Original Article

Serum Lipid Profile in Reproductive Age Women in Abakaliki, South-East Nigeria

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Abstract

Background: Parity has been associated with changes in serum lipid concentrations. This may have implications for cardiovascular health of women. **Aims:** The objective of the study was to evaluate atherogenic risk in a sample of reproductive age women in Abakaliki, southeast Nigeria, using lipid ratios like the Atherogenic Index of Plasma (AIP), Castelli's Risk Index (CRI) and Atherogenic coefficient (AC). **Subjects and Methods:** This questionnaire based survey was conducted in one of the federal tertiary hospital in southeast Nigeria. Sampling was by non-probability purposive sampling technique. Study participants were drawn from women who had come for gynecological consultation, between December 1st 2014 and October 31th 2015. They were arbitrary classified into four groups based on their parity. The survey instrument was administered to the participants after obtaining an informed consent, and blood samples were drawn and analyzed for HDL cholesterol, LDL cholesterol, triglycerides and total cholesterol. Atherogenic risk ratios were derived from these lipid parameters and analyzed for statistical differences. Data analysis was by descriptive and inferential statistics using IBM SPSS Statistics for Windows, version 24.0. Armonk, NY: IBM Corp. **Results:** The age of the women ranged from 17 to 65 years with a mean age of 32.9 (8.6) years. The lipid ratios were significantly different among the groups, especially for the AIP, CRI-I and II (p-values 0.03; 0.02; 0.02 respectively). Bonferroni Multiple Comparison Test demonstrated higher lipid ratios for low parity (para 1 and 2) than the nulliparous (CRI-I; 3.27 ± .196 vs. 4.354 ± 0.277and CRI-II; 1.791 ± 0.178 vs. 2.655 ± 0.251). **Conclusion:** The study demonstrated a higher atherogenic risk for low parity than the nulliparous.

Keywords: Serum lipids changes; Pregnancy; Childbirth

Introduction

Coronary heart disease (CHD) is an important public health concern in developing countries. [1-3] Associations of parity and coronary heart disease have been described in several studies, though results are inconsistent. [4-13] Changes in serum lipid levels during pregnancy have been implicated as a possible mechanism. Pregnancy and childbirth are important events in the life of a woman. Fluctuations of serum sex hormone levels during the process of pregnancy and delivery, perinatal hemodynamic changes, oxidative stress and other gestational factors exert complex influences on the cardiovascular system. Lipid levels rise progressively during pregnancy, and repeated pregnancies may have adverse effects on blood lipid profile. [14-17]

Initial studies on the relationship between parity and cardiovascular risk, demonstrated the increased prevalence of cardiovascular disease with parity number. [5] However, subsequent studies found minimal or no evidence for this association. [18] Incidentally, no such studies relating parity and serum lipids have been carried out in this part of the country. Since women from this part of the country are traditionally known to have large family size, it would be interesting to study lipid profile changes in relation to childbirth. The objective of the study therefore was to evaluate atherogenic risks associated with childbirth using lipid ratios like Atherogenic Index of Plasma (AIP), Castelli's Risk Index I and II (CRI-I and II) in a sample of reproductive age women in Abakaliki, southeast Nigeria.

Subjects and Methods

This was a questionnaire based cross-sectional study carried out at one of the federal tertiary hospital in south east Nigeria. Study participants comprised of women seen at the gynecology clinic of the hospital during the period 1st December 2014 to 31st October 2015. The hospital, located in the heart of the capital city Abakaliki, is the only tertiary health facility in Ebonyi State. Because of its referral status, out-patient consultation rate is very high. Ebonyi state is predominantly agrarian, and most of the women engage in subsistent farming and petty trading. Hospital fees are minimal and affordable. Overall, four hundred and thirteen participants were selected for the study using a non-probability purposive sampling technique. The sample size for the study was determined using GraphPad StatMate version 2.00 for Windows, GraphPad Software, San Diego California USA, www.graphpad.com. Sample size was calculated using an estimated standard deviation of 0.45 from a pilot study, and a significance level (alpha) of 0.05. We determined that a total sample size of 400 had an 80% power to detect a difference between means of 0.18 with significance level of 0.05. The

