

## The Association between Adverse Pregnancy Outcomes and Laboratory Measures as Risk for Cardiovascular Disorders

Haneen Hussein Farhood\*, Manal Khalid Abdulridha\*, Hameedah Hadi Abdulwahid\*\*

\*Clinical Pharmacy department/ College of Pharmacy/ Mustansiriyah University

\*\*Consultant Gynecologist/Karbala Holy Health Directorate

### Article Info:

Received Dec 2022

Accepted Feb 2023

Corresponding Author email:

[haneen.alhassnawy93@uomustansiriyah.edu.iq](mailto:haneen.alhassnawy93@uomustansiriyah.edu.iq)

[orcid: https://orcid.org/0000-0002-5059-7963](https://orcid.org/0000-0002-5059-7963)

### DOI:

### Abstract:

**Background:** Due to the complicated etiology of cardiovascular illnesses, a thorough risk assessment is necessary for screening reasons. Many published studies relate the pregnancy complications and future cardiovascular disease (CVD) risk.

**Objective:** Investigate the association between risk factors of the laboratory measures and adverse pregnancy outcomes (APOs) with level of cardiovascular disorders risk.

**Methods:** Adult women were enrolled in a cross-sectional study, and they were divided into 2 groups according to whether they had a history of adverse pregnancy outcomes or not. Laboratory and clinical measurements were carried out, and The CVD risk was calculated according to Framingham risk score.

**Results:** All women enrolled were over 40 years age, mostly obese, had predominantly A+ve and O+ve blood group phenotypes. As compared to the low-risk category, women with a positive history of pregnancy-induced hypertension and preeclampsia were 7.5 times more likely to be in the intermediate group while those with a positive history of stillbirth were 17.2 times more likely to be in the high-risk group.

**Conclusion:** With reference to the low-risk category, a positive history of pregnancy-induced hypertension and preeclampsia was predictor for intermediate CVD risk, while a positive history of stillbirth was predictor for high CVD risk.

**Key words:** Adverse Pregnancy Outcomes, Cardiovascular Disease, Framingham Risk Score.

## العلاقة بين نتائج الحمل السلبية والقياسات المختبرية كخطر لاضطرابات القلب والأوعية الدموية

حنين حسين فرهود\*, منال خالد عبد الرضا\*, حميدة هادي عبد الواحد\*\*  
\*فرع الصيدلة السريرية/كلية الصيدلة/الجامعة المستنصرية  
\*\*استشاري امراض النساء/دائرة صحة كربلاء

### الخلاصة:

**الخلفية:** نظرا للمسببات المعقدة لأمراض القلب والأوعية الدموية ، من الضروري إجراء تقييم شامل للمخاطر لأسباب الفحص. تتعلق العديد من الدراسات المنشورة بمضاعفات الحمل ومخاطر الأمراض القلبية الوعائية في المستقبل.  
**الهدف:** التحقيق في العلاقة بين عوامل الخطر للتدابير المختبرية ونتائج الحمل السلبية (APOs) مع مستوى مخاطر اضطرابات القلب والأوعية الدموية.

**طرائق العمل:** تم تسجيل النساء البالغات في دراسة مقطعية ، وتم تقسيمهن إلى مجموعات ٢ وفقا لما إذا كان لديهن تاريخ من APOs أم لا. تم إجراء القياسات المختبرية والسريرية ، وتم تطبيق درجة مخاطر فرامنغهام.

**النتائج:** كانت جميع النساء المسجلات فوق سن ٤٠ عاما ، ومعظمهن بدينات ، ولديهن في الغالب أنماط ظاهرية من فصيلة الدم  $A + ve$  و  $O + ve$ . بالمقارنة مع فئة المخاطر المنخفضة ، كانت النساء اللواتي لديهن تاريخ إيجابي من ارتفاع ضغط الدم الناجم عن الحمل وتسمم الحمل أكثر عرضة بنسبة ٧,٥ مرة لأن يكن في المجموعة المتوسطة بينما كان أولئك الذين لديهم تاريخ إيجابي من الإملاص أكثر عرضة بنسبة ١٧,٢ مرة ليكونوا في المجموعة عالية الخطورة.

