Homocysteine and Serum Cholesterol in pregnant Nigerian Women

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Abstract

Hyperhomocysteinaemia and hypercholesterolaemia are implicated in pregnancy and various disease states and conditions including cardiovascular diseases. Their individual effects are known but the use of both in monitoring pregnancy. The aim of this study is thus the determination of serum Homocysteine and cholesterol levels in pregnant Nigerian Women. Healthy fasting adult females had venepuncture while supine and without tourniquet. Homocysteine (tHcy), assay was done using ELISA assay with tHcy binding protein as the capturing enzyme. Excluded from the study were subjects with impaired renal function, liver function and diabetics. Subjects were 60(30 pregnant, 30 non pregnant). Their average age was 26.2 ± 1.7 (CI 0.05 $25.6 - 26.8$ 95%) years for non pregnant controls and 30.7 ± 2.5 (CI 0.05 $29.8 - 31.6$ 95%) years for those pregnant. In the non pregnant group the Mean serum tHcy was $8.0 \pm 4.0 \mu mol/L$ (CI 0.05 $6.6 - 9.4$ 95%). Three females had values $>15 \mu mol/L$. In the pregnant group, Mean tHcy was 4.7 ± 0.9 $\mu mol/L$ (CI 0.05 $3.8 - 5.6$ 95%). Categorization of tHcy is as follows: $<5 \mu mol/L = 8/52(15\%)$, $5-15 \mu mol/L = 41/52(78.8\%)$, $>16 \mu mol/L = 3/52(5.7\%)$.The mean tChol in the pregnant group was $3.26 \pm 1.0 mmol/L$ (CI 0.05 $2.89 - 3.63$) while that for the pregnant group was 4.82 ± 1.0 mmol/L (CI 0.05 $4.45 - 5.19$)
Measuring tHcy and tChol in pregnancy is promising as a good index for monitoring pregnancy. There is a relationship between tHcy and tChol but this needs further investigation.
Keywords: Homocysteine, Cholesterol, Serum, Pregnancy, Nigeria.

1. Introduction

Hyperhomocysteinaemia has been linked in various studies worldwide to the occurrence of cardiovascular disorders, and endothelial cell injury (Holmes 2005). Hypertensive disorders in pregnancy (pre-eclampsia/eclampsia) are among the leading causes of maternal mortality worldwide accounting for approximately 17% of all maternal deaths. Overall perinatal mortality in pre-eclampsia is about 35/1000 total births, but may reach 160/1000 births in severe cases. Pre-eclampsia complicates 3-5% of first pregnancy and 1-2% of subsequent pregnancies with about 5-10% of cases being severe (Keinth 1999).

Homocysteine (Hcy) is a thiol containing amino acid produced by the intracellular demethylation of the essential amino acid methionine. Intracellular Hcy either enters the transulphuration pathway or the remethylation cycle. Apparently 50% Hcy enters the transulphuration pathway, where it is irreversibly combined with Serine by the B_6 dependent enzyme cystathionine beta-synthase to form Cysthathionine (Finkelstein 1990, Perry 1995). This is then metabolized to cysteine and ultimately to sulphate which is excreted in the urine. In the remethylation pathway, Hcy is recycled to methionine by two different reactions catalysed by betaine-Hcy metyltransferase and methionine synthase, which requires 5-methyltetrahydrofolate as methyl donor and vitamin B_{12} as a cofactor (Ueland 1995). When these enzymatic reactions involved in the two metabolic pathways of intracellular Hcy are impaired either due to genetic defects of enzymes for Hcy metabolism or the nutritional deficiency of vitamins such as Folate, B6 and B12, Hcy accumulates in the cells and is exported into the circulation (Malinow 1995). Approximately 80% of circulating Hcy in the blood is protein bound by disulphide linkage (Refsum 1985). The remaining unbound Hcy combines by oxidation either with itself to form the dimmer homocysteine or with cysteine to form the mixed disulphide cysteine-Hcy. Only a small amount circulates as free Hcy. Total Hcy (tHcy) represents the sum of all forms of Hcy including forms of oxidized, protein bound and free.

Hyperlipidaemia has been well documented as a feature of pregnancy in many parts of the world. These findings are from different races (Taylor 1972, De Alvares 1967). Hyperlipidaemia, especially hypercholesterolaemia is frequently associated with hypertension, arteriosclerosis and pre-eclampsia.

Hyperlipdaemia may predispose the pregnant woman to diabetes mellitus. Singly or combined, this can lead to serious problems for the fetus, the mother or both of them. The mechanism of hyperlipidaemia of pregnancy is not fully understood. Genetics and race have been suggested as being pivotal in the aetiology of hyperlipidaemia of pregnancy.

Hyperhomocysteinaemia is a sensitive marker of folate and cobalamin (vitaminB_{12}) deficiency and an independent risk factor for cardiovascular disease. Plasma tHcy concentrations are also related to birth defects, pregnancy complications, Psychiatric disorders, and cognitive impairment in the elderly (Savage 1994, Weir 1998).

