



Prevalence of Thalassemia Trait & Iron Deficiency Anemia during Infancy in 2011-2013 in a Thalassemia Prevalent Region: North Cyprus

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Abstract

Background: Iron Deficiency Anemia (IDA) is an important health problem all around the world especially in developing countries. In the Mediterranean countries another prevalent reason of anemia is Thalassemia. Certain strategies had been established as a government policy to reduce prevalence in North Cyprus, such as pre-marital screening of Thalassemia. The prevalence of thalassemia trait has not been evaluated since then. The aim of this study was to detect the prevalence of IDA, thalassemia trait in infants under regular follow-up and to evaluate the compliance to prophylactic iron supplementation (PIS) and its effect on IDA.

Methods: Healthy children admitted to Department of Pediatrics, Near East University Hospital, in 2011–2013 were included. Data of anthropometric measurements, parental thalassemia trait status, duration of PIS usage, complete blood count, ferritin levels and hemoglobin electrophoresis were collected from hospital database program. Anemic children were grouped as IDA, thalassemia trait, both IDA and thalassemia trait and others.

Results: Eighty-nine infants with a mean age 13.52 ± 2.09 mo were included. Compliance with PIS recommendation was 85.3% and, the mean duration of iron usage was 6.44 ± 3.18 mo. IDA and thalassemia trait were found to be 11.2% and 4.5% respectively, while 3.4% of the infants had both IDA and thalassemia trait.

Conclusion: Prevalence of thalassemia trait was 7.9% demonstrating approximately a 50% decline within 5 decades. This result confirms the success of premarital screening policy in North Cyprus. In addition, prevalence of IDA was relatively low being 14.6% supporting the beneficial effect of PIS on prevention of IDA.

Keywords: Anemia, Thalassemia trait, Iron deficiency, Infant

Introduction

During childhood, anemia is one of the most frequently seen intractable health concern that has both social and economic implications all around the world. WHO estimates that almost one-third of the world's population is anemic, most of which are due to iron deficiency (1). Iron deficiency anemia (IDA) comprises 90% of all anemia cases in the world (2). It usually occurs as a result of insufficient dietary intake of iron as

well as gastrointestinal tract losses and infections (3). IDA is the most encountered form of malnutrition in the world with a prevalence of 43% (4).

American Academy of Pediatrics (AAP) recommends PIS from 4 mo old up to 1 year of age, especially in developing countries (5). Although IDA is usually a concern of developing countries, there is no national data or a study

describing the prevalence of PIS usage or IDA among children in North Cyprus.

Meanwhile, thalassemia is another common reason of anemia, being the most frequent inherited genetic disease worldwide, and especially one of the major causes of anemia in the Mediterranean area, the Middle East, Central Asia, India and the Far East (6). Thalassemia is an autosomal recessively inherited hemoglobinopathy which affects the synthesis of globin chain of hemoglobin. It has three forms based on which globin chain is affected; α , β and δ . β thalassemia is the major type seen in Mediterranean region including Cyprus and it is more prevalent in malaria-endemic areas. In this type; β globin chain synthesis is either decreased or absent leading to three forms of the disease as major, minor or intermediate (7). Carrier frequency varies from 3% to 17% in different populations (8). Over 9000 Thalassemic children are born every year and treatment are very expensive (9). Thalassemia has always been a major challenge in Cyprus. Therefore, strategies for prevention and management of thalassemia had been initiated in 1976 (5). There were only two published studies on thalassemia in North Cyprus up to date conducted in 1946 and 1973 demonstrating frequency of thalassemia trait as 18.2% and 15% respectively in North Cyprus (10, 11).

The main approach for taking thalassemia under control is screening programs, especially in countries with a high number of carriers like Cyprus. As a government policy pre-marital screening is mandatory since 1980 in North Cyprus (5), and as a result no new baby with thalassemia major has been delivered since 2001. Although thalassemia is a major public health problem in Cyprus; no studies have been carried out to investigate the recent prevalence of carrier status in North Cyprus since 1970s.

The objective of this study was to investigate the prevalence of IDA and thalassemia trait in North Cyprus among healthy infants being followed up by Near East University Hospital, Department of Pediatrics. In addition, it was aimed to determine the compliance to PIS recommendation and its effect on the prevalence of IDA.

Methods

This study was a retrospective one. In healthy child follow-up iron supplementation was recommended to children at 4 months up to one year of age. Complete blood count and ferritin levels were evaluated between 10 to 18 mo. The participants were chosen among the children whose complete blood count and ferritin levels were checked between Apr 2011 and Jul 2013 as part of healthy infant follow-up procedure in the Department of Pediatrics, Near East University Hospital, North Cyprus.

The enrollment criteria were as follows;

1. To be in regular follow-up in Near East University University Hospital, Department of Pediatrics.
2. The presence of complete blood count and ferritin levels documented between 10-18 mo of age. Information on birth data (Birth weight, height and percentiles), breastfeeding status, duration of breastfeeding, usage and duration of PIS, weight and height at 1 year of age and percentiles, parental education status and parental thalassemia carrier status had been achieved from hospital database or by phone calls in demand.

