The Association of Body Mass Index and Serum Adiponectin Levels During The Second and Third Trimesters of Healthy Pregnant Women

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ABSTRACT

Background: Adiponectin is a pivotal protein that controls metabolic homeostasis, exhibiting features that enhance insulin sensitivity and reduce inflammation. Adiponectin levels decline progressively during mid- and late pregnancy, following the rise in insulin resistance and the increase in gestational weight gain to support fetal growth and development.

Objectives: The study aims to evaluate the association of serum adiponectin levels with body mass index (BMI) and random blood sugar in healthy pregnant women during the second and third trimesters.

Materials and methods: A case-control study included 100 healthy pregnant women and 100 healthy non-pregnant women as controls; the BMI was calculated manually, random blood sugar was tested using a glucometer, and the enzyme-linked immunosorbent assay technique estimated the serum levels of adiponectin. An independent t-test and a Pearson correlation test were used to analyze the data. Significant results are defined as a p-value less than 0.05.

Results: The serum levels of adiponectin progressively declined from the second to the third trimesters compared with the control group; however, it was statistically non-significant (P-value = 0.901). Adiponectin levels were negatively correlated with BMI in the second and control groups and positively correlated with BMI in the second trimester (r = -0.005, r = -0.129, r = 0.096), respectively. No relationship was found between adiponectin levels and random blood sugar (RBS) in the second and third trimesters and control groups (r = 0.102, r = 0.042, r = 0.050), respectively. No statistically significant associations were observed among each group (P-value > 0.05).

Conclusions: The decline of serum adiponectin levels as pregnancy progresses, in parallel with the rise of BMI and random blood sugar, supports the physiological role of adiponectin in maintaining fetal growth and development.

Keywords: Adiponectin; Pregnancy; Body mass index; ELISA; Hyperglycemia

العلاقة بين مؤشر كتلة الجسم ومستويات الأديبونيكتين في الدم خلال الثلثين الثاني والثالث من الحمل لدى النساء الحوامل الأصحاء

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الخلاصة

الخلفية: الأديبونيكتين هو بروتين محوري يتحكم في التوازن الأيضي، ويظهر ميزات تعزز حساسية الأنسولين وتقلل الالتهاب. تنخفض مستويات الأديبونيكتين تدريجياً خلال منتصف الحمل وأواخره، ويتبعه ارتفاع مقاومة الأنسولين وزيادة الوزن أثناء الحمل لدعم نمو الجنين وتطوره.

الأهداف: تهدف الدراسة إلى تقييم ارتباط مستويات الأديبونيكتين في الدم بمؤشر كتلة الجسم (BMI) وسكر الدم العشوائي لدى النساء الحوامل الأصحاء خلال الثلث الثاني والثالث.

المواد والطرق: شملت دراسة الحالات والشواهد هذه ١٠٠ امرأة من حالات الحمل الأصحاء و١٠٠ امرأة من مجموعات المراقبة الصحية، وتم حساب مؤشر كتلة الجسم يدويًا، وتم اختبار نسبة السكر العشوائي في الدم باستخدام مقياس السكر، وتم تقدير مستويات الأديبونيكتين في المصل بواسطة المقايسة الامتصاصية المناعية للانزيم المرتبط. خضعت البيانات للتحليل بواسطة اختبار t المستقل واختبار ارتباط بيرسون. يتم تعريف النتائج البارزة على أن لها قيمة P أقل من ٠.٠٥.

النتائج: انخفضت مستويات الأديبونيكتين في المصل تدريجياً من الثلث الثاني إلى الثلث الثالث مقارنة بالمجموعة الضابطة، ومع ذلك، كانت ذات دلالة إحصائية غير بارزة (P = 0.901). ترتبط مستويات الأديبونيكتين سلبًا مع مؤشر كتلة الجسم في الأشهر الثلاثة الثانية والمجموعة الضابطة، وترتبط بشكل إيجابي مع مؤشر كتلة الجسم في الأشهر الثلاثة الثانية (r = -0.005 ، r = - 0.129، r = 0.096)، على التوالي. لم يتم العثور على علاقة بين مستويات الأديبونيكتين وسكر الدم العشوائي (RBS) في الثلث الثاني والثالث، ومجموعات المراقبة (r = 0.102 ، r = 0.042، r = 0.050)، على التوالي. لم يلاحظ أي ارتباطات ذات دلالة إحصائية بارزة بين كل مجموعة(P > 0.05).

