



Original Article:

Significant Association of History of Miscarriage with Obesity Among Indian Women of Childbearing Age.

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Abstract: The aim of the present study was to understand the effect of history of miscarriage and still birth on the risk for cardio-metabolic risk factors among women from an endogamous population after controlling for potential confounders. A total of 562 premenopausal women (out of a total of 1014 women) were considered for the present cross sectional study. They were categorized into three groups based on their reproductive history that is as those with miscarriages, still birth and controls (women with successful pregnancy without any complications). Somatometric measurements, biochemical profiles and blood pressure were measured using standard techniques. Binary logistic regression analysis revealed that women with history of miscarriages had two fold significantly increased risk for overweight/abdominal obesity after controlling for potential confounder. It becomes equitable to argue that women with history of miscarriage have an increased risk for cardio-metabolic risk factors later in life. Therefore, utilization of adverse pregnancy outcome as an early intervention marker is needed to mitigate the further escalation of cardiovascular diseases later in life that may occur due to age or menopause.

Key Words: Pregnancy, Miscarriages, Obesity, Still birth, Premenopausal

Introduction:

The risk of cardiovascular diseases has increased worldwide.(1) The American Heart Association 2013 update reports that women more prone to death from cardiovascular diseases as compared to men. Besides these, recent studies (2) from India as well as rest of the world (3) have demonstrated that the risk of cardio-metabolic risk factors is higher among the women as compared to that of men. Reproductive life events like menarche, menopause parity and adverse pregnancy outcomes are important additional risk factors among women as compared to the men that can be used to assess the risk for cardiovascular diseases.

An adverse pregnancy outcome (defined as an event that reduces the chances of having a healthy baby) is an event in a woman's reproductive life that increases her risk of cardiovascular diseases. Several cross sectional and longitudinal studies as well as systematic reviews of epidemiological studies have (4-11) also ascertained the significant associations between pregnancy outcomes and cardiovascular diseases. In line with this, one of the study conducted by Bhasin and Kapoor (12) has suggested that urban Indian women with history of adverse pregnancy outcomes (pregnancy diabetes mellitus, preeclampsia/gestational diabetes, size at gestational age, preterm birth, abnormal birth weight) have increased risk for obesity, 3-8 years post partum. One of the plausible reason evident for these trends (specifically among these Indian populations) are the rapid tempo of economic development that is quiet evident in developing countries like India.(13) The changing lifestyle pattern characterized by sedentarism along with a shift towards the Westernized nutritional profiles, and the ongoing urbanization and globalization has further worsened the situation. Therefore, it is the need of the hour to understand the patterns of cardio-metabolic health among women specifically in light of their reproductive history. The women recruited in the present study belong to a rural background and practice vegetarian diet, which is known to be cardio-protective and hence is expected to have a reduced cardio-metabolic risk. The present study, therefore, has two major objectives. First, to estimate the incidence of adverse pregnancy outcomes in the studied population. Secondly, to assess the effect of adverse pregnancy outcomes on the cardiovascular risk factors among the recruited women.

Materials and Methods

The present population based cross sectional study was conducted as a part of a sponsored research project in which 1014 women aged 30-75 years were recruited through household survey. The participants were recruited from 15

rural villages of Palwal District, Haryana State, India. Of these, only 562 women in the child bearing age were included in the present analysis. Women with natural menopause (n=384) were excluded to reduce the biasness due to in the distribution of cardio-metabolic risk factors.(14) Women with previous history of hysterectomy (n=63) and those in perimenopause (n=5) were excluded to reduce the biasness. The data were collected after informed written consent from the participants. The study protocol was approved by the Ethical Committee of the Department of Anthropology, University of Delhi.

Target Population

Jats are an endogamous caste group of North India. They are primarily an agricultural community involving in physically activity lifestyle. Their food habits involve only vegetarian food and milk products that are likely to protect them from cardiovascular risk. They practice caste endogamy and gotra exogamy. Marriage is monogamous.

Data collection

Data pertaining to socio-demographic variables were collected from the participants using interview schedule. Further, the reproductive performance was also ascertained from the participants through recall method. Based on the response of the participants regarding their reproductive history, they were characterized as cases and controls. Cases were those that had a previous history of still birth or miscarriage. Women with preterm birth and hypertension during pregnancy were also ascertained, but the same were not considered in the present analysis. This was due to lesser number of women in these categories (<1%), which could primarily be attributed to the absence of medical records, since most of the deliveries took place at home.

