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Association between maternal nutrition and fetal developmental profile: Do leptin and adiponectin have a significant role?.

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Abstract

Background: Leptin and adiponectin, which are primarily produced by adipose tissue, have recently been identified as key mediators in the fetal developmental process. Modulation of these adipokines in early life, therefore, provides potential opportunities to improve or reverse the adverse complications associated with an abnormal fetal developmental profile.

Aim : The purpose of this study was to determine the effect of maternal dietary habits on fetal leptin and adiponectin levels and fetal developmental outcomes.

Subjects and Methods: Sixty-two mothers between the ages of 18 and 38, as well as their full-term neonates, were enrolled in this study, whether they had a normal delivery or a Cesarean section, with no birth complications. All mothers were subjected to a full pregnancy history in order to determine their gestational age, as well as a full examination that included measuring and recording all of their anthropometric measurements. Clinical examinations were performed on newborns, and the Apgar score was also recorded. Newborns were classified as small for gestational age (SGA), appropriate for gestational age (AGA), or large for gestational age (LGA) based on their birth weight (LGA). ELISA measured leptin and adiponectin levels in both mother's serum and cord blood serum.

Results: Mothers who consumed fish and fats during pregnancy were not at risk of having SGA babies, and SGA babies had significantly lower adiponectin levels than AGA and LGA babies. Leptin levels increased significantly as they passed from SGA to LGA. Leptin distribution was significantly higher in fetuses of mothers who consumed daily breakfast during pregnancy than those of mothers who did not consume breakfast. Infant adiponectin distribution was significantly higher in fetuses of mothers who ate regular fats than in fetuses of mothers who ate a low fat diet. fetuses adiponectin distribution was significantly higher in infants of mothers who consumed sugary drinks once per day than those of mothers who did not consume sugary drinks. Furthermore, there is a significant positive correlation between infant weight, infant length, infant head circumference, infant mid-arm circumference, and levels of both fetal leptin and fetal adiponectin. A highly significant negative correlation was found between maternal adiponectin and fatel leptin levels, while a highly significant positive correlation was found between maternal leptin and fatel leptin levels.

Conclusion: This study shed light on the important role of maternal nutrition during pregnancy in fetal body fat composition. This study also provides clear evidence for the influence of leptin and adiponectin on fetal development.

Keywords: Maternal nutrition, Leptin , Adiponectin, Gestational age, Fetal developmental profile.

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Introduction

Poor maternal nutrition during pregnancy can have an impact on the course of the pregnancy and fetal growth, resulting in lower GA and poor intrauterine growth [1]. It is well known that GA and birth weight are important predictors of neonatal survival and health [2].

Leptin and adiponectin are the most common hormones associated with adipose depots that influence metabolism and energy homeostasis[3]. The placenta, as well as maternal and fetal adipose tissues, produce leptin during pregnancy, which regulates fetal growth. Leptin has been shown in animal models to play a role in the growth and maturation of the heart, brain, kidneys, and pancreas[4]. Fetal leptin is primarily derived from fetal adipose tissue, whereas the placenta primarily produces leptin for the maternal side [5].

Leptin is detectable in the second trimester and its level rises from the middle of the third trimester to term, according to the reservoir of fetal adipose tissue [6], as it is commonly synthesised by white adipose tissues (WAT) and released into the circulation proportionally to body fat mass [7]. This means that fetal leptin levels rise in tandem with fetal growth [8]. It is worth noting that early-life increases in leptin concentrations are thought to play a role in brain development [9]. It also has protective effects on paediatric neurological diseases [10].

Adiponectin is an insulin-stimulating hormone produced by adipose tissue that increases fatty acid and glucose absorption as well as catabolism in muscle and liver [11]. Adiponectin may play a role in fetal growth and development because insulin regulates it to a large extent [12]. As a result, it is possible to propose

that high levels of adiponectin in the placenta and foetus are associated with fetal growth [13].

However, Sivan et al. [14] proposed that neonatal adiponectin is derived primarily from fetal tissues rather than maternal or placental tissues, and studies on newborn infants show that serum adiponectin levels are positively related to birth weight and leptin levels [15]. These findings are supported by Saito et al. [16], who found that adiponectin levels are significantly higher in large for gestational age (LGA) and appropriate for gestational age (AGA) neonates than in small for gestational age (SGA) neonates (SGA). Adiponectin's role in brain development is noteworthy because it has been discovered that adiponectin acts locally in the brain to govern key processes of brain physiology such as neuronal excitability and synaptic plasticity, neuroprotection, neurogenesis, and glial cell activation regulation [17].