الاستنتاجات: إن انخفاض مستويات الأديبونيكتين في الدم مع تقدم الحمل في هذه النتائج بالتوازي مع ارتفاع مؤشر كتلة الجسم وسكر الدم العشوائي يدعم الدور الفسيولوجي للأديبونيكتين في الحفاظ على نمو الجنين وتطوره.

الكلمات المفتاحية: أديبونيكتين، حمل، مؤشر كتلة الجسم، تقنية إليزا، ارتفاع السكر في الدم.

INTRODUCTION

Pregnancy involves a multitude of physiological transformations, including the growth of the fetoplacental unit, uterine and breast tissue, amniotic fluid, body water, and maternal fat. [1]

During pregnancy, the maternal physiology undergoes dynamic adaptation. These changes manifest in almost the entire body's physiological system, including the respiratory, cardiovascular, neurohumoral, hematologic, renal, and gastrointestinal systems, which are prompted by the hormonal effects of the placenta and the mechanical adjustments necessary to support the expanding fetus. [2,3]

These adaptive changes are intended to promote the fetus's growth through the provision of sufficient amounts of nutrients and oxygen, as well as to get the mother's body ready for birth and nursing. [4]

Adipose tissue is a potent endocrine organ that produces numerous distinct types of adipokines, including adiponectin, leptin, cytokines such as TNFα, resistin, and many other kinds of adipokines, which play essential roles in regulating inflammatory processes and maintaining metabolic homeostasis. [5,6]

Adiponectin (also known as Acrp30, AdipoQ, apM1, and GBP-28) was first discovered by Scherer et al. in 1995 and was then known as an adipocyte complement-related protein of 30 kDa (Acrp30). [7,8] This protein had been isolated using a subtractive cDNA enriched with adipocyte-specific genes. [9]

Adiponectin protein is secreted in large amounts, mainly by the white adipose tissue (WAT) adipocytes. Low quantities of adiponectin secretion are noticed in several tissues, including myocytes, the liver, human murine osteoblasts, epithelial cells, parenchyma cells, and placental tissue. [7]

Adipocytes release adiponectin into the circulation in the form of three oligomeric complexes: a low-molecular-weight (LMW) trimer weighing approximately 60 kDa, a medium-molecular-weight (MMW) hexamer weighing around 150 kDa, and a high-molecular-weight (HMW) multimer weighing about 420 kDa. These complexes are created through a series of intricate signaling and modification processes. [10]

Adiponectin exerts its physiological effects through binding and interaction with its specific receptors, which triggers the activation of downstream signaling pathways. [11]

Three receptors are known to be specific for the adiponectin hormone, including AdipoR1, AdipoR2, and T-cadherin. [12,13]

Adiponectin possesses pleiotropic functions, including enhancing insulin sensitivity, inducing apoptosis in cancer cells, and exhibiting anti-oxidant and anti-inflammatory properties. These activities could result in diverse effects on different body organs. [14]

Adiponectin plays a crucial role in regulating metabolic adaptations and maintaining homeostasis in the body during pregnancy. [15,16] It has been revealed that the maternal adipose tissue is a primary source of adiponectin during pregnancy, whereas there is no evidence of its secretion from the placenta. [17,18] However, the possibility that the placenta could provide an additional supply of this hormone is still controversial. [19]

