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The effects of maternal body weight on iodine concentration in breast milk and cord blood and infant growth

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Abstract

Breast milk (BM) is the only source of iodine and bioactive compounds that influence growth and development in infants. The content of BM may be influenced by maternal body mass index (BMI). The aim of this study was to investigate the effect of maternal weight on BM and cord blood iodine concentrations, growth-related hormones, infant anthropometric measurements. A total of 84 mother-infant pairs participated. Levels of leptin, adiponectin and insulin-like growth factor-I (IGF-I) in postnatal BM and cord blood were analysed by enzyme-linked immunosorbent assay (ELISA), iodine by Sandell-Kolthoff reaction. Dietary iodine intake of women was determined by food frequency questionnaire, and anthropometric measurements of infants at birth and 3 months were evaluated. Dietary iodine intake was found to be similar in normal weight (NW) and overweight/obese (OW/OB) women ($p > 0.05$). Breast milk iodine concentration (BMIC) was 17.4 µg in NW, 18.2 µg in OB/OW women. Adiponectin in cord blood and IGF-I in BM were higher OB/OW than NW women ($p < 0.05$). Positive correlations were found between the infant birth weight and adiponectin in BM, between the infant body weight at 3 months and leptin and adiponectin in BM, between the infant birth head circumference and IGF-I in BM ($p < 0.05$). In multiple linear regression model, leptin and adiponectin in BM had a positive effect on infant body weight ($p < 0.05$). Maternal BMI may influence infant body weight via leptin and adiponectin in BM and infant head circumference via IGF-I. No relationship was found between maternal BMI and iodine levels and anthropometric measurements of the infant. Longitudinal studies are recommended to understand the effect of BMIC on growth.

Introduction

Growth is a process that begins at fertilisation and is influenced by various factors. Iodine is a micronutrient that regulates growth and development through the synthesis/secretion of growth hormone[1] Iodine deficiency during the period of rapid growth and brain development may lead to disorders in thyroid function and musculoskeletal system, low intelligence level, and growth-development retardation.[2] Since most organs do not complete their development in infancy, iodine storage could fall short to catch the fast metabolic rate. Therefore, the iodine requirement of infants is high and health problems related to deficiency are important.[3] Breast milk (BM) contains bioactive components that play a role in the optimal growth of the infant, including enzymes, cytokines, growth factors, hormones such as adiponectin and leptin, in addition to macro- and micronutrients.[4] The highest levels of leptin, adiponectin and insulin-like growth factor-I (IGF-I), which are growth-related factors, are observed in colostrum and their concentrations tend to decrease as the lactation period progresses.[5–7] Growth-related factors such as leptin, adiponectin and IGF-I were also detected in cord blood.[8,9] It has been reported that growth factors in cord blood are associated with the birth weight of the infant.[10] It is unclear whether exposure to high levels of growth factors through BM in the early stages of lactation influences the growth status of infants later in life.[11]

The mammary gland concentrates iodine and secretes it into BM by increasing the expression of the sodium/iodide symporter (NIS).[12] The iodine concentration in BM is highest in colostrum and decreases by more than 40% during the first 6 months of early lactation.[13,14] It is important that breast milk iodine concentration (BMIC) is sufficient to meet daily iodine requirements in exclusively breastfed infants.[15] In breastfed infants, there are insufficient data on urinary iodine concentrations due to the difficulty of urine collection.[16] The threshold for the evaluation of urinary iodine in infants has been determined as ≥100 μg/L, which is based on the results of epidemiological studies in school-age children. However, it is stated that it is not correct to use the same cut-off point since the urine volumes of infants and children are different.[17] Therefore, iodine adequacy in infants is estimated from maternal iodine concentration.[18] In terms of maternal iodine concentration, the level in BM has been reported to be more reliable than maternal urinary iodine.[15,16] While BMIC has recently been reported to be influenced by dietary iodine intake[19] and duration of lactation[20], no clear reference for BMIC corresponding to adequate iodine intake has been established and recommendations are very limited.[21] A BMIC of<100 μg/L has been defined as iodine deficiency, and it has been reported that even if the mother has iodine deficiency, iodine in the infant can be adequately maintained through BM due to the ability of breast epithelial cells to concentrate iodine.[22] In Scandinavian countries the median BMIC required to meet iodine requirements in infants is set at≥100 μg/L, which is also approved by European Food Safety Authority.[23,24]

Although it has been reported that BMIC can be influenced by maternal body weight and health conditions, the effect of maternal health-related factors on BMIC has not been clearly defined.[13] Information on the effect of obesity during pregnancy and lactation on BMIC is limited.[25] Studies have shown that urinary iodine concentration decreases with increasing body mass index (BMI)[26,27] and iodine deficiency is high in morbid obese women.[28] When the relationship between BMI and iodine is evaluated, it can be considered that BMIC may affect obesity in both childhood and adulthood.[25] In our study, it was thought that growth-related factors in cord blood could affect the anthropometric measurements of the infant at birth, while growth-related factors in BM could influence the anthropometric measurements of the infant in the later period (at 3 months).