Anthropometric measurements of participants wearing light clothing and without shoes were ascertained. Anthropometer was used to ascertain the height of the individuals to the nearest of 0.1 cm. Weight was measured in the upright position to the nearest 0.5 kg using a weighing balance. BMI was calculated by dividing weight (kg) by height squared (m²). Cut offs for body mass index (BMI) were defined as per WHO.(15) Waist circumference, hip circumference were measured. Cut offs for waist circumference and waist hip ratio were as defined by Ramachandran et al.(16)

For the estimation of biochemical variables, five millilitres of intravenous blood samples were collected from the participants after 9-12 hours of fasting by trained personnel. Glucose and lipid parameters namely triglyceride (TG), total cholesterol (TC) and High Density Lipoprotein cholesterol (HDL-C) were estimated by spectrophotometer using the commercially available kits.(Randox Laboratories Ltd.) The levels of lipid parameters namely low density lipoprotein (LDL) and very low density lipoprotein (VLDL) were computed using Friedwald and Fredrikson formula.(17) Estimation of plasma homocysteine and serum folate and vitamin B12 levels were done through Immulite 1000 by chemi-luminescence technique at All India Institute of Medical Sciences, New Delhi. The cutoffs of homocysteine, folate and vitamin B12 were as reported by Shukla and Raman.(18)

Statistical Analysis

Statistical analysis was done with SPSS version 16. Descriptive statistics included the computation of mean, SD, median and inter quartile ranges, whereas for inferential statistics t test and Mann Whitney U test was used. Logistic regression analysis was utilized to compute the unadjusted and adjusted odds ratio.

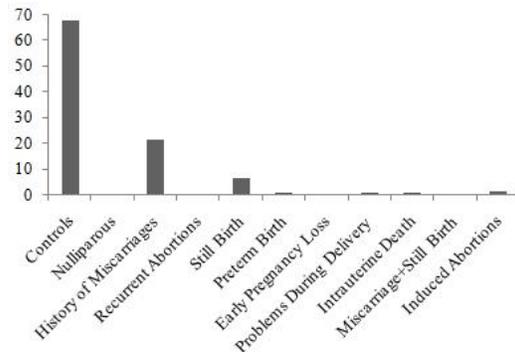


Figure 1: Overview of reproductive performance among the recruited women

Results

Of the 1014 women recruited in the present study, 30.58 % of the women had adverse pregnancy outcomes. Further, when adverse pregnancy outcomes were considered miscarriages (21.4%) was the most prominent adverse pregnancy outcome followed by still birth(6.61 %). The other adverse pregnancy outcomes that were noticeable in the present study were problems during delivery (0.59 %), preterm birth (0.59 %), intrauterine death (0.69 %), early pregnancy loss (0.39 %) and recurrent abortions(0.2 %). Additionally, 0.3 % of the women were found to be nulliparous and 1.08% had induced abortions.

In the present study, among the adverse pregnancy outcomes, the prevalence of miscarriages and still birth were found to be quite high in comparison to other adverse pregnancy outcomes. Therefore, for further analysis of adverse pregnancy outcomes with cardiovascular risk profile only these two phenotypes that is miscarriages and still birth were considered.

Table 1: Baseline characteristics of the study population by reproductive performance

Variables	Controls (1)	History of Miscarriage (2)	Still Birth (3)	p1 (1 vs 2)	p2 (1 vs 3)
Present age (in years)	42(37-50)	43(38-50)	40(35-45)	0.462	0.056
Illiterates Number (%)	241(65.7)	73(62.9)	28(75.7)	0.59	0.219
Agriculturalists Number (%)	194(51.3)	68(53.5)	17(44.7)	0.665	0.439
Smokers Number (%)	103(28.4)	43(34.1)	14(37.8)	0.224	0.228
Age at menarche (in years)	14.92±1.61	14.91±1.51	14.59±1.31	0.952	0.22
Age at first pregnancy (in years)	19.61±2.81	19.22±2.99	18.97±2.49	0.185	0.18
Number of pregnancies	3.6±1.32	5.32±1.55	5.03±1.81	<0.0001	<0.0001

Among the seven baseline characteristics (present age, education, occupation, smoking habits, age at menarche, age at first pregnancy, number of pregnancies) considered in the present study, cases did not differ from the controls with respect to any of the characteristics except for number of pregnancies which were significantly higher among the cases as compared to the controls.

