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Relationship of Vitamin B12 Deficiency with Overweight in Male Jordanian Youth

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Abstract: The purpose of this research was to investigate the association between weights status, as measured by Body Mass Index (BMI) and vitamin B12 levels among male Jordanian youth. Recent studies have shown correlation between Body Mass Index (BMI) and serum vitamin B12 levels in some Middle East countries; however, no data are available for Jordan, where the prevalence of vitamin B12 deficiency has increased at an alarming rate. One hundred and twenty male university students (aged 18 to 24 years) from Amman city, Capital of Jordan, were divided into three groups according to the body mass index namely healthy weight, overweight and obese. Fasting samples were collected for hematological parameters, serum leptin, vitamin B12, folic acid and blood glucose. The mean serum vitamin B12 level was decreased in overweight students (283.2±84.17) pg mL^{-1} comparing with the mean of all groups (353.73±125) pg mL^{-1}. Of all students 16% had B12 deficiency (<200 pg mL^{-1}) and 65% of them were overweight. Serum folate levels were normal in all groups. BMI was positively correlated with serum leptin levels in all groups. Significant elevation was observed of white blood cells count in obese group ($p<0.001$). Present findings suggest that overweight youth are a risk group for vitamin B12 deficiency.

Key words: Vitamin B12, body mass index, BMI, leptin, folic acid, obesity, overweight

INTRODUCTION

Vitamin B12 deficiency remains one of the most common nutritional deficiency in the world and it is frequent among elderly patients (Gupta and Powers, 2008). Most studies of vitamin B12 deficiency in elderly patients correlated this problem with nutritional or hematological factors (Hao *et al*., 2007; Khanduri and Sharma, 2007). Although vitamin B12 deficiency is not common in youth, the prevalence of vitamin B12 deficiency in Jordanian youth has increased at an alarming rate. Several earlier reports has linked behavioral and learning problems among children, adolescents and young adults to Vitamin B12 deficiency (Holst-Schumacher *et al*., 2007; Thauvin-Robinet and Roze, 2007; Strassburg *et al*., 2004). Many researchers reported that, nutritional and hematological observations cannot explain prevalence of vitamin B12 deficiency in young people. Quinlivan (2008) noted that, in vitamin B12 deficiency, high serum folate is associated with increased homocysteine and methylmalonic acid concentrations, beside that, (Johnson, 2007) pointed to a potential adverse interactions between vitamin B12 and folic acid. Elevated homocysteine in blood indicates decrease in vitamin B12 levels in most cases (Fakhrzadeh *et al*., 2006; Meertens *et al*., 2007). Few recent studies have shown a correlation between elevated plasma homocysteine overweight in children and adolescents (Narin *et al*., 2005; Pinhas-Hamiel *et al*., 2006), On the other hand, Thawnashom *et al*. (2005) showed that, folic acid is significantly related to the overweight and obese more than vitamin B12. Furthermore, Papandreou *et al*. (2007) noted that, no difference in homocysteine levels between normal and overweight or obese children. Nonetheless, the data are confusing and the exact role of the obesity gene hormone, leptin (Zhang, 1994) which activates hypothalamic centers that regulate energy intake and expenditure (Pelleymounter, 1995) is still unclear, even though leptin regulates food consumption (Pelleymounter, 1995; Tritos and Mantzoros, 1997), modulates blood formation and immune responses (Hung *et al*., 2005) and its high levels accompanied by overweight (Eikelis and Esler, 2005). Therefore, the aim of the present research is to investigate whether vitamin B12 deficiency is correlated with weight status in Jordanian male university youth.

MATERIALS AND METHODS

This research was carried out at the laboratories of Department of Medical Technology, Applied Science University in January 2008. This cross-sectional study included one-hundred twenty healthy young males with a mean age 21.3±1.25 years (range 18-24) volunteered to participate in the study. Subjects were screened

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by medical history questionnaire, physical examination and fasting blood profile. On the day of the evaluation, height (cm) and weight (kg) were recorded and Body Mass Index (BMI) was calculated and plotted on age-specific percentiles. In accordance with the international classification of weight status, the subjects were categorized as, underweight UW, normal healthy weight HW, overweight OW, or obese OB based on BMIs. In the underweight category were one student, therefore volunteers were grouped into three groups: HW (BMI = 18.5-24.9), OW (BMI = 25-29) and Ob (BMI of 30 or greater).

