

Parity and Atherosclerosis

Riadh Abdul Razzaq Al- Rammadani (MB ChB, M Sc, Ph D)

Summary:

Pregnancies are associated with major physiological changes and increase the risk of ischemic heart disease. The aim of this study was to evaluate the effect of parity on the carotid artery as a representative of arterial atherosclerotic changes in pre and post-menopausal women.

Material and methods: The women included in this study were classified into two groups, group I (pre-menopausal women) and group II (post-menopausal women). Each group has been further classified into subgroups including: a (null-parties), b (1 and 2 parities), c (3 and 4 parities), and d (more than 4 parities). Lipid profile including: total cholesterol (TC), triglycerides (TG), high density lipoprotein (HDL), Low density lipoprotein (LDL) and oxidized low density lipoprotein (oxLDL) was measured biochemically while common carotid artery compliance coefficient (Co) assessed ultrasonographically.

Results: The results showed lower HDL and Co and higher TC, TG, LDL and oxLDL in group II than I. The increase in parity was associated with decrease in HDL and Co and increase in TC, TG, LDL and oxLDL in group I and II.

Discussion: The difference in compliance and lipid profile results between group I and II was referred to menopausal changes including the difference in age and estrogen concentration while the compliance results correlation with parity were explained by the physiological effects of pregnancies on lipid profile. The major conclusions of this work were, post-menopausal women have less elastic arteries than pre-menopausal women and increase parity will decrease the arterial wall elasticity in pre and post- menopausal women.

Key words: Common carotid artery, compliance, parity.

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Introduction

Complications in late pregnancy⁽¹⁾ and history of any spontaneous loss of early pregnancy before the first live birth were associated with an increased risk of ischemic heart disease (IHD)⁽²⁾. Acute myocardial infarction associated with pregnancy has been noted to occur most commonly in multi-gravidas⁽³⁾. Increased parity was associated with increased risk of cardiovascular disease⁽⁴⁾. Data by Humphries et al "2001" demonstrated that there is a positive association between parity and risk of carotid artery plaques in elderly women⁽⁵⁾. Lawlor et al "2003" found associations between number of children and IHD, with the prevalence lowest among those with 2 children and increasing linearly with each additional child above 2⁽⁶⁾.

The mechanical properties of large elastic arteries are important determinants of circulatory physiology⁽⁷⁾. Decrease in arterial compliance, which reflects the ability of an artery to expand and recoil with cardiac pulsation and relaxation⁽⁸⁾. It has been identified as an independent risk factor for cardiovascular disease⁽⁹⁾. The majority of strokes associated with pregnancy were arterial occlusions mostly presented during the third trimester and puerperium⁽¹⁰⁾.

The aim of this study is to measure the effect of parity on the arterial physiological wall property through the measurement of common carotid artery compliance in pre and post-menopausal women with different numbers of parities.

Material and methods:

Subjects:

The subjects included in the current study have been selected from different teaching hospitals in Baghdad at the time extended from Jan, 2004 to Aug 2004. The women involved in this study were classified into two groups' Pre and Post-menopausal women were considered as group I and group II respectively. All the women with the following criteria have been excluded including, habits (smoking and alcohol intake), diseases (cardiovascular, endocrinal and gynecological), drugs (oral contraceptive, hormone replacement therapy) and finally any obstetric complications. Pre-menopausal women who reported irregular monthly bleeding and women who reported presence of climacteric symptoms, defined as perspiration and / or hot flushes, were excluded from the current study. Women were considered to have natural menopause if their menses had ceased naturally for at least 12 months.

The total number of women included in this study were (105) and the remaining of the women after the above exclusion continued to be investigated were (83) including (44) women in group I and (39)

* Al-Kindy Medical College Baghdad University

women in group II. Each subject agreed to participate in the study after being informed of its nature and purpose. The protocol of the study was approved by the local Ethics Committees of the institutions involved.

Parity assessment:

Groups I and II have been further subdivided in subgroups according to their parity number into: a (null-parties), b (1 and 2 parities), c (3 and 4 parities), and d (more than 4 parities).

Common carotid artery compliance coefficient:

The right common carotid artery compliance coefficient was measured ULTRASONOGRAPHICALLY (530D model VOLUSON 530D with 7.5 MHz linear array transducer) as described by Henry et al "2003" (11). Compliance was calculated from diameter, distension and pulse pressure as follows:

$$\text{Compliance coefficient (Co)} = (2D \cdot \Delta D + \Delta D^2) / (4 \cdot \Delta P) \text{ in mm}^2 \cdot \text{KPa}^{-1}$$

Where ΔD is distention, D is diameter and ΔP is pulse pressure.

