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The relationship between maternal and neonatal vitamin B12 and folate levels, anthropometric measurements, and metabolic indicators

Annelerdeki vitamin B12 ve folat düzeylerinin, yenidoğanlardaki vitamin B12 ve folat düzeyleri, antropometrik ölçümler ve metabolik belirteçlerle ilişkisi

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Abstract

Aim: The nutritional imbalances in pregnancy may lead to metabolic problems in newborns, which may cause obesity during childhood and later in life. It is aimed to determine the maternal levels of folate, vitamin B12 at birth and to investigate the correlation between neonatal anthropometric measurements, and metabolic indicators such as serum lipid profile and insulin resistance.

Methods: A total of 102 mothers and newborns were enrolled in this prospective cohort study. The demographic, obstetric features, serum levels of vitamin B12, folate, glucose, high-density lipoprotein (HDL), low-density lipoprotein (LDL), triglycerides, cholesterol, insulin, homocysteine, and homeostatic model assessment (HOMA-IR) were noted. For vitamin B12, levels, ≥191 ng/L were accepted as normal. The correlation between maternal levels of vitamin B12, folate, anthropometric measurements, and metabolic indicators of newborns were evaluated.

Results: Body mass index (P=0.004), serum insulin levels (P=0.012), HOMA-IR (P=0.001), and homocysteine (P=0.001) were increased in neonates born from mothers with lower serum levels of vitamin B12. The maternal vitamin B12 levels were positively, strongly correlated with neonatal vitamin B12 levels (r=0.719, P<0.001). There was an inverse, weak correlation between maternal vitamin B12 levels and neonatal serum insulin levels (r=-0.221, P=0.025), HOMA-IR (r=-0.249, P=0.011), and homocysteine (r=-0.394, P<0.001). Maternal folate levels were strongly, positively correlated with neonatal folate (r=0.735, P<0.001); weakly, positively correlated with neonatal vitamin B12 (r=0.327, P=0.001); moderately, inversely correlated with neonatal homocysteine (r=-0.505, P<0.001).

Conclusion: Optimizing intake of these vitamins levels during pregnancy is important to reduce the neonatal metabolic abnormalities, which may lead to obesity later in life.

Keywords: Pregnancy, Vitamin B12, Folate, Neonates, Insulin resistance, Metabolic indicators

Öz

Amaç: Gebelikteki besin dengesizlikleri yenidoğanın gelecek yaşamında obeziteye neden olan metabolik problemlere yol açabilir. Çalışmamızda, gebeliğin sonunda annelerdeki folik asit, B12 vitamini düzeylerini belirlemek, yenidoğanın antropometrik ölçümleri, serum lipit profili, insülin direnci gibi metabolik göstergeleri arasındaki ilişkiyi araştırmak amaçlandı.

Yöntemler: Toplam 102 anne ve bebek prospektif kohort çalışmaya dahil edildi. Demografik, obstetrik özellikler, serum B12 vitamini, folat, glikoz, yüksek yoğunluklu lipoprotein (HDL), düşük yoğunluklu lipoprotein (LDL), trigliseritler, kolesterol, insülin, homosistein ve homeostatik model değerlendirmesi (HOMA-IR) not edildi. B12 vitamini için, ≥191 ng/L seviyeleri normal olarak kabul edildi. Maternal vitamin B12 ve folat seviyeleri ile yenidoğanların metabolik göstergeleri, antropometrik ölçümleri arasındaki ilişki araştırıldı.

Bulgular: Serum vitamin B12 düzeyi düşük olan annelerden doğan bebeklerde vücut kitle indeksi (P=0,004), serum insülin düzeyleri (P=0,012), HOMA-IR (P=0,001) ve homosistein (P=0,001) düzeyleri artmış olarak saptandı. Maternal B12 vitamini düzeylerinin, yenidoğan B12 vitamini düzeyleri ile kuvvetli korelasyon (r=0,719, P<0,001); serum insülin (r=-0,221, P=0,025), HOMA-IR (r=-0,249, P=0,011), homosistein (r=-0,394, P<0,001) seviyeleri arasında ters zayıf bir korelasyon saptandı. Maternal folat düzeyleri neonatal folat düzeyleri ile kuvvetli pozitif (r=0,735, P<0,001); yenidoğan B12 vitamini düzeyleri ile zayıf pozitif (r=0,327, P=0,001); neonatal homosistein seviyeleri ile orta derecede ters korelasyon gösterdi (r=-0,505, P<0,001).

