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RESEARCH ARTICLE

Serum Iron, Zinc, and Vitamin A Levels in 2-to-6-Year-Old Children with Small or No Appetite

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ABSTRACT

Objective: This study aimed to compare height, weight measurements and serum iron, serum zinc, and serum vitamin A levels of children identified as having small/no appetites by their parents, with healthy controls.
Methods: The research has been designed as a prospective study involving children ages 2-6 years who have been identified as having small or no appetite by their parents, as well as healthy controls from the same age group. After obtaining the informed consent forms, the parents filled out the questionnaire that includes questions about their sociodemographic parameters and children's eating behaviors. The children's medical and family history were taken and their physical examinations regarding systems, height, and weight were examined. The study also evaluated the children's hemoglobin, serum iron, serum zinc, and serum vitamin A levels. For both groups, the study excluded children who were born prematurely, who had a family history of chronic drug use or chronic disease, who had abnormal laboratory tests, or who received pathological findings from their physical examination. The study uses the package program SPSS 15.0 package program for statistical comparisons, the chi-squared test for qualitative variations, and the Student's t test and Mann-Whitney U test for quantitative variations with a value of $p<0.05$ being considered significant. The study also obtained ethical approval from the regional ethical committee.
Results: The study group includes 54 children (50% female, 50% male), and the control group includes 53 children (59% female, 41% male), each group having similar age and gender distributions. Children with weight and height above the 75th percentile are more common in the control group (28% and 30%, respectively) than among the anorexic children group (2% and 4%, respectively; p=0.002). The study group's serum iron and serum zinc levels are lower than the control group's (p=0.026, p=0.002, respectively). The two groups had similar serum vitamin A levels (p>0.05).
Conclusions: Although most children defined as having a small appetite continue to grow normally, evaluating them in terms of iron and zinc deficiencies and supporting them is appropriate in essential cases.

Keywords: Children, appetite, iron, vitamin A, zinc

INTRODUCTION

Appetite is the desire for food. Loss of appetite is the inability to perceive hunger (1). By the end of the second year of life during childhood, nutrient requirements and appetite decline as somatic and brain development slow down. This can lead to picky eating behaviors in children. This physiological decrease in appetite causes concern among parents regarding their children receiving inadequate nutrition (2). Although many children develop and eat normally, they are brought to the physician because they cannot meet the family's demands. A child can be proven to receive adequate nutrition using growth curves that demonstrate normal development, and this alleviates parental concerns (2).

Poor appetite and eating problems lead to medical referrals in 20-35% of healthy children (2-4). While 24% of children have eating problems at the age of two, this percentage is around 17-185 for those aged 3-4 years (5). Limited knowledge is still found regarding the impact loss of appetite has on children's growth, with few long-term studies occurring on this topic (3-7).

A number of organic and social factors can have an impact on a child's appetite. Iron deficiency anemia (IDA) is the most common childhood anemia, with poor appetite a prominent clinical finding (8,9). Additionally, zinc has been reported to be able to impact appetite, with lack of appetite being one symptom of a zinc deficiency (10-12). Animal studies have shown a lack of vitamin A to be able to lead to a reduced

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appetite due to vitamin A affecting both central and taste functions (13-15).

The objective of this study is to assess the growth and iron, zinc, and vitamin A levels in the serum of pre-school children observed by their parents to have small or no appetite and to compare them with children of the same age with normal appetites.

MATERIAL AND METHODS

The study has been conducted as a prospective, cross-sectional, case-control study at the Pediatric Outpatient Clinic of the University of Health Sciences Ankara Training and Research Hospital. The study group consists of 54 children between the ages of 2-6 years who were admitted to the hospital due to poor appetite as reported by their parents. The control group (Group 2) consisted of 53 children who visited the outpatient clinic for a general exam and laboratory tests, which is required by the institution before starting kindergarten, or for routine health check-ups. Group 2's parents reported their children's appetites as normal. The study excluded patients who had low birth weights, were born prematurely, had a family history of chronic drug use or chronic disease, or had abnormal laboratory findings.