In a healthy pregnancy, adiponectin secretion is abundant in the early stages of pregnancy despite the gestational weight gain (GWG), and concentrations of circulating adiponectin, particularly the HMW isoform, decline as the pregnancy progresses and reach the lowest serum levels in the third trimester due to the highest levels of insulin resistance in the mother, and then rise after the postpartum period. This induces a state of insulin resistance that mimics the effects of diabetes. These adaptations meet the growing fetus's ongoing demands for oxygen and nutrients. [10,16,18,20,21]

Low levels of adiponectin during early pregnancy are predictive of the development of insulin resistance and gestational diabetes mellitus (GDM). Even after adjusting BMI, it was shown that women with GDM had reduced adiponectin levels in their fatty tissue**.** [22–24]

MATERIALS AND METHODS

This prospective case-control study was approved by the Ethics Committee of the Ninevah Health Directorate/Ministry of Health in Iraq protocol number (20230131) in October 2023. The study was conducted on 200 subjects and divided into 100 healthy pregnant women, subdivided into 50 in the 2nd trimester and 50 pregnant women in the 3rd trimester; the control group was 100 healthy non-pregnant women. The cases were gathered from pregnant women who received antenatal care at Al-Hadbaa and Al-Quds primary health care centers, at Al-Khansaa Teaching Hospital, Al-Batool Teaching Hospital, Al-Mosul General Hospital, and Al-Salam General Hospital in Mosul City. The control group was also collected simultaneously with the case group from the mentioned places throughout the study period, extending from October 2023 to February 2024.

The inclusion criteria are healthy pregnant women with a single non-twin pregnancy, aged between 18 and 45 years, who were non-smokers, had a BMI between 18.5 and 29.9 kg/m2, had a regular medical condition (no history of hypertension, GDM, diabetes mellitus, or other chronic systemic diseases), and had no history of chronic drug intake.

The data from the subjects were collected for the clinical history and physical examination records (name, age, address, occupation, height, weight, LMP, EDD, BMI before the period of pregnancy, and blood pressure).

The initial investigation was performed to assess the gestational age using an ultrasound of the case group in the same institution. The recent BMI for each participant was calculated manually by estimating the body weight with a digital scale device (Beurer Wellbeing BF105, Germany) and the body height with a soft measuring tape using the standard equation (weight in kg/height in m^2).

The random blood sugar testing for both the case and control groups was performed in the laboratory department of the same institution or manually by using (On.Call®plus, Germany) glucometer.

Five milliliters of venous blood were aspirated from each participant using a clean venipuncture needle.

The blood was placed into a sterile serum-separating gel tube (5 ml). The samples within the tubes were allowed to clot at room temperature and centrifuged at 5000 rpm for 10 minutes. After centrifugation, the serum supernatant was drawn off and transferred into clean and labeled Eppendorf tubes. The samples were then stored in a deep freezer at -20◦C for later use in the Enzyme-linked Immunosorbent Assay (ELISA) test by using a human adiponectin ELISA kit (Bioassay Technology Laboratory, China) to measure adiponectin hormone levels in all samples in a single run.

Statistical Analysis

The data obtained during the search was organized into spreadsheets using Microsoft Excel 2016. The statistical analysis was conducted using IBM-SPSS version 26.

Kruskal-Wallis H test was used to analyze the differences between the socio-demographic characteristics and the adiponectin hormone levels in both the pregnant subjects and the control groups, expressed in both mean and median.

The Pearson correlation test was used to determine the correlation between various study parameters in both the pregnant subjects and control groups, expressed in mean and standard deviation. A P-value less than or equal to 0.05 is considered statistically significant.

RESULTS

A comparison of socio-demographic characteristics between the 100 healthy pregnant women in the 2nd and 3rd trimesters and the 100 healthy non-pregnant women as a control group.

Table (1) demonstrated the studied groups, revealing non-significant differences between the means of cases and the control group (P-value > 0.05).

