has been waived by the IRB at Hamad Medical Corporation due to the retrospective nature of this study.

The authors have no conflicts of interests to disclose.

All data generated or analyzed during this study are included in this published article [and its supplementary information files].

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How to cite this article: Yassin MA, Soliman AT, Nashwan AJ, Alamami AA, Abdulla MA, Hmissi SM, Aldapt MB, Chandra P, Suliman AM, Ibrahim EA, Yassin KS, Allahverdi N, Mohamed SF. Hematological indices reference intervals for a healthy Arab population in Qatar: effect of age, gender, and geographic location. *Medicine* 2022;101:24(e29271).

Received: 4 November 2021 / Received in final form: 22 March 2022 / Accepted: 29 April 2022

<http://dx.doi.org/10.1097/MD.00000000000029271>

1. Introduction

The majority of physicians' medical judgments are based on clinical information supported by laboratory reports.^[1] The availability of a reference interval for different lab values facilitates interpretation.^[2,3] The establishment of a normal reference interval is essential for accurate clarification of the disease diagnosis and follow-up. Moreover, the diagnosis and management of several blood disorders are not possible without the development of various novel blood cell parameters.^[4-6] However, significant differences exist in the reference intervals based on several variables for example, gender, age, genetic, ethnic, geographical and environmental factors.^[7-9]

On the other hand, occupational exposures and dietary habits could affect reference intervals.^[10,11] Reference values were established by large population studies in primarily Western population which is often not directly extrapolatable to Eastern Arab population. Therefore, there is an unmet need for each country/region to establish its guidelines for reference intervals.

To date, no country-specific comprehensive studies on the reference intervals for the Arab population in Qatar considering several variables such as age, gender, and geographic location. Therefore, this is the first study in Qatar intended to investigate reference intervals for complete blood count (CBC) concerning age, gender, and blood grouping. Previous recent published reference values for other Arab gulf countries shall be compared to those from Qatar because of the potential difference due to different geographical and ethnic factors.

2. Methods

2.1. Data collection

The Blood Transfusion Center is under the Ministry of Public Health (MoPH) in Qatar. Before blood donation, a specific assessment must be done to determine eligibility and fitness to donate which include physical examination, demographic, medical, and other information. All methods were performed in accordance with the relevant WHO guidelines and regulations.^[12] As per the WHO Global Database on Anemia, all subjects with hemoglobin <12.0 g/dL for and <13.0 g/dL for men were excluded.^[11]

Ethical approval for the study was obtained from the Institutional Review Board (IRB) at the Medical Research Center (MRC), Hamad Medical Corporation, Doha, Qatar (MRC-01-19-240). The informed consent has been waived by the IRB at Hamad Medical Corporation due to the retrospective nature of this study.

K3EDTA (2 mL) tubes were used to collect the peripheral blood specimens. A sample was collected from each of the 750 eligible healthy Arab adult blood donors (selected from n=1119 subjects screened; n=369 subjects eliminated because of not fulfilling the WHO guidelines for donors) included in the final analysis who donate blood between January 2015 and May 2019. The main reason for exclusion from the study was low hemoglobin level <12 d/dL in females (79/311) and <13 g/dL (58/808) in males.^[11]

Of the 750,515 were males (male donors largely exceeds female donors in Qatar), between 18 and 65 (median age was 30 years). The samples were collected routinely between 8 am and 12 pm and processed within 2 hours. Criteria for donating blood in Qatar (Fig. 1).

2.2. Measurements

The collected blood specimens were analyzed at Hamad General Center (the largest general hospital) in Doha, Qatar. CBC parameters were measured using Cell-Dyn Sapphire (Abbott Laboratories, Diagnostic Division, Abbott Park, IL, USA) and Sysmex XS-1000i (Sysmex Corp., Kobe, Japan) hematology analyzers. Eleven hematology parameters investigated, which including red blood cells count, hemoglobin (Hb), hematocrit (HCT), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), red cell distribution width (RDW), white blood cells count (WBC), absolute neutrophil count (ANC), absolute lymphocyte count (LYMPH), absolute eosinophil count (EOS), absolute basophil count (BASO), absolute monocyte count (MONO), and platelet count (PLT). Anthropometric data, including weight and height, were accurately measured before blood collection; the Body Mass Index and height SDS (HtSDS) were calculated for each adult.

2.3. Quality control & assurance

The hematology laboratory in HMC is accredited by the College of American Pathologists (CAP) Laboratory Accreditation Program. Three different levels (high, medium, and low) of quality control for the respective analyzers; were run thrice a day. Calibration of the analyzers and quality control monitoring were carried out instantly to ensure the validity and reliability of results.

