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The Association of Vitamin B_{12} with Body Weight- and Fat-Based Indices in Childhood Obesity

Mustafa M. Donma, Orkide Donma

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***Abstract*—**Vitamin deficiencies are common in obese individuals. Particularly, the status of vitamin B_{12} and its association with vitamin B_9 (folate) and vitamin D is under investigation in recent time. Vitamin B_{12} is closely related to many vital processes in the body. In clinical studies, its involvement in fat metabolism draws attention from the obesity point of view. Obesity, in its advanced stages and in combination with metabolic syndrome (MetS) findings, may be a life-threatening health problem. Pediatric obesity is particularly important, because it may be a predictor of the severe chronic diseases during adulthood period of the child. Due to its role in fat metabolism, vitamin B_{12} deficiency may disrupt metabolic pathways of the lipid and energy metabolisms in the body. The association of low B_{12} levels with obesity degree may be an interesting topic to be investigated. Obesity indices may be helpful at this point. Weight- and fat-based indices are available. Of them, body mass index (BMI) is in the first group. Fat mass index (FMI), fat-free mass index (FFMI) and diagnostic obesity notation model assessment-II (D2I) index lie in the latter group. The aim of this study is to clarify possible associations between vitamin B_{12} status and obesity indices in pediatric population. The study comprises a total of 122 children. 32 children were included in the normal-body mass index (N-BMI) group. 46 and 44 children constitute groups with morbid obese children without MetS and with MetS, respectively. Informed consent forms and the approval of the institutional ethics committee were obtained. Tables prepared for obesity classification by World Health Organization were used. MetS criteria were defined. Anthropometric and blood pressure measurements were taken. BMI, FMI, FFMI, D2I were calculated. Routine laboratory tests were performed. Vitamin B_9, B_{12}, D concentrations were determined. Statistical evaluation of the study data was performed. Vitamin B_9 and vitamin D levels were reduced in MetS group compared to children with N-BMI ($p > 0.05$). Significantly lower values were observed in vitamin B_{12} concentrations of MetS group ($p < 0.01$). Upon evaluation of blood pressure as well as triglyceride levels, there exist significant increases in morbid obese children. Significantly decreased concentrations of high-density lipoprotein cholesterol were observed. All of the obesity indices and insulin resistance index exhibit increasing tendency with the severity of obesity. Inverse correlations were calculated between vitamin D and insulin resistance index as well as vitamin B_{12} and D2I in morbid obese groups. In conclusion, a fat-based index, D2I, was the most prominent body index, which shows strong correlation with vitamin B_{12} concentrations in the late stage of obesity in children. A negative correlation between these two parameters was a confirmative finding related to the association between vitamin B_{12} and obesity degree.

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

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

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I. Introduction

VITAMIN B_{12} is a water-soluble vitamin, which participates in hematopoietic system and fat metabolism. It is also related to transsulfuration reactions as well as metabolism of nucleic acids. It is unique among the members of water-soluble vitamins family, because it is stored in the body. Due to its involvement in the metabolism of fatty acids, deficiency state of this vitamin is closely associated with memory problems. In recent years, it has also been suggested that vitamin B_{12} deficiency disrupts body's fat metabolism in many ways. Vitamin B_{12} deficiency leads to fatty acid metabolism dysregulation in adipose tissue [1]-[3].

The adipose tissue is considered as both a metabolic and an endocrine tissue. The evaluation of vitamin status is important in obesity associated with excessive fat deposition, because in obese individuals the composition of the diet may be ignored. Most vitamins are deficient in obese individuals. This is confirmed by many studies for vitamin B_{12} as well as vitamin B_9 (folate) and vitamin D performed on both adults and children. Of them, vitamin B_{12} has been less evaluated in cases of obesity [4]-[6].

Recent reports have focused on the status of vitamin B_{12} during pregnancy [1], [2], [7], [8]. Gaining weight is a great problem during pregnancy, because it is quite difficult losing weight afterwards. According to a new study [3], lack of vitamin B_{12}, which is a nutrient that helps the body metabolize fat, may be a possible explanation for this and taking vitamin B_{12} supplements in addition to vitamin B_9 during pregnancy may be a good solution to this problem, which may lead to clinical problems such as diabetes. Deficiency of vitamin B_{12} may also affect fetal development [1], [2].