Fasting blood glucose samples were collected at 8 am Blood glucose was confirmed by using One Touch test strips (Lifescan; Johnson and Johnson, Palmitas, CA).

Clinical hematology parameters measured for all volunteers, were platelet count, total leukocyte count, differential leukocyte counts, hematocrit, hemoglobin and RBC indices (Mean Cell Hemoglobin [MCH], Mean Cell Volume [MCV], mean cell hemoglobin concentration [MCHC]), mean platelets count. Complete blood count was performed on the (COBAS MICROS OT 18, Roche, France).

Serum analysis: The serum was isolated by centrifugation. The electrochemiluminescence immunoassay was used on Cobas e immunoassay analyzer (Roche Diagnostics) for serum vitamin B12 and folic acid using electrochemiluminescence immunoassay (ECLIA) kits (Roche Diagnostics). Quantitative measurement of leptin in serum was performed by enzyme immunoassay or ELISA kit (DRG Diagnostics, Marburg, Germany), according to the manufacturer's instructions.

Statistical analysis: Data were expressed as means±SE and were analyzed with a two-way ANOVA followed by LSD multiple comparison test, using Statistica Software (OK, USA). Differences were considered significant at $p<0.05$.

RESULTS AND DISCUSSION

There were no differences between the means of ages in the three groups (Table 1). In each group and in all subjects, overweight individuals generally demonstrated higher circulating leptin concentrations than healthy-weight volunteers. Mean serum leptin concentrations were more than twice as high in obese than in overweight and four times than in healthy weight of corresponding BMI categories ($p<0.0001$). Figure 2 shows the correlation between BMIs and serum leptin levels in the three groups. Of a total of 120 sera

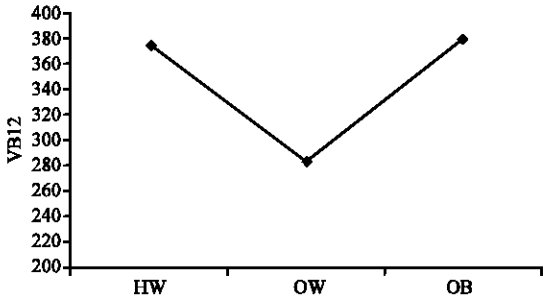

Fig. 1: Correlation between Body Mass Index (BMI) and serum vitamin B12 levels (pg mL^{-1}) belonging to the healthy-weight (HW), overweight (OW) and obese (OB) weight categories

Fig. 2: Relationship between Body Mass Indices (BMIs) and leptin levels (ng mL^{-1}). HW: Healthy weight; OW: Overweight and OB: Obese ($p<0.001$)

Table 1: Distribution of BMIs by age and weight status and statistical results of multiple comparisons and correlations

Age/Weight status	Healthy weight	Overweight	Obese
BMI (n)	64.0	36.00	20.00
Age (year)	21.1±2.8	22.00±1.8	21.00±3.8
Body weight (kg)	71.6±4.8	86.53±11.2	118.46±20.2

Table 2: Clinical chemical and hematological parameters of overweight (OW) and obese (OB) groups comparing with healthy weight (HW) group

Parameter	HW	OW	OB
Haematocrit (%)	47.075±4.947	46.583±4.396	46.070±5.537
Hemoglobin (mmol L^{-1})	15.809±1.164	16.053±1.212	16.180±1.523
MCV (fl)	86.492±5.24	86.919±4.47	88.550±3.776
WBC (10^9 L^{-1})	5.396±1.574	5.865±1.894	7.130±1.796
Serum vitamin B12 (pg mL^{-1})	375.846±125.82	283.222±84.17	379.140±137.226
Serum folic acid (ng mL^{-1})	9.985±3.945	10.0866±3.299	10.848±3.211
Serum leptin (ng mL^{-1})	5.666±2.586	10.874±5.223	24.685±10.224
Blood glucose (mg dL^{-1})	86.923±8.502	86.757±8.988	86.350±5.779

tested, mean vitamin B12 level of all volunteers was (353, 73±125) pg mL^{-1}. The mean level of serum vitamin B12 was decreased (283.222±84.17) pg mL^{-1} comparing with HW group (375.846±125.82) pg mL^{-1} ($p<0.001$). (Fig. 1). 16.66% (n = 20) of all students had B12 deficiency

