Original Article

Complete blood count test in the evaluation of anemia: More than a screening test?

Gokce Celep[1], Zeynep Hulya Durmaz[2]

[1]Department of Pediatrics, Faculty of Medicine, Amasya University, Amasya, Turkey
[2]Department of Biochemistry, Faculty of Medicine, Amasya University, Amasya, Turkey

Abstract

Aim: Anemia is defined as a reduction in the red blood cell mass or blood hemoglobin concentration. Complete blood count (CBC) analyses provide comprehensive information with regard to the classification of anemia. We aimed to determine the prevalence and remind the possible etiologies of anemia in our province using CBC analyses.
Material and Methods: This retrospective study was conducted in a secondary healthcare center in northern Turkey. A total of 2578 healthy children enrolled. Their sociodemographic features, clinical history, and CBC results were retrospectively reviewed from the hospital records. According to CBC analyses, hemoglobin (HGB), hematocrit (HCT), mean corpuscular volume (MCV), mean corpuscular hemoglobin concentration (MCHC), mean corpuscular hemoglobin (MCH) and red cell distribution width (RDW) levels were evaluated.
Results: The prevalence of anemia in the whole study population was 27.6% (n=713). When stratified according to the age subgroups of the study, the prevalances varied between 21.3% and 41.2%. Among the anemic patients, 42.9% (n=306) had microcytic, 56.1% (n=400) had normocytic and 1% (n=7) had macrocytic anemia
Conclusion: The prevalance of anemia was >20% in all the age groups, revealing that anemia is a significant public health problem in our province. Detailed analysis of the CBC provides comprehensive information regarding the classification of anemia. It saves time and money for well-child follow up by facilitating the direct application of etiologic tests.

Keywords: Anemia; complete blood count, well-child

INTRODUCTION

Anemia is defined as a reduction in the red blood cell (RBC) mass or blood hemoglobin (HGB) concentration (1). Complete blood count (CBC) analyses provide comprehensive information regarding the classification of anemia. The threshold for detecting anemia is a hematocrit (HCT) and/ or HGB level less than or equal to the 2.5th percentile according to the age, race, and sex. RBCs constitute the major part of the cellular component of blood. Normal ranges for HGB and HCT vary with age, race, and sex (2). Anemia results from impairment in RBC production and HGB synthesis, excessive destruction of RBC, and acute or chronic blood loss (3,4). Mean corpuscular volume (MCV), mean concentration of corpuscular hemoglobin (MCHC), mean corpuscular hemoglobin (MCH) and red cell distribution width (RDW) are other components of the CBC that guide the preliminary diagnosis of the etiologies of anemia (2,3). Nutritional deficiencies have been reported as the most common cause of anemia, iron deficiency being the lead cause (5-8). Other micronutrient deficiencies

(e.g., folate, riboflavin, vitamins A and B12), acute and chronic infections or inflammations (e.g., malaria, cancer, tuberculosis, and HIV), and inherited or acquired disorders that affect hemoglobin synthesis, RBC production or survival (e.g.,hemoglobinopathies, erythrocyte membrane defects, viral infections, malignancies, toxins, enzymatic deficiencies, hemolysis), and disorders of the bone marrow and reticuloendothelial system are additional causes of anemia (9,10).

Anemia is a global health problem. Children are at increased risk as they grow and become vulnerable to nutritional deficiencies. The World Health Organization (WHO) estimates that approximately one out of every two children is under the negative impact of anemia and related disorders; moreover, its prevalence is higher in developing countries (7,8,11,12). According to the WHO data, the prevalence of anemia with HGB <11g/dl in 6-59 months among Turkish children was estimated to be 29% while that of severe anemia was estimated to be 0.3% (HGB < 7 g/dl). The level of public health significance was reported as "moderate" (8). However, the incidence of anemia in

Turkish children, usually caused by iron deficiency, varied between 5.9–78% in different geographic areas within different age groups, having been decreased in recent years by the supplementation program "Iron-like Turkey Project" based on WHO recommendations (13-17).

