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DISTRIBUTION OF HEMOGLOBINOPATHIES IN TURKEY*

Based on studies conducted at Hacettepe Children's Hospital and reviews of other studies

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Key words: abnormal hemoglobin, hemoglobinopathy, sickle cell anemia, thalassemia

The hemoglobinopathies are not rare in Turkey[1-4]. The two most common hemoglobinopathies, beta thalassemia and sickle cell anemia, create problems both in the treatment of the disease itself and in its prevention by prenatal diagnosis. In many cases early diagnosis has not been possible.

This paper summarizes information about the number and the distribution of thalassemias and other hemoglobinopathies in Turkey.

Material and Methods

All of the 374 patients who were diagnosed in the Hacettepe Children's Hospital during the period 1975 to 1985 as having beta thalassemia major or beta thalassemia intermedia are included in the study. The ages at the time of diagnosis of 323 of the patients are given in Figure 1; the ages of the other 51 patients are not available.

Routine hemotological studies, hemoglobin electrophoresis, as well as Hb A_2 and Hb F determination were carried out by conventional methods[5-7].

Results and Discussion

Beta thalassemia has been found to be present throughout Turkey and the overall frequency is 2%[1-4,8,9] (Figure 2). In some areas the figure is as high as 10.8%[10]. Table I shows the frequency of β -thalassemia the other most common of the hemoglobinopathies and the number of cases of β -thalassemia expected each year.

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* From the Hacettepe University Institute of Child Health, Ankara. A part of this study was presented at the XVII. Meeting of the International Society of Hematology, the European and African divisions, at Warsaw, Poland 8-13 September 1985.

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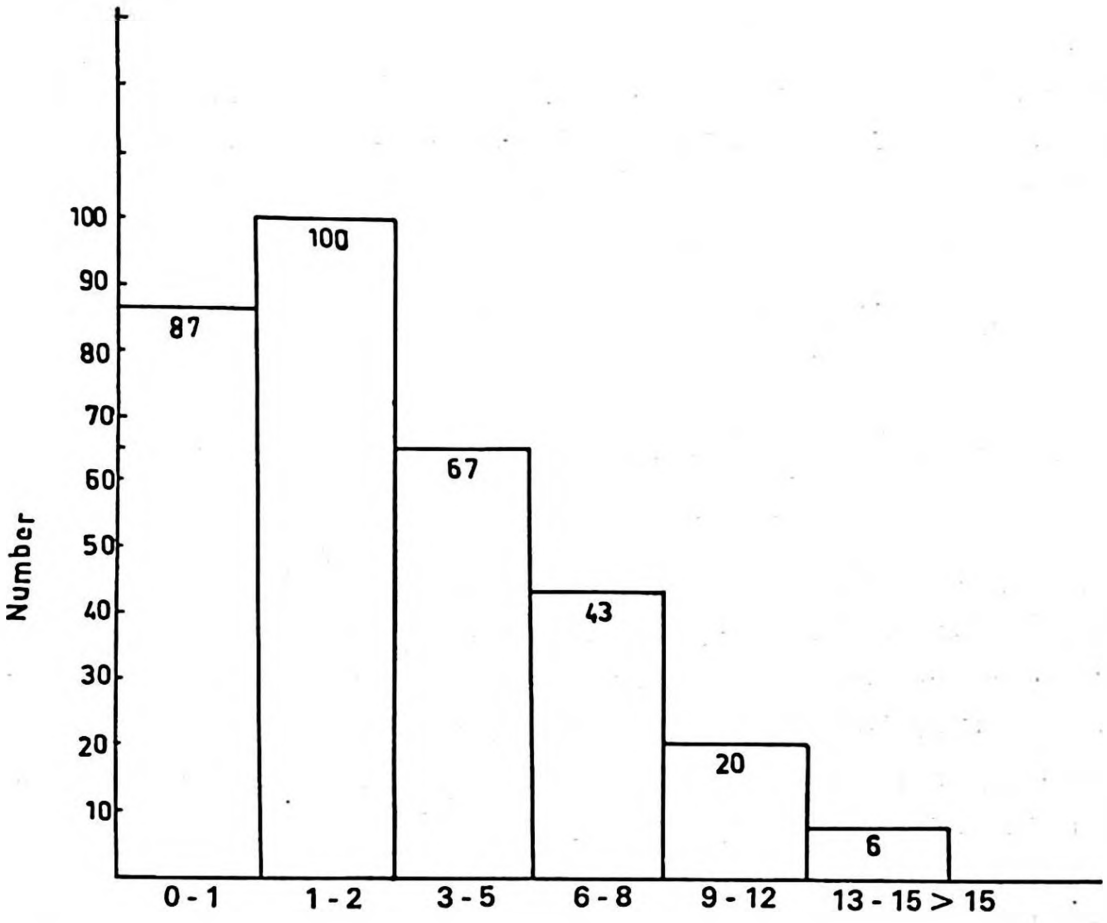

