

Importance of Macromineral Ratios and Products in Association with Vitamin D in Pediatric Obesity Including Metabolic Syndrome

Mustafa M. Donma, Orkide Donma

Abstract—Metabolisms of macrominerals, those of calcium, phosphorus and magnesium, are closely associated with the metabolism of vitamin D. Particularly magnesium, the second most abundant intracellular cation, is related to biochemical and metabolic processes in the body, such as those of carbohydrates, proteins and lipids. The status of each mineral was investigated in obesity to some extent. Their products and ratios may possibly give much more detailed information about the matter. The aim of this study is to investigate possible relations between each macromineral and some obesity-related parameters. This study was performed on 235 children, whose ages were between 06-18 years. Aside from anthropometric measurements, hematological analyses were performed. TANITA body composition monitor using bioelectrical impedance analysis technology was used to establish some obesity-related parameters including basal metabolic rate (BMR), total fat, mineral and muscle masses. World Health Organization body mass index (BMI) percentiles for age and sex were used to constitute the groups. The values above 99th percentile were defined as morbid obesity. Those between 95th and 99th percentiles were included into the obese group. The overweight group comprised of children whose percentiles were between 95 and 85. Children between the 85th and 15th percentiles were defined as normal. Metabolic syndrome (MetS) components (waist circumference, fasting blood glucose, triacylglycerol, high density lipoprotein cholesterol, systolic pressure, diastolic pressure) were determined. High performance liquid chromatography was used to determine Vitamin D status by measuring 25-hydroxy cholecalciferol (25-hydroxy vitamin D₃, 25(OH)D). Vitamin D values above 30.0 ng/ml were accepted as sufficient. SPSS statistical package program was used for the evaluation of data. The statistical significance degree was accepted as $p < 0.05$. The important points were the correlations found between vitamin D and magnesium as well as phosphorus ($p < 0.05$) that existed in the group with normal BMI values. These correlations were lost in the other groups. The ratio of phosphorus to magnesium was even much more highly correlated with vitamin D ($p < 0.001$). The negative correlation between magnesium and total fat mass ($p < 0.01$) was confined to the MetS group showing the inverse relationship between magnesium levels and obesity degree. In this group, calcium*magnesium product exhibited the highest correlation with total fat mass ($p < 0.001$) among all groups. Only in the MetS group was a negative correlation found between BMR and calcium*magnesium product ($p < 0.05$). In conclusion, magnesium is located at the center of attraction concerning its relationships with vitamin D, fat mass and MetS. The ratios and products derived from macrominerals including magnesium have pointed out stronger

associations other than each element alone. Final considerations have shown that unique correlations of magnesium as well as calcium*magnesium product with total fat mass have drawn attention particularly in the MetS group, possibly due to the derangements in some basic elements of carbohydrate as well as lipid metabolism.

Keywords—Macrominerals, metabolic syndrome, pediatric obesity, vitamin D.

I. INTRODUCTION

MACROMINERALS constitute a matter of great concern. In the body, they are involved in many vital functions such as energy metabolism, skeletal structure, and neural transmission. Calcium (Ca) and phosphorus (P) work in a collaborative manner.

Although it is the second most abundant intracellular cation and the fourth most abundant mineral in the human body, there is much less information about magnesium (Mg) and alterations in its concentrations during various disease states. Vitamin D is known for its close associations with macrominerals. Therefore, deficiency state of this vitamin is a major contributing factor underlying in most of the diseases.

The associations among macrominerals and vitamin D have been investigated in many physiological and disease states including asthma, osteopathy and post-menopause, as well as in neurosurgical intensive care unit patients. Experimental studies are also being carried out on the matter [1]-[6]. It is also reported that vitamin D cannot be metabolized without sufficient Mg levels [2], [3].

Macromineral status and the participation of vitamin D have also been investigated in healthy as well as overweight and obese individuals [7]-[11]. Such an integrative report performed on morbid obese (MO) children and those with MetS is also needed in this field.

The aim of this study is to determine serum concentrations of Ca, P, Mg as well as vitamin D to have a notion about their possible alterations in varying obesity classes and also in pediatric MetS in comparison to the values detected in children with normal BMI. Since it is possible to gain more detailed information from the combinations of these macrominerals such as calcium*phosphorus product, calcium/phosphorus ratio, calcium*magnesium product, calcium/magnesium ratio, phosphorus*magnesium product, phosphorus/magnesium ratio, all of these parameters and the associations among them as well as some parameters related to obesity such as BMR and total fat mass will be considered.

