Hematological Values of Healthy Adult Population Living at Moderate Altitude (1869 m, Erzurum, Turkey)

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ABSTRACT

In this study, the normal hematological values in healthy adults living in Erzurum area in Turkey at moderate altitude (1869 m above sea level), and the effect of moderate altitude on these hematological values was investigated. The study population comprised of 929 females and 1204 males aged between 17-95. The mean values for red blood cell and leukocyte counts, and hemoglobin level were significantly higher in males than in females ($p<0.0001$), whereas platelet count was significantly higher in females than in males ($p<0.0001$). In conclusion, we could not find an increase in the number of red blood cells as well as other hematological parameters in healthy adults living in Erzurum area. Hematological values in this study were similar to those reported in the previous studies carried out with those living under 1869 m.

Key Words: Hemoglobin, Leukocyte, Platelet, Healthy adults, Moderate altitude.

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INTRODUCTION

Blood cell values are known to vary according to age, sex, and race. In interpreting a patient's laboratory test results, the clinician usually compares the reported values with the reference values[1]. In clinical practice, reference values are often printed by the laboratory on the same document with the results without specifying where they live[2-5]. Since the absence of a reference range for hemoglobin concentration and other blood cell values, reference values obtained for a predominantly population living in North America and Europe[6].

There is little information regarding normal hematological values at different altitudes above sea level. Hurtado et al published a curve of blood hemoglobin values at altitudes ranging from sea level to 4540 meters. The curve was based on Hurdato's finding in groups of 32 to 40 people living at altitude above 3700 meters and on data reported by his co-workers[7].

It has been reported that up to moderate high altitudes, an adaptation mechanism causes increasingly higher numbers of red blood cell[7,8]. Although the major aim of endurance training at moderate altitude is to increase the amount of total body hemoglobin, the results are conversial[9,10]. It is accepted that moderate altitude does not cause the increase in leukocyte counts. But different opinions concerning the platelet counts are in question[11].

We investigated if moderate altitude had an effect on hematological values and the normal hematological values in a large number of healthy adult population living in Erzurum area (1869 m above sea level).

SUBJECTS and METHODS

The study population consisted of healthy adults living in Erzurum area for at least one year. Subjects were excluded if they had a history of recent infection, any chronic disease, any abnormal bleeding, pica, were at present pregnant or had been pregnant within the last year, and if they had donated blood within the previous 6 months. We did not attempt to detect, ß-thalassemia trait cases because previous studies have shown its much lower prevalence in our region[12].

Fasting prior to the procedure was not required. Biood sample was collected from each subject in tubes containing EDTA and sent for a complete blood cell (CBC) count. The CBC counts were performed between 2 and 3 hour following sampling. The analyzed hematological values were hemoglobin (Hb), hematocrit (Hct), erythrocyte count (RBC), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), leukocyte count, and platelet count. Hematological values were determined on a analyzer (Coulter, Model STKS) according to the manufacturer's instructions. The analyzer was calibrated each day using commercial standards recommended by the manufacturer (Beckman Coulter Company, Florida, USA).

Laboratory results were statistically analyzed using a Statistical Product and Service Solutions (SPSS) program. The dispersion of the hematological parameters within a group is given as mean and SD and the outliners were excluded if the individual values greater or less than 2.5 SDs from the mean. The normal range determined encompasses approximately 95% of population and was derived from 2.5 and 97.5 percentiles for those parameters. The Student's t test was used to estimate the significance of differences in the mean values of the variable between two groups of subjects.

RESULTS

The study population comprised of 2133 subjects (929 females and 1204 males), 2091 participated in this study. The number of reference subjects varied for each index because of the variable number of subjects excluded. The mean ages were 37.2 years for the females and 37.6 years for the males, with ranges from 17 to 95 years for both sexes. The mean ages of females and males were not significantly different ($p > 0.05$).

