Screening of Hemoglobinopathies in Kahramanmaraş, TURKEY

Güneş T. YÜREGİR*, Metin KILINÇ*, Hasan EKERBİÇER, Neşet BİLALOĞLU***, Nermin TEKİN*****

* Department of Biochemistry, School of Medicine, Kahramanmaraş Sütçüimam University,
** Department of Public Health, School of Medicine, Kahramanmaraş Sütçüimam University,
*** Department of Pediatrics, School of Medicine, Kahramanmaraş Sütçüimam University,
**** Technical Health School, Kahramanmaraş, TURKEY

ABSTRACT

Thalassemia and sickle cell anemia are prevalent in southern Turkey. Being in close proximity to Çukurova we screened Kahramanmaraş to assess the prevalence and foci of the diseases. The sample sizes were calculated by Epilnfo 6.0 computer program at 95% confidence level. 1491 subjects aged 2-69 were studied. Hematological parameters were analyzed by an electronic cell counter. Electrophoresis were performed and Hemoglobin A_2 and hemoglobin F levels were determined on samples with MCV< 80 fL. The results of Canatan et al. on Elbistan were included in the final results. Thus, the prevalence of ß-thalassemia, hemoglobin D, Hemoglobin O Arab carriers were 0.68%, 0.28% and 0.013%, respectively. No hemoglobin S was detected. In conclusion, Kahramanmaraş seems not to be a high risk area but the public must be informed about these diseases. Every community in close proximity to high prevalence areas must be enlightened.

Key Words: Carrier screening, ß-thalassemia, Abnormal hemoglobins.

Turk J Haematol 2001;18(2): 79-83.

Received: *24.05.2000* ***Accepted:*** *10.03.2001*

Thalassemias and sickle cell anemia are the most widespread single gene diseases worldwide. Every year 310.000 homozygous or double heterozygous infants are born.

These diseases represent serious medical, social and economic problems to the family and to the public. Preventive measures for these inherited fatal disorders are premarital screening and prenatal diagnosis. However, to start premarital screening, population studies in the region must be done to determine the prevalence of the disease[1,2]. Surveys done in Çukurova encompassing Hatay, İçel, and Adana[3-9] and Antalya[10] on the

Mediterranean region of Turkey were completed and premarital screening programs and prenatal diagnosis have been in effect since 1994[11-13]. Studies for hemoglobinopathies were also conducted in the Elbistan county of Kahramanmaraş[14] and the neighboring provinces as Gaziantep[15] and Şanlıurfa[16]. However, since the prevalence varies from one county or even villge to another, so a single survey does not effectively show the prevalence. Thus, the aim of this study was to determine the prevalence of abnormal hemoglobins and high hemoglobin (Hb) A_2 ß-thalassemia in the province of Kahramanmaraş. Accordingly, it also aims to find the foci of the diseases and if they really exist, emphasize the need for premarital screening and prenatal diagnosis.

MATERIALS and METHODS

This study was conducted in Kahramanmaraş between June 1998 and November 1999 with the participation of 1491 subjects, 601 male, 890 female, aged 2-69 years. The screening survey comprised the counties Göksun, Andırın, Pazarcık, Türkoğlu, Çağlayancerit, Afşin and the central town of Kahramanmaraş. The results of Canatan et al[14] on hemoglobinopathies in Elbistan are also included to the study by the permission of the author. Blood samples were collected from apparently healthy school children, children in day care centers, the university personnel and students, and from the population at the hinterlands of primary health care centers by announcement of the survey by the local authorities. The participation was voluntary.

Blood samples were taken into EDTA tubes and brought to the laboratory in cold chain. Place and date of birth, name of each subject were recorded. Hematological analysis were done on the same day using automated cell counter (Cell Dyne 1700, Abbott Diagnostics). Cellulose acetate electrophoresis were performed according to the method of Kohn. Agar gel electrophoresis was done in Sebia.

The blood samples with MCV levels below 80 fL were analyzed for Hemoglobin F (HbF) by alkali denaturation method and HbA_2 by microcolumn chromatography (Isolab). The subjects with HbF levels > 2% and HbA_2 levels > 3.5% were defined as ß-thalassemia. The sample size were calculated by EpiInfo 6.0 computer program in 95% confidence interval.

