The Rates of and Relationship between Anemia and Deficiency of Iron, Zinc, Vitamin B12 and Folic Acid in Hospitalized Children

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ABSTRACT

Aim: Increased frequency of deficiency due to the insufficient intake of iron, zinc, vitamin B12 and folic acid has been reported in the society. We aimed to investigate the rates of deficiency of these vitamins and minerals, as well as anemia frequency in children admitted to pediatric outpatient clinics of our tertiary hospital in a retrospective three-year period.

Materials and Methods: The frequency of micronutrient deficiency and the relationship between them was determined using statistical methods by evaluating the levels of hematocrit and other micronutritional elements in patients admitted to the general pediatrics outpatient clinics of our hospital between 01.06.2015 and 31.05.2018. The only patient inclusion criteria were being tested for zinc, iron, iron binding, hemogram, vitamin B12, folic acid, ferritin and vitamin D for any reason.

Results: After the evaluation of 64487 patients, we discovered the rates of anemia and iron, zinc, folate, vitamin D, vitamin B12 and ferritin deficiency as 30.8%, 52.1%, 41.1%, 18.2%, 32.4%, 30.8%, 52.1%, 41.1%, 18.2%, 32.4%, 30.8%, 52.1%, 41.1%, 18.2%, 32.4%.
20.1% and 26.7% respectively. Additionally, our results indicate that the frequency of folic acid deficiency decreased over the past years, whereas the rates of zinc and vitamin D deficiency increased over time. The final results show a negative correlation between anemia and folic acid, vitamin D, vitamin B12 and iron binding capacity, and a positive correlation between anemia and iron, ferritin and zinc.

Conclusion: Although it does not reflect the frequency of deficiency in the general population since the data are collected from hospitalized children, it could be argued that multiple micronutrient deficiencies are significantly common in Turkey and zinc and vitamin D deficiency has been increasing over the years, when compared with the results of previous studies.

Keywords: Anemia; iron; zinc; Vitamin D; Vitamin B12; folic acid.

1. INTRODUCTION

Vitamins (A, B, C, D, E, and K) which are organic substances, minerals (sodium, potassium, calcium, phosphorus, fluorine, iron and zinc) and trace elements (iodine, copper, selenium, manganese, chromium and molybdenum) which are inorganic substances are called micronutrients since they are required in very small amounts for living organisms. With that; Carbohydrates, fats and proteins are classified as macronutrients due to the fact that they are substances that are used to provide energy to organisms. Many of the micronutrients play a vital role in human growth, development, physical functions and maintenance of health, as they are cofactors of essential metabolic enzymes [1].

The consumption of snacks has over the years increased and replaced balanced nutritional diets, which has given rise to deficiencies of zinc, iron, vitamin B12, folic acid and lack of other essential diet components. This has led to an increase in our encounter of micronutrient deficiencies in our outpatient clinics in Turkey [2]. These deficiencies can be traced back to low intake, malabsorption, increased metabolic need and excessive loss. Additionally, the deficiency of vitamins has been reported to be more frequent in obese children, which are known to have unhealthy dietary lifestyles [3]. Vitamin D deficiency, on the other hand, occurs from low solar ultraviolet B exposure as well [4].

Zinc is an essential nutrient playing role in the synthesis of protein, lipid and nucleic acid. Zinc deficiency occurs in every part of the world and is inversely proportional to the level of development. Endemic zinc deficiencies are seen in over 1/3 of Southeast Asia and sub-Saharan African countries [5]. It is estimated that zinc deficiency resulting from low intake affects 17% in the whole world. The general trend is that the deficiency level remains stable. However, in a study conducted in China in 2005, it was shown that zinc deficiency decreased from 18% to 8% in China [6]. Vitamin B12 and folic acid are key vitamins and play pivotal roles in maintaining the stability of hematopoietic and nervous system. Vitamin B12 deficiency rate was found to be 81.6% in pregnant women and 42% in infants in a study, conducted with 250 pregnant women and infants in Turkey [7]. Iron and vitamin D deficiencies were also discovered to be prevalent in Turkey. Iron deficiency is the most common nutritional deficiency in Turkey and in the World. It is highly prevalent in developing regions (low-income countries), in infants, adolescents, pregnant women, and iron deficiency was discovered to be correlated with the socioeconomic level of people. When sufficient iron is not taken for hemoglobin synthesis, iron deficiency anemia develops and can give rise to various morbidities [2].

