

## Rate of Common Anemias and Iron Deficiency Without Anemia Among Children Admitted to Antakya State Hospital

Sule UNAL<sup>1\*</sup>, [MD],  
 Turan BAYHAN<sup>1</sup>, [MD],  
 Harika ESKİCİ<sup>2</sup>, [MD],  
 Tülin YÜKSEKGÖNÜL<sup>2</sup>, [MD],  
 Gönül OKTAY<sup>3</sup>, [MD],  
 Tanju ÇELİK<sup>4</sup>, [MD],  
 Cahit ÖZER<sup>1</sup>, [MD]

1 Division of Pediatric Hematology, Department of Pediatrics, Hacettepe University, Faculty of Medicine, Ankara, 2 Department of Pediatrics and 3 Hemoglobinopathy Center, Antakya State Hospital, Departments of 4 Pediatrics, and 5 Family Medicine, Mustafa Kemal University, Faculty of Medicine, Hatay, Turkey

\* Corresponding Author: Şule Ünal, Assoc. Prof., MD, Division of Pediatric Hematology, Department of Pediatrics, Hacettepe University, Faculty of Medicine, Ankara  
 e-mail [suleunal@hacettepe.edu.tr](mailto:suleunal@hacettepe.edu.tr)

Received 25 August 2013, accepted 28 August 2014,  
 published online September 2014

### ABSTRACT

Anemia is one of the common health problems of childhood with significant consequences including growth retardation and increased propensity to infections. Iron deficiency is the most common cause of anemia and still a public health problem. However, iron deficiency is not the only cause and the deficiencies of other nutrients may also be underlying. Additionally, the deficiencies of these nutrients and trace elements may exist in the absence of anemia. On the other hand, the correction of these deficiencies is easy and the treatment has invaluable impact on the general health condition of these children. Herein, we analyzed the frequencies of iron deficiency, iron deficiency anemia, vitamin B12 deficiency, combined deficiencies of iron and vitamin B12 among pediatric and adolescent age group of patients (n=600) who presented to pediatrics out-patient clinic in Antakya State Hospital, where there is no adequate data in the reported literature related to the frequencies of the abovementioned conditions. Patients with hemoglobinopathies were excluded. The rate of anemia was found 16.6% among the pediatric patients presented to out-patient clinic for non-chronic diseases. Iron deficiency was the most common underlying etiology in 68 (73.9%) of the anemic cases. Iron deficiency was detected in 246 (44.4%) patients. Of the 518 patients who were evaluated for vitamin B12, 76 (14.7%) were found to be deficient. Our study was enrolled in 2011 and prior to full-establishment of family physician system and our results may be repeated in order to see the current status after family physician screenings and follow-ups were available.

**Key words:** Anemia, iron deficiency, vitamin B12, Antakya

### Introduction

Iron deficiency (ID) is the most common nutritional deficiency and is still a problem of both developed and developing countries [1,2]. The United States surveys indicated existence of ID without anemia in 7% of toddlers aged 1 to 2 years, 9% of adolescent girls, and 16% of women of childbearing age [2]. During childhood ID has two peaks of prevalence due to rapid growth: first peak occurs at late infancy with additional risks of inadequate iron intake and second peak occurs at adolescent period especially in girls with initiation of menstrual bleeding [3]. Although anemia is the most common consequence of ID, without development of anemia neurocognitive impairment, immune suppression, and inadequate weight gain may occur as complications of ID [2]. Vitamin B12 deficiency is another

nutritional cause of anemia that is characterized by macrocytic anemia. Co-existing iron deficiency anemia (IDA) may mask the macrocytosis of vitamin B12 deficiency [4].

In Turkey, there are a number of studies from different regions of country about prevalence of IDA during childhood [5-9], but there is insufficient data about prevalence of ID without anemia [10-12]. In our study, we aimed to investigate the prevalence of ID, IDA, vitamin B12 deficiency and co-existence of vitamin B12 deficiency and ID, among pediatric and adolescent age groups in Antakya, which is a city in the southern part of Turkey with mostly agriculture based economy.