Our laboratory's statistical quality control (SQC) design adheres to HMO 1301/2007 requirements for frequency of quality control (every 8 hours) and Standard ISO 15189:2013 recommendations for 3 layers of control. To comply with all requirements, 9 control points (3 × 3 model, 3 times/day × 3 control levels N=9) are calculated using stabilized commercially control blood every 24 hours (3 × 3 model, 3 times/day × 3 control levels N=9). Commercial stabilized blood is produced for each of the 2 instruments, Sysmex XT 1800i (Sysmex Corporation, Japan) and Cell-Dyne Ruby (Abbott, Illinois, USA).^[12]

2.4. Statistical analysis

Data were analyzed using the Excel Statistical Package (Version 2010). Horn's algorithm was used to identify the upper and lower extremities' outliers.^[11] The Student *t* test was used to compare hematological and anthropometric data among groups of different variables such as age, gender, and geographical location. ANOVA test was used when multiple comparisons among groups were needed. Nonparametric tests (Wilcoxon Rank and Mann-Whitney tests) were used when the data were not normally distributed. The CBC values between the -2SD and +2SD that included 95% of the sample were calculated. A linear regression model was performed to explore the effect of all variables. HtSDS: Height in cm is converted to height standard deviation score (SDS) by subtracting the mean and dividing by the SD. HtSDS between -2 and +2 is accepted as normal for age, and gender.

3. Results

Hematological data (mean \pm 2SD) at 95% confidence intervals for all the study groups are presented as follows: Arab males (n=515) had significantly higher Hb 14.74, 12.740 (14.614-14.866, 11.770-13.058), Hct 44.03, 38.5 (43.63-44.43, 35.650-39.443),

- 1- The person must be between 18 to 60 years of age.
- 2- He/she must be in good health in general at the day of donation.
- 3- Must not have any chronic heart, lung or circulatory illnesses.
- 4- Weight must be 50 kg and above.
- 5- Donors must not be anemic (Hb <12g/dl), insulin dependent or hypertensive.
- 6- Donors must inform the unit about medications being taken.
- 7- Pregnant, lactating, or menstruating women may not donate.
- 8- Should have not donated blood in the last 8 weeks (56 days)

Figure 1. The exclusion criteria for blood donation.

RDW 15.610, 14.320 (14.979–16.241, 11.930–14.864), ANC 3.17, 2.78 (1.763–4.577, 1.020–3.138), lymphocytes 3.78, 1.94 (2.895–4.665, 1.380–2.058) and monocytes 0.570, 0.390 (0.536–0.604, 0.200–0.429) than adult females (n=235), respectively (Table 1). The hematological data of Asian-Arab females did not differ from those for African-Arab females. Asian-Arab males had significantly higher Hb concentration and higher WBC, lymphocytes and eosinophil count than African-Arab males. Asian Arab young males had significantly higher Hb levels and lymphocyte and lower monocyte counts than old males. African Arab young males had significantly higher lymphocyte 4.690, 1.990 (2.876–6.504, 1.765–2.215) and lower monocyte counts 0.56, 0.7 (0.528–0.592, 0.545–0.855) than old males, respectively. Asian-Arab young females had higher WBC 6.980, 4.920 (4.873 - 9.087, 4.288–5.552), ANC 3.180, 2.490 (2.598–3.762, 1.999–2.981) than old Asian Arab females, respectively. No significant correlation was found between growth parameters (weight, Height, HtSDS, Body Mass Index) and hematological parameters.

Outliers can exist in healthy samples as well as in non-healthy ones. Combining conventional and robust statistical approaches is an effective way of finding outliers in a reference interval context. In general, laboratories lack a well-defined healthy population from which to construct reference intervals. The influence of nonhealthy people in the computation increases the breadth of the reference interval by around 10%. Though, there is a significant variation among analytes. On the other hand, the skewed gender is a result of males are donating blood more than females do. However, the total number of females studied was reasonable acceptable for statistical analysis.

4. Discussion

Most physicians' medical judgments are based on clinical information supported by laboratory reports, where CBC is the most requested. Several studies around the world reported marked differences in some CBC parameters when linked to demographic variables.

