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The Relationship Between Maternal Obesity With Pregnancy-associated Hypothyroidism, Fetal Health, and Pregnancy Outcomes

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ABSTRACT

Introduction: The prevalence of obesity is increasing worldwide, especially among pregnant women. Maternal obesity is a serious risk factor during pregnancy associated with pregnancy-related complications for the mother and her child.

Objective: This study aimed to estimate the prevalence of Jordanian pregnant women who are overweight or obese. The relationship between high body mass index and selected obstetrical conditions was also investigated.

Materials and Methods: A descriptive, correlational, cross-sectional design was used on a purposive convenience sample of 411 pregnant women in Jordan. Results were obtained through structured interviews, antenatal routine lab tests, physical measurements (height and weight), body mass index (BMI), thyroid function tests (free thyroxine [FT4] and 2e [TSH]), and Edinburgh postnatal depression scale. Descriptive statistics, including means, standard deviation, and inferential statistics, such as Pearson correlation, t-test, and ANOVA, were used to describe and examine the relationship among the study variables.

Results: Based on the results, 58.4% of the participants had one to four pregnancies, and 54.5% had at least one abortion. Based on their weight before pregnancy, there was a high frequency of overweight (29.7%) and obesity (25%) among pregnant women. High maternal BMI for the mother is correlated significantly with pregnancy complications and offspring neurocognitive impairments. Additionally, maternal obesity is a risk factor for hypothyroidism. BMI was correlated with hypothyroidism (r=0.141, P=0.004), fetal distress (r=0.217, P=0.0001), postnatal depression (r=0.161, P=0.0001), and preterm labor (r=0.115, P=0.020). The thyroid function tests and thyroid stimulating hormone levels were correlated with maternal and fetal conditions, such as infertility, fetal death, hemorrhage, and cerebral palsy among children.

Conclusion: High BMI associated with old age is a critical factor related to many maternal and infant health conditions. Repeated pregnancy failures, fetal health conditions, and maternal complications, including hypothyroidism, can be associated with maternal obesity. Healthcare providers should raise awareness among mothers and care providers on the serious conditions associated with obesity.

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Highlights

- There is a high prevalence of obesity in pregnant women.
- There is an association between obesity and pregnancy-related complications.
- High body mass index (BMI) among pregnant women affects the well-being of the offspring.
- Maternal obesity is a risk factor for hypothyroidism.

Plain Language Summary

Mother weight and thyroid function are important factors that interfere with maternal, fetal, and born-child well-being. Findings in this study indicated that the greater the mother's weight, the higher the opportunity for the mother and her child to experience health problems, such as gestational diabetes, postpartum hemorrhage, fetal distress and death, and cerebral palsy for the born child. In addition, decreased thyroid function affects the outcome of pregnancy, which might include the mother's and her child's health.

Introduction

Globally, the prevalence of obesity is increasing, especially among women. Over 50% of women were obese in 138 countries [1]. Maternal obesity is a serious risk factor during pregnancy; obesity in the United States affects 0.29% of women before becoming pregnant [2]. Obesity among pregnant women increases the prevalence of pregnancy-related complications for both mother and child [3]. Defining obesity and overweight according to body mass index (BMI) is a widely accepted [4]. High BMI can be defined as overweight (BMI>24.9 kg/m^2) or obesity (BMI >29.9 kg/m^2) [4]. Obesity and overweight have been documented to affect the mother and her offspring. These complications include prematurity, stillbirth, preterm labor, neural defects, congenital anomalies, miscarriage, postpartum hemorrhage, and fetal distress [5-8]. Additionally, obesity has been associated with reproductive system complications even before conception. Infertility, sub-fertility, and irregular cycles were linked to high BMI [9, 10].

Furthermore, a population-based birth cohort study on 2,379 children at early ages in Spain and Greece revealed an association between prepregnancy obesity and neuropsychological impairment with the learning disabilities of the children [11]. Obesity is a risk factor for thyroid dysfunction during pregnancy. Hypothyroidism affects approximately 2%–2.5% of pregnant women; 0.2%–0.5% of pregnancies with overt hypothyroidism [12]. While this condition increases the risk for pregnancy-related complications, subclinical hypothyroidism (increased thyroid stimulating hormone [TSH] and normal free thyroxine [FT4]) and isolated hypothyroxinemia (normal TSH, decreased FT4) were also found to increase the risks of preeclampsia, placental abruption, spontaneous abortion, postpartum hemorrhage, preterm birth, intrauterine growth retardation, fetal distress, stillbirth, low birth weight, congenital malformations, and offspring neuropsychological impairments [13, 14].