Sonuç: Gebelik döneminde annelerde vitamin değerlerinin optimal seviyelerde tutulması, bebeklerin gelecek yaşamlarında obeziteye yol açabilecek metabolik dengesizliklerini azaltmak açısından önemlidir.

Anahtar kelimeler: Gebelik, Vitamin B12, Folat, Yenidoğan, İnsülin direnci, Metabolik belirteçler

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Introduction

Obesity is a major cause of morbidity and mortality worldwide [1]. The prevalence of obesity in the pediatric population exhibits a noteworthy, global increase. Childhood obesity is linked with not only obesity in adulthood, but also increased risk for various metabolic disorders. The nutritional imbalances in pregnancy may lead to decreased serum levels of high-density lipoproteins (HDL), increased triglyceride levels as well as abnormal birth weight [2]. These alterations may enhance the occurrence of obesity, coronary heart disease, type 2 diabetes mellitus (DM) and deterioration of cognitive functions in the later life [3].

Maternal nutritional habits and vitamin deficiencies at the beginning of pregnancy may be related to imbalances of vitamin B12 and folate metabolism [4]. The low levels of vitamin B12, and elevated levels of folate may lead to insulin resistance and metabolic disorders in infants [5-7]. Experimental studies demonstrated that deficiency of vitamin B12 was accompanied by high adiposity, insulin resistance, high blood pressure, and impaired lipid metabolism [8-10]. Low levels of vitamin B12 during pregnancy may alter the methylation pattern of insulin-like growth factor-2 (IGF-2) and influence fetal growth [11], while also restricting the synthesis of S-adenosylmethionine (SAMe), thus leading to increased biosynthesis of cholesterol [12].

Recent studies indicated that vitamin B12 insufficiency during pregnancy was common even in non-vegetarian populations, and that the concentrations of vitamin B12 decreased from the first to the third trimester. No consistent association was reported between vitamin B12 deficiency and birth weight, and the metabolic indicators of newborn such as insulin resistance and blood lipid profiles [13,14].

Our purpose was to assess the correlation between the maternal levels of vitamin B12 and folate, fetal anthropometric measurements at birth, and metabolic indicators such as blood lipid profile, insulin resistance.

Materials and methods

Study design

This prospective cohort was implemented between January 2016 and April 2016 in the pediatric departments of our tertiary care center following the approval of Ethical committee of our institution (Ethic committee of Memorial Hospital-29.01.2016-No:2016/1). Written informed consent was obtained from every participant. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendment or comparable ethical standards.

Initially, 125 women admitted for pregnancy follow-up were enrolled in the study. Since 23 pregnant women declined to participate in the trial, our study group comprised 102 cases with a mean age of 29.15 (4.52) years. A questionnaire form that reviews the socio-demographic features (age, education level, body height, pre-pregnancy body weight, gravida, parity and gestation age, lifestyle, pregnancy history, comorbidities before pregnancy, use of medications before and during pregnancy, family history, and nutritional habits) were filled for every participant. The body-mass indices (BMI) of the pregnant women at the beginning of pregnancy and on the day of labor were noted. Blood samples were collected from brachial veins after at least six hours of fasting and centrifuged within 5 min at 4000 rpm and 4°C. The sera were stored at −80°C until analysis. The serum levels of vitamin B12, folate, glucose, high-density lipoproteins (HDL), low-density lipoprotein (LDL), triglycerides, cholesterol, insulin, and homocysteine were measured in pregnant women. Homeostatic model assessment insulin resistance (HOMA-IR) was evaluated for every participant.

The data on anthropometric measurements of the newborns, including birthweight (g), length (cm) and head circumference, were recorded immediately after birth by a trained assistant. The serum levels of vitamin B12, folate, HDL, LDL, triglycerides, glucose, cholesterol, insulin, and homocysteine were measured from the cord blood of newborns. HOMA-IR levels were assessed for every newborn.

