Association of Pregnancy-Related Factors and Cardiovascular Disease in the Long Term

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Abstract

Aim To observe the association of pregnancy-related factors on the incidence of cardiovascular disease (CVD).

Introduction CVD is one of the leading causes of death in women. It really emphasizes the need for early recognition of cardiovascular risk in women. Heart disease in women poses a major challenge in that the first events are more likely to be fatal. Pregnancy itself predicts cardiovascular disease in later life and is a screening test for CVD.

Methods Total 136 female patients from the outpatient clinic, as well as patients of our hospital, were included in our retrospective single-center study. Along with demographic data and details of risk factors, the reproductive history of all patients such as age at first pregnancy, number of children, any hormonal therapy, and mode and place of delivery were noted. Pregnancy-related data, such as the history of hypertension, diabetes, abortion, pregnancy loss; preterm delivery; and the weight of the newborn were taken into consideration. We excluded unmarried and nulliparous women.

Results The study population comprised 136 female patients. There were 69 (50.74%) in group 1 (coronary artery disease [CAD] group) and 67 (49.36%) in group 2 (non-CAD group). Mean age of patients at enrollment was 53.2 ± 12.52 years. Twenty-seven (19.8%) patients fell under lost pregnancy or child category, and abortions and preterm delivery were faced in 26 (19.1%). Seventy-one (52.2%) patients attained menopause whereas hysterectomy was done in 35 (25.7%). The average age of hysterectomy was 38.37 ± 8.50 years, and that for menopause was 46.78 ± 5.04 years. During pregnancy, the history of hypertension was given only in 4 (3%), diabetes was in given none, and history of a low birth weight of the newborn was given in 3 (2.2%) women. The univariate analysis was done to see the statistical significance of mainly pregnancy factors on long-term cardiac outcomes along with risk factors. Generally, hypertension (p = 0.01) and diabetes (p = 0.01) had significance with cardiac outcomes. In spite of these, the history of a lost pregnancy/child and pregnancy complications both have shown near significance, that is, p = 0.06.

Conclusion Our study suggests an impact of pregnancy loss irrespective of the etiology on the future cardiac outcomes as along with predominant impact factors of hypertension and diabetes.

Keywords
- pregnancy-related factors
- cardiovascular disease
- coronary artery disease

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Introduction

Cardiovascular disease (CVD) is one of the major causes of death in women. Heart disease in women poses a major challenge in that the first events are more likely to be fatal. This emphasizes the need for early recognition of cardiovascular (CV) risk in women. Roberts and Hubel highlight that pregnancy history is hugely significant in the CV risk assessment in women.[1] The pregnancy disorder—preeclampsia that occurs in about 7% of pregnancies—has a well-established relationship with future CVD.[2]

Pregnancy is a normal physiologic state in a woman's life. A complicated pregnancy is a harbinger of future CVD. The complications may be limited to the pregnancy period but leave permanent vascular and metabolic damage, which are predictive of CVD in later life. Hypertension in pregnancy is an established risk factor for coronary heart disease (CHD) and stroke in women. A sibling history of hypertension in pregnancy may be a novel familial risk factor for future hypertension.[3] Gestational diabetes, preterm delivery, and assisted reproductive procedures also have a bearing on the future CV risk of a woman.[4,5] This awareness in the medical community, especially obstetricians, physicians, and cardiologists, would play a crucial role in detecting these complications and monitoring them appropriately.[6,7]

Pregnancy itself soothsays the CVD in later life. Pregnancy can be a screening test for CVD. Obtaining maximum information about pregnancy and exploit on that will help prevent CV events in women's in later life. Based the degree of risk, CVD prevention in women should guide the assessment and management strategies.

Materials and Methods

This is a retrospective single-center study including 136 female patients of the outpatient clinic as well as patients of our hospital. The reproductive history of all patients such as age at first pregnancy, number of children, any hormonal therapy, and mode and place of delivery were noted. Pregnancy-related data, such as history of hypertension, diabetes, abortion, pregnancy loss; preterm delivery; and the weight of the newborn were taken into consideration. Laboratory tests and cardiac history were collected from their recent medical records. All patients underwent electrocardiogram and echocardiography to evaluate their cardiac status and exercise stress testing and coronary angiogram for confirmation whenever the clinical scenario demanded. We excluded unmarried and nulliparous women.