Essential micronutrients are not synthesized in the body, therefore must be taken with diet. Insufficient dietary intake of micronutrients are known to be cause of morbidity and mortality which includes decreased immunity, impaired cognitive functions, and slowing of growth. Lack of micronutrients rarely demonstrate clinical signs until progression to the very late stages. Thus, that kind of subclinical deficiency situation can be described as “hidden hunger” [8]. Micronutrient deficiency, especially zinc, iron, vitamin A and folic acid (folate) deficiency, affect more than 2 billion people in the whole World [9].

Our aim in this study is to determine frequency of micronutrient deficiencies in Turkey and to reveal their relationship with each other, by evaluating the levels of other micronutrient elements accompanied by low hematocrit (HCT) levels in patients admitted to the general pediatrics outpatient clinics of our hospital for any reason between the dates 01.06.2015 and 31.05.2018. Any patient that was simultaneously tested for
zinc, iron, iron binding, hemogram, vitamin B12, folic acid, ferritin, 25-hydroxyvitamin D [25(OH)D] was included in our study.

2. MATERIALS AND METHODS

The frequency of micronutrient deficiency and the relationship between them was determined using suited statistical methods by evaluating the levels of HCT and other micronutritional elements in patients admitted to the general pediatrics outpatient clinics of our hospital between 01.6.2015 and 31.05.2018. Any patient that was simultaneously tested for zinc, iron, iron binding, hemogram, vitamin B12, folic acid, ferritin, 25-hydroxyvitamin D [25(OH)D] was included in our study. In our pediatric outpatient clinic, blood samples for iron, micronutrients and vitamin values are taken in the morning from fasting patients proven to not have any infections.

Patients younger than 1 month and older than 18 years, and those with chronic disease, hematologic, metabolic gastrointestinal and infectious disorders were excluded from the study.

The normal ranges of micronutrients we tested are given below.

Iron (60-180 microgram/dl), Total iron binding capacity (250-450 microgram/dl), Hematocrit (35-55%), Zinc (70-114 microgram/ml), Vitamin B12 (180-914 pg/ml), Folate (5.9-24.08 ng/ml), Ferritin (11-306 ng/ml), 25-hydroxyvitamin D (14-49.8 ng/ml).

We accepted the normal range of zinc as 60 to 135 microgram/ml for 0 to 15 years, 70 to 150 microgram/ml for 15 to 18 years. Normal levels of zinc are considered as 60 to 135mcg/ml for 1 month to 15 years, and 70 to 150mcg/ml for above 15 years of age. It were accepted HCT ranges for anemia; under one year, 1-2 years, 2-12 years and 12-18 years %32, %35, %36 and 12-18 years female %36, male %38 respectively.

Serum folate and B12 levels were analyzed by using UniCellDx 600 autoanalyser (Beckman Coulter, Inc. USA) with chemiluminescence method. Hemogram tests were studied with Sysmex XE-2100 hematology analyzer (TOA Medical Electronics, Kobe, Japan). The internal quality control results of the tests were confirmed to be at ±2 standard deviation on the day of the analysis. The lowest detectable level of folate distinguishable from zero with 95% confidence interval was 0.5 ng/mL (1.1 nmol/L). Total imprecision of folate (CV%) was 4.34. The lowest detectable level of B12 distinguishable from zero with 95% confidence interval was 50pg/mL (37 pmol/L). Total imprecision of B12 (CV%) was 8.4.

All the laboratory tests were analyzed in the biochemistry laboratory of our hospital. Zinc was analyzed using AU2700 Beckman Coulter device. The principle of the method used is based on the formation of a red-colored chelate between zinc and 2-(5-Brom-2-pyridylazo)-5-(N-propyl-N-sulfopropylamino)-phenol. Total amount of zinc was consistent with an increase in its absorbance at 570 nm wavelength. Serum levels of [25(OH)D] were measured by a direct competitive chemiluminescence immunoassay method on the Liaison Analyzer (DiaSorin S.p.A., Italy) [10]. Hemogram was analyzed using Sysmex XE-2100 hematology analyzer (TOA Medical Electronics, Kobe, Japan). Other laboratory tests were conducted by spectrophotometric method using AU2700 biochemical auto-analyzer (Beckman Coulter, Inc. USA).