Therefore, this study aimed to evaluate the effect of maternal body weight during the preconceptional period on BM (colostrum) and cord blood iodine concentrations, growth-related leptin, adiponectin, IGF-I and infant anthropometric measurements.

Method

Study population

The study was conducted with mothers aged 19–45 years and their newborn babies who gave birth in the Gynaecology and Obstetrics Outpatient Clinic of Alanya Training and Research Hospital between March-June 2022. Based on the previous studies in the literature[25,29], it was planned to work with at least 66 mother and infant pairs to determine an intermediate size with 5% error and 85% power. A total of 84 mother-infant pairs, 42 with normal weight (NW, 18.5–24.9 kg/m^2) and 42 with overweight/obese (OW/OB, ≥25.0 kg/m^2), constituted the sample of the study. It was ensured that the characteristics of the mothers (such as gestational age, mode of delivery, number of births, etc.) in each group were similar. The inclusion criteria were that the mothers agreed to participate in the study, were between 19-45 years of age, the mother did not have any disease that could affect metabolism (hyper/hypothyroidism, gestational diabetes, eclampsia, pre-eclampsia, etc.), the mother had a single birth, never smoked or quit smoking 1 year ago, the infant had a normal birth weight (2500–4200 g) and was born at term (37–42 weeks), the newborn did not have any metabolic disease, and the mother fed her infant exclusively with BM.

Socio-demographic, maternal and infant data collection

The questionnaire form, which included descriptive information about the mothers and questions about the use of iodine supplements, was administered by interviewing during postnatal hospitalisation. To determine the amount of dietary iodine intake of the mothers, the consumption of iodine-rich foods (dairy products, seafood and fish, iodised salt, etc.) in the previous month was asked using the food frequency questionnaire. In the food frequency questionnaire, the statements 'every day', '5–6 times a week', '3–4 times a week', '1–2 times a week', 'every 15 days', '1 in a month' and 'never' were used to determine the frequency. The women reported the frequency of food consumption and daily consumption amounts, which were recorded by the researcher. In the evaluation of food frequency questionnaire, frequency values related to food consumption frequency were utilised. The amount of food consumed was multiplied by a coefficient of 1 if consumed 'every day', 0.7855 if consumed '5–6 times a week', 0.498 if consumed '3–4 times a week', 0.2145 if consumed '1–2 times a week', 0.067 if consumed 'every 15 days' and 0.033 if consumed 'once a month' to calculate the average daily consumption.[30,31]

Anthropometric measures

Pre-pregnancy weight and weight gain during pregnancy were recorded from the medical records. Postnatal body weight and height of the mothers were measured with a precision scale calibrated in the hospital and a stadiometer, respectively. BMI was calculated by dividing pre-pregnancy weight by the square of height (kg/m^2). Weight gain during pregnancy was assessed according to Institute of Medicine recommendations.[32] In infants, body weight was measured using a standard baby scale without clothes or nappies, height was measured using infantometer, and head circumference was measured using a non-stretch tape measure. The body weight, height and head circumference of the babies at the 3rd month were measured by the health personnel working at the Family Health Centres and recorded by the researcher. Body weight, height and head circumference measurements of infants were evaluated using the WHO Anthro programme.[33]

Breast milk and cord blood sample collection

Breast milk (colostrum) samples (approximately 5 mL) were collected in a single collection on the day after birth by pumping with a syringe. Cord blood, collected during labour and placed in biochemical tubes, was centrifuged at 3500 r.p.m. for 15 minutes and serum was separated. Samples were placed in eppendorf tubes, barcoded and stored frozen at −80°C until analyses were performed.

Laboratory measurements

Samples were thawed at room temperature on the day of analysis. The measurements of leptin, adiponectin and IGF-I in cord blood and BM samples were performed using an enzyme-linked immunosorbent assay (ELISA) kit from Bioassay Technology Laboratory (BT Lab), Shanghai, China. Leptin and IGF-I were measured in ng/mL and adiponectin in mg/L. The ELISA plates were analysed on a BIOTEK Synergy H1 microplate reader and concentrations were calculated using GEN5 software.[34] The measurement of iodine in cord blood and BM samples was evaluated by the Sandell-Kolthoff reaction, which is a simple, convenient and economical colourimetric method.[35]

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Table 1. Socio-demographic characteristics of women (n = 84)

Socio-demographic characteristics	NW		OW/OB		p
	N	%	N	%	
Age group (years)					
19–30	25	59.5	21	50.0	$\chi^2 = 0.769$ $p^{+} = 0.381$
31–45	17	40.5	21	50.0	
$\overline{X}$±SD	29.7 ± 5.6		31.3 ± 6.0		$t = 1.252$ $p^{++} = 0.214$
Min-Max.	19.0–45.0		20.0–45.0		
Education level					
Primary school graduate	3	7.1	11	25.2	$\chi^2 = 9.937$ $\mathbf{p^{+} = 0.041*}$
Secondary school graduate	10	23.8	15	35.7	
High school graduate	17	40.5	11	26.2	
University graduate	12	28.6	5	11.9	
Occupation					
Officer	4	9.5	–	–	$\chi^2 = 15.382$ $\mathbf{p^{+} = 0.002*}$
Self-employment	4	9.5	–	–	
Unemployed/not working	7	16.7	1	2.4	
Housewife	27	64.3	41	97.6	
Delivery type					
Vaginal birth	18	42.9	12	28.6	$\chi^2 = 1.867$ $p^{+++} = 0.172$
Caesarean section	24	57.1	30	71.4	

$^{+}$ Pearson's chi-square test, $^{++}$ Independent sample *t*-test, $^{+++}$Mann-Whitney *U*-test *$p < 0.05$.