A study in Oman reported that Africans were less susceptible to *Plasmodium vivax* infections as they have a lower reference interval (RIs) for absolute neutrophil counts.^[13] In contrast to RIs for ANC from the US (1800 ± 7700 cells/ μ L),^[14] in our study, RIs for males and females was significantly lower at 1050 ± 4080 cells/ μ L, which is consistent with what has been found in other reports from Africa (500 ± 840 cells/uL).^[4,15,16]

Measuring CBC parameters have been previously published by the International Council for Standardization in Hematology (ICSH).^[17–19] The reference values/ranges are comparable regardless of analyzers, reagents, or analytical principles. Therefore, the laboratories could validate reference intervals on a small number of subjects and combine it with other laboratories from multiple to establish consensus reference intervals.^[20]

There are very few published reports explaining the CBC reference intervals for the Arab populations. In this study, the CBC reference intervals were calculated for a cohort of adult Arabs living in Qatar and analyzed in relation to age, gender, geographical region, and blood subgroups.

In our study, the prevalence of neutropenia (ANC < 1.5×10^9 L) was significantly lower in Arab males (9.8%) compared to Arab females 28% ($P < .001$). These confirmed the relatively

Table 1
Normal hematological reference interval for Arabs in Qatar.

	Age (y)	HSUS	Ht (m)	weight (kg)	BMI	HB g/dL	WBC	PLT	HCT	MCV	MCHC	RDW	ANC	LYMP	MONO	ESINO	BASO	
Arab Females n=225	Mean	-0.72	1.58	75.49	30.02	12.740	5.960	260.920	38.500	83.350	32.840	14.320	2.780	1.940	0.390	0.160	0.080	
	SD	0.36	0.06	17.99	6.73	0.970	2.100	59.490	2.850	11.000	1.280	2.390	1.760	0.960	0.190	0.150	0.030	
	Lower CI (95%)					0.318	0.944	12.845	0.943	2.693	0.709	0.544	0.368	0.118	0.039	0.030	0.006	0.000
	Upper CI (95%)					11.770	3.850	201.430	35.650	72.350	31.560	11.930	11.930	1.020	1.180	0.200	0.100	0.000
Arab Males n=515	Mean	-0.28	1.74	91.52	30	14.740	6.510	250.670	44.030	83.790	32.750	15.610	3.170	3.780	0.570	0.170	0.070	
	SD	0.89	0.06	18.8	5.62	1.270	2.110	65.210	4.000	6.930	2.510	6.300	1.060	0.840	0.340	0.130	0.060	
	Lower CI (95%)					0.126	0.211	6.509	0.400	0.691	0.251	0.631	1.407	0.885	0.034	0.013	0.066	
	Upper CI (95%)					14.614	6.299	244.161	43.630	83.099	32.499	14.979	17.63	2.895	0.536	0.157	0.044	0.136
Asian Females n=130	Mean	-0.77	1.58	77.78	31.02	12.830	5.990	264.960	38.900	83.450	32.870	14.410	2.840	1.930	0.400	0.160	0.030	
	SD	1.01	0.07	18.45	6.76	0.960	2.100	61.800	2.650	10.200	1.290	2.590	1.690	0.570	0.200	0.160	0.030	
	Lower CI (95%)					0.223	1.143	14.314	0.613	2.363	0.290	0.590	0.391	0.131	0.047	0.037	0.006	0.0354
	Upper CI (95%)					12.607	4.847	250.646	38.287	81.087	32.571	13.820	2.449	1.799	0.353	0.123	0.024	0.024
African females n=95	Mean	-0.55	1.6	66.89	26.3	12.350	5.740	243.120	36.830	82.940	32.780	13.910	2.520	1.990	0.390	0.120	0.030	
	SD	0.84	0.06	12.96	5.17	0.940	2.000	43.780	3.050	13.810	1.220	1.490	2.010	0.960	0.130	0.080	0.030	
	Lower CI (95%)					0.496	1.543	23.201	1.562	7.064	0.668	0.760	1.066	0.285	0.065	0.043	0.013	
