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Cobalamin, Folate and Metabolic Syndrome Parameters in Pediatric Morbid Obesity and Metabolic Syndrome

Mustafa M. Donma, Orkide Donma

***Abstract*—**Obesity is known to be associated with many clinically important diseases including metabolic syndrome (MetS). Vitamin B_{12} plays essential roles in fat and protein metabolisms and its cooperation with vitamin B_9 is well-known. The aim of this study is to investigate the possible contributions as well as associations of these micronutrients upon obesity and MetS during childhood. A total of 128 children admitted to Namik Kemal University, Medical Faculty, Department of Pediatrics Outpatient Clinics were included into the scope of this study. The mean age±SEM of 92 morbid obese (MO) children and 36 with MetS were 118.3±3.8 months and 129.5±6.4 months, respectively ($p > 0.05$). The study was approved by Namık Kemal University, Medical Faculty Ethics Committee. Written informed consent forms were obtained from the parents. Demographic features and anthropometric measurements were recorded. WHO BMI-for age percentiles were used. The values above 99 percentile were defined as MO. Components of MetS [waist circumference (WC), fasting blood glucose (FBG), triacylglycerol (TRG), high density lipoprotein cholesterol (HDL-Chol), systolic pressure (SP), diastolic pressure (DP)] were determined. Routine laboratory tests were performed. Serum vitamin B_{12} concentrations were measured using electrochemiluminescence immunoassay. Vitamin B_9 was analyzed by an immunoassay analyzer. Values for vitamin B_{12} < 148 pmol/L, 148-221 pmol/L, > 221 pmol/L were accepted as low, borderline and normal, respectively. Vitamin B_9 levels ≤ 4 mcg/L defined deficiency state. Statistical evaluations were performed by SPSSx Version 16.0. $p \leq 0.05$ was accepted as statistical significance level. Statistically higher body mass index (BMI), WC, hip circumference (C) and neck C were calculated in MetS group compared to children with MO. No difference was noted for head C. All MetS components differed between the groups (SP, DP $p < 0.001$; WC, FBG, TRG $p < 0.01$; HDL-Chol $p < 0.05$). Significantly decreased vitamin B_9 and vitamin B_{12} levels were detected ($p < 0.05$) in children with MetS. In both groups percentage of folate deficiency was 5.5%. No cases were below < 148 pmol/L. However, in MO group 14.3% and in MetS group 22.2% of the cases were of borderline status. In MO group B_{12} levels were negatively correlated with BMI, WC, hip C and head C, but not with neck C. WC, hip C, head C and neck C were all negatively correlated with HDL-Chol. None of these correlations were observed in the group of children with MetS. Strong positive correlation between FBG and insulin as well as strong negative correlation between TRG and HDL-Chol detected in MO children were lost in MetS group. Deficiency state end-products of both B_9 and B_{12} may interfere with the expected profiles of MetS components. In this study, the alterations in MetS components affected vitamin B_{12} metabolism and also its associations with anthropometric body measurements. Further increases in vitamin B_{12} and vitamin B_9 deficiency in MetS associated with the increased vitamin B_{12} as well as vitamin B_9 deficiency metabolites may add to MetS parameters.

***Keywords*—**Children, cobalamin, folate, metabolic syndrome, obesity.

I. Introduction

CHILDHOOD obesity may lead to many severe chronic disease such as diabetes mellitus, MetS, cardiovascular diseases (CVDs) and even cancer in adulthood. Aside from genetic, socioeconomic, and cultural factors, nutritional factors are also important. When excessive intake of macronutrients is combined with micronutrient deficiencies, the principle of sufficient and balanced nutrition is impaired. Cobalamin (vitamin B_{12}) and folic acid (vitamin B_9) are closely interrelated micronutrients and essentially involved in the events related to genetic information. Besides, the deficiency of vitamin B_{12} may lead to hematological, psychiatric and neurological problems, whereas enzymes of vitamin B_9 metabolism serve as targets during cancer chemotherapy.

So far, numerous studies have been performed to be able to detect the levels of vitamin B_{12} as well as those of vitamin B_9. Percent deficiencies have also been the matter of concern. Aside from healthy individuals, women of childbearing age, obese people, pregnant women, those with gestational diabetes have been the center of attraction for the investigations [1]-[4]. The deficiencies of vitamins B_{12} and B_9 were also considered following some bariatric surgery techniques [5]. The profile of this couple was suggested to be examined also for fetal and maternal health in obese pregnancies [6]. However, most of these studies have been carried out on adults.

In very recent studies, vitamin B_{12} and B_9 levels have been reported to be linked with some specific cancers. Low vitamin B_{12} increases risk of gastric cancer [7]. Vitamin B_9 levels in erythrocytes are significantly lower in pancreatic cancer cases [8]. Levels of both vitamins were also investigated in childhood cancers [9].

Data on protective effects of vitamin B_9 obtained from both experimental and clinical studies are inconsistent [10]. There are also some ambiguities concerning the data on vitamin B_{12}.

