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Characteristics of Polycythemia in Sana'a, Yemen

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Abstract

Background: High altitude polycythemia is one of the altitude illnesses. Sana'a region is located at high altitudewhich reaches 3600 meters above the sea level. **Objectives:** To determine the hematological and clinical features of polycythemic patients residingin Sana'a region and to clarify the effect of high altitude in causing polycythemia. **Methods:** Hematological, clinical and demographic data were obtained from 30 polycythemic patients (26 males, 4 females, aged 26 to 85 years residing Sana'a regionand referred to the National Centre of Public Health Laboratories in Sana'a city for the firsttime venesection. **Results:**All studied samples showed high hemoglobinlevels (mean 18.85 g/dL for both sexes), normal platelet counts (228 and 267 $x10^9$/L for males and females, respectively),normal white cell counts in 96.7% of the cases (means 6.01 to 5.98 $x10^9$/L). Their clinical features showed predominance of headache, ruddy cyanosis, dyspnea and night sweating by 86.7%, 76.7%, 70% and 60%, respectively. Hypertension, joint pain, renal disease, peptic ulcer were less commonly mentioned by 36.7%, 20%, 13.3%, and10%, respectively. Hemorrhage, pruritus, splenomegaly, heart disease andliver disease wereobserved by only 6.67% each. **Conclusions:** Findings suggest thatsecondary polycythemia is predominant among polycythemicpatients due to the high altitude of Sana'a region. Findings needs to be confirmed bystudyinga larger sample and extended to investigate the erythropoietin level and JAK2V617F mutation for accurate diagnosis.

Keywords: Polycythemia, Sana'a, Yemen

INTRODUCTION

Polycythemia is an increase in the hemoglobin (Hb) concentration and/or packed cell volume (PCV) above the upper normal limit for age and sex of the patient.(1)It isclassified into absolute polycythemia, in which the total mass of the red cells is raised, and relative polycythemia where the total massof red blood cells is normal but the plasma volume is reduced. Absolute polycythemia is subdivided into primary and secondary polycythemia. Primary polycythemiavera (PV) is caused by a clonal malignancy of a hemopoietic stem cell(myeloproliferative disorder),(2)is associated with trilinear bone marrow proliferation and characterized by a

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raised red cell massandusually associated with leucocytosis and thrombocytosis. Secondary polycythemia (SP) results from an increased erythropoietin, either in the presence or absence of hypoxia.[2,3] The clinical features of the absolute polycythemia (headache, dizziness, dyspnea, hypertension, ruddy cyanosis, night sweating, hemorrhage, gout, splenomegaly, pruritus and peptic ulceration) are related to increased red blood cell mass and total blood volume that results in hyperviscosity, hypervolumia and hypermetabolism.[1]

Yemen is located on the southwestern of Arabian Peninsula. Sana'a region is located in the Middle Western mountainous area of the country at high altitude which reaches 3600 meters at the highest point in the mount Al-NabiShu'ayb. The capital Sana'a city is located in this region at altitude of 2200 meters above the sea level. This high altitude may lead to an increase in total Hb concentration in some people of Sana'a regionto a level that may cause SP [3] due to hypoxia. It is reported that 4% of Hb concentration increases for each 1000 meter which increases in high altitude.[4]

The incidences of high altitude polycythemia (HAP) at two different altitudes in the Tibet Autonomous Region: Lhasa (3650 meters above sea level) and in Naqu-Ando district (4500-4800 meters above sea-level) were 2.39% and 12.95%, respectively[5]. The annual statistical report of the National Blood Transfusion and Research Centre (NBTRC) for the year 2013 in Sana'a city revealed that 582 (6.7%) of the total 8666 donated blood units were from polycythemic cases (therapeutic donation).[6]

Determining the hematological laboratory and clinical features of the polycythemia among Yemeni patients residing Sana'a region are an essential primary step to characterizeits main features and to clarify the role of the high altitude of this region in causing polycythemia. Also to raise the awareness about high altitude polycythemia in order to improve its medical management, and to benefit from using the donated blood of polycythemic patients in transfusion instead of throwing it. The current study was conducted,since there are no pervious studies that addressed this subject.

MATERIALS AND METHODS

The study was conducted among polycythemic patients residing Sana'a regionusing across-sectional approach.A stratified sampling was done and consecutive blood samples were collected from 30 Yemeni polycythemic patients (26 males, 4 females, aged 26 to 85 years) attending the Blood Bank Department between December 2011 and January 2012at the National Centre of Public Health Laboratories (NCPHL)in Sana'a city for first-time venesection. These patients were referred by their doctors for therapeutic donation.