Hemoglobinopathies are endemic in 71% of the world's countries and 300.000 to 400.000 babies are born with these syndromes per year. The most common forms are sickle cell anemia and thalassemia syndromes, being more common in the areas where consanguineous marriages are frequent, like in Turkey. Approximately 7% of the world's population is reported to be hemoglobinopathy carriers and 1.1% of parents are at risk of having an affected baby (18,19). The prevalence of the thalassemia trait was reported to be 2.1% in our country (20). Antenatal and non-antenatal screening tests are applied with different protocols according to the epidemiologic data of different regions and races (21). Pre-marriage screening is not done in the city where this study was conducted.

In this study, we aimed to determine the prevalence and possible etiologies of anemia in our province using the CBC analyses. In addition, we intended to investigate the benefits of a free iron supplementation campaign after a decade and to contribute in detecting other age groups, who could be the target population of a new supplementation program.

MATERIAL and METHODS

This study was conducted in a small city in middle northern Turkey. During a one-year period (January 1st, 2015 to December 31st, 2015), 11842 children were admitted to the pediatric outpatient clinics of a secondary healthcare center and 5251 of them had the CBC test. Participants having chronic illnesses, diagnosed with a chronic illness after the examination, having continuous drug therapy for more than three months or anemia prophylaxis and treatment, treated with blood products, younger than 1 year old and hospitalized after the present administration were excluded from the study. A total of 2578 patients aged 1 to 17 years were enrolled in the study. Their sociodemographic features, clinical history, and test results were retrospectively reviewed from the hospital records. Age, gender, CBC results were noted and the results were compared with reference values presented in "Nathan and Oski's Hematology and Oncology of Infancy and Childhood, 2015" for different age groups (2). The levels of HGB, HCT, MCV, MCHC, MCH and RDW were evaluated. Participants having a HCT or HGB level less than or equal to the 2.5th percentile, according to their age and gender were diagnosed as "anemic," classified as microcytic, normocytic, or macrocytic based on the MCV. Additionally, MCH, MCHC, and RDW were evaluated on the same basis. Mentzer index (MCV/RBC) was calculated for the microcytic anemia group in order to make the preliminary diagnosis of the thalassemia trait (22).

CBC analyses were performed by Mindray BC-6800® (Shenzhen Mindray Bio-Medical Electronics Co. Ltd, China), which is an auto hematologic analyzer device,

analyzing hematologic samples via a laser optic system.

Statistical analyses: The analyses were performed using SPSS® version 15 (SPSS, Inc., Chicago, IL, USA). The data were presented as frequencies, medians and minimum–maximum, ranges or mean ± SD by descriptive statistics, when indicated. Normality tests were applied (histogram and Kolmogorov-Smirnov test) to detect the distribution pattern of the variables. Cross- tables with chi-square test (χ2) were used to identify statistically significant differences between groups at 95% confidence. Probability factor (p) less than 0.05 was regarded as statistically significant.

This retrospective study was approved by the Amasya University, Ethical Committee of Non-Invasive Clinical Researches on 02/27/2020 with the registration number: E.5675

RESULTS

During the study period, 11842 patients were admitted to the pediatric outpatient clinics of the secondary health care center and 2578 patients, who met the eligibility criteria were enrolled in the study. Approximately half of the participants were females (n=1287; 49.9%). The median age of the study group was 7 (IQR: 10) and participants were divided into 6 age groups as follows: Group 1: 1year old, group 2: 2–3 years old, Group 3: 4–6 years old, Group 4: 7–10 years old, Group 5: 11–14 years old, and Group 6: 15–18 years old. The results of the hematologic variables were presented as medians and IQR because they were not normally distributed according to visual or analytical tests of normality.

