https://muthmj.mu.edu.iq

Muthanna Medical Journal
2023; **10**(1):105-112

http://dx.doi.org/10.52113/1/1/2023-105-112

Insulin resistance and lipid profiles in pregnancy complicated by gestational diabetes mellitus

Mashair. E. Ezeldein [1], Hani. Y. Zaky [1.], Elhassan M. Esihag [2], Adil Mergani [3] and Badreldin Elsonni Abdalla [1]

Abstract

Gestational Diabetes Mellitus (GDM) is an important cause of perinatal mortality and morbidity, The abnormalities of the metabolic syndrome and a high-risk health profile are more frequent among women with previous GDM, and the metabolic syndrome is characterized by several risk factors, including central obesity, hypertension, insulin resistance and dyslipidemia. The purpose of this study: was to compare changes in insulin sensitivity and lipid profiles in Sudanese women with GDM. A case-control study was performed at Wed Medani, Teaching Hospital of Obstetrics and Gynecology, Gezira State, central Sudan, and included 200 pregnant women between 24 - 28 weeks gestation, classified into two main groups using oral glucose tolerance test: Normal Glucose Tolerance NGT (n= 100) and GDM (n= 100). Plasma was used for the determination of fasting blood glucose (FBG), and fasting insulin (FI). Serum was used for Total cholesterol (TC), Triglyceride (TG), low-density lipoprotein cholesterol (LDL-C) and High-density lipoprotein cholesterol (HDL-C). Insulin resistance (IR) markers were calculated including glucose/insulin ratio (G/I), fasting insulin resistance index (FIRI) and homeostasis model assessment of insulin resistance (HOMA-IR), Log HOMA-IR, among 200 women, 100 (50%) developed GDM had higher body mass index (BMI; 30.118 vs. 28.604 kg/m2 p= 0.046) and age (29.23 vs. 27.360 years p= 0.010), In comparison to 100(50%) NGT. women with GDM characterized by higher fasting blood sugar was (102.370 vs. 81.920 mg/dl p< 0.000) and had significantly higher Fasting TC (202.630 vs. 182.850 p= -0. 001) and TG (179.530 vs. 159.690 mg/dl P=0 .024)and LDL-C(143.750 vs 130.3200P mg/dl p= 0. 029), while HDL-C and fasting insulin level did not show significant variations between the two groups (p= 0. 417and p =0.359 respectively), insulin resistance (IR) markers were show significant differences (G/I 0.78 vs. 0.56 p= 0.000. FIRI 2.214vs1.61 p= 0.001 HOMA-IR 2.467 vs 1.792 p= 0.001). Correlation analysis showed that Pregnancies complicated with GDM, HOMA-IR was significantly correlated with FBG (r= 0.317, p= 0.001), BMI (r= 0.429, p= 0.000), TG(r= 0.244, p= 0.015) and LDL(r= 0.295, p= 0.013), while it was no significantly correlated with TC (r= 0.194, p= 0.05) and HDL (r=-0.056, p = 0.578).

Our findings provide evidence of GDM as a condition primarily of IR and it also provides evidence of the association of dyslipidemia with IR.

Keywords: Gestational Diabetes Mellitus, Insulin Resistance, Lipid, Sudanese women

* Correspondence author: mashairezeldein@gmail.com
[1] Department of Biochemistry and Nutrition, Faculty of Medicine, University of Gezira, Sudan.
[2] Departments of Obstetrics and Gynecology, Faculty of Medicine University of Gezira, Sudan.
[3]Department of Molecular and Immunogenic, National Cancer Institute University of Gezira, Sudan (NCI-UG)
Received 11 February 2023; revised 20 April 2023; accepted 11 May 2023, available online 07 June