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II. PATIENTS AND METHODS

A. Patients and the Study Protocol

Two hundred and thirty five children aged 06-18 years participated in the study. The study population consisted of five groups, being normal BMI, overweight (OW), obese (OB), MO and MetS. The parents have given written informed consent forms for the involvement of their children into the study. Namik Kemal University, Medical Faculty, Non-interventional Ethical Committee has approved the design of the study.

B. Measurements

Anthropometric measurements were taken. Some obesity-related parameters including BMR, total fat, mineral and muscle masses were determined by body composition monitor (TANITA Corp) using bioelectrical impedance analysis technology.

C. Obesity Classification

Obesity classification was performed using BMI percentile tables for age and sex prepared by the World Health Organization [12]. The values above 99th, those between 95th and 99th, those between 85th and 95th and those between 15th and 85th percentiles were defined as MO, OB, OW, and normal BMI, respectively.

D. MetS Components

The MetS diagnosis was based upon the previously set criteria [13].

MO children with BMI values higher than 99th percentile, systolic and diastolic blood pressures above 130 mm and 85 mm Hg, triacylglycerol (TRG) and high density lipoprotein cholesterol (HDL-C) concentrations above 150 mg/dl and/or below 40 mg/dl, and fasting blood glucose (FBG) levels above 100 mg/dl were considered for inclusion to the MetS group. MO children having two pathological values were defined as MO+MetS.

E. Laboratory Analyses

Hematological analyses were performed. Vitamin D status was determined by measuring 25-hydroxy cholecalciferol (25-hydroxy vitamin D₃, 25(OH)D) using high performance liquid chromatography; values above 30.0 ng/ml were accepted as sufficient. Calcium, phosphorus, magnesium analyses were performed.

Calcium*phosphorus product, calcium/phosphorus ratio, calcium*magnesium product, calcium/magnesium ratio, phosphorus*magnesium product, phosphorus/magnesium ratio were calculated. MetS components (waist circumference, fasting blood glucose, triacylglycerol, high density lipoprotein cholesterol, systolic pressure, diastolic pressure) were determined.

F. Statistical Evaluation of the Data

Data were evaluated by Statistical Package for Social Sciences (SPSS) for Windows, Version 16.0. Values greater than $p < 0.05$ were accepted as statistically significant.

III. RESULTS

35 children with normal-BMI, 20 OW, 47 OB, 97 MO and 36 children with MetS were included into the study.

Any statistically significant difference was not detected among the study groups in terms of calcium, phosphorus, magnesium and the products as well as the ratios of these minerals ($p > 0.05$). Vitamin D levels of the groups did not differ, either.

At this point, correlations have gained importance. Statistically significant correlations were calculated between the vitamin D and magnesium ($r = 0.423$; $p = 0.035$) as well as the phosphorus ($r = 0.684$; $p = 0.001$) levels of children with normal BMI. These findings were confined to this group. Such a correlation could not be found in any other group. Even much stronger correlation was found between vitamin D and the ratio of phosphorus-to-magnesium ($r = 0.768$; $p = 0.001$) (Fig. 1).

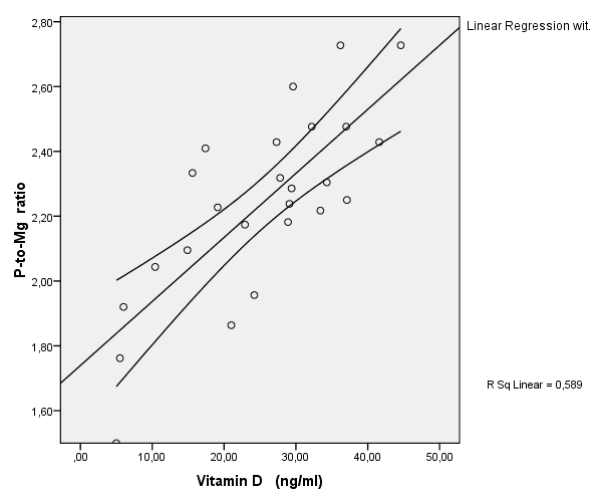
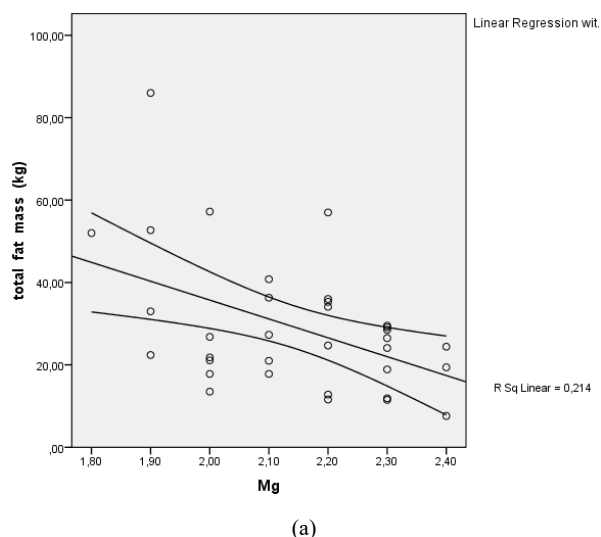