This study population was divided into coronary artery disease (CAD) patients (group 1) and non-CAD patients (group 2) based on the final diagnosis.

The statistical analysis was done with Minitab version 17 (Minitab, Ltd.). The univariate analysis through chi-square test was used for comparison between the two groups. The statistical significance ($p < 0.05$) was taken as significant.

Results

This study population comprised 136 female patients. There were 69 (50.74%) in group 1 (CAD group) and 67 (49.36%) in group 2 (non-CAD group). Mean age of patients at enrollment was 53.2 ± 12.52 years. The demographic data of the entire cohort are mentioned in ►**Table 1**.

Reproductive Risk Factors

The age of menarche was 12.95 ± 1.51 years, and the average number of children per patient was 3.13 ± 1.58. The age at first pregnancy was 19.04 ± 3.99 years. Breast-feeding duration was 1.69 ± 0.97 years. About 117 (86.02%) women had a normal vaginal delivery. The majority had an institutional delivery, that is, 83 (61.02%) patients. Twenty-seven (19.8%) fell under lost pregnancy or child category, and abortions and preterm delivery were faced in 26 (19.1%). Seventy-one (52.2%) patients attained menopause whereas hysterectomy was done in 35 (25.7%). Average age of hysterectomy was 38.37 ± 8.50 years and menopause was 46.78 ± 5.04 years.

During pregnancy, the history of hypertension was given only in 4 (3%), diabetes was given in none, and history of low birth weight of the newborn was given in 3 (2.2%) women.

The biochemical investigations of the study population are mentioned in ►**Table 2**. The lipid profile was done in only 79 patients, of whom 12 had hyperlipidemia.

The univariate analysis was done to see the statistical significance of mainly pregnancy factors on long-term cardiac outcomes along with risk factors. Generally, hypertension ($p = 0.01$) and diabetes ($p = 0.01$) had significance with cardiac outcomes. In spite of these, the history of lost pregnancy/child and pregnancy complications both have shown near significance, that is, $p = 0.06$. Details are mentioned in ►**Table 3** and ►**Fig. 1**.

Table 1 Descriptive statistics of study population

Variable	Mean ± SD
Age (y)	53.2 ± 12.52
Hypertensives (%)	87 (63.9%)
Hypertension duration (y)	7.08 ± 6.99
Diabetics (%)	66 (48.53%)
Diabetics duration (y)	8.12 ± 8.14
Family history (%)	12 (8.82%)
Other risk factors (%)	54 (39.51%)
CAD patients (%)	69 (50.74%)
Height (cm)	157.36 ± 5.2
Weight (kg)	65.09 ±11.4
Systolic blood pressure (mm Hg)	128.12 ± 24.59
Diastolic blood pressure (mm Hg)	81.89 ± 10.02
Pulse rate (beats/min)	81.64 ± 12.21

Abbreviations: CAD, coronary artery disease; SD, standard deviation.

Table 2 Descriptive statistics of laboratory parameters

Variable	Mean ± SD
Hemoglobin (g %)	11.58 ± 1.79
Blood urea (mg/dL)	28.29 ±12.80
Serum creatinine (mg/dL)	0.94 ± 0.56
Random blood sugar (mg/dL)	132.53 ± 69.75
TC (mg/dL)	170.06 ± 46.41
HDL (mg/dL)	52.86 ± 23.54
LDL (mg/dL)	96.63 ± 47.07
VLDL (mg/dL)	23.91± 9.12
Triglycerides (mg/dL)	125.6 ± 73.7
TC/HDL ratio	4.12 ± 2.12
Sodium (NA) (mEq/L)	137.03 ± 19.99
Potassium (K) (mEq/L)	25.1 ± 120.6
Chloride (Cl) (mEq/L)	100.23 ±11.01
T3 (ng/dL)	1.85 ± 1.83
T4 (ng/dL)	11.86 ±15.78
TSH (ng/dL)	4.58 ± 10.09
HBA_{1C} (%)	7.44 ±1.95
hsCRP (mg/L)	4.96 ± 4.01
Vitamin D (ng/mL)	19.33 ± 6.41

Abbreviations: CAD, coronary artery disease; HDL, high-density lipoprotein; hsCRP, high-sensitivity C-reactive protein; LDL, low-density lipoprotein; SD, standard deviation; TC, total cholesterol; TSH, thyroid-stimulating hormone; VLDL, very low-density lipoprotein.