Regarding the distribution of adiponectin serum levels according to the socio-demographic characteristics of the cases and control group enrolled in this study, the means and medians of serum adiponectin levels were slightly higher in pregnant women than in the control group in all the socio-demographic characteristics except for rural residence. The differences were statistically non-significant (P-value > 0.05). The means and medians of serum adiponectin levels were slightly higher in the pregnant cases with a BMI of 18.5 - 24.9 kg/m2 than those with a BMI of 25.0–29.9kg/m2. Still, they did not reach the significance level compared to the control group (P-value = 0.569, P-value = 0.814), respectively, as demonstrated in Table (2).

Table 1. Summary of the socio-demographic characteristics of the study sample.

Parameter	2nd and 3rd trimesters (n=100)		Control (n=100)		P value*
	No.	%	No.	%	
Age (years)					
18 - 30	76	76.0	53	53.0	-
30 - 45	24	24.0	47	47.0	
Mean ± SD	25.96±6.25		29.68±8.24		-
BMI					
18.5 - 24.9	25	25.0	33	33.0	0.213
25.0 - 29.9	75	75.0	67	67.0	
Mean ± SD	26.86±3.05		26.31±3.52		0.240***
Residence					
Urban	60	60.0	72	72.0	0.073
Rural	40	40.0	28	28.0	
Occupation					
Employed	4	4.0	1	1.0	0.369**
Un employed	96	96.0	99	99.0	
Adiponectin (ng/ml)					
Mean ± SD	6.24±4.44		5.79±2.71		0.387***

* Chi-square test was used.
** Fisher exact test was used.
*** An independent t-test was used.

Table 2. The distribution of serum adiponectin levels according to the socio-demographic characteristics of the study sample.

Parameter	Adiponectin (ng/ml)			P value*
	2nd Trimester (n=50)	3rd Trimester (n=50)	Control (n=100)	
	Mean ± SD	Mean ± SD	Mean ± SD	
Age (years)				
18 - 30	(n=36)	(n=40)	(n=53)	0.988
	6.46±6.35	5.54±2.26	5.76±2.60	
Median	5.50	5.38	5.13	
30 - 45	(n=14)	(n=10)	(n=47)	0.264
	7.02±4.20	7.18±2.78	5.83±2.86	
Median	6.13	7.89	5.71	
BMI				
18.5 - 24.9	(n=35)	(n=40)	(n=67)	0.569
	6.88±6.62	5.94±2.35	5.56±2.61	
Median	5.65	6.37	5.06	
25.0 - 29.9	(n=15)	(n=10)	(n=33)	0.814
	6.01±3.17	5.58±2.87	6.26±2.89	
Median	5.99	5.51	5.85	
Residence				
Urban	(n=29)	(n=31)	(n=72)	0.212
	6.53±3.55	6.02±2.12	5.56±2.72	
Median	6.40	6.16	4.92	
Rural	(n=21)	(n=19)	(n=28)	0.393
	6.73±8.03	5.62±2.93	6.39±2.62	
Median	4.51	5.76	6.39	
Occupation				
Employed	(n=1)	(n=3)	(n=1)	0.344
	8.83±---	5.25±2.35	7.44±---	
Median	8.83	4.24	7.44	
	(n=49)	(n=47)	(n=99)	0.837
Unemployed	6.57±5.84	5.91±2.46	5.78 ±2.72	
Median	5.65	6.16	5.29	
Adiponectin (ng/ml)	(n=50)	(n=50)	(n=100)	0.867
	6.62±5.79	5.87 ±2.44	5.79±2.71	
Median	5.75	6.14	5.29	

* Kruskal-Wallis H test was used.

Regarding the correlation of serum adiponectin levels with BMI in each studied group, the means of adiponectin levels were negatively correlated with BMI in the second trimester and the control group and positively correlated with BMI in the second trimester (r = -0.005, r = -0.129, r = 0.096), respectively. The studied data revealed no statistically significant associations (P-value > 0.05), as shown in Table (3).

No relationship was found between means of serum adiponectin levels and the random blood sugar in the second and third trimesters and control groups (r = 0.102, r = 0.042, r = 0.050), respectively. However, no statistically significant associations were observed between serum adiponectin levels and RBS in the studied group (P-value > 0.05), as demonstrated in Table (4).

