DE GRUYTER OPEN

ORIGINAL ARTICLES

Iron deficiency anemia and megaloblastic anemia in obese patients

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Background. The association between obesity and different types of anemia remained uncertain. The present study aimed to assess the relation between obesity parameters and the occurrence of iron deficiency anemia and also megaloblastic anemia among Iranian population.

Methods and Materials. This cross-sectional study was performed on 1252 patients with morbid obesity that randomly selected from all patients referred to Clinic of obesity at Rasoul-e-Akram Hospital in 2014. The morbid obesity was defined according to the guideline as body mass index (BMI) equal to or higher than 40 kg/m^2. Various laboratory parameters including serum levels of hemoglobin, iron, ferritin, folic acid, and vitamin B12 were assessed using the standard laboratory techniques.

Results. BMI was adversely associated with serum vitamin B12, but not associated with other hematologic parameters. The overall prevalence of iron deficiency anemia was 9.8%. The prevalence of iron deficiency anemia was independent to patients' age and also to body mass index. The prevalence of vitamin B12 deficiency was totally 20.9%. According to the multivariable logistic regression model, no association was revealed between BMI and the occurrence of iron deficiency anemia adjusting gender and age. A similar regression model showed that higher BMI could predict occurrence of vitamin B12 deficiency in morbid obese patients.

Conclusion. Although iron deficiency is a common finding among obese patients, vitamin B12 deficiency is more frequent so about one-fifth of these patients suffer vitamin B12 deficiency. In fact, the exacerbation of obesity can result in exacerbation of vitamin B12 deficiency.

Keywords: Anemia, Obesity, Vitamin B12.

INTRODUCTION

Both anemia and morbid obesity are epidemic issues whole of the world along with high economic burden on governments [1]. Although the simultaneous occurrence of these diseases is still doubtful, the molecular association between these two phenomena has been clearly determined [2]. Despite increasing trend of obesity in industrialized countries because of inappropriate nutritional habits, this trend has also been shown to be upward among developing nations mainly due to improper lifestyle as well as tending to inappropriate dietary regimens [3]. The most important consequences of obesity include increased risk for cardiovascular disorders, diabetes mellitus, and also the risk of cancers [4, 5]. Nowadays, an association between obesity and change in iron hemostasis has been also approved. In other words, obesity may lead to iron deficiency anemia through impairment of its gastrointestinal uptake from duodenum [6]. In fact, in the background of dimorphic Iron overload syndrome (DIOS), severe disturbance of iron metabolism can be observed along with fatty liver disease or metabolic syndrome that are own associated with obesity [7]. In this regard, obesity can be associated with iron deficiency anemia due to increased plasma volume, the consumption of high energetic agents, as well as chronic inflammatory reactions in response to excess adiposity [8]. In obese individuals, the serum ferritin level can be increased due to iron metabolic disturbances [9]. Besides, some evidences available in gastrointestinal impairment of vitamin B12 absorption in obese patients may deteriorate anemic condition in these patients, however the association between obesity and different types of anemia remained uncertain [10]. The present study aimed to assess the relation between obesity parameters and the occurrence of iron deficiency anemia and also megaloblastic anemia among Iranian population.

MATERIALS AND METHODS

This cross-sectional study was performed on 1252 patients with morbid obesity that were

DOI: 10.1515/rjim-2016-0046

randomly selected from all patients referred to clinic of obesity at Rasoul-e-Akram hospital in 2014. The morbid obesity was defined according to the guideline from the Consensus Statement from Asia-Pacific Bariatric Surgeons Group as body mass index (BMI) equal to or higher than 40 kg/m^2. In this regard, BMI was calculated by the Quetelet index as the ratio of the subject's body weight (in kg) to the square of the height (in meters). Baseline characteristics and clinical data of study subjects were collected by reviewing the hospital recorded files and recorded at the study checklist. In this study, various laboratory parameters including serum levels of hemoglobin, iron, ferritin, folic acid, and vitamin B12 were assessed using the standard laboratory techniques. In this regard, serum hemoglobin level (g/dL) was measured using the cyanmethemoglobin method with considering the range of 12 to16 g/dL for women and of 14 to17 g/dL for men, as the normal reference. Serum iron concentration (µg/dL) was assessed using the spectrophotometric method (Zist chemistry) with the normal range of 50 to 150 µg/dL. Serum ferritin level (ng/mL) was also measured using the human ferritin enzyme immunoassay test with the normal value of 50 to 200 ng/mL. Also, serum vitamin B12 concentration (pg/mL) was measured using the solid-phase, competitive chemiluminescent enzyme immunoassay method with the reference normal value of 200 to 1000 pg/mL. In this study, the diagnosis of iron deficiency anemia was defined as Hb<12 g/dL for women and <13 g/dL for men; the transferrin saturation index (TSI) <20%; and serum ferritin <30 ng/mL. The TSI was calculated using the formula: (iron/total iron binding capacity) × 10. Also, megaloblastic anemia was defined as MCV> 100 fl and retic<1%.