Furthermore, age is a risk factor for obesity. It plays a negative role in thyroid dysfunction tests. A prospective study on 1035 Dutch Caucasian pregnant women revealed a negative association between obesity, primiparity at a younger age, and FT4; higher TSH, pregnancy complications, and offspring impairments were documented with hypothyroidism [15]. Similar findings has been reported in Poland [6].

Thyroxine deficiency (i.e. decreased FT4) with normal TSH in pregnancy is a risk for developing hypothyroxinemia. This condition occurs in the presence of low maternal iodine intake and high consumption by the fetus. A cluster analysis study on 306 otherwise healthy Mexican pregnant women found that obese women with high BMI are at greater risk of developing hypothyroxinemia [16]. Hypothyroxinemia was documented to negatively impact psychological and neurological development, attention deficit and hyperactivity disorders, and autism among children [17, 18]. Pregnancy outcomes in this study refer to any condition affecting the mother or child during pregnancy and labor.

In Jordan, this issue has not been adequately addressed in empirical studies. Therefore, this study aimed to estimate the prevalence of Jordanian pregnant women who are overweight or obese. This study also investigated the relationship between increased BMI with hypothyroidism and selected obstetrical outcomes.

Materials and Methods

A descriptive, correlational, cross-sectional design was used to assess the frequency of maternal obesity, hypothyroidism, and other obstetrical negative outcomes and their correlation with increased BMI.

The target population presents all pregnant women aged 17-50 years old. The inclusion criteria were as follows: Any pregnant woman with no diabetes or hypertension or previous maternal complications (such as preeclampsia and miscarriage). Participant information was obtained from the medical records. The study sample was pregnant women selected from four mother and child health centers. They were purposively selected as they provided services to the most populated cities in Jordan, Amman, and Zarqa. Both cities represented approximately half of the Jordanian population. These cities have 2763000 females, representing about one-quarter of the total population and more than half the female population in Jordan [19]. Participants should receive antenatal care in these public health centers and have a follow-up file. The total sample size required for the study was calculated based on a confidence level of 95%, a margin of error of 5%, and a population size, assuming inferential tests (Pearson correlation, t-test, and ANOVA). The sample size required to represent the population was found to be 384 pregnant women considering the main variables examined in this study (i.e. pregnancy trimester, BMI, thyroid function, pregnancy outcome) using the statistical software G*Power version 3.1.9.4 (medium effect size 0.25, alpha 0.05, and power 0.95). This number is suitable for all planned tests in this studyy [20]. A total of 411 pregnant women were surveyed to improve representation and decrease margin error. In addition, the attrition rate of 20% and the level of testing (i.e. analysis of variance) were considered when calculating the sample size.

The study questionnaire consists of three parts. Part one was demographic data, which included age, hemoglobin level, number of previous pregnancies, and number of abortions. Part two comprised the physical assessment, which included height, weight, and BMI measurement. Part three of the questionnaire included the lab results (TSH, FT4) and history of complications (such as infertility, missed abortion, fetal death, and fetal distress), anthropometric measurements, which included weight and height that were taken for all participants in light clothing, and no shoes during the three trimesters. Weight before pregnancy was obtained from records and was measured using one digital scale to the nearest 0.1 kg.

All measurements and tests were taken during the interview. Height was measured using measuring tape on the wall with the participant standing without shoes, looking straight with heels together, and recorded to the nearest 0.5 cm. The reliability of the anthropometric measures was maintained using the same protocol by the same person using the same equipment. The digital weight scale was used according to manufacturer instructions and calibrated before data collection, and each time it was moved from the place. BMI was calculated as the ratio of weight (kilograms) to the square of height (meters). Obesity is categorized according to age-sex-specific percentiles of BMI using the international obesity task force (IOTF) for age growth charts [21]. BMI was documented before pregnancy and at the end of each trimester; this information was obtained from the medical records. The study significance and instruction for the structured interview were explained to the participants, who are eligible and agreed to take the antenatal lab tests, physical measurements (height and weight), BMI, and thyroid function tests (TSH and FT4). It was explained to the candidates that neither refusing to participate nor withdraw would produce any burden or influence on the care provided to them. Participation was entirely voluntary and anonymous. The data were treated confidentially using code for names and used only by the researchers for research purposes. Information about women's health during previous pregnancies was taken from the digital and paper medical records in the healthcare center, including complications associated with pregnancy to the mother and the born child (including fetal death, repeated abortions, gestational hypertension, placenta previa, postpartum depression, low birth weight, fetal distress, early delivery, cerebral palsy, and children with a learning difficulty). Postpartum depression was measured using the Edinburgh postnatal depression scale (EDPS), 10 screening questions representing symptoms common in women with depression and anxiety during pregnancy. The EDPS English version is a 4-point Likert scale with a total score range between 0 and 30. A score greater than 8 indicates a higher possibility of depression [22].

