

# Prevalence of thalassaemia, iron-deficiency anaemia and glucose-6-phosphate dehydrogenase deficiency among Arab migrating nomad children, southern Islamic Republic of Iran

M. Pasalar,<sup>1</sup> D. Mehrabani,<sup>2</sup> A. Afrasiabi,<sup>1</sup> Z. Mehravar,<sup>1</sup> I. Reyhani,<sup>2</sup> R. Hamidi<sup>1</sup> and M. Karimi<sup>1</sup>

انتشار الثلاسيميا، وفقر الدم بعوز الحديد، وعوز نازعة هيدروجين الغلوكوز -6- فُسفات بين أطفال البدو المهاجرين العرب، جنوب جمهورية إيران الإسلامية

مهدي باسالار، داوود مهرباني، عبد الرضا أفراشيبي، زهرة مهرآور، إيرما ريجاني، رقية حميدي، مهران كريمي

الخلاصة: لقد تم في هذه الدراسة الاستقصاء عن انتشار فقر الدم بعوز الحديد، وعوز نازعة هيدروجين الغلوكوز -6- فُسفات (G6PD)، وخلّة الثلاسيميا بيتا بين أطفال البدو المهاجرين العرب في جنوب جمهورية إيران الإسلامية. حيث تم تحليل عينات دم من 134 طفلاً من أطفال المدارس الذين تقل أعمارهم عن 18 عاماً (51 ذكور، 83 إناث). فُوجد انخفاض في فيريتين المصل (>12 نانوغرام/دل) لدى 17.9% من الأطفال (21.7% لدى الإناث و 11.8% لدى الذكور). وكان انخفاض خضاب الدم (الهيموغلوبين) مرتبطاً - بشكل كبير - مع انخفاض فيريتين المصل. وكان لدى طفل واحد فقط عوز في عوز نازعة هيدروجين الغلوكوز -6- فوسفات. وكان الخضاب  $HbA2 \leq 3.5$  غ/دل لدى 9.7% من مجموع الأطفال، مما يدل على وجود خلّة الثلاسيميا بيتا (10.8% لدى الإناث و 7.8% لدى الذكور). وكان هناك تشابه بين الخضاب في متوسط حديد المصل وفيريتين المصل والسعة الإجمالية الرابطة للحديد لدى الذكور والإناث. وكان لمؤشر فيريتين المصل نفس دقة مؤشر الهيموغلوبين في تشخيص فقر الدم بعوز الحديد. وكان ارتفاع معدل انتشار خلّة الثلاسيميا بيتا يمثل عاملاً للخطر المحتمل الرئيسي لدى هذه الفئة من السكان.

ABSTRACT This study investigated the prevalence of iron-deficiency anaemia, glucose-6-phosphate dehydrogenase (G6PD) deficiency and  $\beta$ -thalassaemia trait among Arab migrating nomad children in southern Islamic Republic of Iran. Blood samples were analysed from 134 schoolchildren aged < 18 years (51 males, 83 females). Low serum ferritin (< 12 ng/dL) was present in 17.9% of children (21.7% in females and 11.8% in males). Low haemoglobin (Hb) correlated significantly with a low serum ferritin. Only 1 child had G6PD deficiency. A total of 9.7% of children had  $HbA2 \geq 3.5$  g/dL, indicating  $\beta$ -thalassaemia trait (10.8% in females and 7.8% in males). Mean serum iron, serum ferritin and total iron binding capacity were similar in males and females. Serum ferritin index was as accurate as Hb index in the diagnosis of iron-deficiency anaemia. A high prevalence of  $\beta$ -thalassaemia trait was the major potential risk factor in this population.

Prévalence de la thalassémie, de l'anémie ferriprive et du déficit en glucose-6-phosphate déshydrogénase chez des enfants nomades et migrants arabes (sud de la République islamique d'Iran)