It was suggested that vitamin B_{12} deficiency leads to adipocyte dysfunction, fatty acid metabolism dysregulation, increased pro-inflammatory cytokine production, all of which play role in the pathogenesis of obesity [3].

In obesity studies, both weight- and fat-based indices are being used. BMI, which is a frequently used one, is based upon the total weight of the body. However, some studies reported an association between BMI values and vitamin B_{12} status, whereas some others found no significant association between these two parameters [9]-[15].

In a current study performed on B-vitamins and body composition in the elderly, vitamin-B_{12} status was associated with a higher FMI, however, it could not be observed any effect of random allocation with B_{12} and B_9 vitamins on BMI or body composition [15].

The purpose of the present study was to investigate possible associations between vitamin B_{12} status and weight (BMI) as well as fat-based indices (FMI, FFMI, D2I) in pediatric obesity.

II. Patients and Methods

A. Patients

The study was performed on children with N-BMI (n = 32) and morbid obesity (n = 90). Three groups were constituted. N-BMI, morbid obese (MO) without MetS (n = 46) and MO with MetS (n = 44) groups were called as Group 1, Group 2 and Group 3, respectively. Parents of the children, who want to participate in the study have given written informed consent forms. The study protocol was approved by the non-interventional Ethics Committee of Tekirdag Namik Kemal University Medical Faculty.

B. Anthropometric and Blood Pressure Measurements

A portable digital scale and portable stadiometer were used to measure body weight and height, respectively. Circumferences of waist, hip, head and neck were taken using a flexible, non-elastic tape and recorded.

Blood pressure (BP) values of the children were determined by manual BP auscultation method, with an upper arm BP device (sphygmomanometer; ERKA BP monitoring) using adequate cuff and pediatric stethoscope. The child should be seated in a chair prior to and during the measurement, with feet on the floor and arm supported so child's elbow is at about heart level. Talking should be prevented. The cuff should completely cover about 80% of the upper arm. It should be placed on bare skin and on the arm with the arrow on the cuff over the brachial artery. During deflation of the cuff, systolic blood pressure (SBP) and diastolic blood pressure (DBP) were recorded at the Phase 1 and Phase 5 Korotkoff sounds, respectively [16], [17].

C. Classification of Obese Children

Age- and sex-adjusted BMI percentile tables prepared by World Health Organization were used for obesity classification [18]. Children, whose percentile values were above 99 were defined as MO. Percentile values of the children with N-BMI were between 85 and 15. MO children were divided into two groups; those without and with MetS.

D. Criteria for MetS

Aside from central obesity, certain biochemical parameters were used for the diagnosis of MetS [19]. For this purpose, fasting blood glucose (FBG), SBP as well as DBP, triglyceride (TRG) and high-density lipoprotein cholesterol (HDL-C) values were evaluated. FBG values higher than 100 mg/dL, SBP and DBP values higher than 130 mm Hg and 85 mm Hg, respectively, TRG values above 150 mg/dL, HDL-C values below 40 mg/dL were MetS components, which should be taken into consideration. Aside from obesity criteria, at least two of the above must be met to be able to make MetS diagnosis.

E. Biochemical Laboratory Tests

Routine biochemical parameters including FBG, insulin, TRG and HDL-C were measured. Vitamin D, vitamin B_9 and vitamin B_{12} levels were determined. Serum 25(OH)D concentrations were measured by high performance liquid chromatography. Optimal 25(OH)D levels above 30 ng/ml were accepted as sufficient. Immunoassay techniques were used to determine serum vitamin B_{12} and vitamin B_9 levels. Vitamin B_{12} concentrations higher than 221 pmol/L were accepted as normal. Vitamin B_9 levels below 4 mcg/L were considered deficient.

F. Index Calculations

BMI values were calculated from body weight and height (kg/m^2). For computing FMI [total body fat (kg) / height (m) * height (m)] and FFMI values, instead of body weight, total body fat mass and fat free mass were used (kg/m^2). The equation for D2I was D2I = [total body fat mass (kg) * 100/height (cm)]. Homeostatic model assessment for insulin resistance index "HOMA-IR" index values were calculated using: HOMA-IR = [(fasting glucose (mg/dL) * fasting insulin (µIU/ml/ 22.5*0.0555)]

G. Statistical Evaluation

Statistical package for social sciences, Version 16 was used for the evaluation of the data. Mean or median values of parameters studied and indices calculated were tabulated. Correlation analyses were performed. Plot for bivariate correlation with linear regression line was drawn for vitamin B_{12} and D2I values. The statistical significance level was $p < 0.05$.