The aim of this study is to investigate the behavior of these micronutrients within the scope of childhood obesity and MetS.

M. M. D., Prof. Dr., is with the Namik Kemal University, Faculty of Medicine, Department of Pediatrics, Tekirdag, Turkey (corresponding author to provide phone: 00-90-532-371-72-07; fax: 00-90-282—250-99-28; e-mail: mdonma@ gmail.com).

O. D., Prof. Dr., is with the Istanbul University, Cerrahpasa Medical Faculty, Department of Medical Biochemistry, Istanbul, Turkey (e-mail: odonma@gmail.com).

II. Patients and Methods

A. Patients

128 children, who consulted to Pediatrics Outpatient Clinics of Namik Kemal University, Faculty of Medicine, were involved in the study. 92 MO children had the mean age±SEM of 118.3±3.8 months. The corresponding value for 36 children with MetS was 129.5±6.4 months ($p>0.05$). The ethical committee approved the study protocol. The families gave written permission to allow their children to be engaged in the research activity. Demographical characteristics were collected. Anthropometric measurements were taken.

B. Obesity Classification

Children in MO group had the age and sex percentile values of BMI greater than 99 as recommended by WHO.

C. MetS Criteria

For the evaluation of MetS components, WC of the children were measured, FBG, TRG, HDL-Chol analyses as well as SP, DP measurements were performed.

D. Laboratory Analyses

Serum vitamin B_{12} and vitamin B_9 concentrations were determined by immunoassay techniques. Values below 148 pmol/L were defined as low and 148-221 pmol/L as borderline. Concentrations above 221 pmol/L were accepted as normal. Vitamin B_9 levels lower than 4 mcg/L were considered as the deficiency state.

E. Statistical Evaluations

Statistical evaluations were performed by SPSS Version 16.0. p values greater than 0.05 were accepted as statistically significant.

III. Results

In MetS group BMI, WC, hip C and neck C were higher than those of children with MO. Head C values did not differ between the groups.

MetS components were significantly increased in children with MetS (SP, DP $p<0.001$; WC, FBG, TRG $p<0.01$; HDL-Chol $p<0.05$). On the other hand, vitamin B_9 and vitamin B_{12} levels were lower ($p<0.05$) in children with MetS than the other group (Figs. 1 (a) and (b)).

In both groups percentage of vitamin B_9 deficiency was 5.5%. In terms of vitamin B_{12} levels of the study population, there were no cases below 148 pmol/L. However, in MO group 14.3% and in MetS group 22.2% of the cases were in borderline status (Fig. 2).

Negative correlations between B_{12} levels and BMI, WC, hip C, head C were observed in MO group. Negative correlations were also detected between HDL-Chol and WC, hip C, head C, neck C. There was not such a correlation in children with MetS.

It was also interesting to note that strong positive correlation detected between FBG and insulin as well as strong negative correlation observed between TRG and HDL-Chol in MO children were lost in MetS group.

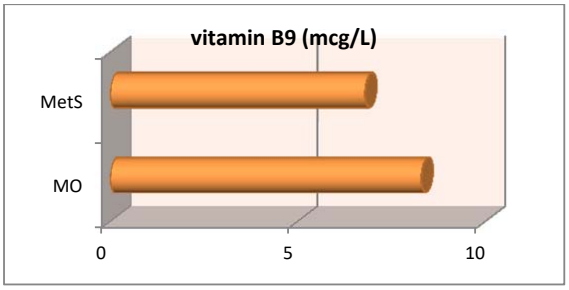

Fig. 1 (a) Vitamin B_9 status of the groups

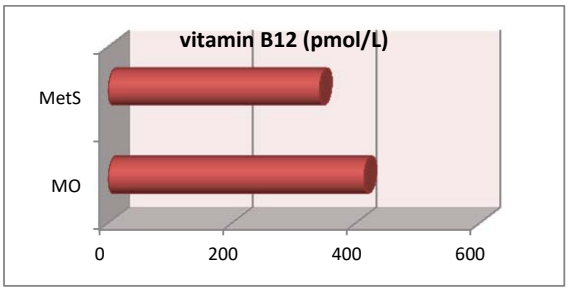

Fig. 1 (b) Vitamin B_{12} status of the groups

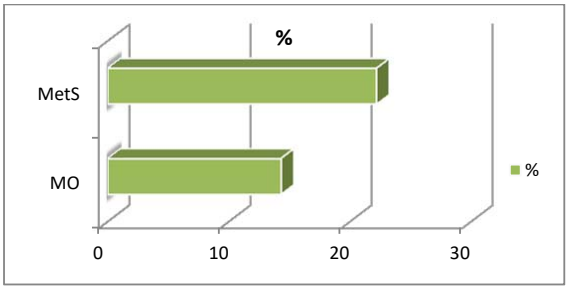

Fig. 2 Percentages of borderline cases based upon vitamin B_{12} levels of the groups

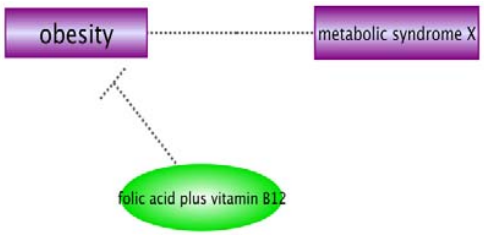

Fig. 3 The possible functional association among vitamin B_{12}, vitamin B_9, obesity, and MetS

IV. Discussion

An interesting functional association may exit among vitamin B_{12}, B_9, and obesity, which in turn gives rise to the development of MetS. Experimental studies have pointed out that supplementation with methyl donors such as vitamin B_9 and vitamin B_{12} prevent transgenerational amplification of obesity suggesting that DNA methylation mechanisms are involved in this process [11] (Fig. 3).

