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Research Article

Is there any Relation between Adiponectin Levels in the First Trimester of Pregnancy and Gestational Diabetes?

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Abstract

Objectives: Pregnancy physiologically causes resistance to insulin which disappears after childbirth. The present study aimed to evaluate the serum levels of adiponectin in the first trimester of pregnancy to predict gestational diabetes.

Methodology: This study is a descriptive-analytical study carried on 100 women in Al-Zahra and Shahid Beheshti Hospitals of Isfahan, Iran in 2014. Adiponectin levels were measured by ELISA after a general screening test of OGCT 50g. Then, between 24 and 28 weeks of pregnancy, OGCT 50g test was done, and if necessary, OGGT 100g test was conducted. Data analysis of logistic regression and ROC (Receiver Operating Characteristics) analysis was done via SPSS (Ver.19) and MedCalc (Ver.9.2) soft wares Using ROC analysis.

Results: The mean age was 24.70 ± 4.72 years and the mean level of adiponectin was 7.19 ± 3.40 milligrams. The role of age and adiponectin level showed that these two factors cannot have a significant impact on gestational diabetes (P value> 0.05). According to the fact that in the adiponectin level of lower/equal to 2.7 micrograms per ml (2.7 µg / ml), test sensitivity, specificity, and the positive predictive value were 26.32%, 92.21%, and 45.5%.

Conclusion: The highest predictive value of adiponectin has been reported as 2.7 µg/ml so in values lower than this level, gestational diabetes is more likely.

Keywords: Adiponectin, Gestational diabetes, First trimester

Introduction

Pregnancy physiologically causes resistance to insulin which disappears after childbirth [1]. In women with pancreatic beta-cell functionless than normal value, insulin secretion may be insufficient to compensate for the resistance and bring about the risk of developing gestational diabetes [2]. Gestational diabetes is defined as the starting point or the initial diagnosis of or glucose intolerance in pregnancy [3]. Prevalence of gestational diabetes, according to different communities and ethnic groups, has been reported between 1 to 14% [4].

Placenta is involved in insulin resistance and fetal development in women with normal pregnancy and gestational diabetes that seems to be generated through the production of hormones in the placenta [5]. Recent research, examining the role of hormones, has also investigated the role of peptides secreted by adipose tissue in the pathogenesis of insulin resistance [6]. Adipose tissue is now considered to be an endocrine organ due to producing adipocytokine, and their presence is vital in many physiological and metabolic processes [7]. Adipocytokines production or secretion disorders affect the pathophysiology of diabetes type II which is a metabolic disorder similar to gestational diabetes [8]. These bioactive substances include adiponectin, visfatin, resistin and the other adipocytokine [9]. Recently, some studies have examined the role of adipocytokine in the development of insulin resistance during pregnancy [10].

Adiponectin is an adipocytokine which has a similar molecular structure to collagen polypeptide and increases insulin sensitivity. Adiponectin serum levels reduce in patients with obesity, coronary artery disease, and diabetes type II. Other important features are known as the anti-diabetic and anti-therogenic properties, anti-inflammatory effects, and a giogenesis. The role of this hormone is regulating the normal pregnancy physiologic performance and abnormal pregnancy disorder such as

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gestational diabetes. The results of some studies have shown the role of the adipocytokine in insulin resistance physiology during pregnancy [11-13].

Previous studies have shown that decreased adiponectin levels in the second trimester of pregnancy plays an important role in the development of gestational diabetes compared with normal pregnancy. In a study on a number of pregnant women it has demonstrated that lower levels of adiponectin in the first trimester of pregnancy resulted in higher insulin resistance and a higher probability of gestational diabetes. But so far, there have been contradictory results about the serum level changes of the adipocytokine found in pregnancy. On the other hand, another research has proved the effect of race difference in plasma concentrations of adiponectin during pregnancy which can be an important factor in increasing the risk of diabetes. Early detection through screening, in order to detect and prevent diabetes type II in women with a history of gestational diabetes, is an appropriate opportunity to lessen the frequency and complications of the disease [13]. Accordingly, evaluating the relationship between adiponectin during pregnancy may be a useful parameter to detect gestational diabetes. Therefore, the present study was designed to evaluate the serum levels of adiponectin in the first trimester of pregnancy to predict gestational diabetes.

Materials and Methods

This study is a descriptive-analytical study carried on in Al-Zahra and Shahid Beheshti Hospitals of Isfahan, Iran in 2014. The study population consisted of 100 pregnant women referred to Al-Zahraand Shahid Beheshti Hospitals in 2013-2014. Inclusion criteria were the pregnant women referred in the first trimester and the individuals consented to participate in the research project. Someone who didn't want to continue the research project was excluded.