III. Results

Children with N-BMI as well as morbid obesity with and without MetS were evaluated for their vitamin profiles, BP values, lipid components and IR, weight- and fat-based indices.

Table I showed the concentrations of serum vitamin B_{12}, B_9 and D for three groups involved in the study.

TABLE I
Vitamin Concentrations of the Groups

Groups	N-BMI (x ± SD)	MO (x ± SD)	MetS (x ± SD)
Vitamin B_{12} (pmol/L)	475 ± 217	385 ± 134	349 ± 125$^{1\text{-}3\ 0.01}$
Vitamin B_9 (mcg/L)	8.1 ± 2.7	8.5 ± 3.4	7.8 ± 2.7^{NS}
Vitamin D (ng/mL)	23.8 ± 20.6	20.2 ± 10.8	18.2 ± 10.0^{NS}

N-BMI = Group 1, MO = Group 2, MetS = Group 3, NS = not significant.

Depressed vitamin B_{12} concentrations were observed in both MO groups without and with MetS in comparison with those in N-BMI group. The difference between N-BMI and MetS groups were statistically significant ($p < 0.01$). Reductions observed for vitamin B_9 and vitamin D in MO groups were statistically insignificant ($p > 0.05$).

Systolic/diastolic blood pressure values and TRG as well as HDL-C concentrations were given in Table II.

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TABLE II
BP, TRG AND HDL-C VALUES OF THE GROUPS

Groups	N-BMI (x ± SD)	MO (x ± SD)	MetS (x ± SD)
SBP (mm Hg)	97.4 ± 12.0	113.3 ± 12.6	$126.2 \pm 14.1^{1\text{-}2,\ 1\text{-}3,\ 2\text{-}3\ 0.001}$
DBP (mm Hg)	60.8 ± 8.5	76.9 ± 11.1	$83.5 \pm 14.0^{1\text{-}2,\ 1\text{-}3\ 0.001;\ 2\text{-}3\ 0.05}$
TRG (mg/dL)	92.4 ± 51.7	103.3 ± 41.1	$174.5 \pm 95.0^{1\text{-}3,\ 2\text{-}3\ 0.001}$
HDL-C (mg/dL)	56.0 ± 12.0	49.5 ± 12.3	$43.4 \pm 7.7^{1\text{-}3\ 0.001;\ 1\text{-}2,\ 2\text{-}3\ 0.05}$

N-BMI = Group 1, MO = Group 2, MetS = Group 3.

Statistically significant increases were detected in MO and MetS groups when BP values and TRG concentrations were considered. On the other hand, significant reductions were found for HDL-C values in MO and MetS groups compared to N-BMI group. Besides, values were much lower in MetS group than MO group ($p < 0.05$).

In Table III, five indices calculated for three groups were shown.

TABLE III
INSULIN RESISTANCE, WEIGHT- AND FAT-BASED BODY INDICES OF THE GROUPS

Groups	N-BMI (x ± SD)	MO (x ± SD)	MetS (x ± SD)
HOMA-IR ^{m}	1.7	4.0	$7.2^{1\text{-}3\ 0.001}$
BMI (kg/m^2)	16.6 ± 2.2	28.6 ± 5.6	$31.0 \pm 5.6^{1\text{-}2,\ 1\text{-}3\ 0.001}$
FMI (kg/m^2)	3.1 ± 1.3	10.4 ± 3.8	$11.3 \pm 3.9^{1\text{-}3,\ 2\text{-}3\ 0.001}$
FFMI (kg/m^2)	12.9 ± 1.6	17.9 ± 2.8	$19.1 \pm 3.0^{1\text{-}2,\ 1\text{-}3\ 0.001}$
D2I (kg/m)	4.2 ± 2.5	15.4 ± 6.8	$17.6 \pm 7.0^{1\text{-}2,\ 1\text{-}3\ 0.001}$

N-BMI = Group 1, MO = Group 2, MetS = Group 3, ^{m} median.

