Early Pregnancy Serum Adiponectin and Serum Triglycerides Level For Detection of Gestational Diabetes Mellitus

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Abstract: Pregnancy is associated with profound alterations in hormonal metabolism. These changes include hyperinsulinemia and insulin resistance together with large increases in the concentrations of cortisol, estrogen, progesterone and human placental lactogen. The first two trimesters of pregnancy are considered to be predominantly anabolic, and pregnant women normally deposit a certain amount of fat stores. The last trimester of pregnancy is characterized by increased catabolism, increased lipolysis, elevations of the concentrations of free fatty acids, minimal or no fat deposition, and significant increases in triglyceride concentrations. Gestational diabetes mellitus, defined as a carbohydrate intolerance of varying severity, is the most frequent metabolic disorder of pregnancy, affecting 2-3% of all pregnancies. Although most of the women with GDM return to normal glucose tolerance after delivery, they have increased risk of developing diabetes, mainly type 2 diabetes mellitus, later on, with an incidence ranging from 6-62%, depending on the population examined and the length of the follow up considered. The offspring of women with GDM are prone to adverse side effects such as macrosomia, which is strongly associated with fetal death, prematurity, birth trauma and respiratory distress syndrome and equally important, these offspring have a high risk of developing obesity, impaired glucose tolerance and type 2 diabetes in adulthood. Cytokines, through their ability to interfere with insulin signaling, have been implicated in insulin resistance in GDM. So adipokines secreted by adipose tissue are required for a number of physiological and metabolic processes. Despite the potential importance of these agents as mediators of metabolic disorders, they have implicated in GDM and macrosomia. Adiponctin is adipocytokine that produced by adipose tissue and also the placenta, could play a role in complicated interactions involving the regulation of appetite and fat metabolism in human pregnancy. Adiponctin level have been reported to be decreased. The aim of this study was to assess the relation of early pregnancy serum adiponectin, triglycerides and HDL-cholesterol levels and the risk of GDM. The study was conducted upon 115 pregnant women from anti natal clinic at El Shatby maternity university. **The results of this study showed that:** 75.5% (n=87) of the cases were GCT<140 while 24.3% (n=28) had GCT>140. adiponectin was statistically significantly different between the two groups (p<0.01). Based on this significance, the researchers used ROC analysis to estimate a cut-off point for serum adiponectin, TG and HDL-cholesterol level. The research detected that adiponectin level <5.5 µg/ml, triglycerides concentrations >155 mg /ml and HDL concentration < 68 ng /ml measured, on average, 11-14 weeks pregnancy were associated with a 3.4-fold increased risk of developing GDM with 96.43% sensitivity and 98.85% specificity positive prediction (AUC=0.985, p<0.001). **In conclusion:** We found adiponectin levels have been shown to be lower in cases with high triglycerides level and lower HDL level and these all are associated with increased risk (3.4 fold) of GDM. **Recommendations:** we recommend for measuring serum adiponectin, serum triglycerides and HDL-Cholesterol in early pregnancy as an early screening for GDM.

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1. Introduction

Gestational diabetes mellitus (GDM) is the most common medical complication of pregnancy. It is associated with maternal and neonatal adverse outcomes. Maintaining adequate blood glucose levels in GDM reduces morbidity for both mother and baby. There is a lack of uniform strategies for screening and diagnosing GDM globally.(**Hartling et al, 2014)**

Gestational diabetes mellitus (GDM) is carbohydrate intolerance resulting in hyperglycemia with onset or first recognition during pregnancy. If untreated, perinatal morbidity and mortality may be increased. Accurate diagnosis allows appropriate treatment. Use of different tests and different criteria will influence which women are diagnosed with GDM. **(Han et al., 2012)**