Coexistence of hyperhomocysteinaemia and hypercholesterolaemia in a pregnancy can be a serious challenge to the care givers of the pregnant woman, the pregnant woman and the baby. Thus, the measurement of tHcy and lipid profiles in the clinical setting is thus of potentially great importance (Carmel 2001).

Before diagnosis could be made using tHcy level, it is important to know the normal or reference level in the target population. There are some data in the Hcy field in Nigeria and there is an increased interest in this which is good. However, few data exist when it comes to data about lipids and homocysteine in pregnancy in the sub-Saharan Africa.

In this study, we therefore looked at the relationship between serum lipids and tHcy in the Nigerian society with particular reference to healthy pregnant adult females.

2. Materials and Methods

Fifty pregnant females attending antenatal clinic at the Lagos University Teaching Hospital (LUTH) in 2004 were randomly recruited. These were recruited in the third trimester of pregnancy. Fifty healthy age matched female adults were randomly recruited from among the staff of the college of medicine and the teaching hospital and students as controls. The exclusion criteria are; family history of diabetes mellitus, previous big babies (>5Kg), previous gestational diabetes, glycosuria, proteinuria, hypertension, obesity and previous history of pre-ecclampsia or ecclampsia, with malignant diseases, acute infections, cardiovascular diseases, liver and renal disease. Clearance was obtained from the institutional ethical review committee and informed consent obtained from the subjects and controls. The subjects had venepuncture while supine and without tourniquet. Participants provided a complete medical history and were subjected to a thorough clinical examination. Collected blood (10ml) 5ml was transferred to disposable tubes containing Lithium Heparin and the other 5ml into tubes containing no anticoagulant and allowed to clot. After centrifugation at 3000rpm for 5minutes, the recovered plasma (from heparinized tubes) was emptied into dry plastic tubes and stored at -20^oc until assayed. Serum was separated from the clotted sample into dry plastic tubes and equally stored frozen till analysis. Plasma homocysteine concentration was measured by Enzyme-linked Immunosorbent Assay (ELISA) using the micro-well technique of the Diazyme laboratories,3550 General Atoms ct, San Diego, CA and expressed as μmol/L (Frantzen 1998). Serum cholesterol was measured by an enzymatic method.

3. Result

Subjects were 60(30 pregnant, 30 non pregnant). Their average age was 26.2 ± 1.7 (CI 0.05 25.6 – 26.8 95%) years for non pregnant controls and 30.7 ± 2.5 (CI 0.05 29.8 - 31.6 95%) years for those pregnant. In the non pregnant group the Mean serum tHcy was 8.0 ± 4.0μmol/L (CI 0.05 6.6 – 9.4 95%). Three females had values >15μmol/L. In the pregnant group, Mean tHcy was 4.7 ± 0.9 μmol/L (CI 0.05 3.8 – 5.6 95%). Categorization of tHcy is as follows: <5μmol/L = 8/52(15%), 5-15μmol/L = 41/52(78.8%), >16μmol/L= 3/52(5.7%).

The mean tChol in the pregnant group was 3.26 ± 1.0mmol/L (CI 0.05 2.89 – 3.63 95%) while that for the pregnant group was 4.82 ± 1.0 mmol/L (CI 0.05 4.45 – 5.19)

Results were presented as mean ±SD. Pearson's correlation coefficient® was used to show correlation between parameters. P ≤0.05 was considered statistically significant.

4. Discussion

In this study, the mean serum total homocysteine (tHcy) was found to be significantly lower in the pregnant group, 4.7 vs 8.8 μmol/L [Table 1]. The mean total cholesterol (tChol) was however significantly higher in the pregnant group, 4.8 vs 3.3mmol/L.

The finding of a lowered tHcy in the pregnant group is in agreement with many studies. Glew *et al* found a 30% lower mean tHcy in pregnant women compared with their non pregnant controls in Abuja, (7.1 vs 10.1) Nigeria (Glew 2002). Walker and his group got tHcy at 36-42weeks gestation of 5.5(CI 3.3 7.5 95%), in the non pregnant control group they got 7.9(CI 6.2 9.6, 95%) (Walker 1999). It has been widely accepted that tHcy only increase in pregnant women developing preeclampsia. This rise in tHcy in pregnancy has been linked with the formation of reactive oxygen species as well as the promotion of smooth muscle cell growth. Thus, a low level of tHcy in pregnancy is a good prognostication factor.

There have been conflicting reports about the behaviour of tChol in normal pregnancy. Some authors found a rise from 1st through the 3rd trimester of pregnancy while others found an initial rise from 1st to 2nd trimester and a fall in the 3rd trimester (Sitadevi 1981, Brizzi 1999). Continuous rise throughout pregnancy has been found by earlier workers in Nigeria, United States of America, Asia and Europe (Ajose 2002). However, Das and Isichie, Adegoke and coworkers reported a fall in the third trimester (Das 1996, Adegoke 2003). It is known that in early pregnancy there is maternal fat accumulation but in the late phase of pregnancy maternal response to increased fetal demand ensures that fat which yields more energy per mole is utilized preferably to glucose.