Figure 1

Age distribution of the patients with thalassemia major at diagnosis.

TABLE I

The Frequency of Beta Thalassemia and Some Other Common Hemoglobinopathies and the Expected Number of Beta Thalassemia Cases at Birth Calculated from the Population and the Birth Rate.

Turkish population in 1985	50×10^6
Birth rate	31 per 1000
Mean frequency of β-thalassemia	2%
Expected no of β-thalassemia major (at birth)	150 per year
Pregnancy at risk	600 per year
Infant mortality rate	98 per 1000
β-thalassemia major at 1 year of age	136
Frequency of Hb S (In Eti Turks)	3-37%
Frequency of Hb E (In Eti Turks)	0.5%

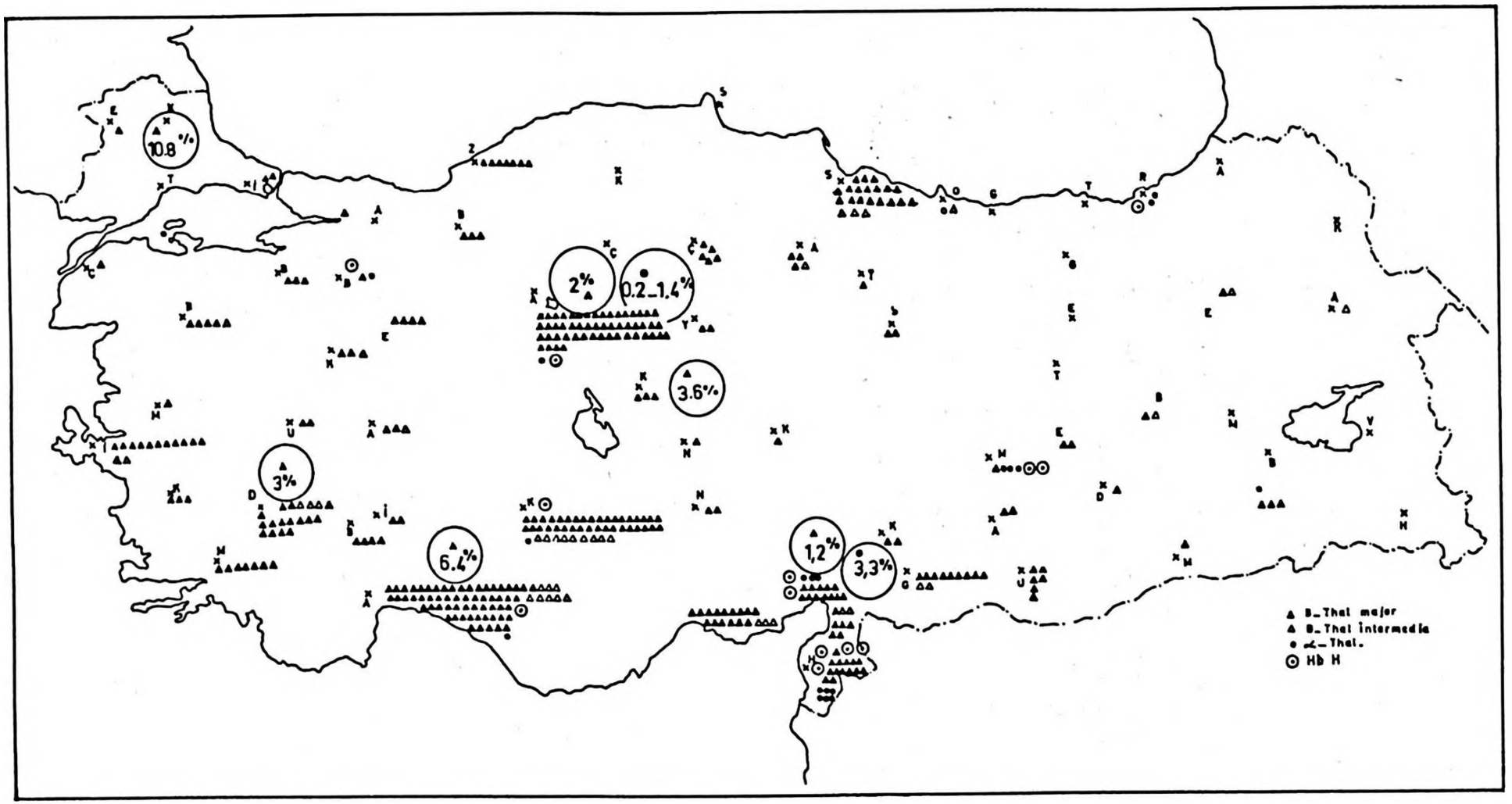

Figure 2

Distribution of beta thalassemia and alpha thalassemia in Turkey diagnosed in Hacettepe Children's Hospital. Figure inside the wide circle indicates the frequency of the hemoglobinopathies obtained by surveys.

It is expected that a total of 150 of the infants born each year will be affected with beta thalassemia major and since the number of consanguineous marriages is 21% the actual number of thalassemic patients is probably higher[11]. The frequency of alpha thalassemia was found, by cord blood studies, to be 0.2-3.3%[3,12,13]. Among populations with hemoglobin S the frequency of alpha thalassemia is reported to be even higher, 17-32%[14,15]. Hemoglobin H disease has also been found in various part of Turkey (Figure 2)[16].

Figure 3 shows the age distribution, at present, of beta thalassemia major in 92 patients. Although the expected number of patients with beta thalassemia under 10 years of age is 1000, in our institution during the last 10 years only 374 patients have been diagnosed as having beta thalassemia. Seventy-seven of these are at present under the age of 10 years (Figure 3). It would seem that there are many living undiagnosed or dying before diagnosis has been made. This assumption explains the discrepancy between the actual figures and the expected figures.

At least seven different mild beta thalassemia determinants exist and these (Table II) result in beta thalassemia intermedia in the homozygous condition or, in cases of compound heterozygosity, in mild and severe beta thalassemia[17-20].