Metabolic adaptation during pregnancy is essential to meet the physiological demands of pregnancy as well as the adequate growth and development of the fetus. These metabolic changes are progressive and may be accentuated in women who develop gestational diabetes mellitus. Fasting glucose values fall in early pregnancy together with rise in plasma free fatty acids, Enhanced ketogenesis and fall in plasma amino acids. Decreased hepatic insulin sensitivity in later pregnancy plays a key role in bringing about appropriate changes in carbohydrate, lipid and amino acid metabolism which are essential for normal fetal development and survival. Maternal lipid metabolism is altered during pregnancy but little is known about the influence of these alterations on either intrauterine fetal development or maternal wellbeing. **(Daniel et al, 2005)**

Adiponectin is a protein hormone that modulates a number of metabolic processes, including glucose regulation and fatty acid oxidation**. (Chen et al, 2006)** Adiponectin is exclusively secreted from adipose tissue (and also from the placenta in pregnancy into the blood stream and is very abundant in plasma relative to many hormones**. (Ukkola et al, 2002).** Levels of the hormone are inversely correlated with body fat ratio in adults. **(Cawthorn et al, 2014)**

Adiponectin effects:

1. Glucose influx

a. Decreased gluconeogenesis. **(Schumann, 1991)**

b. Increased glucose uptake. **(Han et al, 2012) (Cawthorn et al., 2014)**

2. Lipid catabolism. **(Vasseur et al, 2003)**

a. B-oxidation. **(Cawthorn et al, 2014)**

b. Triglyceride clearance**. (Cawthorn et al, 2014)**

3. Protection from endothelial dysfunction (important facet of atherosclerotic formation). **(Lara-Castro, 2007)**

4. Insulin sensitivity**. (Matsuzawa et al, 2004)**

5. Weight loss.

6. Control of energy metabolism**. (Liu et al, 2012)**

7. up regulation of uncoupling proteins**. (Ukkola,2002)**

8. Reduction of TNF-alpha (tumor necrosis factor alpha).

Adiponectin is up regulated during adipogenesis and down regulated in insulin-resistant states. The mechanism (s) governing the re-arrangements from adipogenesis to facilitated lipolysis during pregnancy are unknown but the adiponectin changes relate to decreased insulin sensitivity of glucose disposal rather than alterations of lipid metabolism. **(Liu et al,2012)**

Adiponectin level is inversely correlated with adiposity in humans, and positively correlated with insulin sensitivity in humans and rodents. Adiponectin and HMW (high molecular weight) Adiponectin is negatively correlated with serum triglycerides and positively with HDL (high density lipo protein) and cholesterol. **(Lara-Castro, 2006; Wright, 2012)**

Aim of the Work

The aim of the study is to investigate the possible measurement of serum Adiponectin and serum triglycerides HDL-cholesterol level in early pregnancy (11-14 weeks) and the subsequent risk of GDM.

2. Patients and Methods

The study was carried out on pregnant women admitted to antenatal clinic El Sayed Galal University Hospitals, after taking their consent for participation of this work. Then later at 12-14 weeks of gestation 115 pregnant females of matched age and parity were selected from those women who had visited the antenatal clinic. Those cases was selected randomly from high risk group for gestational diabetes.

Selected cases was classified later at 24-30 weeks of gestation according to the results of GCT into 2 groups retrospectively:

Group I (study group)

Included 28 pregnant females complicated at this pregnancy with GDM that confirmed by GCT.

Group II (control group)

Included 87 healthy pregnant females with normal GCT.

Selection criteria

Females in this study should have the following inclusion and exclusion criteria.

Inclusion criteria:

Obese (BMI of 30kg/m2 or higher).

Giving birth to a baby that weighed more than four kilograms (nine pounds).

Using corticosteroid medication.

Having gestational diabetes in a previous pregnancy.

Having a parent, brother or sister with type 2 diabetes.

Having polycystic ovary syndrome (PCOS) or acanthosisnigricans (darkened patches of skin).

Pregnant females had the same range of age (25-35 years).

Normal fasting blood glucose level at first trimester.

Exclusion criteria

Prediabetic.

All cases were subjected in the first visit to detailed history taking regarding,

Consent: written consent was taken on admission for participation in the study after explaining the procedure and the aim of this study for both the study and the control groups.

Personal history: Name, age, occupation, residence.

Menstrual history: and estimation of expected date of delivery.