After completing the children's examinations and analyses, the investigators interviewed the parents face-to-face during the same visit and asked them about their demographic characteristics, whether the child had been breastfed or not, the duration of breastfeeding in children who had been, the time complementary foods started being added, which food groups the child preferred, which food groups they do not like (the parents were informed that more than one group could be marked), snacking habits, whether the parents gave the children multivitamins or not, and how the parents described their child's appetite. Families' monthly income levels were classified according to data from the Confederation of Turkish Workers' Trade Unions (16). The height (cm) and weight (kg) of the children in the study and control groups were measured by the same researcher using the same scale and height measuring device, with the values being recorded as percentiles (17). Blood samples were taken for a hemogram test and serum iron, serum zinc, and serum vitamin A level tests and sent directly to the laboratory without delay. The immunoturbidimetric method was used to determine serum iron and serum zinc levels at a wavelength of 570-700 using the Olympus AU 2700 from Japan and the Randox kit from the UK. The normal ranges for erythrocyte indices were determined based on the reference values provided for the corresponding age and gender (18). Recommended normal ranges for serum zinc levels were used as a reference (19).

Vitamin A levels were determined by high-performance liquid chromatography (HPLC) (Agilent 1100, Germany; kit-chromsystems, Germany). The reference values for serum vitamin A levels were used to determine the normal ranges for that age group (20).

Written informed consent was obtained from parents for participation in the study. The study adheres to the ethical standards outlined in the 1975 Declaration of Helsinki, as revised in 2000 by the Committee on Human Experimentation. The study received ethical approval from the Local Ethics Committee (Approval No. 3640 dated on 10/26/2011).

The package program SPSS 15.0 was used to analyze the statistical data. The Kolmogorov-Smirnov test was used to calculate the distribution of the data. Normally distributed parameters (i.e., hemoglobin, zinc, and vitamin A levels) were expressed as mean±standard deviation. Non-normally distributed parameters (i.e., age, duration of breastfeeding and vitamin D, age when complementary foods were added to breastfeeding, iron levels) were expressed as median (minimum-maximum). Statistical comparisons were made using the chi-squared test for qualitative variables, while the Student's t test and Mann-Whitney U test was used for the correlation analyses of the quantitative variables. Statistical significance was defined as $p<0.05$.

RESULTS

The median age of the 107 children included in the study is 4 years (2-6 years). No difference was found between the two groups in terms of age or gender ($p>0.05$; Table 1). Parents reported that poor appetite had been present since birth in 22 (40.7%) of the 54 children with small or no appetite. All families in the study had an income below the starvation threshold.

More children in the control group had weights and heights above the 75th percentile than the children with small or no appetite ($p=0.002$; Table 1).

The children's least favorite food group was vegetables, and their most favorite was fruit. Children with small or no appetite were found to be less likely to prefer vegetables compared to the controls ($p=0.005$; Table 2). No significant relationship was found for food preference with gender; age; maternal education level; weight and height percentiles; and hemoglobin, serum iron, serum zinc, and serum vitamin A levels ($p>0.05$). Children's preference for milk and fruit was observed to decrease as the father's level of education increased ($p=0.029$). Six of the eight parents (75%) of children who did not like fruit reported giving their child appetite syrup ($p=0.001$).

Serum iron and serum zinc levels were found to be lower in children with small or no appetite compared to the control group ($p=0.026$; $p=0.002$, respectively; Table 3). In addition, the proportion of children with low serum iron and serum zinc levels was statistically higher in children with small or no appetites compared to the control group (48% vs. 28%; 13% vs. 2%, respectively), while no difference was found between the two groups' vitamin A levels. A positive correlation has been found between serum iron and serum zinc levels ($p=0.024$; $r=0.218$).

