RESEARCH PAPER

Serum Magnesium in Overweight Children

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Objective: To determine whether overweight children and adolescents have lower serum concentration and lower dietary intake of magnesium compared to those with normal weight; and to study the correlation of serum magnesium levels with components of metabolic syndrome in children and adolescents.

Design: Cross-sectional, comparative study.

Setting: General/Pediatric Endocrinolgy OPD tertiary care medical centre. Study done from July 2007 to March 2009

Participants: 55 overweight and 53 normal weight children and adolescents aged 4 years to 14 years.

Methods: We compared fasting levels of serum magnesium, insulin, glucose, total and HDL-cholesterol, triglycerides and dietary magnesium intake.

Results: The serum magnesium levels were significantly lower in overweight (2.12 ± 0.33 mg/dL) compared to normal weight group (2.56 ± 0.24 mg/dL, P<0.001), while the dietary intake of magnesium (adjusted for calorie intake) was higher in overweight group (0.20 ± 0.06 mg/kcal) compared to normal weight (0.17 ± 0.05 mg/kcal; P= 0.005). Serum magnesium levels were inversely correlated with body mass index, systolic blood pressure, diastolic blood pressure, waist circumference and fasting insulin levels.

Conclusions: Serum magnesium levels were significantly lower in overweight children compared to those with normal weight in spite of a higher dietary intake.

Key words: *Child, India, Magnesium, Metabolic syndrome, Overweight.*

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Overweight adults have lower serum and intracellular magnesium compared to healthy normal weight controls [1-3]. An association is also reported between lower serum/ intracellular magnesium and insulin resistance (IR), type 2 diabetes mellitus (DM), hypertension and metabolic syndrome (MS) [1-3]. This association is biologically plausible because magnesium containing ATPases are important co-factors for many of the enzymes of the carbohydrate metabolism pathway [4]. Impaired cellular glucose uptake, impaired action of insulin at receptor level, and impaired tyrosine kinase activity are other mechanisms by which magnesium deficiency impairs insulin action at cellular level [5-7].

It is being increasingly recognized that the foundations for obesity and metabolic syndrome are laid down in childhood with subsequent tracking into adulthood [8]. We conducted this study to test the hypothesis that the association of lower serum magnesium with obesity and metabolic syndrome develops in childhood itself. The objectives of the study were to determine whether serum magnesium and dietary intake of magnesium were lower in overweight children compared to normal weight and to assess the correlation of serum magnesium with parameters of metabolic syndrome.

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METHODS

Subjects included 55 overweight children (BMI >85th centile for age and gender as per Agarwal's growth charts for Indian children) and 53 normal weight children, aged between 4 to 14 years enrolled from the general pediatric outpatient or Pediatric endocrinology clinic. Children with genetic/endocrine/syndromic causes of obesity, diabetes mellitus, medical conditions predisposing to hypomagnesemia (gastroenteritis, chronic kidney disease and chronic liver disease) or on medications predisposing to hypomagnesemia (*e.g.* diuretics, amphotericin were excluded. The study was approved by the institutional ethics committee. Written informed consent from all parents and assent from subjects, wherever appropriate, were obtained.

Detailed dietary history was obtained in both groups using a validated food frequency question-naire (based on 24-hour as well as a monthly recall) by an experienced pediatric dietician. Enrolment of cases and controls was done simultaneously to avoid seasonal bias in dietary characteristics. A detailed clinical examination including anthropometry (height, weight and waist circumference (WC)), markers of insulin resistance (acanthosis nigricans and skin tags), and blood pressure (BP) was performed in all subjects. Sexual maturity rating (SMR) was evaluated in all subjects and they were grouped into pre (Tanner 1), early (Tanner 2, 3) and advanced puberty (≥Tanner 4) [9]. Weight was measured with an accuracy of 0.1 kg and height to the nearest 0.5 cm using a calibrated digital weighing scale with a stadiometer (Seca, Germany, model no: 7892317109) and BMI was calculated. WC was measured to an accuracy of 0.5 cm, using a non elastic tape at the midpoint of iliac crest and the lower border of rib cage. BP was measured in duplicate using mercury sphygmomanometer (Elkometer-300, India) in sitting position in the right arm with appropriate sized cuffs after the child had rested for five minutes.

