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Preeclampsia and Fetal Growth Restriction as Warning Signs for Maternal Cardiovascular Disease in Later Life

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ABSTRACT

Globally, cardiovascular diseases (CVDs) continue to be the primary cause of mortality for women. Even though conventional risk factors raise the risk of CVD in later life, pregnancy-related problems also affect a woman's potential risk of CVD. Specifically, endothelial dysfunction, inflammation, vasospasm, and hypercoagulability are mother defects that lead to preeclampsia and fetal growth restriction (FGR) as well as placental dysfunction and maternal cardiovascular maladaptation to pregnancy. Certain pregnancy problems and CVDs may share pathophysiologic mechanisms. This analysis sought to show how certain unfavorable pregnancy outcomes are linked to subsequent cardiovascular disease (CVD) and how crucial it is to take a woman's pregnancy history into account when determining her risk for CVD. We also intended to draw attention to the part that maternal cardiovascular maladaptation plays in the emergence of particular pregnancy problems like FGR.

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INTRODUCTION

At around one in three, females die because of cardiovascular diseases; the world's primary driver of death for women [1]. Compared to men, women have a considerably higher population-adjusted risk of dying from CVDs (21% against 15%, respectively) [2]. Often, the fundamental risk factors exist for many years before the clinical manifestation of cardiovascular diseases. Furthermore, there is mounting evidence that women who have experienced specific pregnancy difficulties in the past are more likely to acquire cardiovascular diseases later on [3].

Preeclampsia, gestational hypertension, and fetal development abnormalities are examples of these negative pregnancy consequences (APOs) (refer to Table 1) and figure 1[4]. There could additionally be a relationship between the etiologic routes of pregnancy problems and CVDs (such as inflammation, vascular dysfunction, or metabolic syndrome) [5]. The most recent strategies, which ultimately imply a pregnancy experience as a component of the regular assessment of women's cardiovascular risk, have highlighted the significance of these connections. It is more obvious that Implications of a lack of variation of the maternal cardiovascular system enhance the vulnerability to the manifestation of cardiovascular disorders following pregnancy. Our goal was to methodically assess and measure the data about the association between particular APOs and the risk of cardiovascular disease in the future for mothers.

Preeclampsia

A condition unique to pregnancy, preeclampsia is thought to affect 2–8% of all pregnancies and is linked to elevated rates of infant, maternal, and neonatal sickness and death [5]. (Table1) offers a comprehensive definition of preeclampsia.

Maternal Cardiovascular Threat with Preeclampsia

Preeclampsia and subsequent maternal CVDs have been identified in several studies [6]. Preeclampsia and CVDs share certain risk factors, aside from age and pregnancy-specific factors, but a clear causal link between the two conditions was not established. During an average follow-up of roughly eight years, Kestenbaum et al. discovered that the risk of cardiovascular events more than tripled for women with a history of severe preeclampsia (hospitalizations because of Stroke, myocardial infarction and as well as percutaneous coronary artery interventions) (HR: 3.3; 95% CI: 1.7–6.5) and increased thromboembolic actions (HR: 2.3; 95% CI: 1.3 to 4.2) [6]. Peripheral arterial, cerebrovascular, or coronary vascular disease, at minimum ninety days following the date of delivery discharge) in preeclamptic women without traditional indicators of risk for CVD (HR: 2.1; 95% CI: 1.8–2.4) [7]. Additionally, different large cohort research found that women with a history of preeclampsia had an increased risk of dying from CVD (HR: 2.14; 95% CI: 1.29–3.57), and that the risk increased markedly if preeclampsia developed before 34 weeks of pregnancy (HR: 9.54; 95% CI: 4.5–20.26) [8]. Nonetheless, the first ten years after having a preeclamptic pregnancy saw an even greater rise in the threat of stroke, cardiac failure, and mortality from CVD [9].

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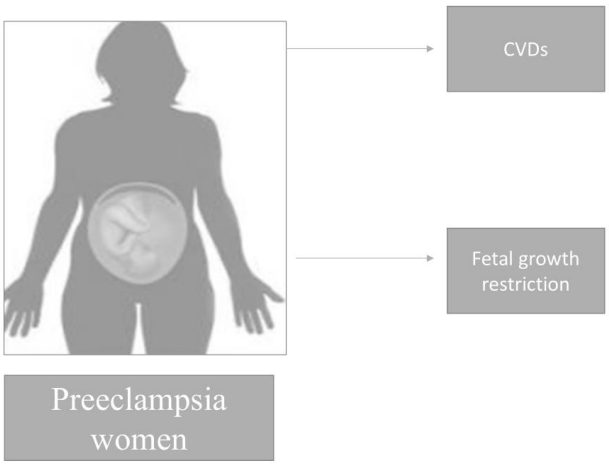

Figure 1. Associated of preeclampsia with fetal growth restriction and warning sign of cardiovascular disease