Data were collected using a standardized interview to fill in the study questionnaire and take physical measurements by assigned data collectors to maintain consistency. The data collection was conducted in the period from March 2019 to March 2020 when the lockdown took place because of COVID-19. Each interviewee was interviewed in person and in the vicinity of the healthcare center in a private room, which was provided by the center manager for the researcher.

All data analyses were performed using SPSS software, version 21 (SPSS, Chicago, IL, USA) software. Minimum values, maximum values, and frequency tables were explored to identify missing data and outliers.

Descriptive statistics, including Means±SD and percentages, were used as appropriate to present the demographic variables, physical measurements, and results of lab tests. Further, percentages were used for pregnancy and offspring complications. Inferential statistics were used to measure the relationship between thyroid and BMI values on pregnancy conditions, such as the Pearson correlation, t-test, and ANOVA according to testing groups.

Results

A total number of 411 pregnant women participated in this study. More than half of the participants (58.4%) had one to four pregnancies, and many participants (54.5%) had at least one abortion (Table 1). It is worth noting here that elective abortion is illegal in Jordan, except in case of expected physical harm to the pregnant. Therefore, all abortions reported in this study were based on medical conditions. Previous abortions were reported in more than 45.5% of the participants, with 25.8% reporting more than two abortions (n=104).

This study found that 51.6% of participants were overweight or obese (Table 2). Of the obese participants, 14.6% had class-1 obesity, 5.6% had class-2 obesity, and 1.7% had class-3 morbid obesity. Just under half of the women (41.6%) were anemic (hemoglobin <11 mg/dL), and the majority (58.4%) had the minimum acceptable hemoglobin during pregnancy, more than 11.0 mg/dL. The value for TSH in the first trimester was 0.1-2.5 mIU/L, 0.2-3 mIU/L for the second, and 0.3-3.5 mIU/L for the third trimester. The normal value is < 3.5 mIU/L [12]. The FT4 is at the lower limit in the first trimester (13.68 Pmol/L; reference range: 12.1-19.6 Pmol/L). Most thyroid function using TSH and FT4 (73%) results were within the normal serum levels accounting for trimester-related levels. High serum levels of TSH distributed across the three trimesters were present in 26% of participants. Low FT4 levels were detected in 12.6% of participants. The relationship between high BMI (>25 kg/m^2) and thyroid dysfunction test showed no statistically significant correlation.

Table 3 presents the rate of pregnancy conditions among the participants. There are high percentages noticed in conditions like postpartum depression (24.6%), fetal death (15.6%), and infertility conditions (14.4%) among obese/overweight compared with non-obese women. The correlations between BMI and the pregnant and the offspring health outcomes were tested using the Pearson correlation coefficient. High BMI was associated with higher postnatal depression (r=0.161,

Table 1. Participants' demographic and reproductive characteristics (n=411)

Factor		Mean±SD/No. (%)	Range
Age (y)		29.65±6.32	17-47
Hemoglobin (mg/dL)		11.10±1.40	7.0-16.0
Pregnancy trimester	1st 2nd 3rd	157(38.2) 77(18.7) 177(43.1)	
Number of pregnancies		4.1±1.1	1-4: 240(58.4) 5-8: 147(35.8) >8: 24(5.8)
Number of abortions		0.99±0.25	0: 224(54.5) 1: 81(19.7) 2-4: 97(23.6) >4: 9(2.2)

Table 2. Physical measurement among participants (n=411)

Variables	Category	Description	No. (%)	Mean±SD
BMI category (kg/m^2)	Underweight	<18.5	5(1.2)	26.33±5.77
	Normal	18.5-24.9	194(47.2)	
	Overweight	25-29.9	122(29.7)	
	Obese class1	30-34.9	60(14.6)	
	Obese class 2	35-39.9	23(5.6)	
	Obese class 3	>40	7(1.7)	
Hemoglobin (mg/dL)		<11	41.6	11.10±1.87
TSH (mIU/L)	1st trimester	0.1-2.5*	157(38.2)	2.872±.54
	2nd trimester	0.2-3*	77(18.7)	2.74±.37
	3rd trimester	0.3-3.5*	177(43.1)	2.45±.54
	Combined		2.67*	
Interpretation of serum levels of TSH	Low		6(1.5)	
	Normal		297(72.3)	
	High		107(26)	
FT4 (Pmol/L)	1st trimester	12.1-19.6**	157(38.2)	13.68±1.98
	2nd trimester	9.6-17**	77(18.7)	11.87±2.13
	3rd trimester	8.4-15.6**	177(43.1)	12.17±2.08
	Combined		12.69**	
Interpretation of serum levels of FT4	Low		53(12.9)	
	Normal		341(83)	
	High		17(4.1)	

Abbreviations: FT4: Free thyroxine; FT3: Free triiodothyronine; TSH: Thyroid-stimulating hormone; BMI: Body mass index.