Serum studies

Serum levels of glucose, cholesterol, triglycerides, HDL, and LDL were studied by a commercially available kit (GMI Inc., Bunker, Minnesota, USA). Fried Ewald formula was employed for measurement of LDL cholesterol, whereas HOMA-IR was assessed with Homeostasis Model Assessment 2 computer model (HOMA 2), based on fasting blood glucose and insulin levels [15-17].

Electrochemiluminescence immunoassay method was utilized for studying serum levels of insulin, vitamin B12 and folate (Roche Cobas e411 Immunology Analyzer, Roche Diagnostics, Basel, Switzerland). For vitamin B12, levels ≥191 ng/L were accepted as normal. The homocysteine levels from serum and cord blood were investigated using the microparticle enzyme immunoassay (MEIA) method (Abbot IMX®, Abbott Lab., Abbott Park, IL, USA).

Exclusion criteria were unwillingness to participate, presence of a chronic disease and use of medications other than multivitamin or folate supplements for the mothers, and congenital anomalies and prematurity for the newborns.

Statistical analysis

Analysis of data was performed by IBM Statistical Package for Social Sciences (SPSS) Statistics v.21 software (SPSS Inc., Chicago, IL, USA). Quantitative variables are presented as mean (standard deviation) or median, minimum, and maximum values, while categorical variables are expressed as number and percentage. The assumption of normality needed for the utility of parametric tests has been investigated with the Shapiro – Wilks test. The significance of the difference between two groups was evaluated with either T-test or Mann Whitney U test. The significance of the correlation between variables was assessed using Pearson or Spearman correlation coefficient. *P*-value <0.05 was considered statistically significant.

Results

A total of 102 mothers and their newborns were analyzed. An overview of maternal and neonatal baseline descriptive data is presented in Table 1. The mean maternal age was 29.15 (4.52) years (range: 19-49); the mean BMI values before and at the end of pregnancy were 25.1 kg/m^2 (3.9) and

30.5 kg/m^2 (3.7), respectively. While none of the mothers used vitamin B12 supplements, 55.4% of the mothers used folate supplements, and 5 (4.9%) of the mothers were vegetarian. The mean vitamin B12 level of the mothers were 228.3 ng/ml; 32 (31.4%) mothers had low vitamin B12. The mean folate level was 15.1 µg /ml. None of the mothers had low folate levels. The mean gestational age of the newborns was 38.8 (0.8) weeks. The mode of delivery was cesarean section (C/S) in 73 cases (71.6%), and vaginal delivery (28.4%) in 29 cases.

The baseline descriptive data for neonates is presented in Table 2. The pregnant women gave birth to 45 female (44.1%) and 57 male (55.9%) neonates. The average BMI of neonates was 13.18 (1.27) kg/m^2.

Table 3 displays the serum maternal and neonatal levels of vitamin B12, folate and other markers. The mean serum levels of vitamin B12 in the mother and newborn were 246.37 ng/ml (99.12) and 460.7 ng/ml (339.95), respectively. The mean maternal and neonate folate levels were 15.89 µg /ml (4.36), and 18.90 µg /ml (2.22), respectively.

Table 1: Baseline descriptive data of mothers in our series (n=102)

Variable		Mean (SD)	Min – Max
Age		29.15 (4.52)	19 – 49
BMI (before pregnancy)		25.12 (3.93)	43 – 86
BMI		30.6 (3.79)	22 – 42
Gravidity		1.64 (1.04)	1 – 7
Gestational age (weeks)		38.77 (0.82)	38 - 41
		Number	Percentage
Educational level	PS	7	6.9
	SS	49	48.0
	University	46	45.1
Mode of delivery	Vaginal	29	28.4
	C/S	73	71.6
Folate use	No	45	44.1
	Yes	57	55.9
Vegetarian	No	97	95.1
	Yes	5	4.9
Smoking	No	94	92.2
	Yes	8	7.8

BMI: body-mass index, PS: primary school, SS: secondary school, C/S: cesarean section