Group 1 consisted of 286 participants; 154 (53.8%) males and 132 (46.2%) females. Median HCT and HGB concentration of this group was 35.3 % (IQR: 3.3) and 11.4 g/dl (IQR: 1.2) respectively. Sixty-one (21.3%) of the group members had anemia and 41.0% (n=25) of them were females, but the ratio between genders was not statistically significant (p= 0.55). Twenty six (42.6%) of the anemic participants had normocytic and 35 (57.4%) had microcytic anemia according to the MCV levels. Nineteen participants (6.6%) had RBC count < 2.5 percentile, 8 (2.8%) had RBC count >97.5%. Only one patient had MCHC >97%, pointing to a possible erythrocyte membrane defect. MCH levels were low in 82.1% (n=50) of the anemic participants. Forty- two (14.7%) participants in this group had microcytic anemia and approximately half of this group (n=17; 48.6%) had increased RDW.

In group 2, there were 410 participants, 194 (47.3%) being females. The cut-off HGB level for this age group was defined as 11 g/dl, but the median was 11.6 g/dl (IQR: 1.4) for our participants. The prevalence of anemia was 29.3% (n=120), the ratio between females and males was 0.7 without statistical significance (p=0.44). Median HCT was 35.6% and RBC count was 4.62 (IQR: 0.53). Twenty-four percent of the group (n=98) had microcytosis and 50% (n=49) of them had anemia. The rate of normocytic anemia was 23.1% (n= 71). Only four participants had macrocytosis. MCHC was >97.5 percentile in three children

and MCH was low in 33.2% (n=136) of the participants. RDW was high in 33.4% (n=137) of the participants. Forty-three (87.8%) participants in the microcytic anemia group had increased RDW and while it was within the normal range in 6 participants (12.2%).

Group 3 consisted of 259 males (53.4%) and 225 females (46.4%), totally 485 children. The median HGB level was 12.0 g/dl (IQR: 1.4) and HCT was 36.8% (IQR: 4). Children having HGB levels < 11 g/dl were diagnosed as "anemic" in this age group and the prevalance of anemia was 41.2% (n=200) in this group. The incidence of anemia was 39.8% (n=103) in males and 43.1% (n=97) in females. RBC count was high in 42 participants (8.7%). Microcytosis rate was 26.8% (n=130) and only one participant had macrocytosis. The rate of microcytic anemia among anemic patients was 38% (n= 76) and normocytic anemia was detected in 124 (62%) patients. MCHC was high in 8 participants (1.6%) and MCH was low in approximately half of the group (n=237; 48.9%). RDW of the 285 (58,8%) participants was high and 65 (85.5%)of the microcytic anemia group had increased RDW.

Group 4 had 496 participants; 269 males (54.2%), and 227 females (48.8%). Median HCT was 39.0% (IQR: 3.4) and median HGB level of the group was 12.8 g/dl (IQR: 1.3). The anemia cut-off level was 12.0 g/dl for this age group, the prevalence of anemia was 23.6% (n=117), and 66 (56.4%) of them were females. RBC count was low in 10 (2%) patients and high in 51 (10.3%) of the participants. The median MCV of the group was 81.4 fl (IQR: 5.1). MCV< 78 fl was defined as "microcytosis" for this age group and its rate was 22% (n= 109) in our group, 9 (1.8%) participants had macrocytosis. Rates of microcytic and normocytic anemia were 40.2% (n=47) and 57.3% (n=67), respectively and 40 members (85.1%) of the microcytic anemia group had increased RDW. Three patients had macrocytic anemia. MCH was low in 38.9% (n=193)of the patients and MCHC was high in 3 participants.

There were 442 participants in group 5 and 203 (45.9%) were males. The median HGB levels of females and males were 13.1 g/dl (IQR: 1.4) and 13.2 g/dl (IQR:1.4), respectively. One hundred and fourteen of the participants (25.8%) were anemic. The anemia rate in males was 26.1% (n=53) and 25.5% (n=61) in females; however; the difference between genders was not significant (p=0.09). Rate of microcytosis in anemic females was 45.9% (n=28) and 46.3% (n=25) in anemic males. Three participants had macrocytic anemia. MCH levels of 34.8% (n=154) of the participants were low and MCHC levels of 7 participants (1.6%) were high. Approximately half of the participants had (52%; n=230) increased RDW levels.

