The Role of Serum Adropin Level in Diagnosis of Gestational Diabetes Mellitus

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ABSTRACT:

BACKGROUND:

In pregnancy, Gestational Diabetes Mellitus is considered as intolerance to carbohydrate which discovered in pregnancy. It is a glucose metabolism abnormality associated with long and short-term morbidities that could affecting both of the offspring and mother such as shoulder dystocia, preeclampsia or hypertension.

OBJECTIVE:

To evaluate the level of serum adropin in pregnant ladies with Gestational Diabetes Mellitus (GDM) in comparison with that of normal euglycemic pregnant patient.

METHODS:

At National Diabetes Center and AL-Yarmouk teaching hospital, a case-control study was done for the period from January 2020 to October 2020. Forty pregnant ladies with Gestational Diabetes Mellitus (cases) and fifty healthy pregnant ladies (controls) were involved. Lipid concentration and serum adropin were evaluated between 24th-28th weeks of pregnancy for the two groups. The results were compared between them using independent sample t-test.

RESULTS:

Serum adropin was significantly correlated with maternal age, and fasting blood sugar and 2-hour blood glucose measurement after subjecting them to 75-gram Oral Glucose Tolerance Test (p-value: 0.004, 0.001, 0.001) respectively but, serum adropin was significantly negatively associated with Gestational Diabetes Mellitus (AUC: 0.927, PV=0.001, 95%CI: 0.860-0.964) the cutoff point of 38.05 with sensitivity of72.5% and specifity of 98% was considered as the most accurate point of adropin concentration for diagnosis of Gestational Diabetes Mellitus.

CONCLUSION:

Low level of serum adropin is independent diagnostic factor for Gestational Diabetes Mellitus.

KEYWORDS: Adropin hormone, Gestational Diabetes Mellitus, oral glucose tolerance test.

INTRODUCTION:

Gestational Diabetes Mellitus (GDM): Has been recognized as hyper glycaemia first seen during pregnancy. And recently described by the American Diabetes Association (ADA) as 'diabetes discovered for the first time in pregnancy during the second or third trimester that is not obviously frank diabetes [1]. The incidence is between 10-15% of pregnancies, depending on criteria used for diagnosis [2].

During pregnancy, pancreatic β_cell response is increased and there is also hyperinsulinaemia and in women with GDM there is an exaggeration of resistance to insulin which occured possibly due to a difficulty for pancreatic β_cell to increase the secretion of insulin and this may show an early marker of decreased in the function of pancreatic β_cell [3].

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Adropin is a peptide hormone which has a significant role in lipid and glucose homeostasis regulation. Adropin was discovered since 2008 by Kumar et al. It is the only hormone encrypted by the energy homeostasis associated (Enho) gene. It is synthesized in liver and also brain, in addition to peripheral tissues such as gastrointestinal tract and heart. Also, adropin is found in the circulation. [4]. Many studies showed that levels of adropin in serum are depend upon metabolic diseases and affected by diet [5].

Adropin influence on expression of an inducible nitric oxide synthase, which can explain the potential role of adropin in prediction of endothelial dysfunction in patients with diabetes mellitus [6]. Several studies improved significant association between reduction in serum adropin level and development of gestational diabetes mellitus [7].

PATIENTS AND METHOD:

A case control study carried out in the National Diabetes Disease Center and AL-Yarmouk Teaching Hospital from January 2020 to October 2020.

From Scientific Counsel of obstetrics and gynecology / Iraqi Board for medical specialization, Verbal consent was taken from a pregnant women attending consultation clinic before enrollment into the study.

The current study included 40 pregnant ladies with gestational age between 24wks_28wks of pregnancy diagnosed as GDM (case group) and 50 healthy pregnant ladies with the same gestational age after exclusion of GDM as (control group).

Inclusion criteria: Pregnant women with gestational age between 24wks_28wks of gestation for both case and control groups, Age group <35 years, BMI<30 Kg/m^2(pre pregnancy), Singleton pregnancy.