Introduction

Gestational diabetes mellitus (GDM), is defined as any degree of glucose intolerance with onset or first recognition during pregnancy (1). The prevalence of GDM is increasing as a consequence of the increased prevalence of obesity and type 2 diabetes mellitus (DM) in addition to advancing maternal age (2). It is believed that 2%–5% of pregnancies worldwide are complicated with GDM(3). During pregnancy, the growing fetus requires nutrition and placental hormones, and some of the Chronic inflammation factors, such as tumor necrosis factor α, can antagonize the action of insulin, leading to a state of insulin resistance (IR) (4). Even though it may be transient(5), it is associated with a variety of adverse pregnancy outcomes, which not only cause preeclampsia, excessive amniotic fluid, dystocia and postpartum hemorrhage in pregnant women, Insulin resistance but also neonatal hypoglycemia, malformation, cardiac insufficiency fetal distress, stillbirth, and hypocalcemia in neonates, and Women who have had previous GDM are at increased risk of type 2 diabetes or cardiovascular disease (CVD) in later life (6). During normal pregnancy, exogenous insulin supply modifies lipid metabolism and the changes that are typical of GDM may disappear (7). Though a lot of study has been made there is still doubt in the relationship between maternal Insulin resistance and lipid alteration and certain pregnancy complications and perinatal outcomes in GDM; which could be explained by difference in trimester of pregnancy, condition of glycemic control, race/ethnicity and sample size, but the real causes remain unknown(8). The aim of this study was to compare Insulin resistance and triglyceride (TG) and total cholesterol (TC) (HDL-C) (LDL-C) levels, between those with GDM and those with normal glucose tolerance, following an OGTT in Sudanese women.

Materials and Methods

Two hundred pregnant women (Their ages ranged from 18 to 39 years) with a singleton pregnancy were recruited from the Wed Medani, Teaching Hospital of Obstetrics and Gynecology ,Gezira State, central Sudan, from May 2016 to September 2017. All women were between 24 - 28 weeks' gestation and classified to (100 normal glucose tolerance NG and 100 pregnant women with (GDM). Inclusion criteria: We followed the WHO diagnostic criteria developed by the International Association of Diabetes and Pregnancy Study Group (IADPSG) for the classification of gestational diabetes mellitus (GDM). Accordingly, GDM

was diagnosed if the fasting blood sugar (FBS) was equal to or more than 92 mg/dL, and 2 hr post-glucose load blood sugar equal to or more than 153 mg/dL.(9). Women had the following conditions were excluded from the study, previously medical complications during pregnancy such as type 1 or 2 diabetes, history of hypertension hyperthyroidism, hypothyroidism, polycystic ovary syndrome, and inflammatory diseases, treated with hormones or drugs that may affect glucose or lipids concentrations.

The OGTT involved participants drinking 75g of glucose powder dissolved in approximately 250 ml of water. Drinks were consumed within five minutes and the participants remained seated throughout the process. Venous blood samples were drawn an, one hour and two hours post-glucose load. Blood was collected in vacutainers containing fluoride and oxalate. Blood samples were immediately sent to the laboratory on site and processed in real-time so as to reduce further glycolysis in the blood collection tubes analysis. Serum and plasma samples were separated at 4000 rpm at room temperature for 15 minutes, lipid profile levels were estimated immediately, and remaining Serum was stored at-20°Cuntil further analysis of insulin levels. Serum glucose was measured using a glucose oxidase method; insulin was measured with a chemiluminescence's immunoassay; Lipid profiles which include serum TG, TC, HDL-C, LDL-C were measured using the Tinder enzymatic method. IR was evaluated with the homoeostasis model assessment method m(HOMA-IR), which uses fasting glucose and insulin levels at baseline HOMA-IR was calculated using the following equation:

HOMA-IR = (Glucose mg/L × Insulin μU/L) / 405

Log (HOMA-IR): Log (HOMA-IR) transforms the skewed distribution of fasting insulin values to determine a much stronger linear correlation with glucose clamp estimates of insulin sensitivity when extensive ranges of insulin sensitivity / resistance are being studied (10).

