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Premarital Screening for Thalassemia Among Young Adults: A Study in Zabol, Sistan and Baluchistan Province of Iran

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Abstract

Introduction: There is a high prevalence of hemoglobinopathies, including thalassemia, in Sistan and Baluchistan province of Iran. It is important to appropriately screen young adults to control the birth of new cases of thalassemia. In many less-equipped centers, this practice only relies on cell blood count. This study investigated the hematological parameters of young adults referring to the Central Laboratory of Sistan, Zabol, for premarital screening for thalassemia.

Methods: This was a descriptive cross-sectional study conducted in Zabol, Sistan and Baluchistan province of Iran from August 2020 to August 2021. Complete blood count (CBC) parameters of 2926 young adults were collected using a Sysmex KX-21 device and were compared with available reference intervals according to the Clinical and Laboratory Standard Institute.

Results: The means of women's and men's age were 38.84±16.32 and 36.64±14.14 years, respectively. The average values for each parameter in the studied population were red blood cell (RBC) (4.78±0.55), hemoglobin (13.19±2.46 g/dL), hematocrit (40.11±3.57%), mean corpuscular volume (MCV) (85.16±28.33), neutrophil (52.12±9.98), lymphocyte (37.84±9.03), mixed leukocytes (10.00±3.51), platelets (244.02±62.32). The mean values of hemoglobin (14.48±5.17 vs. 12.69±1.39 g/dL), hematocrit (43.01±3.89 vs. 38.97±3.45%), serum ferritin (115.4±74.3 vs. 69.20±12.36 g/dL), total iron-binding capacity (316.84±1.38 vs. 320.95±41.01, $P=0.01$), and serum iron (85.05±28.51 vs. 76.25±28.22, $P=0.02$) were significantly lower in women than in men. Out of 2,926 people who entered this study, 195 (6.66%) were suspected of having thalassemia because of their low MCV (71.61±7.33 fL) and mean corpuscular hemoglobin (MCH) (23.67±2.66 pg).

Conclusion: The relatively low hemoglobin in females referring for premarital screening for thalassemia awakens healthcare experts to carefully examine these cases for the possibility of thalassemia minor after excluding other common possible reasons such as iron deficiency anemia using iron studies and hemoglobin electrophoresis.

Keywords: Hemoglobinopathy screening, Thalassemia, Normal ranges

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Introduction

A complete blood count (CBC) test is one of the important tests for the diagnosis, screening, and a follow-up of patients for hemoglobinopathies, especially in less-equipped centers.[1] The CBC test involves measuring parameters such as red blood cell (RBC) indices, hemoglobin, and differential count of white blood cells (WBCs).[2,3] This test provides a relatively cheap and widely available screening for detecting anemias such as iron deficiency anemia and thalassemia.[4-7] Based on the results

of CBC, suspected cases can be further analyzed by iron studies, hemoglobin electrophoresis, high-performance liquid chromatography (HPLC), or molecular studies to confirm a diagnosis, which imposes additional costs on countries' healthcare systems.[4]

In the southeast of Iran and Sistan and Baluchistan province, pre-marital screening tests for thalassemia are extremely important because of the high rate of familial marriage and the high penetrance of thalassemic alleles.[8,9] About 10% of thalassemia major patients of the country belong to Sistan and Baluchistan province, and 2500 patients with thalassemia major, in need of regular blood transfusions, live in this province.[10] The penetrance of the beta thalassemia gene in the province has been reported to range from 6.2% to 12.9%,[8] highlighting the importance of pre-marital screening tests to identify these cases. In the present study, we aimed to determine the basic CBC parameters of the young adults referring for pre-marital screening for thalassemia in Zabol, Sistan and Baluchistan province.

Methods and Materials

Study Design

This descriptive cross-sectional study was conducted in Zabol, Sistan and Baluchistan province, southeast of Iran from August 2020 to August 2021. This province is the host of a mixed population from different races and ethnic groups, from Sistani to Baluch as well as Afghan refugees. The data were gathered retrospectively from the records of the young adults referring to the Central Laboratory of Zabol for premarital screening tests.

Sample Size

All samples referring within a year were enrolled in this study; accordingly, the data of 2926 young adults were analyzed.

Sample Collection

Anticoagulated venous blood samples were collected in ethylenediamine tetraacetic acid tubes. To minimize laboratory interferences and the effects of physiological changes, all samples were collected in the morning and processed within 24 hours of blood collection.