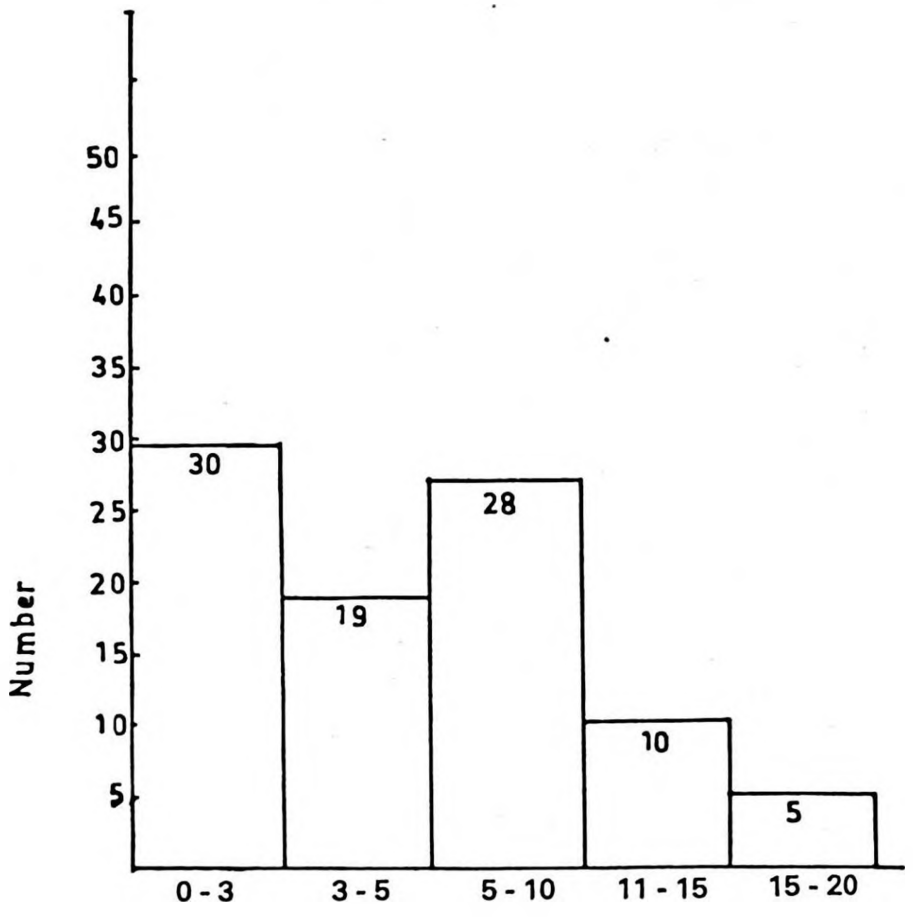

Figure 3

Ages of the patients with beta thalassemia major at present.

TABLE II

Genotypic Analysis of the Patients with Beta Thalassemia Intermedia

Group no	Genotype	Number of patients	Other studies
I-	6β - thal		
	a- $^{G}\gamma 6\beta/^{G}\gamma 6\beta$	2 (1)	–
	b- $^{GA}\gamma\gamma 6\beta/^{GA}\gamma\gamma 6\beta$	2 (2)	1 (1)
	c- $^{GA}\gamma\gamma 6\beta/\beta^{o}$	1 (1)	1
II -	$A_2F\beta^{\bullet}/\beta^{o}$ or β^{+}; $A_2F\beta^{+}/A_2F\beta^{+}$	14 (12)	2
III -	β^{o}/β^{o}	3 (3)	12
IV -	$A_2N\beta^{+}/\beta^{+}$ or silent β^{+}/β^{+}	4 (2)	–
V -	$A_2N\beta^{+}/A_2N\beta^{+}$	–	7
	Low HbF		
VI -	a- β^{++}/β^{++}	6 (5)	3
	b- β^{+} or β^{o}/β^{A}	10 (9)	–
VII -	$\beta^{th}/\beta^{th}\alpha^{th}$	3 (3)	–

a- Figure in parenthesis refers to the number of families.

They include:

1) A_2F β -thalassemia (thalassemia determinant which is characterized by increased Hb F and Hb A_2 in heterozygote),
2) Mild β^0-thalassemia,
3) Silent β -thalassemia,
4) β ++ thalassemia which is characterized by slightly increased Hb F and increased Hb A_2 in the homozygote. The latter is the most common mild β -thalassemia determinant[18].

The number of patients with sickle cell anemia diagnosed in our center is much fewer than for beta thalassemia major, the ratio is about 1:5 (Figure 4). However these patients are cumulated in a particular area in southern Turkey and they