As a result, adipokines like leptin and adiponectin, which are primarily produced by adipose tissue, have been identified as key molecules in processes underlying many phenotypic traits associated with embryonic programming.
As a result, manipulating adipokines early in life has revealed potential options for improving or reversing the unfavourable consequences of atypical programming, as well as insight into some of the mechanisms implicated in the development of chronic disease across the life course [18].

Aim of the work

This study was undertaken to explore the impact of fetal leptin and adiponectin that may result from the maternal dietary habits during pregnancy on the developmental outcomes of the neonates.

Subjects and Methods

Sixty-two mothers and their neonates were recruited from the Obstetrics and Gynecology Department, El Galaa Teaching Hospital. Parental written informed consent was obtained from all study participants after explaining the aim and the implementation procedures of the study. Inclusion criteria included women between 18 and 38 years of age and their full-term babies from normal delivery or Cesarean section, without any birth complications like perinatal asphyxia, or acute fetal suffering signs. Exclusion criteria included women presenting with diabetes, preeclampsia, antiphospholipid syndrome, connective tissue diseases, chronic infection, alcoholism, or smoking during pregnancy. All mothers were subjected to a full history of pregnancy to detect their gestational age, a full examination that included measuring and recording of all their anthropometric measurements. All anthropometric measurements have been obtained using standardised equipment and following the recommendations of the International Biological program **[19].** Maternal anthropometric measurements were made on the participants wearing a minimum amount of clothing. The weights of pregnant women were measured using a digital weighing balance with a sensitivity of 100 g. Total gestational weight gain was estimated by subtracting the early first trimester weight (self-reported in the hospital interview) from the last measured weight before delivery. and a nutrition sheet including a questionnaire about the maternal nutritional food intake during pregnancy. A semi-structured questionnaire and a data record form were used to collect information about the mother's profile.

The paediatrician performed a thorough clinical examination on the neonates, which included a chest, heart, abdomen, and central nervous system examination. The Apgar score, which ranges from 1 to 10, was also used to assess neonatal condition at birth at 1 and 5 minutes after delivery. Infants were scored on a scale of 0 to 2 in five categories (skin colour, muscle tone, reflexes, respiratory effort, and heart rate), and the total score was calculated by adding the points from each category [20]. Anthropometric data was collected prior to the start of breast feeding. Without diapers, newborns were weighed (in kilogrammes) on an electronic digital infant scale (Laka).The length (in centimeters) was measured in the supine position, using a stadiometer (Seca 416) composed of a stationary head-board and a movable foot board. head and mid upper arm circumferences (cm) were also measured **[21].** Newborns were assigned to small for gestational age SGA (lower than 10th percentile), appropriate for gestational age AGA (between 10th and 90th percentile) and large for gestational age LGA (higher than 90th percentile).

Venous blood samples (5 ml) were withdrawn from each mother participating in the study immediately before labour, and 5 ml were taken from the cord blood. The serum of the mother's blood and the cord blood were separated by centrifugation under cooling at 4°C for 10 min. and storedat200°C for determination of leptin and adiponectin by ELISA using Glory Science (USA) according to manufacturer's manuals.
This study was conducted in strict accordance with the regulations and guidelines of the ethics committee for Medical Research of the National Research Centre, which approved the study protocol under the Registration Number (20 122).

Statistical analysis.

Statistical analysis was performed using the statistical package for social sciences (SPSS) version 21 for windows (IBM Corp., Armonk, NY, USA). Continuous data was expressed as mean standard deviation, minimum, maximum. Pearson's correlation analysis was conducted to evaluate the association between continuous exposure and continuous covariates. Categorical data was expressed as frequencies and percentages, and was analyzed with the two-tailed chi square test. Continuous data was compared according to nutritional groups and social factors using Mann-Whitney U and Kruskal-Wallis as nonparametric tests. Multiple linear regression analysis was done to identify the effect of multiple maternal factors on a dependent variable (infant serum leptin). $P<0.05$ was accepted as statistically significan

Results

A total of 62 mother-newborn pairs were enrolled in this study. The mean of maternal age was 26.03 ± 5.267 years. Mothers mean of BMI were 30.519± 5.835.The mean of gestational age was 37.60± 1.38 weeks. The maternal and neonatal demographic , anthropometric and laboratory data are shown in Table 1.