Complete blood count (CBC), ferritin and if present hemoglobin electrophoresis results had been obtained from hospital database program.

Diagnosis of IDA and thalassemia trait are as follows:

Anemia was defined as hemoglobin level below 10.5 gr/dl whereas mean corpuscular volume (MCV) below 70fL has been used to indicate microcytic anemia (12, 13).

Within the microcytic anemia group; if ferritin level was below 15mg/ml and Mentzer index (MCV/RBC) was above 13, this was considered as IDA, while high RBC level, normal RDW value and Mentzer index smaller than 13 was considered as Thalassemia trait (12).

The ethical committee code YDU/2015/32-214.

Statistical Analysis

Statistical analyses were performed by means of SPSS 17 (Chicago, IL, USA) software.

Results are expressed as the mean \pm SD or percentages. Groups were compared by means of Students T test. A *P* value of <0.05 was considered as statistically significant.

Results

The study group consisted of 89 infants, 44.9% being female and 55.1% being male (Table 1).

Compliance with PIS recommendation of the study group was 85.3% and, the mean duration of iron usage was 6.44 ± 3.18 mo. According to the pre-marital screening results 11.2% of mothers and 4.5% of fathers had been diagnosed as thalassemia trait.

Table 1: Demographic findings of the study group

Demographic findings	
Sex: Males/females (n (%))	40 / 49 (44.9 / 55.1)
Mean age \pm SD (Months)	13.52 \pm 2.09
Compliance to prophylactic iron supplementation (n (%))	76 (85)
Prevalence of Anemia (n (%))	23 (25.8)
Breastfed infants (n (%))	81 (91)
Duration of breastfeeding (months)	7.88 \pm 6.16
Parent's educational status:	
* (n (%))	55 (84.6)
** (n (%))	10 (15.4)
Compliance to iron prophylaxis recommendation (n (%))	76 (85.3)
Mean duration of iron usage (months)	6.44 \pm 3.18
Thalassaemia trait prevalence of parents:	
Mothers / Fathers (n/n (%/%))	10 / 4 (11.2/4.5)

* at least one parent's educational status was graduation from university or above

** both parents were graduated from high school or below

Among infants IDA and thalassemia trait have been found to be 11.2% and 4.5% respectively. Percentage of infants having both IDA and thalassemia trait was 3.4%. Anemia has not been detected in 74% of the cases while 6.7% of cases had anemia other than IDA and Thalassemia. Seven infants were diagnosed as thalassemia trait based on the described criteria and three of them confirmed by hemoglobin electrophoresis.

Frequencies of IDA – thalassemia trait and PIS usage are summarized in Table 2.

Infants with and without IDA were compared based on demographic characteristics, usage and duration of PIS demonstrating no significant differences ($P>0.05$). Comparison of breastfeeding, PIS and growth between iron deficiency anemia and non-anemic group are summarized in Table 3.

Table 2: Frequency of anemia and compliance to prophylactic iron supplementation

Frequency of Anemia and Compliance to PIS	n (%)
Compliance to prophylactic iron supplementation	76 (85)
Frequency of Anemia	23 (25.8)
Iron deficiency anemia only	10 (11.2)
Thalassemia trait only	4 (4.5)
Iron deficiency anemia and thalassemia trait together	3 (3.4)
Thalassemia trait confirmed by hemoglobin electrophoresis	3 (3.4)
Anemia other than IDA and thalassemia trait	6 (6.7)
Non-anemic	66 (74.2)

Table 3: Comparison of breastfeeding, prophylactic iron supplementation, duration and growth between iron deficiency anemia and others

Demographic characteristics	IDA n:13	Others n:76	P-values
Birthweight (gr) (mean± SD)	3212.3 ± 520.6	3121.7 ± 534.4	0.57
Duration of breastfeeding (months) (mean± SD)	10.1 ± 6.8	7.6 ± 6.0	0.25
Weight at 1 year (gr)(mean± SD)	9944.5 ± 1097.7	9770.9 ± 1248.3	0.67
Height at 1 year (cm) (Mean± SD)	78.9 ± 3.1	75.2 ± 3.2	0.11
Duration of PIS (Mean± SD) (months)	7.8 ±2.8	6.7 ± 2.9	0.34
Usage of PIS (%)	100	94	0.43

Discussion

Cyprus had been the region with the highest prevalence of Beta thalassemia since the 19th century (14,15). Screening of thalassemia trait in Turkish Cypriot population has not been performed since then. A frequency of 7.9% which shows a 50% decline in the prevalence of thalassemia trait compared to the study results of 1973. This result confirms the necessity and success of the premarital screening policy in Cyprus. In addition, the frequency of IDA was found to be 14.6% which is lower than other developing countries. The importance of AAP recommendation of PIS for the prevention of IDA in early childhood. Moreover, there were no significant differences between infants with and without anemia based on weight and height at birth and 1 year of age, duration of breastfeeding and compliance to PIS.