Exclusion criteria: women with type 1or 2 Diabetes Mellitus, multiple pregnancies, infectious and inflammatory disease, hypertension, cardiovascular, hepatic, renal disease (association between adropin level and these diseases), cancers and smoking.

Investigation: For all women in both groups the following tests were done:

1. Oral Glucose Tolerance Test (OGTT).
2. Serum adropin.
3. Serum Lipid profile.

Oral Glucose Tolerance Test (OGTT) was done in the morning after eight hours fasting but not more than fourteen hours and after minimum of three days of unrestricted diet and physical activities, and no smoking. Venous plasma was obtained to measure glucose level at fasting and two hours after ingestion of 75 g glucose melted in 300 ml of water.

Gestational diabetes was diagnosed according to National Institute for Health and Care Excellence (NICE) Guideline by the presence of one of the two criteria including [8]:

Fasting plasma glucose level≥100 mg/dl (5.6 mmole/L).

2 hrs. Plasma glucose level≥ 140 mg/dl (7.8 mmol/L).

Forty pregnant with GDM (diagnosed by abnormal fasting or 2hr. post prandial glucose level or both of them after OGTT) were considered as a case group and were matched for gestational age, body mass index (BMI), parity with 50 healthy pregnant ladies with fasting or 2 hr. post prandial blood glucose level after OGTT are within normal as controls.

Five ml of venous blood were obtained from both groups during 24th-28th wks of gestation after an overnight fasting. The blood centrifuged and serum were stored at -20 C° to be assessed later on.

Lipid profile and adropin level were measured for women in case and control groups in fasting state for 12 hours. Serum high density lipoprotein (HDL), low-density

lipoprotein (HDL), Triglyceride and cholesterol level were measured by auto analyzer using colorimetric method and serum adropin concentration were assessed by ELISA method kit (Human adropin –ENHO-ELISA KIT) catalog number: CSB-EL007669HU. The significance level was set at p value <0.05 to determine the cut-off point for serum adropin as a significant marker for GDM.

RESULTS:

Table 1: show us demographic characteristics of case and control groups. The mean age of case group (30.08±2.28 year) was significantly higher than the control group (28.56±2.1 year), (p-value = 0.001). There was no significant difference between the studied groups including BMI, gravidity, parity, abortion and GA at sampling.

Table 1: Demographic characteristics of the studied groups.

	Case N=40 Mean ±SD	Control N=50 Mean ±SD	p-value
Maternal age (year)	30.083± 2.2831	28.560±2.1011	0.001
BMI (kg/m^2)	26.833±1.6162	26.548± 1.2031	0.341
Parity	1.65 ±1.847	1.38 ±1.483	0.444
History of abortion	0.83 ±1.217	0.54 ± 0.862	0.197
GA at sampling (weeks)	26.13 ±1.305	26.04 ±1.277	0.757

BMI: body mass index, GA: gestational age

Table 2: show us the biochemical measurements of the studied groups. Mean serum adropin concentrations in the case group (38.62 ±4.23) were significantly beneath that of the control group (49.84±3.68), (p-value= 0.001). There was no significant association between adropin levels and lipid profile (HDL, LDL, triglyceride and cholesterol concentration) (P-value >0.05 in all conditions). Mean fasting blood glucose (97.28±6.9) and 2 h (144.83±11.47) blood glucose 2hr. after 75 g glucose (OGTT) were significantly higher in GDM case group in comparison with control group (80.40±3.703,111.64±6.170) respectively, p- value=0.001 in all cases.

Table 2: Biochemical measurements of the studied groups.

