LIPID PROFILE AND INSULIN RESISTANCE IN PREGNANT WOMEN WITH FAMILY HISTORY OF DIABETES MELLITUS

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ABSTRACT

Background: *A history of diabetes mellitus in first degree relatives is a major risk factor for diabetes mellitus (DM) and Gestational Diabetes Mellitus (GDM). The underlying disorders in DM and GDM are known to have genetic predispositions. The pregnancy state is a stressor that reveals underlying metabolic derangements particularly with respect to glucose and lipid metabolism. We investigated if the lipid profile and insulin resistance in pregnant women with family history of DM is different from those without such history.*

Method: *Glucose, insulin and lipids (total cholesterol, triglyceride, high density lipoprotein and low density lipoproteins) were measured at 26 to 32 weeks of pregnancy in fasting blood samples obtained from 75 pregnant non diabetic women (Twenty five with a history of first degree relative with DM and fifty women without such history). The insulin resistance was assessed using Homeostatic Assessment Model (HOMA-IR).*

Results: *The ages of the subjects ranges from 20 to 40 years with a mean (S.D) of 30.6 (4.8). The mean gestational age of the subjects was 28.2 (1.2) years. The mean fasting glucose, fasting insulin and Total Cholesterol, Triglyceride, High Density Lipoprotein, Low Density Lipoprotein and HOMA-1R were not significantly different in both groups. Family history of DM was significantly associated with severe insulin resistance ($P < 0.05$).*

Conclusion: *The underlying pathophysiologic derangements in diabetes may well be ongoing in women with family history of DM. A strict follow-up plan should be instituted for this category of pregnant women during and after pregnancy.*

Key words: *Family History of Diabetes Mellitus, insulin resistance, fasting glucose, fasting insulin, lipid profile*

INTRODUCTION

The incidence of type 2 diabetes mellitus (T2DM) in Nigeria is on the increase in parallel with the global trend.[1,2] The number of women going into pregnancy with disorder of glucose metabolism is also thought to be rising.[3] The reasons for this trend are multi-factorial. The increase in prevalence of obesity, affluence, sedentary life style and western-oriented eating habits has been posited as possible explanation for this trend.[1,4]

Genetic factors have been shown to increase the risk of DM. Several genes influence insulin secretion by modulating pancreatic β cell function and insulin action by modifying insulin receptor response. Genetics has also been fingered in other aspects of glucose metabolism and metabolic conditions such as energy intake and expenditure and lipid metabolism that increase risk of T2DM.[5]

Pregnancy is a physiologic condition which places enormous strain on maternal metabolism of glucose and lipids. A general increase in plasma glucose, triglyceride and free fatty acid levels has been attributed to physiologic increase in insulin resistance which is thought to become prominent in the second half of pregnancy.[6-9] These physiologic adaptations are however exaggerated in gestational diabetes mellitus.

Pregnant women with history of DM in first degree relatives are deemed at higher risk for GDM. However there is dearth of data in our local setting to verify the independent association of a family history of DM and key indices of glucose and lipid metabolism in pregnancy. To address this question, this study seeks to determine if the lipid profile and insulin resistance in women with family history of DM is different from those without such history.

METHODOLOGY

This study was conducted in the metabolic research unit of the department of chemical pathology of the Jos University Teaching Hospital using women recruited from the antenatal clinic of the Hospital. A total of seventy five (75) non-diabetic women were recruited for the study. Twenty five (25) of these had a history of first degree relative with DM (positive FH subjects) while fifty (50) women did not have such history (negative FH subjects). The two groups were matched for age and gestational age.

Glucose, insulin and lipids were measured in fasting blood samples obtained from 75 pregnant women at 26 to 32 weeks of pregnancy. The insulin resistance was assessed using Homeostatic Assessment Model (HOMA-IR).