Variables	Controls (1)	History of Miscarriage (2)	Still Birth (3)	p 1 (1 vs 2)	p 2 (1 vs 3)
Body Mass Index (kg/m ²)	21.19(19.01-24.26)	22.05(18.76-24.28)	22.01(19.84-24.04)	0.529	0.29
Waist Circumference (cm)	78(70.93-86)	79.12(70.98-86.13)	79.1(72.1-87.72)	0.594	0.315
Waist Hip Ratio	0.85(0.79-0.90)	0.86(0.82-0.9)	0.86(0.8-0.89)	0.334	0.866
Fasting Blood Glucose (mg/dl)	77.82(69.31-86.07)	76.71(68.37-87.34)	75.91(66.06-82.93)	0.992	0.295
Cholesterol (mg/dl)	164.22(139.27-192.73)	154.32(134.93-180.78)	159.31(141.51-179.73)	0.044	0.411
Triglyceride (mg/dl)	89.89(67.05-134.28)	92.73(71.74-134.76)	84.11(61.64-119.73)	0.275	0.475
High Density Lipoprotein (HDL) (mg/dl)	51.2(41.6-60.2)	50.23(41.01-59.16)	47.23(42.81-54.88)	0.525	0.242
Low Density Lipoprotein (LDL) (mg/dl)	93.93(70.14-115.39)	87.94(66.79-107.35)	86.14(74.01-114.48)	0.052	0.773
Very Low Density Lipoprotein (VLDL) (mg/dl)	17.96(13.39-26.84)	18.55(14.35-26.95)	16.82(12.33-22.33)	0.257	0.338
Homocysteine (μmol/l)	16.1(11.98-23)	16.15(12.2-24.6)	15.1(12.65-19)	0.405	0.372
Folate (ng/ml)	3.69(2.86-5.6)	3.86(2.36-5.61)	4.15(2.76-6.25)	0.809	0.604
Vitamin B12	253(196-362.5)	228(186-324)	221(187.5-393.5)	0.095	0.255

*p value based on Mann Whitney test for continuous variables

Table 2 reveals the somatometric and biochemical characteristics of the population. It can be seen that the three groups that is the control group and those with history of miscarriages and still birth had a tendency towards abnormal waist hip ratio and hyperhomocystenemia. Further, none of the risk factors considered showed significant differences between control women and those with history of still birth. Only cholesterol and LDL levels were significantly higher among the controls as compared to those with history of miscarriages.(Table 2)

Variables	Controls (1)	History of Miscarriage (2)	Still Birth (3)	p 1 (1 vs 2)	p 2 (1 vs 3)
Traditional Risk Factors					
a. BMI					
Underweight(<18.5 kg/m ²)	69(18.5)	26(20.63)	4(10.52)	0.229	0.188
Overweight (23-24.9 kg/m ²)	52(13.94)	25(19.84)	7(18.4)	0.04	0.804
Obese (≥25 kg/m ²)	77(20.64)	28(22.22)	6(15.78)	0.269	0.368
b. Abdominal Obesity					
Waist Circumference(=80 cm)	166(44.62)	60(47.62)	19(50)	0.55	0.525
Waist Hip Ratio(<0.8)	271(73)	108(85.71)	30(78.94)	0.004	0.431
c. Blood Glucose and Dyslipidemia					
Hyperglycemia(≥110 mg/dl)	12(6.25)	8(12.31)	1(2.6)	0.115	0.768
Cholesterol(≥200mg/dl)	75(19.89)	19(15.08)	4(10.52)	0.23	0.161
Triglyceride(≥150mg/dl)	63(16.76)	23(18.25)	7(18.42)	0.699	0.794
High Density Lipoprotein (HDL) (<50mg/dl)	330(71.1)	98(21.1)	36(7.8)	0.761	0.322
Low Density Lipoprotein (LDL) (≥130mg/dl)	58(15.59)	15(12.2)	6(15.78)	0.357	0.974
Very Low Density Lipoprotein (VLDL) (≥30mg/dl)	63(16.71)	23(18.25)	6(15.79)	0.699	0.884
Non Traditional Risk Factors					
Hyperhomocystenemia (>15micromol/l)	208(56.67)	72(57.6)	20(52.63)	0.856	0.632
Folate deficiency (<3ng/ml)	106(28.89)	43(37.06)	10(26.3)	0.09	0.738
Vitamin B12 deficiency (<220pg/ml)	173(50)	67(56.3)	21(58.33)	0.235	0.34

* p value based on chi square test for categorical variables

Among the obesity related parameters, women with history of miscarriages had the highest prevalence for underweight, overweight and obesity. The prevalence of women with overweight were significantly higher among women with history of miscarriages as compared to the controls. Among the measures of central obesity, women with high waist hip ratio were also significantly higher among women with history of miscarriages. In contrast to this, high waist circumference was most prevalent among women with still birth, showing no significant difference between the case and the control group. Further when the lipid parameters were considered, women with history of miscarriages had higher prevalence of hyperglycemia and high VLDL. In contrast to this, women with still birth had a higher prevalence of hypertriglyceridemia

and high LDL. Control women had the highest prevalence for hypercholesterolemia. Among the non traditional risk factors, the prevalence of hyperhomocystenemia and folate deficiency was highest among women with history of miscarriages, whereas that of Vitamin B12 deficiency is highest among those with still birth. However, these observed differences were not found to be statistically significant. (Table 3)

