# Blood glucose and serum lipid profiles during pregnancy

C N Ekhator and M I Ebomoyi


## Abstract

Pregnancy is associated with significant changes in the functions of the normal liver and understanding these changes is essential to a proper clinical evaluation of liver abnormalities during pregnancy. This study aimed at determining blood glucose level, triglyceride (TG), high-density lipoprotein (HDL), total cholesterol (TC), and low-density lipoprotein (LDL) in the three trimesters of pregnancy among women in Benin City, Nigeria. This was a prospective cohort study, in which 50 blood samples were collected at each mid trimester of pregnancy. Controls were age-matched, non-pregnant women. Data were analysed using ANOVA and $p<0.05$ was considered statistically significant. The results showed that glucose concentration was significantly higher in pregnant women than the control group, and it was highest in the third trimester of pregnancy. Lipid profile results showed that TG was significantly lower in the control group than in pregnant women. TG was highest in first trimester pregnancy and least in the control group. HDL was significantly lower in the first trimester than in the control group, second or third trimester. Delayed TG clearance is a function of increased blood TG levels and when this occurs with high blood pressure in pregnancy, it could lead to the development of pre-eclampsia. This association may be significant in understanding the process of pre-eclampsia and may help in developing strategies for prevention and early diagnosis of pre-eclampsia.


## Introduction

The pregnant woman experiences physiological changes to support foetal growth and development. Pregnancy is associated with significant change in the functions of the normal liver. Although the precise mechanisms underlying these various alterations are not clear in every case, their recognition is essential to a proper clinical evaluation of liver abnormalities during pregnancy.[1]

During early pregnancy, glucose tolerance is normal or slightly improved and peripheral (muscle) sensitivity to insulin and hepatic basal glucose production is normal.[2] Glucose production increases with maternal body weight, such that glucose production per kilogram body weight does not change throughout pregnancy.[3]

Lipid metabolism changes during pregnancy.[4,5] Natural rising of plasma lipids is seen in normal pregnancy, but this event is not atherogenic and it is believed this process is under hormonal control;[6] but in complicated pregnancy, there is a possible defect in the mechanism of adjusting physiologic hyperlipidaemia.[7] Plasma lipid profiles in the first trimester of pregnancy may predict the incidence and severity of pre-eclampsia.[8] The anabolic phase of early pregnancy encourages lipogenesis and fat storage in preparation for rapid foetal growth in late pregnancy.[9] Lipolysis is increased as a result of insulin resistance, leading to increased flux of fatty acids to the liver promoting the synthesis of very low-density lipoproteins (LDLs) and increased triglyceride (TG) concentrations. Because of a decrease in the activity of lipoprotein lipase, very-LDL remains in the plasma for longer and leads to the accumulation of LDL. An increase in LDL is associated with the development of atherosclerosis.[10] Abnormal lipid metabolism also seems important in the pathogenesis of pregnancy-induced hypertension (PIH). Obviously, the association of serum lipids with gestational proteinuric hypertension is highly suggestive of a role for lipid profile analysis as a diagnostic tool.[11]

During the course of normal pregnancy, plasma triglyceride and cholesterol concentrations rise and as pregnancy progresses both become normal.[12] Hormonal variations during pregnancy affect lipid metabolism. The endogenous female sex hormones have a significant effect on serum lipids.[12] During pregnancy, there is an increase in the hepatic lipase activity and decrease in lipoprotein lipase activity.[12.] Hepatic lipase is responsible for the increased synthesis of the TGs at the hepatic level, whereas the decreased activity of lipoprotein lipase is responsible for the decreased catabolism at the adipose tissue level, the net effect of which will be an increase in circulating TGs and the second step of uptake of the remnant chylomicrons by the liver is delayed so it leads to accumulation of TGs in plasma.[13]

Another hypothesis is that hypertriglyceridemia is probably a consequence of competition between chylomicrons and very LDL cholesterol for the lipoprotein lipase. Classically, chylomicron clearance occurs in two sequential steps: (1) TG hydrolysis by lipoprotein lipase;