No statistically significant difference was found for the hemoglobin, serum iron, serum zinc, and serum vitamin A levels with several factors (i.e., gender, age, parental education,

Table 1: Characteristics of children with poor appetite (Group 1) and controls (Group 2)

	Total (n= 107) (%)	Group 1 (n=54) (%)	Group 2 (n=53) (%)	p
Female /male (n, %)	58 /49 (54.2/45.8)	27/27 (50/50)	31/22 (59/41)	0.440
Mother's education level (n, %)				0.131
≤ 5 years	80 (75)	36 (67)	44 (83)	
6-8 years	16 (15)	10 (18)	6 (11)	
High school and above	11 (10)	8 (15)	3 (6)	
Father's education level (n, %)				0.689
≤ 5 years	66 (62)	33 (61)	33 (62)	
6-8 years	26 (24)	12 (22)	14 (27)	
High school and above	15 (14)	9 (17)	6 (11)	
Exclusive breastfeeding duration (months) [median (min-max)]	14 (0-18)	18 (0-18)	12 (0-8)	0.287
Introduction to complementary foods (months) [median (min-max)]	6 (2-18)	6 (3-18)	6 (2-10)	0.708
Vitamin D intake (n, %)	81 (75.7)	38 (70.0)	43 (81.0)	0.142
Duration of vitamin D supplementation (months) [median (min-max)]	6 (0-24)	6 (1-18)	6 (1-24)	0.205
Multi-vitamin use (n, %)	23 (21.5)	10 (18.0)	13 (24.0)	0.488
Weight (n, %)				0.002
< 10th percentile	7 (6,5)	4 (7)	3 (6)	
10-75th percentile	83 (77,5)	48 (89)	35 (66)	
> 75th percentile	17 (16)	2 (4)	15 (28)	
Height (n, %)				0.002
< 10th percentile	10 (9)	3 (6)	7 (13)	
10-75th percentile	77 (72)	47 (87)	30 (57)	
> 75th percentile	20 (19)	4 (7)	16 (30)	

Table 2: Comparison of dietary habits between children with poor appetite (Group 1) and Controls (Group 2)

	Total (n= 107) (%)*	Group 1 (n=54) (%)*	Group 2 (n=53) (%)*	p
Snacking habits (n, %)	22 (21)	10 (18)	12 (27)	0.859
Disliked foods (n, %)**				
Milk	15 (14)	9 (17)	6 (11)	0.583
Egg	18 (17)	12 (22)	6 (11)	0.273
Meat	32 (30)	17 (32)	15 (28)	0.889
Vegetables	39 (36)	26 (48)	13 (25)	0.005
Fruits	8 (7,5)	4 (7)	4 (8)	0.552
Bread	11 (10)	7 (13)	4 (8)	0.385
Cereal	18 (17)	12 (22)	6 (11)	0.290

*: Column percentage, **: More than one food group

Table 3: Comparison of hemoglobin, serum iron, zinc and vitamin A levels in children with poor appetite (Group 1) and controls (Group 2)

	Total (n= 107) (%)*	Group 1 (n=54) (%)*	Group 2 (n=53) (%)*	p
Hemoglobin (gr/dl) [median (min-max)]	12.2±0.9 (9.1-14)	12.2±0.9 (9.1-13.7)	12.3±0.9 (9.5-14)	0.729
Low (n, %)	5 (5)	3 (6)	2 (7)	1.000
Iron (µg/dl) [median (min-max)]	78 (30-140)	75 (30-140)	80 (35-140)	**0.026**
Low (n, %)	41 (48)	26 (48)	15 (28)	**0.047**
Zinc (µmol/L) [median (min-max)]	14.7±4.2 (7.3-36.7)	13.6±3.3 (9-22)	15.8±4.7 (7.3-36.7)	**0.002**
Low (n, %)	8 (7.5)	7 (13)	1 (2)	**0.042**
Vitamin A [median (min-max)]	0.9±0.2 (0.3-1.7)	0.9±0.2 (0.5-1.7)	0.8±0.2 (0.3-1.5)	0.079
Low (n, %)	24 (22)	11 (20)	13 (25)	0.649

*: Column percentage

multivitamin use, height percentile, breastfeeding, introduction of complementary foods, and eating habits (p>0.05).

