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# Leptin Placental Expression in Pregnant Women with Diabetes: A Case **Control Study**

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#### ABSTRACT **Article Info** Background & Objective: One of the worldwide healthcare problems is Diabetes doi) 10.30699/jogcr.8.2.167 mellitus (DM), and the prevalence of this disease increases steadily, particularly in pregnancy. The several metabolic disorders in the pregnancy were revealed by the Received: 2022/08/27; placenta. The pathogenesis of diabetes mellitus is associated with hyperglycemia, Accepted: 2022/12/10; insulin resistance, and oxidative stress, and it negatively impacts the mother-placenta-Published Online: 22 Feb 2023; fetus system. This research aims to compare the amount of leptin expression, as well as its score and intensity, in the placentas of women with diabetes with those of healthy Use your device to scan and read the controls. article online Materials & Methods: In this work, we used a case-control methodology. Thirty women were diagnosed with diabetes and were placed in one group, while the other 40 served as a comparison. Primary monoclonal antibodies were used for the immunohistochemical analysis of leptin (Abcam, UK). Results: The patients group showed the greatest percentage (23%) of placental expression of leptin. The expression of leptin was high in around 53% of the patient population. The intensity of leptin expression was significantly higher in DM patient than control groups (P>0.05). About 77% of patients group had moderate intensity of leptin expression, while 37.5% of control group had no leptin expression. Conclusion: Diabetes mellitus was related with alterations in expressions of leptin Corresponding Information: as metabolic placental factor. Leptin may affect the pregnancy diverse disorders and Zinah Hammad. pregnancy outcome. Collage of Medicine, University of Babylon, Babil, Iraq Keywords: Leptin, Diabetes mellitus, Pregnancy Email: zinahammad9@gmail.com Copyright © 2023, This is an original open-access article distributed under the terms of the Creative Commons Attribution-noncommercial 4.0 International License <u>© () ()</u>

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# Introduction

One of the worldwide healthcare problems is Diabetes mellitus (DM), and the prevalence of this disease increases steadily, particularly in pregnancy (1). Recently, there has been an uptick in the incidence of diabetes due to factors including pregnant women's increasing age and the rising risk of obesity (2). Frequent complications wererelated to DM in pregnancy includes macrosomia, respiratory distress syndrome, and neonatal death (2).

During gestation, the placental formation is critical for embryonic development and pregnancy consequence, metabolic exchange, hormones, growth factors, and cytokines cross over (3). There are two types of trophoblast cells, known as "extravillous and villous trophoblast," that develop during pregnancy. It is between the decidua and the myometrium of the mother that cytotrophoblasts, which are responsible for implantation, proliferation, differentiation, and infiltration. Through a process known as "the villous route," a syncytiotrophoblast is formed (4). The trophoblast invasion is a pivotal event in the process of reshaping the mother's spiral arteries to provide enough blood flow to the growing placenta and baby (5).

The placenta shows many metabolic abnormalities throughout pregnancy. Hyperglycemia, insulin resistance, and oxidative stress all have a role in the pathogenesis of diabetes, which in turn has negative effects on the mother-placenta-fetal system. Because of this, morphology and physiologically active chemicals undergo changes in production, whose altered expression may suggest several pathological processes (6).

During pregnancy, adipose tissue and the placenta create leptin, a 16-kiloda protein hormone (7), which is considered as essential biomarker. Leptin regulates energy metabolism (8).

Specifically, Leptin influences the production of proinflammatory cytokines, such as tumour necrosis factor alpha and interleukin-6, which in turn influence insulin resistance, endothelial dysfunction, and the development of placental ischemia (9). The

pathophysiology of gestational diabetes mellitus as it relates to the placenta, since difficulties associated with GDM ameliorate after birth. Therefore, placental functions, including placental overgrowth, worry about problems from GDM. Insulin resistance, hyperinsulinemia, and hyperleptinemia are all linked to gestational diabetes, and they all interfere with placental transport and food delivery to the fetus (10).

