A community-based study of common hereditary blood disorders in Oman

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دراسة مجتمعيةُ المُرتكَز حول اضطرابات الدم الوراثية الشائعة في سلطنة عُمان

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خلاصة: قمنا بتقييم درجة انتشار ثلاثة من اضطرابات الدم الوراثية الشائعة، وهي الخَلّة المنجلية، والثلاسيمية، وعَوَز نازعة هيدروجين فوسفات 6 غلوكوز، بين العُمانيين وذلك بإجراء مقابلات مع عينة ممثلة تتكون من 6103 من العُمانيين وفحص 6342 عينة من عينات الدم لأطفال تقل أعمارهم عن خمس سنوات، وقد تبين أن 27 بالمئة من العُمانيين الذكور قد ورثوا عوز نازعة هيدروجين فوسفات 6 غلوكوز، بالمقارنة مع 11 بالمئة من العُمانيات، مع انتشار في كامل عُمان لمعدلات تبلغ 5.8٪ بالنسبة للمنجلية و2.2٪ بالنسبة للثلاسيمية. وكان هناك ترابط قوي بين الاضطرابات الثلاثة ومناطق البلاد.

ABSTRACT We assessed the prevalence of three common hereditary blood disorders (sickle-cell and β-thalassaemia traits and glucose 6-phosphate dehydrogenase deficiency) among the Omani population. We interviewed a representative sample of 6103 Omani households and blood samples from 6342 children aged 0–5 years were collected. About 27% of Omani males had inherited glucose-6-phosphate dehydrogenase deficiency (compared with 11% of females) while countrywide prevalence rates for the sickle-cell and β-thalassaemia traits were estimated to be 5.8% and 2.2% respectively and showed no significant gender differences. There was a significant association between all three disorders and region of the country.

Etude communautaire des maladies héréditaires du sang courantes à Oman

RESUME Nous avons évalué la prévalence de trois maladies héréditaires du sang courantes (trait drépanocytaire, trait bêta-thalassémique et déficit en glucose-6-phosphate-déshydrogénase) dans la population omanaise. Nous avons interviewé un échantillon représentatif de 6103 ménages omanais et procédé à des prélèvements sanguins sur 6342 enfants âgés de 0 à 5 ans. Environ 27 % des garçons omanais présentaient un déficit en glucose-6-phosphate-déshydrogénase héréditaire (contre 11 % des filles) et on estime que le taux de prévalence au niveau national pour le trait drépanocytaire et le trait bêta-thalassémique s'élève à 5,8 % et 2,2 % respectivement, ne montrant pas de différence significative en fonction du sexe. Il y avait une association significative entre les trois maladies et la région du pays.

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Introduction

Studies are available from the neighbouring countries of Oman on the prevalance of haemoglobinopathies and glucose-6-phosphate dehydrogenase (G6PD) deficiency [*1–3*]. The most commonly encountered abnormal haemoglobin in the area is sickle haemoglobin (Hb S $^{\beta 6\ Glu \rightarrow Val}$). In addition, both G6PD deficiency and the thalassaemias coexist at a high frequency [*4,5*]. There has been no community-based study in Oman, but a study on blood donors at the Sultan Qaboos University Hospital showed the carrier frequency for β-thalassaemia to be 1.5%, 6% for sickle haemoglobin, and 27% for G6PG deficiency in males [*6*].

The inherited disorders of haemoglobin synthesis, which are some of the commonest disorders known in humans are high in regions of the world in which *Plasmodium falciparum* malaria is endemic, including the Mediterranean region, the Middle East, Africa, India and South-East Asia. Oman is known to have a high frequency of malaria-associated erythrocyte disorders [*4,6*].

Oman has a relatively young health care system, with comprehensive medical care universally available only during the past 20–25 years. While infant mortality has been reduced from 118 per 1000 live births in 1972 to less than 18 per 1000 live births in 1995 [*7,8*], the morbidity and mortality due to inherited red cell disorders have remained high. Therefore, any further reduction of early childhood morbidity and mortality will depend to a large extent on control of the major haemoglobinopathies. Thus, a national prevention programme is being considered.