Children whose weight was under the 10th percentile were found to have vitamin A levels of 0.8±0.3 µmol/l. Children whose weight was between the 10th-75th percentiles had vitamin A levels of 0.9±0.2 µmol/l, while children in the 75th or higher weight percentile had a vitamin A level of 0.7±0.1 µmol/l. Namely children in 10th-75th weight percentile had higher serum vitamin A levels compared to those in the 75th or higher weight percentiles (p=0.025).

DISCUSSION

Loss of appetite is a common complaint that causes parents to bring their children to the doctor. The impact of reduced appetite on growth remains unclear, and a limited number of long-term studies are found on this topic (3,6,7). Bekem et al. (6) assessed the nutritional characteristics of children with poor appetites and found 63.9% to be malnourished. Malnutrition was more common in children who experienced a loss of appetite before the age of seven months (6). A study was conducted to evaluate the relationship between parents' reports of their children's appetite levels and their weights two years later. The study found that children with poor appetites had body mass indexes below the baseline and remained below at the end of two years compared to children with normal or high appetite levels (7). A follow-up study examining the relationship between eating problems and children's growth found 20% of children aged 30 months to have feeding problems. Children who do not have eating problems were observed to gain more weight (3). The current study found the height and weight percentiles to be lower in the small or no appetite group than in the control group.

One third of the world's population is deficient in vitamins and minerals, especially iron, zinc, and vitamin A (21). Even without anemia, iron deficiency is known to have significant adverse health effects in children and adults, ranging from maternal and infant mortality in the perinatal period to adverse effects on children's physical and mental development and physical motor capacity (22). Iron deficiency anemia (IDA) is a major global nutritional problem that particularly affects infants, children, and pregnant women. According to the World Health Organization (WHO), about 30% of children in Türkiye have hemoglobin levels <11 g/dL (23), with this being 28% in pregnant women. A study conducted in Greece found 7.9% of children aged 12-24 months to have IDA. The study also reported children with IDA to have poor appetite, be sick more often, drink less breast milk, and consume more cow's milk and tea, as well as consume less meat, vegetables, and fruit (24). A study in China found 24.3% of preschool children to be iron deficient, with iron deficiency being more common in urban than in rural areas (25). Öktem et al. (26) conducted a study comparing the serum iron levels of two groups with different socioeconomic backgrounds: the low socioeconomic status group that was nourished on legumes and unleavened bread had lower serum iron levels than the high socioeconomic status group that was nourished on meat and leavened bread. The current study has found iron deficiencies to be present in 48% of the study group, which is higher than reported in the literature. Namely, 48% of the children with small or no appetite were found to be iron deficient, compared to 28% of the control group. Having small or no appetite is a significant indicator of being iron deficient. Iron deficiency has been reported to lead to loss of appetite due to the effect serum iron levels have on ghrelin levels, an appetite-stimulating hormone (8). Although the present study found iron deficiency to occur more frequently in children with small or no appetites than in the control group, no difference was found between the two groups regarding the presence of low hemoglobin levels and anemia. Another finding of the present study was the presence of a positive correlation between serum zinc and serum iron levels, which is in agreement with the literature (27,28).

Zinc plays a key role in the human growth, immune, and reproductive systems. Zinc deficiency causes a loss of appetite, growth retardation, skin problems, and hypogonadism (19). Zinc deficiency rates in the world are reported to range between 4-73% and average at 31%. According to zinc surveys conducted in Türkiye, approximately 25% of children have low serum zinc levels (21, 29). Zinc deficiency results from inadequate dietary intake or malabsorption and, to a lesser extent, losses due to diarrhea. Low levels of animal foods in the diet and elevated levels of phytates (i.e., absorption inhibitors) reduce zinc absorption (21). Zinc deficiency in humans has been reported to be associated with income level. A study in China found 38.2% of preschool children to have low serum zinc levels, and these levels to be lower in people living in rural areas with lower socioeconomic status compared to those living in urban areas (25). In the United States, 42.8% of 12- to 36-month-old children from low-income families were found to have low serum zinc levels. The study also found a positive correlation between zinc levels and consuming over 15 g of meat per day (30). A study conducted in Isparta compared the zinc levels of children from two schools with different socioeconomic backgrounds and found the children from lower socioeconomic backgrounds to have lower zinc levels (26). The current study found low serum zinc levels in 7.5% of all children, which is a lower frequency than in other studies despite being conducted over a very low-income population. The reason for the lower incidence of zinc deficiency in this study despite being conducted over a sample with a low economic level is believed to be able to be related to the widespread use of medications containing zinc in Turkish society, especially for children with small or no appetites.