Instruments

We used a Sysmex KX 21 device (Sysmex Corporation, Kobe, Japan) for CBC testing and a minidry BS480 device for biochemical tests (ferritin, total iron-binding capacity, and serum iron). Hematological parameters were those routinely checked, including CBCs, erythrocyte indices, hemoglobin, and hematocrit. Further, the erythrocyte sedimentation rate was determined by the standard western green method. The calibration of all devices was checked regularly with quality control programs. Finally, the parameters were analyzed and compared with reference values.

Statistical Analysis

The data were analyzed using SPSS version 27 software. A P value of < 0.05 was considered to be statistically significant.

Results

Study Population Characteristics

Samples from 2926 people, including 829 males (28.3%) and 2097 females (71.7%), who agreed to participate in this study were analyzed. The mean age of the participants was 37.27 ± 14.82 years. Moreover, Table 1 provides means, upper and lower limits of WBC, RBC, hemoglobin, hematocrit, mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), MCH concentration, red cell distribution width-standard deviation, platelets, mean platelet volume, counts of lymphocyte, neutrophil, eosinophil, and monocyte, as well as erythrocyte sedimentation rate for both genders.

Hemoglobin, RBC, and hematocrit were significantly higher in men than in women; however, there were no significant differences between men and women in terms of MCV, MCH, MCH concentration, red cell distribution width, WBC, differential leukocyte%, and platelet count. Serum ferritin, serum iron, and total iron-binding capacity were significantly higher in men than in women. Furthermore, out of 2926 people who entered this study, 195 (6.66%) were suspected of having thalassemia because of their low MCV and MCH (Means: 71.61 ± 7.33 fL and 23.67 ± 2.66 pg, respectively).

Discussion

Iran is located in the Middle East, a region with a high prevalence of thalassemia and other hemoglobinopathies, where premarital screening programs are strictly followed.[11] This is especially important because a main cause of the transmission of thalassemia in various populations is consanguineous marriages, reaching up to 60% in some Arab states.[12] Countries such as Jordan,[13] Saudi Arabia,[14] Palestine,[15] Lebanon,[16] and Iran[17] have implemented mandatory premarital screening programs for thalassemia, resulting in significant reductions in the birth of affected neonates. Nevertheless, even voluntary programs such as that in Turkey can be effective in reducing the birth of newborns with this disorder.[18]

The findings revealed that out of 2926 people who entered this study, 195 (6.66%) people were suspected of thalassemia with the average MCV and MCH of 71.61 ± 7.33 fL and 23.67 ± 2.66 pg, respectively. CBC is a simple and cost-effective screening tool to differentiate thalassemia carriers from individuals with iron deficiency anemia.[19] However, a ratio of carriers may not be revealed by CBC based on erythrocyte indices or even by HPLC, requiring further investigation through molecular

Table 1. Hematological Parameters in Young Adults Referring for Premarital screening

Hematologic Parameters	Gender		Lower Limit (95% CI)		Upper Limit (95% CI)		*P* Value
	Female n=2097 (71.7%)	Male n=829 (28.3%)	Female	Male	Female	Male	
Age (y)	36.64±14.14	38.84±16.32	8.36	6.2	64.92	71.48	0.01
WBCs, $\times 10^3/\mu L$	6.62±1.73	6.48±1.83	3.16	2.82	10.08	10.3	0.07
RBCs, $\times 10^6/\mu L$	4.65±0.52	5.12±0.63	3.61	3.86	5.69	6.38	0.001
Hemoglobin, g/dL	12.69±1.39	14.48±5.17	9.91	4.14	15.47	24.82	0.001
Hematocrit %	38.97±3.45	43.01±3.89	32.07	35.23	45.87	50.79	0.001
MCV, fL	85.11±27.98	85.32±28.88	29.33	27.56	141.07	143.08	0.85
MCH, pg	27.67±6.8	28.46±8.04	14.07	12.38	41.27	44.58	0.79
MCHC, g/dL	32.78±9.04	33.29±1.69	14.66	29.91	50.86	36.67	0.31
RDW-SD, fL	13.76±3.30	13.70±1.87	7.16	9.96	20.36	17.44	0.60
Platelets, $10^3/\mu L$	251±62.36	226.39±62.22	126.28	101.95	375.72	350.83	0.001
MPV, fL	9.47±0.93	9.35±0.92	7.61	7.51	11.33	11.19	0.01
Neutrophil	3.53±1.40	3.39±1.41	6.33	0.57	6.33	6.21	0.64
Lymphocyte %	37.82±8.91	37.91±9.34	20.0	19.23	55.64	56.59	0.08
Monocyte	9.75±3.83	10.64±2.72	2.06	5.2	17.41	16.08	0.01
Eosinophil	2.5±0.98	1.09±0.24	0.54	0.61	4.46	1.57	0.001
Ferritin, g/dL	69.20±12.36	115.4±74.3	44.48	0.00	93.92	264	0.001
TIBC, g/dL	320.95±41.01	316.84±1.38	238.93	314.08	402.97	319.6	0.01
Serum iron, g/dL	76.25±28.22	85.05±28.51	19.81	28.03	132.69	142.07	0.02
ESR, mm/h	6.73±5.11	4.60±3.87	0.00	0.00	16.95	12.34	0.001