The required sample size of the study was determined using the sample size estimating formula for prevalence studies and taking into account the level of confidence as 95% (Z1-a/2 = 1.96). Adiponectin test sensitivity was considered 0.5 (p = 0.5) duet lack of a similar study, and accepting the error rate of 10% (d = 0.1), the number of samples was estimated 96; for a greater certainty, 100 patients were selected and studied. After obtaining the informed consent, pregnant women entered the study for general screening of diabetes. Exclusion criteria were diabetes and twin pregnancy. Four women were excluded because of their unwillingness to continue the study. After wards, adiponectin levels were measured by Human Adiponectin (ADPN) ELISA Kit (glory science.co.ltd [United States]) after a general screening test of OGCT 50g. Then, between 24 and 28 weeks of pregnancy, OGCT 50g test was done, and if necessary, OGGT 100g test was conducted.

Data analysis of logistic regression and ROC (Receiver Operating Characteristics) analysis was done via SPSS (Ver.19) and MedCalc (Ver.9.2) software's, and the significance level was considered less than 0.05. Using ROC analysis, the cut-off point of the determined adiponectin, and based on that, the diagnostic value, the percentage of sensitivity, specificity, positive predictive value, negative predictive value, false positive rate, false negative rate, and the accuracy of diagnostic test of adiponectin were determined.

Results

In the present study, of 96 pregnant women, 19 patients (19.8%) suffered gestational diabetes and 77 (80.2%) were free of diabetes. The averages of the first two factors in this study consisted of an average age of 24.70 ± 4.72 years and an average adiponectin level of 7.19 ± 3.40 milligrams per milliliter (Table 1). The results of logistic regression, assessing the role of age and adiponectin level in gestational diabetes, showed that (despite the opposite and minimal effect of age and adiponectin on gestational diabetes) these two factors cannot have a significant impact on gestational diabetes (P value > 0.05) (Table 2).

On the other hand, the results of ROC analysis generally showed that since the area under curve (AUC) is less than 70% in the ROC chart, so adiponectin variable is not a good diagnostic criteria for gestational diabetes (P > 0.05). But, according to the fact that in the adiponectin level of lower/equal to 2.7micrograms per ml (2.7 µg / ml), test sensitivity, specificity, and the positive predictive value were 26.32%, 92.21%, and 45.5%, respectively, hence this level has the highest predictive value and high specificity compared to other levels of adiponectin in the present study (Table 3 and Figure 1). And therefore, at lower levels of

Characteristic	Total	GDM		P value
		Positive(n=19)	Negative(n=77)	
Maternal age	24.70 ± 4.72	24.14 ± 4.18	24.66 ± 4.59	0.320
Gestational age (wk)	25.66 ± 0.98	27.1 ± 0.6	25.3 ± 1.02	0.0005
BMI(km/m^2)	26.848 ± 5.18	27.36 ± 5.09	26.72 ± 4.82	0.365
TC (mg/dl)	204.95 ± 26.51	225 ± 26.87	200 ± 26.12	<0.0001
LDL(mg/dl)	121.77 ± 10.3	135.33 ± 11.08	118.42 ± 9.50	<0.0001
HDL(mg/dl)	53.59 ± 10.91	51.08 ± 10.61	54.21 ± 11.23	0.145
Adiponectin(µg/ml)	7.16 ± 3.49	7.06 ± 3.69	7.22 ± 3.35	0.855

Table 1: Basic and clinical characteristics of the studied pregnant women

GDM*	Factors	Mean ± SD	Beta	OR(95% CI)	P value
Positive(n=19)	Age	24.47 ± 4.78	-0.013	0.987(0.886-1.099)	0.811
Negative(n=77)		24.76 ± 4.74			
Positive(n=19)	Adiponectin	7.06 ± 3.69	-0.014	0.987(0.850-1.145)	0.859
Negative(n=77)		7.22 ± 3.35			

*dependent variable

Table 2: Results of logistic regression to assess the role of age and adiponectin level in gestational diabetes

Area under the ROC curve			0.512			
Standard error			0.074			
95% Confidence interval			0.408 to 0.615			
Significance level P (Area=0.5)			0.8715			
Criterion	**Sensitivity**	**95% CI**	**Specificity**	**95% CI**	**+PV**	**-PV**
<=2.7 *	26.32	9.2 - 51.2	92.21	83.8 - 97.1	45.5	83.5

*The proposed cut-off point

Table 3: Results of ROC analysis to determine the optimal cut-off point of adiponectin level vs. developing gestational diabetes