Data analysis

SPSS 22.0 software was used for statistical analyses. Descriptive statistics are presented as percentage (%), frequency, mean ($\overline{X}$), standard deviation (SD) and median, minimum-maximum (min-max). Normality distribution of the data was analysed by Kolmogorov Smirnov test. In the comparisons of quantitative data between two groups under parametric test conditions, independent sample *t*-test was used if there was normal distribution, otherwise Mann-Whitney *U*-test was used. The relationships between categorical variables were determined by Pearson chi-square and Fisher's exact chi-square test. Pearson correlation test was used for correlations between quantitative data under parametric conditions. Multiple linear regression model was used to evaluate the independent effects of factors that may have an effect on anthropometric measurements such as body weight, height and head circumference of infants. For statistical significance, $p < 0.05$ was accepted.

Ethical considerations

Ethics committee permission numbered 10354421-2022/02-01 was obtained from Alanya Alaaddin Keykubat University Faculty of Medicine Clinical Research Ethics Committee and research permission was obtained from Alanya Training and Research Hospital. The study was conducted in accordance with the principles of the Declaration of Helsinki. Written informed consent was obtained from the volunteer mothers and the infants' participation in the study was approved by their mothers.

Results

Study population

Eighty-four mother-infant pairs, who met the inclusion criteria, participated in the study. Socio-demographic information of the women is given in Table 1. The educational level of NW women was higher than that of OW/OB women ($p = 0.041$). Most of both NW (64.3%) and OW/OB women (97.6%) were housewives ($p = 0.002$).

Table 2 shows information about the anthropometric measurements of the mothers and their infants. The head circumference of the infants of OW/OB women was found to be higher than that of NW women (35.9 ± 0.8 and 35.3 ± 1.2 cm, respectively $p = 0.014$). It was found that 73.8% of the infants participating in the study had normal birth body weight, 72.6% had normal birth length and 40.5% had normal birth head circumference (15–85th percentile) (data not shown). NW women had higher weight gain during pregnancy than OW/OB women ($p = 0.007$).

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Table 2. Anthropometric measurements according to women's pre-pregnancy BMI

Anthropometric measurements	NW ($n = 42$)			OW/OB ($n = 42$)			t/U	*p*
	$\overline{X}$±SD	Median	Min-Max.	$\overline{X}$±SD	Median	Min-Max.		
Birth (Infant)								
Body weight (g)	3276 ± 447.0	3195	2500–4200	3313 ± 405.0	3290	2500–4200	t = −0.390	0.698^{+}
Height (cm)	50.3 ± 1.8	50.0	46.0–55.0	50.4 ± 1.6	50.0	45.0–53.0	*U* = 813.0	0.527^{++}
Head circumference (cm)	35.3 ± 1.2	35.5	33.0–37.0	35.9 ± 0.8	36.0	34.0–37.0	*U* = 621.5	**0.014**$^{++}$
3rd month(Infant)								
Body weight (g)	6210 ± 655.0	6275	5000–7500	6331 ± 723.0	6375	5000–8200	t = −0.800	0.426^{+}
Height (cm)	60.2 ± 3.3	60.0	55.0–67.0	60.8 ± 3.6	61.0	51.0–68.0	t = −0.853	0.396^{+}
Head circumference (cm)	39.8 ± 1.2	40.0	38.0–43.7	39.9 ± 1.0	40.0	30.0–43.0	*U* = 800.0	0.450^{++}
Pre-pregnancy body weight (kg)	57.9 ± 6.4	57.0	40.0–70.0	72.7 ± 9.4	71.5	58.0–110.0	t = −8.382	**<0.001**$^{+}$
Pre-pregnancy BMI (kg/m^2)	21.8 ± 1.8	22.0	18.6–24.8	29.4 ± 3.6	28.0	25.1–40.0	*t* = 11.998	**<0.001**$^{+}$
Height (cm)	162.6 ± 6.4	162.0	146.0–175.0	157.4 ± 5.5	157.0	150.0–173.0	*t* = 4.007	**<0.001**$^{+}$
Body weight at the end of pregnancy (kg)	72.4 ± 9.9	73.5	49.0–92.0	83.6 ± 10.1	81.0	69.0–123.0	t = −5.092	**<0.001**$^{+}$
BMI at the end of pregnancy (kg/m^2)	27.7 ± 2.5	27.1	21.3–32.4	33.8 ± 3.6	33.1	28.4–43.1	*t* = 11.988	**<0.001**$^{+}$
Weight gain in pregnancy (kg)	14.6 ± 5.4	13.7	3.0–25.0	10.3 ± 6.5	12.0	(−3.0)–25.0	*t* = 2.765	**0.007**$^{+}$

$^{+}$ Independent sample *t*-test, $^{++}$ Mann-Whitney *U*-test, $p < 0.05$.