Note. CI: Confidence interval; WBC: White blood cell; RBC: Red blood cell; MCV: Mean corpuscular volume; MCH: Mean corpuscular hemoglobin; MCHC: Mean corpuscular hemoglobin concentration; RDW-SD: Red cell distribution width-Standard deviation; MPV: Mean platelet volume; TIBC: Total iron-binding capacity; ESR: Erythrocyte sedimentation rate.

investigations such as next-generation sequencing.[20]

Carrier screening is one of the viable methods used to prevent thalassemia major, especially in countries where this condition prevails such as those in the Mediterranean region and Middle East (e.g., Iran).[21,22] Countries have witnessed a sharp reduction in the incidence of neonates with thalassemia since the beginning of screening measures.[23] The extent of screening measures is suggested to be extrapolated to all ethnicities in which the penetrance of defected globin genes is high.[24] Along with screening programs, there is a need to elevate public awareness about the disease through mass media, school education, workshops, and the like.[25] Nevertheless, achieving desirable outcomes may take a relatively long times.[26] For example, successful screening programs in Spain comprised both premarital and prenatal screening programs, especially targeting at-risk ethnicities.[27] The effectiveness of these programs can be increased by creating registries for recording the data of carriers and patients.[28] In Portugal, carriers were offered a card for better screening and counseling results,[22] and screening programs for hemoglobinopathies in the UK include CBC, HPLC, capillary electrophoresis, and isoelectric focusing.[29]

Strategies for screening programs vary in countries, but generally, they include MCV and MCH as primary indicators,[30] followed by checking serum ferritin levels to exclude iron deficiency in suspected cases. Further, the quantification of various hemoglobin molecules (e.g., hemoglobin subunit alpha 2 and hemoglobin F) can be among screening tests, particularly for those who show borderline ferritin and serum iron levels. The most definite way of determining if someone is a carrier is DNA testing; however, this test is not always available.[31] As mentioned, Iran's national premarital screening is a pillar of the country's measures for preventing the birth of thalassemia major patients. The same program is undergoing in many countries, and its effectiveness has been proven.[32] Since Iran has a high prevalence of thalassemia carriers, it is recommended to perform such screening for adolescents, young adults, parents, and siblings of children with thalassemia major, using inexpensive tests such as CBC, hemoglobin electrophoresis, HPLC, or DNA testing.[33] Nonetheless, implementing a large-scale screening program for this target population requires appropriate infrastructure.[34] Strengthening infrastructure with the collaboration of international organizations can obviate financial barriers in this area and enable large-scale national screening of populations. This strategy can help determine the burden and actual frequency of carriers in the country and, subsequently, improve the effectiveness of pre-marital screening programs.[35]

Conclusion

In Sistan and Baluchistan province, the high prevalence of hematological diseases such as hemoglobinopathies (e.g., thalassemia) renders pre-marital screening tests vital. In this regard, special care must be exercised to have a proper interpretation of the test results. In this study, CBC parameters of 2926 young adults referring for pre-marital screening tests in Zabol, Sistan and Baluchistan province, were analyzed, and 195 (6.66%) people were suspected of having thalassemia due to low MCH and MCV. It is recommended to provide equipment for hemoglobin electrophoresis and molecular testing at referral centers in this province to offer better screening services to the public.