	Mean	**Std. Deviation**
Maternal age (Years)	26.03	5.267
Maternal weight (kg)	76.556	15.7245
Maternal height (cm)	158.31	6.373
Maternal BMI (Kg/cm^2)	30.519	5.835
Infantile BMI	2.31	.801
Infantile weight (kg)	2.856	.8773
Infantile length (cm)	46.73	3.842
Infantile head circumference (cm)	33.90	2.288
Infantile mid arm circumference (cm)	10.024	1.6357
Apgar score at first minute	5.47	1.561
Apgar score at fifth minute	7.91	1.443
Gestational age (weeks)	37.60	1.384
Maternal adiponectin(pg/ml)	1185.56	299.928
fetal adiponectin (pg/ml)	1205.43	344.517
Maternal leptin (pg/ml)	8.019	1.6504
fetal leptin (pg/ml)	7.321	2.1109

Table 1. Demographic , anthropometric and laboratory data of mothers and their infants

Table 2 illustrates the effect of maternal nutrition on gestational age categories. The results reveal insignificant association (p>0.05) between maternal breakfast and gestational age regarding AGA and SGA (Table 2a) as well as AGA and LGA (Table 2b).The data in Table (2c) show that mothers with irregular fish consumption are more at risk of having infants SGA comparing with frequent fish consumption one or more days in a week (p = 0.031).The results of Table (2c) also demonstrate that mothers with irregular fat consumption are more at risk of having SGA infants compared to those with regular fat consumption (p = 0.003). Moreover, the findings of Table (2c) indicate that there is no significant association between frequent sugary drinks taken by the mother and gestational age (p > 0.05) regarding AGA and SGA. The data in Table (2d) display that there are no significant associations between maternal intake of fish or sugary drinks and having infants LGA (p > 0.05). However, mothers who are eating fat once per week or more are more at risk of having LGA infants compared to those not having fat in diet (p = 0.04).

			Gestational age categories		Total	P	OR
			Small for gestational age	Appropriate for gestational age			
Daily breakfast	Yes	Count	14	15	29	0.951	1.037
		% within Daily breakfast in pregnancy	48.3%	51.7%	100.0%		
	No	Count	9	10	19		
		% within Daily breakfast in pregnancy	47.4%	52.6%	100.0%		

Table 2a. Effect of mother's breakfast during pregnancy on gestational age categories: Comparison between small for gestational and appropriate for gestational age.

			Gestational age categories		Total	P	OR
			Large for gestational age	Appropriate for gestational age			
Daily breakfast	Yes	Count	11	15	26	0.273	0.135
		% within Daily breakfast in pregnancy	42.3%	57.7%	100.0%		
	No	Count	2	10	12		
		% within Daily breakfast in pregnancy	16.7%	83.3%	100.0%		

Table 2b. Effect of maternal breakfast during pregnancy on gestational age categories: Comparison between large for gestational and appropriate for gestational age.

			Gestational age categories		Total	p	OR
			Small for gestational age	Appropriate for gestational age			
Fish intake	No	Count	17	3	20	0.031*	6.927
		% within Fish intake	85.0%	15.0%	100%		
	Once /w	Count	7	7	14		
		% within Fish intake	50.0%	50.0%	100%		
	2-3 times/w	Count	0	1	1		
		% within Fish intake	0.0%	100.0%	100%		
Fats	No	Count	1	0	1	0.003*	11.484
		% within Fats	100.0%	0.0%	100%		
	once/w	Count	8	0	8		
		% within Fats	100.0%	0.0%	100%		
	> once/w	Count	15	25	40		
		% within Fats	37.5%	62.5%	100%		
Sugary drinks	No	Count	12	4	16	0.070	7.055
		% within Sugary drinks	75.0%	25.0%	100%		
	Once/d	Count	8	12	20		
		% within Sugary drinks	40.0%	60.0%	100%		
	1-2 times /d	Count	3	8	11		
		% within Sugary drinks	27.3%	72.7%	100%.		
	3 times/d	Count	1	1	2		
		% within Sugary drinks	50.0%	50.0%	100%		

Table 2c. Effect of other nutritional factors during pregnancy on gestational age categories: Comparison between small for gestational and appropriate for gestational age. *$p < 0.05$ is significant

			Gestational age categories		Total	p	OR
			Small for gestational age	Appropriate for gestational age			
Fish intake	No	Count	1	3	4	0.772	0.517
		% within Fish intake	25.0%	75.0%	100%		
	Once /w	Count	1	7	8		
		% within Fish intake	12.5%	87.5%	100%		
	2-3 times/w	Count	0	1	1		
		% within Fish intake	0.0%	100.0%	100%		
Fats	No	Count	0	0	0.0%	0.04*	4.060
		% within Fats	0.0%	0.0%	100%		
	once/w	Count	2	0	2		
		% within Fats	100.0%	0.0%	100%		
	> once/w	Count	11	25	36		
		% within Fats	30.6%	69.4%	100%		
Sugary drinks	No	Count	2	4	6	0.280	3.838
		% within Sugary drinks	33.3%	66.7%	100%		
	Once/d	Count	8	12	20		
		% within Sugary drinks	40.0%	60.0%	100%		
	1-2 times/d	Count	1	8	9		
		% within Sugary drinks	11.1%	88.9%	100%.		
	3 times/d	Count	2	1	3		
		% within Sugary drinks	66.7%	33.3%	100%		