Methods

The 1993 national population census was used as a frame for a two-stage, stratified probability sample. In the first stage, a systematic probability proportionate to sample size of 264 primary sample units was chosen from all Oman's districts. In the second stage, an updated listing of Omani households from the primary sample units was made and 25 households from each PSU were selected using a systematic random technique. Altogether 6600 households were designated for the survey. Based on the prevalence of haemoglobinopathies reported by White et al. [*6*] the required sample size was estimated to be 6000.

The haemoglobinopathy survey in the current study was linked to a family health survey which had been planned to study growth and other parameters among Omani children aged 0–5 years. The fieldwork was carried out between October 1995 and December 1995. Trained interviewers visited the designated households and filled in the forms. Data obtained included number of children, socioeconomic background and level of consanguinity. Out of the 6600 households selected, 6103 (92.5%) were successfully interviewed. There were 9033 children aged 0–5 years; of these 6342 (70.2%) children were taken by their parents to health centres or hospitals for blood collection; 3–5 mL whole blood in potassium EDTA (79.4%) or, if there was difficulty in collection as in babies (20.6%), blood was spotted on to Whatman BFC 180 specimen collection cards. We excluded 20 blood samples (0.3%) from the sample because of leakage, clotting or absence of accompanying

data. Of the remaining 6322 samples, 5020 (79.4%) were in EDTA and 1302 (20.6%) were on filter paper. Consent was obtained from parents and the survey was authorized by the Ministry of Health.

Complete blood counts and blood indices, screening for haemoglobin S, G6PD activity and quantification of Hb A2 and Hb F, as well as screening for haemoglobin variants were performed. Hb A2 values > 3.5% in the absence of an abnormal haemoglobin were considered confirmatory of β-thalassaemia trait.

Table 1 **Distribution of the three common hereditary blood disorders according to age group, sex and region**

Variable	β-thalassaemia trait N = 6283[a]		Sickle-cell trait N = 6322		G6PD deficiency N = 6322	
	No.	%	No.	%	No.	%
Age group (years).						
0–<1	18	1.6	75	6.6	226	20.0
1–<2	33	2.6	71	5.5	239	18.6
2–<3	31	2.3	64	4.8	240	18.0
3–<4	32	2.5	70	5.4	242	18.6
4–5	24	1.9	85	6.6	239	18.7
Total	138	2.2	365	5.8	1186	18.8
Statistical data	$\chi^2 = 4.04$, $P = 0.4$		$\chi^2 = 6.3$, $P = 0.17$		$\chi^2 = 1.8$, $P = 0.77$	
Sex						
Male	68	2.1	182	5.6	861	26.6
Female	70	2.3	183	5.9	325	10.6
Total	138	2.2	365	5.8	1186	18.8
Statistical data	$\chi^2 = 0.23$, $P = 0.6$		$\chi^2 = 0.31$, $P = 0.58$		$\chi^2 = 274.4$, $P = 0.000$	
Region						
Muscat	20	3.0	55	8.1	133	18.9
North Batinah	56	3.6	50	3.1	296	16.9
South Batinah	15	2.1	58	8.0	189	26.1
Musandam	1	1.6	3	4.7	7	10.9
Al Dhahira	14	2.3	26	4.1	133	21.0
Al Dakhiliyah	19	1.7	103	9.3	321	29.0
North Sharqiyah	4	0.9	45	10.1	72	16.2
South Sharqiyah	7	1.2	24	3.9	53	8.7
Al Wusta	0	0.0	0	0.0	0	0.0
Dhofar	2	0.5	1	0.2	9	2.1
Total	138	2.2	365	5.8	1186	18.8
Statistical data	$\chi^2 = 33.54$, $P = 0.00$		$\chi^2 = 127.2$, $P = 0.00$		$\chi^2 = 286.98$, $P = 0.00$	

[a] *Data were missing for 39 children.*
N = *number examined.*
G6PD = glucose-6-phosphate dehydrogenase.

Results

Table 1 shows the distribution of the three common hereditary blood disorders according to age group, sex and region. There was no significant association between these blood disorders and age group. Sex was only significantly associated with G6PD deficiency. Region was significantly associated with all three disorders ($P < 0.5$).

