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Blood boron levels and anthropometric measurements in prepubertal children

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ABSTRACT

This study was conducted to assess the blood boron levels (BBL) in prepubertal children in the West and Central Anatolia regions of Turkey and its relationship with chosen anthropometric measurements. A multistage sampling design that combined multicluster (West Anatolia vs. Central Anatolia regions and rural vs. urban residents) and simple random sampling methods were used for the sample selection. BBL was measured using inductively coupled plasma mass spectrometry. Weight, height, mid-arm circumference, and triceps skinfold thickness were measured. Z-scores for weight-for-age, height-for-age, and body mass index (BMI)-for-age were calculated. Furthermore, arm-muscle area, arm-fat area, and fat percentage were measured. This study enrolled 2126 children, of whom 50.7% were male. The mean age was 8.9 years. The mean concentration of BBL was 15.6 μg/L (interquartile range: 11.7–19.6 μg/L). Children in urban areas had significantly higher BBL than those in rural areas (17.2 ± 5.5 vs. 11.9 ± 4.6 μg/L; $p < .001$). Children in the West Anatolia region had significantly lower BBL than those in the Central Anatolia region (14.5 ± 5.9 μg/L vs. 17.8 ± 5.0 μg/L; $p < .001$). BBL was not affected by maternal education, occupation, sex, and anemia. BBL was found to be significantly lower in children with low BMI, low triceps skinfold thickness, low arm fat area, and low-fat percentage. Change in BBL was associated with the region and residence in Turkey. BBL differed between well-nourished and malnourished children. Further studies are needed to evaluate the relationship between anthropometry and BBL.

1. Introduction

The health and well-being of children essentially depend on the environment in which they live [1]. Boron is widely distributed in nature and is usually consumed through food or tap water. Boron exposure can also occur in glass-, ceramic-, or enamel-related industries [2,3]. The World Health Organization (WHO) has classified boron as "probably essential" for humans [4]. The role of boron in humans is not exactly known, although some studies have suggested its beneficial effects [2,3]. Boron appears to be required for bone and joint functions, has the ability to improve the antioxidant defense *in vivo*, and has some controversial effects on lipid metabolism [2,5–8]. Considering the evidence that boron acts as a regulator of energy substrate utilization, the effect of boron on obesity requires further research. Previously, in a study involving female adults, a positive relationship was demonstrated between the content of boron in drinking water and the degree of obesity (%), but not with any other weight-related variables including body mass index (BMI), body fat (%), lean mass, and visceral adipose tissue ($r = 0.322$, $p < .01$) [9]. However, the effect of boron on obesity development remains unclear in the analyses of experimental and clinical data [10–12]. Additionally, the relationship between arm anthropometry and blood boron levels (BBL) has not been evaluated and the knowledge about BBL in children is limited [12–15].

Boron is supposed to regulate the metabolism of some minerals [2,16]. However, no study has been published about the association between anemia and BBL. Aside from toxic metals and bioactive substances, cigarette smoke contains more than 4000 chemicals, including boron [17,18]. These chemicals undergo complex interactions with human biological systems [17–20]. However, the effect of smoking on BBL remains unknown as well.

The purpose of this study was to determine BBL in healthy prepubertal children and to evaluate the relationship between BBL and anthropometric measurements [weight, height, BMI, mid-upper arm circumference (MUAC), triceps skinfold thickness (TSF), arm-muscle area (AMA), arm-fat area (AFA), and fat percentage] in a sample representing two geographical regions (West Anatolia vs. Central Anatolia regions) and residences (rural vs. urban) in Turkey. Additionally, we aimed to evaluate the effect of exposure to smoking

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and the presence of anemia on BBL in prepubertal children.

2. Material and methods

2.1. Study design and sampling

Turkey is included in the Nomenclature of Territorial Units for Statistics (NUTS) and divided into 12 NUTS-1 geographical regions. For this study, two geographical regions, Central Anatolia and West Anatolia, involving 11 provinces, were enrolled. A multistage sampling design that combined multicluster (West Anatolia vs. Central Anatolia regions and rural vs. urban residences) and then simple random sampling methods was used to select the sample. Firstly, the Turkish Statistical Institute (TURKSTAT) calculated the sample size according to the population density of children for each geographic region, province, and residence. Secondly, TURKSTAT selected the blocks as primary sampling units from every stratum. A total of 47,352 households were selected in the survey. Subsequently, the lists were prepared after a field operation for the presence of a suitable child.

The study was carried out according to the guidelines of the Helsinki Declaration. The study was approved by the local ethics committee in medical research of Hacettepe University Faculty of Medicine (291207TBK07/14), and a written informed consent was obtained from each parent.

2.2. Study protocol

Information about the children such as age, sex, birth weight, gestational period, number of siblings, maternal education and occupation, and presence of smoking at home were obtained from their mothers using a structured questionnaire.

All anthropometric measurements (height, weight, MUAC, and TSF) were measured twice by a team of nurses, who had received similar training and practice by the investigators, and the averages were recorded. During measurements, the children were dressed in light indoor clothing and were barefoot or wore stockings. The subjects were weighed to the nearest 0.1 kg using an electronic scale (Seca 767 digital medical scale, Hamburg, Germany) and the height was measured to the nearest 0.1 cm with a stadiometer (Seca 220 measuring rod, Hamburg, Germany) in a vertically erect position. Field surveys were periodically supervised.