Table 2d. Effect of other nutritional factors during pregnancy on gestational age categories: Comparison between large for gestational and appropriate for gestational age. *p < 0.05 is significant

the findings in Table 3 show that leptin distribution in fetuses of mothers with regular breakfast intake is significantly higher than that of mothers with irregular daily breakfast (p = 0.033). fetal adiponectin distribution of mothers with high consumption of fat is significantly higher than that of mothers with low fat intake (p= 0.013). Moreover, fetal adiponectin distribution of mothers taking fat more than once per week is significantly higher than that of mothers taking fat once per week (p = 0.013). Fetal adiponectin distribution of mothers taking sugary drinks once per day is significantly higher than that of mothers not taking sugary drinks per day (p = 0.008). However, leptin distribution in fetuses of mothers not taking sugary drinks is significantly lower than that in fetuses of mothers taking frequent sugary drinks once or more per day (p = 0.027).

	regular breakfast intake	**N**	**Mean Rank**	**P**
Maternal adiponectin (pg/ml)	Yes	29	21.78	0.602
	No	15	23.90	
fetal adiponectin (pg/ml)	Yes	30	22.72	0.837
	No	15	23.57	
Maternal leptin (pg/ml)	Yes	27	22.07	0.684
	No	15	20.47	
Fetal leptin (pg/ml)	Yes	27	24.50	0.033*
	No	15	16.10	
	Fish intake	**N**	**Mean Rank**	**P**
Maternal adiponectin (pg/ml)	No	14	11.04	0.534
	1 day/week	6	9.25	
Fetal adiponectin (pg/ml)	No	15	9.53	0.081
	1 day/week	6	14.67	
Maternal leptin (pg/ml)	No	14	11.07	0.162
	1 day/week	5	7.00	
Fetal leptin (pg/ml)	No	14	8.89	0.148
	Fats	**N**	**Mean Rank**	**P**
Maternal adiponectin (pg/ml)	No	1	35.50	0.602
	once/week	8	21.50	
	> once/week	36	22.99	
Fetal adiponectin (pg/ml)	No (a)	1	2.00	0.013* a&b a&c b&c
	once/week (b)	9	14.11	
	> once/week (c)	36	26.44	
Maternal leptin (pg/ml)	No	1	39.00	0.074
	once/week	8	28.88	
	> once/week	34	19.88	
Fetal leptin (pg/ml)	**No**	**1**	9.00	0.186
	Once/day	8	16.31	
	> once/day	34	23.72	

	Sugary drinks	N	Mean Rank	P
Matrnal Adeponectin	No	12	23.50	0.965
	Once/day	21	23.19	
	> once/day	12	22.17	
Fetal adiponectin	No (a)	12	15.42	0.008* (a&b)
	Once/day (b)	22	29.59	
	> once/day (c)	12	20.42	
Maternal Leptin	No	11	26.09	0.294
	Once/day	20	22.20	
	> once/day	12	17.92	
Fetal leptin	No (a)	11	14.45	0.027* (a&b) (a&c)

Table 3. Effect of maternal nutritional factors during pregnancy on materno-fetal adiponectin and leptin levels. *p < 0.05 is significant

Table 4 represents the effect of delivering time on adiponectin and leptin levels in mothers and their infants, fetal adiponectin distribution of mothers delivered in winter is significantly higher than that of mothers delivered in summer (p = 0.002), While, maternal leptin distribution is significantly higher in those delivered in summer than those delivered in winter (p = 0.001).