Table 3. Information on women's iodine intake

Iodine intake	NW ($n = 42$) *N*	%	OW/OB ($n = 42$) N	%	*p*
Use of iodine supplements during pregnancy					
Yes	–	–	–	–	–
No	42	100.0	42	100.0	
Type of salt used					
Sea salt	–	–	1	2.4	$p^{+} = 0.520$
Rock salt	4	9.5	6	14.3	
Iodised salt	38	90.5	35	83.3	
Iodised table salt consumption g/day ($n = 73$)					
$\bar{X}$±SD	10.7 ± 5.5		9.3 ± 5.0		$U = 778.5$ $p^{++} = 0.342$
Min-Max.	0–18.0		0–20.0		
Median	9		8.5		
****Daily maternal dietary iodine intake (μg)**					
$\bar{X}$±SD	184.4 ± 73.8		186.6 ± 72.3		$U = 866.0$ $p^{++} = 0.886$
Min-Max.	67.6–428.4		72.9–387.5		
Median	172.0		171.0		

$^{+}$Fisher's exact test, $^{++}$Mann-Whitney *U*-test, *$p < 0.05$.
***Iodised salt is taken into account.*

Leptin, adiponectin, IGF-I and iodine status

Information on iodine intake of women is given in Table 3. All women, both NW and OW/OB, did not use iodine supplements during pregnancy ($p > 0.05$). The type of salt used in food preparation and at the table, the amount of iodised salt and daily dietary iodine intake did not show a significant difference between the groups ($p > 0.05$).

Table 4 shows the levels of leptin, adiponectin, IGF-I and iodine in cord blood and BM according to BMI of women. Median leptin concentrations in cord blood and BM were higher in OB/OW women than in NW women ($p > 0.05$). Median adiponectin concentration in cord blood was significantly higher in OB/OW mothers compared to NW women ($p = 0.021$). IGF-I concentration in BM of OB/OW women was found to be higher than IGF-I concentration in BM of NW women ($p = 0.002$). There was no difference between cord blood and BM iodine concentrations in NW and OB/OW women ($p > 0.05$).

The relationship between women's BMI and leptin, adiponectin, IGF-I and iodine levels in cord blood and BM is given in Table 5. A low level positive correlation was found between pre-pregnancy BMI and IGF-I concentration in BM ($r = 0.282$, $p = 0.009$) and cord adiponectin concentration ($r = 0.221$, $p = 0.044$). A low level negative correlation was observed between weight gain during pregnancy and IGF-I concentration in BM ($p = 0.036$). No significant correlation was found between iodine concentration and maternal BMI or weight gain during pregnancy ($p > 0.05$).

Table 6 shows the relationship between anthropometric measurements of infants and leptin, adiponectin, IGF-I and iodine in BM and cord blood. A positive correlation was found between adiponectin in BM and birth weight of the baby ($r = 0.220$, $p = 0.045$). A positive correlation was observed between the body weight of the infant at 3 months and leptin concentration in BM ($r = 0.216$, $p = 0.049$) and adiponectin concentration in BM ($r = 0.292$, $p = 0.007$). There was no correlation between infant height and leptin, adiponectin, IGF-I and iodine in BM and cord blood ($p > 0.05$). There was a positive correlation between the head circumference of the baby at birth and IGF-I in BM ($r = 0.222$, $p = 0.043$). Positive correlations were observed between the 3-month weight gain of the infant and leptin in BM ($r = 0.264$, $p = 0.015$), and between the change in the infants' 3-month length growth and IGF-I in BM ($r = 0.273$, $p = 0.012$).

Table 7 shows the regression model of the relationship between the anthropometric measurements of the infant at the third month and leptin, adiponectin, IGF-I and iodine in cord blood and BM. After adjustment for maternal age, education level, pre-pregnancy BMI and weight gain during pregnancy, 1.0 ng/mL increase in leptin in BM increased the weight of the infant by 0.208 g. Leptin in BM had a borderline positive effect on infant weight (β=0.208; $p = 0.055$). An increase of 1.0 mg/L of adiponectin in BM increased the body weight of the infant by 0.291 g and adiponectin in BM had a positive effect on the body weight of the infant (β=0.291; $p = 0.009$). According to the model, leptin, adiponectin, IGF-I and iodine in both BM and cord blood had no significant effect on the infant's height at 3 months ($F = 1.538$, $p = 0.199$; $F = 1.413$; $p = 0.237$, respectively). In addition, none of the leptin, adiponectin, IGF-I and iodine variables in cord blood and BM included in the model showed a significant effect on the infant's head circumference at 3 months ($F = 0.428$, $p = 0.788$; $F = 1.350$; $p = 0.259$, respectively).