Serum glucose was assayed within 4 hour of sampling. Serum for insulin assay and lipid assays were stored at -20°C and -80°C respectively and analysed within 90 days of sampling.. Blood samples were analysed for glucose and lipids using commercial kits on the Roche/Hitachi 902 automatic analyzer (LDLc was calculated from Friedewald's formula).[10] Insulin was assayed using DRG Human insulin ELISA kits (DRG International, Inc. U.S.A). The intra-batch and inter-batch coefficient of variation (CV) were within limits as quoted by the kit manufacturers. The data was analysed using Statistical Package for Social Sciences (SPSS Incorporated Chicago Version 15.0) softwares. The level of significance was set at $P < 0.05$.

ETHICAL CONSIDERATION

This study was undertaken after due approval from the Ethical Committee of the Jos University Teaching Hospital (JUTH). Informed consent was obtained from all subjects.

RESULTS

The ages of the subjects in this study ranges from 20 to 40 years with a mean (S.D) of 30.6 (4.8) years while the mean gestational age was 28.2 (1.2). The mean (S.D) weight of the subjects was 77.7 (16.7). (see table 1) The median gravidity and parity were 3 and 2 respectively.

Table 1 General characteristics of the subjects

VARIABLE	MEAN	STANDARD DEVIATION
AGE	30.6	4.8
GESTATIONAL AGE	28.2	1.2
GRAVIDITY	3.1	1.0
PARITY	1.8	1.7
WEIGHT	77.7	16.7

The mean (S.D) fasting glucose and insulin were 4.3 (3.9) mmol/L and 10.4 (6.4) mmol/L respectively. The mean (S.D) HOMA-IR was 1.3 (0.8). The mean TC, TG, HDLc and LDLc were 5.2 (0.8) mmol/L, 1.7 (0.5) mmol/L, 1.8 (0.8) mmol/L and 2.6 (1.1) mmol/L respectively (see table 2).

Table 2 - Biochemical characteristics of the subjects

VARIABLE	MEAN	STANDARD DEVIATION
Fasting Glucose (mmol/L)	4.3	3.9
Fasting Insulin (mIU/L)	10.4	6.4
HOMA-IR	1.3	0.8
TC (mmol/L)	5.2	0.8
TG (mmol/L)	1.7	0.5
HDLc (mmol/L)	1.8	0.8
LDLc (mmol/L)	2.6	1.1

TC- Total Cholesterol, TG- Triglyceride,
HDLc- High Density, Cholesterol, LDLc- Low Density Cholesterol

The mean (S.D) fasting glucose was higher in the positive FH group (4.5(1.0) mmol/L) compared to the negative FH group (4.2(1.4) mmol/L). This observed difference was however not significant. The fasting insulin and HOMA-IR were also higher in the postive FH compared to the negative FH subjects although this was not statistically significant. The serum TG levels between the two groups were similar. The TC and LDLc were higher and the HDLc lower in the positive FH compared to the negative FH subjects but this finding was also not statistically significant. (See table 3).

Table 3 - Comparison of the mean (S.D) between POSTIVE FH and NEGATIVE FH women usingindependent sample t- test.

VARIABLE		POSTIVE FH n = 25	NEGATIVE FH n = 50	P-VALUE
AGE	(years)	31.4 (5.0)	30.1 (4.6)	0.28
GA	(wks)	28.2 (1.3)	28.2 (1.2)	1.00
WEIGHT	(kg)	81.8 (19.1)	75.7 (15.1)	0.14
Fasting Glucose	(mmol/L)	4.5 (1.0)	4.2 (1.4)	0.39
Fasting Insulin	(mIU/L)	11.9 (7.9)	9.7 (5.5)	0.17
TC	(mmol/L)	5.2 (0.8)	5.2 (0.8)	0.84
TG	(mmol/L)	1.7 (0.5)	1.7 (0.5)	0.90
HDLc	(mmol/L)	1.7 (0.7)	1.9 (0.8)	0.29
LDLc	(mmol/L)	2.8 (1.0)	2.6 (1.1)	0.33
HOMA-IR		1.5 (0.9)	1.1 (0.6)	0.11

The subjects with HOMA-IR ≥ 1.9 were categorized as having severe insulin resistance. Only 17 subjects (22.7%) in this study had such level of insulin resistance. A family history of DM was significantly associated with severe insulin resistance (P = 0.01) but not with maternal obesity (P = 0.28). The significant association of family history of DM with severe insulin resistance remained after controlling for age, gestational age grand-multiparity and maternal obesity.