**الاستنتاج:** بالإشارة إلى فئة المخاطر المنخفضة ، كان التاريخ الإيجابي لارتفاع ضغط الدم الناجم عن الحمل وتسمم الحمل مؤشرا على خطر متوسط للإصابة بالأمراض القلبية الوعائية ، في حين أن التاريخ الإيجابي للإملاص كان مؤشرا على ارتفاع مخاطر الإصابة بالأمراض القلبية الوعائية.

**الكلمات المفتاحية:** نتائج الحمل السلبية ، أمراض القلب والأوعية الدموية ، درجة مخاطر فرامنغهام.

## Introduction

The prevalence of the most common cardiovascular diseases (CVDs) is the result of long-term processes involving intricate interactions between risk factors that are both modifiable and immutable. The majority of CVD cases can be linked to changeable risk factors, hence they should be viewed as preventable<sup>[1]</sup>. According to the developed world's greatest CVD death rates (>400 deaths per 100,000 people, in both genders) were in the Caucasus and Central Asia regions. The Oceania area was expected to have the lowest CVD fatality rates (85 deaths per 100,000 population, in both genders)<sup>[2]</sup>. Nearly 80% of these deaths occurred in low- and middle-income countries, where premature death rates are highly disparate<sup>[3]</sup>. According to statistics from the national health and nutrition examination survey (NHANES) for the years 2013 to 2016, the prevalence of CVD, which includes coronary heart disease (CHD), heart failure (HF), stroke, and hypertension, is 48.0% in persons under the age of 20 and rises with age in both men and women. Women have a higher population-adjusted risk of dying from CVD than do men (20.9% versus 14.9%, respectively)<sup>[4]</sup>. Due to the complicated etiology of cardiovascular illnesses, a thorough risk assessment is necessary for screening reasons<sup>[5]</sup>. Traditional CVD risk factors, such as hypertension, diabetes, smoking, and hypercholesterolemia, have sparked the creation of risk prediction models and significant advances in treatment<sup>[6]</sup>. Major contributors to CVD include

cardiometabolic, behavioral, environmental, and social risk factors<sup>[7]</sup>. Unhealthy eating, inactivity, usage of tobacco products, and abusing alcohol are the main behavioral risk factors for heart disease and stroke. Individuals may experience the effects of behavioral risk factors like elevated blood pressure, elevated blood glucose, elevated blood lipids, and overweight and obesity<sup>[8]</sup>. There are numerous prediction models that can be used to estimate the risk of having symptomatic CVD, which varies widely between individuals. An individual can be categorized into low, middle, or high risk categories with the accompanying treatment options based on the estimated risk for CVD in the upcoming ten years<sup>[9]</sup>. Framingham risk score (FRS) is a standardized and widely used method for determining the risk of coronary artery disease (CAD). Age, gender, total cholesterol (TC), high density lipoprotein cholesterol (HDL), smoking behavior, and systolic blood pressure are the six coronary risk factors taken into account by the FRS. The most accurate method for estimating a person's likelihood of developing long-term CVD is the FRS<sup>[10]</sup>. In addition to increased insulin resistance, adipose tissue deposition, hypercoagulability, cardiac remodeling, and decreased vascular resistance, pregnancy causes a number of vascular, metabolic, and physiological changes in the mother<sup>[11]</sup>. Preeclampsia, gestational hypertension, gestational diabetes, preterm delivery, fetal growth restriction, having a neonate with a low birth weight or a low birth weight indexed to a referent sample based on gestational

age, and placental abruption are just a few examples of maternal or fetal complications<sup>[11]</sup>. These adverse pregnancy outcomes (i.e. hypertensive disorders of pregnancy [HDPs], gestational diabetes, preterm birth prior to 37 weeks of gestation, and intrauterine growth restriction) are linked to a 2-fold increased risk of developing cardiovascular disease in the future. CVD may also be linked to stillbirth and placental abruption<sup>[12]</sup>. APOs are not uncommon, with 30% of women at risk of developing one. This includes gestational hypertension (3–14%), pre-eclampsia (2–5%), gestational diabetes (5%), preterm delivery (6–12%) and the delivery of a small-for-gestational-age infant<sup>[13]</sup>. Attempts to engage women in learning about their future CVD risk should be prompted by pregnancy associated with APOs or CVD manifestations<sup>[14]</sup>. This study aimed to investigate the association between potential risk factors of some clinical and laboratory measures and adverse pregnancy outcomes with risk levels of developing cardiovascular disorders.