Obstetric history: Gravidity, Parity, mode of previous delivery, pre-eclampsia or gestational diabetes in any previous pregnancies.

Past history: Medical disease especially hypertensive disorders and diabetes, surgical and gynecological history.

Family history: of type 2 diabetes mellitus in first or second degree relatives.

Clinical examination:

I) General examination: including:

Vital signs including blood pressure in mmHg, pulse, temperature.

Weight, height then we calculate BMI.

Chest & heart examination.

Oedema.

II) Obstetric examination:

Abdominal examination. (Including routine abdominal ultrasound).

Vaginal ultrasound if indicated.

III) Assessment of body mass index (BMI) (Liu M et al, 2012)

Body mass index (BMI= weight kg/(height)2m2)

BMI in normal individuals is 20-24.

BMI in obese individuals is >25

Subdivided as following:

- mild obesity: 25-29
- moderate obesity: 30-34
- Severe obesity: >35.

Lab investigations:

In the first visit in the 1st trimester at 12-14 weeks of gestation:

All patients included in the study will be subjected to:

- Routine investigations of early pregnancy including (Hb in gm/dl, Rh typing, FBS in mg/dl, complete urine analysis). **(Dacie JV, Lewis SM,1995)**

- Serum adiponectin level, triglycerides HDL-cholesterol concentrations in mg/dl using fasting for 8 hours venous blood sample, the blood samples were centrifuged to separate the serum and were stored at -20o C till examined by enzyme-linked immunosorbent assay (ELISA) technique. **(Grundy S, et al, 2002)**

- Estimation of glycosylated haemoglobin (HbA1c) normal level = 4.2-6.2%. **(Scherer PE et al,1995)**

In the second trimester between 24-28 weeks' gestation:

A) Screening tests:

*** Glucose challenge test:"** O'Sullivan test**"**

Done at any time of the day irrespective to meals, by giving 50 gm of oral glucose and measuring blood glucose level after one hour, Levels more than140 mg% is considered positive. **(Agarwal MM et al, 2007)**

If negative, the test was repeated again at 34-36 weeks.

B) Confirmatory tests:

Positive cases with glucose challenge test were confirmed using.

*** 3 hours glucose tolerance curve:**

Patient fasting 8-14 hrs at rest after three days of normal diet.

Fasting blood sample is collected then patient is given 100-g of glucose in 300 cc water and samples are collected every hour.

Special Biochemical Investigations:

Adiponectin enzyme immunoassay for DRG (USA)

Kit provides materials for the quantitative determination of adiponectin in serum. **(Scherer PE et al, 1995)**

Principal of the Assay for adiponectin

The Assay Max Human Adiponectin ELISA Kit is designed for detection of adiponectin in human urine, plasma, serum and cell culture supernatants. This assay employs a quantitative sandwich enzyme immunoassay technique that measures adiponectin in less than 4 hours. A polyclonal antibody specific for adiponectin has been pre-coated onto a microplate. Adiponectin in standards and samples is sandwiched by the immobilized antibody and biotinylated polyclonal antibody specific for adiponectin, which is recognized by a streptavidin-peroxidase conjugate. All unbound material is then washed away and a peroxidase enzyme substrate is added. The color development is stopped and the intensity of the color is measured. **(Scherer PE et al, 1995)**

Principal of the assay for triglycerides

1. Triglycerides lpl glycerol+ fatty aids.
2. Glycerol + ATP GK glycerol-3- phosphate +ADP.
3. Glycerol-3-phosphate + O2 GPO dihydroxyacetone phosphate + H2O2.
4. 2H2O2 + 4-APP + 4-cholesterol pod Quinoneimine dye + 4H2O.

Principal of the assay for cholesterol

The series of the reactions involved in the assay system is as follows

1. Cholesterol esters CE cholesterol + fatty acids.
2. Cholesterol+O2 CHOD cholest-4-en-3-one +H2O2.
3. 2H2O2 + phenol +4AA POD Quinoneimine dye + 4H2O. **(Grundy S et al,2002)**

Principal of the assay for HDL cholesterol

Low density lipoproteins (LDL) and very low density lipoproteins (VLDL) in sample precipitate with phosphotungstate and magnesium ions.