## Material and Methods

Study was performed among 600 consecutive patients, prospectively who came to Pediatrics Out-patient Clinic of Antakya State Hospital between February 2011 and August 2011 and who were older than six months of age at admission. The patients who came to clinic for any reason other than homozygous state for a hemoglobinopathy or a chronic disease (such as autoimmune disorders, chronic renal failure, cardiac disease, malignancy or a chronic infection like tuberculosis) were included. The patients who have no chronic infection, but have presented to clinic with an acute infection such as upper respiratory tract infection, acute gastroenteritis or urinary tract infection were also included. Of the study group, 291 were males and male to female ratio was 0.94. All patients were evaluated with complete blood count, serum iron (SI) and serum ferritin (SF). Serum iron was measured with calorimetric method. Serum ferritin analyses were done with enzyme-linked immunoassays. Patients were considered as anemic if hemoglobin (Hb) level is less than two standard deviation for their age and gender [2]. Of the study group 560 were further tested for vitamin B12 and folic acid deficiency. Serum vitamin B12 level below 200 pg/ml was defined as vitamin B12 deficiency, whereas serum ferritin below 10 ng/ml was taken as a cut-off value iron deficiency state.

Iron deficiency anemia is the overt stage of ID with accompanying anemia to ID, whereas stage 1 ID is defined as iron deficiency without anemia [2]. Antakya is an endemic region for sickle cell anemia and thalassemia, so hemoglobin electrophoresis with high pressure liquid chromatography (HPLC) was achieved in 433 of the patients in order to define the heterozygous states for  $\beta$  thalassemia and Hb variants including Hb S, C, D and E. Of these patients, those who have HPLC and were found to be heterozygous for a hemoglobinopathy were excluded from the analyses for iron status. Local Ethical Committee approval was obtained.

## Results

Mean age of cases were  $84.5 \pm 51.3$  months (6-106). Of the patients whose HPLC results were available 27 (6.2%) were found to have  $\beta$ -thalassemia trait, on the other hand 15 (3.5%) were found to have sickle cell trait. The rates of Hb C, Hb D and Hb E trait among this study group was found as 0.46%, 0.23% and 0.23%, respectively. These 46 patients were

excluded from analyses and anemia and etiology evaluations were made among the remaining 554 patients. Hematological evaluations and iron status revealed: Hb:  $11.9 \pm 1.2$  g/dl (5.4-15), hematocrit:  $36.5 \pm 3.2\%$  (24-43), MCV:  $75 \pm 7.4$  fl (31.5-92.9), SI:  $49.3 \pm 36.4$   $\mu$ g/dl (2-292), SF:  $43.7 \pm 49.5$  ng/dl (1.09-464). Anemia was detected in 92 (16.6%) of the patients according to their age and gender normals. Mean Hb level of anemic patients were  $10 \pm 0.95$  g/dl (5.4-10.9). Iron deficiency was the underlying etiology in 68 (73.9%) of the anemic cases. Iron deficiency was detected in 246 (44.4%) patients and 72.3% of patients with iron deficiency were found to have normal Hb levels for their age and gender.

Of the 518 patients who were evaluated with vitamin B12 analysis 76 (14.7%) were found to have vitamin B12 deficiency. Nineteen (25%) of the patients who had vitamin B12 deficiency were found to be anemic, whereas 45 (59.2%) had ID and 17 (22.3%) had IDA. In all study group of the 89 anemic patients whose vitamin B12 levels were available, 19 (21.3%) were found to have vitamin B 12 deficiency. None of the patients were found to have folic acid deficiency.

When patients were grouped according to their age, anemia prevalence was 47.6% in age group between 6 months and 2 years-old, 20.3% between 2 and 5 years-old, 9.3% between 6 and 10 years-old, and 4.5% in patients who were older than 10 years of age. Iron deficiency rates were 70.9%, 52.6%, 34%, and 34.6% among each age group, respectively (Table 1).

## Discussion

Insufficient dietary intake of iron is the most common reason of ID and IDA among pediatric age group [2] and ID is more prevalent among countries with less advanced economies [13]. Besides, 1/4 of world children suffer from IDA [14].