Table 2: Baseline descriptive information for newborns in our series (n=102)

Variables		Mean (SD)	Min – Max
Body-mass index (kg/m^2)		13.18 (1.27)	10.15 – 16.55
Head circumference (cm)		34.24 (1.52)	30 - 37
		Number	Percentage
Sex	Female	45	44.1
	Male	57	55.9

SD: Standard deviation

Table 3: Serum levels of laboratory parameters under investigation

Variable	Maternal	Neonatal
Vitamin B12 (ng/ml)	246.37 (99.12)	460.7 (339.95)
Folate (µg/ml)	15.89 (4.36)	18.90 (2.22)
Glucose (mg/dl)	82.36 (16.17)	71.75 (26.42)
Cholesterol (mg/dl)	258.67 (45.76)	60.93 (15.65)
TG (mg/dl)	265.72 (89.23)	28.82 (16.01)
HDL (mg/dl)	73.93 (19.51)	29.91 (10.83)
LDL (mg/dl)	134.73 (41.98)	25.25 (8.44)
Insulin (mIU/l)	20.12 (19.43)	12.16 (11.55)
HOMA-IR	4.31 (6.33)	2.34 (2.89)
Homocysteine (µmol/l)	5.46 (2.75)	5.53 (1.56)

TG: triglyceride, HDL: high-density lipoprotein, LDL: low-density lipoprotein, HOMA-IR: homeostasis model assessment insulin resistance

The distribution of maternal serum parameters with respect to cut-off points is shown in Table 4. The results indicated that 32 pregnant women (31.4%) had low levels of vitamin B12 (<191 ng/ml). Notably, serum folate levels were sufficient (≥4.9 µg/ml) in all pregnant women.

Table 4. The distribution of maternal serum parameters with respect to cut-off points

Variable		Number	Percentage
Body-mass index (kg/m^2)	18.5 - 24.9	6	5.9
	25 – 29.9	39	38.2
	≥ 30	57	55.9
Vitamin B12 (ng/ml)	< 191	32	31.4
	≥ 191	70	68.6
Folate (µg/ml)	< 4.9	0	0.0
	≥ 4.9	102	100.0
Glucose (mg/dl)	≤ 125	99	97.1
	> 125	3	2.9
Cholesterol (mg/dl)	≤ 200	5	4.9
	> 200	97	95.1
TG /mg/dl)	≤ 150	9	8.8
	> 150	93	91.2
HDL (mg/dl)	≤ 40	1	1.0
	> 40	101	99.0
LDL (mg/dl)	< 130	50	49.0
	≥ 130	52	51.0
Insulin (mIU/l)	< 10	29	28.4
	≥ 10	73	71.6
HOMA-IR	< 2	34	33.3
	≥ 2	68	66.7
Homocysteine (µmol/l)	≤ 15	101	99.0
	> 15	1	1.0

TG: triglyceride, HDL: high-density lipoprotein, LDL: low-density lipoprotein, HOMA-IR: homeostasis model assessment insulin resistance

Table 5 demonstrates a comparative analysis of descriptive and laboratory parameters with respect to maternal and newborn serum vitamin B12 levels. In terms of maternal vitamin B12 levels, BMI, serum vitamin B12, insulin, homocysteine and HOMA-IR were found to differ significantly in neonates. Newborns of mothers with lower serum vitamin B12 levels (<191 ng/ml) had remarkably higher BMI (P=0.004), higher levels of insulin (P=0.012), HOMA-IR (P=0.001), homocysteine (P=0.001) and lower levels of serum vitamin B12 (P<0.001).