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survey instrument used was a semi-structured questionnaire with both closed and open-ended questions. The questionnaire was validated in a pilot study by testing for both content and constructs validity. The first part of the questionnaire asked questions on the socio-demographic characteristics of the participants (age, parity, educational status, occupation of husband, oral contraceptive use, menopausal status, and alcohol use and smoking), while the second part contained baseline measurements of blood pressure, weight, height, fasting blood sugar and the serum lipid levels of each participant. Two research assistants administered the survey instrument to the women as they waited for gynaecological consultation. Informed consent was obtained prior to this. The participants were instructed to observe an overnight fast during the next scheduled gynecological appointment, when fasting venous blood was collected through venepucture of the large antecubital veins in the chemical pathology department of the hospital, for analysis. The blood samples were analyzed for total cholesterol, HDL-cholesterol, triglycerides and LDL-cholesterol (millimole per liter) using the appropriate kits for Randox (Crumlin, County Antrim, BT294QY, United Kingdom). Atherogenic lipid ratios were then derived from these lipid parameters. The logarithmically transformed ratio of plasma TG to HDL-C (known as Atherogenic Index of Plasma, AIP) correlates closely with the LDL particle size and can serve as an indicator of the atherogenic lipoprotein phenotype. Clinical studies have shown that AIP predicts cardiovascular risk and that it is an easily available cardiovascular risk marker. [19] Castelli's Risk indexes (CRI) are based on three important lipid profile parameters i.e. TC, LDL-C and HDL-C. CRI-I calculated as the ratio of {TC/HDL-C} and CRI-II as {LDL-C/HDL-C}. [20] The laboratory analysis was conducted by one of the medical laboratory scientist specially enlisted for the research. The specimen used for the analysis was fasting plasma and all the samples were collected in heparinized containers which does not alter the concentration of analytes. The samples were analyzed using a semi-automated colorimetric method using CHEM-7 machine, which is manufactured by Erba Manheim, Germany. Pipetting was carefully done and all through the process of analysis, only one set of pipettes were used. Also, the equipment used was the same used for routine laboratory investigations which were calibrated daily. Quality control specimens were used along with routine samples for validation of results. LDL cholesterol was calculated using the Friedewald's equation. For the analysis, the women were grouped into social classes using the classification of Olusanya and Okpere. [21] The height and weight were also entered into the questionnaire and used to calculate the body mass index (BMI), using the formula weight/height squared. A self-report physician diagnosis of diabetes or use of hypoglycemic agents or insulin was used to exclude diabetes mellitus. Hypertension was defined as a self-report physician diagnosis of hypertension, antihypertensive use, or systolic blood pressure (SBP) ≥140 mmHg or diastolic blood pressure (DBP) ≥ 90 mmHg. Parity was defined as live births, since this is more likely to be recalled accurately than pregnancies or miscarriages. This eliminates errors which might arise due to recall bias. The women were arbitrary categorized into four groups for this study: Para 0 (nulliparous), Para 1-2 (low parity), Para 3-5 (moderate parity), and Para ≥ 6 (high parity). The exclusion list for the study include; breastfeeding women, hypertensive women, diabetic women, women with history of hormonal contraceptive or alcohol use and those who smoked cigarette. This research was conducted in accordance with the guidelines of the Helsinki declaration. Ethical approval for this study was obtained from the hospital ethics committee.

Statistical Analysis

Statistical analysis was performed using IBM SPSS Statistics for Windows, version 24.0. Armonk, NY: IBM Corp. Preliminary analysis involved a description of baseline characteristics of the participants. Descriptive statistics for continuous variables were presented in form of means, standard deviations and or confidence intervals where appropriate, while categories were stated as percentages and proportions. We compared mean differences in serum lipid concentrations using the One-way ANOVA test. The atherogenic ratios (Atherogenic Index of Plasma (AIP); Castelli Risk Index-1 and 11 (CRI-1 and 11); and the Atherogenic coefficient (AC) were derived from the lipid parameters and tested for statistical differences. Statistical significance was taken as $P<0.05$ [Table 1].

Results

Majority of the participants were married women (350/414 or 84.5%). The age of the women ranged from 17 to 65 years with a mean of 32.9 (8.6) years. The nulliparous and the low parity women were relatively younger (30 and 35 years respectively) when compared to the high parity group (46 years). Majority (52%) of the women had post-secondary education. About 47% of the study participants were from the low social class, while the middle (social class III) and high social classes (social class I and II) made up 25.4% (105/413) and 27.4% (114/413) respectively. Table 2 shows the mean serum lipid concentrations for HDL cholesterol, LDL cholesterol, triglycerides and total cholesterol. The p- values for the ANOVA were not statistically significant (p-values of 0.11, 0.10, 0.32 and 0.08 for HDL, LDL, Triglycerides and Total cholesterol respectively). Table 3 shows the values of the lipid atherogenic ratios: Atherogenic Index of Plasma (AIP), Castelli Risk ratio-I and II (CRI-I and II) and Atherogenic Coefficient (AC), with p-values. The ratios were significantly different among the groups ($p<0.05$) especially for the AIP, CRI-I and II (p-values 0.03; 0.02; 0.02 respectively). Bonferroni Multiple Comparison Test demonstrated a higher atherogenic risk value for low parity than the nulliparous (CRI-I; 3.27 ± .196 vs. 4.354 ± 0.277and CRI-II; 1.791 ± 0.178 vs. 2.655 ± 0.251).