RÉSUMÉ La présente étude a évalué la prévalence de l'anémie ferriprive, du déficit en glucose-6-phosphate déshydrogénase et de la bêta-thalassémie mineure chez des enfants nomades et migrants arabes dans le sud de la République islamique d'Iran. Des échantillons de sang de 134 écoliers de moins de 18 ans ont été analysés (51 garçons, 83 filles). Des taux de ferritine sérique faibles (< 12 ng/dL) ont été observés chez 17,9 % des enfants (21,7 % chez les filles et 11,8 % chez les garçons). Un faible taux d'hémoglobine (Hb) était significativement corrélé à un faible taux de ferritine sérique. Seul un enfant était atteint de déficit en glucose-6-phosphate déshydrogénase. Au total, 9,7 % des enfants présentaient un taux d'HbA2 supérieur ou égal à 3,5 g/dL, signe d'une bêta-thalassémie mineure (10,8 % des filles et 7,8 % des garçons). Le taux moyen de fer sérique, de la ferritine sérique et la capacité de liaison du fer total étaient similaires chez les deux sexes. Le taux de ferritine sérique était aussi précis que le taux d'Hb pour le diagnostic de l'anémie ferriprive. La forte prévalence de la bêta-thalassémie mineure représentait le principal facteur de risque dans cette population.

<sup>1</sup>Haematology Research Centre, Nemazee Hospital; <sup>2</sup>Stem Cell and Transgenic Technology Research Centre, Department of Pathology, Shiraz University of Medical Sciences, Shiraz, Islamic Republic of Iran (Correspondence to M. Karimi: karimim@sums.ac.ir).

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## Introduction

There are a number of different nomad tribes of different ethnicities in the Islamic Republic of Iran and the haematological problems of their children may not be the same as in the wider community. Beta-thalassaemia is a common health problem in the Islamic Republic of Iran (1) which drastically affects the family and personal life of sufferers and is a drain on health resources (2). Beta-thalassaemia is caused by a deficient synthesis of  $\beta$ -chains of haemoglobin leading to hypochromic microcytic red cells, ineffective erythropoiesis and haemolytic anaemia and is the result of a decrease in haemoglobin (Hb)F synthesis during the first year of life (3). There have been several studies on  $\beta$ -thalassaemia mutation spectrum in the Iranian population since 1997 when the national thalassaemia screening programme was implemented (2,4). Up to the end of 2001, 2.7 million prospective couples had been screened and 10 298 at-risk couples had been identified, showing acceptable coverage of screening plus an annual 7.4% increase in the number of people reaching marriageable age. The average prevalence of carrier couples detected increased from 3.0/1000 to 4.5/1000 (5).

Iron-deficiency anaemia too is a common haematological problem worldwide, and is a public health problem in many developing countries. It is estimated that more than 500 million people worldwide are affected by iron-deficiency anaemia (6).

Glucose-6-phosphate dehydrogenase (G6PD) deficiency is another important haematological disorder in the Islamic Republic of Iran, where it is a major public health problem in many areas (7). G6PD is an X-chromosome linked disorder, leading to acute haemolytic anaemia following ingestion of fava beans, certain drugs and bacterial or viral infections (8).

Nutritional deficiency, familial marriage, illiteracy and certain cultural beliefs in different nomadic groups may produce variations in the prevalence of thalassaemia, G6PD deficiency and iron-deficiency anaemia (9,10). National data collection from different nomadic groups may help in planning health services more efficiently. The aim of this study was to investigate the prevalence of iron-deficiency anaemia,  $\beta$ -thalassaemia, and G6PD deficiency in Arab migrating nomads in Fars Province, southern Islamic Republic of Iran.

## Methods

### Sample

This cross-sectional study was conducted on Arab migrating nomad children in rural areas of Fars province in the southern part of the Islamic Republic of Iran. These nomads migrate between summer and winter quarters each year by up to 500 km. A total of 134 school-children in the age range 6–18 years were recruited from all 17 Arab nomad schools in the region. Their ethnicity determined by their registration in selected schools for Arab nomads. The total Arab students registered in any of schools were selected by their identification number using a computer program through simple random sampling, without replacements. According to our previous local data and the following statistical formula, the consultant statistician calculated 133 persons as the sample size:

$$n = [Z^2 (1 - \alpha/2) \times P (1 - P)] / d^2$$

with confidence interval = 95%,  $d = 5.1\%$  and  $P = 10\%$ .

The entire study group were of the same middle socioeconomic class and known to have a moderate-calorie diet intake. We excluded students who had any recognized haematological disease.

The study was approved by the ethics committee of Shiraz University

of Medical Sciences. Written consent was taken from each student within the legal age range and the remaining participants signed the consent with their parents signing as witnesses. None of the selected students refused participation in the study.

### Data collection

The study was performed over a 6-month period from March to July 2012. Data collection and blood sampling were performed by 3 of the current authors at the students' schools.