The height and weight data were used to calculate BMI (kg/m^2) using the following formula: weight (kg) divided by height (m) squared. Weight-for-age (W/A), height-for-age (H/A), and BMI-for-age (BMI/A) were expressed as z-scores based on WHO-2007, which was referenced using WHO AnthroPlus [21]. These measurements were divided into three categories (z-scores < -1; $-1 \leq$ z-scores $\leq +1$; z-scores $> +1$).

With respect to arm anthropometry, MUAC was measured using a non-elastic paper tape to the nearest 0.1 cm on the left arm, halfway between the acromion process and the olecranon process. TSF was measured to the nearest 0.1 mm using Holtain skinfold calipers (Holtain Ltd, Crymych, UK) [22]. AMA, arm area (AA), AFA, and fat percentage (%) were calculated based on the following formulae [23–25]:

$$\text{AMA (cm}^2\text{)} = (\text{MUAC} - \pi\text{TSF})^2/4\pi$$

$$\text{AA (cm}^2\text{)} = \text{MUAC}^2/4\pi \ (\pi = 3.1416)$$

$$\text{AFA (cm}^2\text{)} = \text{AA} - \text{AMA}$$

$$\text{Fat\%} = \text{AFA} \times 100/\text{AA}$$

Percentile values for each arm anthropometric data were calculated and measurements were classified into three categories: low < 15%, 15% ≤ normal ≤85%, and high > 85%.

2.3. Blood analysis

Venous blood samples were collected in two metal-free tubes containing the anticoagulant ethylene diamine tetraacetic acid (3 mL per tube) for measuring BBL and hemoglobin values.

The complete blood count was evaluated from the first sample itself. Anemia was defined as a hemoglobin value < 11.5 g/dL, which is the cutoff point for anemia in children aged 5–11 years [26].

The collected blood samples were stored at 4 °C. Blood samples were analyzed for BBL using inductively coupled plasma mass spectrometry (ICP-MS; Agilent 7500cx, Agilent Technologies, USA). ICP-MS was operated under suitable conditions (radio frequency power supply 1500 W, plasma argon flow rate of 15 L/min, auxiliary argon flow rate of 1.1 L/min, and nebulizer argon flow rate of 0.94 L/min). Only high-purity deionized water (ultra-pure, resistivity of 18.2 MΩ cm) was used for the washing of vials and preparation/dilution of samples and standards. Additionally, Suprapur® nitric acid (65% w/w), Triton X100, and multi-element standard solutions from Merck (Darmstadt, Germany) were used.

During sample preparation, 0.4 mL of whole blood was added into 3.5 mL diluent with Rh (1 ppb) as the internal standard [27]. The diluent consisted of 0.5% (v/v) butanol, 0.65% (w/v) nitric acid, and 0.1% (v/v) triton. The blanks and standards were prepared in the same manner as the samples. In the six calibrated standard preparations, the concentrations of the single-element standard solutions of boron were, 0, 1, 2, 5, 10, and 20 μg/L.

Method validation included accuracy, precision, and limit of detection (LOD) assay steps. Because boron-certified reference materials were not available, the spiked recoveries of doped samples (+50 μg/L) were used for determining accuracies. The mean spike recovery was found at 93.2%, which was adequate. Precision was determined by replicating the quality control material (20 μg/L) for every 20 samples in a run. Day-to-day precision was determined by replicating quality control material for 10 consecutive days. LOD was calculated as three times the standard deviation (SD) of the boron concentration in the blank. LOD was 1.5 μg/L and the results were expressed as μg/L. Sixteen cases (0.8%) were below the LOD and were expressed as LOD/√2. The mean coefficient of variation was between 5% and 10%, which was adequate.

2.4. Statistical analysis

Statistical analyses were performed using SPSS version 23.0 for Windows (IBM Corp., Armonk, NY, USA). Descriptive statistics were expressed as mean, SD, interquartile range (IQR), and 95% confidence intervals (CI) for continuous variables and percentages for categorical variables.

The distribution of BBL was outlined using Kolmogorov–Smirnov test. The shape of the distribution, asymmetrical and skewed, was not corrected after log-transformation. Therefore, "a two-step approach for transforming non-normally distributed continuous variables to normal" was applied. Step 1 involved transforming the variable into a percentile rank, which gave uniformly distributed probabilities. Step 2 applied the inverse-normal transformation to the results in "Step 1" to form a variable consisting of normally distributed z-scores [28]. Then, data of "z-scores" were converted to original value with specified mean and SD using intensity–duration–frequency (IDF) ["IDF.NORMAL (probability, mean, SD). Numeric." Formulation].

A Student's *t*-test was used to compare the two groups. One-way ANOVA was performed to compare more than two groups. When a significant difference among means existed in one-way ANOVA, post hoc analyses were performed using Duncan's test.

After adjusting for sex, age, residence, and region, the relationship between anthropometric measurements and BBL was further analyzed using general linear models. Fisher's least significant difference test was used for post hoc comparisons.