	Delivery time				P
	Winter		Summer		
	N	Mean Rank	N	Mean Rank	
Maternal adiponectin (pg/ml)	30	24.83	15	19.33	0.184
Ftetal adiponectin (pg/ml)	30	28.05	16	14.97	0.002*
Maternal leptin (pg/ml)	28	17.18	15	31.00	0.001*
Fetal leptin (pg/ml)	28	23.27	15	19.63	0.364

Table 4. Effect of delivery time on adiponectin and leptin levels *p < 0.05 is significant

The results in Table 5 reveal a highly significant positive correlation between infant weight, infant length, and infant head circumference with fetal adiponectin level. A significant positive correlation is noticed between infant mid arm circumference and fetal adiponectin level. A highly significant positive correlation is found between infant weight, infant length, infant head circumference, and infant mid arm circumference with fetal leptin level. A significant positive correlation is detected between infant weight and infant mid arm circumference with maternal weight. A highly significant negative correlation is observed between infant weight and infant length with maternal adiponectin level and a significant negative correlation is detected between infant mid arm circumference and mother's adiponectin level. Also, the data in Table 5 indicate the presence of a highly significant negative correlation between maternal adiponectin levels and maternal leptin as well as fetal leptin levels. A highly significant negative correlation is found between fetal adiponectin level and maternal leptin level. Maternal leptin level shows a highly significant positive correlation with fetal leptin level.

		Maternal age (Years)	Maternal weight (kg)	Maternal height (cm)	Gestational age (weeks)	Maternal adiponectin (pg/ml)	Fetal adiponectin (pg/ml)	Maternal leptin (pg/ml)	Fetal leptin (pg/ml)
Infant weight (kg)	Pearson Correlation	-0.015	0.289*	0.205	0.088	-0.456**	0.484**	-0.023	0.756**
	Sig. (2-tailed)	0.909	0.023	0.110	0.497	0.002	0.001	0.884	0.000
Infant length (cm)	Pearson Correlation	-0.001	0.243	0.170	0.225	-0.381**	0.427**	-0.057	0.637**
	Sig. (2-tailed)	0.993	0.057	0.188	0.078	0.010	0.003	0.715	0.000
Infant head circumference (cm)	Pearson Correlation	-0.100	0.227	0.126	0.194	-0.223	0.559**	-0.152	0.548**
	Sig. (2-tailed)	0.438	0.076	0.330	0.130	0.141	0.000	0.329	0.000
Infant mid arm circumference (cm)	Pearson Correlation	0.030	0.323*	0.164	0.098	-0.380*	0.335*	-0.042	0.617**
	Sig. (2-tailed)	0.815	0.010	0.202	0.446	0.010	0.023	0.790	0.000
Apgar score at first minute	Pearson Correlation	-0.124	0.040	0.230	0.001	-0.129	0.316	-0.359	-0.191
	Sig. (2-tailed)	0.418	0.792	0.129	0.996	0.503	0.095	0.072	0.351
Apgar score at fifth minute	Pearson Correlation	0.042	0.135	0.191	-0.148	-0.256	0.325	-0.108	0.037
	Sig. (2-tailed)	0.784	0.378	0.208	0.331	0.180	0.085	0.600	0.859
Gestational age (weeks)	Pearson Correlation	-0.099	-0.034	0.081	1	0.188	0.071	-0.177	-0.216
	Sig. (2-tailed)	0.442	0.792	0.531		0.216	0.638	0.257	0.164
Maternal adiponectin (pg/ml)	Pearson Correlation	-0.073	-0.125	-0.210	0.188	1	-0.113	-0.401**	-0.546**
	Sig. (2-tailed)	0.634	0.412	0.167	0.216		0.461	0.008	0.000
Fetal adiponectin (pg/ml)	Pearson Correlation	-0.154	0.085	0.084	0.071	-0.113	1	-0.405**	0.143
	Sig. (2-tailed)	0.307	0.576	0.580	0.638	0.461		0.007	0.359
Maternal leptin (pg/ml)	Pearson Correlation	0.115	0.202	-0.123	-0.177	-0.401**	-0.405**	1	0.422**
	Sig. (2-tailed)	0.461	0.195	0.433	0.257	0.008	0.007		0.005
Fetal leptin (pg/ml)	Pearson Correlation	-0.045	0.328*	0.163	-0.216	-0.546**	0.143	0.422**	1
	Sig. (2-tailed)	0.772	0.032	0.296	0.164	0.000	0.		

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Table 5. Correlation between mother and infant anthropometric measurements and Apgar scoring *Correlation is significant at the 0.05 level.

To further analysis the effect of different factors on fetal leptin level, we conducted multiple linear regression analysis using fetal leptin as a dependent variable and mother's characteristic manifestations. The data in Table 6 show that fetuses with high leptin levels are significantly associated with mothers taking breakfast daily, taking fats once per week, delivering in winter, mothers of low serum adiponectin, mothers of increasing height, and mothers with infants of low Apgar score in first minute and high Apgar score in fifth minutes.