Iron deficiency anemia is the overt stage of ID, which corresponds to decrease in hemoglobin levels 2SD below the age and gender appropriates, in addition to low transferrin saturation and low SF levels [2]. A very important social and economical consequence of ID is the neurocognitive impairment of children and adults with chronic, severe ID during infancy period, which may even persist after iron treatment [15-18].

In Turkey, ID prevalence has been reported in a few studies with variable values based on area where it was performed. Ürk et al. have carried on their investigation on 848 healthy children with ages

**Table 1.** Anemia, iron deficiency, and iron deficiency without anemia prevalences according to age groups

Age groups	Group size	Anemia n (%)	Iron deficiency anemia n (%)	Iron deficiency without anemia n (%)	Iron deficiency (with or without anemia) n (%)
6 months–2 years	86	41 (47.6)	31 (36)	30 (34.8)	61 (70.9)
2–5 years	133	27 (20.3)	20 (15)	50 (37.6)	70 (52.6)
6–10 years	182	17 (9.3)	12 (6.5)	50 (27.4)	62 (34)
>10 years	153	7 (4.5)	5 (3.2)	48 (31.3)	53 (34.6)

of between 7-12 years from Manisa and showed ID and IDA prevalences 24.7% and 1.4%, respectively [11]. Berçem et. al. [12], have found ID in 30.7% and IDA 5.5% of 328 adolescents from Sivas and they pointed out that both ID and IDA were significantly more frequent among girls. In another study from Adana, Koçak et. al. [10] have notified ID prevalence according to age ranges as 48% between 0-2 years, 19.6% in 3-14 years, and 14.7% in children above 14 years of age. In contrast IDA was detected in 12.9% of 0-2 years, and in 18.3% of 3-14 years of patients [10]. Although this study by Kocak et al. [10] includes data of almost 20 years ago from a region close to Antakya, unfortunately our results at infancy is worse with 70.9% rate of ID and 36% rate of IDA. However, our sample includes patients who came to out-patient clinic with any type of infection, whereas the study by Koçak et al includes a population based screening [10]. In our study, the concomitant acute infections of the patients who presented to the out-patient clinic may even have normal SF levels, that may caused some of the patients with stage 1 ID to be evaluated as normal and the exact rate of ID may even be higher than this rate. On the other hand, our study reflects the rate among patients who came to hospital for an acute disease and the rates of anemia, ID or IDA of this current study may not reflect the rates in the all population. However, the very high rates of both ID and anemia among children in Antakya, emerges the importance of size of this problem in Antakya.

Iron deficiency anemia rate in our study is also greater than previous reports from Turkey. For instance Kara et al. [6] found IDA in 5.8% of 338 adolescents from Kocaeli. In another investigation from Şanlıurfa, Koç et al. [8] showed IDA in 3.1% of 2913 children with ages between 6-16 years. Low value of IDA rate in this study has been attributed to dietary habits of this area which includes consumption of large amounts of meat.

In Turkey, Ministry of Health initiated a programme named “Iron-Like Turkey” in 2004 which involves iron supplementation to infants under 12 months of age [9]. In a cross-sectional study that was performed by Yalçın et al. [9] to search IDA rate in different regions of Turkey after initiation of iron supplementation programme, they found IDA in 59 (3.7%) of 1589 children with ages of 12-23 months. However our study denotes that ID is still an important health problem of Turkish infants among some parts of the country.

Co-existence of vitamin B12 deficiency and ID is common among elderly patients with pernicious anemia [19]. However, malnourished children may also have vitamin B12 deficiency and ID, concomitantly especially when their diet is poor for meat sources [20]. During childhood vitamin B12 deficiency may cause neurodevelopmental delay, impairment in overall growth and development, hypotonia, feeding difficulties, lethargy, tremors, hyperirritability, and coma; in addition to peripheral neuropathies, and cytopenias [21]. In a previous study vitamin B12 deficiency frequency was reported as 5.9% among adolescents in Turkey [22]. Co-existence of vitamin B12 deficiency and IDA has been examined in a study from Turkey by Isik Balcı et al. [23] and they found the rate of IDA as 3.3%, on the other hand the concomitant presence of IDA and vitamin B12 deficiency was found in 2.3% of 1120 adolescents living in Denizli [23]. Of the anemic patients, 21.3% were found to have vitamin B12 deficiency in our study and almost half of vitamin B12 deficient children had concomitant ID and one-fifth had IDA. These results may indicate that the cause of deficiency in both of these nutrients may be related to lesser available sources of meat in the diet of the children. Dried beans and dark green leafy vegetables are especially good sources of iron for individuals who have a diet poor in animal sources. However, although Antakya is a place with agricultural economy, the soils are