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Table 4. Cord blood and breast milk leptin, adiponectin, IGF-I, iodine concentrations according to pre-pregnancy BMI of women (n = 84)

Growth-related factors		NW (n = 42)			OW/OB (n = 42)			t/U	p
		$\overline{X}$±SD	Median	Min-Max.	$\overline{X}$±SD	Median	Min-Max.		
Leptin (ng/mL)	Cord blood	4.2 ± 3.4	1.5	0.4–21.0	5.7 ± 3.6	1.5	0.47–29.4	873.0^{++}	0.936
	Breast milk	1.0 ± 0.4	0.9	0.4–2.3	1.1 ± 0.6	1.1	0.4–4.4	769.0^{++}	0.312
Adiponectin (mg/L)	Cord blood	141.8 ± 124.9	106.1	39.1–780.3	201.4 ± 170.5	140.4	57.1–940.3	623.0^{++}	**0.021***
	Breast milk	80.2 ± 38.3	69.5	38.8–244.2	93.5 ± 78.2	75.6	37.5–546.1	785.5^{++}	0.388
IGF-I (ng/mL)	Cord blood	271.6 ± 187.7	242.0	37.7–992.7	325.7 ± 235.3	247.2	59.6–936.0	769.0^{++}	0.442
	Breast milk	165.1 ± 136.3	104.7	42.8–565.5	290.7 ± 192.8	241.8	52.2–635.8	543.0^{++}	**0.002***
Iodine (μg/L)	Cord blood	32.9 ± 4.8	34.3	18.9–39.0	31.9 ± 6.7	34.4	10.5–38.7	783.5^{++}	0.378
	Breast milk	16.6 ± 4.9	17.4	4.8–29.0	18.2 ± 6.7	18.2	2.4–32.0	1.434^{+}	0.155

$^{+}$ Independent sample *t*-test, $^{++}$ Mann-Whitney *U*-test; *$p < 0.05$.

Table 5. The relationship between women's pre-pregnancy and birth at BMI, weight gain in pregnancy and cord blood and breast milk leptin, adiponectin, IGF-I, and iodine levels (n = 84)

Growth-related factors		Pre-pregnancy BMI (kg/m^2)		BMI at birth (kg/m^2)		Weight gain in pregnancy	
		r	*p*	*r*	*p*	*r*	*p*
Cord blood	**Leptin**	0.023	0.826	−0.047	0.673	−0.133	0.226
	Adiponectin	0.221	**0.044***	0.157	0.153	−0.189	0.084
	IGF-I	0.139	0.207	0.123	0.265	−0.070	0.528
	Iodine	−0.092	0.403	−0.024	0.827	0.161	0.143
Breast milk	**Leptin**	0.139	0.207	0.156	0.157	0.012	0.916
	Adiponectin	0.144	0.190	0.146	0.186	0.017	0.881
	IGF-I	0.282	**0.009***	0.181	0.100	−0.230	**0.036***
	Iodine	0.059	0.597	0.095	0.388	0.045	0.685

Pearson correlation test, *$p < 0.05$.

Discussion

BM is an important nutritional source that supports normal growth and development in infants and influences long-term health status.[36] Milk composition varies depending on the duration of lactation, maternal age, general health and educational status, pre-pregnancy body weight, diet and lifestyle factors.[11] Iodine is an important mineral that supports growth and development, and iodine levels in foods other than fish, shellfish and oceanic plants are very low.[37] The use of iodine-enriched salt or iodine supplements is recommended to meet the iodine requirement during pregnancy, when the requirement is increased.[38] Although 90.5% of NW women and 83.3% of OW/OB women who participated in this study stated that they use iodised salt, studies conducted in different regions of Turkey have found pregnant women who do not use iodised salt.[39–41] Since iodine is a mineral that is quickly affected by heat and humidity conditions and is easily lost, it should be stored in dark coloured and sealed containers, and it is recommended to add iodised salt after the food is cooked since it may be lost with cooking.[42] However, it was determined that most of the women participating in this study added salt as soon as they put the food on the stove and stored iodised salt in a transparent glass container in a place where light could see (data not shown). There are iodine-containing foods in the daily diet and the amount of iodine taken with the diet varies from day to day. The exact determine of dietary iodine intake depends on the type, amount and frequency of consumption of iodine-containing foods.[43] The most practical way to ensure iodine intake through food is iodised salt, but the amount of salt consumption of individuals varies and it is difficult to determine the exact amount.[44] In this study, the frequency of consumption of foods with high iodine content, including iodised salt consumption in the last month of pregnancy was analysed and it was found that dietary iodine intake was 184.4 ± 73.8 μg/day in NW women and 186.6 ± 72.3 μg/day in OW/OB women. In a study conducted in Japan, it was found that 73.3% of women had normal BMI before pregnancy and the daily iodine intake was 437.5 ± 167.9 μg according to food consumption frequency.[45] In a study conducted in Spain, it was found that the dietary iodine intake of women was 137 μg per day, regardless of the maternal pre-pregnancy body weight.[46] According to the Turkish Dietary Guidelines 2022, it is recommended that adult pregnant and lactating women should receive 200 μg of iodine daily through diet.[47] In this study, although

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Table 6. Association of infant body weight, height and head circumference at birth and 3 months with leptin, adiponectin, IGF-I and iodine concentrations in cord blood and breast milk (n = 84)