Table 5: Comparative analysis of descriptive and laboratory parameters with respect to maternal and newborn serum vitamin B12 levels

	Maternal		*P*-value	Neonatal		*P*-value
	<191 ng/ml	≥191 ng/ml		<191 ng/ml	≥191 ng/ml	
Age	28.59 (3.93)	29.40 (4.77)	0.406	-	-	-
BMI	25.45 (3.83)	24.97 (3.99	0.570	-	-	-
BMI**	30.83 (3.52)	30.5 (3.93)	0.681	13.70 (1.10)	12.93 (1.27)	0.004
Folate	15.30 [5 - 20]	18.25 [7 - 20]	0.097	20 [10 - 20]	20 [13 - 20]	0.230
Glucose	82 [50 - 186]	81.5 [60 - 126]	0.845	63 [48 - 156]	65.5 [26 - 156]	0.405
Cholesterol	251.53 (35.48)	261.93 (49.65)	0.289	61.81 (14.63)	60.53 (16.18)	0.703
TG	290.19 (109.77)	254.53 (76.40)	0.061	26.5 [11 - 99]	25 [7 - 84]	0.662
HDL	71.16 (18.08)	75.20 (20.12)	0.334	27.5 [10 - 55]	28 [11 - 66]	0.806
LDL	124.81 (36.71)	139.26 (43.67)	0.107	25.09 (6.07)	25.33 (9.36)	0.880
Insulin	14.5 [2 - 114]	13.95 [2 - 112]	0.968	11.25 [4 - 65]	8.45 [0 - 68]	0.012
HOMA-IR	3.15 [0 - 52]	2.60 [0 - 25]	0.700	2.2 [0 - 15]	1.20 [0 - 20]	0.001
Homocysteine	5.65 [2.8 – 29.6]	4.9 [2.9 – 8.8]	0.109	6.27 (1.73)	5.19 (1.36)	0.001

BMI*: body-mass index before pregnancy, BMI**: BMI on the day of labour, TG: triglyceride, HDL: high-density lipoprotein, LDL: low-density lipoprotein, HOMA-IR: homeostasis model assessment insulin resistance

Table 6: An overview of maternal and neonatal serum vitamin B12 and folate levels with respect to various characteristics of the mother

		Maternal				Neonatal			
		Vitamin B12	*P*-value	Folate	*P*-value	Vitamin B12	*P*-value	Folate	*P*-value
Mode of delivery	V	211 [99 - 571]	0.873	14.8 [5 - 20]	0.013	373 [123 - 1916]	0.659	20 [14 - 20]	0.280
	C/S	227 [59 - 563]		18.9 [7 - 20]		368 [98 - 1983]		20 [10 - 20]	
Folate use	No	224 [59 - 571]	0.928	15.5 [5 - 20]	0.151	378 [98 - 1916]	0.835	20 [13 - 20]	0.652
	Yes	227 [99 - 563]		18.6 [7 - 20]		368 [123 - 1983]		20 [10 - 20]	
Vegetarian	No	227 [59 - 571]	0.125	17.5 [5 - 20]	0.887	371 [98 - 1983]	0.303	20 [10 - 20]	0.718
	Yes	158 [120 - 370]		14.1 [11 - 20]		231 [182 - 1715]		20 [14 - 20]	
Smoking	No	227 [59 - 571]	0.463	16.9 [5 - 20]	0.097	366 [98 - 1983]	0.538	20 [10 - 20]	0.317
	Yes	195 [99 - 352]		19.85 [11 - 20]		389 [123 - 771]		20 [14 - 20]	

V: vaginal, C/S: cesarean section

An outline of maternal and neonatal serum vitamin B12 and folate levels with respect to various characteristics of the mother is given in Table 6. Notably, mothers who gave birth via C/S had higher levels of folate than those who underwent vaginal delivery (P=0.014). Interestingly, folate supplementation did not yield a significant difference in neither maternal (P=0.151) nor neonatal (P=0.652) serum folate levels.

The results of correlation analysis for maternal serum levels of folate and vitamin B12 and neonatal biomarkers is shown in Table 7. We noted that maternal vitamin B12 levels was positively and strongly correlated with neonatal vitamin B12 levels (r=0.719, P<0.001). There was an inverse and weak correlation between maternal vitamin B12 levels and neonatal serum levels of insulin (r=-0.221, P=0.025), HOMA-IR (r=-0.249, P=0.011) and homocysteine (r=-0.394, P<0.001). Maternal folate levels were strongly and positively correlated with neonatal folate (r=0.735, P<0.001), weakly and positively correlated with neonatal vitamin B12 (r=0.327, P=0.001), moderately and inversely correlated with neonatal homocysteine (r=-0.505, P<0.001).