The students were interviewed concerning family history of thalassaemia and G6PD deficiency, signs and symptoms of iron-deficiency anaemia and anaemia, such as pica, agitation, anorexia and pale conjunctiva, and also availability of safe (piped, potable) drinking water. For young children, their parents answered the questions.

A 5 mL blood sample was collected from the participants by antecubital venepuncture and put in an icebox and immediately transported to Dastgheyb Hospital laboratory (affiliated to Shiraz University of Medical Sciences) for analysis.

Routine haematological parameters were measured immediately after blood sampling using an automated cell counter (Sysmex K1000 haematology analyser). These included: red blood cell (RBC) count, haemoglobin (Hb), haematocrit (Hct), mean corpuscular volume (MCV), mean corpuscular haemoglobin (MCH), mean corpuscular haemoglobin concentration (MCHC) and red-cell distribution width (RDW). Serum iron and total iron binding capacity (TIBC) were determined by a calorimetric procedure, and serum ferritin was determined by enzyme-linked immunosorbent assay method (Dynex). The degree of G6PD deficiency was measured by fluorescent spot testing. Determination of different kinds of haemoglobin was performed using high performance liquid chromatography (Hb-Gold).

Haemoglobin alpha-2 (HbA2)  $\geq$  3.5 g/dL was considered diagnostic of  $\beta$ -thalassaemia trait. MCV  $<$  80 fL, MCH  $<$  27 pg and Hb A2  $\geq$  3.5% were considered as criteria for diagnosis of beta-thalassaemia. Anaemia was defined as Hb concentration below the World Health Organization cut-off for age and sex, i.e.  $<$  12 g/dL for females and 6–14-year-old males, and  $<$  13 g/dL for 15-year-old males. The degrees of iron deficiency was determined by the following criteria: iron depletion was defined as serum ferritin concentration  $<$  12 ng/mL; and iron deficiency anaemia as anaemia accompanied by serum ferritin  $<$  12 ng/mL.

### Data analysis

Pearson correlation test was performed to examine the association of Hb concentration with serum ferritin. Statistical analysis was performed using SPSS software, version 18. Student *t*-test used to compare the mean values of male and female participants. Statistical significance was set at  $P < 0.05$ .

## Results

Out of 134 schoolchildren 51 (38.1%) were male and 83 (61.9%) were female. The mean age of participants was 11.7 (SD 3.5) years, and the age range was 6–18 years, including 48 primary (6–11 years), 35 intermediate (12–15 years) and 51 secondary schoolchildren (16–17 years).

Regarding risk factors related to anaemia, 33 (24.6%) children did not have access to safe drinking water; 6 (4.5%) had a family history of thalassaemia and 4 (3.0%) had a family history of favism. The prevalence of symptoms which by themselves are non-specific, but are related to iron deficiency, was relatively high (Table 1).

The mean HbA2 level of the children was 2.7% (SD 0.8%), Hb was 13.1 (SD 1.3) g/dL and Hct was 42.8% (SD

**Table 1 Prevalence of different risk factors related to anaemia in Arab migrating nomad schoolchildren (n=134)**

Parameter	Yes		No	
	No.	%	No.	%
Availability of safe drinkable water	101	75.4	33	24.6
Family history of thalassaemia	6	4.5	128	95.5
Family history of favism	4	3.0	130	97.0
Pica	24	17.9	110	82.1
Anorexia	12	9.0	122	91.0
Agitation	43	32.1	91	67.9
Pallor	25	18.7	109	81.3

3.1%) (Table 2). The mean serum ferritin was 27.3 (SD 23) ng/dL.

The mean Hb levels of males [13.6 (SD 1.2) g/dL] were significantly higher than for female children [12.7 (SD 1.3) g/dL] ( $P < 0.001$ ) and so were the Hct [44.5% (SD 2.6%) versus 41.8% (SD 2.9%) respectively] ( $P < 0.001$ ) and MCHC values [30.6 (SD 1.6) g/dL versus 29.2 (SD 3.2) g/dL respectively] ( $P = 0.004$ ). None of the other parameters (MCV, MCH, RDW, HbA2, HbF, serum iron, serum ferritin and TIBC) showed significant differences between males and females

Among the participants, only 1 child had G6PD deficiency (Table 3). A total of 24 children (17.9%) had serum ferritin  $<$  12  $\mu$ g/dL (Table 3), and the prevalence of low serum ferritin was higher in females than males (21.7% versus 11.8%), although the difference was not statistically significant ( $P = 0.223$ ). The prevalence of low Hb showed a statistical correlation with low serum ferritin ( $P < 0.05$ ). A total of 13 children (9.7%) had HbA2 levels  $\geq$  3.5% and the prevalence of  $\beta$ -thalassaemia trait was higher, but not significantly so, in female than male children (10.8% versus 7.8%) ( $P = 0.787$ ) (Table 3).