(<200 pg mL^{-1}), most prevalence of these cases was among overweight group (n =13). Serum folate levels were normal in all groups. However, except slightly increased MCV there was no significant difference between HW and OW or Ob groups in terms of glucose, hemoglobin and PCV (Table 2). Nevertheless, significantly higher of white blood cells count were observed in OB group comparing with HW group ($p<0.001$).

We found that low levels of serum vitamin B12 were more prevalent among Jordanian overweight male youth. These findings may explain part of the results of one study on Jordanian adults in 2005. Fora and Mohammad (2005) reported that, a high frequency of suboptimal serum vitamin B12 level among Jordanian which is an early sign of negative B12 balance. A number of different factors have been proposed to explain the vitamin B12 deficiency in young people, including inadequate diet, with limited intake of B12-rich foods (Flier, 1997) therefore low supplementation of vitamin B12 shows abnormality in blood indices (Khanduri and Sharma, 2007). For this purpose we examined hematological parameters in all volunteers. We didn't find any correlation between vitamin B12 deficiency and hematological indices results in overweight subjects with vitamin B12 deficiency. Furthermore, in contrast to Quinlivan (2008) study results, folic acid levels in our study were within normal ranges in all volunteers. Nearly, all patients with vitamin B12 deficiency also have substantially increased levels of homocysteine (Wiersinga *et al*., 2006; Meertens *et al*., 2007). Narin *et al*. (2005) has demonstrated that leptin and apo B are main correlates of homocysteine levels in obese children and adolescents. Similarly, Pinhas-Hamiel *et al*. (2006) has also reported that obese children and adolescents are a risk group for low vitamin B12 concentration. These results are in agreement with our results in that serum levels of vitamin B12 were decreased in overweight, but not obese youth. On the other hand, Papandreou *et al*. (2007) has pointed out that no difference was observed in homocysteine levels between normal and overweight and obese children. It is well known that leptin plays important role in the regulation of body weight and energy balance (Rafail *et al*., 2008). In present study significant positive correlation ($p<00.1$) was observed between serum leptin levels and BMIs of all groups. Several earlier repots have been confirmed theses findings. Little is known about vitamin B12 levels and hormonal balance in obese. Garanty-Bogacka *et al*. (2006) has shown correlation between serum homocysteine levels and simple obesity in children. However, numerous studies have reported that leptin has been shown to stimulate hematopoietic stem cells (Claycombe *et al*., 2008; Cymbaluk *et al*., 2008) and vitamin B12 is one of the factors that affect the response to erythropoiesis-stimulating agents (Jauréguy and Choukroun, 2006). This is supported by previous lines of evidence that indicate that low vitamin B12 levels inhibit the suppression of erythropoietin response in nonanemic pregnant women probably through MCHC modifications (Carretti *et al*., 1998). Similarly, Hung *et al*. (2005) has also reported that increasing energy intake improves erythropoiesis, which may be mediated in part by an increase in serum leptin levels. These studies showed agreement with part of our findings that, serum leptin levels were positively correlated with white blood cells count, mean corpuscular volume and hemoglobin in obese and overweight youth comparing with control group. However, some related studies have reported that hyperhomocysteinemia correlates with insulin resistance in obese prepubertal children (Atamer *et al*., 2008; Martos *et al*., 2006). Accordingly, our assumption is that leptin may modulate vitamin B12 levels during hematopoiesis in overweight and obese hyperinsulinemic youth. Further studies are recommended to be made as to provide further support to this assumption

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