*C N Ekhator, Department of Physiology, Faculty of Basic Medical Sciences, College of Medicine, Ambrose Alli University, Ekpoma, Nigeria; and M I Ebomoyi, Department of Physiology, School of Basic Medical Sciences, College of Medical Sciences, University of Benin, Benin City, Nigeria.*
*Correspondence to: Dr Maureen Ebomoyi.*
*Email: maureenebomoyi@gmail.com*

(2) uptake of the remnants by the liver. Delay in the second step leads to accumulation of remnants in plasma and is generally thought to represent the atherogenic risk of hypertriglyceridaemia. The conclusion of another study also indicated that there exists a consistent positive association between elevated maternal TG and the risk of pre-eclampsia.[14]

Increased fasting blood glucose in pregnant women could indicate danger signs which pose a threat to both the woman and the foetus since glucose is an important substrate for metabolism.[15.] A high increase in blood glucose during pregnancy could lead to gestational diabetes which is characterised by difficulty during delivery, abnormal foetal weight, adolescent obesity, and neonatal hypoglycaemia.[16–18]

This study was therefore undertaken to determine the blood glucose level, TG, HDL, total cholesterol (TC), and LDL in the three trimesters of pregnancy in women in Benin City, Nigeria.

## Patients and methods

### Study group

This was a prospective cohort study. Subjects were recruited from pregnant women before the sixth week of pregnancy referred for prenatal care in Modic Medical Centre, Ise Clinic and Maternity, and Edo Medical Center – all in Benin City. They were between the ages of 25 and 34 years. Non-pregnant women of the same age group served as controls. The demographic characteristics and midwifery information were collected by questionnaire. Written informed consent was obtained from all women who participated in the study and then fasting venous blood samples were taken from subjects at mid trimester during the first, second and third trimesters of pregnancy. Blood was also taken from non-pregnant women used as controls. Plasma was separated from blood and assayed.

Individuals with a background of pregnancy complications were excluded: e.g. abortion, preterm delivery, pre-eclampsia, intra uterine foetal death (IUFD); patients having systematic disorders such as chronic hypertension, diabetes, and other chronic diseases were also excluded. Blood pressure was recorded in each trimester throughout the pregnancy.

### Control group

A group of 50 non-pregnant women between the ages of 25 and 34 years attending the same hospitals served as the control group.

### Biochemistry

Blood glucose and lipid profiles were determined using standard methods.

### Statistical analysis

Mean and standard error of mean were calculated for both control and study groups. Level of significance between control and study groups was analysed using one way ANOVA. Data were presented as mean ± standard error of mean. A p value of $< 0.05$ was considered statistically significant.

### Ethics

The ethical committee of the School of Basic Medical Sciences, University of Benin, approved the study.

## Results

The characteristics of the study subjects are presented in Table 1. There was a significant difference in the HDL, LDL, and TC concentrations between the various groups (see Table 2). As shown in Table 2, blood glucose concentration was significantly higher in pregnant women than the control group, and it was highest in the third trimester of pregnancy.

TG was significantly lower in the control group than in the first, second, or third trimester. However, among the pregnant women, TG concentration in the first trimester

*Table 1 Age and clinical characteristics of control and pregnant women*

| Parameter | Non-pregnant controls (n=50) | Pregnant women (trimesters) 1st (n=50) | 2nd (n=50) | 3rd (n=50) |
|---|---|---|---|---|
| Age (years) | 28.0±0.3 | 28.0±0.4 | 28.0±0.4 | 28.0±0.4 |
| Packed cell volume (%) | 38.1±0.2[a] | 33.3±0.3[b] | 30.8±0.1[c] | 30.1±0.4[c] |
| Systolic BP (mmHg) | 100.8±0.5[a] | 105.6±0.7[b] | 98.9±0.5[c] | 103.6±1.2[d] |
| Diastolic BP (mmHg) | 62.1±0.6[a] | 74.6±1.1[b] | 60.3±0.8[c] | 71.8±1.2[d] |

Note
1. All the parameters in this table are expressed as means ± SEM.
2. Means with different superscript letterss are significantly different for the respective parameters at $p<0.05$.
3. Means with the same superscript letterss are not significantly different for the respective parameters at $p<0.05$.