Tests of iron and iron binding were performed in Beckman Coulter AU2700 Clinic chemistry analyzer, ferritin test in Beckman Coulter DXI 800 Immunoassay analyzer using Becman Coulter branded ready commercial kits.

2.1 Statistical Method

SPSS 15.0 for Windows program was used in the statistical analysis. Descriptive statistics of assessment results were given as number and percentage for categorical variables, and as mean, standard deviation, minimum, maximum for numeric variables. The rates in independent groups were tested using Chi-square analysis. Relationships between rates in groups were investigated by Linear-by-Linear Association, and by Spearmen Correlation Analysis since relationships between numerical variables did not provide normal distribution conditions. A p value of <0.05 was accepted as statistical significance level.

3. RESULTS AND DISCUSSION

During the 3-year period, the total number of patients whose variables were simultaneously or separately evaluated in the study was 64487. We also used separately analyzed data in deficiency rate calculations. However, synchronously
analyzed values were used in correlation calculations. The average age of the group was 7.1±5.4 years. The group consisted of 33191 females and 32896 males. Age and gender distribution of the group were given in Table 1.

The number of patients in which variables were examined, the mean value, the median value and the lowest and highest values are shown in Table 2.

There was a significant difference between male and female in all variables except folate. We discovered the rates of anemia and iron, zinc, folate, vitamin D, vitamin B12 an ferritin deficiency, as 30.8%, 52.1%, 41.1%, 18.2%, 32.4%, 20.1% and %26.7 respectively. The distribution of the variables by gender, ages are shown in Table 3.

There was a positive significant correlation between HCT and iron and zinc, in addition we found a significant negative correlation between HCT and folic acid, [25(OH)D], vitamin B12 and iron binding capacity. The relationship between variables is shown in Table 5.

A difference between genders in terms of micronutrient values in the groups was determined, with the exception of folate. While low HCT was more common in men under two years, zinc, folate, [25(OH)D], vitamin B12, and ferritin deficiencies were significantly more common in women (p<0.05) (Table 3).

Some micronutrient deficiencies especially zinc, have been increasing over the years (Table 4). While a positive significant correlation between HCT and iron and zinc was observed as expected, a significant positive correlation with zinc was also detected (p<0.001 for each) (Table 5). However, this relation is plausible when one considers that the usual intake of iron and zinc are mostly maintained both with animal sources. A significant negative correlation between HCT and nutrients such as folic acid, [25(OH)D], vitamin B12 is found, and as expected a negative correlation iron binding capacity is noted too.(p<0.001 for each) (Table 5). Folic acid deficiency frequency has decreased significantly over the years (Table 4). However, while a similar relationship is expected in people consuming both B12 and iron-rich foods such as red meat and offal, the negative relationship between HCT and vitamin B12 was not the case. Similar to previous results, we observed a negative relationship between [25(OH)D] and HCT. Multiple micronutrient deficiencies occur simultaneously in underdeveloped countries as a result of protein energy malnutrition. Global hidden hunger is particularly common in India, Afghanistan, Southeast Asia and sub-Saharan Africa. In the population, pregnant women, children under 5 years old and adolescents are more sensitive groups [11]. Although the mean age of our study group is 7 years, the presence of children under the age of 5 in the

### Table 1. Age and gender distribution of the patients

|        | Mean±SD(Year) | Min-Max |
|--------|---------------|---------|
| Age    | 7.1±5.4       | 0-17    |
| Gender |               |         |
| Male   | 32896         | 49.8    |
| Female | 33191         | 50.2    |
| Total  | 64487         |         |