Fasting insulin resistance index (FIRI): FIRI was formulated by Duncan et al. (1995) for estimation of insulin resistance. This was calculated by the equation: FIRI = (fasting glucose mmol × fasting insulin μU/mL) / 25.

Statistical analysis

Statistical analysis was performed using IBM computer using SPSS (statistical program for social science) as follows; descriptive statistics are shown as mean ± Standard mean error (SME) of the mean. . Independent-Samples T Test "t" was performed for comparing means for two groups Pearson's correlation was used to measure how HOMA-IR related with BMI, FBG, lipids parameters, Independent Samples 'P value less than 0.05 was considered statistically significant.

The Results

Results revealed that pregnancies complicated with GDM had significantly higher maternal age and were presented with increased BMI compared to matched normal pregnancy group; however, both groups were matched for gestational age (p-value 0.010, p= 0.046. (Table 1) Lipid parameters :Data obtained from this study revealed significantly higher means for cholesterol and TG and LDL-C in pregnancy complicated with gestational diabetes mellitus compared to normal glucose tolerance group(p= 0. 001, p= 0 .024, p= 0.,029. On the other hand, pregnancy complicated with GDM showed no significant of the mean values HDL p= 0 .417studied groups (Table 1).

Table 1.

Subjects' characteristics and lipid parameters in normal pregnancy and in GDM (Mean ± SME).

Parameter	**GDM (n = 100)**	**Normal** (n = 100)	**P value**
Maternal age (year)	29.23 ± 0.497	27.360 ± 0.519	0.010
BMI (kg/m2)	30.118 ± 0.526	28.604 ±0.538	0.046
TC (mg\dl)	202.630 ±4.141	182.850 ± 4.440	0. 001
TG (mg\dl)	179.530 ±62.93037	159.690 ±5.997	0 .024
HDL(mg\dl)	35.170 ±7.348	33.880 ± 1.404	0. 417
LDL(mg\dl)	143.750 ±43.198	130.320± 4.304	0. 029

Fasting blood glucose and insulin and markers of insulin resistance Compared to NGT women, pregnant group with GDM had elevated fasting blood glucose and markers of insulin resistance which include (fasting insulin resistance index, Homeostasis model in HOMA-IR, and Log HOMA-IR) . There was no significant difference in fasting insulin levels between the two groups the (Table 2).

Table 2.

Fasting blood glucose and markers of insulin resistance in normal pregnancy and in GDM groups

Parameter	**GDM (n = 100)**	**Normal** (n = 100)	**P -value**
FBG (mg\dl)	102.370±0.046	81.9200±0.521	0.000
1 hor	189.87±0.508	-	-
2 hour	176.580±0.536	-	-
FI µU\ml	9.373 ±0.523	8.840±.0.246	0.359
G/I	0.78±0.05	0.56±0.019	0.000.
FIRI	2.214±0.168	1.61±0.04	0.001
Homa IR	2.467±0.185	1.792±0.514	0.001
log Homa IR	0.307±.0.026	0.232±0.014	0 .014

FBG: Fasting blood glucose, FI: Fasting insulin, G/I: Glucose/insulin ratio, FIRI: Fasting insulin resistance index; HOMA-IR: Homeostasis model assessment of insulin resistance *P* value < 0.05 is significant.

Person's correlations

Between HOMA-IR and each of BMI, FBG and lipids parameters in GDM groups:

Pregnancies complicated with GDM, HOMA-IR was significantly correlated with FBG, TG, LDL, and BMI (p= 0.001), (p= 0.015), (p= 0.003) and (p= 0.000) respectively (Table 3).

Table 3.

Person's correlations between HOMA-IR and each of BMI, FBG and lipids parameters in normal and GDM groups.