Discussion

There is an influence of several factors on women's risk for CAD. Despite traditional CAD risk factors, there are several risk factors exclusive and foremost to women who also confer an increased CV risk. The effect and complexity of biological, physiologic, and hormonal factors on women with CAD risk cannot be understood or explained with simply knowledge of heart diseases in men. Through this study the authors would like to highlight the women-specific predominant risk factors for the burden of CAD.

The well-known facts about pregnancy-related risk factors are the increased CV risk associated with gestational diabetes mellitus (GDM),[8–10] gestational hypertension, pre-eclampsia, and eclampsia.[11–15] Less well-known facts are the association of CAD with other pregnancy-related factors such as preterm delivery,[16–18] spontaneous pregnancy loss, and history of stillbirth. Recurrent miscarriages play a role as the future risk for CAD/CHD. Meta-analysis of nearly 10 studies has shown it to be associated with higher likelihood of developing future CHD.[19,20] As per the literature, > 3.5 times higher risk of myocardial infarction (MI) was associated with history of stillbirth. The recurrent miscarriage (more than three occurrences) was associated with nearly nine times higher risk of MI.[21]

In our study also, CAD was associated significantly with lost pregnancy and/or child, and abortions and preterm delivery were $p = 0.06$.

Table 3 Comparison of outcomes with pregnancy parameters and risk factors

Variable	Group A: Cardiac ($n = 69$)	Group B: Noncardiac ($n = 67$)	p Value
Hypertensives	51 (73.9%)	36 (53.7%)	0.01
Nonhypertensives	18 (26.1%)	31 (46.3%)	
Diabetics	39 (56.5%)	24 (35.8%)	0.01
Nondiabetics	30 (43.5%)	43 (64.2%)	
Other risk factors—present	30 (43.5%)	24 (35.8%)	0.36
Other risk factors—absent	39 (56.5%)	43 (64.2%)	
Family history—present	6 (8.7%)	6 (8.9%)	0.95
Family history—absent	63 (91.3%)	61 (91.1%)	
Any hormone intake—yes	9 (13.04%)	7 (10.4%)	0.63
Any hormone intake—no	60 (86.96%)	60 (89.6%)	
Lost pregnancy/ child—yes	18 (26.1%)	9 (13.4%)	0.06
Lost pregnancy/ child—no	51 (73.9%)	58 (86.6%)	
Normal delivery	60 (86.9%)	57 (85.1%)	0.75
Cesarean section (C-section)	9 (13.1%)	10 (14.9%)	
Home delivery	24 (34.8%)	30 (44.8%)	0.23
Hospital delivery	45 (65.2%)	37 (55.2%)	
Pregnancy complications—yes	17 (24.6%)	9 (13.4%)	0.06
Pregnancy complications—no	52 (75.4%)	58 (86.6%)	

These women-specific risk factors are not only limited to above, but following factors also play a role in future CVD. However, these have not been analyzed in our study as the study was focused on the pregnancy-related factors only. Premature menopause predisposes to CAD; however, menopausal hormone therapy for the primary or secondary prevention of CVD was not recommended.[22,23] Psychosocial factors have additionally been related to CHD.[24] In every age group compared with men, the more women have