## Methods

A cross-sectional study was carried out between February and June of 2022. In addition to the obstetrics and gynecology teaching hospital in Karbala, a convenient sample of 257 women, aged 40 and older, was chosen during their visit to the private clinics. These women were divided into two groups: those with and those without a history of APOs. Women who had already developed CHD, stroke, or another atherosclerotic disease were not included, nor were women whose APO history had missing information or those who were taking aspirin and lipid-lowering medications. The women were divided into two main groups: Group 1 (G1), which consisted of 103 women to be assessed for cardiovascular risk presented without a history of APOs (control group), and Group 2 (G2), which consisted of 154

women to be assessed for cardiovascular risk presented with a history of APOs. The institutional scientific and ethical committee of Pharmacy College at Mustansiriyah University and the Governorate Health Directorate in Karbala gave their approval to the study. After thorough explanation of the study's purpose and assurance of the accuracy of the data gathered, written consent was obtained. The 1964 Helsinki Declaration and its later amendments<sup>[15]</sup>, as well as the institutional research committee's ethical standards<sup>[15]</sup>, were all followed in all methods used in the study involving human participants. The information was gathered from the case sheets of the women and included sociodemographic data, a history of APOs, comorbidities, laboratory investigations, medical history, and medication history. A specific data collection sheet was created by the research team to match study objectives. Each participant had their height, weight, and blood pressure measured according to standard procedures<sup>[16]</sup>. Fasting blood glucose was also measured using an on-call plus glucometer in addition to measuring the lipid profile (serum total cholesterol, serum triglyceride, serum high-density lipoprotein cholesterol, and serum low-density lipoprotein cholesterol) using a Mindray autoanalyzer<sup>[17]</sup>. Based on the 10-year Framingham risk score variables, the CVD risk was calculated<sup>[18]</sup>. The Framingham calculator was created as a tool to assess the risk of CAD in individuals aged 30-74 without a history of CAD, a diagnosis of the disease, or any symptoms. The risk of developing CAD over the next 10 years is calculated by adding up risk factors on a score sheet tailored to each gender. Age, total cholesterol, HDL, blood pressure, diabetes, and smoking status are all risk factors that are assigned points based on their presence or level. After adding the points for each risk factor, a score is generated<sup>[19]</sup>. Low risk was defined as a risk score of 10% or less, intermediate risk as a score between

10% and 20%, and high risk as a score 20% or above<sup>[19]</sup>. Among the unfavorable pregnancy outcomes that were included in the current study<sup>[20]</sup> were a history of placenta previa, placenta abruption, preterm delivery, abortion, stillbirth, pregnancy-induced hypertension/preeclampsia<sup>[21]</sup>, gestational diabetes, and ectopic pregnancy. For statistical analysis, the collected data were imported into Microsoft Excel 2016 and loaded into SPSS V 20. Percentages were used to represent categorical variables. The format for continuous variables was (Means  $\pm$  SD). To compare means within the same group, an ANOVA was used. Odds ratios (OR) were estimated using multinomial logistic regression. A p-value of  $< 0.05$  was considered significant and  $p < 0.01$  was considered highly significant.

