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Gestational Diabetes as a Risk Factor for Cardiovascular Disorders

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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Original Research Article

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ABSTRACT

Background: Gestational diabetes (GD) is identified as a risk factor for increasing the onset of cardiovascular disorders (CVD). However, it is not clear whether this risk is linked with the intercurrent pathogenesis of type 2 diabetes mellitus. Thus, it is essential to identify markers and risk factors responsible for the pathogenesis of CVD and develop therapeutic strategies to decrease the cardiovascular health burden in affected women.
Objective: The present study aims to evaluate the effect of GD on the future onset of CVD and assess the impact of type 2 diabetes mellitus in this context.
Study Design: A cohort study was conducted in Karachi Institute of Heart Diseases Karachi Pakistan from June 2017 to June 2018. A total of 227 females who give birth to at least one kid were included in this study. Females with previous history of cardiovascular disorders and any

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other chronic disorders were excluded from this study. Using a biennial questionnaire behavioral, life style characters and health outcomes were evaluated. Multivariable Cox model was used to measure hazardous risk and ratio for cardiovascular disorders with 95 % confidence interval.
Results: In this study, 11.8% of participants were diagnosed with gestational diabetes with a mean age of 31.6 ± 2.6 years. 28% of women with GD were developed hypertension later on compared to the non-GD participants (8%), indicating a positive association between GD and hypertension. A multivariate Cox analysis revealed that women with GD had a 28% increased risk of incidence of hypertension as compared to the non-GD group (HR. 1.24 [95% CI 1.13 – 1.65); P<0.01).
Conclusion: Females with GD are at higher risk for developing CVD later in their life. This association might be due to obesity and sedentary lifestyle.

Keywords: Diabetes mellitus; hypertension; cardiovascular; risk factors.

1. INTRODUCTION

Gestational diabetes (GD) is considered one of the most prevalent endocrinopathies, defined as impaired glucose metabolism during pregnancy, and it affects approximately 8 – 12 % of pregnant women worldwide [1]. Pregnancy is accompanied by different physiological changes and alters the hormones' levels; in the late stages of pregnancy, the placenta produces human placental lactogen, which modulates metabolism and leads to insulin resistance. During pregnancy, if the pancreatic beta cells futile to remunerate maternal insulin resistance, it might lead to the pathogenesis of GD [2]. GD is linked with adverse fetal outcomes, including premature fetus delivery and fetal macrosomia [3]. Studies also suggested that GD is linked with the increased onset of cardiovascular disorders (CVD), including coronary vascular disease, ischemia, stroke, and myocardial infarction. However, it is unclear whether the increased risk for CVD is ascribed to the subsequent pathogenesis of type 2 diabetes mellitus or pre-diabetes or the accompanying risk factors for CVD, for instance, hyperlipidemia or obesity [4].

In women, diabetes is inimical to cardiovascular health, and the risk for the pathogenesis of CVD associated with type 2 diabetes mellitus is higher in women compared with men. This increased risk in women might be linked with obesity, or women spend more time in hostile metabolic conditions of pre-diabetes than men who have type 2 diabetes mellitus [5,6]. In women, GD is considered as another diabetes-linked risk to cardiovascular health. During pregnancy, there is an increased cytokine production and insulin resistance promoting atherogenesis [4,7]. However, there is also the possibility that before pregnancy, some women might have a high-risk cardiovascular phenotype, which may be identified during the routine checkup and for screening of GD [4]. It is also identified that a healthy lifestyle and dietary patterns are essential for reducing the risk for progression of GD to obesity and chronic CVD, including hypertension and type 2 diabetes mellitus [8]. The present study aims to assess the risk of cardiovascular disorders in women who were previously identified with GD.

2. METHODOLOGY

2.1 Study Design

2.1.1 Study population

After the approval from the institutional ethical committee, a longitudinal study was begin in Karachi Institute of Heart Diseases Karachi Pakistan from June 2027 to June 2018 to assess the link of GD with CVD. A total of 227 participants, ages 24 – 34 years with an average age of 30.7±3.8 years, were included in this study. Using a baseline questionnaire, the history of GD was recorded, follow-up was taken after every two years. Participants reporting their first pregnancy with GD were grouped as exposed. Participants reporting GD with a previous history of type two diabetes were not considered as exposed. Follow-up was conducted after every two years to evaluate changes in lifestyle characters and health-related information. Females who have given birth to one child at the age of twenty years were included in this study. Participants with any chronic disorders, including diabetes and cancers, were excluded from this study. In 2020, the last follow-up was conducted in which GD and other reproductive characters were assessed, because after that, half of participants had passed their age.