*Table 2 Blood glucose and lipid profile of control and pregnant women*

| Parameter | Non-pregnant controls (n=50) | Pregnant women (trimesters) 1st (n=50) | 2nd (n=50) | 3rd (n=50) |
|---|---|---|---|---|
| Glucose (mmol/l) | 1.86±0.0.02[a] | 0.22±0.2[b] | 2.23±0.09[b] | 9.41±0.002[c] |
| TG (mmol/l) | 3.32±0.01[a] | 7.50±0.22[b] | 6.05±0.07[c] | 5.94±0.007[c] |
| HDL (mmol/l) | 1.40±0.01[a] | 1.15±0.007[b] | 1.46±0.02[c] | 1.35±0.012[d] |
| LDL (mmol/l) | 1.99±0.03[a] | 4.27±0.03[b] | 3.31±0.05[c] | 3.01±0.02[d] |
| TC (mmol/l) | 4.33±0.04[a] | 5.39±0.02[b] | 5.20±0.02[c] | 5.54±0.02[d] |

Note
1. All the parameters in this table are expressed as means ± SEM.
2. Means with different superscript letters are significantly different for the respective parameters at $p<0.05$.
3. Means with the same superscript letters are not significantly different for the respective parameters at $p<0.05$.

was significantly higher than in the second and third trimester. The second and third trimester TG concentrations were not significantly different.

HDL was significantly lower in the first trimester than in the control group, second, or third trimester. LDL was highest in first trimester pregnancy and least in the control group. TC was significantly higher in pregnant women than in the control.

## Discussion

In this study we investigated the changes in glucose and lipid profile throughout the course of normal pregnancy. Age distributions among the pregnant women were the same because the same subjects were studied from first trimester to the third trimester. Age-matched non-pregnant women were used as controls. We observed significantly increased TG, TC, and LDL levels during the course of the pregnancy, which provide evidence of abnormal lipid metabolism during pregnancy.

The increase in TG, TC, and LDL levels observed in pregnant women is in agreement with earlier observations that lipid metabolism changes during pregnancy[4] and a natural rise in plasma lipids is seen in normal pregnancy due to hormones.[8] This rise in TG, TC, and LDL may be due to an increase in hepatic lipase activity and a decrease in lipoprotein lipase activity.[12] Hepatic lipase is responsible for the increased synthesis of triglycerides at the hepatic level, whereas the decreased activity of lipoprotein lipase is responsible for the decreased catabolism at the adipose tissue level, the net effect of which will be an increase in circulating TGs. The second step of uptake of the remnant chylomicrons by the liver is delayed so it leads to accumulation of TGs in plasma.[13]

Some previous studies showed that the most dramatic change in the lipid profile in normal pregnancy is serum hypertriglyceridaemia, which may be two- to three-fold higher during pregnancy compared with the levels in non-pregnant women. In our study also, this observation holds true.[14,19–22] The principle modulator of this hypertriglyceridaemia is oestrogen, as pregnancy is associated with hyperoestrogenaemia. Oestrogen induces hepatic biosynthesis of endogenous TGs, which are carried by very-LDL.[23] This process may be modulated by the hyperinsulinaemia found in pregnancy.[24] The above mentioned interactions along with increased endothelial TG accumulation may result in endothelial cell dysfunction.[25] Increased TG, found in pregnancy-induced hypertension, is likely to be deposited in predisposed vessels, such as the uterine spiral arteries and contributes to the endothelial dysfunction, both directly and indirectly through generation of small, dense LDL.[5] Moreover, this hypertriglyceridaemia may be associated with hypercoagulability.[26] In our study, the rise in serum TG in the third trimester of pregnancy was statistically significant ($p<0.05$) compared with the non-pregnant women. Moreover, very-LDL which carries the endogenous TG is also synthesised in the liver and the increase in TG in gestosis is estimated mainly in the very-LDL.[27]

Hypertriglyceridaemia is probably a consequence of competition between chylomicrons and very-LDL cholesterol for the lipoprotein lipase. Classically, chylomicron clearance occurs in two sequential steps: (1) TG hydrolysis by lipoprotein lipase, (2) uptake of the remnant by the liver. Delay in the second step leads to accumulation of remnants in plasma and is generally thought to represent the atherogenic risk of hypertriglyceridaemia.