*Milli-international unit per liter, **Picomoles per litter.

P=0.001), preterm labor (r=0.115, P=0.02), and fetal distress (r=0.217, P=0.001).

A significant correlation was also between BMI>30 kg/m2 and hypothyroidism (r=0.141, P=0.004). No statistically significant relationship was found between pregnancy conditions and high BMI (Table 4).

Thyroid function and BMI had statistically significant correlations with the categories of a range of pregnancy conditions, including fertility (P=0.005), fetus death (P=0.023), thyroid disease (P=0.0001), and cardiovascular disease (P=0.001) due to Table 5.

Discussion

This study showed a high prevalence of overweight and obese pregnant women in all age groups. Similar results were reported in the USA [2]. Another study reported that 45% of pregnant women from South-Asian countries were either overweight or obese during their pregnancy [7]. However, one study reported that 26% of Southern European women were overweight or obese [11]. Another study reported that 29% of Australian pregnant women were overweight [23].

Table 3. Reported pregnancy-related conditions among women (n=411)

Condition	No. (%)	
	Yes	No
GDM	20(4.1)	391(95.1)
Infertility condition	59(14.4)	352(85.6)
Fetal death	64(15.6)	347(84.4)
Repeated abortions	2(0.5)	409(99.5)
Gestational hypertension	4(1)	407(99)
Placenta previa	4(1)	407(99)
Postpartum depression	101(24.6)	310(75.4)
Low birth weight	56(13.6)	355(86.4)
Fetal distress	38(9.2)	373(90.8)
Early delivery	45(10.9)	366(89.1)
Cerebral palsy	36(8.8)	375(91.2)
Children with a learning difficulty	7(1.7)	404(98.4)

GDM: Gestational diabetes mellitus.

Findings in this study have shown that many obstetrical complications have been associated with obesity, such as postnatal depression, preterm labor, and fetal distress. Similarly, numerous reports in the literature indicate significant associations between obesity and obstetrical and offspring complications [4, 6-8]. Furthermore, many of these outcomes were associated with hypothyroidism [6]. This study also revealed the association between high BMI and the risk of hypothyroidism.

In addition, age and high BMI (>35 kg/m^2) were associated with pregnancy complications, offspring malformation, and cognitive impairments. Individuals over 35 are at an increased risk of developing hypothyroidism with either increased TSH level or decreased FT4. Older-age pregnant women are even at more risk for other pregnancy complications such as gestational diabetes, repeated miscarriages, gestational hypertension, and preterm labor, and have negative outcomes for offspring such as children with learning difficulties [13, 23] otherwise, complicated cases before pregnancy, such as fertility problems [9, 10].

Table 4. Correlation between BMI and pregnancy outcomes

Association		r**	P
BMI	Hypothyroidism	0.141	0.004
	Postnatal depression	0.161	0.0001
	Preterm labor	0.115	0.020
	Fetal distress	0.217	0.0001

Gestational diabetes, abortion, stillbirth, preeclampsia, premature, congenital anomaly, gestational hypertension, subfertility secondary infertility (delayed conception), and postpartum hemorrhage had no significant statistically significant correlation (P>0.05).

**The Pearson correlation.

Table 5. Differences in the correlation of thyroid function, body mass index, and pregnancy-associated conditions