planted for at least three times a year and this may cause a decline in the micronutrients of the soil and in turn those of the beans and vegetables.

Unlike previous reports from Turkey in our study we tried to investigate both iron and vitamin B12 status of pediatric population. As mentioned before, deficiency of both of these nutrients can cause clinical impairments without anemia [2,21]. In our study, only one-fourth of the children with vitamin B12 deficiency were found to have anemia, in Antakya.

In our study, we found the rates of  $\beta$ -thalassemia trait and sickle cell trait as 6.2% and 3.5%, respectively among the pediatric patients who came to out-patient clinic. The prevalences of  $\beta$ -thalassemia trait and sickle cell trait have previously reported as between 2.3-4.6% and 3-47%, respectively in various studies in Çukurova region, where Antakya is also included [24].

Our study group includes patients who came to out-patient clinic for any reason other than a hemoglobinopathy disease or a chronic disease and is not a population-based screening. This may be a limiting factor in the prediction of the exact rate of ID or IDA. Since most of the patients who came to our out-patient clinic were those who had acute infections and IDA has been reported to potentially increase the risk of common childhood infections [25], this may have caused higher rates of ID or IDA

among our study group. On the other hand, as SF is an acute phase reactant some of the ID patients in stage 1, may have been underestimated. Additionally, a survey for the investigation of the cause of the anemia would be rational to have a more definitive idea about the cause of the anemias in this region. Although each physician who got involved in the patient recruitment in this current study, investigated for the underlying potential etiologies for anemia prior to treatment initiation, including nutritional causes and bleeding, this data have not been recorded as to be reported within the study, since the aim was to define the frequencies of these nutritional deficiencies.

Our study was held in 2011 and the family physician system has been established by the end of 2010. After that time, the iron supplementations of the infants were held by the responsible family physicians and this may have caused a decline in the iron and anemia status of infants in Antakya. The current status of ID and IDA in Antakya should be repeated in order to test the current effectivity of our system in terms of prevention of ID and IDA.

In conclusion, preventive strategies for iron and vitamin B12 should be built and dietary recommendations should be given to population of this area. Besides, similar studies should be performed in different areas of Turkey to detect children at risk.