	Unstandardized Coefficients		Standardized Coefficients	t	Sig.
	B	Std. Error	Beta		
Constant	15.241	13.505		1.129	0.278
Daily breakfast in pregnancy	-2.272	0.717	-0.459	-3.168	0.007*
Fats	-4.601	1.852	-0.403	-2.484	0.026*
Delivery time	-4.401	1.490	-0.844	-2.954	0.010*
Maternal weight (kg)	-0.001	0.020	-0.005	-0.037	0.971
Maternal height (cm)	0.131	0.051	0.421	2.592	0.021*
Apgar score at first minute	-1.776	0.716	-1.306	-2.480	0.026*
Apgar score at fifth minute	1.750	0.747	1.031	2.342	0.034*
Gestational age (weeks)	-0.409	0.219	-0.273	-1.867	0.083
Maternal adiponectin (pg/ml)	-0.004	0.002	-0.555	-2.578	0.022*
Maternal leptin (pg/ml)	0.186	0.299	0.143	0.621	0.544

Table 6. Multiple linear regression analysis for factors affecting fetal leptin
*$p < 0.05$ is significant

Discussion

The purpose of this study was to elucidate the effect of maternal nutrition on gestational age and the construction of adipose tissue in fetuses. Also, our aim was extended to examine the implications of fetal leptin and adiponectin on the fetal developmental profile.

In the present study, we found that mothers taking fish during pregnancy were not at risk of having infants with SGA. This result matched the study of Amezcua-Prieto et al. [22], who stated that women with a total intake of marine n-3 fatty acids during pregnancy had a low risk of having a SGA newborn. N-3LCPUFAs pass through the placental circulation during pregnancy, affect fetal development and extend the gestation time [23]. The improved fetal growth could be due to the fact that n–3 LCPUFAs raise the ratio of prostacyclin to thromboxane, lowering blood viscosity and encouraging increased placental blood flow, both of which are beneficial to fetal growth [24]. It is worth mentioning that the high consumption of fish and sea food is likely to be profitable for the offspring, as maternal fish intake in pregnancy has been associated with positive fetal neurodevelopmental outcomes [25].

The results of the current work indicated that mothers who were eating fat more than once/week during pregnancy were not at risk of having infants with SGA. This finding is on par with that of the study by Mani et al. [26] which elucidated that high consumption of dietary fat in early pregnancy is linked with increased birth weight and decreased risk of SGA. The tabulated results in the present study demonstrated that leptin distribution in infants of mothers taking daily breakfast during pregnancy was significantly higher than in infants of mothers not taking daily breakfast during pregnancy. It has been reported that a nutrient-rich and energy-appropriate diet during pregnancy is crucial for optimal development and growth of the fetus [27]. According to the reservoirs of fetal adipose tissue, fetal leptin can be detected as early as the second trimester, and its concentration increases from the middle of the third trimester towards term [6]. This means that fetal leptin levels increase in parallel with fetal development [8]. Moreover, fetal leptin has been found to be positively correlated with neonatal weight [28].

This correlation reflects the increment of adipose tissue along with gestational progress, especially during late gestation [29]. It is worth noting that the release of fetal leptin precedes fetal adiponectin of mothers taking breakfast regularly during pregnancy. This phenomenon was explained by Leipala et al. [30]. who stated that fetal leptin is liberated by adipocytes in late stages of differentiation, but adiponectin is secreted only by fully differentiated adipose cells. Thus, fetal leptin secretion started before fetal adiponectin release, as shown in the current study.

Our results demonstrated that the fetal adiponectin level of mothers having regular fat in their diet was significantly higher than that of fetuses of mothers with irregular fat consumption. As mentioned above, the high intake of fats is correlated with increased birth weight and a decreased risk of SGA [26]. Prenatal growth and gestational age play a crucial role in adipose tissue maturation and deposition, altering adipokine production, endocrine release and metabolic functions [30]. The histology of adipose tissue in newborns revealed two populations of cells; small cells

that do not store fat and larger cells that contain fat but have a smaller width than adult fat cells. These cells are responsible for enhanced adiponectin generation in neonates [31]. The current findings show that the fetal adiponectin distribution of mothers taking sugary drinks once per day was significantly higher than that of fetuses of mothers not taking sugary drinks per day. In accordance with our results, Lustig [32]. reported an increased glucose transfer to the fetus from sugar-sweetened beverages during pregnancy that may result in insulin-mediated effects on offspring adiponectin levels, as adiponectin is a well-known insulin-sensitive hormone that plays a vital role in glucose and lipid metabolism [33]. It has also been confirmed in fetal lambs, that an enhancement in fetal glucose feeding during late gestation stimulates fetal adipose tissue deposition [34]. Thus, sugary drinks during pregnancy lead to high fat deposition in the fetus and, in turn, high adiponectin levels.