The MetS, a significant consequence of obesity, is

characterized by extended WC, low HDL-C, high TRG, impaired FBG and elevated blood pressure. There are complex relations among these parameters. Within this context, the possible involvement of vitamin B_{12} as well as vitamin B_9 still keeps its enigma (Fig. 4).

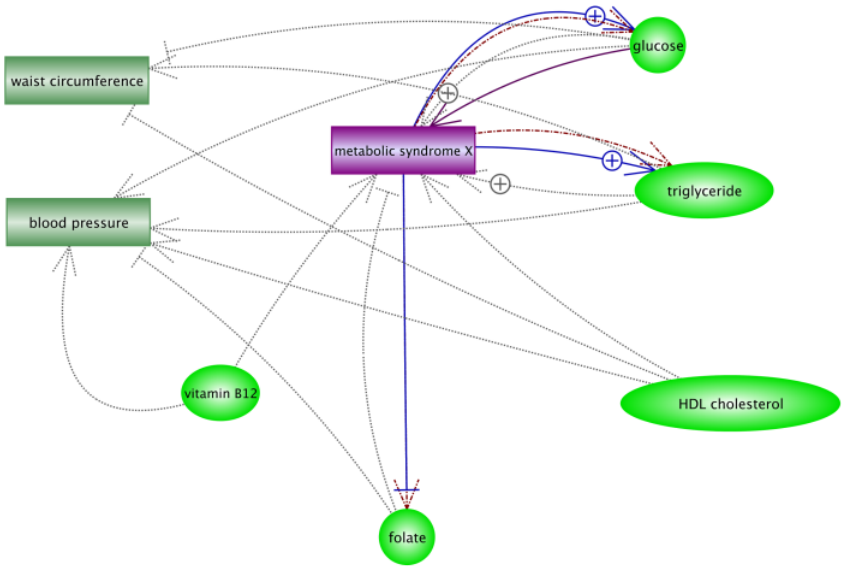

Fig. 4 Network among vitamin B_{12}, vitamin B_9 and MetS parameters

There are many studies on vitamin B_{12} as well as B_9 performed on adults with MetS [12]-[14]. However, to the best of authors' knowledge, not much attention has been paid to the roles of vitamin B_{12} and B_9 within the network of obesity-MetS parameters particularly in children.

Lower vitamin B_9 levels were reported in subjects with MetS than those without MetS [12]. Indian patients with MetS exhibit strong associations with reduced levels of vitamin B_{12} and B_9 [13]. Serum concentrations of both vitamins were found to be inversely associated with MetS in Turkish women [14].

In a study performed on children, an increase in BMI was reported to be associated with a decrease in vitamin B_{12} levels [15]. In another study, about a third of obese adolescents had a low or borderline serum vitamin B_{12} status. In the same study, vitamin B_9 levels did not differ among the groups with low, borderline and normal vitamin B_{12} [16].

In our study, both vitamin B_9 and vitamin B_{12} levels were decreased in children with MetS in comparison with MO children. However, vitamin B_9 deficiency percent detected for both groups were the same. Although, none with vitamin B_{12} deficiency was detected in the study population, percentage of children with borderline vitamin B_{12} status was greater in children with MetS than those in the other group.

Low vitamin B_9 intake is suggested as one of the predictors of MetS. It should be paid attention particularly during the primary care of patients [17]. In another report, this vitamin was introduced as a new biomarker of MetS, particularly suitable for screening purposes in general population [18].

Among all, people mostly wondered how blood pressure would be in relation to this complicated network. Considering the fact that vitamin B_{12} and vitamin B_9 work in a collaborative manner as coenzymes in the regeneration of methionine from homocystein, this couple may have synergistic effects on blood pressure or endothelial function [19], [20]. Increases in blood pressure have been shown to be reduced by vitamin B_9 and vitamin B_{12} administration [21].

The metabolisms of vitamin B_9 and vitamin B_{12} are impaired during their deficiency. The end products synthesized may affect and interact with MetS components. This study points out vitamin B_{12} fluctuations possibly caused by the variations in MetS components. The associations between vitamin B_{12} and anthropometric measurements are also altered. As a result of the increases in severity as well as percent of both vitamin B_9 and vitamin B_{12} deficiency in MetS, the concentrations of deficiency metabolites will also increase. This may affect the status of MetS parameters.

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