Data regarding their age, sex, originalresidence, family historyof polycythemia, chewing at(fresh green leaves of Catha Edulis) and cigarette smoking were collected. Other information included their clinical presentation at time of sample collection (headache, dyspnea, night sweating, pruritus, ruddy cyanosis, splenomegaly, peptic ulcer, hemorrhage, hypertension, joints pain, heart disease, liver disease and renal disease).

Venous blood samples were collectedfrom each patientand were analyzed on the same day for complete blood count (CBC) at the NCPHL using the hematological analyzer MYTHIC 22 (Orphee, Geneva, Switzerland).[7] Samples with Hb level more than 17.5 g/dL in adult males and 15.5 g/dL in adult females and PCV more than 51 L/L in males and 48 L/L in females were diagnosed as polycythemia.[1]

RESULTS

All the blood samples (26 males, 4 females) showed Hb levels> 17.5 g/dL(mean 18.85 g/dLin both sexes),and PCV > 51 L/L (mean 55.77 L/L for men, 55.15 L/L for women), so they wereconsidered as polycythemia that could be either PVor SP. Theirred cell counts were close or higher than the upper normal limit (mean 6.22 $x10^{12}/L$ for males, 5.8 $x10^{12}/L$ for females). Twenty nine (96.7%) of them had white cell count within the normal range (4.0 - 11 $x10^{9}/L$) and none had platelet count more than 400 $x10^{9}/L$. Two cases had low platelet count(39.0, 104 $x10^{9}/L$) (table 1).

Table 1: Hematological parameters of polycythemic patients

Hematological parameters	Male *(n=26)*			Female *(n=4)*		
	Mean	**SD**	**Range**	**Mean**	**SD**	**Range**
Hb (g/dL)	18.85	0.8	17.8 – 20.1	18.85	0.07	18.4 – 18.9
PCV (L/L)	55.77	2.4	52.7 – 58.3	55.15	0.92	54.5 – 55.8
RBC ($x10^{12}/L$)	6.22	0.66	5.4 – 7.9	5.8	0.14	5.7 – 5.9
MCH (pg)	30.7	2.6	24[a] – 34.9	31.66	0.35	31.4 – 31.9
MCV (fL)	90.16	6.16	75[a] – 100	93.95	0.92	93.3 – 94.6
MCHC (g/dL)	33.8	0.79	32.2 – 35.2	33.75	0.07	33.7 – 33.7
RDW (%)	12.12	1.15	10.2 – 14.6	12.65	2.05	11.2 – 14.1
WBC ($x10^{9}/L$)	6.01	3.05	22- 19.5[b]	5.98	1.44	3.9 – 7
Platelet ($x10^{9}/L$)	228	68.23	39 – 325[c]	276	33.3	253 - 325

[a] One case with low MCH and MCV
[b] One case with WBC count > the upper limit of the normal range
[c] Two cases with platelet count <150 $x10^{9}/L$

Table 2 shows the ages, weights and body mass index (BMI) of the polycythemic patients. All the patients were adults with a mean age of 52.76 years for men and 64.5 years for women. Also their mean weight and BMI were 75Kg and 26.4 for men and 88.5 kg and31.5 for women.

Table 2: The age and weight of the polycythemic patients

Parameter	Male (*n=26*)			Female (*n=4*)		
	Mean	SD	Range	Mean	SD	Range
Age (years)	52.76	18.32	26 – 85	64.5	22.16	33 – 85
Weight (kg)	75	17.9	33 – 102	88.5	14.4	70 - 105
IBM	26.4	3.7	15.1 – 33.7	31.5	4.0	26 – 35.5

All patients were living in the Sana'a region,about half of them (46.7%) were cigarette smokers and two- thirds (76.7%) were chewing qat. Also only one (3.33%) had a family history of polycythemia (table 3).

As presented in table 3, their clinical features showed predominance of headache, ruddy cyanosis, dyspnea and night sweating by 86.7%, 76.7%, 70% and 60%, respectively. Hypertension, joint pain, renal disease, peptic ulcerwere less commonly mentioned by 36.7%, 20%, 13.3%, and10% of the patients respectively. Hemorrhage, pruritus, splenomegaly, heart disease and liver disease were uncommonly observed by 6.67% each.