Growth-related factors		Body weight (g)				Height (cm)				Head circumference (cm)				3-month weight gain		3-month height growth	
		Birth		3rd month		Birth		3rd month		Birth		3rd month					
Cord blood		*r*	*p*	*r*	*p*	*r*	*p*	*r*	*p*	*r*	*p*	*r*	*p*	*r*	*p*	r	p
	Leptin	0.001	0.991	0.129	0.243	0.026	0.813	0.058	0.603	0.063	0.568	0.095	0.391	0.160	0.147	0.050	0.650
	Adiponectin	−0.080	0.470	−0.119	0.279	−0.216	0.048	−0.180	0.102	−0.036	0.743	−0.068	0.541	−0.088	0.428	−0.081	0.465
	IGF-I	−0.077	0.484	−0.126	0.254	−0.120	0.276	0.106	0.339	−0.026	0.817	0.004	0.973	−0.098	0.377	0.187	0.088
	Iodine	0.038	0.732	0.055	0.617	0.068	0.536	0.017	0.875	0.015	0.890	0.037	0.741	0.040	0.719	−0.079	0.473
Breast milk	**Leptin**	0.007	0.951	0.216	**0.049***	0.044	0.694	0.100	0.365	0.209	0.057	0.174	0.114	0.264	**0.015***	0.088	0.424
	Adiponectin	0.220	**0.045***	0.292	**0.007***	0.116	0.293	0.212	0.052	0.190	0.084	0.161	0.143	0.195	0.076	0.175	0.111
	IGF-I	−0.051	0.644	0.068	0.540	−0.087	0.432	0.198	0.071	0.222	**0.043***	0.128	0.247	0.124	0.261	0.273	**0.012***
	Iodine	−0.078	0.480	−0.048	0.664	0.085	0.441	0.002	0.986	−0.133	0.228	−0.082	0.461	0.000	0.999	0.103	0.350

Pearson's correlation test, $^{*}p < 0.05$.

iodised salt was included in dietary iodine intake in both NW and OW/OB women, it was found that daily iodine intake recommendations were not met. In countries where BMIC has been evaluated, despite the mandatory iodisation of salt, BMIC have been found to be low, and it has been reported that iodised salt consumption does not meet the increased iodine requirements during lactation and infancy.[17]

Maternal BMI in the pre-pregnancy period and excessive weight gain during pregnancy may affect the obesity frequency of the newborn in the following years.[48] Anthropometric measurements of the newborn, such as body weight, height and head circumference, are essential for the evaluation of the growth in the postnatal period.[49] The infants of OW/OB mothers who participated in the study had higher birth weight and head circumference compared to the infants of NW mothers. In studies, it was observed that the body weight and head circumference at birth of infants of OW/OB mothers were higher compared to NW mothers, and the body weight of the mother was positively correlated with the body weight of the newborn.[50,51] In addition, it has been reported that as the BMI of the mother in the pre-pregnancy period increases, the height, body weight and head circumference measurements of the infants at birth also increase.[52]

During intrauterine life, iodine is transferred from the mother to the foetus, and the amount transferred to the foetus is influenced by the mother's dietary iodine intake.[20] The iodine intake of breastfed infants is entirely dependent on BMIC, and it is assumed that approximately 40–45% of the iodine intake of the mother passes into the milk.[13,19] The reference range for BMIC during lactation has not been established and generally<100 μg/L indicates iodine deficiency.[21,22] All women participating in this study had BMIC<100 μg/L (inadequate), these results suggest that adequate iodine is not being provided to infants through the consumption of iodised salt. It is thought that this situation may be due to the fact that the dietary iodine intake of the women participating in the study was below the recommendations and that although they used iodised salt, they did not know the correct storage and use conditions. In the United States, the median iodine level in BM obtained up to 60 hours after birth was 51.4 μg/L.[53] In New Zealand, the iodine status of infants was assessed at 3, 6 and 12 months after birth, and it was reported that the median BMIC was <75 μg/L at all time points, which may indicate iodine deficiency in infants.[54] In Moroccan mothers with moderate to severe iodine deficiency, BMIC measured between 1–6 weeks of lactation was <50 μg/L.[55] Among Norwegian breastfeeding women, 76% of them had a median BMIC of 68 μg/L (inadequate) and an average dietary iodine intake of 121 μg/day (inadequate).[14] It has also been reported that in iodine-deficient areas, BMIC is usually <50 μg/L and the likelihood of meeting the Recommended Dietary Allowances of 90 μg/day for iodine in infants is reduced.[56] Similar to our study results, it has been found that BMIC are insufficient in women who use iodised salt, are well-nourished, but do not take iodine supplements during pregnancy.[57–59]

Maternal body weight leads to changes in the bioactive components of BM that affect infant growth.[60] The importance of questioning the pre-pregnancy body weight of the mother has been emphasised in studies to understand the effect of maternal metabolic status on BMIC.[25] Although there are limited studies evaluating the effect of maternal BMI during pregnancy on BMIC, a negative correlation was found between maternal urinary iodine concentration and BMI.[23,27,28] Although iodine deficiency is high in morbidly obese people, the physiological pathways linking