## Result

### Demographics and obstetrical history of participants

The 257 women who were enrolled had a mean age of  $48.5 \pm 6.7$  years, with 62.1%

of group 1 and 56.5% of group 2 being between the ages of 40 and 49 (103 in the group 1 and 154 in women with APO in group 2). There was no statistically significant difference between the two groups ( $P > 0.05$ ), table (1). The difference between group 1 and group 2 in the number of participants in each BMI category was statistically not significant ( $P > 0.05$ ). Women in both study groups had predominantly A+ve and O+ve blood group phenotypes, ( $P > 0.05$ ). The mean number of deliveries in the entire sample was  $(5.22 \pm 2.29)$  ranging from 0-13 child. The majority (79.9%) of the group 2 and (73.8%) of the group 1 had more than 3 deliveries. In the APO group (G2), (11%) preterm births, (33.1%) preeclampsia/pregnancy-induced hypertension), and (6.5%) gestational diabetes were past events. The most frequent unfavorable outcome was abortion (76%). (20.8%) of the group 2 recalled experiencing a stillbirth. Other APOs (placenta previa, placental abruption, ectopic pregnancy) was only 3.9%.

**Table (1): Demographics and obstetrical history of participants**

		G1 (n= 103)		G2 (n=154)		Total		
Variable		No	%	No	%			P value
Age								0.469 <sup>NS</sup>
	40-49	64	62.1%	87	56.5%	151	58.8%	
	50-59	29	28.2%	56	36.4%	85	33.1%	
	60-69	9	8.7%	9	5.8%	18	7%	
	≥70	1	1%	2	1.3%	3	1.2%	
BMI								0.128 <sup>NS</sup>
	Normal	2	1.9%	5	3.2%	7	2.7%	
	Overweight	38	36.9%	39	25.3%	77	30%	
	Obese	63	61.2%	110	71.4%	173	67.3%	
ABO group								0.441 <sup>NS</sup>
	A	45	44.1%	54	35.1%	99	38.7%	
	B	18	17.6%	36	23.4%	54	21.1%	
	AB	7	6.9%	9	5.8%	16	6.3%	
	O	32	31.4%	55	35.7%	87	34%	
Rh								0.148 <sup>NS</sup>
	Positive	99	97.10%	153	99.40%	252	98.4%	
	negative	3	2.90%	1	0.60%	4	1.6%	
Number of deliveries								0.364 <sup>NS</sup>
	1-3	27	26.2%	31	20.1%			
	>3	76	73.8%	123	79.9%			

Data presented as Number(N) and percentage (%), Chi-Square test comparing categorical variables, P-value ≥0.05, NS, non-significant.

### The Impact of History of Adverse Pregnancy Outcomes on Cardiovascular Disease Risk Score level

Referring to Table (2) which presented the effect of APOs on CVD risk according to the

three-tiered FRS. Among type of APOs, only gestational diabetes exhibits significant high predicting score among women within high CVD risk level compared to intermediate and low level (P <0.01).

**Table (2): The prevalence of adverse pregnancy outcomes according to Framingham's score**

	Framingham Risk Score						
	Low CVD risk (<10%) n=169		Intermediate risk (10-19%) n=56		High CVD risk (20-29%) N=31		
APO	No	%	No	%	No	%	P
preterm delivery	11	6.5%	4	7.1%	1	3.2%	0.748 <sup>NS</sup>
Hypertension	36	21.3%	8	14.3%	7	22.6%	0.483 <sup>NS</sup>
Abortion	74	43.8%	31	55.4%	11	35.5%	0.161 <sup>NS</sup>
Stillbirth	20	11.8%	10	17.9%	4	12.9%	0.514 <sup>NS</sup>
Gestational DM	4	2.4%	1	1.8%	5	16.1%	0.001
Others APO	3	1.8%	1	1.8%	2	6.5%	0.272 <sup>NS</sup>

P-value by Chi Square test comparing categorical variables. NS, nonsignificant.



### The Impact of Clinical and Laboratory Measurements on Cardiovascular Disease Risk Score level

As presented in Table (3), laboratory measures among women in both study groups showed that the systolic blood pressure (SBP), diastolic blood pressure (DBP) and fasting blood sugar (FBS) were

significantly higher in intermediate and high -risk categories compared to low-risk categories ( $P<0.01$ ). Similarly, all lipid profile measurements were significantly deranged in the high Framingham risk group compared to the low-risk group. These differences were equally seen in both groups.