The fetal leptin distribution of mothers not taking sugary drinks during pregnancy was lower than that of fetuses of mothers taking sugary drinks during pregnancy. The study by Tomoo and his co-workers indicated that leptin is principally produced by the white adipose tissue and liberated into the circulation proportionally to the quantity of body fat mass [7]. hus, the absence of sugary drinks during pregnancy causes a reduction in fetal adiposity, which in turn leads to the lowering of fetal leptin levels as shown in the present work. So, leptin and adiponectin could be applied as markers for adipose tissue development and the amount of adipose tissue in the fetus [30].

In this study, the fetal adiponectin distribution of mothers delivered in winter was significantly higher than that of mothers delivered in summer. In winter, if the maternal temperature descends, umbilical or uterine blood flow will be decreased. Reduced umbilical flow can put fetal and placental nutrition, oxygenation, and metabolic waste disposal at risk. The increase in the fetal metabolic rate due to cold stress will reduce hypothermia and increase the energy demand [35]. Fetal energy demands utilize carbohydrates as the primary fuel, which accounts for 80% of fetal energy. Although the placenta maintains a continuous interrupted supply of maternal glucose to the fetus, the fetal glucose metabolism depends on fetal insulin production to enhance the utilization of glucose by sensitive tissues [36]. As adiponectin enhances insulin sensitivity and improves glucose metabolism, so adiponectin increases in fetal compartments [37].

As shown in the present results, maternal leptin distribution was significantly higher in those delivered in summer than in those delivered in winter. The study of Al-Azraqi [38] found that heat stress significantly increases leptin concentrations in the exposed group compared to the thermo neutral control group. The oxidative stress induced by heat stress has been found to increase lipid peroxidation [39]. The increased fat oxidation was found to be correlated with an increased leptin concentration [40].

The data in this study demonstrated that SGA infants have significantly lower adiponectin than AGA and LGA. Also, significant differences in leptin between the three groups were detected with an increase in leptin level passing from SGA to LGA. The depletion in adiponectin level in SGA is comparable to that obtained in the study of Kamoda et al. [41] which indicated that the level of serum adiponectin shows a significant decline in SGA than in AGA neonates owing to the decreased quantity of brown adipose tissue in SGA neonates. Our results go hand in hand with the study of Martinez-Cordero et al. [42] which recorded lower leptin levels in SGA than in AGA infants. As a result, it appears that gestational age, which indicates maturity, is a significant operator of leptin levels in the fetus. In the present approach, a highly significant positive correlation has been detected between infant weight, infant length, infant head circumference and fetal adiponectin level. A significant positive correlation has been detected between infant mid arm circumference and fetal adiponectin level. These findings come in line with more than one study as adiponectin levels were assigned to be affected by being born SGA and weight gain [43]. Also, strong positive correlations between adiponectin level at birth and weight, length, head circumference, and gestational age have been reported. [44].

Hansen-Pupp et al. [45] stated that adiponectin concentrations at birth have a significant positive correlation with anthropometric measures and gestational age at birth. In terms of the mechanism by which adiponectin regulates growth, it has been established that fetal adiponectin has a role in both insulin sensitivity and the availability of nutrients such as fatty acids, which may affect both fetal and childhood growth [46]. This positive correlation is compatible with the suggestion that in newborns the adipose tissue is composed mainly of small, newly differentiated adipocytes that lack the factors that are responsible for inhibition of adiponectin production. Thus, the prevalence of small adipocytes in newborns' adipose tissue may explain the extremely high levels of adiponectin in cord blood. A highly significant positive correlation has been found in the present study between infant weight, infant length, infant head circumference, infant mid arm circumference and fetal leptin level.

In term infants, leptin levels showed a positive correlation with birth weight, gain in fat mass, and body mass index (BMI) [47]. Compelling evidence indicates the role of leptin in fetal growth and development [48]. Leptin levels of infants at birth have been found to be positively correlated with BMI and head circumference [47]. This could indicate either a basic association with adipose tissue or an active involvement of leptin in fetal growth, as leptin is known to influence both fetal and neonatal development, including head circumference [49].

Moreover, leptin deficiency has been linked to alterations in brain volume and structure [50]. In accordance with our results, it has been reported that in full-term newborns, the leptin and adiponectin levels showed a strong correlation with all anthropometric variables [51].