Table 7. Regression analysis for the relationship between anthropometric measurements of the infant at the third month and leptin, adiponectin, IGF-I and iodine in cord blood and breast milk

	Body weight (g)			Height (cm)			Head circumference (cm)		
	β	Standard error	*p*	*β*	Standard error	*p*	*β*	Standard error	*p*
Cord blood									
Leptin (ng/mL)	0.215	0.016	0.069	0.101	0.080	0.389	0.131	0.026	0.276
Adiponectin (mg/L)	−0.149	0.001	0.209	−0.252	0.003	**0.035***	−0.109	0.001	0.368
IGF-I (ng/mL)	−0.146	0.000	0.208	0.147	0.002	0.205	−0.003	0.001	0.977
Iodine (μg/L)	0.071	0.013	0.519	0.005	0.065	0.961	0.039	0.021	0.730
$R^2 = 0.021$; $F = 1.435$; $p = 0.230$				$R^2 = 0.020$; $F = 1.413$; $p = 0.237$			$R^2 = 0.028$; $F = 0.428$; $p = 0.788$		
	β	Standard error	*p*	*β*	Standard error	*p*	*β*	Standard error	*p*
Breast milk									
Leptin (ng/mL)	0.208	0.126	**0.055***	0.063	0.649	0.572	0.159	0.210	0.156
Adiponectin (mg/L)	0.291	0.001	**0.009***	0.174	0.006	0.124	0.139	0.002	0.220
IGF-I (ng/mL)	−0.047	0.000	0.672	0.147	0.002	0.204	0.056	0.001	0.625
Iodine (μg/L)	−0.066	0.012	0.533	0.015	0.064	0.894	−0.083	0.021	0.452
$R^2 = 0.086$; $F = 2.946$; $\boldsymbol{p = 0.025}$*				$R^2 = 0.025$; $F = 1.538$; $p = 0.199$			$R^2 = 0.017$; $F = 1.350$; $p = 0.259$		

*Multiple linear regression analysis, *p < 0.05.*
The model was adjusted for maternal age, education level, pre-pregnancy BMI, and weight gain during pregnancy.

obesity to iodine deficiency are not clear.[27] It is thought that iodine absorption may be inhibited due to the increased amount of fat in the diet of obese individuals, inflammatory cytokines secreted by adipocytes and insulin resistance may modulate NIS expression on the apical surface of enterocytes, leading to a decrease in active iodine accumulation.[28] In a study conducted in Thailand, it was reported that maternal body weight may affect BMIC.[61] In another study, no significant difference was observed between the BMICs of NW and OW/OB women.[25] In our study, no significant difference was found between women's pre-pregnancy BMI and BMIC. Because the dietary iodine intake of women in both groups was inadequate and at similar levels, which led to inadequate BMIC in both NW and OW/OB groups.

It has been reported that leptin in maternal serum, cord blood and BM may affect infant growth in later years.[62] Leptin in BM is influenced by maternal adiposity and tends to increase with maternal body weight.[63] In this study, it was found that leptin in BM of OW/OB women was higher than that of NW women. Other studies have also reported higher leptin concentrations in breast milk of OW/OB women.[60,64,65] Adiponectin concentration in BM is affected by maternal BMI.[11] In our study, adiponectin concentrations in cord blood and BM of OW/OB women were found to be higher than NW women. Previous studies have also found a positive correlation between adiponectin concentration in BM and maternal BMI.[66,67] In our study, a positive correlation was found between pre-pregnancy BMI and cord adiponectin, suggesting that adiponectin passing through cord blood to infants of mothers with high BMI may affect the birth weight of infants. On the other hand, since there are also studies that did not find a relationship between maternal BMI and adiponectin concentration in milk[64,68,69] no definite inference can be made.

It has been reported that IGF-I level in cord blood reflects fetal IGF-I at birth and affects the birth weight of the infant.[5] In our study, IGF-I concentrations in BM and cord blood of OW/OB women were found to be higher. In a study, it was found that leptin and IGF-I in the milk of NW and OB mothers did not differ.[70] In another study, it was reported that IGF-I in BM did not differ significantly according to pre-pregnancy BMI.[64] In our study, a positive association was found between maternal BMI and IGF-I in BM, whereas a negative association was observed between weight gain during pregnancy and IGF-I concentration in BM. It was thought that this may be due to the fact that most of both NW and OW/OB women had weight gain in pregnancy within the normal range and obese women gained less weight during pregnancy. Hormones such as adiponectin, leptin and IGF-I in BM have an effect on supporting growth, regulating appetite and energy intake, and shaping body composition later in life.[71] In infants, leptin levels are involved in the expansion of energy stores necessary for survival and rapid growth.[72] In our study, a positive correlation was found between the body weight of infants at the third month and weight gain during this period and leptin concentration in BM. Considering that infants born to mothers with high BMI may have high leptin exposure and this may lead to leptin resistance in the infant, it has been reported that appetite regulation in the infant may be impaired and the risk of obesity may increase in later years of life.[73] In the light of the available data, no definite inference can be made between growth-body composition and leptin in early life because leptin in BM may vary depending on maternal adipose tissue.[36] One of the important mediators linking growth in early infancy with maternal metabolic status is BM adiponectin.[67] It has been reported that adiponectin levels in BM differ depending on the BMI of the mother, show pleiotropic properties in the first years of life depending on nutrient availability, and support body weight gain and survival in children.[74] In our study, adiponectin concentration in BM showed a positive correlation with the body weight of the infant both at birth and at 3 months. In a study conducted in the Philippines, it was found that infants exposed to high levels of adiponectin through BM had a higher weight at 2 years of age.[75] A positive correlation was found between adiponectin concentration in BM samples taken at 4 and 6