Fig. 1 Correlation between phosphorus-to-magnesium ratio and vitamin D level in children with normal-BMI



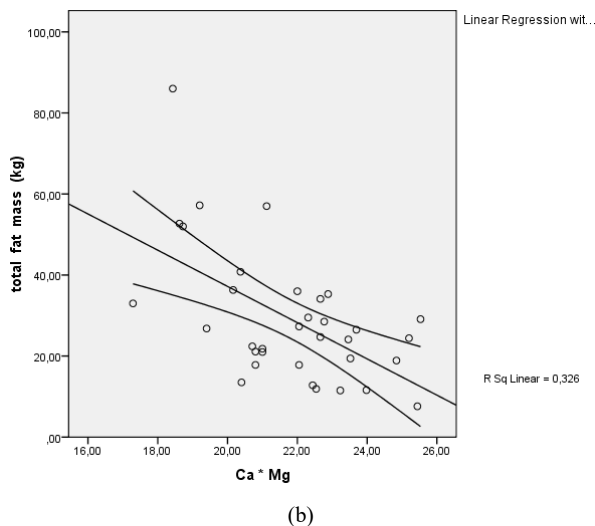


Fig. 2 Correlations between total fat mass and (a) Mg as well as (b) Ca*Mg product in morbid obese children with MetS

There was a negative correlation between magnesium and total fat mass ($r = -0.463$; $p = 0.006$) in MetS group. This finding was observed only in this group. This finding was the indicator of the inverse relationship between magnesium levels and obesity degree. Also, the correlation between calcium*magnesium product and total fat mass was the strongest one ($r = -0.571$; $p = 0.001$) among all groups (Figs. 2 (a) and (b)).

A negative correlation between BMR and calcium*magnesium product, which is confined to children with MetS, was detected ($r = -0.350$; $p = 0.043$) (Fig. 3).

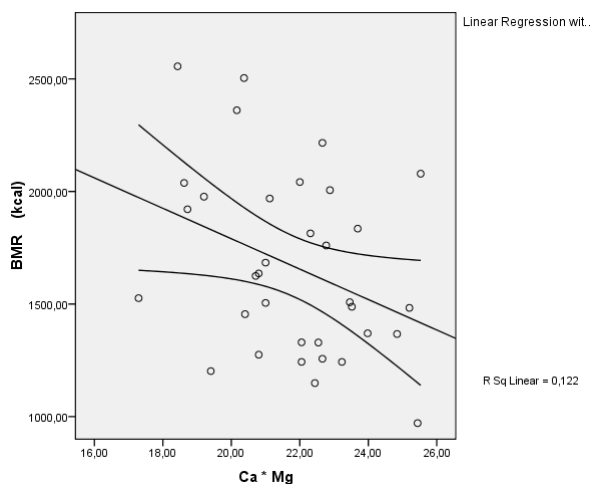


Fig. 3 Correlation between BMR and Ca*Mg product in morbid obese children with MetS

IV. DISCUSSION

Obesity is associated with nutritional, metabolic and biochemical alterations. Minerals participate in many reactions within this context. Mutual interactions take place between minerals and the components of the metabolic reactions.

Therefore, it is plausible to investigate some possible findings, which may be beneficial during the evaluation of obesity and an extreme case, MetS.

Significant associations between Mg and vitamin D levels were reported among students [8]. We have also found a correlation between vitamin D and phosphorus-to magnesium ratio in children with normal BMI. This finding was lost in groups with higher BMI.

In another study performed on asthma in adults, it was reported that both vitamin D and magnesium may serve as important markers of asthma severity [1]. In OW and OB children, significantly lower magnesium levels were observed [9], [10]. In our study, although statistically significant reductions were not detected in any of the groups with elevated BMI, negative correlations found between total fat mass and magnesium and calcium*magnesium product have pointed out inverse relations between magnesium status and morbid obesity with MetS.