Group 6 consisted of 462 participants; 190 males (41.1%) and 271 females (58.7%). The anemia rate in the whole group was 22% (n=102). The median HGB levels of females and males were 14.6 g/dl (IQR: 1.4) and 12.9 g/dl (IQR:1.4) respectively. Anemia rate (HGB<13.7g/dl) in males was 23.4% (n=45) and 21% (n=57) in females. Microcytosis was present in 82 participants (17.7%) and 61 (74.4%) of them were females, the difference was

statistically significant within genders (p=0.012). Twelve males (6.3%) had microcytic anemia and 32 (16.8%) had normocytic anemia. The rate of microcytic anemia in females was 12.5% (n=34) and normocytic anemia 8.1% (n=22). The rates of microcytic and normocytic anemia were statistically different within genders (p=0.007; p<0.001 respectively). Twenty-two (4.8%) members had macrocytosis (MCV>95 fl). The rate of high MCHC was 1.7% (n=8) and low MCH was 29% (n=134). RDW was high in 198 (73.1%) of females.

When considering all the groups anemia rate was 27.6% (n=713) and 42.9% (n=306) of the anemic patients had microcytic, 56.1% (n=400) had normocytic and 1% (n=7) had macrocytic anemia. MCH was low in 36.6% (n=945) of the study group. High MCHC levels were detected in 30 (1.2%) participants. Anemia was most frequent in Group 3. The rate of increased RDW in microcytic anemia group was 88.9% (n=272), revealing iron deficiency anemia as one of the preliminary diagnoses. Additionally, RDW was within normal ranges in 34 (11.1%) members of the microcytic anemia group and Mentzer index was <13 in 13 (4.2%) participants of this group, revealing possible thalassemia syndromes.

DISCUSSION

Anemia is a common public health problem throughout the world and in our province with a prevalance of approximately 30% in the pediatric population. The incidence was >20% in all groups (21.3%-41.2%) revealing that anemia is a significant public health problem in our province. Anemia causes impairment in the biochemical reactions, cellular functions, growth-development, cognitive –behavioral improvement, immunity, physical capacity, thermoregulation, gastrointestinal and cardiovascular systems (2,23). Anemia can be screened or diagnosed by chance during the examination of different health problems through CBC analyses which is one of the most requested analyses during medical examination

The weaning of fetal hemoglobin and high rate of growing up increase iron demand; that is why iron deficiency is the most frequent cause of anemia in childhood and adolescence unless dietary intake or supplementation is sufficient (24,25). In Turkey, 1–2mg/kg/day iron supplementation is recommended and provided freely for healthy infants aged 4 to12 months within the concept of "iron-like Turkey project" by Turkish Republic, Ministry of Health since 2004 (26). Screening for anemia at 9-12 months, 5 years old and adolescence are recommended and performed by measurement of HGB with different methods (27). Most studies in Turkey have been reported before these interventions whereas our study reported the changes after a decade of these processes.

Incidence of anemia was reported to be over 20% even in well-developed countries (28). Anemia was detected in 28% in the screening study of 6–11 years old children in İstanbul and 15% of this population had microcytic anemia (29). In 2011, a comprehensive study was

conducted by Gazi University to evaluate the efficiency of the supplementation programs of the Turkish Ministry of Health in 6–17 months old babies. HGB levels were <11.5 g/dl in 56.5% of the study group and iron deficiency was detected in 28.7% according to ferritin levels (30).