Table 2 shows the distribution of the three common hereditary blood disorders according to the level of haemoglobin and history of blood transfusion during the 12 months preceding the study. Sickle-cell trait was not significantly associated with anaemia while the other two blood disorders were ($P < 0.05$). Only G6Pd deficiency was associated with history of blood transfusion. ($P < 0.05$)

The mean Hb S level in the EDTA samples of 219 children aged 2–5 years was 28.8% (Table 3). There was no significant difference in the mean levels of Hb S between the regions ($F = 1.32$, $P = 0.23$). The Tukey-B test showed that no two

Table 2 **Distribution of the three common hereditary blood disorders according to the haemoglobin (Hb) level and history of blood transfusion during the last 12 months**

Parameter	β-thalassaemia trait		Sickle-cell trait		G6PD deficiency	
	No.	%	No.	%	No.	%
Hb level (g/dl)						
Normal (Hb ≥ 11)	30	1.2	154	6.2	363	14.6
Mild anaemia (Hb = 10–10.9)	73	3.2	140	6.0	563	24.2
Moderate anaemia (Hb = 9–9.9)	6	3.1	10	5.2	37	19.1
Severe anaemia (Hb < 9)	0	0.0	0	0.0	2	16.7
Total	109	2.2	304	6.1	965	19.3
Statistical data	$N = 4982$, $\chi^2 = 23.3$, $P = 0.00$		$N = 5016$, $\chi^2 = 1.9$, $P = 0.6$		$N = 5012$, $\chi^2 = 71.00$, $P = 0.00$	
History of blood transfusion						
No	94	1.9	297	6.1	917	18.8
Yes	1	1.9	4	7.5	18	34
Total	95	1.9	301	6.1	935	18.9
Statistical data	$N = 4909$, $\chi^2 = 0.00$, $P = 0.97$		$N = 4955$, $\chi^2 = 0.03$, $P = 0.87$		$N = 4939$, $\chi^2 = 6.9$, $P = 0.01$	

N = *number examined.*
G6PD = glucose-6-phosphate dehydrogenase.

Table 3 **Hb S levels (%) in children age 2–5 years (EDTA samples) by region**

Region	Number	Lowest Hb S level	Highest Hb S level	Median level	Mean level
Musandam	1	26.6	26.6	–	26.6
North Batinah	30	20.4	40.2	30.0	29.9
South Batinah	33	23.9	39.0	27.6	28.8
Al Dhahira	20	16.9	36.8	29.6	29.3
Muscat	32	16.4	37.6	26.0	27.4
Al Dakhiliyah	56	23.2	42.7	26.7	28.4
North Sharqiyah	32	18.0	39.7	27.5	28.5
South Sharqiyah	14	19.9	40.7	31.3	31.4
Al Wusta	0	0.0	0.0	0.0	0.0
Dhofar	1	32.6	32.6	–	32.6
Total	219	16.4	42.7	28.5	28.8

F = 1.32, P = 0.23.

Table 4 **Association of first cousin consanguinity with all homozygous hereditary blood disorders**

Consanguinity level	Homozygous blood disorders		All others (normal + heterozygous)		Total	
	No.	%	No.	%	No.	%
First cousin consanguinity	12	0.6	2111	99.4	2123	33.6
All other cousins or non relatives	10	0.2	4189	99.8	4199	66.4
Total	22	0.3	6300	99.7	6322	100

Likelihood ratio $\chi^2 = 4.04$, P = 0.04.

groups (regions) were significantly different at the 0.05 level.

Table 4 shows that 33.6% of the studied sample was offspring of first cousin marriage. There was a significant association of consanguinity of first degree cousins with homozygous blood disorders ($\chi^2 = 4.04$, $P = 0.04$).

Table 5 compares the prevalence of the three common disorders between Oman and other GCC countries. Oman had the highest prevalence of the three disorders in comparison to United Arab Emirates and Saudi Arabia.

Combining our figures with information from the national census data, December

Table 5 **Comparison of prevalence (%) of common hereditary blood disorders with neighbouring countries of the Gulf Cooperation Council**

Country	Hb S	β-thalassaemia trait	G6PD deficiency
Oman	5.8	2.2	18.8
United Arab Emirates [4]	1.9	1.7	8.7
Saudi Arabia [18–21]	1.2	2.4	6.2

G6PD = glucose-6-phosphate dehydrogenase.

1993, on the total number of children under 5 years of age (1995 projection: 252 669), it was calculated that there are 14 314 children aged 5 years and under with sickle-cell trait, 5392 with β-thalassaemia trait and 44 733 with G6PD deficiency in Oman.