The combinations of macrominerals in terms of ratios as well as products including those of magnesium suggested stronger correlations than each of the mineral alone. Particularly magnesium and its ratios and products obtained with the other macrominerals must be considered due to its interesting associations with vitamin D, fat mass and MetS. Findings have pointed out that unique correlations of magnesium as well as calcium*magnesium product with total fat mass have drawn attention particularly in MetS group, possibly due to the alterations in some parameters related to carbohydrate as well as lipid metabolism.

REFERENCES

- [1] M. N. Shaikh, and B. R. Malapati, R. Gokani, B. Patel, M.Chatriwala, "Serum magnesium and vitamin D levels as indicators of asthma severity," *Pulm. Med.*, vol.2016; pp.1643717, 2016.
- [2] American Osteopathic Association, "Low magnesium levels make vitamin D ineffective: Up to 50 percent of US population is magnesium deficient," *ScienceDaily*, 26 Feb. 2018. www.sciencedaily.com/releases/2018/02/180226122548.htm.
- [3] A. M. Uwitonze, and M. S. Razzaque, "Role of magnesium in vitamin D activation and function," *J. Am. Osteopath. Assoc.*, vol.118, pp. 181-189, Mar. 2018.
- [4] E. B. Schmitt, J. Nahas-Neto, F. Bueloni-Dias, P. F. Poloni, C. L. Orsatti, and E. A. Petri Nahas, "Vitamin D deficiency is associated with metabolic syndrome in postmenopausal women," *Maturitas*, vol.107, pp.97-102, Jan. 2018.
- [5] S. H. Ardehali, S. Dehghan, A. R. Baghestani, A. Velayati, and S. Z. Vahdat, "Association of admission serum levels of vitamin D, calcium, Phosphate, magnesium and parathormone with clinical outcomes in neurosurgical ICU patients," *Sci. Rep.*, vol. 8, pp. 2965, Feb. 2018.
- [6] S. Kurstjens, J. A. van Diepen, C. Overmars-Bos, W. Alkema, R. J. M Bindels, F. M. Ashcroft, C. J. J. Tack, J. G. J. Hoenderop, and J. H. F. de Baaij, "Magnesium deficiency prevents high-fat-diet-induced obesity in mice," *Diabetologia*, vol.61, pp. 2030-2042, Sep. 2018.
- [7] A. R. Oliveira, K. J. Cruz, J. S. Severo, J. B. Morais, T. E. Freitas, R. S. Araújo, and D. D. Marreiro, "Hypomagnesemia and its relation with chronic low-grade inflammation in obesity," *Rev. Assoc. Med. Bras.*, vol.63, pp.156-163, Feb 2017.
- [8] R. Kelishadi, E. Ataci, G. Ardalan, M. Nazemian, M. Tajadini, R. Heshmat, M. Keikha, and M. E. Motlagh, "Relationship of serum magnesium and vitamin D levels in a nationally-representative sample of Iranian adolescents: The CASPIAN-III Study," *Int. J. Prev. Med.*, vol. 5, pp.99-103, Jan. 2014.
- [9] R. Chaudhary, A. Kumar, and R. B. Sinha, "Assessment of serum magnesium in overweight children at a tertiary care hospital of Bihar," *Int. J. Med. Health Res.*, vol. 4, pp. 159-161, 2018.

- [10] M. G. Huerta, J. N. Roemmich, M. L. Kington, V. E. Bovbjerg, A. L. Weltman, V. F. Holmes, J. T. Patrie, A. D. Rogol, and J. L. Nadler, "Magnesium deficiency is associated with insulin resistance in obese children," *Diabetes Care*, vol.28, pp.1175-1181, May 2005.
- [11] E. Stokic, A. Romani, B. Ilincic, A. Kupusinac, Z. Stosic, E. R. Isenovic, "Chronic latent magnesium deficiency in obesity decreases positive effects of vitamin D on cardiometabolic risk indicators," *Curr. Vasc. Pharmacol.*, vol. 16, pp.610-617, 2018.
- [12] World Health Organization (WHO). The WHO Child Growth Standards. Available at: [http:// www.who.int /childgrowth/en/](http://www.who.int/childgrowth/en/). Accessed on June 10, 2016.
- [13] P. Zimmet, K. G. Alberti, F. Kaufman, N. Tajima, M. Silink, S. Arslanian, G. Wong, P. Bennett, J. Shaw, S. Caprio, and IDF consensus group, "The metabolic syndrome in children and adolescents-an IDF consensus report", *Pediatr. Diabetes*, vol: 8, no.5, pp. 299-306, Oct. 2007.