**Table (3): The clinical and lab test measurements**

	Framingham Risk Score						
Variables	Low CVD risk (<10%) n=169		Intermediate CVD risk (10-19%) n= 57		High CVD risk (20-29%) n= 31		P value
	Mean	±SD	Mean	±SD	Mean	±SD	
SBP (mmHg)	125.7	18.1	146.9	22.3	148.7	15.3	<0.001
DBP (mmHg)	83.7	12.5	93.8	12.3	95.5	9.2	<0.001
TC (mg/dL)	183.3	31.7	200.6	34.0	221.8	46.8	<0.001
HDL (mg/dL)	47.3	9.8	43.3	7.2	41.6	6.1	<0.001
LDL (mg/dL)	113.7	29.7	126.4	32.2	135.4	44.3	<0.001
TG (mg/dL)	118.2	55.3	143.1	74.1	175.7	84.6	<0.001
FBS (mg/dL)	112.6	33.4	137.9	57.8	172.3	74.5	<0.001

P-values by ANOVA were used to compare continuous variables. Abbreviations: SBP, systolic blood pressure; DBP, diastolic blood pressure; TC, total cholesterol; HDL, high-density lipid; LDL, low-density lipid; TG, triglyceride; FBS, fasting blood sugar.

### Association between adverse pregnancy outcomes and clinical and laboratory measures as risk factors of cardiovascular disorders

Compared to the low-risk category which has been set as a reference group in the logistic regression model, the odd ratio (OR) of having different parameters was tested as a predictor for being in a higher risk group as shown in Table (4). Out of these, older age, higher SBP and FBS, and lower HDL showed significant association with being in the higher Framingham risk category. Older age by a year had 58% more likely to be in the intermediate risk group and was 2.1 times more likely to be in the high-risk group as compared to the low-risk group (the reference group). Increasing SBP by 1mmHg increased the likelihood of being in the intermediate and

high-risk categories by 16% and 19% respectively as compared to the low-risk group. There was a slight but significant increase in the probability of patients being in intermediate (3%) and high risk (5%) groups when they had a 1 mg/dL increase in their FBS. Additionally, having 1mg/dL lower HDL increased the probability of being in the intermediate and high-risk groups by 20% and 29% respectively. When comes to adverse pregnancy outcomes, women with a positive history of pregnancy-induced hypertension and preeclampsia were 7.5 times more likely to be in the intermediate group than the low-risk group while those with a positive history of stillbirth were 17.2 times more likely to be in the high-risk group compared to the low-risk group. The associations with other APO

outcomes (preterm delivery, abortion and gestational DM) were statistically not significant.

**Table (4): Correlation between risk factors of the lab and adverse pregnancy outcomes and risk for cardiovascular disorders**

Parameter	Framingham Risk Score						
	Low CVD risk	Intermediate CVD risk			High CVD risk		
		OR	95% CI		OR	95% CI	
Age (year)	ref	*1.58	1.30	1.91	*2.13	1.67	2.72
BMI (Kg/m <sup>2</sup> )	ref	1.04	0.91	1.19	0.95	0.79	1.15
Having a family history of CVD vs. no family history	ref	2.67	0.77	9.19	1.89	0.31	11.51
Having > 3 deliveries vs. having ≤ 3	ref	0.33	0.07	1.44	0.51	0.06	4.66
SBP per mmHg	ref	*1.16	1.09	1.24	*1.19	1.10	1.30
DBP per mmHg	ref	1.004	0.93	1.09	1.05	0.94	1.17
TC per mg/dL	ref	1.02	0.98	1.07	1.04	0.99	1.09
HDL per mg/dL	ref	*0.80	0.71	0.91	*0.71	0.60	0.84
LDL per mg/dL	ref	1.007	0.97	1.05	1.002	0.96	1.05
TG per mg/dL	ref	0.99	0.98	0.99	0.99	0.976	1.003
FBS per mg/dL	ref	*1.03	1.02	1.05	*1.05	1.03	1.07
<b>Having adverse pregnancy outcome</b>							
Preterm delivery	ref	0.39	0.06	2.77	0.60	0.01	33.21
Pregnancy-induced HT/preeclampsia	ref	*7.53	1.57	36.17	1.64	0.18	15.01
Abortion	ref	0.77	0.23	2.58	1.70	0.29	10.17
Stillbirth	ref	2.46	0.48	12.56	*17.2	1.21	242.94
Gestational DM	ref	1.63	0.05	52.13	0.02	0	0.96
Anemia	ref	4.05	0.99	16.58	5.67	0.62	51.43