## Discussion

As the results indicate, 1 student had G6PD disorder (0.7%) and 24 (17.9%) showed low serum ferritin ( $<$  12  $\mu$ g/

dL), indicative of iron-deficiency anaemia. The mean serum ferritin in our study was 27.3 (SD 23) ng/dL. Thirteen participants had HbA2  $\geq$  3.5 g/dL and therefore 9.7% of our sample were classified as having  $\beta$ -thalassaemia trait. The mean HbA2 level was 2.7% (SD 0.8%) in the current research. The mean levels of Hb, Hct and MCHC showed statistically significant differences between male and female students, while other haematological parameters and iron indices showed no significant differences. The low Hb and Hct values correlated significantly with low serum ferritin ( $P < 0.05$ ). Hence, it seems that serum ferritin index is as accurate as the Hb index in the diagnosis of iron-deficiency anaemia.

The prevalence of iron-deficiency anaemia in our research was 17.9%. This figure is consistent with previous reports in southern Islamic Republic of Iran (9–12), but is lower or higher than the prevalence found in other developing countries (13,14). The prevalence of iron-deficiency anaemia in developed countries has declined in recent decades, but there has been little change in developing countries. The most common reason for iron-deficiency anaemia in children is poor intake of iron in the diet. This finding is particularly prominent in developing countries where the low level of iron intake is accompanied by malaria and intestinal parasitic infestations (15). There is a big difference in the prevalence of iron-deficiency

**Table 2 Haematological parameters and iron indices in Arab migrating nomad schoolchildren**

Parameter	Males (n=51)	Females (n=83)	Total (n=134)	P-value
	Mean (SD)	Mean (SD)	Mean (SD)	
Hct (%)	44.5 (2.6)	41.8 (2.9)	42.8 (3.1)	< 0.001
Hb (g/dL)	13.6 (1.2)	12.7 (1.3)	13.1 (1.3)	< 0.001
MCV (fL)	83.6 (6.1)	81.5 (7.6)	82.3 (7.1)	0.097
MCH (pg/cell)	25.7 (2.8)	25.1 (3.1)	25.3 (3.0)	0.261
RDW (%)	13.8 (1.8)	13.7 (1.8)	13.7 (1.8)	0.755
MCHC (g/dL)	30.6 (1.6)	29.2 (3.2)	29.8 (2.8)	0.004
HbA2 (g/dL)	2.6 (0.7)	2.7 (0.9)	2.7 (0.8)	0.499
HbF (g/dL)	0.5	0.5	0.5	-
Serum iron (µg/dL)	89.2 (39.5)	91.4 (35.1)	90.5 (36.7)	0.737
TIBC (µg/dL)	319.8 (28.6)	325.4 (44.6)	323.2 (46.2)	0.424
Serum ferritin (µg/dL)	30.5 (28.6)	25.4 (18.6)	27.3 (23.0)	0.213

Hct = haematocrit; Hb = haemoglobin; MCV = mean corpuscular volume; MCH = mean corpuscular haemoglobin; RDW = red-cell distribution width; MCHC = mean corpuscular haemoglobin concentration; HbA2 = haemoglobin alpha-2; HbF = haemoglobin F; TIBC = total iron binding capacity. SD = standard deviation.

anaemia between developing and industrialized countries. In a study by Jain et al. the prevalence of iron-deficiency anaemia was 59.9% in India (13), while in a nutritional investigation in Madrid, Spain, the prevalence of iron-deficiency anaemia and iron deficiency state were 0.94% and 4.94% respectively (16). Although the prevalence of iron-deficiency anaemia in this study of Arab migrating nomads of the southern Islamic Republic of Iran is lower than the prevalence found in some other developing countries (17), it is still alarmingly high. Therefore,

improved nutrition and educational programmes by the public health authorities may help to decrease the risk of iron deficiency and iron-deficiency anaemia.