Discussion

There are conflicting reports regarding the relationship between parity, High Density Lipoprotein Cholesterol (HDL-C), Low Density Lipoprotein Cholesterol (LDL-C), Triglycerides (TG) and Total Cholesterol (TC). Previous studies had found a lower mean HDL-C (and higher TG, LDL-C and TC) values in parous women than in nulliparous women, with obvious negative health implications. Mankuta et al. [22] reported a cumulative effect of consecutive pregnancies on lowering HDL cholesterol levels, while Gunderson et al. reported a decline

Table 1: Baseline characteristics of study participants stratified against parity shown as percentages, mean with standard deviation.

	Parity			
	Nulliparous (n=187)	**Low parity (n=94)**	**Moderate parity (n=88)**	**High parity (n=45)**
Marital status				
Married	125 (35.7%)	92 (26.3%)	88 (25.1%)	45 (12.9%)
Unmarried	62 (96.9%)	2 (3.1%)	0 (0.0%)	0 (0.0%)
Social class				
I	7 (50.0%)	4 (28.6%)	0 (0.0%)	3 (21.4%)
II	43 (43.0%)	21 (21.0%)	29 (29.0%)	7 (7.0%)
III	79 (75.2%)	14 (13.3%)	7 (6.7%)	5 (4.8%)
IV	43 (44.3%)	13 (13.4%)	31 (32.0%)	10 (10.3%)
V	15 (15.3%)	42 (42.9%)	21 (21.4%)	20 (20.4%)
	Mean (SD)*	Mean (SD)	Mean (SD)	Mean (SD)
Age (years)	30 (6)	30 (7)	35 (9)	46 (7)
***BMI (kg/m²)**	23.64 (5.3)	23.12 (3.2)	25.37 (4.8)	24.33 (3.9)

Footnotes: *SD=Standard deviation; †BMI=Body Mass Index

Table 2: Mean serum lipid concentrations for parity with 95% CI.

	Parity								
Lipid profile	**Nulliparous (n=187)**		**Low parity (n=94)**		**Moderate parity ((n=88)**		**High parity n=45**		
	Mean	**95% CI§**	**Mean**	**95% CI**	**Mean**	**95% CI**	**Mean**	**95% CI**	**P value**
†HDL (mmol/l)	1.01	0.95-1.08	0.94	0.85-1.03	0.98	0.87-1.08	1.18	1.0-1.36	0.11
‡LDL (mmol/l)	1.51	1.37-1.65	1.44	1.27-1.62	1.26	1.05-1.47	1.30	1.01-1.59	0.10
ʅTG (mmol/l)	0.88	0.78-0.99	0.80	0.70-0.90	1.22	1.01-1.44	0.75	0.65-0.84	0.32
ϕTC (mmol/l)	2.90	2.74-3.07	2.82	2.67-2.90	2.76	2.50-3.03	2.82	2.42-3.21	0.08

Footnotes: *mmol/dl= millimole per liter; †HDL cholesterol= High density lipoprotein cholesterol; ‡LDL cholesterol= Low density lipoprotein cholesterol; ʅTG= Triglycerides; ϕTC=Total cholesterol; §CI= confidence interval

Table 3: Atherogenic ratios ± SEM.

			Parity		
lipid ratios	**Nulliparous (n=187)**	**Low parity (n=94)**	**Moderate parity (n=88)**	**High parity (n=45)**	
	mean ± SEM	mean ± SEM	mean ± SEM	mean ± SEM	p-value
AIP	-0.129 ± 0.028	-0.069 ± 0.040	0.0002 ± 0.042	-0.169 ± 0.057	0.033
CRI-1	3.270 ± 0.196	4.354 ± 0.277	3.348 ± 0.292	3.489 ± 0.400	0.013
CRI-2	1.791 ± 0.178	2.655 ± 0.251	1.657 ± 0.266	2.081 ± 0.364	0.021
AC	1.904 ± 0.080	1.822 ± 0.113	1.764 ± 0.119	1.818 ± 0.163	0.781

AIP: Atherogenic Index of Plasma Calculated as Log TG/HDL; CRI-1: Castelli Risk Index-1 calculated as TC/HDL; CRI-2: Castelli Risk Index-2 calculated as LDLc/HDL; AC: Atherogenic Coefficient calculated as (TC– HDL)/HDL