After centrifugation, the cholesterol concentration in the HDL fraction, which remains in the supernatant, is determined.

Cholesterol esters CE cholesterol + fatty acids.

Cholesterol +1/2O2+ H2O CO cholestenone +H2O2.

2H2O +4-Aminoantipyrine + phenol peroxidase Quinoneimine dye + 4H2O. **(Grundy S et al,2002)**

Follow up:

Routine antenatal visits with general & obstetric examinations. (Every month till 28 w. then twice/ month till 36 w. then weekly till delivery.)

Mode of delivery:

Either normal vaginal delivery or caesarian section.

Statistical analysis of the data

Data were fed to the computer and analyzed using IBM SPSS software package version 20.0**.** **(**Armonk, NY: IBM Corp**)** Qualitative data were described using number and percent. The Kolmogorov-Smirnov test was used to verify the normality of distribution Quantitative data were described using range (minimum and maximum), mean, standard deviation and median. Significance of the obtained results was judged at the 5% level.

The used tests were

1 - Student t-test

For normally distributed quantitative variables, to compare between two studied groups

2 - Mann Whitney test

For abnormally distributed quantitative variables, to compare between two studied groups

3 - Receiver operating characteristic curve (ROC)

It is generated by plotting sensitivity (TP) on Y axis versus 1-specificity (FP) on X axis at different cut off values. The area under the ROC curve denotes the diagnostic performance of the test. Area more than 50% gives acceptable performance and area about 100% is the best performance for the test. The ROC curve allows also a comparison of performance between two tests.

4 - Sensitivity

The capacity of the test to correctly identify diseased individuals in a population "TRUE POSITIVES". The greater the sensitivity, the smaller the number of unidentified case "false negatives"

5 - Specificity

The capacity of the test to correctly exclude individuals who are free of the disease "TRUE NEGATIVES". The greater the specificity, the fewer "false positives" will be included

6 - Positive Predictive value (PPV)

The probability of the disease being present, among those with positive diagnostic test results.

7 – Negative Predictive value (NPV)

The probability that the disease was absent, among those whose diagnostic test results were negative.

8 – Accuracy

Rate of Agreement = (True positives + True negatives) / Total tested x 100

3. Results

This study was performed in El Sayed Gala University Hospitals on 115 patient from antenatal care clinic.

All cases were selected after fulfilling criteria of inclusion into the study.

Descriptive data

The mean age for all patients was 38.0 years (standard deviation 28.66 years). 46.1% (n=53) were less than 30 years and 53.9% (n=62) were more than 30 years. (table1)

Table (1): Distribution of the studied cases according to demographic data (n = 115)

	No.	%
Age		
<30	53	46.1
≥30	62	53.9
Min. – Max.	30.0 – 18.0	
Mean ± SD.	38.0 ± 28.66	
Median	5.03	

The mean gestational age was 14.0 weeks (standard deviation 12.90weeks. (table 2)

Table (2): Distribution of the studied cases according to gestational age (n = 115)

Gestational age	
Min. – Max.	13.0 – 11.0
Mean ± SD.	14.0 ± 12.90
Median	0.94

The mean Adiponectin level for all patient was 11.73 (standard deviation 4.57) with minimum 7.16, maximum of 16.3 and median of 9.56.

The mean TG level for all patient was129.89 (standard deviation 68.38) with minimum 40.0, maximum of 290.0 and median of 110.50.

The mean HDL level for all patient was 48.10 (standard deviation 10.41) with minimum 30.0, maximum 68.0 of and median of 46.0.

