

Is Parity a Risk Factor for Coronary Heart Disease?

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Abstract

Introduction- Coronary artery disease (CAD) is the second cause of mortality in women over the age of 40. The risk factors for CAD in females include: age over 55, BP>140/90, smoking and hyperlipidemia. As we know, the plasma lipoprotein level changes significantly during pregnancy, and low density lipoprotein reaches its peak approximately in the 36th week of pregnancy. Hypercholesterolemia induced by pregnancy may be atherogenic. The purpose of this study was to evaluate any relation between multiparity and CAD.

Methods- In this case-control study, 230 women over 50 years old were studied. Of this total, 115 were considered as the case group, who were selected from among patients with CAD admitted to the cardiac ward. Another 115 patients without CAD who were admitted to the internal and surgery wards with normal cardiovascular consultation were selected as the control group. Patients with known risk factors such as hypertension, hyperlipidemia, diabetes, obesity, active and passive smokers, type A personality and any record of hormone replacement therapy were excluded. The data were analyzed using the commercially available software package SPSS, version 11. Student's t-test and χ^2 were used for analysis, and results were expressed as mean \pm SD. *p* value <0.05 was considered statistically significant.

Results- The mean age of the subjects at first parity in the case and control groups was 16.09 \pm 2 and 16.3 \pm 2 years, respectively (*p*=NS). The mean number of parities in the case group was 7.5 \pm 3.1, and 5.9 \pm 1.9 in the control group (*p*<0.001). Body mass index (MI) was 23.6 and 24.8, respectively; and mean cholesterol level, LDL and HDL in the case and control groups were within normal limits, with no patients being overweight. The average cholesterol, HDL, and LDL levels for the case and control groups were 164.2 vs. 164.1, 102.6 vs. 105.4 and 34.5 vs. 40.5, respectively.

Conclusion- Exposure to repeated periods of hyperlipidemia induced by pregnancy may be responsible for an increased risk of CAD, especially in women with parity above four. The patient's age at first pregnancy was not observed to be a risk factor for CAD (*Iranian Heart Journal 2007; 8 (4): 43-46*).

Key words: coronary artery disease ■ parity ■ risk factor

Coronary heart disease is the second cause of mortality and disability in women over the age of 40 years old.¹ The risk factors for coronary artery disease (CAD) in females include: age over 55, smoking, BP>140/90mmHg, diabetes, HDL<35mg/dl and positive family history.²

It is known that plasma lipoproteins undergo both quantitative and qualitative changes during pregnancy.³ There is a gradual two-to-threefold increase in triglyceride level, and these levels reach their peak (200-300mg/dl) at term and gradually fall thereafter, approaching pre-pregnancy levels 6 weeks post-partum.

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Total cholesterol level at term changes less dramatically, with only a 50-60% rise above pre-pregnancy levels. The 95th percentile value for 36th week of gestation and 6th week post-partum are 318mg/dl and 265mg/dl, respectively.

As in the case with triglycerides, all lipoprotein particles at 36 weeks of gestation increase their cholesterol content.³ The cholesterol increase in low-density lipoprotein is proportional to that of total cholesterol and remains elevated up to 8 weeks after delivery. HDL (high-density lipoprotein cholesterol) levels display a unique pattern of fluctuation, peaking at week 25, and then decreasing until week 32, and finally remaining constant for the remainder of the pregnancy.⁴ The mechanisms for all pregnancy-induced lipoprotein and TG changes are not completely understood. The rise in plasma TG parallels the rise in estrogen levels during pregnancy. Estrogens have been shown to increase the synthesis of VLDL, which is the major carrier for TG in the fasting state. There is evidence, however, that estrogens are negative regulators of lipoprotein lipase activity. The increase in estrogen levels during late pregnancy theoretically should decrease the level of LDL-C. This, however, does not occur and instead, elevation in LDL-C is observed. These elevations are poorly understood; nonetheless, they could be secondary phenomena caused by increased conversion of the abundant VLDL.⁴ High progesterone levels during late pregnancy also could be a contributing factor. Increase in LDL-C has been shown most frequently with synthetic progesterone; however, it is unclear whether natural progesterin has the same effect. Falling HDL-C levels in the last half of pregnancy, along with LDL-C changes, correlates with rising levels of human placental lactogen, insulin and insulin resistance. The enrichment of LDL-C and HDL-C in triglycerides could be related to the decrease in hepatic lipase activity that is observed during gestation. Changes in LDL patterns during pregnancy

might be used to identify those women who later in life may be predisposed to coronary heart disease.⁴ It seems legitimate to question whether repeated exposure to lipids and lipoprotein changes during consecutive pregnancies has an adverse effect on these and other protective mechanisms, thereby increasing the risk for atherosclerosis and CAD in the otherwise healthy female. Several studies have attempted to answer this question. Unfortunately, no clear answer is available. Both the Framingham study and British study found no link between parity and risk for CAD.⁵ One Swedish study found an increased risk for CAD after multiple pregnancies or abortions.⁵ Beard et al. found a relative risk to develop CAD of 1/5 in women with a history of four or more pregnancies.⁵ More significant was the finding that relative risk for CAD was 1/8 in women whose age at first pregnancy was less than 25 years and highest when the age at first pregnancy was less than 20 years.⁵ This last age cutoff for first gestation also was found to increase the relative risk for CAD in Vecchia's study. Rosenberg also reported a 1/9 relative risk for CAD in this same age group, but this value did not achieve statistical significance.⁵ The contradictory data on the correlation between the number of pregnancies and the risk for CAD suggests that if such a link exists, it is probably very subtle.