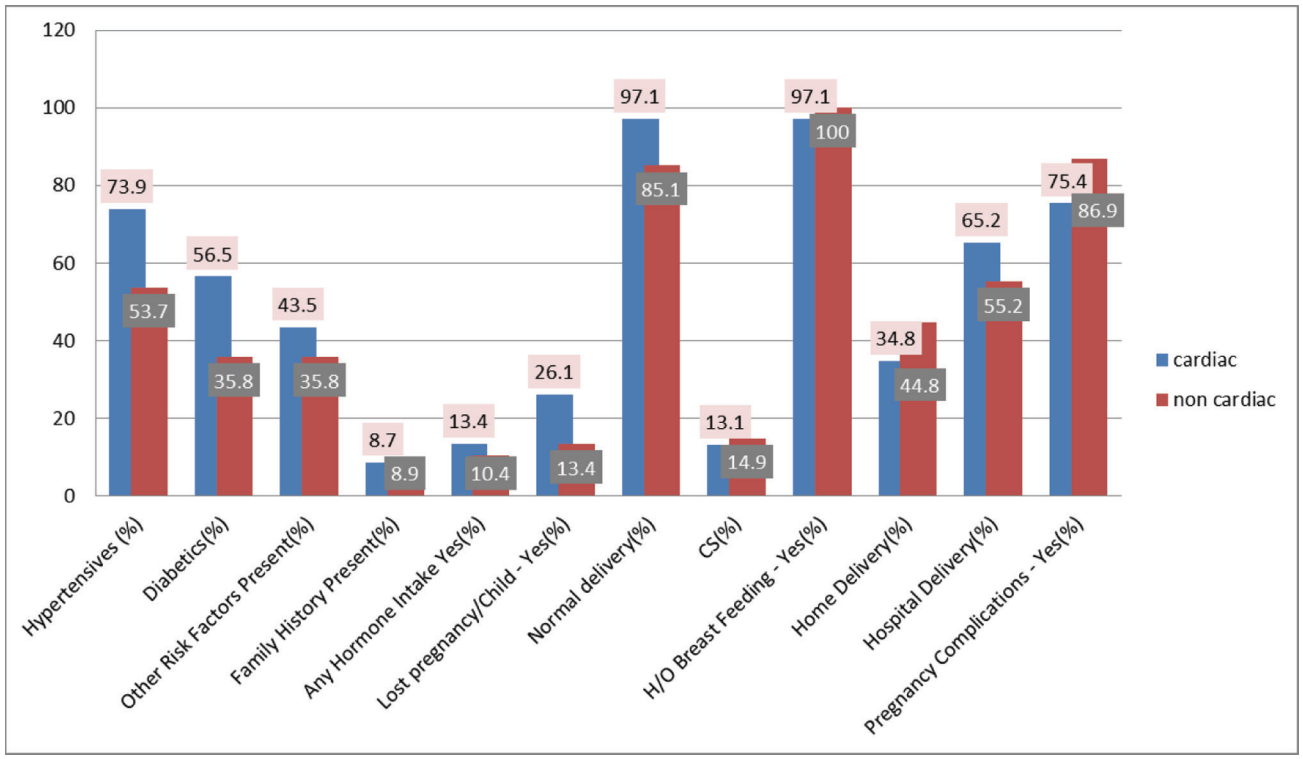

Fig. 1 Comparison between groups A and B.

depression and the depression rate was nearly twice,[25–27] and studies have shown that symptoms of depression are directly associated with CHD risk.[28] According to the American Heart Association/American College of Cardiology Foundation recommendations, the treatment of depression has not been shown to improve CV outcomes.[29]

The risk assessment for women with CAD should involve history, clinical examination, and laboratory testing. The direct preventive strategies to reduce CAD in asymptomatic women should develop through risk assessment calculators. The increased awareness of women-specific risk factors for CAD has led to educating women so that we can decrease the future cardiac events.

The reproductive years are an ideal time to evaluate preclinical CVD risk and launch approaches to prevent or delay the onset of disease in women. Therefore, the early detection of risk unmasked by pregnancy offers a great opportunity to improve the health of women, but not yet tested. Further, implements are required to translate this potential into meaningful improvements in the health of women. The contribution of a tool to obtain valid pregnancy history information via maternal recall is an important step in this direction.

There is a requirement to update risk factors for CVD in women by including the pregnancy-related events. Understanding the mechanisms that link pregnancy loss and CVD and how to include information of pregnancy loss (and other adverse pregnancy events) for CVD assessment is still required to be determined.

Limitation

As it was a retrospective study, patients were not able to recollect the details of pregnancy complications such as gestational hypertension, diabetics, preterm delivery, and low birth. This was a small population study and requires confirming the results in larger population.

Conclusion

Our study suggests that there is an impact of pregnancy loss irrespective of the etiology on the future cardiac outcomes as along with predominant impact factors of hypertension and diabetes.

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