There were highly statistically significant differences for all hematological values between females and males ($p < 0.0001$). The mean values

Table 1. The hematological values of all the subjects

	Male		Female		Total		p
	n	Mean ± SD	n	Mean ± SD	n	Mean ± SD	
RBC, $x10^{12}$/liter	1174	5.12 ± 0.4	912	4.64 ± 0.4	2086	4.90 ± 0.5	< 0.0001
Hb, g/dL	1186	15.4 ± 1.3	901	13.6 ± 1.2	2087	14.6 ± 1.6	< 0.0001
Hct, %	1185	45.0 ± 3.9	910	40.0 ± 3.8	2095	42.9 ± 4.6	< 0.0001
MCV, fL	1181	88.2 ± 4.0	883	86.7 ± 4.6	2064	87.5 ± 4.3	< 0.0001
MCH, pg	1183	30.2 ± 1.6	886	29.4 ± 1.8	2069	29.9 ± 1.7	< 0.0001
MCHC, gr/dL	1182	34.1 ± 0.9	909	3.8 ± 0.9	2091	34.0 ± 0.9	< 0.0001
WBC, $x10^{9}$/liter	1167	7.8 ± 2	908	7.46 ± 2	2075	7.6 ± 2	< 0.0001
Platelet, $x10^{9}$/liter	1176	235 ± 52	901	253 ± 56	2077	243 ± 55.1	< 0.0001

for RBC and leukocyte counts, Hb level, Hct value, MCV, MCH level, and MCHC were higher in males, whereas the mean values for platelet count was higher in females. The hematological values of all the subjects are shown according to sex for the study population in Table 1.

DISCUSSION

Data derived from unselected populations, or populations selected for disease by virtue of having laboratory investigations performed, are likely to yield biased values. Even with the best of reference standards, there will be an overlap of laboratory values of mildly affected, abnormal individuals into the normal reference range[2,3]. The values reported here were derived from a large population sample and that subjects were excluded by using rational, statistically driven criteria, we argue that it is appropriate to compare hematological values derived from our study.

High altitudes will cause tissue hypoxia leading to the release of erythropoletin, and in turn an increase in the rate of red cell production, eventually a polycythemia with an enhanced oxygen carrying capacity[13-15]. On the other hand, there is a risk that the stress hormones may induce a relative depression of the bone marrow particularly in the early phase of altitude training when adaptation is minimal and the stress reaction is most accentuated[14].

An increase of total red cell volume as a result of the stimulated erythropolesis at moderate altitude was reported. In recent reports, however, investigators suggested that the marked erythrocytosis at altitude reported in early studies (25 to 30% higher hemoglobin concentration, hematocrit, and red cell mass values in high Andean natives than in subjects at sea level) may largely reflect selection of subjects with pulmonary disease because an agrarian population from the same area exhibited only a 10 to 12% increase above values obtained at sea level[16]. But this increase rate mentioned has been found out for the altitudes much more above 1869 m.

We could not an increase in the number of red blood cells as well as other hematological parameters in healthy adults living in Erzurum area. Hematological values in this study were similar to those reported in other studies with large, well-selected samples[5,9,17]. However, Akdag et al reported that median values of RBC, Hb, Hct, and MCV at 1869 m altitude have been found to be higher than the study carried by Yip et al with the group aged between 6-14 living at sea level values (0.47 x 10^{12}/1for RBC, 1.3 gr/dL for Hb, 4% for Hct, 2 fL for MCV)[18]. But we saw that there was not a significant difference between our study and the study carried out by Yip et al[19]. (Their study uses different age groups and we recalculated the median value for 17-74 years old in order to be able to compare the results). The median values of RBC, Hb, and Hct were slightly higher in our study, MCV slightly lower than the sea level values (0.22

x 10^{12}/1 for RBC, 0.3 gr/dL for Hb, 0.9% for Hct, 2 fL for MCV). We are in the opinion that for an accurate result the study should be carried out with the same group both at sea level and at high altitude.

But the studies failed to demonstrate an increase in total body hemoglobin during training at moderate altitude[20]. Gore et al reported that in highly trained athletes, four weeks of training at an altitude of 1740 m produced no change in mass of hemoglobin in the blood and only a small increase in maximum oxygen consumption[21]. At the same time Friedmann et al reported that 18 days of endurance training at an altitude of 1800 m does not lead to an increase in total body hemoglobin[15]. It is possible, however, that an altitude greater than 1869 m may be required to induce an increase in Hb mass.