Venous blood samples were obtained after an overnight fast of at least 10 hours for estimation of serum magnesium, insulin, total and HDL-cholesterol (HDL-C) and triglycerides in all subjects. Serum was separated and stored at -80°C until analysis. An oral glucose tolerance test was also performed in overweight children by measuring fasting and 2 hour plasma glucose after loading with 1.75 g/kg of glucose. Serum magnesium was analyzed using flame atomic absorption spectrometer (Avanta M, GBC, Australia). Standard curves were prepared using international magnesium standards (Merck, Germany). The validation of these curves was done using two different seronorms (Sero, A/S, Norway) of known concentrations. Intra-assay quality control was ensured by repeating the pooled serum magnesium analysis after every 10 samples. The maximum accepted intra-assay variation was 10%. Serum insulin was measured using a commercially available radioimmuno-assay kit (Medicorp, Montreal, Canada). Total cholesterol, triglyceride and HDL-C were measured by enzymatic end point method using the principle of enzymatic hydrolysis and oxidation using a commercially available kit (Randox, UK). LDL cholesterol was calculated using 'Friedewald's formula [10] [LDL = total cholesterol – (triglyceride/5 + HDL)] and non-HDL cholesterol (non-HDL-C) was calculated as total cholesterol –HDL-C.

The daily magnesium and calorie intake of each subject was calculated by entering the dietary record into nutrient calculator software (Diet soft), which has data on the calorie content, micro and macro-nutrient composition of most Indian foods as per National Institute of Nutrition, Hyderabad, guidelines [11]. The daily magnesium intake was expressed as mg/kcal to factor in the higher calorie intake in the overweight group.

Metabolic syndrome was defined according to the International Diabetes Federation criteria for children and adolescents as abdominal obesity (waist circumference ≥90th percentile for age and gender or adult cut off) and the presence of 2 or more other features (triglycerides ≥1.7 mmol/L (150 mg/dL); HDL-C <1.03 mmol/L (40 mg/dl); BP ≥130 mm Hg systolic or ≥85 mm Hg diastolic; fasting glucose ≥5.6 mmol/L (100 mg/dL) or type 2 DM [12].

Data were recorded in a predesigned proforma and managed in an Excel spread sheet. Comparison of physical, biochemical parameters and dietary magnesium intake between the overweight and normal weight groups was done using either Student's t-test or Wilcoxon rank sum test. Bivariate (unadjusted) correlations of serum magnesium with BP, WC, serum HDL-C, non-HDL-C and insulin were examined using Spearman's rank correlation. Log transformed values of variables not normally distributed (fasting insulin and lipid parameters) were used to examine the BMI adjusted linear correlations between serum magnesium and the variables found to be significant in unadjusted comparison. STATA 9.0 statistical software was used for data analysis. P <0.05 was considered significant.

RESULTS

***Table* I** compares the baseline anthropometric and biochemical variables in two groups. ***Table* II** compares the outcome variables between overweight and normal weight children. Lower serum magnesium levels in the overweight group persisted even when subgroup analysis was done for children ≤10 years and >10 years.

Prevalence of metabolic syndrome in overweight adolescents (≥10 years of age) was 45%. Systolic hypertension was seen in 20%, diastolic hypertension in 35%, low HDL-C in 75%, hypertriglyceridemia in 10% and deranged oral glucose tolerance test in 17.5% of the overweight adolescents.