The mean cholesterol level for all cases was 193.07 (standard deviation of 26.39) with minimum of 119.0, maximum of 253.0 and median of 191.0. (table 3)

Table (3): Descriptive analysis of the studied cases according to Lipid profile (n = 115)

Lipid profile	Min. – Max.	Mean ± SD.	Median
Adiponectin	7.16 – 16.3	11.73 ± 4.57	9.56
Triglycerides "TG"	40.0 – 290.0	129.89 ± 69.51	113.0
HDL	30.0 – 68.0	48.10± 10.41	46.0
Cholesterol	119.0– 253.0	193.07± 26.39	191.0

75.5% (n=87) of the cases were GCT<140(have gestational diabetes) while 24.3% (n=28) had GCT>140(have not gestational diabetes). (table4)

Table (4): Distribution of the studied cases according to GCT (n = 115)

	No.	%
GCT		
<140	87	75.7
>140	28	24.3
Min. – Max.	110.0 – 83.0	
Mean ± SD.	290.0 ± 121.74	
Median	39.17	

Table (5): Relation between GCT and different parameters

	GCT		Test of Sig.	P
	<140 (n = 87)	>140 (n = 28)		
Adiponectin				
Min. – Max.	11.88 – 19.10	3.24 – 8.50	MW= 7.761*	<0.001*
Mean ± SD.	15.49± 3.61	5.92 ± 2.68		
Median	12.38	5.50		
Triglycerides "TG"				
Min. – Max.	62.40 – 129.70	101.0 – 290.0	MW= 7.704*	<0.001*
Mean ± SD.	96.05 ± 33.65	235.04 ± 40.45		
Median	87.0	238.0		
HDL				
Min. – Max.	31.0 – 68.0	30.0 – 64.0	t=1.936	0.055
Mean ± SD.	49.15 ± 9.98	44.82 ± 11.22		
Median	46.0	45.0		
Cholesterol				
Min. – Max.	143.0 – 253.0	119.0 – 228.0	t=0.114	0.909
Mean ± SD.	193.23 ± 25.18	192.57 ± 30.35		
Median	188.0	201.0		

*: Statistically significant at p ≤ 0.5.

Early maternal total serum adiponectin concentration were lower in women who developed GDM cases vs. non-GDM controls (mean ± SD) 5.92 ± 2.68 vs. 15.49 ± 3.61 µ g/ml, adiponectin levels showed a statistically significant difference (p<0.001). (Among the study cases 23 % of women were adiponectin deficient (total adiponectin<5.5 µg/ml). (table 10, figure 9)

Early maternal serum triglycerides level was higher in women who developed GDM (mean ± SD) cases vs. non-GDM controls 235.04 ± 40.45vs. 96.05± 33.65 n g/ml, TG levels showed a statistically significant difference (p<0.001). (Among the study cases 23 %of women were triglycerides higher concentrations (total TG> 155 mg /ml). (table 10, figure 10)

Early maternal serum HDL level was lower in women who developed GDM (mean ± SD) cases vs. non-GDM controls 44.82 ± 11.22 vs 49.15 ± 9.98 HDL showed a statistically significant difference (p<0.005). (Among the study cases 23 %of women were HDL lower concentrations (total HDL < 45 ng /ml). (table 10, figure 11)

Cholesterol level among the study was not statistically significant difference (p<0.9). (table 5)

T, p: t and p values for Student t-test for comparing between the two categories MW, p: p values for Mann Whitney test comparing between the two categories.

Women with lower adiponectin concentration at first trimester has higher risk of GDM than higher adiponectin concentration (**C.I 95%).** (table 6)

Table (6): Agreement (sensitivity, specificity and accuracy) for adiponectin to predict diabetic cases (GCT)

	Cutoff	Sensitivity	Specificity	PPV	NPV
Adiponectin	≤5.5	96.43	100.0	100.0	98.9

Women with Higher triglycerides concentration at first trimester has higher risk of GDM than lower triglycerides concentration (0.96 – 1.01 **C.I 95%).** (table 7)

Table (7): Agreement (sensitivity, specificity and accuracy) for Triglycerides "TG" to predict diabetic cases (GCT >140)

	Cutoff	Sensitivity	Specificity	PPV	NPV
Triglycerides "TG"	>155	96.43	98.85	96.4	98.9

This demonstrates that there is an inversely relation between serum adiponectin and triglycerides level and the risk of GDM as lower adiponectin level, lower HDL level and higher triglycerides level increase the risk of GDM by 3.4 fold.