	Case N=40 Mean ±SD	Control N=50 Mean ±SD	p-value
Adropin level pg/ml	38.623± 4.2389	49.844± 3.6852	0.001
total cholesterol mg/dl	211.58 ±17.888	219.26 22.583	0.083
HDL mg/dl	54.63± 5.994	55.72± 5.010	0.384
LDL mg/dl	112.88 ±7.796	115.14 ±6.433	0.135
Triglyceride mg/dl	213.70± 28.492	223.82 ±19.312	0.059
FBS mg/dl	97.28± 6.910	80.40± 3.703	0.001
2 hr. pp after OGTT mg/dl	144.83 ±11.467	111.64 ±6.170	0.001

FBS, fasting blood sugar; HDL, high-density lipoprotein;
LDL, low-density lipoprotein; OGTT, oral glucose tolerance

Table 3: show us significant negative correlation between serum adropin levels and maternal age, (r=-0.303, p v=0.004), as well as FBS (r=-0.715, p-value =0.001) and 2 hr. post prandial after OGTT (r=-0.771, p-value =0.001) There was non-significant negative correlation between serum adropin levels and lipid profile (LDL, HDL, triglyceride and cholesterol concentration) as well as BMI P-value >0.05 in all conditions.

Table 3: Correlation between adropin level and other studied variable.

variable (s)	R value	P value
Maternal age (year)	-0.303	0.004
FBS mg/dl	-0.715	0.001
OGTT 2hr	-0.771	0.001
BMI	-0.082	0.444
Total cholesterol	-0.031	0.770
HDL	-0.184	0.083
LDL	0.198	0.062
Triglyceride	-0.183	0.084

BMI: body mass index, HDL: high density lipoprotein,
LDL: low density lipoprotein, OGTT: oral glucose tolerance

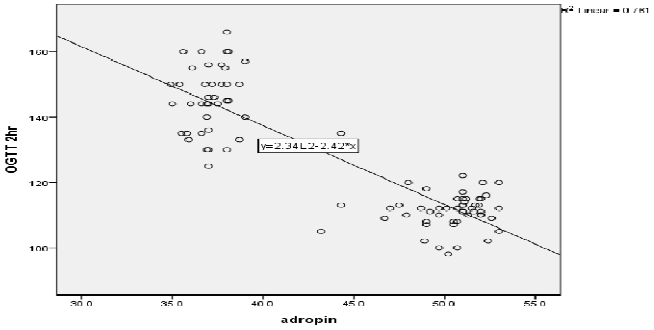

Figure 1: Shows correlations between adropin level and OGTT after 2 hr.

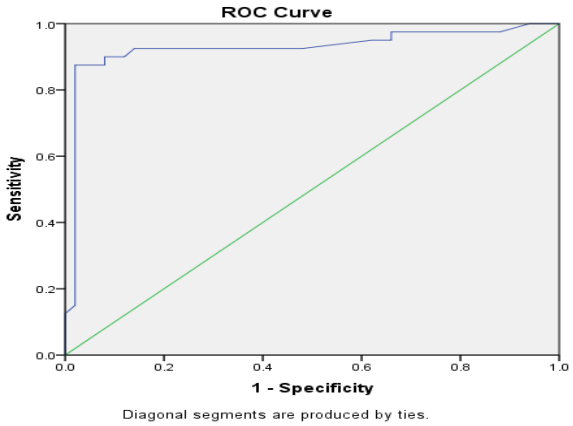

Figure 2: ROC for association between serum adropin concentration and GDM.

In figure 1,2& and related tables ROC found that adropin is an independent diagnostic parameter of GDM (AUC: 0.927,p-value=0.001, 95%CI: 0.860–0.964). The cut-off point of 38.05 with sensitivity of 72.5% and specificity of 98% was determined as the best point of adropin concentration for diagnosis of GDM.

Area Under the Curve				
Test Result Variable(s): adropin				
Area	Std. Error	Asymptotic Sig.[b]	Asymptotic 95% Confidence Interval	
			Lower Bound	Upper Bound
.927	.034	0.001	.860	.994

Coordinates of the Curve		
Test Result Variable(s): adropin		
Positive if Less Than or EqualTo[a]	Sensitivity	Specificity
37.950	0.625	0.99
38.050	0.725	0.98
38.400	0.775	0.90
38.850	0.825	0.85
40.000	0.875	0.81
48.350	0.925	0.78

DISCUSSION:

Understanding the mechanisms of adropin and factors which affect its release may influence new possibilities for management of different metabolic disorders like diabetes, obesity, GDM [9,10].