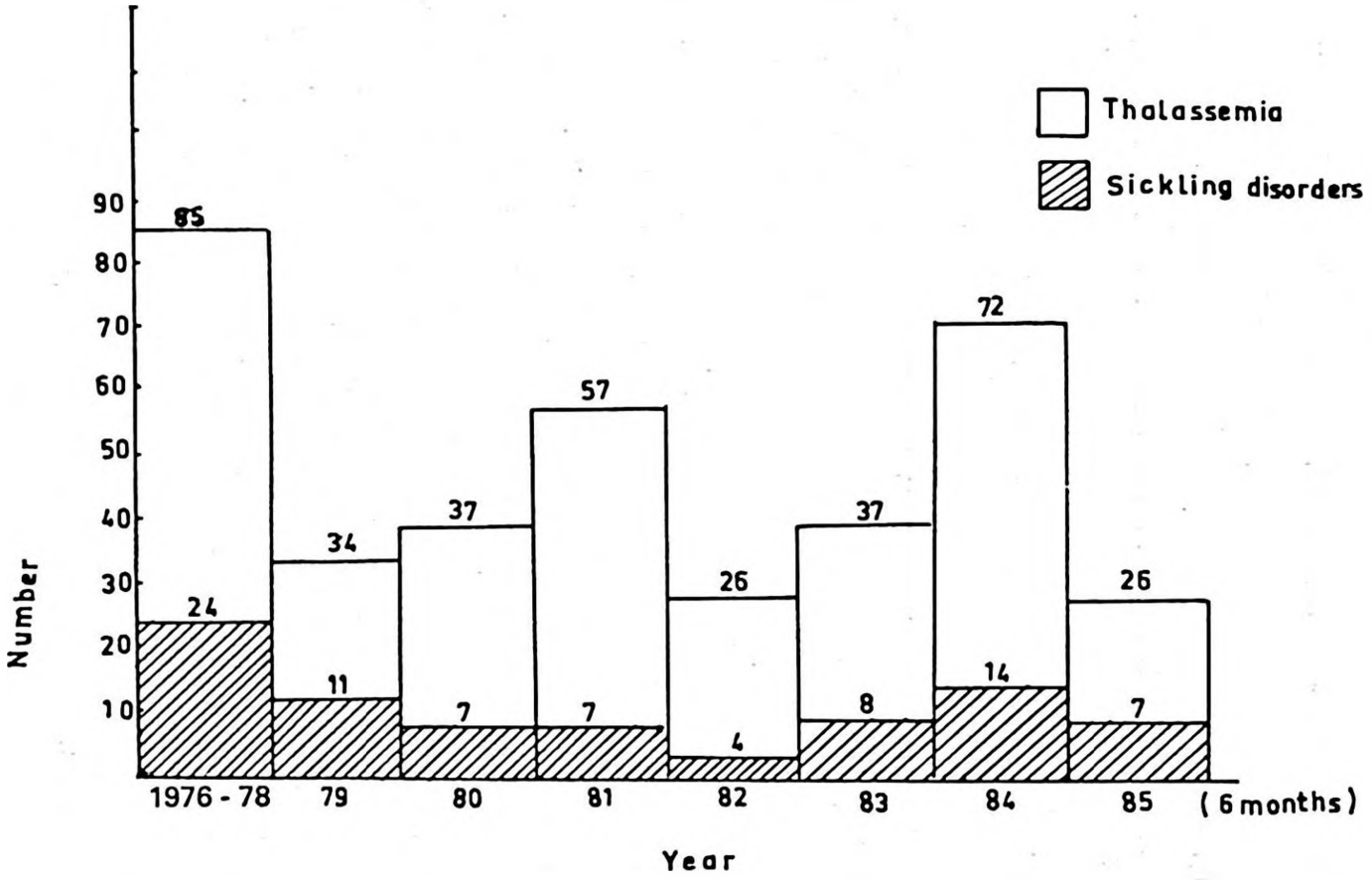

Figure 4

Distribution of beta thalassemia and sickling disorders in Turkey diagnosed in Hacettepe Children's Hospital.

constitute one of the major health problems in that area (Figure 5). Also the number of pregnant women seeking help for prenatal diagnosis is low. The presence of a total of 19 abnormal hemoglobins has been reported in Turkey[21-24] (Table III, Figure 5).