4. Discussion

Adiponectin is a physiologically active polypeptide hormone derived from adipose tissue and exhibits insulin-sensitizing, anti-atherosclerotic, and anti-inflammatory properties**. (Metzeger and Coustan, 1998)**

Adiponectin has an important role in the pathophysiology of insulin resistance and diabetes, atherosclerosis, hypertension, dyslipidemia and angiogenesis. Moreover, adiponectin has been suggested to play a regulatory role in the metabolic adaptation during human pregnancy and a solid body of evidence supports the role of adiponectin in normal gestation and pregnancy complications**. (Guariguata et al, 2014)**

Only a handful of studies have addressed the maternal adiponectinmultimers concentrations and their relative distribution.

Glucose metabolism disorder is a common complication during pregnancy and its pathogenesis associated with insulin resistance and deficiency of insulin secretion. It has been presumed for a long time that glucocorticoids and placental secreted hormones (human placental lactogen (HPL), progesterone, estrogen, prolactin, etc) mediate the insulin resistance. **(Seshiah et al, 2004)**

However studies have focused on several new factors including leptin and adiponectin which could lead to insulin resistance. But most studies measured the levels of the above factors only after GDM had clearly diagnosed. **(Swami et al, 2008)**

This study was carried on 115 pregnant females with matched age and parity. They were selected from those women who had visited the antenatal clinic of El-Sayed Galal Maternity University Hospital, to investigate the possible role of early pregnancy serum adiponectin and triglycerides and the risk of GDM.

In the present study the serum adiponectin level was significantly lower in early pregnancy associated with higher triglycerides level

Our findings are similar to some previous studies that investigated early pregnancy serum adiponectin and serum triglycerides status and GDM risk, but were different from others.

(Catalano et al,2010) conducted a longitudinal study in which total, HMW and LMW adiponectin were measured in 10 normal lean women, before pregnancy, in both early (12–14 weeks) and in late gestation (34–36 weeks). The authors reported that maternal circulating HMW adiponectin and HMW/Total adiponectin ratio were lower in late gestation than in non-pregnant state, and that there were no significant differences in circulating adiponectinmultimers between early and late gestation.

In current study showed that early pregnancy serum adiponectin was lower in concentration in the cases that developed GDM later on.

(Paradisi et al, 2010) observed a larger decrease in adiponectin levels between 2nd to 3rd trimester and 1st to 2nd trimester. If adiponectin was implicated in the pregnancy-related rise in insulin resistance, we would expect a decrease of adiponectin levels before the known rise in insulin resistance characteristic of 2nd trimester.

Nevertheless, our results demonstrate that low adiponectin levels at 1st trimester are independently associated with risk of developing GDM and suggest that they are likely the reflection of baseline insulin resistance. (Retnakaran, et al,2004) the HMW/Total adiponectin ratio, measured between 28 to 31 weeks of gestation, was decreased in pregnant women of Indo-Asian descent (n=30) as compared to Caucasian women (n=65).

(Lain KY et al, 2008) described a higher maternal concentration of HMW adiponectin and an elevated HMW/Total adiponectin ratio in patients with preeclampsia (n=14) than in normal pregnant women (n=14). Investigators have reported that decreased plasma adiponectin concentrations, measured in early pregnancy, was found in women who had GDM compared with non-diabetic pregnant women.

(La croix m et al, 2013) found that low circulating adiponectin concentration has been associated with several components of the metabolic syndrome, including intra-abdominal body fat distribution, hyper lipidemia and insulin resistance. Taken together, these observations simply that decreased maternal adiponectin levels may be a link between obesity and GDM.

In the current study we found that there is an inverse relation between serum adiponectin and serum triglycerides level and the risk of GDM as lower adiponectin concentration has a higher triglycerides level and increased risk of GDM by 3.8 fold.

Cseh et al （2004) demonstrated a significantly inverse relation between maternal adiponectin level and increased BMI, fasting C-peptide concentration and C-peptide/glucose ratio in women who have GDM.