Pearson correlation		BMI	T c	TG	HDL	LDL	FG
IR (normal)	R	0.270	-0.043	-0.081	-0.009	-0.052	0.597
	P-value	0.007	0.664	0.425	0.926	0.607	0.000
(IR GDM)	r	0.429	0.194	0.244	-0.056	0.295	0.317
	P -value	0.000	0.053	0.015	0.578	0.003	0.001

Discussion

Women with GDM are at higher risk of feto-maternal complication during pregnancy. As metabolic changes of mother leads to several metabolic complications, it was observed that abnormalities of carbohydrate metabolism in GDM lead to other abnormalities, especially lipid abnormalities(11). Physiological insulin resistance underlies all pregnancies beginning around 24–28 weeks of gestation and progressing through the third trimester. Altered maternal lipid metabolism is also common in pregnancy with modest increases in lipids early in pregnancy and significant elevations of lipids later in pregnancy, specifically, triglycerides and to a lesser extent phospholipids and cholesterol(12). With increasing gestational age, the placenta-synthesized lactose, oestrogens, progesterone, and maternal adrenocorticotropic hormones can become resistant to insulin, showing physiological insulin resistance(4). All tissues during pregnancy show decreased sensitivity to insulin, and to maintain glucose metabolism and to stabilize hyperinsulinism, especially pancreatic β-cell hyper function; insulin secretion can be increased to meet the needs of the body and to maintain normal blood glucose levels (Wan g *et al*.2013; Kelstrup *et a*l.2013). However difference In insulin levels between those with and those without GDM remain unclear and the metabolic reasons for dyslipidemia in GDM are not well-established(13) (5). The present study, which reports on changes in Insulin resistance levels both in those with GDM and those with NGT following an OGTT at 24 – 28 weeks' gestation, demonstrates that, although fasting insulin levels in the GDM group were higher than those seen in the normal pregnancy group (9.373 ±0.523µU\ml and 8.840±.0. µU\ml, respectively), the difference was not statistically significant. It may be because the sample size selected in this study was not large enough, blood glucose levels were higher than the standard upper limit indicating an increased presence of IR. In normal pregnancy, as intestinal fat absorption capacity increases significantly, and, under the influence of high levels of oestrogens and progesterone, very low-density lipoproteins generated by the liver are significantly increased and tissue lipase activity decreases (Vejrazkova et al. 2014). TG and TC levels, as markers for lipid metabolism, change significantly, which results in a physiological hyperlipidemia. Normal lipid metabolism, with the absorption, synthesis, and metabolism of lipids in a state of relative equilibrium, is a necessary condition for a healthy pregnancy. Many studies suggest that in women with GDM, there are increased level of triglyceride, LDL-C and total cholesterol and lower level of HDL-C; but these finding are not consistent(13). Results from the present study revealed significantly higher TG and TC levels, , LDL-C and IR indices in the GDM group, and also demonstrated that , LDL-C and TG levels were positively correlated with IR in this group. Hexeberg et al., who studied data , Found that IR was a

common causative factor in metabolic lipid disorders, including hypertriglyceridaemia (14). Scymanska et al. monitored blood lipids, insulin levels and IR indices in 81 GDM women and in 41 normal pregnant women(15). They found that lipids, insulin and IR indices in the GDM group were higher than those observed in the control group which is in agreement to our study. The results suggest that symptoms of IR are present in GDM women. They are characterized by higher serum triglycerides, insulin, and increased IR. These metabolic disorders induce the accumulation of TG in β cells, causing cell toxicity(16). This includes changes such as the formation of lipid droplets in the islet cells, a decreased number of cells, and fibrosis, all of which can aggravate IR and affect β -cell function. indices in 55 GDM women and in 50 normal pregnant women (17), They also found that lipids, insulin and IR indices in the GDM group were higher than those observed in the control group. The results suggest that symptoms of IR are present in GDM women. They are characterized by higher serum TG.TC, LDL and increased IR

Conclusion and recommendations

In summary, this study provides evidence of the association of dyslipidemia with IR. More prospective studies may be conducted in this area including large number of subjects and diverse races, to explore the relationship of lipidemic status and its impact on feto- maternal health and potential method on reducing glycaemia load and improving insulin sensitivity

Ethical approval

Committee of Faculty of Medicine, University of Gezira was approved the Ethics of this study. All the participants of the study were informed about the study objectives.