The incidence of anemia varies according to age, gender, socioeconomic status, habitat, nutritional sources and habits (1). In group 1, the incidence was lower when compared with the other age groups; we thought that this was the benefit of the iron prophylaxis program as Vatandaş et al. reported before (31). The peak was in 4–6 years old group and this was a different result from the literature. The reason for this result may be the life changes at those ages: In Turkey, children begin to kindergarten and school at 4–6 years old. The rate of infectious diseases and parasities increase and feeding problems become apparent (32). The incidence is higher in the first three years of life and adolescence with male dominance in the first and female dominance in the second group (33,34). In our study, there is no significant difference in anemia prevalence between genders in all groups, but the distribution of the anemia types was different. There are different reports with different results.

Normocytic anemia was detected in 15.5% (n=400) of this population. Chronic illnesses, inflammation, infections, acute or chronic blood loss, and parasites may be the reasons for the normocytic anemia or folate and vitamin B12 insufficiency accompanying iron deficiency may result in normocytosis instead of macrocytosis (3).The rate of normocytic anemia was higher than that microcytic anemia in all age groups except group 1. Since iron, folate, vitamin B12 or reticulocyte ratio and acute phase reactants such as white blood cell count or C-reactive protein or geita microscopy were not mentioned, it is impossible to make a certain comment about the etiology which is one of the limitations of the present study.

Microcytic anemia was present in 306 patients (11.9%). The most common causes of microcytic anemia are iron deficiency, thalassemia syndromes, lead poisoning, and copper deficiency (3). The rate of microcytic anemia was higher in adolescent females and the normocytic anemia rate was higher in the males of the same age group. Gaining bad dietary habits such as consuming fast and manufactured food in both genders is an important problem in adolescent age group which results in nutritional deficiencies. Iron loss of females during menstruation causes iron deficiency leading to microcytic anemia and fast increasing of muscular mass in males may cause normocytic anemia with increasing demand of vitamin B12 and folate for cellular proliferation and growth (33,35). In an anemic patient existence of microcytosis with increased RDW is an important clue for iron deficiency anemia and normal RDW for thalassemia trait. The rate of increased RDW in microcytic anemia group was 88.9% (n=272) in this study population, revealing iron deficiency anemia as the preliminary diagnose. The prevalence of

thalassemia trait or syndromes was not known because HGB electrophoresis records of the susceptible patients were not mentioned which one of the limitations of the study is. However, rate of microcytic anemia with normal RDW was 11.1% (n=34) and Mentzer index was <13 in the 4.2% of the patients, pointing thalassemia trait or syndromes as preliminary diagnoses. It was reported that the incidence of iron deficiency anemia was approximately 80% and rate of thalassemia minor was 16.4% in a sample of anemic patients in a recent study (36). According to the data of Turkish Society of Haematology there are approximately 1300000 thalassemia carriers and 4500 thalassemia patients in Turkey (37). Macrocytic anemia was detected in 0.3% (n=7) participants. It is not common in the pediatric population and usually related with B12 or folate deficiency and bone marrow impairment (3). The incidence of B12 deficiency was reported as 2.2% (36). In the present study we did not measure B12 or folate levels, reticulocyte count and evaluate peripheral blood or bone marrow smears which is another limitation.

In the present study we focused on diagnosis of anemia through CBC which is one of the common tests applied during hospital administrations. This study has great limitations, because of being a retrospective report based on hospital records. We did not mention the socioeconomic status, consanguineous marriage of the parents, personal and family history, dietary habits, smoking habits of the participants. Consanguity is important for genetic causes of anemia such as hemoglobinopathies, erythrocyte membrane defects and enzymatic deficiencies. We did not mention the results of the further examinations that we referred above.

CONCLUSION

In conclusion, we would like to restate that the data provided by CBC is comprehensive for the primary healthcare physicians to evaluate anemia and determine the preliminary etiologic diagnosis. The detailed interpretation of a CBC can provide time and cost effectiveness in the further evaluation of the etiology of anemia. We aimed to draw attention that any administration to the healthcare settings may be a chance of starting well-child follow up to manage other problems, such as anemia. After the solution of the current problem, the patient may be evaluated with more target specific tests by the interpretation of the CBC results.