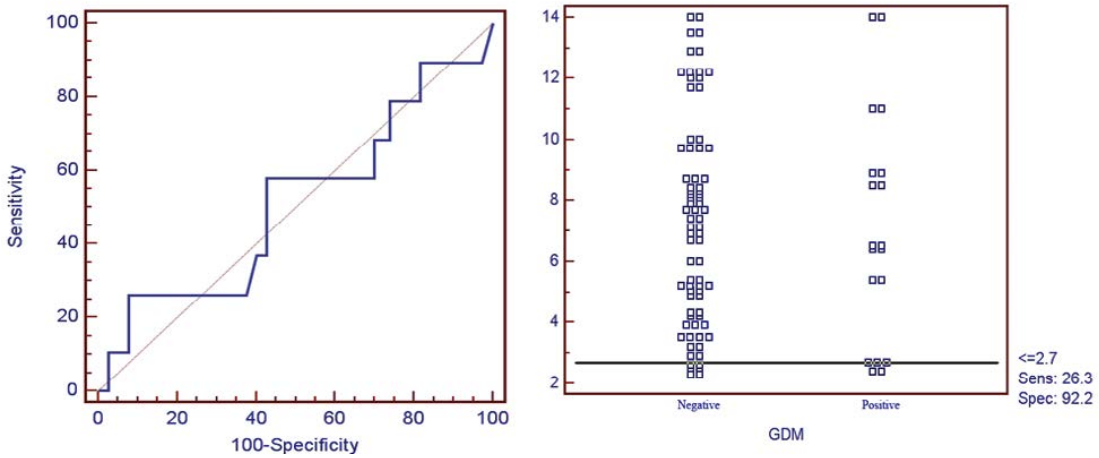

Figure 1: ROC curve and interactive dot diagram of gestational diabetes vs. adiponectin level

adiponectin levels (eg, 2.7 μg/ml) developing gestational diabetes is more likely.

Discussion

Gestational diabetes mellitus (GDM) can affect between 1% and 20% of pregnancies, depending on diagnostic criteria and studied population, and is associated with a range of adverse maternal and neonatal outcomes. Improvement of targeted screening by inclusion of the first trimester biomarkers may be feasible, facilitating stratified care and early intervention. The results of several reviews have also supported the role of adipocytokines in the physiology and pathophysiology of insulin resistance during pregnancy [14,15]. Diabetes mechanism has not been clearly defined; however, factors related to obesity play an important role [16,17].

It seems serum concentration of adipocytokine changes is under the effect of metabolic status of pregnancy in women with gestational diabetes and these changes are associated with insulin resistance in these patients [18,19]. Changes in some hormone factors such as the amount of estrogen, progesterone, cortisol, and human chorionic lactogen, glucagon and leptin are associated with metabolic disorders of gestational diabetes [20].

The findings of the present study revealed the lower serum levels of adiponectin in women with gestational diabetes compared with women without gestational diabetes. That the difference was not much and could be ignored; in other words the difference was not statistically significant (P Value < 0.05). Similar to the findings of the current study, a lot of studies have also pointed out the same issue; however, in most of such studies the observed difference has been statistically significant. In a systematic review it has been revealed that adiponectin levels in the first or second trimester of pregnancy were lower among pregnant women who later develop GDM than non-GDM women, whereas leptin levels are higher [21]. It has also pointed to this topic by Lacroix, et al. that pregnant women with lower adiponectin levels at 1st trimester have higher levels of insulin resistance and are more likely to develop GDM independently of adiposity or glycemic measurements [7]. Lower adiponectin levels have notably been associated with subclinical inflammation, while low levels of adiponectin in pregnancy have been associated with women of South Asian origin and this may have a significant impact on the development of GDM [22]. Moreover, down regulation of adiponectin in the first trimester of pregnancy is an independent predictor of impending GDM [23,24]. Also; the present study has addressed the role of age on gestational diabetes and showed that age has no effective role in the occurrence of gestational diabetes. It should be noted that there exists a dearth of research on the impact of age on gestational diabetes. But, in general, further studies seems necessary in this regard since as women become older, they become more obese; consequently, they will have a higher level of adiponectin compared to young women; perhaps, it can be said that this issue could also be effective in gestational diabetes. Because low adiponectin is well established to cause insulin resistance and decreased IGFBP-1 indicates increased IGF-I bioavailability, we propose that these changes are mechanistically linked to the development of GDM in obese women [25].

The weakness of this study can be this fact that the two groups of case and control were not considered from the beginning of the study and this has led to considerable differences between the frequency of normal individuals and diabetic patients. But the strength of this work may be simultaneously evaluation of the previous fixed criteria (blood sugar test) in comparison

with adiponectin test and so we found 19 diabetic mothers with previous method, but 22 diabetic ones have been diagnosed using adiponectin test which indicates the higher sensitivity than the previous routine test.

Finally, to determine the cut-off point of the variable of adiponectin in order to diagnose gestational diabetes, the ROC curve has been used. This curve is an efficient way of showing the relationship between sensitivity and specificity of a test with continuous values. In this study, the area under the curve was reported as less than 70%; accordingly, it is not solid evidence of the validity and the reliability of the test to diagnose gestational diabetes (P-Value> 0.05); and the sensitivity of the test has been low. However, the number proposed by the software with the highest predictive value and characteristics has been reported as 2.7 µg/ml. The report has been stated merely because in values lower than this level, gestational diabetes is more likely. Therefore, in future studies, its validity and reliability can be evaluated using the proposed cut point since the normal range of adiponectin level in adults is 4-19.4 µg / ml.

Many studies have provided a normal or abnormal range in some diseases, but few studies have evaluated the cut point for the diagnosis of gestational diabetes.

Conflict of interest

There was no conflict of interest between the authors.

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