The first epidemiologic study on thalassemia in Cyprus demonstrating a thalassemia carrier status of 18.2% (10). Thereafter, the second study, among Turkish and Greek Cypriots showing a frequency of thalassemia trait of 15% (11). A study performed 25 yr later in 1998 revealed Cyprus as the region with the highest frequency of thalassemia trait worldwide (14, 15). The frequency of thalassemia trait was 7.9% in 2011-2013 among Turkish Cypriot infants. This decrease since 1946 is most probably due to the strict adherence to the pre-marital thalassemia trait screening policy.

Malaria is the leading cause of the increase in thalassemia frequency in malaria endemic regions

and eradication of malaria in Cyprus in 1948 might have a role on the decreasing frequency in each generation (14, 15). The mandatory national screening program in Cyprus is the leading cause of this decrease. Moreover, current prenatal diagnostic techniques such as chorionic villus sampling and DNA analysis might have contributed to this decrease (5).

After national screening law came into force in North Cyprus in 1980, the rate of thalassemia major births decreased dramatically and eventually no new thalassemia major case has been delivered since 2001 (5). National screening programs have also been established in Italy, Greece and the UK. When compared to these countries, Cyprus has the lowest prevalence of thalassemia major births (16).

For prevention of IDA the recommendation of AAP is to initiate PIS at the age of 4 mo continuing at least for 8 mo till the age of 1yr (17). Our institution's routine healthy infant follow-up protocol includes the recommendation of PIS from 4 mo to 12 mo of age. Complete blood count and serum ferritin level are checked in-between the age of 12-18 mo to evaluate the presence of IDA and thalassemia trait, as well (18).

The frequency of IDA among infants in our study group was found to be 14.6%. Our results were compared with those of Turkey due to the similarity in ethnicity. The frequency of IDA between ages 0-5 in Turkey is around 50% according to a national study (13). Another study was performed on 1881 children from 3 geographical regions of Turkey. Compliance to

PIS was found to be 43% and mean duration of usage was 1-2 mo, while the frequency of IDA between 12-23 mo was reported as 16.3% (19). Accordingly, compliance to PIS in North Cyprus was 85.3% and mean duration of the prophylactic supplementation was 8 mo. Rate and duration of compliance to PIS was also higher than Turkey, supporting the finding of lower frequency of IDA.

Moreover, several studies were carried out in low and high-income countries. Although UK has low IDA prevalence, frequency of IDA in inner cities approached to those in developing countries (20). Frequency of IDA in infants aged 6-24 mo of low socioeconomic families, especially of the ethnic minorities, changed between 25-40% (21). Frequency of IDA in infants from high socioeconomic level families was 5% whereas 20% in those of low socioeconomic level (21). Social status was determined by educational level of parents demonstrating no significant difference between IDA and non-anemic groups. A study carried out in Cuba among infants of 6-23 mo of age concluded that prevalence of IDA was 23.8% and 28.5% in urban and rural regions, respectively (22). Another study which collected data from several European cities (Athens, Bilbao, Budapest, Dublin, Madrid, Naples, Porto, Rostol, Santiago, Umea and Vienna) used levels of Hb, ferritin, MCV, transferrin saturation and transferrin receptor and found out that infants aged 12 mo have frequency of iron deficiency and IDA as 7.2% and 2.3%, respectively (23). In Iceland and Norway, the frequency of IDA at 12 mo of age was reported as 2.7% and 10%, respectively (23). When compared to developed countries, IDA frequency in North Cyprus was higher.

The prevalence of IDA in low socioeconomic countries is much higher (24). In Sub-Saharan Africa, IDA in 10-23 mo aged infants changed between 59 and 99.4% throughout 2001-2006. In Armenia and Egypt, it was above 50% in 2005 and in India it was around 76% in 1999. In Latin America and Caribbean countries, a frequency of IDA changing between 53.1 and 87.8% was

reported. Therefore, based on the results of our preliminary study, frequency of IDA in North Cyprus seems to be between developed and developing countries.

Although thalassemia has been a major public health problem in Cyprus since the mid-1900's, no studies investigating the rate of in frequency of thalassemia trait status have been carried out in North Cyprus during the last five decades. Likewise; there are no reports on the frequency of IDA among infants in North Cyprus. Although preliminary with a small sample size, this is the first study evaluating IDA frequency and adherence to PIS during infancy. Another limitation is that; it is a single center study. More studies with nationwide sampling are required to generalize our results for North Cyprus.

Conclusion

Thalassemia trait frequency was 7.9% among infants demonstrating a decline of more than 50% since 1946 in North Cyprus. This result confirms the success of strict adherence to pre-marital screening policy conducted since 1980. In addition, prevalence of IDA was relatively low in this region compared to other developing countries, supporting the beneficial effect of PIS on prevention of IDA.

Ethical considerations

Ethical issues (Including plagiarism, informed consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc.) have been completely observed by the authors.

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The authors declare that there is no conflict of interests.

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