Table 4: Showing the odds ratio (95% confidence interval) of central obesity (abnormal waist hip ratio) according to history of miscarriages			
	Control	History of Miscarriages	p value
Waist Hip Ratio			
Odds Ratio (Unadjusted)	1.00 (reference)	2.358 (1.364-4.075)	0.002
Odds Ratio (Adjusted for number of pregnancies)	1.00 (reference)	2.233 (1.214-4.013)	0.01
Overweight			
Odds Ratio (Unadjusted)	1.00 (reference)	1.790(1.007-3.183)	0.047
Odds Ratio (Adjusted for number of pregnancies)	1.00 (reference)	2.144 (1.09-4.217)	0.027

Premenopausal women with history of miscarriage(s) had more than 2 fold increased risk for central obesity and overweight both in unadjusted and adjusted (number of pregnancies) models. (Table 4)

Discussion

In the present study, the prevalence of miscarriage was 21.4%. The reported prevalence of miscarriages in the cohort is lower as compared to the study by Patki et al, who reported the prevalence of miscarriages to be 32 % among 2400 patients from five cities.(19) Review of literature suggests that there are no studies that report the prevalence of miscarriages with respect to ancestry. In the present scenario, it is essential that population specific studies are undertaken to understand the risk for adverse pregnancy outcomes, since predisposing factors might be population specific. Dietary habit (vegetarian/ non vegetarian) is an important risk factor for adverse pregnancy outcomes.

Kaur L et al reported vegetarianism to be a risk factor for adverse pregnancy outcomes.(20) The women recruited in the present study had South east Asian ancestry and practiced vegetarian diet. Since the women in the present study are vegetarian it is likely that this dietary habit is an important factor that is predisposing them to an adverse pregnancy outcome (example miscarriage). In contrast to this, several studies (21-24) have postulated vegetarianism to be cardio-protective. These findings suggest that adverse pregnancy outcomes could act as a risk factor to identify individuals at risk for cardiovascular diseases.

The present study further reports that in the case group, those with history of miscarriages had a two-fold significant increased risk for overweight/abdominal obesity (abnormal waist hip ratio). The women with history of still birth also had higher, though not significant, prevalence for overweight/abdominal obesity (abnormal waist hip ratio). These findings highlight that among populations practicing vegetarian diets which are generally thought of as cardio-protective, women with adverse pregnancy outcome may be at higher risk as compared to men. Several studies (25-28) from South Asia and also the world have reported the prevalence of obesity to be significantly higher among the females as compared to the males. Similar findings were reported by Bhasin and Kapoor

(12) in a hospital and household survey of an urban caste group where they showed that the risk for obesity was higher among women with a history of gestational diabetes mellitus, hypertensive disorder of pregnancy, birth weight, preterm birth and inappropriate size at gestational age.

Dyslipidemia characterized by abnormal lipid profile is one of the major reasons of cardiovascular morbidity and mortality.(29) In the present study, women with history of miscarriages have a higher, though not significant, prevalence of hyperglycemia, hypertriglycerdemia and high VLDL as compared to the controls. Further, women with a history of still birth also had a higher though not significant prevalence for hypertriglycerdemia. In the present study, prevalence of hypertriglycerdemia in both the types of adverse pregnancy outcomes, suggests that there might be an increased risk of future cardiovascular disease in these two subgroups as compared to controls.

Further with respect to non-traditional factors that is hyperhomocysteinemia, folate deficiency and vitamin B12 deficiency all the three groups are found to have a similar distribution. However, folate deficiency is less as compared to the vitamin B12 deficiency, which can be attributed to their vegetarian diet. The high prevalence of hyperhomocystenemia and vitamin B12 deficiency (accounting to more than 50 percent) among premenopausal women (median age of 42 years) with adverse pregnancy outcomes that is miscarriages and still birth is a matter of major concern since these nutritional deficiencies are likely to predispose these women to numerous other complex disorders.

In conclusion, the observed association between history of miscarriages and obesity among premenopausal women is a matter of concern, since the condition is likely to aggravate with age and menopause. The findings of the present study further needs to be validated among women with diverse ethnic background and larger sample size. This would help in identifying women with adverse pregnancy outcomes at risk for cardio-metabolic risk factors/nutritional deficiencies/other complex disorders that were not under the purview of the present study.

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