### Table 2. Number, mean, median and minimum-maximum values of variables

|                      | N     | Mean±SD     | Min-Max   | Median (IQR)     |
|----------------------|-------|-------------|-----------|------------------|
| HCT(%)               | 64457 | 37.0±4.1    | 17-66.6   | 36.8 (34.4-39.3) |
| Zinc (mcg/ml)        | 7016  | 83.6±36.6   | 0.3-596.8 | 75 (63.4-93.0)   |
| Folate (ng/ml)       | 7814  | 9.8±4.4     | 1.8-24.8  | 8.87 (6.54-12.1) |
| [25(OH)D] (ng/ml)    | 13666 | 21.9±16.3   | 1.9-214.6 | 17.9 (12.6-25.7) |
| Vitamin B12 (pg/ml)  | 17187 | 304.3±162.4 | 46-1462   | 264 (195-368)    |
| Iron (mcg/dl)        | 17043 | 63.4±36.6   | 0-380.2   | 58.1 (35-85)     |
| Total iron binding capacity (mcg/dl) | 16363 | 310.0±69.5 | 18.6-1097.7 | 303.8 (265-348.3) |
| Ferritin(ng/ml)      | 18635 | 24.1±28.9   | 0.6-1242.9| 17,9 (10.5-29.1) |
| Variable       | <2 years |            |            |            | 2-12 years |            |            |            |            | >12 years |            |            |            |
|----------------|----------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|
|                | Male     | Female     | Male       | Female     | Male       | Female     | Male       | Female     | Male       | Female     | Male       | Female     |            |
|                | n    | %  | n   | %  | p     | n    | %  | n   | %  | p      | n    | %  | n   | %  | p      | n    | %  | n   | %  | p      |
| HCT            | 5053  | 53.3 | 3892 | 47.5 | <0.001 | 6018 | 35.5 | 5417 | 33.6 | 0.001 | 606  | 10.6 | 3543 | 44.2 | <0.001 |
| Normal         | 4375  | 46.2 | 4260 | 52.0 | 0.061  | 10929 | 64.5 | 10702| 66.4 | 0.001 | 5089 | 89.3 | 4472 | 55.8 |        |
| High           | 45    | 0.5  | 41   | 0.5  | 2      | 0.0  | 1   | 0.0  | 1      | 0.0  | 1     | 0.0  | 3    | 0.0  | 1        | 0.0  | 3    | 0.0  | 1    | 0.0  |
| Zinc           | 285   | 43.6 | 280  | 42.7 | 0.061  | 753   | 40.8 | 725  | 40.7 | 0.262 | 231  | 33.0 | 609  | 44.1 | <0.001 |
| Normal         | 224   | 34.3 | 259  | 39.5 | 0.018  | 870   | 47.1 | 869  | 48.8 | 0.001 | 395   | 56.3 | 659  | 47.7 |        |
| High           | 144   | 22.1 | 116  | 17.7 | 0.018  | 223   | 12.1 | 186  | 10.4 | 0.001 | 75    | 10.7 | 113  | 8.2  |        |
| Folate         | 7     | 1.5  | 5    | 1.2  | 0.777  | 210   | 10.3 | 199  | 9.5  | 0.701 | 328   | 35.6 | 671  | 35.6 | 1,000  |
| Normal         | 451   | 98.5 | 407  | 98.8 | 0.018  | 1829  | 89.7 | 1896 | 90.5 | 0.018 | 593   | 64.4 | 1215 | 64.4 |        |
| High           | 0     | 0    | 0    | 0    |          | 1     | 0.0  | 1    | 0.0  |        | 0     | 0    | 1    | 0.1  |        |
| 25(OH)D        | 135   | 9.3  | 99   | 7.5  | 0.102  | 1018  | 28.0 | 1306 | 37.5 | <0.001 | 529   | 39.0 | 1345 | 55.7 | <0.001 |
| Normal         | 1114  | 76.5 | 1003 | 76.1 | 0.018  | 2567  | 70.5 | 2122 | 60.9 | 0.001 | 808   | 59.6 | 1020 | 42.3 |        |
| High           | 208   | 14.3 | 216  | 16.4 | 0.018  | 54    | 1.5  | 55   | 1.6  | 0.001 | 18    | 1.3  | 49   | 2.0  |        |
| Vitamin B12    | 169   | 13.7 | 150  | 13.1 | 0.153  | 494   | 11.4 | 468  | 11.0 | 0.864 | 803   | 38.6 | 1365 | 33.1 | <0.001 |
| Normal         | 1037  | 83.8 | 974  | 85.4 | 0.018  | 3812  | 87.7 | 3744 | 88.1 | 0.001 | 1268  | 60.9 | 2746 | 66.5 |        |
| High           | 32    | 2.6  | 17   | 1.5  | 0.018  | 41    | 0.9  | 39   | 0.9  | 4.018  | 10    | 0.5  | 18   | 0.4  |        |
| Iron           | 1429  | 71.4 | 1232 | 67.8 | 0.048  | 2183  | 49.2 | 1954 | 47.9 | 0.428 | 484   | 31.8 | 1591 | 50.0 | <0.001 |
| Normal         | 570   | 28.5 | 582  | 32.0 | 0.018  | 2243  | 50.5 | 2111 | 51.7 | 0.001 | 1000  | 65.6 | 1561 | 49.1 |        |
| High           | 3     | 0.1  | 4    | 0.2  | 0.018  | 13    | 0.3  | 15   | 0.4  | 0.018  | 40    | 2.6  | 28   | 0.9  |        |
| TIBC*          | 290   | 14.8 | 333  | 19.0 | 0.001  | 734   | 17.2 | 703  | 18.1 | 0.075 | 413   | 28.2 | 443  | 14.6 | <0.001 |
| Normal         | 1574  | 80.6 | 1356 | 77.5 | 0.018  | 3466  | 81.3 | 3112 | 79.9 | 0.001 | 1011  | 69.1 | 2390 | 78.6 |        |
| High           | 9     | 4.6  | 60   | 3.4  | 0.018  | 62    | 1.5  | 79   | 2.0  | 0.001 | 39    | 2.7  | 208  | 6.8  |        |
| Ferritin       | 715   | 34.4 | 506  | 29.0 | 0.001  | 839   | 17.1 | 959  | 20.6 | <0.001 | 262   | 15.9 | 1703 | 47.0 | <0.001 |
| Normal         | 1356  | 65.2 | 1231 | 70.7 | 0.018  | 4050  | 82.7 | 3688 | 79.3 | 0.001 | 1385  | 84.0 | 1915 | 52.9 |        |
| High           | 9     | 0.4  | 5    | 0.3  | 0.018  | 6     | 0.1  | 3    | 0.1  | 0.018  | 1     | 0.1  | 2    | 0.1  |        |