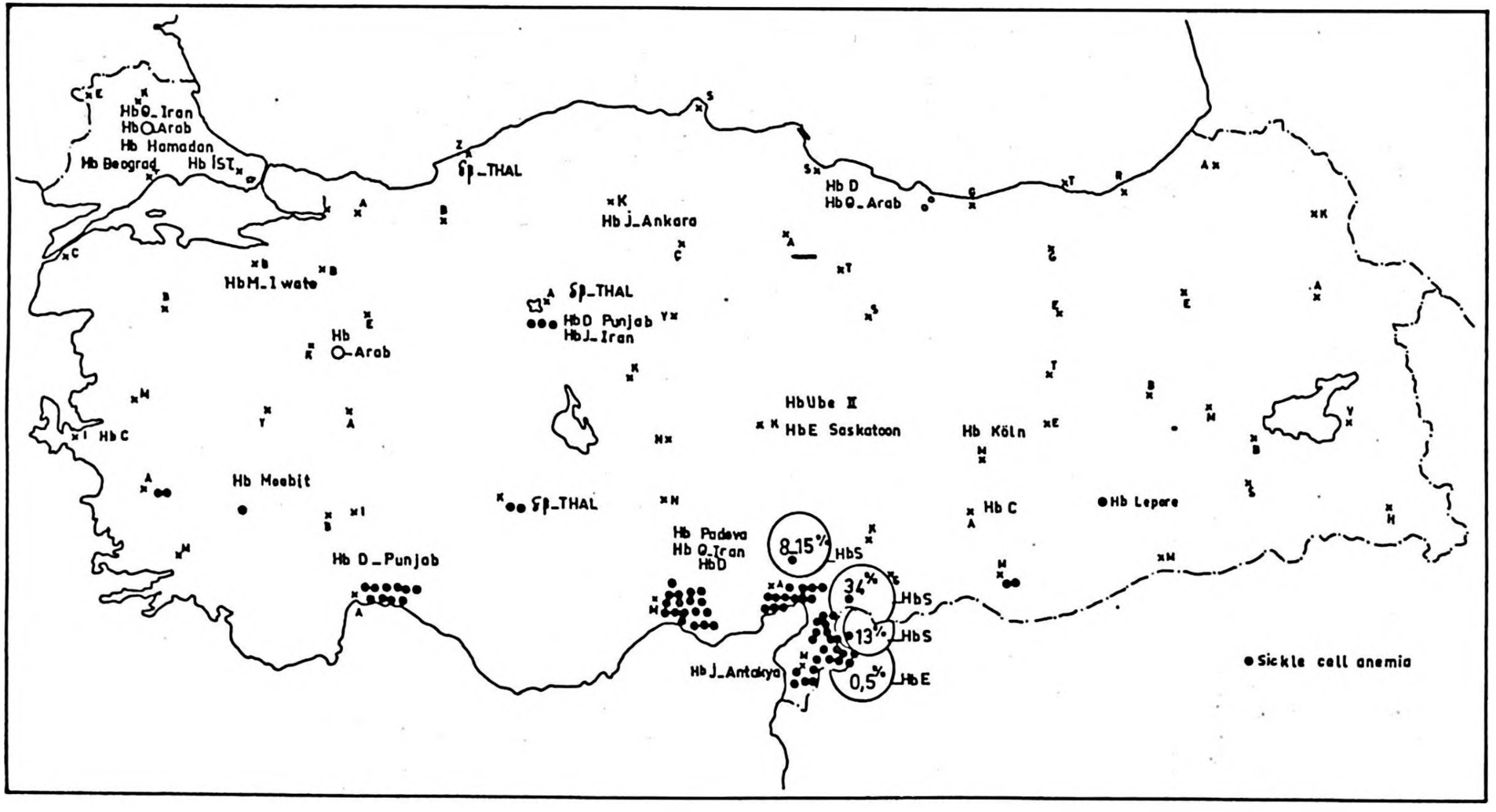

Figure 5

Distribution of sickle cell anemia and delta beta thalassemia diagnosed at Hacettepe Children's Hospital and abnormal hemoglobins reported in Turkey. The figure inside the circle indicates the frequency of abnormal hemoglobin obtained in surveys.