The current results demonstrated a significant positive correlation between infant weight, infant mid arm circumference and mother weight. Rijvi et al. [52] recorded that there is a strong association between maternal weight gain and the birth weight of the fetus. There was a proportional increase in mean birth weight with an increase in maternal weight gain throughout pregnancy, and this increase was statistically significant. Our finding shows parallelism with the study of Nagmoti et al. [53], which demonstrated a positive association between maternal BMI and weight with infantile parameters. This suggests that maternal size has the greatest impact on fetal growth as measured by birth weight, length, and head circumference. [54]. A highly significant negative correlation has been found between infant weight, infant length and maternal adiponectin level. A significant negative correlation has been detected between infant mid arm circumference and maternal adiponectin level. The association between maternal adiponectin concentration and fetal growth is less clear. A negative correlation between maternal adiponectin and fetal birth weight has been reported by the study of Ong et al. [55]. The maternal blood adiponectin levels were significantly lower than those of the umbilical blood and the cord blood adiponectin was positively associated with anthropometric measures at birth [56].

The data in this study indicated the presence of a highly significant negative correlation between maternal adiponectin levels and maternal leptin as well as fetal leptin levels. During pregnancy, there is an elevated level of leptin in the mother's body due to the enhancement of total fat content [57]. and this leads to a decrease in the maternal adiponectin concentration [58]. Human pregnancy is connected with increased food intake, which prevents maternal nutrient depletion and allows for enhanced nutrient delivery to the growing fetus, in contrast to leptin's normal influence on satiety [59]. Injection of leptin directly into the brains of pregnant Sprague-Dawley rats had little effect on lowering food intake, according to the study by Ladyman and Grattan [60].

This disparity is caused by central leptin resistance, which arises during the second trimester of human pregnancy and is thought to be caused by a decrease in hypothalamic ObRb expression. [61].As a result, elevated leptin concentrations and signalling play a significant role in the control of food intake during pregnancy. These data imply that fetal leptin levels are directly related to fetal fat mass (as in adults), with the maternal contribution being minor [62]. As shown in the present work, a highly significant negative correlation has been found between fetal adiponectin level and maternal leptin level. This was related to the study of Dridi and Taouis, [63] which found a negative association between cord adiponectin and maternal weight gain. The mechanisms that control fetal plasma adiponectin levels are largely unclear.

The present results revealed a highly significant negative correlation between maternal leptin level and maternal adiponectin level and this is in concurrence with Manoharan et al. [58] study which revealed that the level of adiponectin is negatively correlated with body fat. The amount of leptin in the body is proportional to the amount of adipose tissue present [64]. Since the quantity of adipose tissue in the maternal body increases during pregnancy, the level of adiponectin decreases [65]. Maternal leptin level showed a highly significant positive correlation with fital leptin level. This coincides with Lucasa et al. [66] study which showed higher leptin concentrations in both cord blood and post-delivery maternal serum. During pregnancy, there is an elevated concentration of leptin in the maternal body due to the increase in total fat content, production of this adipokine in the human placenta, and increasing energy requirements of the mother, placenta, and fetus [57].

Leptin is thought to have a role in maximising the availability of substrates needed for fetal growth, particularly through mobilizing maternal fat stores, which are linked to the newborn's birth weight. According to Perichart-Perera et al. [67], the concentration of leptin during pregnancy may be a predictor of newborn size at birth and is linked to the mother's weight.

Multiple linear regression analysis revealed that fetal leptin levels are significantly dependent on maternal characteristics and manifestations during pregnancy, such as taking daily breakfast and fat once per week, delivering in winter, increasing height, decreasing Apgar score in the first minute, increasing Apgar score in the fifth minute, and adiponectin decreasing levels.

Finally, it is important to mention that leptin has a possible role in brain development [68], neurogenesis [69], particularly during the development of the CNS, [70]. Leptin has also been shown to enhance cognition through the regulation of hippocampal function. Moreover, leptin can significantly improve cAMP-response element binding protein (CREB) phosphorylation *via the* MAP kinase/extracellular signal-regulated protein kinase (ERK1/2) pathway [71]. ERK1/2 phosphorylation (pERK1/2) can directly activate the protein signaling cascade regulating a variety of cellular processes such as nerve growth, survival, and neuroplasticity. Similarly, adiponectin may help restore neuronal insulin signalling, which is crucial for synaptic plasticity and memory, by modulating glutamate receptor trafficking. [72].

Conclusion

The outcomes of this research shed light on the significance of maternal nutrition during pregnancy and its impact on fetal body fat composition. This study provides clear evidence of the influence of the fetal fat secretome (leptin and adiponectin) on the overall fetal developmental profile, including central nervous system development, which may pave the way for later neurodevelopmental consequences.

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