*Chi-square analysis  1-Total iron binding capacity
study may have biased the percentages of deficiencies to be higher. A difference between genders in terms of micronutrient values in the groups was determined, with the exception of folate. While low HCT was more common in men under two years, zinc, folate, [25(OH)D], vitamin B12, and ferritin deficiencies were significantly more common in women (p<0.05) Table 3.

Some micronutrient deficiencies especially zinc, have been increasing over the years Table 4. While a positive significant correlation between HCT and iron and zinc was observed as expected, a significant positive correlation with zinc was also detected (p<0.001 for each) Table 5. However, this relation is plausible when one considers that the usual intake of iron and zinc are mostly maintained both with animal sources. A significant negative correlation between HCT and nutrients such as folic acid, [25(OH)D], vitamin B12 is found, and as expected a negative correlation iron binding capacity is noted too (p<0.001 for each) Table 5. Folic acid deficiency frequency has decreased significantly over the years Table 4. However, while a similar relationship is expected in people consuming

Table 4. Changes in variables by years

| Year | 2015 | 2016 | 2017 | 2018 | P** |
|------|------|------|------|------|-----|
|      | n    | %    | n    | %    | n    | %    | n    | %    |<--.001|
| HCT  |      |      |      |      |      |      |      |      |      |
| Low  | 2765 | 24.3 | 6621 | 31.8 | 7199 | 33.2 | 3248 | 30.7 |      |
| Normal | 8590 | 75.5 | 14178| 68.1 | 14446| 66.7 | 7318 | 69.2 |      |
| High | 26   | 0.2  | 34   | 0.2  | 16   | 0.2  | 16   | 0.2  |      |
| Zinc |      |      |      |      |      |      |      |      |      |
| Low  | 5    | 1.3  | 288  | 15.5 | 1511 | 46.8 | 1079 | 70.4 |<--.001 |
| Normal | 186  | 46.7 | 1140 | 61.3 | 1502 | 46.5 | 448  | 29.2 |      |
| High | 207  | 52.0 | 431  | 23.2 | 214  | 6.6  |      |      |      |
| Folate |      |      |      |      |      |      |      |      |      |
| Low  | 114  | 22.7 | 362  | 20.7 | 1511 | 46.8 | 448  | 29.2 |<--.001 |
| Normal | 385  | 76.7 | 1390 | 79.3 | 2656 | 81.0 | 1960 | 85.9 |      |
| High | 3    | 0.6  | 0    | 0.0  | 0    | 0.0  |      |      |      |
| 25(OH)D |      |      |      |      |      |      |      |      |      |
| Low  | 271  | 29.7 | 771  | 22.9 | 1547 | 27.2 | 1843 | 49.8 |<--.001 |
| Normal | 578  | 63.4 | 2405 | 71.4 | 3888 | 68.4 | 1763 | 47.7 |      |
| High | 62   | 6.8  | 193  | 5.7  | 253  | 4.4  | 92   | 2.5  |      |
| Vitamin B12 |      |      |      |      |      |      |      |      |      |
| Low  | 397  | 23.0 | 1002 | 22.8 | 1134 | 17.4 | 916  | 20.1 |<--.001 |
| Normal | 1318 | 76.3 | 3371 | 76.6 | 5301 | 81.5 | 3591 | 78.8 |      |
| High | 12   | 0.7  | 29   | 0.7  | 66   | 1.0  | 50   | 1.1  |      |
| Iron |      |      |      |      |      |      |      |      |      |
| Low  | 1099 | 52.7 | 2668 | 52.2 | 3403 | 52.1 | 1703 | 51.4 | 0.750 |