In the current study we found significant positive association between GDM and maternal age (P value=0.001) and this fact improved by many studies such as a study done by Yueli.Li, et al. in a systematic review and meta-analysis of over 120 million participants) they demonstrate that GDM increased linearly with increased age (p-value=0.001) [11]. Another study done by Han.Y, et al. which included 120 Chinese women with singleton pregnancies and they found significant association between the GDM and increased maternal age [12].

In current study adropin level was not significantly associated with lipid profile (low density lipoprotein, high density lipoprotein, cholesterol, triglyceride and concentration (P-value>0.05) in

our study and this agrees with study done by change.J.B., et al. aimed to identify the relationship between adropin levels and body composition and lipid profile in adolescents in Taiwan and they found there is no difference in lipid profiles in low or high adropin concentrations [13].

In the present study there was significant negative association between serum adropin level and GDM, Patient with GDM showed significantly lower serum adropin concentration as compared to control group (P-value = 0.001) and this result is similar to a study done by Beigi.A, et al. a case-control study included 80 Iranian pregnant women ,40 of them diagnosed with GDM (case group) and 40 normal healthy pregnant women (control group), they found significant lower serum adropin level among patient with GDM as compared to control group[14]. Another study done by Celik, E., et al. they studied the maternal levels of adropin in Gestational Diabetes Mellitus, in their study done on 40 pregnant women (20 of them with GDM and 20 healthy pregnant ladies) they found that the mean maternal adropin levels in GDM were significantly lower than those of control group, and this agree with the current study [15]. Also study done by Ayden, S. et al. they also found significant negative association between serum adropin level and GDM and this also support our study result [9].

The result of current study shows a high correlation between serum adropin level and fasting blood glucose and 2hr blood glucose level post 75g OGTT. This is a significant finding as it offers an opportunity for early diagnosis of GDM, especially among pregnant women who cannot easily tolerate the OGTT (R value: 0.715, 0.776 and 0.771 respectively with P-value: 0.001 in all of them), and this agrees with a study done by zang. H. ,et al. A total of 116 pregnant with GDM and 60 control Chinese pregnant women he found that serum adropin level reduced in Chinese patients with GDM compared with control group and there is negative correlation between serum adropin level and FBS and 2 hr. blood glucose level post 75 g OGTT [16]. This strongly support us to confirm that adropin is an independent diagnostic factor of GDM (AUC: 0.927, P-value: 0.001, 95% CI: 0.860-0.994).

And disagrees with a study done by beige, A .et al which mentioned above, they didn't found significant correlation between serum adropin level and maternal blood glucose level at fasting and 2hr. post 75g OGTT because they regress this confounding factor from their study [14].

Depending on our study result showed that Area under the curve 927 with a standard error .034, The Confidence interval 95% (lower bound 860 and upper bound 994). The cut-off point of 38.05 with sensitivity of 72.5 % and specificity of 98 % was set on as the leading point of adropin concentration for prediction of GDM, because when we used a point less than it the sensitivity of test will drop.

CONCLUSION:

1. Serum adropin concentration is significantly reduced in patients with gestational diabetes mellitus.
2. There is negative correlation between serum adropin concentration and maternal age, FBS and 2hr.OGTT.
3. The study revealed non-significant negative association between serum adropin level with BMI and Lipid profile
4. ROC found that adropin is an independent diagnostic factor of GDM (AUC: 0.927, p-value=0.001, 95%CI: 0.860–0.964) The cut-off point of 38.05 with sensitivity of 72.5% and specificity of 98%.

Recommendation:

1. Using of s. adropin level as a diagnostic marker for GDM in high risk group.
2. Future studies including higher sample size and evaluate the relation between adropin in pregnancy and neonatal morbidity also future invention of maternal diabetes, neonatal diabetes and insulin resistance are justifying to affirm our study findings.

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