Funding

None

Conflicts of Interest

The author declares that he has no competing interests.

Study registration

Not required.

References

1. ADA. 14. Management of diabetes in pregnancy: standards of medical care in diabetes—2019. Diabetes care. 2019;42(Supplement 1):S165-S72.
2. Zhu Y, Zhang C. Prevalence of gestational diabetes and risk of progression to type 2 diabetes: a global perspective. Current diabetes reports. 2016;16(1):7.
3. Rosik J, Szostak B, Machaj F, Pawlik A. The role of genetics and epigenetics in the pathogenesis of gestational diabetes mellitus. Annals of human genetics. 2020;84(2):114-24.
4. Barbour LA, McCurdy CE, Hernandez TL, Kirwan JP, Catalano PM, Friedman JE. Cellular mechanisms for insulin resistance in normal pregnancy and gestational diabetes. Diabetes care. 2007;30(Supplement 2):S112-S9.
5. Catalano P. Trying to understand gestational diabetes. Diabetic Medicine. 2014;31(3):273-81.
6. Sullivan SD, Umans JG, Ratner R. Gestational diabetes: implications for cardiovascular health. Current diabetes reports. 2012;12(1):43-52.
7. Rojas-Rodriguez R, Lifshitz LM, Bellve KD, Min SY, Pires J, Leung K, et al. Human adipose tissue expansion in pregnancy is impaired in gestational diabetes mellitus. Diabetologia. 2015;58(9):2106-14.
8. Jin W-Y, Lin S-L, Hou R-L, Chen X-Y, Han T, Jin Y, et al. Associations between maternal lipid profile and pregnancy complications and perinatal outcomes: a population-based study from China. BMC pregnancy and childbirth. 2016;16(1):1-9.
9. WHO. Diagnostic criteria and classification of hyperglycaemia first detected in pregnancy. World Health Organization; 2013.
10. Duncan MH, Singh BM, Wise PH, Carter G, Alaghband-Zadeh J. A simple measure of insulin resistance. Lancet. 1995;346(8967):120-1.
11. Layton J, Powe C, Allard C, Battista M-C, Doyon M, Bouchard L, et al. Maternal lipid profile differs by gestational diabetes physiologic subtype. Metabolism. 2019;91:39-42.
12. Herrera E, Ortega-Senovilla H. Disturbances in lipid metabolism in diabetic pregnancy–are these the cause of the problem? Best practice & research Clinical endocrinology & metabolism. 2010;24(4):515-25.
13. Herrera E, Ortega-Senovilla H. Implications of lipids in neonatal body weight and fat mass in gestational diabetic mothers and non-diabetic controls. Current Diabetes Reports. 2018;18(2):1-13.
14. Hexeberg S, Retterstøl K. Hypertriglyceridemia--diagnostics, risk and treatment. Tidsskrift for den Norske laegeforening: tidsskrift for praktisk medicin, ny raekke. 2004;124(21):2746-9.
15. Szymanska M, Bomba-Opon DA, Wielgos M. Blood pressure and lipid changes in gestational diabetes mellitus. Neuroendocrinology Letters. 2008;29(3):328-33.
16. Ryckman K, Spracklen C, Smith C, Robinson J, Saftlas A. Maternal lipid levels during pregnancy and gestational diabetes: a systematic review and meta-analysis. Bjog: an international journal of obstetrics & gynaecology. 2015;122(5):643-51.
17. Liang Z, Wu Y, Zhu X, Fang Q, Chen D. Insulin resistance and lipid profile during an oral glucose tolerance test in women with and without gestational diabetes mellitus. Journal of Obstetrics and Gynaecology. 2016;36(3):337-9.