Factor	Variables	Mean Square	df	P**
FT4 level	Fertility condition	0.286	2	0.005
	Fetus death	0.244	2	0.023
	Cerebral palsy children	0.060	2	0.006
TSH	GDM	0.054	236	0.009
	Cardiovascular disease	0.056	236	0.0001
	Thyroid disease	0.051	236	0.0001
	Fertility condition	0.150	236	0.0001
	Fetus death	0.169	236	0.0001
	PP hemorrhage	0.107	236	0.010
	PP thyroiditis	0.203	236	0.0001
	PP depression	0.224	236	0.0001
	Low weight birth	0.140	236	0.0001
	History of fetal distress	0.102	236	0.0001
	Preterm labor	0.130	236	0.0001
	Cerebral palsy children	0.110	236	0.0001
BMI category	Fertility condition	0.139	4	0.036
	Fetal death	0.170	4	0.033
	PP Thyroiditis	0.567	4	0.0001
	Low weight birth	0.186	4	0.0001
	Cerebral palsy children	0.083	4	0.0001
FT4 level & TSH	Fetus death	0.146	8	0.024
	Hemorrhage history	0.160	8	0.030
	Thyroiditis history	0.179	8	0.011
	Depression history	0.305	8	0.001
	Low weight birth	0.082	8	0.003
	History of fetal distress	0.144	8	0.0001
	Preterm labor	0.104	8	0.009
	Cerebral palsy children	0.057	8	0.0001
TSH & BMI	Fertility condition	0.149	41	0.0001
	Fetus death	0.102	41	0.025
	Thyroiditis history	0.183	41	0.0001
	Depression history	0.150	41	0.015
	Low weight birth	0.122	41	0.0001
	History of fetal distress	0.059	41	0.006
	Cerebral palsy children	0.066	41	0.0001

Abbreviations: FT4: Free thyroxine; FT3: Free triiodothyronine; TSH: Thyroid-stimulating hormone; BMI: Body mass index; GDM: Gestional diabetes melitus.

**The t-test and ANOVA test.

With FT4 levels outside the normal range, offspring are likelier to have low birth weight, cerebral palsy, and other pregnancy complications [16]. We found an association between abnormal TSH/FT4 levels, antepartum hemorrhage (placenta previa), thyroid dysfunction symptoms, and postpartum depression. Similarly, pre-eclampsia hypertension, preeclamptic toxemia (PET), and eclampsia were 3.5 times, 2.8 times, and 4.5 times higher for overweight pregnant women than non-overweight pregnant women in India [14, 25]. In Pakistan, PET, in obese pregnant women was more than 15% higher compared to normal-weight pregnant women, eclampsia was three-fold greater in obese women, and gestational diabetes mellitus was higher at 23.3% as compared to 6.7% in non-obese [26].

Older age pregnant women are more likely to develop thyroid dysfunction, pregnancy complications, and congenital or neurocognitive fetal complications [15, 26, 27]. However, other studies have suggested that obesity, primiparity, and younger age had abnormal levels of FT4 at all trimesters, higher TSH, pregnancy complications, and offspring problems [27, 28].

A study in India found that higher maternal age and high BMI are risk factors for developing hypothyroidism during pregnancy among 1000 women at a rate of 9.2%, with 8.5% subclinical and only 0.7% having overt hypothyroidism [29]. Extreme obesity also results in high levels of thyroid-stimulating hormone due to abnormality of the hypothalamic-pituitary-thyroid axis [30], supported by this study's findings. As reported in the literature [31], obesity has been associated with both physiological and psychological problems among different groups of individuals, such as pregnant mothers [32]. Therefore, we recommend conducting studies that examine associations between maternal obesity, long term psychological health outcomes. We also recommend conducting larger-scale studies to determine obstetric and offspring conditions after pregnancy among obese women and the subsequent impact on future health conditions and pregnancies.

There were limitations that we experienced in this study. The first limitation is the limited budgeting and data collection settings. This study did not receive any funds, and the research carried out study steps independently. Therefore, it was impossible to include more numbers of women, which represents a second and important limitation. In addition, convenience sampling, which was limited in the place and the time, is another limitation that could be avoided in future more presentative studies. Finally, another limitation is the absence of regional or local reference levels of tests. Hence, we urge researchers to conduct future research on a much greater scale and include plans of defining reference values that apply to middle eastern populations.

The findings in this study documented many pregnancy-associated complications of obesity. Therefore, it is imperative to work on different aspects leading to increased safety of the pregnant woman and the pregnancy. BMI and hypothyroidism are risk factors that can be recognized and thus managed at a low cost. Screening of women, especially among women older than 35 years of age, is a proactive step toward eliminating pregnancy complications related to these conditions.

Ethical Considerations

Compliance with ethical guidelines

Permission was obtained from the Jordanian Research Ethics Committee at the Ministry of Health (No.: 12264).

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Authors' contributions

Conceptualization, data analysis and writing the drafting the manuscript: Lourance Al Hadid and Omymah Z. Al-Rajabi; Data conduction, curation: Marwa Al Barmawi and Omymah Z. Al-Rajabi; Writing editing & review: Ahmad Yahya AL-Sagarat and Marwa Al Barmawi; Final approval: All authors.

Conflict of interest

The authors have declared no conflict of interest.

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