Table 7: Analysis of the correlation between maternal serum levels of vitamin B12 and folate and neonatal variables under investigation

	Maternal vitamin B12		Maternal folate	
Neonatal	r	*P*-value	r	*P*-value
Vitamin B12	0.719	<0.001	0.327	0.001
Folate	0.118	0.236	0.735	<0.001
Glucose	0.062	0.538	0.007	0.947
Cholesterol	0.004	0.971	0.073	0.463
TG	0.035	0.728	-0.165	0.097
HDL	-0.049	0.623	0.077	0.441
LDL	0.078	0.434	0.043	0.668
Insulin	-0.221	0.025	0.084	0.400
HOMA-IR	-0.249	0.011	0.050	0.617
Homocysteine	-0.394	<0.001	-0.505	<0.001

TG: triglyceride, HDL: high-density lipoprotein, LDL: low-density lipoprotein, HOMA-IR: homeostasis model assessment insulin resistance, correlation coefficients (r): 1 - 0.90: very strong association; 0.89 – 0.70: strong association; 0.69 – 0.40: moderate association; 0.39 – 0.20: weak association; 0.19 – 0.0: no associations

Discussion

Suboptimal concentrations of vitamin B12 may be independently associated with abnormal birth weight, an adverse lipid profile, and higher insulin resistance in neonates. Therefore, that may serve as surrogate markers for metabolic disorders such as obesity, type 2 diabetes, and metabolic syndrome in later life in many populations [2]. We investigated the serum levels of vitamin B12 and folate in pregnant women to investigate whether they are correlated with metabolic indicators and fetal anthropometric measurements at birth. Results of the current study imply that low levels of maternal vitamin B12 were associated with an increased likelihood of obesity and glucose intolerance in neonates.

There is an association between vitamin B12 levels and indicators of metabolic risk (such as lipid profiles) at birth [2]. The increased levels of homocysteine in the patients with low vitamin B12 suggest that these low levels can be clinically significant and represent a frank insufficiency at the tissue level [2,15]. The recent studies have reported a rate of 40% for low vitamin B12 level in mothers, which was attributed to hemodilution, changes in binding proteins, active transport to the fetus as well as consumption of processed foods and improved hygiene [2,18].

Adaikalakoteswari et al. [2] proposed that decreased levels of maternal vitamin B12 were linked with fetal insulin resistance, lower HDL and higher triglycerides. Similarly, an experimental study demonstrated that adverse lipid profile was detected in rats born to vitamin B12 restricted dams [19]. It can be postulated that low maternal vitamin B12 status may unfavorably influence the lipid profile in the newborn. We observed that maternal vitamin B12 levels were positively correlated with neonatal vitamin B12 levels and inversely correlated with neonatal insulin, HOMA-IR, and homocysteine levels. On the other hand, no remarkable association could be established between maternal and neonatal lipids. Further trials are warranted to unveil the roles of lipids in vitamin B12, folate and glucose metabolism during pregnancy.

Supplementation of vitamin B12 and folate in pregnant women may be useful for reduction of metabolic risks for neonate and achievement of more favorable perinatal outcomes. Our data is important since we observed that maintenance of sufficient folate levels in the mother was accompanied with adequate folate level and diminution of homocysteine in the neonate. Maternal vitamin B12 levels were inversely correlated with neonatal head circumference and neonatal triglyceride levels. Thus, we speculate that maternal vitamin B12 supplementation is crucial for regulation of favorable fat and glucose metabolisms in the newborn.

Interestingly, the relationship between maternal folate and neonatal homocysteine became insignificant when maternal homocysteine level was included in the analysis. Hence, the effect of folate on neonatal homocysteine may be mediated through maternal homocysteine while the impact of vitamin B12 may be partly independent of it. In accordance with this data, low levels of maternal vitamin B12 were predictive for hyperhomocysteinemia in both the newborns and the mothers [20].