Preeclampsia was linked to an more risk of heart failure (RR: 1.6, 95% CI: 0.73–3.5), stroke (RR: 1.18; 95% CI, 0.95–1.46), disease of coronary artery (RR: 1.46; 95% CI: 0.95–2.25), and death from coronary artery disease (RR: 2.10; 95% CI, 1.25–3.51) or cardiovascular disease (RR: 2.21; 95% CI, 1.83–2.66), according to a recent meta-analysis [9]. However, another study reported hypertension, CAD, angina, and venous thromboembolism that found2.35 (2.08–2.65), 1.65 (1.26–2.16),1.53 (1.09–2.15),1.62 (1.09–2.41), respectively [10]]

Desirable Mechanisms Connecting the Development of Future Maternal Cardiovascular Disorders with Preeclampsia

There is a discussion of several possible reasons why cardiovascular disease and preeclampsia are related. It has been suggested that preeclampsia could predict cardiovascular events via different mechanisms [9]. However, the association between preeclampsia and future CVD may be partially caused by risk factors that are common to both of these conditions. Permanent vascular alterations with severe endothelial dysfunction are a different idea that may be connected to the previous one and that minimizes future cardiovascular disease risk [11]. The basis of primary ischemia of the uterus is thought to be abnormal alterations to the placental arteries, which is a feature of preeclampsia. Ineffective spiral artery remodeling causes mother circulation to circulate at the intervillous space with a high velocity (about 1-2 m/s), with a greater surge that destroys the villi and forms echogenic cystic lesions lined with thrombus that can also be discharged into the mother's circulation [12]. These antiangiogenic indicators are thought to play a major role in endothelial injury throughout preeclamptic pregnancy, nonetheless they avoid stay noticeably higher following delivery. According to theory, the arterial injury incurred during preeclamptic pregnancy endures and has a role in the development of CVD in these patients. Inflammation is linked to endothelial dysfunction, which hence leads to atherosclerosis. The new theory relates CVD development and acute atherosis in the future to cellular fetal micro chimerism (cFMC) [13]. When fetal cells are discharged into the Pregnant mother's tissues and blood, cFMC develops [13]. Fetal cells are thought to move more readily into the mother's bloodstream in a malfunctioning placenta, where they trigger an immune response against the fetal cells that exhibit exogenous peptides on the HLA surface. Abnormal endothelium to mesenchymal transitions is another potential reason for endothelial dysfunction observed in equally atherosclerosis and pregnancy. According to the theory, endothelial integrity is not entirely restored in preeclamptic women, and they continue to be more vulnerable to inflammatory or stress-related stimuli, as seen in atherosclerosis. Additionally, even after controlling for body mass index, age, and blood pressure, women who had a prior Preeclampsia makes pregnancy more difficult also had significantly higher coronary artery calcium score (CACS), one of the preclinical indicators of CVD. EVs, or extracellular vesicles, are crucial mediators in maternal CVDs associated with preeclampsia, according to new findings [14]. Despite maintaining global systolic function as measured by ejection fraction, women with preeclamptic pregnancies exhibit impaired systolic strain and biventricular diastolic dysfunction [15]. In women who were previously preeclamptic, mild dysfunction in contractions may already manifest, avoiding the ejection fraction being lost, suggesting that global strain is a sensitive metric for the early identification of aberrant cardiac function [16].

Fetal Growth Restriction

A disorder of placental etiology, fetal growth A disorder of placental etiology, restriction of fetal growth is characterized by an improper adaptation of the mother's circulatory system during pregnancy. The fetus in this APO does not develop to its full biological potential because of compromised placental function, which is caused by several things. Depending on whether fetal growth limitation with an abrupt or gradual onset is taken into account, the origin of FGR varies. Two potential pathways about placental anomalies as well as the cardiovascular system of mother’s adaptability account for the occurrence of early-onset FGR. [17].

Maternal Cardiovascular Threat and Fetal Growth Restriction

According to earlier research, women whose pregnancies were complicated by FGR are at risk of developing cardiovascular diseases later in life. Like CVDs, FGR is typified by oxidative stress and persistent inflammation [18]. Even so, according to updated HUNT (Nord-Trøndelag Health) analyze category and insight model found that issues of pregnancy, like preterm gestational age, only slightly improved a ten- forecast of parous women's risk for Cardiovascular of disease [5]. Pregnancy complications history, besides, may enhance

clinical risk prediction prior to the fifty years old and is recognized for forecasting the emergence of conventional risk factors for cardiovascular disease at earlier ages.]. Pregnancy complications history, on the other hand, may enhance clinical risk prediction prior to the age of fifty and is known to predict the emergence of traditional CVD risk factors at earlier ages.

Table 1. Descriptions of adverse pregnancy outcomes (APOs).