Table 3: Clinical and demographic features of the polycythemic patients

Clinical feature	Patients number (n=30)	Positive %
Headache	26	86.7
Dyspnea	21	70.0
Night sweating	18	60
Pruritus	2	6.67
Rruddy cyanosis	23	76.7
Splenomegaly	2	6.67
Peptic ulcer	3	10.0
Hemorrhage	2	6.67
Hypertension	11	36.7
Joint pain	6	20.0
Heart disease	2	6.67
Renal disease	4	13.3
Liver disease	2	6.67
Living at high altitude	30	100.0
Family history for polycythemia	1	3.33
Smoking cigarette	14	46.7
Chewing qat	23	76.7

DISCUSSION

This study was the first attempt to evaluate polycythemia in Sana'a region which has a total population of 3.2 millions.[8] It was chosen because of the following reasons: first, its high altitude that was reported in many studies as a cause of SP especially HAP[3-5] and, secondly, it includes the capital Sana'a city that has a residence of about 2.0 millions[8] who came from different regions of the country with other causes of polycythemia. The criteria of polycythemia diagnosis was based on Hb concentration above 17.5 g/dL for men and 15.5 g/dL for women and PCV value more than 51 L/Lin males and 48 L/Lin females. The Hb concentration and PCV values of all these patients were applied withthis criterion. All the patients were adults with malepredominance. Their clinical features generally support the diagnosis of polycythemia (table3), where none of them had a combined absence of all the common clinical features ofpolycythemia such as headache, dyspnea or ruddy cyanosis. Also none of them wassuffering from dehydration or burnat the time of the study which excluded relative polycythemia to a certain limit.

The high Hb levels of these patients are generally correlated with the high PCV valuesand red cell counts in all the blood samples whichindicated the validity of theseresults (table 1).The obtained hematological parameter values showedno association between the increased Hb concentrations or PCV values with leucocytosis and/or thrombocytosis except leucocytosis (19.5 $x10^9$/L)in only one case (table 1) which may suggestthe absence of marrow panmyelosis (trilinear proliferation).

Nevertheless, this study was mainly planned as a first attempt to determine thecharacteristic hematological parameters and clinical features of polycythemic patients residing in Sana'a region, and also to evaluate the effects of its high altitudein causing SPrather than verifying or specifying all causes or types of polycythemia. However, the analysis of the obtained data revealedsome evidencesofthe possible causes and types of polycythemia. At the time of this study, the technology for JAK2V617F mutationand erythropoietin level investigation wereunavailable inYemen which interfered partially with applying the 2008 World Health Organization (WHO) criteria of PV diagnosis.(9) However, 21 patients (17 men >18.5 g/dL, 4 women >16.5 g/dL) had high Hb levels that fit within the first part of the major WHO criteria of PV diagnosis. Because none of these showed a combined increase in RBC, WBC and platelet counts which may suggest the absence of marrow trilinear proliferation, in addition to absence of splenomegaly in any of them. These findings may exclude these cases from having PVaccording to the WHO criteria and the PV Study Group.(9,10) In order to confirm their exclusion, they should be investigated for JAK2V617F mutation(11) and erythropoietin level(12) which are almost associated with PV rather than SP.

Despitethat the sample size was small and that firm conclusion could not be drawn, the findingsof this study suggestedthat the common cause of polycythemia among Yemeni patients residing Sana'a region was SP.(13) Thiswas supported by normal WBC counts in 96.67% ofthe patients, platelet counts not exceeding 400 $x10^9$/L in any of them and very low coexistence of palpable splenomegaly (6.67%),(13)in addition to the rare incidence of PV which is between 2/100,000 people in USA, Europe to 2/million people in Africa and Asia,(14)high altitude was reported in many studies as a cause of SP due to hypoxia.(3) All patients in the current study were exposed to this factor due to their place of living.About half of them (46.7%) were cigarette smokers[66.7% of them were mild smokers (<15 cigarettes/day)](15)that may suggest smoking isnot the main cause of SP, also its effects need to be confirmed by measuring the level of carboxy hemoglobin.(16)The relation between chewing qat and increased Hb level has not been reported in any study yet.About two-thirds of patients were qat chewers and this needs further investigation.The average weightBMI among them were75 Kg and 26.4 for men and 88.5 kg and 31.5 for women which is not sufficientlyindicatingthat obesityis a major factor of causing SP, since the majority of the patients were men. Renal, heartand liver diseases were found in low percentages 13.7, 6.67 and 6.67, respectively, also suggesting that theydo not play a major role in causing SP(table 3).

High altitude is the main cause of SP among Yemeni polycythemic patients residing Sana'a region. Furtherinvestigation including determination of erythropoietin level and JAK2V617F mutationin order to accurately diagnose polycythemia is warranted.Confirmation of diagnosis will raise the need to provide the HAP patient more medical careattention by expanding the blood transfusion services throughout Sana'a region to facilitate therapeutic phlebotomy, and to get another source of blood supplyfor transfusion.

CONCLUSION

It could be concluded from the current study thatSP is predominant among Yemeni polycythemic patients residing in Sana'a region due to its high altitude.A larger sample-size is needed and other studies are needed to investigate JAK2V617F mutation and erythropoietin levelto confirm theprimary findings.

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