This implies that there might be a kind of threshold of how high living and how long a training camp at altitude must be to sufficiently stimulate erythropolesis for an increase of total body hemoglobin. The normal difference in hemoglobin concentrations can be estimated to be about 12% between permanent residents at sea level and at 2500 m above sea level. This difference indicates a necessary adaptation time of about 12 weeks[14]. Levine and Stray-Gundersen suggested that the altitude in erythropolesis stimulation for an increase of total body hemoglobin should be at least 2000-2500 m and this altitude has been suggested above 3000 m by Arnaund[22,23]. An increase in total body hemoglobin or red blood volume has been found in athletes who for 28 days either lived at about 2500 m or in another study lived in apartment in normobarric hypoxic conditions equivalent to approximately 2500 m[22-24].

Physiological variations in leukocyte count may occur in healthy people. Diurnal variations may effect the total leukocyte count as well as other celi types[3]. Previous studies show that the leukocyte count often is normal in those living at high altitude[11]. We, too, could not found a significant difference.

Platelet counts usually are normal or high in those living at high altitude[11]. Sharma reported that the highlanders living at 3658 m had a significantly high platelet count than lowlanders living at sea level[25]. Hudson et al reported that the mean platelet counts were low in the residents of low altitude than high altitude and demonstrated a significant and sustained elevation in platelet numbers within 48 h of ascent to high altitude[26]. But almost all of the studies have been carried out much more above 1869 m. We could not found a significant difference in platelet count. It is not suitable to compare the platelet count between the studies above and our study since the altitudes are quite different.

In addition, the mechanisms of adaptation to living at altitude apparently are multiple, and differ for different ethnic groups[23,27-29]. Previous studies of the erythropoletic response to hypoxia in high-altitude natives suggest that the hematocrit and hemoglobin values in Himalayan natives (Sherpas) are lower than expected for the altitude, perhaps because of a genetic adaptation[27,29]. In adaptation mechanisms, genetic factors are most likely to be relevant. There is sex difference in total leukocyte counts, and platelet counts which are apparent in all ethnic groups and this seems to be a genuine biological difference[4-6]. The cause is unknown[4].

In conclusion, we could not find increased number of red blood cells as well as other hematological parameters in healthy adults living in Erzurum area. Hematological values in this study were similar to those reported in the previous studies carried out with living under 1869 m. In addition, the hematological values presented here are derived from a large, representative population sample; therefore, the results are likely to applicable to the subjects in other areas in Turkey.

REFERENCES

1. Castro OL, Haddy T, Rana SR. Age- and sex- related blood cell values in healthy black Americans. Public Health Reports 1987;102:232-7.
2. Kelly A, Munan L. Haematologic profile of natural populations: Red cell parameters. Br J Haematol 1977;35:153-60.
3. Tsang CH, Lazarus R, Smith W, Mitchell P, Koutts J, Bunett L. Hematological indices in an older popu-

lation sample: Derivation of healthy reference values. Clin Chem 1998;44:96-101.