RESULTS

Hematological data for different age groups are presented in Table 2. For each age group the data given in Wintrobe for the lower limit of normal values for RBC, Hb, Hct, MCV and MCH were accepted and our data were accordingly evaluated[1].

For the age group 2-5, 6-12, 13-18 M, 13-18 F, 19-39> M, 19-39> F, 40-< M, 40-< F; 20, 10, 6, 9,7, 65, 8, 9 cases were below the lower limit of normal values, respectively.

These cases would be considered as iron deficient or iron deficient anemia. Results of the 19-39 female group are note worthy. In Table 2, the results of abnormal hemoglobins and high A2 ß-thalassemia in the counties of Kahramanmaraş are shown. No hemoglobin S was detected.

In the districts that we have investigated (n= 1491), the prevalence for high A2 ß-thalassemia was 0.47%, HbD trait 0.27%, and one case of Hb O-Arab was detected. Taking Canatan's results into consideration (n= 995), the overall prevalence for ß-thalassemia trait is 0.68%, HbD trait 0.28% and HbO Arab trait 0.04%.

DISCUSSION

Sickle cell anemia and ß-thalassemia are important public health problems in the southern part of Turkey. The presence of these diseases in Çukurova was first reported by Aksoy et al in 1955 and 1958, respectively[17,18]. Studies in the region in further years showed variable incidences ranging from 0.5-44.2% for sickle cell trait and 1.4-10.8% for ß-thalassemia trait[3-9]. A systematic sur-

Table 1. The means, standart deviations and ranges of hematological parameters in different age groups and sexes

Age (Year)	Sex	RBC* (*)	Hb* (*)	Hct* (*)	MCV* (*)	MCH* (*)	RDW* (*)
2-5	M + F	4.71 ± 0.39	13.27 ± 1.27	38.67 ± 3.44	82.24 ± 6.85	28.21 ± 2.51	14.71 ± 1.56
	n= 82	3.35 - 6.05	6.70 - 16.70	23.60 - 49.80	51.30 - 99.80	15.20 - 34.00	11.90 - 24.00
6-12	M + F	4.57 ± 0.33	12.73 ± 0.95	36.73 ± 2.76	82.24 ± 6.85	27.93 ± 2.03	14.44 ± 1.19
	n= 293	3.49 - 6.30	8.40 - 15.70	26.80 - 46.90	52.50 - 92.70	16.50 - 34.40	12.60 - 21.00
13-18	M	4.89 ± 0.36	13.77 ± 1.11	39.84 ± 3.27	81.76 ± 5.75	28.18 ± 2.32	14.58 ± 1.15
	n= 116	3.89 - 6.05	10.10 - 16.70	31.60 - 49.80	60.60 - 96.40	18.80 - 32.30	12.10 - 20.20
	F	4.58 ± 0.36	12.91 ± 1.27	37.79 ± 3.31	82.60 ± 7.58	28.23 ± 2.64	14.81 ± 1.80
	n= 154	3.35 - 5.89	6.70 - 16.00	23.60 - 46.80	51.30 - 99.80	15.20 - 34.00	11.90 - 24.00
19-39	M	5.09 ± 0.44	15.05 ± 1.55	43.36 ± 4.28	85.20 ± 6.02	29.62 ± 2.27	14.46 ± 1.18
	n= 180	3.92 - 6.74	8.70 - 15.10	28.20 - 59.60	57.20 - 96.40	18.60 - 33.30	12.50 - 21.90
	F	4.52 ± 0.42	12.70 ± 1.46	37.07 ± 3.83	82.27 ± 7.64	28.14 ± 2.88	15.12 ± 1.84
	n= 439	3.34 - 6.14	7.00 - 18.80	23.30 - 53.90	55.00 - 95.70	16.50 - 32.70	10.80 - 23.90
40-<	M	5.03 ± 0.55	14.56 ± 1.78	42.07 ± 4.60	84.09 ± 7.13	29.00 ± 2.73	15.08 ± 1.65
	n= 87	3.64 - 6.56	10.60 - 22.00	31.00 - 52.10	60.20 - 94.50	19.10 - 34.30	13.10 - 22.60
	F	4.62 ± 0.45	13.24 ± 1.56	38.40 ± 4.52	83.45 ± 6.86	28.69 ± 2.58	14.98 ± 2.02
	n= 136	3.51 - 6.37	7.40 - 18.80	24.00 - 55.40	56.00 - 96.30	17.80 - 33.30	11.70 - 24.80