2.2 Covariate Assessment

Demographic data were captured at baseline. Family history of diabetes, myocardial infarction

(MI), and stroke were recorded at baseline, and the data was updated every four years. Health-linked characters, including smoking, alcohol consumption, and diagnosis of other health problems were recorded every two years. Reproductive characters including pregnancy, use of contraceptives, preeclampsia were also recorded. A questionnaire including questions related to physical activity were recorded at baseline and follow-up were conducted every four years. The dietary routine was assessed every four years using a semi qualitative food frequency questionnaire.

2.3 Statistical Analysis

SAS statistical software (version 9.1) was used to evaluate the statistical significance of the data. Study participants were assessed every two years from the time of their first delivery to the onset of CVD (vascular obstruction, myocardial infarction). Using the multivariable Cox hazard model, the hazard risks and ratio were evaluated. 98% confidence interval was used for the relation between GD's history versus the onset of CVD. Using a multivariable model, various reproductive characters of study participants were evaluated, including pre and post-pregnancy BMI, family history of CVDs, menstrual cycle history, menopause status, information related to hormonal therapy if used, and ethnicity. The lifestyle factors affecting cardiovascular health, including obesity, alcohol and smoke consumption, physical activity, and use of aspirin, were evaluated using the secondary multivariable model.

3. RESULTS

The present study included 227 pregnant women free of hypertension and diabetes at the study's baseline. All the women were aged between 24 – 34 years with an average of 30.7±3.8 years at the baseline. Among them, 11.8% of women were exposed to gestational diabetes during their first or subsequent pregnancy. The mean age of first pregnancy is 27.6 years, and a significant difference of age of first pregnancy was found between GD and non-GD. Most of the participants at their baseline are multiparous, and among them, 30% of the women were ever exposed to GD during their gestational period. Women with GD were found to be overweight, have less physical activity, have a family history of diabetes or hypertension, and regularly smoke compared to the non-GD participants (Table 1).

During follow-up, 28% of the GD participants have developed hypertension, and 20% were diagnosed with diabetes mellitus (Table 2). Pregnancy BMI is positively associated with the increased risk of gestational diabetes (Table 1). There is a significant association of family history of diabetes and hypertension with the risk of hypertension ($p<0.01$). There is a significant age, BMI-, multivariable-adjusted association between GD and the future incident of hypertension. Exposure to GD is significantly associated with a 28% increased risk of future hypertension (HR. 1.24 [95% CI 1.13 – 1.65); $P<0.01$) (Table 3). Among all participants, 25% of females have developed diabetes, of whom 47% were previously exposed to GD before the development of diabetes (Table 2). A significant association is found between GD and incidence of hypertension with an HR (1.17 [1.02 – 1.35]; $p<0.05$). The incidence of hypertension is associated with diabetes and GD with an HR of (1.16 [1.03 – 1.34]; $p<0.05$).

4. DISCUSSION

In this observational study, women exposed to GD are at high risk of incidence of hypertension in the future after adjusting the major risk factors of hypertension. However, the precise mechanism for this association is unclear yet. There may be factors that are associated with hypertension. To maintain the glucose supply to the developing fetus, the maternal tissue becomes insulin resistant [9,10]. Studies reported that the women who develop GD during their pregnancy are more susceptible to developing diabetes in the near future due to the metabolic challenge (chronic insulin resistance and β-cell dysfunction) they faced during pregnancy [11]. Chronic insulin resistance and insufficient insulin secretion are both associated with increased hypertension risk [10,11]. Our results also reflected a positive association between GD and future incidence of diabetes and hypertension. All these factors show a clear association between GD and the future incidence of hypertension. Elevated plasma glucose subsequently results in metabolic dysfunction and vascular damage results in an increased risk of hypertension. Therefore, metabolic dysfunction during pregnancy may be a risk factor for hypertension years later [12,13]. The association of GD and subsequent hypertension reflected the common risk factors involved in the pathogenesis of hypertension and diabetes [13]. This study also reflects the common risk factors associated with metabolic and vascular