Categories	Descriptions
Gestational hypertension	Following 20 weeks of pregnancy, developing de novo hypertension: Systolic blood pressure of 140 mmHg or more AND/OR two distinct instances of diastolic pressure of 90 mmHg or above within an individual whose was previously normotensive and free of additional end-organ pathology or proteinuria [6].
Preeclampsia	following 20 weeks of gestation, de novo hypertension occurs AND: A urine protein: creatinine ratio of 0.3 g/g or +1 by urine dipstick indicates proteinuria (⩾300 mg/24 hours). OR When there is no proteinuria: - platelet count < 150 000/μL - alkaline or aspartate transaminase > 40 IU/L - serum creatinine ⩾ 90 μmol/L Seriou's headaches, clonus, blindness, stroke, changed mental status, and chronic visual scotomata are examples of neurological consequences. - uteroplacental dysfunction, which includes stillbirth, aberrant examination of the umbilical artery Doppler waveform, and fetal growth disorders [10,11].
Fetal growth restriction	The measuring of many fetal parameters, such as weight and abdominal circumference, by lower third percentage. but ten percentage that indicated the waist circumference and the umbilical artery's lack of end diastolic flow.
Gestational diabetes mellitus	At any point during pregnancy, at least one of the following requirements was satisfied: - 91–125 mg/dL (5.1–6.9 mmol/L) of fasting plasma glucose 1-hour plasma glucose after a 75 g oral glucose load ⩾ 10.0 mmol/L (180 mg/dL) [13].

Table 2. Designated published research of preeclampsia and future warning of cardiovascular disease

Research/First Author (Reference)	Design	Number of participants	Measure of Outcome	Outcome Measures' Threat HR (95% CI)
Kestenbaum [6]	Retrospective	31,239	CV events Thromboembolic events	2.2 (1.3–3.6) (mild pre-eclampsia) and 3.3 (1.7–6.5) (severe pre-eclampsia) 2.3 (1.3–4.2) (severe pre-eclampsia)
Wu [9]	Metanalysis	6,400,000	CAD CAD-related death Heart failure stroke CVD-related death	1.46 (0.95–2.25) 2.1 (1.25–3.51) 1.6 (0.73–3.5) 1.18 (0.95–1.46) 2.21 (1.83–2.66)
Mongraw-Chaffin [8]	Retrospective	14,403	CVD-related death	2.14 (1.29–3.57) 9.54 (4.50–20.26) if onset of preeclampsia before 34 weeks' gestation
Hannaford [10]	Prospective	23,000	Hypertension CAD Angina Venous thromboembolism	2.35 (2.08–2.65) 1.65 (1.26–2.16) 1.53 (1.09–2.15) 1.62 (1.09–2.41)

Possible Mechanisms Connecting Future Maternal Cardiovascular Disease Development with Fetal Growth Restriction

Despite being distinct conditions, preeclampsia and FGR exhibit similarities in their pathophysiology, including insufficient placentation, obstetrics, vascular dysfunctions and discomfort [19]. According to Melchiorre et al., despite having maintain ejection fraction and geometry as measured of women who are pregnant, a majority were affected by FGR had 12 weeks after birth. worse a third exhibited obvious diastolic chamber dysfunction, and a third had diastolic reserve with compromised myocardial unwinding [20]. The majority of patients with FGR-complicated pregnancies were found to have aberrant LV strain values. A tiny placenta, decidual arteriopathy, placental infarcts with diminished of ability placental parenchyma, and anomalies of the placental villous tree, including distal villous

hypoplasia, are examples of vascular dysfunction symptoms in FGR. Vascular fibrinoid necrosis and acute atherosis are brought on by insufficient trophoblastic invasion, smooth muscle persistence in the arterial walls, and vascular injury [21]. Mutations in the genes producing glucokinase, angiotensinogen, coagulation factors, and G proteins are linked to a greater likelihood of coronary artery disease and FGR. Additionally, contrast to women with no complication of pregnancies, it was shown that patients with FGR have a greater inflammatory response that persists over time.

Conclusion

Fetal growth restriction and preeclampsia are two harmful pregnancy outcomes that are closely associated with the threat of long-standing maternal CVDs. These pregnancy issues most expected have analogous pathophysiologic mechanisms and are associated with comparable danger signs for women. However, there is still a lack of clarity regarding a liaison mechanism behind this association. Pregnancy offers a special chance to assess a woman's risk of developing CVDs later in life and implement effective risk-reduction techniques because it happens early in life, usually before the development of clinically noticeable CVDs.

Authors contribution

Umme Salma: Conception and design; drafting of the article. Md Sayed Sheikh: Analysis and interpretation of the data and final approval of the article. Ahmed Baker A. Alshaikh and Maged Elshamy: Critical revision of the article for important intellectual content.

Conflicts of Interest

No conflict of interest in this article was reported.

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