RBC: $10^6/mm^3$, Hb: g/dL, HTC: %, MCV: fL, MCH: pg, RDW: % M: Male, F: Female, n: Number analyzed,
*: Mean ± standart deviation, (*): Range.

vey done in collaboration with the municipal health authorities encompassing the provinces of Hatay, Adana and İçel showed that the prevalence for HbAS was 10.3%, 9.3%, 10.5% and ß-thalassemia carrier status was 5.7%, 1.8%, 3.3%, respectively[7]. In Şanlıurfa[16] and Gaziantep[15] preliminary reports showed prevalences of 3.9% and 3.89%. Forty homozygous ß-thalassemia cases in Kayseri suggest high prevalences there too (Personal com). Kahramanmaraş being in close proximity to Adana, Hatay, Gaziantep

Table 2. The distribution of hemoglobinopathy carriers in Kahramanmaraş

District	n	ß-thalassemia	Hb D	Hb O Arab	Total
K. Maraş (Central)	751	7 (0.93%)	2 (0.27%)	1 (0.13%)	10 (1.33%)
Göksun (Tombak village)	112	-	1 (0.89%)	-	1 (0.89%)
Çağlayancerit	127	-	1 (0.79%)	-	1 (0.79%)
Elbistan*	995	10 (1.0%)	3 (0.3%)	-	13 (1.31%)
Other districts**	501	-	-	-	-
Total	2486	17 (0.68%)	7 (0.28%)	1 (0.04%)	24 (0.97%)

* Canatan et al.[14]
** ß-Thalassemia, Hb D and Hb O Arab carriers were not detected in. Pazarcık (Narlı Town) (n: 101), Andırın (Central) (n: 87), Andırın (Efirağızlı village) (n: 46), Andırın (Yeşilova village) (n: 27), Türkoğlu (n: 90), Afşin (n: 150).

and Şanlıurfa, one would have expected high prevalences here too. However this province is quite different from the others in that immigration from the east and the south seems to have the minimal effect. It seems to be a closed community. Though Çukurova has a very heterogenous population for hundreds of years, Kahramanmaraş exhibits traits of a homogenous community with least immigration from neighboring areas.

The screening study done by Canatan et al in Elbistan district of Kahramanmaraş showed that the prevalence of ß-thalassemia trait as 1% (n= 995). No hemoglobin S was detected and there were 3 HbD carriers[14]. Our study, which included several districts of the province showed that the ß-thalassemia trait as 0.47% and HbD was 0.27% and for the first time Hb O Arab was detected here. Thus, there seems to be no need to screen every couple before marriage in order to detect carriers of hemoglobin disorders in Kahramanmaraş and environs.

However, a note of precaution is necessary. Since there are high prevalences of hemoglobinopathies in the southern part of Turkey and people are mobile, now every individual must have knowledge about these fatal diseases. A prevention program which depends on education, the detection of carriers, genetic counselling and prenatal diagnosis are in effect in Italy[19] for twenty years and homozygous births are almost nil there. Aside from hemoglobinopathy survey, the analysis of hematological parameters show that iron deficiency is an important health problem in Turkey and preventive measures must also be taken seriously.

In conclusion, being on the Mediterranean and the migratory nature of our population, hemoglobinopathy maps of screening surveys and evaluation of hematological parameters in provinces bordering and neighboring the Mediterranean sea must be continued.

ACKNOWLEDGEMENT

We would like to thank Öznur Ekiz, Aysel Tatlıyer and Fatih Büyükdereli for the tecnical assistance and Assoc. Prof. Dr. Duran Canatan for providing additional data.