This research aims to compare the amount of leptin expression, as well as its score and intensity, in the placentas of women with diabetes with those of healthy controls.

### Methods

There was a case-control study. Patients were enrolled at privatehospitals in Babylon province, Iraq.

DM (n = 30) and control (n = 40) were the two comparison groups, comprised of a total of 70 pregnant women.

Immunohistochemistry was performed using a primary monoclonal antibody against leptin. Micrographs were captured using an Olympus BX46

#### Table 1. Age in diabetic pregnancy and control groups

microscope and Cell Sens 47 Entry software, both components of a microscopic image fixation system. The quantitative evaluation of the outcomes of immunohistochemistry experiments was conducted. The photography was done with a 200x and 400x magnification. The photographs did not include the fields of view with tissue abnormalities, staining faults, or artifacts.

With the aid of the software VideoTest-Morphology 5.2, the number of cells expressing the investigated marker was computed

SPSSV.23.0 software was used to conduct the statistical analysis. The mean of continuous data was calculated using the t-test. We employed the Chi test or the fisher exact test for qualitative data. P value <0.05 is regarded as significant.

# Results

<u>Table 1</u> displays the ages of the research groups. The age of DM patients did not differ substantially from that of control groups (P>0.05).

Age years	Patients	Control	P value
Mean ± SD	30.27± 6.33	$29.85{\pm}7.43$	> 0.05
Range	22 - 38	20 - 40	

\*P<0.05 was significant

The Placental expression of leptin in diabetic pregnancy and control, presented in <u>Table 2</u>. The Placental expression was significantly higher in DM

patient than control groups (P>0.05). About 23% of patients group had positive placental expression of leptin.

 Table 2. Placental expression of leptin in diabetic pregnancy and control

Leptin Expression	Patients	Control	P value	
Positive	7	0	0.004*	
Negative	23	40		

\*P<0.05 was significant

The scoring of leptin expression in diabetic pregnancy and control is presented in <u>Table 3</u>. The scoring of leptin expression was significantly higher in

DM patient than control groups (P>0.05). About 53% of patients group had high score of leptin expression, while 67.5% of control group had no leptin expression.

Table 3. Scoring of leptin expression in diabetic pregnancy and control

Scoring	Patients	Control	P value
High	16	0	
Moderate	0	10	0.01*
Low	14	3	0.01
Negative	0	27	

\*P<0.05 was significant

The intensity of leptin expression in diabetic pregnancy and control, presented in Table 4. The intensity of leptin expression was significantly higher in DM patient than control groups (P>0.05). About

77% of patients group had moderate intensity of leptin expression, while 37.5% of control group had no leptin expression.

Fable 4.	Intensity of <b>b</b>	entin expressi	on in diabetic	pregnancy	and control
	intensity of r	cpun capi cooi	on in unaberio	presnancy	and control

Intensity	Patients	Control	P value
М	23	0	
S	0	14	0.01*
W	0	11	0.01
Negative	7	15	
*P<0.05 was significant			