| Normal | 972  | 46.6 | 2410 | 47.1 | 3097 | 47.4 | 1588 | 47.9 |      |
| High | 13   | 0.6  | 36   | 0.7  | 32   | 0.5  | 22   | 0.7  |      |
| TIBC |      |      |      |      |      |      |      |      |      |
| Low  | 354  | 17.6 | 821  | 17.0 | 1166 | 18.8 | 575  | 17.4 | 0.002 |
| Normal | 1559 | 77.4 | 3824 | 79.0 | 4885 | 78.9 | 2641 | 79.7 |      |
| High | 102  | 5.1  | 197  | 4.1  | 143  | 2.3  | 96   | 2.9  |      |
| Ferritin |      |      |      |      |      |      |      |      |      |
| Low  | 652  | 30.2 | 1389 | 27.8 | 1909 | 26.9 | 1034 | 23.6 |<--.001 |
| Normal | 1507 | 69.7 | 3598 | 72.0 | 5179 | 72.9 | 3341 | 76.3 |      |
| High | 2    | 0.1  | 9    | 0.2  | 12   | 0.2  | 3    | 0.1  |      |

**Linear-by-Linear Association 1- Total iron binding capacity

Table 5. Correlation between hematocrit and zinc, and other variables

|          | HCT  | ZINC  |
|----------|------|-------|
|          | rho  | p     | Rho  | p    |
| Zinc     | 0.107 | <0.001 | 0.037 | 0.057 |
| Folate   | -0.293 | <0.001 | 0.152 | <0.001 |
| 25(OH)D  | -0.211 | <0.001 | 0.033 | 0.017 |
| Vitamin B12 | -0.188 | <0.001 | 0.115 | <0.001 |
| Iron     | 0.380 | <0.001 | -0.065 | <0.001 |
| TIBC     | -0.127 | <0.001 | 0.027 | 0.067 |
| Ferritin | 0.172 | <0.001 |      |      |

1- Total iron binding capacity
both B12 and iron-rich foods such as red meat and offal, the negative relationship between HCT and vitamin B12 was not the case. Similar to previous results, we observed a negative relationship between [25(OH)D] and HCT.

Multiple micronutrient deficiencies occur simultaneously in underdeveloped countries as a result of protein energy malnutrition. Global hidden hunger is particularly common in India, Afghanistan, Southeast Asia and sub-Saharan Africa. In the population, pregnant women, children under 5 years old and adolescents are more sensitive groups [11]. Although the mean age of our study group is 7 years, the presence of children under the age of 5 in the study may have biased the percentages of deficiencies to be higher.

The most common micronutrient deficiency in the World is iron deficiency. Anemia develops in the late stages of iron deficiency. World Health Organization estimates that over 50% of the women in the whole World have iron deficiency anemia. The aim for 2025 is to reduce this rate to 50% [12]. In our large sample size of 64457 patients, we discovered the rate of iron deficiency to be at 50.2% and that of anemia to be at 30.8% (Table 3). Our results are coherent with the literature. These results show us that although there was no anemia, 20% of the patients still had iron deficiency. We can prevent the morbidities caused by anemia by recognizing this group earlier and treating iron deficiency before the development of anemia. The importance of this comes from a study conducted in Sri Lanka, where it was demonstrated that iron deficiency, even if it did not cause anemia, could impair growth, cognitive and behavioral characteristics, immunity, hormone balance, performance and working capacity [13].