The significance of the general trend toward an increased risk for CAD when age at first pregnancy is in the early 20s is unclear. Socioeconomic factors could be confounding factors, although most of the studies mentioned have corrected for such variables.⁶ Although it is unclear whether the sum of all pregnancy-related changes is atherogenic, it is certain that the elevations in plasma lipids could identify a patient with latent hyperlipidemia. Many consider elevations in plasma lipids beyond the 95th percentile at 36 weeks gestation or failure of values to normalize at 6 weeks postpartum to be the first indicator of latent hyperlipidemia.⁴ Lawlor et al. in their study in 4286 women

between 60 and 79 years of age found that increased parity due to changes in body mass index (BMI) can increase the risk of CAD.⁶ Therefore, the aim of the present study was to compare parity in women with CAD and a control group without known risk factors. This investigation might be helpful in isolating a subgroup of women at higher risk of CAD.

Methods

In a prospective, case-control study, 115 women admitted to the CCU with chest pain and changes in serial EKG or elevated enzymes and without a history of diabetes, hypertension and hyperlipidemia were compared with 115 women admitted to other units of the hospital with the same criteria and normal cardiovascular consultation and EKG, exercise test and echocardiography. Lipid profile and blood sugar tests were done after admission.

Data on age, BMI, parity, job and smoking were collected and analyzed with t-test using SPSS v. 10.

Results

The demographic and clinical data of the study population are shown in Table I. There was no significant difference in the mean of BMI between the two groups (Table II).

Table I. Demographic and clinical data of study population

	case	control	PV
Mean age	66.23	64.01	0/235
Job	94.2%	95.7%	
Use of OCP	1.02%	1.36%	0/526
Gravidity	6.78	4.82	0/0001**
Para	5.42	3.78	0/0001**
Obesity BMI>29	7.2%	18.8%	0/0021**
Exposure to smoke	54%	48%	

Table II. Comparison between BMI in women over 50 years with and without CAD

Groups	No	Mean BMI	SD	Min	Max
Case	115	23/6	2/5	17/5	29/4
Control	115	24/8	1/8	20/3	30/8

Distribution of parity in women over 50 years with/without CAD is shown in Table III. These data show that the mean parity in women with CAD was significantly higher than that in the control group ($p=0.000$). These data show that women with four or more pregnancies had a significantly higher risk for CAD (OR=1.73, Table III).

Table III. Distribution of parity in women over 50 years with/without CAD

Parity	case		control		Total		P value
	No	%	No	%	No	%	
0-3	6	5.2	10	8.7	16	7	0.000
4-7	58	50.4	83	72.2	141	61.3	significant
>7	51	44.4	22	19.1	73	31.7	
Total	115	100	115	100	230	100	

The fasting glucose, cholesterol and lipid profile did not differ significantly, and Table IV gives a comparison of the mean value of the fasting glucose, cholesterol and lipid profile in women over 50 years with/without CAD.

Table IV. Mean laboratory results in women over 50 years with/without CAD

Mean lab result	Case (mean±SD)	Control (mean±SD)
FBS	112.6±28.4	155.3±26.3
Cholesterol total mg/dl	164.2±34.6	164.1±27.7
LDL mg/dl	102.6±26.8	105.4±9.1
HDL mg/dl	34.5±11	40.5±9.8
TG mg/dl	97.8±32.1	85.6±25.1

Comparison between mean age of the first pregnancy in women over 50 years with/without CAD is depicted in Table IV.

Table IV. Comparison between mean ages of first pregnancy in women over 50 years with/without CAD

Groups	No.	Mean (y)	SD	Min	Max	P value
Case	109	16/09	2	13	20	0/4
Control	115	16/3	2	13	20	

Discussion

The finding of this study shows that multiparity, aside from the obstetric point of view, is also a comprehensive problem with a variety of associated metabolic changes (hyperlipidemia and dyslipidemia). It was previously reported that women had lower risk of CAD when the age at first pregnancy was less than 20 years (OR=1.9).⁵ Our present study does not show any significant difference between the two groups, but mean age was significantly lower than that in previous studies due to the difference in cultural and religious factors.

Mean parity in women with CAD and without known risk factors such as obesity hypertension, hyperlipidemia, etc. was significantly higher than that in women in the control group (7.5±3.1 vs. 5.9±1.9, $p=0.000$). These data show that multiparity is a risk factor for CAD. This has been reported by Lawlor et al.⁷ The Framingham study and British study found no link between parity and risk for CAD.⁹

Beard et al. found a relative risk to develop CAD of 1.5 in women with a history of four or more pregnancies,¹⁰ which chimes in with our results. Hunpher et al. suggested in women with a history of four pregnancies or more, BMI and waist ratio increased per pregnancy.⁶ BMI was controlled in this study and it was normal in both groups. Lawlor et al. reported a 36% increased risk of atherosclerosis in multiparous women vs. primiparous, and the risk increased to 64% in

women with a history of four pregnancies or more. In agreement with earlier reports, we found a positive impact of four pregnancies or more on incidence of CAD.

Conclusion

The results of the present study suggest a strong correlation between multiparity and CAD. However, no difference was demonstrated between age at first pregnancy and risk of CAD.

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