P<0.05 was significant

### Discussion

The Placental expression of leptin in diabetic pregnancy and control, is presented in Table 2. The Placental expression was significantly higher in DM patient than control groups (P>0.05). About 23% of patients group had positive placental expression of leptin. Leptin and its receptor are expressed more frequently in the placenta in cases of GDM, as was discovered in (11). In spite of the fact that placentally generated leptin has been hypothesized to have both autocrine and paracrine roles, its precise role is still up for debate. Human placental leptin has the same size, charge, and immunoreactivity as leptin from adipose tissue and uses the same promoter, but it also contains an upstream enhancer that is unique to the placenta. This suggests a potential role for placental leptin during pregnancy and demonstrates a difference between the placenta and adipose tissue in the regulation of leptin gene expression. Human placenta and fetal membranes have been found to contain both short and long splice variants of the leptin receptor (12), indicating that leptin may play a role in foetal growth and development, maternal leptin transfer to the foetus, or elimination of leptin from the maternal-fetal circulation. Placental leptin may have autocrine and paracrine effects, although its precise function is still unclear. Human placental leptin has the same size, charge, and immunoreactivity as adipose-derived leptin; it also shares the same promoter but additionally a placenta-specific enhancer. includes This demonstrates that placental leptin and adipose leptin are controlled differently, suggesting that placental leptin may play a specific function during pregnancy. As both the short and long splice variants of the leptin receptor have been identified in the human placenta and foetal membranes, leptin may play a role in the growth and development of the foetus, the transport of maternal leptin to the foetus, or the elimination of leptin from the maternal-fetal circulation. Leptin has been detected in human beings, making all of this possible (13). Leptin expression in the placenta of women with GDM may be partially decreased by bioactive dietary ingredients such as polyphenols that may lower circulating leptin levels. The end result is

improved placental nutrition transport and a reduction in central leptin resistance (14, 15).

Previous studies (16, 17) have shown that leptin may be transferred from mother to child via the placenta. Which receptor is mediating this transit is not yet understood, though. The placenta responds physiologically to leptin by undergoing angiogenesis, growth, and immunomodulation (18). The placenta's proliferation, invasion, apoptosis, and protein synthesis are all controlled by leptin throughout the early stages of pregnancy (19, 20). Placental leptin acts as an immunological modulator by regulating the production of T cell cytokines, nitric oxide, and the degradation products of arachidonic acid, which is in agreement with? (21). It's interesting to note that IL-6, IL-1, IL-1, and IFN- all control leptin expression (22).

Increased leptin expression is a hallmark of type 2 diabetes, suggesting that the pro-inflammatory actions of leptin may play a pivotal role in the pathogenesis of this condition. The downregulation of intrauterine proinflammatory cytokines is associated with a healthy pregnancy, and placental leptin may explain why these levels are increased in certain pregnancy illnesses (23).

Leptin expressions have been reported to rise in the placenta following GDM (24), and leptin has even been recommended as a first-trimester biochemical predictor of GDM (25). Additionally, it was hypothesized that hyperinsulinemia would govern the generation of placental leptin, which would operate as a circulating signal to regulate fetal homeostasis (26). Furthermore, it is known that leptin levels in cord blood are controlled by maternal hyperglycemia, which may assist to explain why neonates exposed to GDM have an increased risk of obesity (27). When comparing the placental gene expression profile of normal and diabetic pregnancies, researchers found that GDM was associated with increased leptin synthesis and the production of pro-inflammatory cytokines like IL-6 and TNF, which together create a chronic inflammatory environment that boosts leptin production (28).

Increased amniotic fluid volume, or polyhydramnios, is related with gestational diabetes; this correlation raises the possibility that aquaporins (AQP) such as AQP9 expression is altered in GDM (29). When the mother's blood sugar is under control, the amniotic fluid volume is also normal. Glycerol is another substance that AQP9 can transport, therefore the fetus might possibly receive this substance from it. In this context, we discovered that placentas from women with GDM exhibit excessive AQP9 mRNA and protein expression. These findings could imply that the increased glycerol transport to the fetus during GDM, which is correlated with greater leptin plasma levels which is shown in (30), it may serve to offset any potential increase in the baby's energy requirements during this prenatal metabolic disease.

# Conclusion

The main objective of the current research was to compare the amount of leptin expression, as well as its

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score and intensity, in the placentas of women with diabetes with those of healthy controls. The results demonstrated that diabetes mellitus was related with alterations in expressions of leptin as metabolic placental factor. Leptin can be an effective factor in pregnancy diverse disorders and pregnancy outcome.

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None.

# **Conflicts of interest**

The authors declare no known conflicts of interest.

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