Table 3. Correlation of adiponectin levels with BMI in the studied group.

Parameter	Adiponectin (ng/ml)	Body Mass Index (Kg/m^2)	r (correlation coefficient value)	P value*
	Mean ± SD	Mean ± SD		
2nd Trimester (n=50)	6.62±5.79	26.42±3.40	-0.005	0.973
3rd Trimester (n=50)	5.87 ±2.44	27.31±2.61	0.096	0.505
Control (n=100)	5.79±2.71	26.31±3.52	-0.129	0.199

* Pearson correlation was used.

Table 4. Correlation of adiponectin levels with RBS in the studied group.

Parameter	Adiponectin (ng/ml)	Random blood sugar (mg/dL)	r (correlation coefficient value)	P value*
	Mean ± SD	Mean ± SD		
2nd Trimester (n=50)	6.62±5.79	104.40±17.87	0.042	0.773
3rd Trimester (n=50)	5.87 ±2.44	104.68±16.02	0.102	0.482
Control (n=100)	5.79±2.71	106.47±15.56	0.050	0.618

* Pearson correlation was used.

DISCUSSION

The physiology of resistance to insulin during pregnancy is quite intriguing since it has evolutionarily developed a pseudo-diabetogenic state to restrict maternal glucose use and prioritize the provision of glucose to the developing fetus, which primarily relies on glucose as its primary energy source. However, the causative mechanisms and determinants of insulin resistance during pregnancy are intricate and not entirely revealed. [21,25]

During pregnancy, several adipokines, including leptin, adiponectin, and cytokines such as interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-α), are released from the white adipose tissue and the placenta, which function as endocrine organs. [26]

In this study, the mean serum adiponectin levels were not significantly decreased from 6.62±5.79 ng/dL in the 2nd trimester to 5.87 ±2.44 ng/dL in the 3rd trimester (P-value = 0.867), which was in line with previous studies, which reported that adiponectin levels were inversely associated with insulin and insulin resistance, and they declined with pregnancy progression. [16,27–29]

In both subgroups of BMI, the means of adiponectin progressively declined in mid and late pregnancy. The Pearson correlation analysis means of adiponectin levels were negatively correlated with BMI in the second trimester and control group and positively correlated with BMI in the second trimester (r = -0.005, r = -0.129, r = 0.096), respectively, with no statistically significant associations (P-value > 0.05). Goyal et al. study reported a statistically significant (P-value <0.001) but negative correlation between serum adiponectin levels and BMI at both the mid and late stages of gestation in fifty normal pregnant women (r = -0.476, r = -0.441), respectively.[30] This variation in results could be explained by geographical and ethnic diversity among the subjects in the different study samples.

Pregnancy is the only stage in life characterized by hyperglycemia, and because it supplies the fetus with enough glucose, hyperglycemia plays a critical role in its nutrition and development. [31] Recent research has shown that the adipokines leptin and adiponectin contribute to normal pregnancy and that disruption of these adipokines is associated with GDM and preeclampsia (PE).[32]

The study found that serum adiponectin levels decreased gradually from the second to the third trimesters of gestation. In contrast, there was only a slight increase in the average random blood sugar levels as gestation progressed. However, no notable relationship was observed between the serum adiponectin levels and RBS in the second and third trimesters, as well as the control groups (r = 0.102, r = 0.042, r = 0.050), respectively. Furthermore, no statistically significant correlations were found between groups (P-value > 0.05). This could be attributed to the poor compliance of the participants in performing the fasting glucose test (FBG) or the oral glucose tolerance test (OGGT), which provides more accurate data for the screening of insulin resistance. [33]

CONCLUSIONS

Adiponectin plays a vital role in normal pregnancy. The decline of serum adiponectin levels as the pregnancy progresses. These findings, in parallel with the rise of the BMI and random blood sugar, support adiponectin's physiological role in maintaining fetal growth and development.

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