Discussion

The results of this nationwide survey generally support the findings of an earlier hospital-based study on Omani blood donors [6]. The distribution of the three common hereditary blood disorders was variable, with the densely populated northern regions showing the highest prevalence.

The overall prevalence of sickle-cell trait (5.8%) was higher than the 1.9% reported from the neighbouring United Arab Emirates [1] but still much lower than the rate in Bahrain (11.3%) [2]. However, North Batinah and Al Dhahira, which are regions adjoining the United Arab Emirates showed prevalence rates similar to that of the United Arab Emirates but lower than the other northern regions. It is difficult to explain this regional variation. For instance, there is no apparent explanation for the large difference in the prevalence of sickle-cell trait between North Batinah (3.1%) and South Batinah (8.0%); both areas are similar geographically and in their ethnic composition.

The mean and median levels of Hb S showed no statistically significant difference between the various northern regions while the ranges indicate that β-thalassaemia is endemic throughout these areas. It should be noted that, using blood counts supported by molecular investigations, a previous hospital-based study on Omani blood donors found a high frequency of β-thalassaemia [6].

Molecular studies have shown that the majority of β-thalassaemia mutations in Oman originated in the Indian subcontinent, particularly from Baluchistan [6,9]. The presence of Baluchi tribes, who settled as a cohesive community along the northern Batinah coast and did not migrate inland for various reasons, could explain the higher incidence of β-thalassaemia in this coastal area.

There was a huge variation in G6PD deficiency, with certain areas showing some of the highest prevalence rates ever reported (Al Dakhiliyah: 29.0%, South Batinah: 26.1%). Molecular studies have confirmed that the commonest deficient enzyme in Oman is G6PD^{MED} [10], similar to that described in Saudi Arabia [11], the United Arab Emirates [12] and the Mediterranean [13]. Despite the historical data, which suggest that the tribes of Oman originated from the Republic of Yemen following the breaking of the Ma'arib Dam in the 5th century AD [14], G6PD deficiency in Yemenis is reported at a much lower prevalence of 6.2%, but no molecular data are available [4].

There was no significant association between any of the three blood disorders and age groups of the studied sample.

G6PD deficiency was the only hereditary blood disorder that was significantly associated with gender. Males had almost double the rate than females. The opposite was reported by Mohammed et al. [2] but they suggested that the findings warranted some explanation. Anaemia was significantly associated with thalassaemia trait and G6PD deficiency and not with sickle cell traits. History of blood transfusion during the 12 months prior to the study was only significantly associated with G6PD deficiency proportionately with the highly significant association of the disorder with anaemia.

Consanguinity rates and rates of first cousin marriage are high in Oman. The first cousin marriage rate in our study was higher (33.6%) than that of Egypt (11.4%), Iraq (30%), Jordan (32%), Kuwait (30.2%), Lebanese Muslims (17.3%) and Saudi Arabia (31.4) [*15*].

First cousin consanguinity was significantly associated with all homozygous blood disorders in the study, which constituted 0.3% of the sample. Although marriages between close relatives are looked upon unfavourably in Europe and north America and are illegal in some places, in other parts of the world they account for 20%–50% of all marriages [*16*]. Many of these regions are predominantly Islamic. This association has arisen for cultural and historical reasons rather than religious ones. If consanguineous marriages form a high enough proportion (30% or more) of all marriages in a community, the distribution of autosomal recessive diseases will be altered [*17*].

Our results confirm that the inherited haemoglobinopathies are widespread in Oman and are of a level to be of national concern. Oman has the highest prevalence of the three disorders in comparison with the United Arab Emirates and Saudi Arabia as is shown in Table 5 [*4,18–21*]. With the figures obtained from our survey and using the Hardy–Weinberg equation, it was calculated that the number of children in Oman affected with a major haemoglobinopathy born yearly is 2 per 1000 live births. Correcting for 30%–40% consanguineous marriages that are known to occur, this figure rises to 3 per 1000 live births. With total births of 42 000 per year, Oman can expect about 125 children affected with a major haemoglobinopathy to be born annually, resulting in a heavy burden on the health services. Therefore, strengthening of the already existing national programme for detection, genetic counselling and health education is of prime importance in the future health planning of Oman.

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