dysfunction and increased risk of diabetes and hypertension. However, there is a need to evaluate the biological causal risk factors before, after, and during the pregnancy associated with hypertension. Our results reflect the positive association between GD and the future incidence of hypertension indicating that GD may use it to intervene the high-risk women by modifying their lifestyle and precautions to delay the incidence of hypertension [14]. However, further research is needed to identify the underlying biological mechanism involved in the pathogenesis of GD-associated hypertension and management of GD by modifying the identifying risk factors. It a notably found in previous studies that cardiovascular disorders including hypertension, metabolic syndrome, dyslipidemia, etc. are found to be more prevalent in women with a history of GD [14,15]. All these studies supported the emerging concept that women with GD have previously had some metabolic dysfunction identified clinically during pregnancy and associated with the incidence of hypertension, metabolic syndrome, and diabetes years later [16].

Table 1. Summary of baseline characteristics of participants of the study (N=227)

Baseline Characteristics	GD	Non-GD	*p*-value
No. of participants;(%)	27 (11.8)	200 (88.2)	
Age; (mean ± SD)	31.6 ± 2.6	29.8 ± 3.8	>0.01
Age at first pregnancy (mean ± SD)	28.9 ± 2.4	26.4 ± 3.2	<0.01
≤ 30; %	72	80	
>30; %	28	24	
Pre-pregnancy BMI (mean ± SD)	21.5 (2.5)	20.5 (2.2)	<0.01
Normal BMI (< 25.0); %	85	94	
Overweight (> 25.0); %	15	6	
BMI during pregnancy (mean ± SD)	24.6 (2.6)	23.2 (2.6)	<0.01
Normal BMI (< 25.0)	52	75	
Overweight/obese (> 25.0)	48	25	
Total physical activity (minutes/week) (mean ± SD)	250 (112)	280 (150)	<0.01
Vigorous physical activity (minutes/week) (mean ± SD)	80 (70)	105 (95)	<0.01
Smoking; %	5	1.8	<0.01
Parity			
Primiparous; %	25	20	<0.01
Multiparous; %	75	80	<0.01
Gestational Diabetes (ever); %	30	2	
Gestational Hypertension (ever); %	18	8	
Family history of Diabetes; %	32	12	<0.01
Family history of Hypertension; %	20	15	<0.01
Lipid lowering medicine; %	8	7	<0.01
Use of Aspirin; %	9	8	<0.01
Use of oral contraceptives (ever); %	14	12.8	>0.01

Table 2. Incidences of outcomes in term of hypertension and diabetes

Outcomes	GD (%)	Non-GD (%)	*p*-value
Hypertension	28	8	<0.01
Diabetes	20	5	<0.01

Table 3. Association of GD with future incidence of hypertension

Model	HR (95% CI)	*p*-value
Model 1: age	1.86 (1.63-2.13)	<0.01
Model 2: + BMI	1.48 (1.20-1.68)	<0.01
Model 3: + first pregnancy age	1.36 (1.29-1.65)	<0.01
Model 4: history of gestational hypertension	1.29 (1.11-1.58)	<0.01
Model 5: family history of diabetes or hypertension, total physical activity, smoking status, OC use	1.24 (1.13-1.65)	<0.01

This study may open a window to identify the GD as a risk factor for hypertension and consciously manage the high-risk population. There is a potential limitation associated with the current study. All the factors are self-reported by the participants so, the accuracy may be affected. The study represents a specific group of population. A large cohort study may reflect the actual situation of incidence of disease in the population. Although the confounders were carefully controlled, there might be some residual unmeasured confounding factors that may bias the response.

5. CONCLUSION

Considering all these facts, it is concluded that GD may be a possible risk factor for the future prognosis of hypertension. Women with GD were more prone to develop hypertension in the near future than the non-GD participants. Correlation with previous reports indicated the GD as a unique factor that reflects the future risk of hypertension, thus providing a possible modifier or tool for early risk management and prevention of women's leading cause of mortality.

CONSENT

As per international standard or university standard, patients' written consent has been collected and preserved by the author(s).

ETHICAL APPROVAL

As per international standard or university standard written ethical approval has been collected and preserved by the author(s).

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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