Authors' Contribution

Conceptualization: Omolbanin Sargazi-Aval.
Data Curation: Omolbanin Sargazi-Aval,Hojat Shahraki, Alireza Khiabani, Mohammad Mehdi Rahimi Ghahroudi.
Formal Analysis: Alireza Khiabani.
Funding Acquisition: All Authors.
Investigation: All Authors.
Methodology: Omolbanin Sargazi-Aval, Hojat Shahraki, Mahsa Rahgoshay.
Project Administration: Omolbanin Sargazi-Aval.
Resources: Hojat Shahraki, Alireza Khiabani.
Supervision: Omolbanin Sargazi-Aval.
Validation: Hojat Shahraki.
Visualization: Hojat Shahraki.
Writing—Original Draft: Omolbanin Sargazi-Aval, Hojat Shahraki, Alireza Khiabani.
Writing—Review and Editing: All Authors.

Competing Interests

None to declare.

Ethical Approval

This study was approved by the Ethics Committee of Zabol University of Medical Sciences (Code: IR.ZBMU.REC.1398.176). Informed consent was obtained from all participants.

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References

1. Jones G, Barker A. Reference intervals. Clin Biochem Rev. 2008;29(Suppl 1):S93-97.
2. Van den Bossche J, Devreese K, Malfait R, et al. Reference intervals for a complete blood count determined on different automated haematology analysers: Abx Pentra 120 Retic, Coulter Gen-S, Sysmex SE 9500, Abbott Cell Dyn 4000 and Bayer Advia 120. Clin Chem Lab Med. 2002;40(1):69-73. doi:10.1515/cclm.2002.014
3. Rasouli M, Pourmokhtar M, Sarkardeh S. Hematological Reference Intervals for Healthy Iranian Blood Donors. Int J Hematol Oncol Stem Cell Res. 2017;11(4):305-312.
4. Dosoo DK, Asante KP, Kayan K, et al. Biochemical and hematologic parameters for children in the middle belt of Ghana. Am J Trop Med Hyg. 2014;90(4):767-773. doi:10.4269/ajtmh.13-0098
5. Ramezani A, Shams M, Zarinfar N, et al. Hematological reference values for healthy males in the central part of Iran. Iran J Pathol. 2014;9(1):50-55.
6. Sirdah MM, Tarazi IS, El Jeadi H, Al Haddad RM. Normal blood cells reference intervals of healthy adults at the Gaza Strip-Palestine. J Clin Lab Anal. 2008;22(5):353-361. doi:10.1002/jcla.20265
7. Wu X, Zhao M, Pan B, et al. Complete blood count reference intervals for healthy Han Chinese adults. PLoS One. 2015;10(3):e0119669. doi:10.1371/journal.pone.0119669
8. Miri-Moghaddam E, Sargolzaie N. Cut off determination of discrimination indices in differential diagnosis between iron deficiency anemia and β- thalassemia minor. Int J Hematol Oncol Stem Cell Res. 2014;8(2):27-32.
9. Rashid M, Bin Majid O, Dehghani M, Karimi M. Normal hemoglobin and hematological indices in southwest of Iran. Iran J Blood Cancer. 2009;1(3):99-102. [Persian].
10. Miri-Moghaddam E, Eshghi P, Sanei Moghaddam E, Hashemi S. Prevalence of hemoglobinopathies in Sistan and Balouchistan province in the southeast of Iran. Sci J Iran Blood Transfus Organ. 2013;9(4):406-413. [Persian].
11. Hamamy HA, Al-Allawi NA. Epidemiological profile of common haemoglobinopathies in Arab countries. J Community Genet. 2013;4(2):147-167. doi:10.1007/s12687-012-0127-8
12. Al-Gazali L, Hamamy H, Al-Arrayad S. Genetic disorders in the Arab world. BMJ. 2006;333(7573):831-834. doi:10.1136/bmj.38982.704931.AE
13. Hamamy H, Al-Hait S. Premarital screening program for beta-thalassemia in Jordan. The Ambassadors Online Magazine. 2007;10(1):52-60.
14. Alhamdan NA, Almazrou YY, Alswaidi FM, Choudhry AJ. Premarital screening for thalassemia and sickle cell disease in Saudi Arabia. Genet Med. 2007;9(6):372-377. doi:10.1097/gim.0b013e318065a9e8
15. Tarazi I, Al Najjar E, Lulu N, Sirdah M. Obligatory premarital tests for beta-thalassaemia in the Gaza Strip: evaluation and recommendations. Int J Lab Hematol. 2007;29(2):111-118. doi:10.1111/j.1751-553X.2006.00836.x
16. Abi Saad M, Haddad AG, Alam ES, et al. Preventing thalassemia in Lebanon: successes and challenges in a developing country. Hemoglobin. 2014;38(5):308-311. doi:10.3109/03630269.2014.939279
17. Samavat A, Modell B. Iranian national thalassaemia screening programme. BMJ. 2004;329(7475):1134-1137. doi:10.1136/bmj.329.7475.1134
18. Canatan D. Haemoglobinopathy prevention program in Turkey. Thalass Rep. 2011;1(s2):e4. doi:10.4081/thal.2011.s2.e4
19. Tong L, Kauer J, Wachsmann-Hogiu S, Chu K, Dou H, Smith ZJ. A new red cell index and portable RBC analyzer for screening of iron deficiency and thalassemia minor in a Chinese population. Sci Rep. 2017;7(1):10510. doi:10.1038/s41598-017-11144-w
20. Shang X, Peng Z, Ye Y, et al. Rapid targeted next-generation sequencing platform for molecular screening and clinical genotyping in subjects with hemoglobinopathies. EBioMedicine. 2017;23:150-159. doi:10.1016/j.ebiom.2017.08.015
21. Cao A, Furbetta M, Galanello R, et al. Prevention of homozygous beta-thalassemia by carrier screening and prenatal diagnosis in Sardinia. Am J Hum Genet. 1981;33(4):592-605.
22. Martins MC, Olim G, Melo J, Magalhães HA, Rodrigues MO. Hereditary anaemias in Portugal: epidemiology, public health significance, and control. J Med Genet. 1993;30(3):235-239. doi:10.1136/jmg.30.3.235
23. Cowan RS. Moving up the slippery slope: mandated genetic screening on Cyprus. Am J Med Genet C Semin Med Genet.