Biochemical estimation:

Serum total cholesterol (TC), triglycerides (TG), and high density lipoprotein (HDL) were determined by totally enzymatic methods (Bio Merieux Company – France). Low density lipoprotein (LDL) was calculated from Friedewald's Formula (12). Determination of oxidized low density lipoprotein (oxLDL) was done according to the procedure of Harris et al "1996" (13).

Statistical analysis:

Data were analyzed with (SPSS Vr. 11.0) software. The results were presented as number, and mean \pm standard deviation (SD). The data were analyzed by using Student's (unpaired) t-test where pre-menopausal women have been considered as control to be compared with post-menopausal women. One way ANOVA (using LSD) has been used to evaluate compliance and lipid profile statistically between the subgroups in group I and II, where null parity subgroup has been considered as control. $P < 0.05$ has been considered as the lowest limit of significance.

Results:

The data of the present study showed that there was a difference in age (32.6 ± 6.7 years, 54.4 ± 7.8 years $P < 0.01$) between groups I and II respectively. The Total cholesterol, triglyceride, low density lipoprotein and oxidized low density lipoprotein were lower in group I than group II but it was the reversed for high density lipoprotein and compliance which were higher in group I than group II (table 1). The relation between parity and compliance was very obvious as has been shown in table 2 and 3, where the mean of compliance decrease with increase in parity in group I and II. In group I there were no significant difference in the mean of compliance between subgroup Ia and Ib

but this difference was statistically significant between subgroup Ia and subgroup Ic and Id. These observations were true in group II and can be extended to include HDL in group I and II. The above observation was reversed for TC, TG, LDL and oxLDL.

Discussion:

The results have shown the physiological effects of menopause by decreasing the compliance and changes in lipid profile, this could be explained according to the following explanations:

First: The ages of the postmenopausal women were higher than that of the pre-menopausal women. The incidence of cardiovascular disease in women rise sharply after middle age, and menopause is thought to be a major determinant of this increase (14). Aging is associated with an increase in vessel stiffness (15). McGrath et al "1998" have shown that there was a reduction in the arterial compliance with the progress of age (16), and that aging process could be the cause behind the decrease in compliance.

Second: Menopause is well known to be associated with a decrease in estrogen level (17). There is a strong link between menopause and an increased incidence of cardiovascular disease (18) and observational studies suggest that postmenopausal estrogen replacement therapy reduces cardiovascular disease risk by about half (19). Perhaps the most dramatic evidence suggesting that loss of endogenous estrogen increases cardiac risk is the sharp increase in LDL cholesterol that begins in the pre-menopausal period and continues to at least 60 years of age (20). Kuller and colleagues "1994" found that the "menopause" is associated with increase LDL, and decrease HDL levels (21). The decrease in estrogen level associated with menopause could be the cause behind the changes in lipid profile. The data of the present study showed obvious effects of parity numbers on the development of atherosclerosis, evaluated through the measurement of common carotid artery compliance coefficient in addition to the changes in lipid profile. The most possible explanations of these observations are that, the pregnancy is associated with major physiological changes including major lipid profile changes. The pregnant women had significantly higher concentrations of total cholesterol, triglyceride, and LDL cholesterol and lower HDL than the non-pregnant women in early (22) and the late pregnancy (23). Gunderson et al "2004" prospectively examined the association between childbearing and changes in fasting plasma lipids. HDL cholesterol declines of -3 to -4 mg/dl after a first birth persisted during the 10 years of follow-up independent of weight, central adiposity, and selected behavior changes (24). Plasma cholesterol levels were higher than control at birth and during lactation with increase in LDL-size particles (25). Lipid metabolism is altered during