Zinc is involved in the synthesis of neuropeptides, which are bioactive peptides. These substances have been reported have an effect in regulating food intake (29). The secretion of neuropeptide Y, a peptide involved in appetite regulation, is impaired by zinc deficiency (31). Zinc can affect appetite through its impact on the hypothalamus, ghrelin, leptin, and zinc receptors. Additionally, animal experiments have demonstrated zinc to be able to increase appetite (10). That study found serum zinc levels to be lower in the group with small or no appetites and the number of children with zinc deficiencies to be higher, and therefore suggested that zinc deficiency may be a cause of small or no appetite in preschool children.

The current study has been unable to make a comparison between groups in terms of diverse levels of income. When comparing the dietary habits of the two groups, no correlation was found between zinc levels and children's fondness for meat products. Because the current study did not calculate the amount of food consumed, it is unable to provide data on this issue.

Vitamin A plays a significant role in vision, epithelial cell differentiation, growth, reproduction, and the immune system. Low dietary intake, malabsorption, and increased excretion due to illness can lead to vitamin A deficiency (21). Groups particularly at risk of vitamin A deficiency include infants, children under 5 years of age, and women during the postpartum period when rapid growth increases daily requirements. Children under 5 years of age, especially in infancy and during puerperium, are particularly at risk of vitamin A deficiency due to rapid growth and increased daily requirements. WHO considers the prevalence of serum vitamin A levels below 0.70 µmol/l of 20% or more in preschool children and pregnant women to be a significant public health issue for that population (20). A study conducted over a low-income region of China evaluated the vitamin A levels in children under the age of five and found 20.2% of children to suffer from vitamin A deficiency and this frequency to increase with age (32). A Brazilian study found 15% of the sample with low fruit, vegetable, and meat intake to be vitamin A deficient (33). WHO conducted a study on the prevalence of serum vitamin A levels in preschool children in Türkiye and found 12.5% of children to have a serum vitamin A level under 0.70 µmol/l, indicating a moderately high health problem in Turkish society (34). The current study also found a higher prevalence of vitamin A deficiency in children aged 2-6 years. This may be due to the low economic level of the group in which the study was conducted. Infection and iron deficiency have negative impacts on serum vitamin A levels. Iron and zinc, together with vitamin A, are required for the bidirectional functioning of many pathways, including absorption of vitamin A and minerals, retinol-binding protein synthesis, cell maturation, signaling pathways and the immune system (35). The present study found no association between vitamin A levels and serum iron and serum zinc levels. Vitamin A deficiency has been reported to cause loss of appetite in animals (13,14), with loss of appetite having been described as the earliest sign of vitamin A deficiency. In humans, however, no clear association between poor appetite and vitamin A deficiency has yet to be identified. The present study also found no relationship between the level of vitamin A and appetite. However, this study was conducted only in a low-income group. Conducting the same study over different income levels and larger groups is believed to be appropriate.

The study has several limitations. Firstly, the patients were only asked whether they were taking vitamins or not, without any further inquiry into the name, amount, or content of the vitamin preparations. Additionally, the amounts of food groups in the diet were not calculated. Finally, the study had a small sample size.

In conclusion, poor appetite is a common reason for children to be referred to a doctor. Although most children continue to grow normally, assessing their growth and development and checking for iron and zinc deficiencies are important, as well as providing treatment for necessary cases.

Ethics Committee Approval: The study received ethical approval from the Local Ethics Committee (Approval No. 3640 dated on 10/26/2011).

Informed Consent: Informed consent was obtained from the participants.

Peer Review: Externally peer-reviewed.

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