## REFERENCES

- [1] **Baker RD, Greer FR.** Diagnosis and prevention of iron deficiency and iron-deficiency anemia in infants and young children (0-3 years of age). *Pediatrics* 2010;126:1040-1050.
- [2] **Andrews NC, Ullrich CK, Fleming MD.** Disorders of iron metabolism and sideroblastic anemia. In: Stuart H. Orkin DGN, David Gingsburg, A. Thomas Look, David E. Fisher, Samuel E. Lux, editor. Nathan and Oski's Hematology of Infancy and Childhood. 7th ed: *Saunders and Elsevier*; 2009. p 521-570.
- [3] **Lanzkowsky P.** Iron-deficiency anemia. In: Lanzkowsky P, editor. Manual of Pediatric Hematology and Oncology. 5th ed. United States of America: *Elsevier*; 2011:38-57.
- [4] **Remacha AF, Sarda MP, Canals C, et al.** Combined cobalamin and iron deficiency anemia: a diagnostic approach using a model based on age and homocysteine assessment. *Ann Hematol* 2013;92:527-531.
- [5] **Derman O, Okstuz-Kanbur N, Yenicesu I, et al.** Iron deficiency anemia in a group of Turkish adolescents: frequency and contributing factors. *Int J Adolesc Med Health* 2005;17:179-186.
- [6] **Kara B, Cal S, Aydoğan A, et al.** The prevalence of anemia in adolescents: a study from Turkey. *J Pediatr Hematol Oncol* 2006;28:316-321.
- [7] **Kilinc M, Yuregir GT, Ekerbicer H.** Anaemia and iron-deficiency anaemia in south-east Anatolia. *Eur J Haematol* 2002;69:280-283.
- [8] **Koc A, Kosecik M, Vural H, et al.** The frequency and etiology of anemia among children 6-16 years of age in the southeast region of Turkey. *Turk J Pediatr* 2000;42:91-95.
- [9] **Yalcin SS, Tezel B, Yurdakok K, et al.** A community-based iron supplementation program, "Iron-Like Turkey", and the following prevalence of anemia among infants aged 12-23 months. *Turk J Pediatr* 2013;55:16-28.
- [10] **Kocak R, Alparslan ZN, Agrıdag G, et al.** The frequency of anaemia, iron deficiency, hemoglobin S and beta thalassemia in the south of Turkey. *Eur J Epidemiol* 1995;11:181-184.
- [11] **Ürk V OA, Çiftdoğan DY, Özyurt BC, Gülen H.** Manisa yöresinde ilköğretim çocuklarında demir eksikliği anemisi prevalansı. *Ege Pediatri Bülteni* 2007;14:79-86.
- [12] **Berçem İD, Cevit Ö, Ergür AT, Berçem G, Gültekin A, Sütçü İ.** Sivas'ta 12-18 yaş grubu adolesanlarda demir eksikliği ve demir eksikliği anemisi prevalansı. *Türkiye Klinikleri J Pediatr* 1999;8:15-20.
- [13] **Stoltzfus RJ.** Iron interventions for women and children in low-income countries. *The J Nutr* 2011;141:756S-762S.

- [14] **WHO.** Global health risks: mortality and burden of disease attributable to selected major risks. *Geneva*, 2009.
- [15] **Lozoff B, Jimenez E, Hagen J, et al.** Poorer behavioral and developmental outcome more than 10 years after treatment for iron deficiency in infancy. *Pediatrics* 2000;105:E51.
- [16] **Lozoff B, Smith JB, Kaciroti N, et al.** Functional significance of early-life iron deficiency: outcomes at 25 years. *J Pediatr* 2013;163:1260-1266.
- [17] **Lukowski AF, Koss M, Burden MJ, et al.** Iron deficiency in infancy and neurocognitive functioning at 19 years: evidence of long-term deficits in executive function and recognition memory. *Nutr Neurosci* 2010;13:54-70.
- [18] **Shafir T, Angulo-Barroso R, Calatroni A, et al.** Effects of iron deficiency in infancy on patterns of motor development over time. *Hum Mov Sci* 2006;25:821-838.
- [19] **Demiroglu H, Dunder S.** Pernicious anaemia patients should be screened for iron deficiency during follow up. *N Z Med J* 1997;110:147-148.
- [20] **Bhardwaj A, Kumar D, Raina SK, et al.** Rapid Assessment for Coexistence of Vitamin B12 and Iron Deficiency Anemia among Adolescent Males and Females in Northern Himalayan State of India. *Anemia* 2013;2013:959605.
- [21] **Stabler SP.** Vitamin B12 deficiency. *N Engl J Med* 2013;368:2041-2042.
- [22] **Wetherilt H, Ackurt F, Brubacher G, et al.** Blood vitamin and mineral levels in 7-17 years old Turkish children. *Internationale journal for vitamin and nutrition research Internationale Zeitschrift fur Vitamin- und Ernährungsforschung Journal International de Vitaminologie et de Nutrition* 1992;62:21-29.
- [23] **Isik Balci Y, Karabulut A, Gurses D, et al.** Prevalence and Risk Factors of Anemia among Adolescents in Denizli, Turkey. *Iran J Pediatr* 2012;22:77-81.
- [24] **Kılınc Y.** Hemoglobinopathies in Turkey. *Turk J Hematol* 2006; 23:214-216.
- [25] **Strauss RG.** Iron deficiency, infections, and immune function: a reassessment. *Am J Clin Nutr* 1978;31:660-666.