4. Bain BJ. Ethnic and sex differences in the total and differential white cell count and platelet count. J Clin Pathol 1996;49:664-6.
5. Arumanayagam M, Lam YM, Swaminathan R, Donnan SPB, Hom BL. Blood cell values in healthy Hong Kong Chinese adults. Clin Lab Haematol 1987;9:263-9.
6. Saxena S, Wong ET. Heterogeneity of common hematologic parameters among racial, ethnic, and gender subgroups. Arch Pathol Lab Med 1990;114: 715-9.
7. Hurdato A, Merino C, Delgrado A. Influence of anoxemia on hematopoetic activity. Arch Intern Med 1945;75:284-323.
8. Ruiz-Arguelles GJ. Sanchez-Medal L, Loria A, Piedras J, C6rdova MS. Red cell indices in normal adults residing at altitudes from sea to 2670 meters. Am J Hematol 1980;8:265-71.
9. Tikly M, Blumsohn D, Solomonos HD, Govender Y, Atkinson PM. Normal haematological reference values in the adult black population of the Witwatersrand. S Afr Med J 1987;72:135-6.
10. Savourey G, Garcia N, Besnard Y, Guinet A, Hanniquet AM, Bittel J. Preadaptation, adaptation and de-adaptation to high altitude in humans: Cardioventilatory and haematological changes. Eur J Appl Physiol 1996;73:529-35.
11. Athens, Lee GR. Polycythemia: Erythrocytosis. In: Lee GR, Bithell TC, Foerster J, Athens JW, Lukens JN, eds. Wintrobe's Clinical Hematology gth ed. Philadelphia: Lea & Febiger 1993:1245-61.
12. Gencelli Y. Screening of ß-thalasemia trait status by hemoglobin electrophoresis in East Anatolia (doctoral thesis). Erzurum, Turkey: Ataturk University Medical Faculty, 1983.
13. Knaupp W, Khilnani S, Sherwood J, Scharf S, Steinberg H. Erythropoletin response to acute normobaric hypoxia in humans. J Appl Physiol 1992;73: 837-40.
14. Berglund B. High-altitude training. Aspects of haematological adaptation. Sports Med 1992;5:289-303.
15. Friedmann B, Jost J, Rating T, Weller E, Werle E, Eckardt KU, Bartsch P, Mairbaurl H. Effects of iron supplementation on total body hemoglobin during endurance training at moderate altitude. Int J Sports Med 1999;20:78-85.
16. Garruto RM, Dutt JS. Lack of prominent compensatory polycythemia in traditional native Andeans living at 4.200 meters. Am J Phys Anthropol 1983; 61:355.
17. BaÞak M, Gul S, Kucukkaral› Y, Çank›r Z, Öztürk A, Öztosun M, Yazgan Y, Özcan A, Yaylac› M, Danac› M. A trial randomized reference hemogram results in Turkey. THOD 1998;8:69-72.
18. Akda¤ R, Energin M, Kalayc› G, Karakelleoglu C. Reference limits for routine haematological measurements in 7-14-year-old children living at an moderate altitude (1869 m, Erzurum Turkey). Scand J Clin Lab Invest 1996;56:103-9.
19. Yip R, Johnson C, Dallman PR. Age-related changes in laboratory values used in the diagnosis of anemia and iron deficiency. Am J Clin Nutr 1984;39: 427-36.
20. Dill DB, Adams WC. Maximal oxygen uptake at sea level and at 3.090 m altitude in high school champion runners. J App Physiol 1971;30:854-9.
21. Gore CJ, Hahn AG, Burge CM, Telford RD. VO2 max and haemoglobin mass of trained athletes during high intensity training. Int J Sports Med 1997; 18:477-82.
22. Levine BD, Stray-Gundersen JA. Practical approach to altitude training: Where to live and train for optimal performance enhancement. Int J Sports Med 1992;13:209-12.
23. Arnaud J, Quilici JC, Riviere G. High-altitude haematology: Quechua-Aymara comparisons. Ann Hum Biol 1981;8:573-8.
24. Laitinen H, Alopaeus K, Heikkinen R, Hietanen H, Mikkelsson I, Tikkanen H, Rusko HK. Acclimatization to living in normobaric hypoxia and training in normoxia at sea level in runners. Med Sci Sports Exerc 1995;27:109.
25. Sharma SC. Platelet count in permanent of high altitude. Indian J Physiol Pharmacol 1981;25:65-8.
26. Hudson JG, Bowen AL, Navia P, Rios-Dalenz J, Pollard AJ, Williams D, Heath D. The effect of high altitude on platelet counts, thrombopoietin and erythropoietin levels in young Bolivian airmen visiting the Andes. In J Biometeorol 1999;43:85-90.
27. Beall CM, Brittenham Gm, Strohl KP, Blangero J, Williams-Blangero S, Goldstein MC, Decker MJ, Vargas E, Villena M, Soria R, Alarcon AM, Gonzales MC. Hemoglobin concentration of high-altitude Tibetans and Bolivian Aymara. Am J Phys Anthropol 1998;106:385-400.
28. Beall CM, Reichsman AB. Hemoglobin levels in a Himalayan high altitude population. Am J Phys Anthropol 1984;63:301-6.
29. Winslow RM, Chapman KW, Gibson CC, Samaja M, Monge CC, Goldwasser E, Sherpa M, Blume FD, Santolaya R. Different hematologic responses to hypoxia in Sherpas and Quechua Indians. J App Physiol 1989;66:1561-9.

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