In this study, we found a tChol level of 3.3 in the non-pregnant controls and 4.8mmol/L in the pregnant group. This finding is comparable with that reported by Ajose (2002) and Ahaneku (1999) in the third trimester of pregnancy.

The association between tHcy and tChol in pregnant group in this study shows a correlation of 0.2 (r=0.2) while that between the tHcy and tChol in the non-pregnant controls was -0.4(r=-0.4).

This may indicate that an increased tChol in presence of low tHcy may be a good prognostic tool in monitoring pregnancy. However, more studies are needed to fully establish the relationship between tHcy and tChol in pregnancy such that it can be used to monitor pregnancy effectively. A longitudinal or cohort study involving a sizable number of pregnant women from 1st through the third semester will be ideal.

5. Conclusion

Measuring tHcy and tChol in pregnancy is promising as a good index for monitoring pregnancy. When the precise relationship is established alongside its aetiopathogenesis, it will be possible to introduce these tests in hospitals for the monitoring of pregnancy.

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Table 1: Mean Age, tHcy and tChol in studied groups

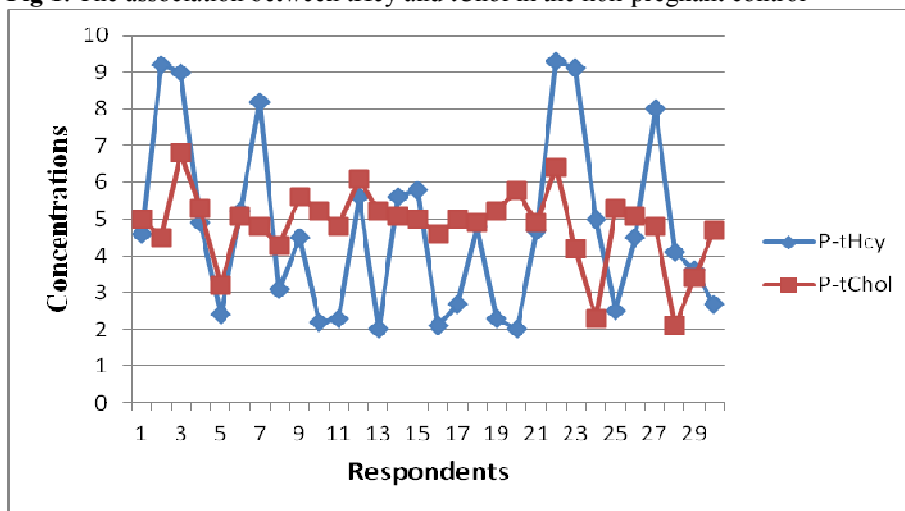|	Non Pregnant		Pregnant	
Mean age (Yrs)	26.2[a]	3.5[b]	30.7[a]	5.0[b]
tHcy	8.0	8.0	4.7	4.8
tChol	3.3	2.0	4.8	2.0

Where a = mean values
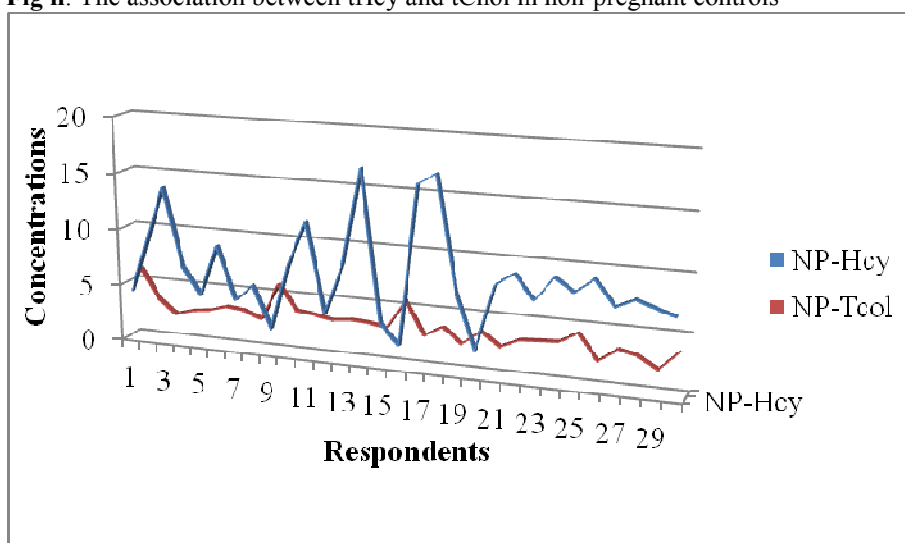   b = 2SD
  tHcy = total Homocysteine
  tChol= total Cholesterol

Fig 1: The association between tHcy and tChol in the non-pregnant control

There is a correlation of -0.37 between tHcy and tChol in the pregnant women.

Fig ii: The association between tHcy and tChol in non-pregnant controls

There is a correlation of 0.2 between tHcy and tChol in the non pregnant control group.

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