Table 4- Association between family history of DM with severe insulin resistance and maternal obesity

VARIABLE		POSTIVE FH	NEGATIVE FH	P-VALUE	ODD RATIO	ADJUSTED ODD RATIO†
SEVERE IR*	YES	10 (58.8%)	7 (41.2%)	0.01	4.1 (1.3-12.7)	1.1 (1.0 -13.1)
	NO	15 (25.9%)	43 (74.1%)			
OBESITY	YES	6 (46.2%)	43 (53.8%)	0.28		
	NO	19 (30.6%)	43 (69.4%)			

* SEVERE IR- severe insulin resistance (HOMA-IR ≥ 1.9).
† Adjusted for age, gestational age grand-multiparity and maternal obesity.

DISCUSSION

Family history of DM predisposes individuals to increase risk of hyperglycaemia and dyslipidaemias. The results from this study show a consistent pattern of higher fasting glucose, fasting insulin, HOMA-IR, TC and LDL levels in the positive FH group compared to the negative FH group

Higher glucose levels among positive FH group compared to the negative FH group was not significant in this study as was found in another study though among non pregnant population.[11] The same study demonstrated significantly higher fasting insulin and HOMA-IR among the positive FH subjects compared to the negative FH subjects. These findings lend credence to the fact that genetic predisposition to insulin resistance among positive FH individuals restrain insulin mediated suppression of endogenous glucose production resulting in higher fasting plasma glucose and stimulation of a feedback loop that results in higher insulin secretion.[12,13]

The TG levels have been shown to be higher among diabetic compared to non diabetic subjects.[14-16] In this study, the TG levels were similar in both positive FH and negative FH groups. The cluster of higher HOMA-IR, weight and levels of glucose, insulin, TC, LDL as well as lower HDL in the positive FH subjects in this study mimics the metabolic and clinical features in metabolic syndrome and type 2 DM.[17-19]

There are no generally accepted cut-off values to classify individuals with insulin resistance particularly in pregnancy, however, it is suggested that individuals within the higher 20th percentile of insulin resistance of a given health population may have severe insulin resistance with associated increased cardiovascular risk.[20] In this study, this cut point was determined to be a HOMA-IR of 1.9. This study showed clearly that women with a family history of diabetes were more likely to have severe insulin resistance (HOMA-IR ≥ 1.9). This suggests that increased insulin resistance, the underlying defect in metabolic disorders characterized by obesity, glucose intolerance and dyslipidaemias may be genetically programmed in this group of women. Although accompanying obesity and derangements in glucose and lipid metabolism did not appear to be significantly different in the positive FH subjects compared to the negative FH subjects in this study, the progression of the metabolic disorder may be the influence by environmental and lifestyle.[21,22] Therefore counseling and follow up of this category of women would be necessary to delay this progression.

CONCLUSION

The underlying pathophysiologic derangement in diabetes may well be ongoing in women with family history of DM. A strict follow up plan should be instituted for this category of pregnant women during and after pregnancy.

DECLARATION: The authors declare no conflict of interest.

REFERENCE

1. Ebenezer AN , Osaretin JO, Anele EI , Aaron O, Seye B. Type 2 diabetes in adult Nigerians: a study of its prevalence and risk factors in Port Harcourt, Nigeria. Diabetes Research and Clinical Practice 2003; 62:177-185