	Upper CI (95%)					11.854	4.197	219.919	35.268	75.876	32.024	13.150	1.454	1.705	0.325	0.077	0.017	0.017
Asian Males n=355	Mean	-0.35	1.74	90.53	29.88	14.880	6.720	252.380	44.320	83.890	32.780	15.610	3.740	4.000	0.600	0.190	0.040	
	SD	0.85	0.06	18.34	5.63	1.280	2.200	65.650	3.440	7.570	2.620	6.280	1.240	10.790	0.360	0.150	0.040	
	Lower CI (95%)					0.196001	0.254199	6.244144	0.432009	0.95075	0.330649	0.793866	0.282967	1.361	0.046	0.018	0.04673	
	Upper CI (95%)					15.038	6.470	244.140	43.890	82.940	32.410	14.810	3.480	1.722	0.554	0.172	0.036	0.044
African Males n=160	Mean	-0.15	1.75	93.23	30.2	14.510	6.140	247.700	43.510	83.610	32.690	15.620	3.170	3.390	0.530	0.140	0.130	
	SD	0.94	0.07	19.46	5.59	1.240	2.210	64.300	4.790	5.630	2.290	6.330	2.080	3.430	0.300	0.100	0.180	
	Lower CI (95%)					0.206	0.368	10.712	0.798	0.937	0.381	1.054	3.828	0.570	0.050	0.017	0.181	
	Upper CI (95%)					14.304	5.772	236.988	42.712	82.673	32.309	14.566	-0.658	2.820	0.480	0.123	-0.051	0.311
Asian young males n=222	Mean	-0.24	1.75	90.63	29.62	14.990	6.860	259.990	44.590	83.180	32.580	16.200	3.720	4.690	0.560	0.200	0.040	
	SD	0.85	0.06	19.3	5.86	1.190	2.080	65.540	3.130	7.730	2.920	7.120	1.700	12.400	0.220	0.160	0.040	
	Lower CI (95%)					0.357	0.460	15.495	1.061	1.699	0.328	0.413	0.862	0.225	0.155	0.023	0.007	
	Upper CI (95%)					14.183	5.860	214.155	42.469	84.311	33.022	13.467	2.928	1.765	0.545	0.147	0.033	0.047
African young males n=99	Mean	-0.13	1.76	91.49	29.58	14.550	6.240	252.890	43.680	83.480	32.550	15.850	3.240	3.610	0.490	0.140	0.140	
	SD	0.97	0.07	17.31	4.65	1.250	2.200	62.280	4.940	5.720	2.380	6.700	2.140	3.570	0.180	0.100	0.160	
	Lower CI (95%)					0.221	0.392	11.071	0.878	1.016	0.424	1.191	4.351	0.635	0.032	0.018	0.205	
	Upper CI (95%)					14.329	5.848	241.819	42.802	82.464	32.126	14.659	-1.111	2.975	0.458	0.122	-0.065	0.345
African old males n=61	Mean	-0.27	1.75	104.68	34.3	14.250	5.450	209.570	42.310	84.580	33.690	13.990	2.610	1.780	0.810	0.130	0.030	
	SD	0.7	0.05	27.36	8.65	1.140	2.120	66.360	3.290	4.820	0.910	1.370	1.180	1.130	0.650	0.080	0.020	
	Lower CI (95%)					0.568	1.054	33.000	1.634	2.397	0.463	0.680	0.586	0.032	0.324	0.040	0.010	
	Upper CI (95%)					13.662	4.396	176.570	40.676	82.183	33.237	13.310	2.024	1.219	0.486	0.090	0.020	0.040
Asian young females n=87	Mean	-0.64	1.59	77.42	30.44	12.810	6.980	276.760	38.350	83.820	33.020	14.260	3.180	2.020	0.440	0.160	0.040	
	SD	1.18	0.08	21.81	7.66	1.060	6.500	67.300	2.500	5.040	1.160	1.420	1.790	0.560	0.230	0.140	0.030	
	Lower CI (95%)					0.344	2.107	21.815	0.809	1.634	0.383	0.469	0.582	0.182	0.074	0.044	0.010	
	Upper CI (95%)					12.466	4.873	254.945	37.541	82.186	33.637	13.791	2.588	1.331	0.366	0.116	0.030	
Asian old females n=43	Mean	-0.91	1.57	78.15	31.61	12.840	4.920	252.840	39.470	83.080	32.730	14.570	2.490	1.840	0.350	0.170	0.030	
	SD	0.77	0.05	14.19	5.62	0.850	1.960	52.920	2.680	13.590	1.390	3.310	1.490	0.680	0.160	0.180	0.020	
	Lower CI (95%)					0.279	0.632	17.393	0.881	4.467	0.455	1.087	0.491	0.183	0.052	0.060	0.008	
	Upper CI (95%)					12.561	4.288	235.447	38.589	78.613	32.275	13.483	1.999	1.657	0.298	0.110	0.022	0.038

* P < .05 among the 2 groups.
BMI = Body Mass Index.