Results were presented as mean ± standard deviation (SD) for quantitative variables and were summarized by absolute frequencies and percentages for categorical variables. Normality of data was analyzed using the Kolmogorov-Smirnoff test. Categorical variables were compared using chi-square test or Fisher's exact test when more than 20% of cells with expected count of less than 5 were observed. Quantitative variables were also compared with t test or Mann-Whitney U test. The association between study variables was assessed using the Pearson's correlation test or Spearman's test. Also, multivariate logistic regression model was used to assess the relation between BMI and iron deficiency anemia. For the statistical analysis, the statistical software SPSS version 16.0 for windows (SPSS Inc., Chicago, IL) was used. P values of 0.05 or less were considered statistically significant.

RESULTS

The mean age of patients was 39.77 ± 10.74 ranged from 10 to 70 years. The mean age was significantly lower in men than in women (35.81 ± 10.24 years *versus* 40.74 ± 10.64 years, p < 0.001). In total, 19.7% were male and 80.3% were female. The mean BMI was 49.99 ± 5.87 kg/m^2, more in men than in women (48.52 ± 6.98 kg/m^2 *versus* 46.62 ± 5.51 kg/m^2, p < 0.001). As shown in Table 1, among all baseline laboratory indices, the mean levels of serum hemoglobin, ferritin, and iron were all lower in women compared with men, but no difference was found in other parameters including vitamin B12, folic acid, MCV, and TIBC between the two genders. Regarding association between age and laboratory indices, a direct association was found between age and vitamin B12 (r = 0.141, p = 0.003) and folic acid (r = 0.168, p = 0.003) as well as an adverse association between age and serum hemoglobin (r = -0.087, p = 0.002). BMI was adversely associated with serum vitamin B12 (r = -0.062, p = 0.029) (Figure 1), but not associated with other hematologic parameters. The overall prevalence of iron deficiency anemia was 9.8% (8.9% in men and 10.0% in women, p = 0.589). The prevalence of iron deficiency anemia was independent of patients' age and also of body mass index (the mean BMI in those with and without iron deficiency anemia was 46.57 ± 5.36 kg/m^2 and 47.04 ± 5.93 kg/m^2, p = 0.358) (Figure 1).

The prevalence of vitamin B12 deficiency was 20.9% (20.6% in men and 21.0% in women, p = 0.904). The patients' age did not depend on the prevalence of vitamin B12 deficiency; however, the mean BMI was significantly higher in the patients with vitamin B12 deficiency than in those without this diagnosis (47.86 ± 6.55 kg/m^2 *versus* 46.77 ± 5.66 kg/m^2, 0.008). Based on the definition, only one patient had MCV higher than 100 fL thus had a normal serum vitamin B12 level.

According to the multivariable logistic regression model (Table 2), no association was revealed between BMI and the occurrence of iron deficiency anemia adjusting gender and age (OR = 1.014, p = 0.419). A similar regression model (Table 3) showed that a higher BMI could predict occurrence of vitamin B12 deficiency in morbid obese patients (OR = 1.031, p = 0.007).

Table 1
Laboratory parameters in men and women with morbid obesity

Index	Men	Women	P-value
Serum hemoglobin	15.40 ± 1.40	13.20 ± 1.33	< 0.001
Serum ferritin	144.39 ± 111.68	59.48 ± 60.00	< 0.001
Serum vitamin B12	322.13 ± 211.09	327.19 ± 180.26	0.729
Serum TIBC	340.88 ± 53.22	347.12 ± 65.25	0.504
Folic acid	9.77 ± 3.85	10.11 ± 4.37	0.549
Serum MCV	83.13 ± 12.26	83.25 ± 6.93	0.938
Serum iron	95.66 ± 35.44	72.29 ± 37.08	< 0.001