2. Nwaneli C.U. Changing Trend in Coronary HeartDisease in Nigeria. *Afrimedic Journal 2010; 1(1): 1-4*
3. Coetzee EJ. Pregnancy and diabetes scenario around the world: Africa. International Journal of Gynecology and Obstetrics 2009; 104: S39S41
4. Nwafor A, Owhoji A. Prevalence Of Diabetes Mellitus Among Nigerians In Port Harcourt Correlates With Socio-Economic Status. J. Appl. Sci. Environ. Mgt. 2001; 5 (1): 55-57
5. World Health Organisation. Genetics and Diabetes. Available from http://www.who.int/genomics/about/Diabetis-fin.pdf (Accessed on 10th February 2014)
6. Ekhator CN, Ebomoyi MI. Blood glucose and serum lipid profiles during pregnancy. African Journal of Diabetes Medicine. May 2012; 20(1): 16-20
7. Cetin I, Alvino G, Cardellicchio M. Long chain fatty acids and dietary fats in fetal nutrition (2009). *J Physiol* 587(14): 34413451
8. Catalano PM. Obesity, insulin resistance, and pregnancy outcome. Reproduction (2010) 140 365371
9. Catalano P. The Diabetogenic State of Maternal Metabolism in Pregnancy. *NeoReviews* 2002;3;e165-e172
10. Friedewald WT, Levy RI, Fredrickson DS. Estimation of the concentration of low density lipoprotein cholesterol in plasma, without use of preparative ultracentrifuge. Clin Chem 1972; 18:499-502
11. Thejaswini K.O , Dayananda G , Chandrakala S.P. Association Of Family History Of Type 2 Diabetes Mellitus With Insulin Resistance International Journal Of Basic Medical Sciences, Sept 2013; 4(3) Available from:http://www.ijbms.com/physiology/association-of-family-history-of-type-2-diabetes-mellitus-with-insulin-resistance-thejaswini-k-o-dayananda-g-chandrakala-s-p/#.UviyXGJdWNY (Accessed on 10th February 2014)
12. Di Cianni G, Miccoli R, Volpe L., Lencioni C, Del Prato S. Intermediate metabolism in normal pregnancy and in gestational diabetes. Diabetes Metab Res Rev 2003; 19: 259270
13. Butte NF Carbohydrate and lipid metabolism in pregnancy: normal compared with gestational diabetes mellitus. The American Journal of Clinical Nutrition Available from: http://ajcn.nutrition.org/content/71/5/1256s.full (Accessed 10th of February, 2014)
14. Krauss RM. Lipids and lipoproteins in patients with type 2 diabetes. Diabetes Care. Jun 2004;27(6):1496-504.
15. Solano MP, Goldberg RB. Lipid Management in Type 2 Diabetes. Clinical Diabetes. January 2006; 24(1): 27-32
16. Boden G , Laakso M. Lipids and Glucose in Type 2 Diabetes:What is the cause and effect? Diabetes Care September 2004; 27(9): 2253-2259
17. Lavie CJ, Milani RV, O'Keefe JH. Dyslipidemia intervention in metabolic syndrome: emphasis on improving lipids and clinical event reduction. Am J Med Sci. 2011 May;341(5):388-93
18. Brinton EA. Lipid abnormalities in the metabolic syndrome. Curr Diab Rep. 2003;3:6572
19. Grundy SM., Brewer HB, Cleeman JI, Smith SC, Lenfant C . Definition of Metabolic Syndrome: Report of the National Heart, Lung, and Blood Institute/American Heart Association Conference on Scientific Issues Related to Definition. Circulation 2004; 109: 433-438
20. Kernan WN, Inzucchi SE, Viscoli CM, Brass LM, Bravata DM, Shulman GI *et al*. Pioglitazone Improves Insulin Sensitivity Among Nondiabetic Patients With a Recent Transient Ischemic Attack or Ischemic Stroke. *Stroke*. 2003;34:1431-1436.
21. Ershow AG. Environmental Influences on Development of Type 2 Diabetes and Obesity: Challenges in Personalizing Prevention and Management Journal of Diabetes Science and Technology July 2009; 3(4):727-734
22. Abbasi A, Corpeleijn E, van der Schouw YT, Stolk RP, Spijkerman AM, van der A DL et al. Maternal and paternal transmission of type 2 diabetes: influence of diet, lifestyle and adiposity J Intern Med. 2011 Oct;270(4):388-96.