Among the components of metabolic syndrome, a significant inverse correlation of serum magnesium was observed with serum insulin (P<0.005), BMI (P<0.0001), WC (P<0.001), systolic BP (P=0.001) and diastolic BP (P=0.0009). After adjusting for BMI, the correlation of serum magnesium with WC remained

TABLE I COMPARISON OF BASELINE CHARACTERISTICS OF OVERWEIGHT AND NORMAL WEIGHT SUBJECTS

Characteristic	Overweight (*n*=55)	Normal weight (*n*=53)	*P* value
Gender (M/F)	44/11	37/16	0.36
Age (years)	10.6 ± 2.7	10.2 ± 2.1	
SMR stage			
Tanner 1 (males)	28 (18)	27 (17)	
Tanner 2,3 (males)	21(20)	21(17)	0.56
>Tanner 4 (males)	6 (6)	5 (3)	
BMI (kg/m^2)	24.8 ± 5.0	14.8 ± 2.2	<0.001
Waist circumference (cm)	85 ± 8.9	58.3 ± 6.8	<0.001
Systolic BP (mm Hg)	118 ± 16	102 ± 10	<0.001
Diastolic BP (mm Hg)	78 ± 12	68 ± 7	<0.001
Total cholesterol (mg/dL)	137 (117-170)	130.4(119-140)	0.127
Triglycerides (mg/dL)	107 (90 - 144)	94 (69 -116)	0.037
HDL cholesterol (mg/dL)	36 (31-41)	29 (24-39)	0.001
Non-HDL cholesterol(mg/dL)	103 (126)	99 (86-112)	0.28
Serum insulin (µIU/mL)	6.5 (4.1-11.9)	3.2 (2.2-5.6)	<0.001

* *Data presented as mean ± S.D or median (inter-quartile range).*

significant (P< 0.001) while all others became non-significant.

DISCUSSION

Our study has shown that overweight children, even those ≤10 years of age have significantly lower serum magnesium levels as compared to normal weight children. We speculate that the lower serum magnesium levels further aggravate the insulin resistant state in overweight children and predispose them to type 2 diabetes and cardiovascular diseases in adulthood.

Human and animal studies suggest that supplementation with magnesium improves insulin-mediated glucose disposal and insulin secretion [13-15].

TABLE II SERUM AND DIETARY MAGNESIUM IN OVERWEIGHT AND NORMAL WEIGHT CHILDREN

Variable	Overweight (*n*=55)	Normal weight (*n*=53)	*P* value
Serum Mg (mg/dL)	2.12 ± 0.33	2.56 ± 0.24	<0.001
age ≤10 y	2.14 ± 0.37	2.58 ± 0.21	<0.001
age >10 y	2.10 ± 0.29	2.56 ± 0.26	<0.001
Dietary Mg (mg/Cal)	0.20 ± 0.06	0.17 ± 0.05	0.005
Unadjusted Mg intake (mg/day)	303 ± 15	192 ± 8.5	<0.005

Mg: magnesium

In one small (*n*=25) pediatric study by Huerta, *et al*. [16], overweight children had lower serum levels as well as lower calorie-adjusted intake of magnesium compared to normal weight children. However, we found the unadjusted as well as calorie-adjusted dietary intake of magnesium to be higher in the overweight group, which was even greater than the RDA for magnesium (140-290 mg/day).We postulate that the lower serum levels of magnesium in our overweight group in spite of a higher dietary intake might be due to either decreased absorption or increased excretion of magnesium. Increased fractional excretion of magnesium in urine in patients with type 2 DM, hypertension and obesity has been previously reported in adults [17]. Association of lower serum magnesium levels with BMI, systolic and diastolic BP, WC and serum insulin level in our study suggests that the origin of the association of insulin resistant state with low serum magnesium starts in childhood itself.

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Contributors: BJ: patient enrolment, data acquisition, data analysis and drafting of manuscript; VJ: concept and design, data acquisition, analysis, drafting and critical review of the manuscript. She will serve as guarantor of the study; NV: data analysis and interpretation, laboratory analysis and critical revision of the manuscript; AA: data acquisition, data analysis and interpretation; SS: laboratory analysis and interpretation of lab results.
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WHAT IS ALREADY KNOWN?

- Serum and intracellular magnesium is low in obese and hypertensive adults.

WHAT THIS STUDY ADDS?

- Overweight children have lower serum magnesium levels compared to normal weight children.
- Serum magnesium has a significant inverse correlation with waist circumference.

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