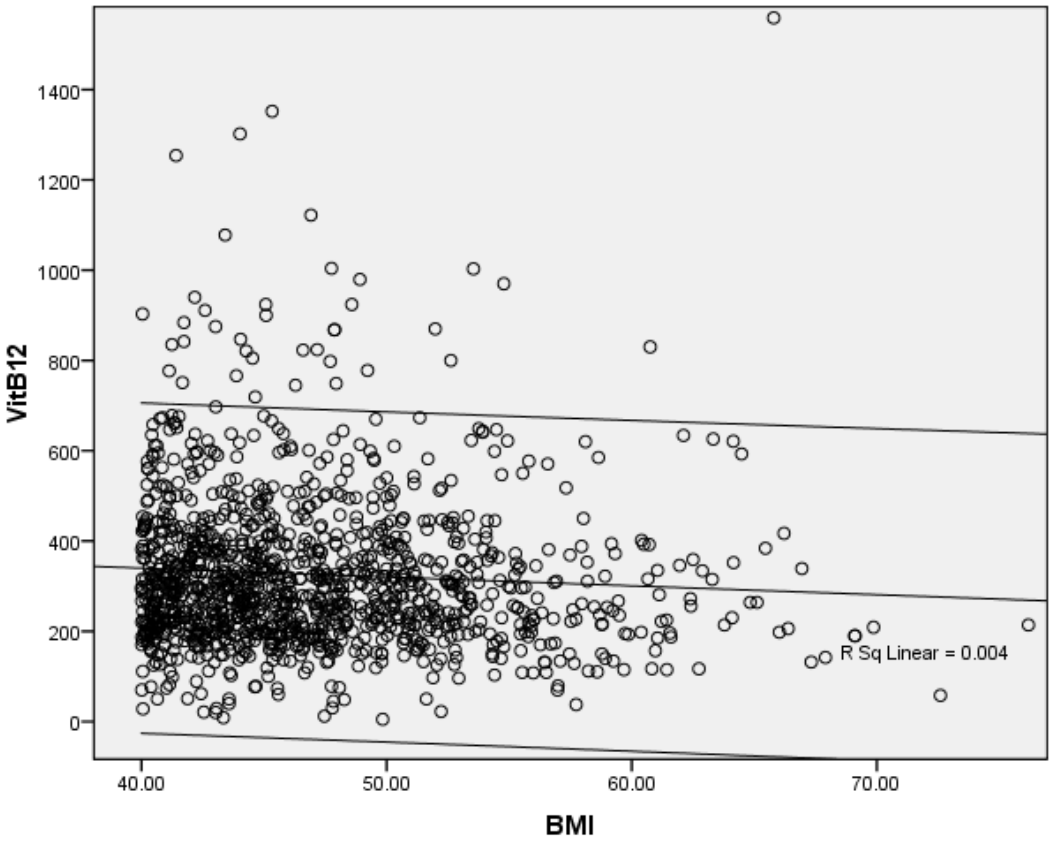

Figure 1. Association between BMI and vitamin B12 level (r = -0.062, p = 0.029).

Table 2
Multivariate logistic regression model to assess relation
between BMI and iron deficiency anemia

	B	S.E.	Wald	Sig.	Exp(B)
BMI	.014	.017	.652	.419	1.014
Sex	-.119	.253	.221	.638	.888
Age	.003	.009	.087	.767	1.003
Constant	1.671	.996	2.816	.093	5.316

Table 3
Multivariate logistic regression model to assess relation
between BMI and vitamin B12 deficiency

	B	S.E.	Wald	Sig.	Exp(B)
BMI	-.031	.011	7.306	.007	.970
Sex	-.143	.182	.619	.431	.867
Age	.012	.007	3.099	.078	1.012
Constant	2.566	.695	13.627	.000	13.018

DISCUSSION

Some important points were obtained in the present study. First, the overall prevalence of iron deficiency anemia among morbid obese patients was 9.8%, while the prevalence of vitamin B12 deficiency was revealed to be 20.9%, about two times iron deficiency anemia. In fact, although iron deficiency anemia is an own prominent finding among obese patients, but the prevalence of vitamin B12 deficiency should be more considered because about one-fifth of the obese patients suffer vitamin B12 deficiency that may lead to pernicious anemia in these patients if progressed. The second point was that the increase in BMI in obese patients can result in reducing vitamin B12 status; however, the increase in BMI may not be associated with significant changes in other hematopoietic indices, even serum hemoglobin level. In fact, by increasing BMI, only deterioration of vitamin B12 deficiency is expected in obese patients.