Vitamin B12 is supposed to be the strongest driver of homocysteine, and an established metabolic risk factor [5,21]. There is a strong inverse correlation between maternal vitamin B12 and neonatal homocysteine levels [2]. In the relevant literature, BMI was higher in patients with low vitamin B12 [22]. However, the causality of this association has not been yet elucidated. The biochemical basis for increased metabolic risk due to low vitamin B12 may be due to 2 pathways: Vitamin B12 is a cofactor for conversions of homocysteine to methionine and methyl malonyl Co-A to succinyl Co-A. Thus, oxidation of free fatty acids will be impaired, and lipogenesis will occur in the case of deficiency of vitamin B12 [5]. Low maternal vitamin B12 and high folate status may be involved in the epidemic of adiposity and type 2 DM. Our data is coherent with these results.

Our results imply that the dietary supply of methyl donors like folate and vitamin B12 during pregnancy is necessary for normal growth, development, and physiological functions of newborn. Maternal deficiency of vitamin B12 was reflected as higher BMI, increased levels of insulin, HOMA-IR and homocysteine in neonates. Therefore, we suggest that monitorization of maternal vitamin B12 and replacement of any deficiency detected during pregnancy may avoid further adverse metabolic consequences in the newborn. Deficiency of vitamin B12 is particularly associated with altered lipid profile and increased metabolic risk [12]. Sukumar et al. [23] suggested that vitamin B12 insufficiency during pregnancy was common even in non-vegetarian populations and there was no clear association

between vitamin B12 and low birth weight. Vitamin B12 exhibits a crucial function in adipose metabolism, and its deficiency causes increased levels of homocysteine and cholesterol. There were remarkable associations of vitamin B12 deficiency with BMI, triglycerides, and total cholesterol [12]. Thus, maintenance of adequate levels of vitamin B12 during periconceptional period is important and special risk groups such as vegetarians and patients with malabsorption need to be evaluated carefully [12]. However, we did not come across any adverse metabolic outcome due to a vegetarian diet.

Experimental studies have shown that maternal folic acid supplementation can alter DNA methylation and gene expression in the developing fetus, which may confer disease susceptibility later in life. Maternal folic acid supplementation affects tissue folate concentrations, DNA methylation and gene expression in the offspring in a gestation-period-dependent and organ-specific manner [24]. Even though low maternal folate levels were initially correlated with metabolic risk markers in the newborn, these associations became invisible after regression analysis [2]. A folate supply may contribute to the implantation and development of the placenta and improvement of the endothelial function [25]. There is a remarkable interaction between metabolisms of folate and vitamin B12, and a high folate intake may hinder the hematologic and neurodegenerative symptoms of vitamin B12 deficiency. The investigation of the link between sociodemographic factors with vitamin B12 status revealed that gender and income were not associated with serum vitamin B12 levels. On the other hand, obesity was negatively correlated with vitamin B12 status [26]. We suggest that maternal supplementation of vitamin B12 and folate may be the initial step in the combat with obesity and DM.

Limitations

The modest sample size and data restricted to the experience of a single institution. Furthermore, the impact of confounding variables such as social, environmental, genetic, metabolic, and ethnic factors may have affected our results. Hence, interpretation of our results must be made cautiously. Further multi-centric trials on larger series are warranted to identify the consequences of deficiencies of folate and vitamin B12 in pregnant women.

Conclusion

The main strength of this study was the investigation of the relationship between multiple metabolic indicators and folate, vitamin B12. In conclusion, we suggest that the achievement of optimal serum levels of vitamin B12 and folate during pregnancy are important for reducing the likelihood of neonatal DM and obesity. Identification of deficiency of these vitamins in the periconceptional period is important to provide adequate nutritional support to avoid obesity and related metabolic morbidities. Levels of vitamin B12 may have a significant potential to affect the health of future offspring. Policies and recommendations should be developed for food fortification and supplement use to decrease risks for metabolic hazards such as type 2 DM, obesity, and cardiovascular diseases.

The achievement of optimal serum levels of vitamin B12 and folate during pregnancy are important for reducing the likelihood of neonatal glucose metabolism abnormalities and obesity in later life. Identification of deficiency of these vitamins during the periconceptional period is important to provide adequate nutritional support to avoid obesity and related metabolic morbidities.

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