On the other hand, increased TGs play a part in decreasing the HDL-cholesterol. HDL particles carry cholesterol from peripheral tissues to the liver. Impaired transport of cholesterol from peripheral tissues to the target area of utilisation may cause the decrease in HDL-cholesterol in serum. According to Pirzado et al,[28] there is a direct correlation between adipose tissue lipoprotein lipase activity and plasma HDL cholesterol. This direct correlation may be responsible for low levels of HDL cholesterol.

It is well known that pregnancy is accompanied by significant alterations in glucose metabolism,[3,29,30] yet the control mechanisms regulating these changes have not been well defined and its assessment is limited in pregnant women. The results obtained in this study showed variability in blood glucose level in non-pregnant and pregnant women. Our result showed that there was a significant ($p<0.05$) increase in glucose production throughout the course of pregnancy when compared with non-pregnant women.

It is believed that the increase in glucose levels helps provide the foetus with a constant glucose environment that is ideal for development, and which makes no demands on its control mechanisms until it is separated from the mother.[31] Perhaps the tendency to greater fluctuation of glucose concentration prepares the foetus for extra-uterine life by increasing the sensitivity of the foetal beta-cell to glucose. However, it is of great importance that the maternal glucose level is controlled as an unstable glucose environment may have adverse effects on the developing foetus. Many workers have suggested that poor glucose control in early pregnancy may be responsible for abnormal foetal development; and neurological defects have been seen in the offspring of diabetic mothers.[31] More specifically, the frequent nocturnal hypoglycaemia observed among insulin-treated diabetic patients may, in severe cases, be a factor responsible for abnormal embryogenesis or perhaps for unexpected death of the foetus during the last trimester of pregnancy.[31]

In summary, as shown in this study, glucose production is increased from the onset of pregnancy to the last trimester. Also, the findings reported in this research suggest that the pregnant women studied had elevated TG, TC, and LDL levels. Increased TG levels are usually associated with delayed TG clearance, and high blood pressure, if present at the same time, could lead to the development of pre-eclampsia. This association may be significant in understanding the pathological process of pre-eclampsia and may help in developing strategies for prevention and early diagnosis of pre-eclampsia. This is however the subject of future research.