Reviewing the literature shows those most previous studies emphasized on high prevalence of iron deficiency anemia among morbid obese patients, but few studies focused vitamin B12 deficiency in this patient's population. In a study by Zhao *et al*. [11], obese patients had lower levels of hemoglobin as well as lower serum ferritin when compared to non-obese ones. In a study by Manios *et al*. [12], both obese men and women had lower serum hemoglobin and serum ferritin than non-obese patients. In another study by Pinhas Hamiel *et al*. [13], an association was found between BMI and serum iron. Also, Cheng *et al*. [14] indicated the prevalence of anemia and iron deficiency as 10% and 17%, respectively. In their study, BMI could predict lower levels of serum iron, TIBC, and also CRP. In another survey by Karl *et al*. [15] and similar to our study, no difference was found between obese and non-obese patients in terms of iron deficiency anemia. In another report by Tijerina-Sáenz *et al*. and in line with our survey, BMI, body fat percentage or dietary intakes were not independent contributors to stages of iron depletion; however, they pointed an association between body fat content and serum ferritin level [16]. More interestingly, Kordas *et al*. [17] also indicated that overweight and obese women had a lower likelihood of anemia than normal-weight women. In total, the results of the studies which remained paradoxical regarding association between obesity and iron deficiency might be due to the difference in the definition of obesity or employing different techniques to assess laboratory parameters.

Regarding the relationship between obesity and megaloblastic anemia, only a study focused on this association. Crowley *et al*. [18] reported a notable decrease in both indices of vitamin B12 and folic acid found after gastric bypass surgery in obese patients, which may be a decreasing intrinsic factor following this operation. However, our study could show that vitamin B12 deficiency may occur regardless of any therapeutic intervention on these patients. In other words, vitamins B12 deficiency can be a result of obesity itself because of its pathophysiological nature.

CONCLUSION

Totally, although iron deficiency is more frequent in morbid obese patients so about one-fifth of the patients suffer from vitamin B12 deficiency. In fact, the exacerbation of obesity can result in exacerbation of vitamin B12 deficiency.

Acknowledgment. Authors wish to thank Rasoul-e-Akram Hospital Clinical Research Development Center for technically supported implementation of the project.

Conflict of interest: The authors declare no conflict of interest.

Introducere. *Asocierea dintre obezitate şi anemie rămâne incertă. Studiul prezent îşi propune să evalueze relaţia dintre parametrii asociaţi obezităţii şi apariţia anemiei megaloblastice şi a celei feriprive în cadrul populaţiei Iraniene.*

Materiale şi Metode. *A fost realizat un studiu transversal pe 1252 de pacienţi cu obezitate morbidă dintre pacienţii ce s-au prezentat la Spitalul Rasoul-e-Akram în anul 2014. Obezitatea morbidă a fost definită folosind ghidurile internaţionale (index BMI>40 kg/m^2). Au fost analizaţi mai mulţi parametri, incluzând aici nivelurile sideremiei, a hemoglobinei, feritina, acidul folic şi vitamina B12 serică.*

Rezultate. *BMI a fost asociat negativ cu nivelurile serice ale vitaminei B12 însă nu a fost asociat cu alţi parametri hematologici. Prevalenţa anemiei feriprive a fost de 9.8%. Prevalenţa anemiei feriprive a fost independentă de vârsta pacienţilor*

sau de BMI-ul acestora. Prevalența deficitului de vitamina B12 a fost de 20.9%. Realizând o analiză de regresie logistică multivariată nu s-a găsit nicio asociere între anemia feriprivă şi BMI după ce s-a ajustat după vârsta şi genul pacientului. Un model de regresie similar a arătat că nivelurile mai mari ale BMI ar prezice niveluri scăzute ale vitaminei B12 la pacienții cu obezitate morbidă.

***Concluzii**. Deşi anemia feriprivă este o caracteristică comună printre pacienții obezi, deficitul de vitamina B12 este mai frecvent, o cincime din aceşti pacienți prezentând acest deficit. De fapt, exacerbarea obezității poate duce la exacerbarea deficitului de vitamina B12.*

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Received May 10, 2016