REFERENCES

1. Sandoval C. Approach to the child with anemia. https://www.uptodate.com/contents/approach-to-the-child-with-anemia. access date: 23.10.2019.

2. Brugnara C, Oski FA, Nathan DG. Diagnostic approach to the anemic patient. In: Orkin SH, Fisher DE, Ginsburg D, eds. Nathan and Oski's Hematology and Oncology of Infancy and Childhood. 8th edition. Philadelphia: WB Saunders 2015;293.

3. Lerner NB. The anemias. In: Kliegman RM, Stanton BF, St Geme JW, Schor NF, eds. Nelson Textbook of Pediatrics. 20th edition. Philadelphia (PA): Elsevier; 2015;2309-12.

4. Yazıcı S, Çelik T, Seyrek K. (Anemia Prevalance among Children). İzmir Dr. Behçet Uz Çocuk Hast Derg 2012;2:6-9.

5. Stevens GA, Finucane MM, De-Regil LM, et al. Global, regional,and national trends in hemoglobin concentration and prevalence of total and severe anemia in children and pregnant and non-pregnant women for 1995–2011: a systematic analysis of population-representative data. Lancet Glob Health 2013;1:16-25.

6. United Nations Children's Fund, United Nations University, World Health Organization. Iron deficiency anemia assessment, prevention, and control: a guide for programme managers. Geneva: World Health Organization; 2001 (WHO/NHD/01.3; available at: http://www.who.int/nutrition/ publications/en/ida_assessment_prevention_control.pdf, access date: 22.12.2019).

7. Stoltzfus RJ, Mullany L, Black RE. Iron deficiency anemia. In: Ezzati M, Lopez Ad, Rodgers A, Murray CJL, eds. Comparative quantification of health risks: global and regional burden of disease attributable to selected major risk factors. Geneva: World Health Organization; 2004:163-210.

8. World Health Organization. The global prevalence of anemia in 2011. Geneva: World Health Organization; 2015.

9. Balarajan Y, Ramakrishnan U, Ozaltin E, et al. Anemia in low-income and middle-income countries. Lancet. 2011;378:2123-35.

10. Tolentino K, Friedman JF. An update on anemia in less developed countries. Am J Trop Med Hyg 2007;77:44-51.

11. Marotta C, Di Gennaro F, Pizzol, D, et al. The at risk child clinic (ARCC): 3 years of health activities in support of the most vulnerable children in Beira, Mozambique. Int. J. Environ. Res. Public Health 2018;15:1350.

12. McLean E, Cogswell M, Egli I, et al. Worldwide prevalence of anemia, WHO Vitamin and Mineral Nutrition Information System, 1993-2005. Public Health Nutr 2009;12:444-54.

13. Gedikoğlu G, Koç L. Marmara bölgesinde demir eksikliği taraması.(Research of iron deficiency in the Marmara region) Tıp Fak Mecm 1975;38:19-33.

14. Karagun BS, Korkmaz O, Gursu AH, et al. The Prevalence of Anemia Among Children Aged 1-15 Admitted to Hospital in Sivas. The J Current Pediatrics 2014;2:67-72.

15. Turkish Society of Hematology (Türk Hematoloji Derneği). The Guideline of Diagnosis and Treatment of Iron Deficiency Anemia in Children, part 2, 2011. available at: www.thd.org.tr/file access date: 23.10.2019

16. T.C. Sağlık Bakanlığı, Anne Çocuk Sağlığı Genel Müdürlüğü. 12-23 aylık çocuklarda demir kullanımı araştırması raporu, 2009, Ankara.

17. World Health Organisation, Iron Deficiency Anemia Assessment, Prevention, and Control, A Guide for Programme Managers, WHO, Geneva, 2001. available at: https://www.who.int/nutrition/publications/micronutrients/anaemia_iron_deficiency/WHO_NHD_01.3/en/ access date: 28.2.2020.