high prevalence of neutropenia in the Arab population. In a previous study, benign neutropenia (BN) was present in 10.7% of Arab adults, of whom 2.3% of individuals had moderate neutropenia (ANC $0.5\text{--}1.0 \times 10^9/\text{L}$). In 22 tribe-family groups, the prevalence of benign neutropenia varied between 0% and 38%. Unlike our study that showed a higher prevalence of neutropenia in females, others found no difference in the sexes' frequency.^[21] In another study, the frequency of neutropenia (NP) in Arab children (a neutrophil count $< 1.5 \times 10^9/\text{L}$) was found to be: Green Crescent Arabs 9.8%, Peninsular Arabs 10.9%, and North African Arabs 15.4%. On the other hand, the NP's frequency was 10.6% in 12,703 Emirati children same as their adult counterparts.^[16] Although the inheritance of benign neutropenia in Arabs was consistent with an autosomal dominant pattern; the presence of more than 1 genetic variant for this trait could explain the diversity of the observed phenotypes.^[16,21]

These data indicated that due to the high prevalence of low neutrophil count in our Arab population, measures should be taken to prevent the inappropriate investigations of a healthy individual with benign neutropenia. A lower interval for ANC can be adopted.

Our hematological data, including Hb, Hct, PLT, was comparable to data recently published for Omani, Saudi and Sudanese adults (3 Arab countries). However, the lower limit intervals for WBC in our study ($2.3 \times 10^9/\text{L}$ for males and $1.7 \times 10^9/\text{L}$ in females) were lower compared to those in the Omani study ($2.78\text{--}8.1 \times 10^9/\text{L}$, Saudi study ($3.3 \times 10^9/\text{L}$) and Sudanese study ($2.9 \times 10^9/\text{L}$). However, in the Saudi study, the lower interval was taken as 25th percentile not 2.5th percentile as our study.^[22,23] The reduced lower limit interval for WBC count comparable to those reported in our study was reported in 2 African studies from Togo 4.1 ($1.9\text{--}10.1$) and Uganda $4.9 \times 10^9/\text{L}$ ($2.8\text{--}8.2$).^[24,25]

On the other hand, another study from Kuwait showed that ANCs, in adult Kuwaiti population were 2.6 to 8 and (2.0–7) for women and 2.7 to 8 and (2.0–7) for men, respectively. Both the WBC and ANC counts were higher compared to reference data for adults in the UK.^[26]

Arab males had significantly higher Hb, Hct, RDW, WBC, lymphocytes, and monocytes compared to Arab females. It is already known that males and females have variant mean hemoglobin levels. It is probably a direct effect of sex hormones, both estrogen, and androgens, on erythropoiesis.^[14,27]

In our study, Asian-Arab males had significantly higher Hb concentration and higher WBC, lymphocytes, and eosinophil counts compared to African-Arab males. The differences from between Asian-Arabs and African-Arabs is due to ethnic descent rather than geographical location.

Arab-Asian young males had significantly higher PLT, WBC, and lymphocyte counts compared to old Asian males. Arab-Asian young females had higher WBC and ANC counts compared to older Asian Arab females. These supported previously published data by Nah et al confirming age-related changes in the WBC and platelet counts with the highest counts occurred during childhood and decreased with age.^[28,29] A large cohort study found that women before age 50 had significantly higher ANC%, lower LY%, and higher neutrophil-to-lymphocyte ratio (NLR) than women after 50 years. These results show that blood leukocyte composition differs between women before and after menopausal age.^[30] Another large Korean study

showed that age displayed the strongest association with the hemoglobin level in both men and women.^[31]

It must be mentioned that within-day biological variation and hour-to-hour reference change values for hematological parameters. However, our blood samples were taken randomly all over the day between 7 am and 9 30 pm which decrease the possibility of the effect of time variation on the results.^[32]

4.1. Limitations

The relatively small sample (n=750) of the studied population was calculated to give a margin of error between 3% and 5%. Bigger sample and prospective design can increase the accuracy of the results. The disproportionately lower number of females was unavoidable because we chose to take sequential samples from all subjects coming during this specific time and usually female donors are less than male donors. However, this shall not significantly affect the margin of error (between 5% and 7%).

5. Conclusions

In the studied Arab population, we found important differences in the hematological parameters based on gender, age, and geographical area (African versus Asian Arabs). The lower limit interval of Arabs for ANC appeared to be markedly lower than the internationally reported reference lower limit. These Arab – specific reference intervals for hematological tests may help improve disease diagnosis, allow for better diagnosing, tracking, and monitoring of health status, and can facilitate clinical decision making.

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