A family history of favism was reported for 3.0% of children. Favism has been reported as a common disease in some northern (13) and southern regions of the Islamic Republic of Iran (14,15). Newborn screening in a tertiary-care centre in north Lebanon showed a prevalence of favism of 2.1% (62/3009), significantly higher in males than females (18).

In Sana'a, Yemen, of the total 508 male blood donors recruited into a study, 36 were G6PD deficient, giving a likely G6PD deficiency prevalence of 7.1% (19). In Thailand, 4 and 7 G6PD variants were observed in samples collected from Burmese and Thai populations, with a prevalence of G6PD of 6.6% (21/317) and 14.2% (26/183) in the different populations respectively (20). In Saudi Arabia, the prevalence of G6PD deficiency was reported to be 6.9% (21). The current study showed a much lower prevalence than the above-mentioned reports. We only found only

**Table 3 Prevalence of glucose-6-phosphate dehydrogenase deficiency, iron deficiency and beta thalassaemia minor in Arab migrating nomad schoolchildren**

Parameter	Males (n = 51)		Females (n = 83)		Total (n = 134)	
	No.	%	No.	%	No.	%
<b>G6PD deficiency</b>						
Present	1	2.0	0	0.0	1	0.7
Absent	50	98.0	83	100.0	133	99.3
<b>Serum ferritin level (µg/dL)</b>						
< 12	6	11.8	18	21.7	24	17.9
≥ 12	45	88.2	65	78.3	110	82.1
<b>HbA2 level (g/dL)</b>						
< 3.5	47	92.2	74	89.2	121	90.3
≥ 3.5	4	7.8	9	10.8	13	9.7

G6PD = glucose-6-phosphate dehydrogenase; HbA2 = haemoglobin alpha-2.

1 case of G6PD deficiency in our study, in a male child. The prevalence of G6PD deficiency was 0.74%, which is lower than some data reported from high-prevalence areas in northern and southern regions of the Islamic Republic of Iran (9,10). The difference from other studies may be due to variations in age groups studied, or to sociocultural or climate differences between the regions.

The prevalence of  $\beta$ -thalassaemia trait was 9.7% in our study, which is higher than in previous findings in nomads in southern Islamic Republic of Iran (9,10). The rate of  $\beta$ -thalassaemia carriage has a wide range worldwide. In Bangladesh, it was reported to be as high as 28% (17). In Malaysia, it was estimated that 4.5% of the population were carriers for thalassaemia, and this is similar to our finding (22). In Turkey the frequency of  $\beta$ -thalassaemia carriers in the city of Adiyaman was low (1.91%) (23).

Although most patients who have  $\beta$ -thalassaemia trait are asymptomatic and are found accidentally by a minor decrease in Hb level and MCV, the detection of such cases is important in the prevention of  $\beta$ -thalassaemia major. In the Islamic Republic of Iran, marriage registrars routinely refer prospective couples to a designated local laboratory

for premarital screening. The man's red cell indices are checked first. If he has a microcytic cells (mean corpuscular haemoglobin < 27 pg or mean corpuscular red volume < 80 fL) the woman is tested. When both the man and woman are microcytic, HbA2 concentration would then be measured. If both have a concentration of  $\geq 3.5$  g/dL (diagnostic of thalassaemia trait), the couple are referred to a local designated health centre for genetic counselling. At-risk couples attend as many counselling sessions as they need to reach an informed decision about marriage (an average of 2.5 sessions, range 1–5). Those who marry after counselling are referred to their local health centres or health houses for follow up until they have completed their family (24). Recently, there has been great success in the field of bone-marrow transplantation of thalassaemia major patients in the Islamic Republic of Iran (25), but obviously improving the screening programmes is a better way to deal with the issue than this complicated and expensive procedure.

To the authors' knowledge, there are no reports of iron-deficiency anaemia, G6PD and  $\beta$ -thalassaemia trait in migrating nomads from other countries with which to compare our results.

## Conclusions

According to our results, we should be aware of the signs and symptoms of anaemia and common haematological disorders associated with anaemia (such as G6PD) in this population. The relatively high prevalence of  $\beta$ -thalassaemia trait seems to be a major potential risk in our area and a careful application of the Iranian thalassaemia programme seems to be needed. As iron-deficiency anaemia is a prevalent disease in migrating Arab nomads, establishment of educational programmes for these tribes is necessary. Early diagnosis and treatment is mandatory in the prevention of mortality and morbidity in this neglected population and we call on the Ministry of Health to pay special attention to this group.

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