**References**

1. Angel GAL. Effect of pregnancy on pre-existing liver disease: physiological changes during pregnancy. *Ann Hepatol* 2006; 5: 184–6.
2. Catalano PM, Tyzbir ED, Wolfe RR. Carbohydrate metabolism during pregnancy in control subjects and women with gestational diabetes. *Am J Physiol* 1993; 264: E60–E67.
3. Assel B, Rossi K, Kalhan S. Glucose metabolism during fasting through human pregnancy: comparison of tracer method with respiratory calorimetry. *Am J Physiol* 1993; 265: E351–E356.
4. Brizzi P, Tonolo G, Esposito F. Lipoprotein metabolism during normal pregnancy. *Am J Obstet Gynecol* 1999; 181: 430–4.
5. Sattar N, Greer IA, Louden J. Lipoprotein subfraction changes in normal pregnancy: threshold effect of plasma triglyceride on appearance of small dense low density lipoprotein. *J Clin Endocrinol Metab* 1997; 82: 2483–91.
6. Rovinsky JJ, Jaffin H. Cardiovascular hemodynamics in pregnancy. III. Cardiac rate, stroke volume, total peripheral resistance, and central blood volume in multiple pregnancy. Synthesis of results. *Am J Obstet Gynaecol* 1966; 95: 787–94.
7. Cunningham FG, Leveno KJ, Bloom SL, et al. *Williams Obstetrics*. 22nd ed. New York: McGraw-Hill, 2005; pp 762–808 and pp 126–32.
8. Setareh A, Mitra MG, Sedigheh B, et al. Maternal plasma lipid concentrations in first trimester of pregnancy and risk of severe pre-eclampsia. *Pak J Med Sci* 2009; 25: 563–7.
9. Kaaja R. Insulin resistance syndrome in pre-eclampsia. *Sem Reprod Endocrinol* 1998; 16: 41–6.
10. Ross R. Atherosclerosis: an inflammatory disease. *N Engl J Med* 1999; 340: 115–26.
11. Jayanta D, Ananda KM, Pradip KS. Study of serum lipid profile in pregnancy-induced hypertension. *Ind J Clin Biochem* 2006; 21: 165–8.
12. Patrizia B, Giancarlo T, Franca E, et al. Lipoprotein metabolism during normal pregnancy. *Am J Obstet Gynecol* 1999; 181(2): 430-4.
13. Rubina A, Tabassum M. Pre-eclampsia and lipid profile. *Pak J Med Sci* 2007; 23: 751–4.
14. Ray JG, Diamond P, Singh G, Bell CM. Brief overview of maternal triglycerides as a risk factor for pre-eclampsia. *Br J Obstet Gynaecol* 2006; 113: 379–86.
15. Famakinwa TT. *A synopsis of medical-surgical nursing*. 3rd ed. Agbor: Krisbec Publications, 2002: pp 315–62.
16. Green D, Stephen M. Fetal maternal metabolism relationship. *J Obstet Gynaecol* 2002; 33: 11–18.
17. Afolabi BB, Abudu OO, Oyeyinka O. Fasting plasma glucose levels in normal pregnant Nigerians. *J Obstet Gynaecol* 2003; 23: 128–30.
18. Mark AB. Association of essential hypertension and insulin resistance. *J Obstet Gynaecol* 2007; 196: 39.
19. Enquobahrie DA, Williams MA, Butler CL, et al. Maternal plasma lipid concentration in early pregnancy and risk of preeclampsia. *Am J Hypertens* 2004; 17: 574–81.
20. Gractacose E, Casals E, Gomez O, et al. Increased susceptibility to low density lipoprotein oxidation in women with a history of pre-eclampsia. *Br J Obstet Gynaecol* 2003; 110: 400–4.
21. Winkler K, Wetzka B, Hoffmann MM, et al. Triglyceride-rich lipoproteins are associated with hypertension in pre-eclampsia. *J Clin Endocr Metab* 2003; 88: 162–66.
22. Toescu V, Nuttall SL, Martin U, et al. Changes in plasma lipids and markers of oxidative stress in normal pregnancy and pregnancy complicated by diabetes. *Clin Sci* 2004; 106: 93–8.
23. Glueck CJ, Fallet RW, Scheel D. Effects of oestrogenic compounds on triglyceride kinetics. *Metab* 1975; 24: 537–45.
24. Adegoke OA, Iyare EE, Gbenebitse SO. Fasting plasma glucose and cholesterol levels in pregnant Nigerian women. *Niger Postgrad Med J* 2003; 10: 32–6.
25. Mikhail MS, Basu J, Palan PR, et al. Lipid profile in women with preeclampsia: relationship between plasma triglyceride levels and severity of preeclampsia. *J Assoc Acad Minor Phys* 1995; 6: 43–5.
26. Kokia E, Barkai G, Reichman B et al. Maternal serum lipid profile in pregnancies complicated by hypertensive disorders. *J Perinat Med (Germany)* 1990; 18: 473–8.
27. Yamaguchi K. Triglycerides and apoproteins in toxaemia of pregnancy, *Nippon Sanka Fujika Gakkai Zasshi (Japan)* 1988; 40: 1875–82.
28. Pirzado ZA, Sangi SA, Malik R. High density lipoprotein cholesterol (HDL) metabolism and its role in the ischemic heart disease. *Pak J Med Res* 1999; 38: 38–41.
29. Connolly CC, Holste LC, Aglione LN, et al. Alterations in basal glucose metabolism during late pregnancy in the conscious dog. *Am J Physiol Endocrinol Metab* 2000; 279: E1166–77.
30. Catalano PM, Tyzbir ED, Wolfe R, et al. Longitudinal changes in basal hepatic glucose production and suppression during insulin infusion in normal pregnant women. *Am J Obstet Gynecol* 1992; 167: 913–19.
31. Gillmer MDG, Beard RW, Brooke FM, Oakley NW. Carbohydrate metabolism in pregnancy: Part I – diurnal plasma glucose profile in normal and diabetic women. *Brit Med J* 1975; 3: 399–404.