in HDL-cholesterol up to 10 years after the first pregnancy. [23] Hubert et al. [24] assessed 8-year changes in lipid levels amongst offspring of the Framingham cohort who were aged 20-29 at entry into the study. Women experienced approximately 1 mg/dl declines in HDL-cholesterol with each birth after adjusting for a variety of potentially confounding factors. Lv et al. [25] also found a correlation between parity and lipid metabolism in Chinese women. They observed that women with higher parity appeared to have a lower total cholesterol in blood. Conversely, Kritz-Silverstein et al. [26] reported that number of childbirths was unrelated to HDL cholesterol concentrations in women, particularly for low parity women. Lock et al. [27] also found that parity did not affect lipid concentrations among Singaporean women. Although there was no difference in the mean serum lipid concentrations of HDL-C, LDL-C, TG and TC in the present study, the lipid ratios based on these parameters were statistically different among groups ($p<0.05$). The p-values for the AIP, CRI-I and CRI-II were 0.03, 0.01 and 0.02 respectively. These ratios can contribute significantly to the estimation of atherogenic risks, especially when absolute values of lipid profile parameters are not markedly deranged. The ratios have been found to be a better mirror of the metabolic and clinical interactions between lipid fractions. They therefore have more relevance over individual lipid parameters. It has also been shown that in situations where other atherogenic risk parameters like TG and HDL-C appear normal, AIP may be a diagnostic alternative. [28] According to Grover, either the ratio of LDLC/HDL-C or TG/HDL-C is the best related predictor of

future cardiovascular events. [29] The Castelli's Risk Index-I and II showed significantly higher atherogenic risk values for low parity than for nulliparous (CRI-I; 3.270 ± 0.196 vs. 4.354 ± 0.277, p-value 0.01 and CRI-2; 1.791 ± .178 vs. 2.655 ± .251, p-value 0.03). Dior et al.[10] reported higher atherogenic risk value for mothers of 1 child (HR = 1.18; 95% CI, 1.04–1.4), mothers of 5–9 children (HR = 1.21; 95% CI, 1.09–1.33), and mothers of ≥ 10 children (HR = 1.49; 95% CI, 1.12–1.99) than mothers of 2–4. Most reports show a nonlinear association between parity and lipid ratios. Gallagher et al. [30] showed slightly increased atherogenic risk associated with more than five births while Jaffe confirmed that the risk estimates were higher among women with no children (HR 2.43, CI 1.49, 3.96) and women with more than 8 children (HR 1.64, CI 1.02, 2.65) than those with two children. [31,32] In contrast, a cohort study reported by Jacobs et al. suggested that women with more than 4 pregnancies were at lower CVD mortality risk, [11] with further reduction of mortality as parity increases. [33] Several potential mechanisms might have been proposed but the exact biologic mechanisms are not fully understood. The protective effect from moderate parity reported by some researchers may be linked with the enhanced endothelial function in pregnancy, which results in greater bioavailable nitric oxide. [11] It is worth mentioning that increased endothelial function from pregnancy, unlike its concurrent metabolic change and other temporary disorders, may continue postpartum. [34] Furthermore, numerous pregnancies always result in prolonged exposure to high levels of estrogen and progesterone, which may reduce atherogenic risk. However, numerous pregnancies also relate to older maternal age, inflammation and oxidative stress, which are tightly associated with adverse predictors to cardiovascular disease, as was seen in some of these studies.

Some researchers have expressed the view that the rise in atherogenic risk with parity may be as a result of residual confounding due to socioeconomic position [4] or lifestyle risk factors and stress associated with child-rearing. [35] Increased atherogenic risk was more likely to be attributable to lifestyle factors such as anxiety, stress, even fear of raising children. [36,37] Socioeconomic factors may also enhance the relationship between parity and atherogenic risk for Cardiovascular disease, because both Cardiovascular disease and high parity have higher frequency in lower social classes. [10] Also, higher parity, for example, may lead to unhealthy behaviors, such as smoking and alcohol consumption which then impact on lipid levels. However, the effects of these factors are difficult to measure using biological assays, [36] and are even more difficult to fully include in studies.

This research addressed an important aspect of women's reproductive health which had been relatively under-investigated in black women, especially in Nigeria. The survey data and measurements were collected first hand, and this contributed to completeness of data. The gynecology clinic is an organized setting where it was relatively easy to identify the group needed for the research. If the respondents were unclear about the meaning of a question they could ask for clarification. Response rate was almost 100 percent since the researcher could give the questionnaire to those who were present and be sure to get immediate feedback. The selection criteria for the participants was quite stringent, and although it affected recruitment, it made the sample population more homogenous in terms of addressing the effects of confounding variables. Parity was defined as live births, thereby eliminating the effect of recall bias. There are however some limitations to this study. Being a hospital-based study, findings from this study may not be generalized to the general population, since only a segment of the women in Abakaliki may have visited our facility. We also observe that there is an inherent imprecision in a single, cross-sectional determination of lipid levels because lipid levels may change with time.

Conclusion

In conclusion, the study demonstrated a higher atherogenic risk ratio for low parity than the nulliparous. There is yet no agreement on the influence of parity on lipid atherogenic risks. This remains an area of controversy and a subject for further prospective research.

Conflict of Interest

All authors disclose that there was no conflict of interest.

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