human pregnancy, with low-density lipoproteins (LDL) becoming more susceptible to oxidation (26). oxLDL levels in plasma and carotid plaques from 44 patients undergoing carotid endarterectomy and oxLDL levels in 17 control plasma and 9 normal intima samples were determined. In paired samples from individual patients, plaque oxLDL was nearly 70 times higher than plasma oxLDL. Plasma oxLDL undergoing carotid endarterectomy was significantly higher than in the controls (27). Toikka et al "1999" study have shown that the compliance of the carotid artery varies inversely with concentration of plasma oxLDL. Their study demonstrated an in vivo association between oxLDL and arterial elasticity suggesting that oxidative modification of LDL may play a role in the alteration of arterial wall elastic properties (28). From above we can conclude that repeated pregnancies increase the exposure to lipid profile and oxidized lipid changes that increase the possibility of atherosclerotic changes observed as a decrease in arterial compliance. Therefore, increasing parity increases the possibility of development of atherosclerosis. The major conclusions of this work are, post-menopausal women have less elastic arteries than pre-menopausal women and increase parity will decrease the arterial wall compliance in pre and post- menopausal women.

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Table 1. Mean ± SD for total cholesterol , triglyceride , high density lipoprotein , low density lipoprotein , oxidized low density lipoprotein and common carotid artery compliance coefficient in pre-menopausal women(group I) and post-menopausal women (group II).

	Pre-menopausal women No.=44	Post-menopausal women No.=39	P value
Age(years)	32.6±6.7	54.4±7.8	P<0.01
Total Cholesterol (mg/dl)	194.4±16	217.0±21.3	P<0.01
Triglyceride (mg/dl)	158.3±21.8	177.8±22.8	P<0.01
High density lipoprotein (mg/dl)	56±4.6	47.7±4.8	P<0.01
Low density lipoprotein (mg/dl)	106.7±17	133.7±21.6	P<0.01
Oxidized low density Lipoprotein(μ mol/L)	0.37±0.1	1.1±0.3	P<0.01
Compliance (mm ² .KPa ⁻¹)	0.58±0.05	0.52±0.06	P<0.01

Table 2. Mean±SD of TC(total cholesterol) , TG(triglycerides) , high density lipoprotein (HDL) , LDL(low density lipoprotein) , oxLDL (oxidized low density lipoprotein) and Co(compliance coefficient) in group I subgroups , where NS: not significant, * : P<0.05 , ** :P<0.01.

Group I				
	Ia (Number =12)	Ib (Number=12)	Ic (Number=12)	Id (Number=8)
TC(mg/dl)	183.9±8.8	187.5±10.6 ^{NS}	199.6±13.9 ^{**}	212.5±16.7 ^{**}
TG(mg/dl)	143.8±18.4	148.3±17.8 ^{NS}	164.6±13.7 ^{**}	185.6±12.4 ^{**}
HDL(mg/dl)	59.9±3.2	58.4±3 ^{NS}	53.8±2.9 ^{**}	50±1.6 ^{**}
LDL (mg/dl)	95.3±11.3	99±12.3 ^{NS}	112.8±13.2 ^{**}	125.4±17.1 ^{**}
Oxldl (mg/dl)	0.27±0.06	0.31±0.03 ^{NS}	0.43±0.04 ^{**}	0.53±0.04 ^{**}
Co (mm ² .KPa ⁻¹)	0.61±0.04	0.6±0.04 ^{NS}	0.56±0.04 ^{**}	0.52±0.04 ^{**}

Table 3. Mean ± SD of TC(total cholesterol) , TG(triglycerides) , high density lipoprotein (HDL) , LDL(low density lipoprotein) , oxLDL (oxidized low density lipoprotein) and Co(compliance coefficient) in group I subgroups , where NS: not significant, * : P<0.05 , ** :P<0.01.

Group II				
	Ila Number =9	Iib Number = 10	Iic Number = 9	Iid Number = 11
TC(mg/dl)	201.1±20.4	212±21.5 ^{NS}	221.1±16.2 [*]	231.3±16.8 ^{**}
TG(mg/dl)	149.4±15	174±15.1 ^{**}	183±10 ^{**}	200±10.5 ^{**}
HDL(mg/dl)	51.7±3.5	50.4±3.4 ^{NS}	47.2±3.1 ^{**}	42.5±3.1 ^{**}
LDL(mg/dl)	119.6±21.1	126.8±21.4 ^{NS}	137.2±16.7 ^{NS}	148.7±17.1 ^{**}
Oxldl(mg/dl)	0.68±0.07	0.91±0.07 ^{**}	1.1±0.2 ^{**}	1.4±0.16 ^{**}
Co(mm ² .KPa ⁻¹)	0.56±0.05	0.54±0.03 ^{NS}	0.5±0.05 ^{**}	0.47±0.04 ^{**}