2009;151C(1):95-103. doi:10.1002/ajmg.c.30202
24. Loukopoulos D. Haemoglobinopathies in Greece: prevention programme over the past 35 years. Indian J Med Res. 2011;134(4):572-576.
25. Cao A, Kan YW. The prevention of thalassemia. Cold Spring Harb Perspect Med. 2013;3(2):a011775. doi:10.1101/cshperspect.a011775
26. Lena-Russo D, Badens C, Aubinaud M, et al. Outcome of a school screening programme for carriers of haemoglobin disease. J Med Screen. 2002;9(2):67-69. doi:10.1136/jms.9.2.67
27. Mañú Pereira M, Corrons JL. Neonatal haemoglobinopathy screening in Spain. J Clin Pathol. 2009;62(1):22-25. doi:10.1136/jcp.2008.058834
28. Cela E, Bellón JM, de la Cruz M, et al. National registry of hemoglobinopathies in Spain (REPHem). Pediatr Blood Cancer. 2017;64(7):e26322. doi:10.1002/pbc.26322
29. Cell NS. Thalassaemia Screening Programme, Handbook for Laboratories. 2017. http://www.sickleandthal.org.uk/publications.htm#LabHandbook. Accessed September 2006.
30. Hoppe CC. Newborn screening for hemoglobin disorders. Hemoglobin. 2011;35(5-6):556-564. doi:10.3109/03630269.2011.607905
31. Chern JP, Lin KH, Lu MY, et al. Beta-thalassemia major births after National Screening Program in Taiwan. Pediatr Blood Cancer. 2008;50(1):58-61. doi:10.1002/pbc.21185
32. Fucharoen S, Weatherall DJ. Progress toward the control and management of the thalassemias. Hematol Oncol Clin North Am. 2016;30(2):359-371. doi:10.1016/j.hoc.2015.12.001
33. Mudiyanse RM, Senanayake MP, Rathnayake RM. "Safe marriages" for thalassaemia prevention: a KAP survey in Sri Lanka. Transl. Biomed. 2015;6(3):1-5.
34. Ansari SH, Shamsi TS, Bohray M, et al. Molecular epidemiology of β-thalassemia in Pakistan: far reaching implications. Blood. 2011;118(21):5309-5309. doi:10.1182/blood.V118.21.5309.5309
35. McGann PT, Hernandez AG, Ware RE. Sickle cell anemia in sub-Saharan Africa: advancing the clinical paradigm through partnerships and research. Blood. 2017;129(2):155-161. doi:10.1182/blood-2016-09-702324