It is known that the iron deficiency anemia affects physical and cognitive development, physical and reproductive performance in adults, and also has negative effects on pregnancy [14]. Iron deficiency leads to several morbidities even if it does not cause anemia [15]. In a study conducted in Sri Lanka, it was shown that iron deficiency in children mostly occurred ilk the first 2 years. The mean rate decreased to 2.4% in the following 8 years, and increased to 15.4% in the following years [16].

In terms of gender, iron deficiency in children under two years (p<0.048) was more common in boys than girls, but in adolescent period more common in girls than boys (upper 12 years) (p<0.001) Table 3. Under two years anemia rate was %50, although in Turkey, iron prophylaxis is applied to babies up to the age of one. However, there is a significant difference in favor of women in adults for iron deficiency [15] and we also found same results in our study.

Zinc plays a critical role in cell differentiation, enzyme functions, protein and DNA synthesis, maintenance of normal pregnancy and growth of the child. The mortality and morbidity of diarrhea, acute upper respiratory tract infection and malaria increase in zinc deficiency [17]. We discovered that the deficiency rate of zinc to be 41.1%. Another interesting finding was that the deficiency increased significantly from 2015 to 2018 (Table 4). The continuous dietary intake of zinc is essential since it cannot be stored to meet the needs for a long time, unlike iron storages. The deficiency of zinc, which is abundant in animal and seafood, is more common in those following a plant-based diet. World Health Organization estimates that each year 800 thousand people die of the causes related to zinc deficiency [17]. 17.3% percent of the world population and 30% of the South Asian population are under the risk of inadequate intake of zinc [11]. Our results demonstrate that zinc deficiency in our country was more common compared to the results of previous studies. According to World Health Organization’s report, our country is classified among countries where subclinical deficiency occurs [18]. Therefore, it is estimated that there are a significant number of patients whose clinical symptoms do not fully appear, serum values are at the lower limit of normal with tissue zinc levels being low.

In children with iron deficiency and iron deficiency anemia, other micronutrient deficiencies, especially zinc deficiency must be kept in mind, when iron deficiency and anemia do not resolve even if iron treatment is applied [19]. It is also stated that administering zinc concomitantly with iron provides better anemia treatment results in children with iron deficiency anemia [20].

Vitamin B12 deficiency also causes neurological findings due to the increase in serum methyl malonic acid and homocysteine, before laboratory values decrease too much. Besides, megaloblastic anemia related to vitamin B12 and folate acid deficiency can occur during long-lasting and very low levels of vitamin B12, and anemia does not develop in many children with low levels [21]. In our study, we found that vitamin...
B12 and folic acid deficiency rates were about 20% [22]. We detected that the frequency of deficiencies remained stable or even decreased from 2014 to 2018.

Generally, multiple simultaneous micronutrient deficiencies (MND) are more common than a single deficiency, and are more common in children and adolescents. In a cohort of preschool aged children, more than one MND was found in 62% of the children. In the sample, 38.3%, 17.7%, and 6% of the children, respectively, had two, three, or four or more multiple micronutrient deficiencies at the same time. Only 7.3% had no deficiency [22]. Another study found that among adolescent school children with iron deficiency, folate deficiency was 1.8 times higher than normal population, and also zinc deficiency was 1.7 times higher. Similarly, it was detected that iron deficiency was 1.3 times higher and folate deficiency was 1.2 times higher in people with zinc deficiency [23].

4. CONCLUSION AND LIMITATIONS

The limitations of our study is that we used retrospective hospital data collected from children admitted to the hospital, included the post-treatment control values of the same patient, and that our samples are not an accurate reflection of the whole population.

High rates of micronutrient and vitamin deficiencies that have increased over the years in children admitted to the hospital require new health plans to determine the prevalence in the general population and to eliminate the deficiencies.

Although it does not reflect the frequency of deficiency in the general population since it consisted of hospital data, it can be said that multiple micronutrient deficiencies are significantly common in our country, and zinc and vitamin D deficiency has been increasing over the years.

CONSENT AND ETHICS APPROVAL

This study was approved by Haseki Ethical Committee on 18.09.2019 with a registry number 30/2019.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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