TABLE III

List of Abnormal Hemoglobins Reported From Turkey

Name and Structure	Origins of the Subjects	Name of the Authors
1. Hb J-Ankara ($\beta^{10Ala-Asp}$)	Kastamonu	Arcasoy at al[24]
2. Hb J-Antakya* ($\beta^{65Lys-Met}$)	Antakya	Huisman et al[25]
3. Hb Beograd ($\beta^{121Glu-Val}$)	Yugoslavia**	Aksoy et al[20]
4. Hb C ($\beta^{6Glu-Lys}$)	Gaziantep, İzmir	Altay et al[26], Göksel and Tartaroğlu[27]
5. Hb D-Punjab ($\beta^{121Glu-Gln}$)	More than one place	Aksoy and Lehmann[28], Çavdar and Arcasoy[29] Özsoylu[30]
6. Hb E ($\beta^{26Glu-Lys}$)	More than one place	Aksoy[31], Arcasoy et al[3] Altay et al[1]
7. Hb E-Saskatoor ($\beta^{22Glu-Lys}$)	Kayseri	Prozorova-Zamani et al[21]
8. Hb Hamadar ($\beta^{56Gly-Arg}$)	Western Thrace**	Aksoy et al[10]
9. Hb İstanbul ($\beta^{92His-Gln}$) (St. Etienne)	Caucasia**	Aksoy et al[32]
10. Hb J-İran ($\beta^{77His-Asp}$)	Ankara	Arcasoy et al[33]
11. Hb Köln ($\beta^{98Val-Met}$)	Malatya	Gürgey and Altay[34]
12. Hb Lepore (Füzyon Hb)	Diyarbakır	Çavdar and Arcasoy[35]
13. Hb M Iwate ($\alpha^{87His-Tyr}$)	Bursa	Özsoylu[36]
14. Hb O-Arab ($\beta^{121Glu-Lys}$)	Kütahya, Western Thrace**	Altay et al[22] Aksoy[23]
15. Hb O-Padova ($\alpha^{30Glu-Lys}$)	Adana	Kılınç et al[37]
16. Hb Q-İran ($\alpha^{75Asp-His}$)	Adana, Western Thrace**	Aksoy et al[38]
17. Hb Moabit ($\alpha^{86Leu-Arg}$)	Denizli	Knuth et al[39]
18. Hb Ube-2 ($\alpha^{68Asn-Asp}$)	Kayseri	Bilginer et al[40]
19. Hb A_2'	İmroz	Aksoy[41], Arcasoy et al[3]

* This abnormal hemoglobin was formerly reported as Hb Hacettepe. $\alpha_2B_2^{127Gln-Glu}$. Reinvestigation of this variant indicated that the original characterization was in error. The variant was renamed Hb J Antakya $\alpha_2B_2^{65\ Lys-Met}$ after the city where the family resides.

** Immigrants.

Other hemoglobinopathies such as alpha thalassemia and the abnormal hemoglobins listed in Table III do not create a health problem.

This study indicates that the number of patients actually diagnosed as having β -thalassemia major is far less than that of the expected number as calculated. Both the general public and people in the medical professions must be made more thalassemia conscious so that more attention well be given to the hemoglobinopathies in diagnosis and treatment. In Turkey every effort must be made to eradicate hemoglobinopathies by means of prenatal diagnosis.

Summary

From the information obtained from 374 patients diagnosed in Hacettepe Children's Hospital during the years 1975 - 1985, and from the surveys and publications made by other authors, the distribution of hemoglobinopathies in Turkey has been determined.

Population studies indicate that Hb S is present only in Çukurova, Manavgat and İstanbul. Beta thalassemia has been found to be present all over Turkey but most frequently in west and southwest Turkey.

The number of patients with β -thalassemia major was also found to be higher in certain areas such as Çukurova, Ankara, Konya and western Anatolia.

Detailed hematological examination of the patients with β -thalassemia intermedia revealed the presence of at least seven different mild β -thalassemia determinants.

It has been reported that 19 abnormal hemoglobin variants are to be found in Turkey but in some isolated areas the only common ones are Hb S and Hb E.

The number of patients actually diagnosed as having β -thalassemia major was much lower than the expected figure arrived at by calculation. The reasons for the discrepancy in these figures are discussed. The importance of prenatal diagnosis in the eradication of hemoglobinopathies is stressed.

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