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months after birth and body weight and height of the infant.[76] In addition, high adiponectin concentrations in BM at 1, 3, 5 and 6 months after birth were found to be associated with rapid weight gain in the 2nd year of life.[66] On the other hand, there are studies indicating that there is no relationship between adiponectin in BM and infant height and body weight.[9,77] IGF-I is one of the BM hormones involved in fetal growth, and there is limited literature indicating that IGF-I is associated with body weight and height of infants.[78] Although there is a positive correlation between weight gain in the early stages of life and IGF-I in BM, the net effect of endogenously produced IGF-I in BM is not known.[70] In our study, IGF-I in BM was found to be positively correlated with birth head circumference and height growth at three months. In a study, it was found that infants born to diabetic mothers were exposed to higher IGF-I through BM and this was positively correlated with infant body weight.[79] It has also been reported that there is a relationship between IGF-I concentration in BM and weight-for-height z-scores of infants.[70] Further studies are needed to draw clear conclusions about the relationship between IGF-I in BM and infant growth.[80] In our study, no significant effect of iodine concentration in cord blood and BM on body weight, height and head circumference at birth and 3 months was found. In our study, after adjustment for confounding factors such as maternal age, education level, pre-pregnancy BMI and weight gain during pregnancy, a significant and positive relationship was observed between leptin and adiponectin concentrations in BM and infant body weight at 3rd months. However, no relationship was found between growth-related hormones (leptin, adiponectin, IGF-I) and iodine concentration in BM and cord blood and body weight and head circumference of the infant at 3rd months. The reason why no correlation was found between anthropometric measurements of infants and iodine in our study may be attributed to the fact that BMIC was insufficient in all mothers. In a systematic review, no association was observed between iodine intake and infant growth due to the heterogeneity of the populations in terms of iodine sufficiency.[81] Iodine supplementation in iodine-deficient mothers could increase BMIC, thereby allowing a clearer understanding of the effects of iodine on infant growth. In a study, it was reported that body weight increased more in the first year of life in infants with higher levels of iodine intake through BM and that iodine intake in the early period of life may affect the growth trajectory of the infant independently of the mother's pre-pregnancy body weight.[25] Another factor that may hinder clear conclusions regarding the BMIC and infant growth across studies could be the differences in the methods used for analysing BMIC. In future studies, BMIC of women living in different regions of Turkey should be determined, and the impact of maternal iodine levels, both low and high, on infants' growth patterns should be assessed.

Limitations

Dietary iodine intake of the mothers was evaluated by food frequency questionnaire. It is recommended that urine iodine concentration should also be analysed to clearly determine iodine intake, but the fact that urine iodine concentration could not be analysed in the mother due to limited budget is one of the limitations of the study. In addition, reasons such as the inability to work with a larger sample size due to limited budget, the fact that the region where the study was conducted receives a lot of rainfall and is risky in terms of iodine deficiency, and the fact that the study was carried out in a population with low education and socio-economic level prevent the generalisability of the results to the whole population. It is thought that different methods were used in BM collection and BMIC analysis in the studies and these differences in analytical methods may have prevented a clear demonstration of the relationship between iodine and growth parameters. Therefore, standardisation of milk collection and analysis methods is recommended. Furthermore, it is suggested that variants in the SLC5A5 gene encoding the NIS gene may be a factor that may affect BMIC and this should be taken into consideration in future studies.

Conclusion

Our study showed that maternal pre-pregnancy BMI may affect infant body weight through leptin and adiponectin concentrations in BM. In addition, it was revealed that the pre-pregnancy BMI of the mother was positively associated with IGF-I in BM and affected the birth head circumference and height growth of the infants. BMIC of the women who participated in our study was found to be severely inadequate. No relationship was observed between maternal BMI and iodine concentration. Iodine concentration in BM and cord blood did not significantly affect the anthropometric measurements of infants. In order to better understand the impact of BMIC on growth, well-planned studies with large samples are needed.

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Competing interests. 'None'. All authors declare that they have no conflicts of interest.

Ethical Standards

Ethics committee permission numbered 10354421-2022/02-01 was obtained from Alanya Alaaddin Keykubat University Faculty of Medicine Clinical Research Ethics Committee and research permission was obtained from Alanya Training and Research Hospital. The study was conducted in accordance with the principles of the Declaration of Helsinki. Written informed consent was obtained from the volunteer mothers and the infants' participation in the study was approved by their mothers.

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