This study was supported by KSU Research Fund Medical Faculty No.1

REFERENCES

1. Lee GR, Bithell TC, Foerster J, Athens JW, Lukens JN. Wintrobe's Clinical Hematology (ninth ed). London: Lea Febiger, 1993;1023-1145:2304.
2. WHO. Guidelines for the control of hemoglobin disorders, Modell B (Ed) World Health Organization. Hereditary Disease Programme. Document of the VI th Annual meeting of the WHO Working Group on Hemoglobinopathies, Sardinia, 1989. (WHO/HDP/HB/GL/94.1);1994:1-62.
3. Çavdar AO, Arcasoy A. The incidence of - ß thalassemia and abnormal hemoglobins in Turkey. Acta Haematol 1971;45:312-8.
4. Arcasoy A. Hemoglobinopathies in Turkey. Hematology Reviews and Communications 1992;6:61-7.
5. Altay Ç, Yetkin S, Özsoylu S, Kutsal A. Hemoglobin S and some other hemoglobinopathies in Eti-Turks. Hum Hered 1978;28:56-61.
6. Yüregir GT, Donma O, Dikmen N, İsbir T, Çınar M. Population studies Hemoglobin S and other Variants in Çukurova, the southern part of Turkey. Acta Hematol Jap 1987;50:757-65.
7. Yüregir GT, Arpacı A, Aksoy K, Tuli A, Dikmen N, Özgönen FT, Kılınç Y. Population at risk for Hemoglobinopathies in Çukurova, Türkiye: Need for Prenatal Diagnosis. Ann Med Sci 1995;4:61-9.
8. Kılınç M, Koçak F, Yuregir G, Aksoy K. İçel ilinde orak hücre anemisi ve ß-talasemi taşıyıcılık sıklığı. Ç.Ü. Tıp Fak. Der 1999;24:62-5.
9. Altay Ç, Gürgey A. Distribution of hemoglobinopathies in Turkey. Turkish J Pediatr 1986;28.219-29.
10. Bircan Y, Şişli S, Güven A, Çalı S, Yegin O, Ertug H, Güven AG, Akar N. Hemoglobinopathies in the district of Antalya, Turkey. Pediatr Hematol Oncol 1993;10:289-91.
11. Altay Ç, Yılgör E, Beksaç S, Gürgey A. Premarital screening of hemaglobinopathies: A pilot study in Turkey. Hum Hered 1996;46:112-4.
12. Gali AE, Polat G, Doğdu Ö, Akgöl M, Parlar HR, Arpacı A, Aksoy K, Yüreğir G. A premarital screening programme of Hemoglobinopathies in Hatay. Ann Med Sci 1999;8:88-92.
13. Atilla G, Çürük MA, Arpacı A, Özgönen FT, Kılınç Y, Aksoy K, Yüregir GT. Prenatal diagnosis of He-

moglobinopathies in Southern Turkey. Ann Med Sci 1999;8:93-7.

14. Canatan D, Bor S, Arcasoy A, Yeşil N. Elbistan yöresinde Anormal Hb ve HbA_2 yüksekliği ile karakterize ß -thalassemia taşıyıcı taraması. Doğa Tr J Med Sci 1990;14:555-61.
15. Ahi S. Gaziantep ve yöresinde hemoglobinopati ve Talasemi sıklığının hemoglobin elektroforezi ile saptanması. Thesis, M.S. Gaziantep University, 1998. (Unpublished data)
16. Yıldırmak Y, Tanyer G, Dallar Y, Çağıl H, Yeşil N. Şanlıurfa ilinde beta talasemi ve anormal hemoglobin taraması. XXVI Ulusal Hematoloji Kongresi Ankara,1998,168.
17. Aksoy M, Sickle cell trait in South Turkey, Lancet 1955;19:589.
18. Aksoy M, Ikin EV, Maurant AE, Lehmans H. Blood groups, hemoglobins and thalassemia in southern Turkey and Eti Turks. J Brit Med 1958;2:937.
19. Cao A, Saba L, Galanello R, Rosatelli MC. Molecular diagnosis and carrier screening for beta thalassemia. JAMA 1997;278:1273-7.

Address for Correspondence:

Güneş T. YÜREGİR, MD

P.O. Box: 1030
Gar, Adana, TURKEY