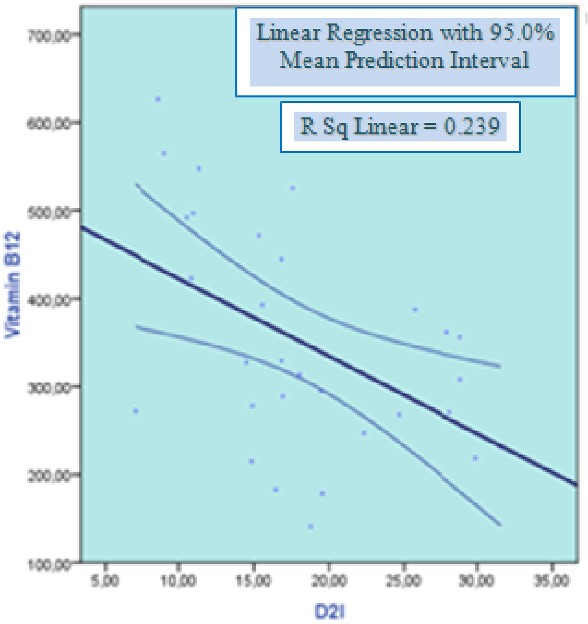

Fig. 1 Bivariate correlation with linear regression line between vitamin B_{12} concentrations and diagnostic obesity notation model assessment index-II values in MO children with MetS

First index, HOMA-IR is an IR index. Great increases were calculated both in MO and MetS groups. Second index was the well-known BMI. In this study, it was the representative of weight-based indices of the body. Within the scope of fat-based indices, three individual formulas, FMI, FFMI and D2I were available. Great increases for all indices were calculated both in MO and MetS groups.

In the second part of the study, the findings deduced from correlation analysis were examined. Negative correlations were obtained between vitamin D and HOMA-IR in MO ($r = -0.312$; $p = 0.039$) and MetS ($r = -0.309$; $p = 0.049$) groups. Such an association was not present in N-BMI group.

Within the scope of indices, interesting correlations were found for vitamin B_{12}. In N-BMI group, vitamin B_{12} was correlated with none of the indices. No statistically significant correlation was found between vitamin B_{12} and BMI, FMI, FFMI or D2I. In MO group, neither BMI nor FMI was correlated with this vitamin. However, a significant correlation was found with D2I ($r = -0.379$; $p = 0.039$). Vitamin B_{12} was correlated with all indices [with BMI ($r = -0.350$; $p = 0.020$), with FMI ($r = -0.423$; $p = 0.020$), with D2I ($r = -0.489$; $p = 0.006$)] in MetS group (Fig. 1).

Upon examination of these correlations, the strongest correlation was between vitamin B_{12} and D2I in MetS group.

IV. DISCUSSION

The association between vitamin B_{12} and obesity has been investigated in many studies. However, the independent role of vitamin B_{12} on lipid metabolism has not been widely studied [20].

Associations between increased BMI and reduced vitamin B_{12} were observed in the early stage of pregnancy [21], [22]. Children born to mothers with low B_{12} levels appear to develop higher adiposity and IR [23]. In a similar manner, vitamin B_{12} concentrations were significantly lower in obese children and were negatively associated with the severity of obesity [24]. In another clinical report, lower concentrations of vitamin B_{12} in obese were observed than those in overweight and normal weight individuals [25].

Vitamin B_{12} deficiency, which is a serious disorder, is more common in the elderly. In general, during the treatment with vitamin B_{12}, younger patients have better outcomes compared to older individuals [26].

Obese children and adolescents constitute a risk group for low vitamin B_{12} concentration. Therefore, it is recommended that vitamin B_{12} deficiency should be considered in obese children [27].

Under the light of above studies, it is clear that there is an immediate need for exploring the possible associations between vitamin B_{12} and weight- and fat-based obesity indices as the indicators of the severity of obesity status in pediatric population.

In this study, it was demonstrated that fat-based indices are much closely associated with vitamin B_{12} concentrations. In N-BMI children, vitamin B_{12} was correlated with neither BMI (a weight-based index) nor fat based indices (FMI; FFMI; D2I). In MO children, the association was observed only with D2I. In MetS group, all indices were correlated with vitamin B_{12}, being the strongest correlation was detected with D2I, which is a fat-based index. These findings have confirmed that a negative correlation found between vitamin B_{12} and D2I is the best indicator of the association between vitamin B_{12}

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deficiency and advanced obesity in MO children with and without MetS.

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