18. Modell B, Darlison M. Global epidemiology of hemoglobin disorders and derived service indicators. Bull World Health Organ 2008;86:480-7.

19. Williams TN, Weatherall DJ. World distribution, population genetics, and health burden of the hemoglobinopathies. Cold Spring Harb Perspect Med 2012;2:1-14.

20. Canatan D, Kose MR, Ustundag M, et al. Hemoglobinopathy Control Program in Turkey. Community Genet 2006;9:124-6.

21. Lee SY, Yap ES, Lee EYP, et al. Evaluation of Thalassaemia Screening Tests in the Antenatal and Non-Antenatal Populations in Singapore. Annals Academy of Med 2019;48:5-15.

22. Kilic A, Gokcay G. Cocuklarda demir eksikliği anemisine yaklaşım. Surekli Tıp Eğitimi Dergisi 1999; 8(11). Available at: http://www.ttb.org.tr/STED/sted1199/st1 1992. html. http://www.ttb.org.tr/STED/index.php/eskisayilar.

23. Pasricha SR. Should we screen for iron deficiency anemia? A review of the evidence and recent recommendations. Pathology. 2012;44:139-47.

24. Janus J, Moerschel, SK. Evaluation of anemia in children. Am. Fam. Physician 2010;81:1462-71.

25. Iannotti LL, Tielsch JM, Black MM, et al. Iron supplementation in early childhood. Am J Clin Nutr 2006;84:1261-76.

26. Ilarslan Cullas NE, Gunay F, Ileri DT, et al. Investigation of the frequency of iron insufficiency among infants in a population in which routine iron supplementation is implemented. Turk J Pediatr.2018;60:22-31.

27. Bebek, Çocuk, Ergen İzlem Protokolleri, T.C. Sağlık Bakanlığı Halk Sağlığı Genel Müdürlüğü, yayın no: 1112, Ankara, 2018.

28. Irwin JJ, Kirchner JT. Anemia in children. Am Fam Physician 2001;648:1379-86.

29. Gur E, Yıldız I, Celkan T. Prevalence of anemia and the risk factors among school children in Istanbul. J Trop Pediatr 2005;51:346-50.

30. Gazi Üniversitesi, Tıp Fakültesi. Türkiye'de 6-17 Aylık Çocuklarda ve Annelerinde Hemoglobin Ferritin D -Vitamini Düzeyi ve Demir Eksikliği Anemisi Durum Belirleme Yürütülen Programların Değerlendirilmesi Araştırması. Sağlık Bakanlığı Yayınları, No: 873, Ankara,2011.

31. Vatandas N, Atay G, Tarcan A, et al. Hayatın ilk yılında demir profilaksisi ve anemi. Çocuk Sağlığı ve Hastalıkları Derg 2007;50:12-5.
32. 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;42:91-5.
33. André HP, Sperandio N, Siqueira RL, et al. Food and nutrition insecurity indicators associated with iron deficiency anemia in Brazilian children: a systematic review. Cien Saude Colet 2018;23:1159-67.
34. Balci YI, Karabulut A, Gurses D, et al. Prevalence and risk factors of anemia among adolescents in Denizli, Turkey. Iran J Pediatr 2012;22:77-81.
35. Zuffo CR, Osório MM, Taconeli CA, et al. Prevalence and risk factors of anemia in children. J Pediatr (Rio J). 2016;92:353-60.
36. Duyuran O, Acipayam C, Akkececi NS, et al. Etiology of anemia in children aged between 6 months and 18 years. J Surg Med 2019;3:402-5.
37. Turk Hematoloji Derneği. Eritrosit Hastalıkları ve Hemoglobin Bozuklukları Tanı ve Tedavi Kılavuzu 2019, Beta talasemi tanı ve tedavi kılavuzu. available at: www.thd.org.tr/file access date 24.10.2019.