Cseh et al (2004) also mentioned that maternal plasma adiponectin levels correlated positively with the birth weights of newborns of women who had GDM and those who did not. However, Chan, et al. reported that maternal adiponectin levels at delivery were unrelated to birth weights of neonates of normal pregnant women.

Williams et al (2004) have shown a significantly inverse association between adiponectin levels in early pregnancy and subsequent risk of GDM after

controlling for prepregnancy BMI. Similar results were reported by Lain et al and LaCroix et al.

Hotta *et al* (2000) reported that plasma adiponectin concentrations were statistically significantly reduced in patients with type 2 diabetes as compared with controls.

Recently, investigators reported that low plasma adiponectin concentrations, measured at baseline, were associated with an increased risk of incident type 2 diabetes in Pima Indians.

This observation was corroborated by **Spranger *et al*, (2003)**, who designed a nested, case-control study within the population-based European Prospective Investigation into Cancer and Nutrition Potsdam cohort.

Taken together, results from available animal studies, as well as those from clinical and population-based epidemiological studies, suggest that adiponectin is likely to play a role in the pathogenesis of insulin resistance and type 2 diabetes.

On the basis of these observations, and given that gestational diabetes mellitus (GDM) is biochemically and epidemiologically similar to type 2 diabetes in nonpregnant adults, we used available data from a prospective cohort study to evaluate the extent to which plasma adiponectin concentrations in early pregnancy are associated with the subsequent risk of GDM. We hypothesized that lower plasma adiponectin concentrations would be associated with an increased risk of GDM. **(Pendergrass et al, 1995)**

In this study we found that early pregnancy plasma TG levels≥155mg/dl were associated with a 3.4-fold higher risk of GDM. this result is similar to **Enquobahrie et al (2016)** found that early pregnancy plasma TG levels 137 mg dl−1 were associated with a 3.5-fold higher risk of GDM and that each 20 mg dl−1 increase in TG level was associated with a 10% increase in GDM risk.

Li et al (2009) also reported a 1.58 to 2.7-fold increased risk of GDM among lean and obese women when TG 1.58 mmol l−1 as well as a 50% risk reduction when HDL-C 2.22 mmol l−1.

A meta-analysis published recently showed that in the first trimester, only a high level of TG was a risk factor for GDM, while low HDL-C levels were only significantly associated with GDM in the second and third trimester.

Our results showed that high TG levels and low HDL levels were all risk factors for GDM in early pregnancy; however, a low TG level could have a protective role in the development of GDM.

The underlying mechanisms of the associations between lipid profiles and GDM are not entirely understood. However, some etiologies have been hypothesized. Some studies have shown that abnormal lipid metabolism can lead to the direct destruction of the function of β cells of the pancreas, whereas other studies have shown that excessive lipid accumulation may lead to elevated oxidative stress, which correlates with insulin resistance. Elevated plasma lipid and lipoprotein levels can also directly induce endothelial dysfunction. **(Kettunen et al, 2016)**

In contrast, lipids, especially TG, can cross the placenta in various forms and are transported to the fetus as important nutrients for foetal development. Above all, dyslipidaemia could have a causal role in GDM, PE, preterm birth, LGA, SGA and macrosomia. **(Inouye et al, 2010) (Ritchie et al, 2015)**.

Conclusion and Recommendations

From the present study we concluded that:

Low adiponectin levels in early pregnancy is an early event in the natural history of GDM and is an important one-step analysis in antenatal screening for GDM.

High level of TG in early pregnancy is an early event in the natural history of the disease and is an important one-step analysis in antenatal screening for GDM.

Low HDL concentration is an early event in the disease and is an important one-step analysis in antenatal screening for GDM.

Serum adiponectin is inversely related to serum TG and positively to HDL.

The study was of a small sample size, more research is needed to confirm this finding with different inclusion criteria, using different scores are warranted to fully address this point.

In view of good correlation between serum adiponectin and gestationsl diabetes routine use of early pregnancy measurement of serum adiponectin level is recommended.

In view of good correlation between serum TG and gestationsl diabetes routine use of early pregnancy measurement of serum TG level is recommended.

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