Odds ratios (OR) were estimated using multinomial logistic regression. \* Denotes significant result P< 0.05. Abbreviations: CVD, cardiovascular disease; SBP, systolic blood pressure; DBP, diastolic blood pressure; TC, total cholesterol; HDL, high-density lipid; LDL, low-density lipid; TG, triglyceride; FBS, fasting blood sugar; HT, hypertension; DM, Diabetes mellitus; APO, adverse pregnancy outcome.

## Discussion

Some studies show persistent anti-angiogenic, coagulopathic, and inflammatory states in women with APOs, along with structural and functional changes to the cardiovascular system. However, it is unclear whether the elevated

long-term CVD risk linked to APOs is caused by these shared risk factors or if there are additional mechanisms and characteristics that play a role<sup>[22]</sup>. It is challenging to determine whether the associations between APOs and an increased risk of future maternal CVD are

caused by shared risk factors because many of the studies that describe these associations have not fully adjusted for potential confounding baseline cardiovascular risk factors. It is still unclear what causes women with APOs to have an elevated risk of CVD; it may be due to shared baseline risk profiles, APOs acting independently as risk factors, unmeasured confounders, unidentified complex mechanisms, or a combination of the aforementioned factors<sup>[13]</sup>.

### **The Impact of History of Adverse Pregnancy Outcomes on Cardiovascular Disease Risk Score**

Few studies have supported the inclusion of pregnancy risk factors in risk prediction scores, despite the fact that current CVD prevention guidelines emphasize the significance of pregnancy history in evaluating CVD risk<sup>[23]</sup>. Two studies in particular looked at the incremental value of adding intrauterine growth restriction, low birth weight, preterm delivery, and HDP to known risk factors, and they found no change in the risk category<sup>[23,24]</sup>. HDP and preterm delivery status did result in reclassification of CVD risk in one study using a Norwegian population-based registry, but it had negligible clinical significance<sup>[25]</sup>. In spite of being independently associated with increased 10-year CVD risk, incorporating HDP into a study of a US cohort of women at low risk for CVD did not enhance predictive discrimination<sup>[23]</sup>. These studies used cohorts and population-based registries to create sample populations of parous women  $\geq 40$  without a history of CVD; consequently, a sizable portion of the women in these groups were past the age of childbearing<sup>[22]</sup>. In the current study, average age of participant was 48.5 years. In a previous Australian study among obstetric women, it was noted that the majority of women with obstetrical histories and APOs were obese, and that an increase in maternal BMI was associated with harmful health outcomes for both the

mother and unborn child<sup>[26]</sup>. The risk associated with APOs may have been underestimated by sampling older women because the prevalence of comorbid conditions like diabetes, obesity, dyslipidemia, and hypertension rises with aging. It is also challenging to determine each APO's individual risk because they can happen simultaneously and are not independent of one another. Therefore, in the future, any risk prediction modeling studies should include risk factors that are independently highly predictive of CVD and include populations that reflect the intended target population for screening (i.e., women of reproductive age)<sup>[22]</sup>. To determine the extent of elevated CVD risks in women with a history of APOs using recognized cardiovascular risk tools, additional research is needed. It will then be necessary to assess how well these scores perform in the postpartum population. It will continue to be challenging to develop efficient risk reduction strategies in this population until the true levels of CVD risks are fully understood, for example, the ideal timing, setting, and types of intervention required to ameliorate or prevent the progression of adverse cardiovascular events<sup>[13]</sup>. In our study, Women in both study groups had predominantly A+ve and O +ve blood group phenotypes. Maternal ABO blood group was linked to the risk of preeclampsia, but not to gestational diabetes (GDM), preterm delivery, low birth weight, or small for gestational age, according to a study on Thai women<sup>[27]</sup>. Unlike another study on the Iranian population, which found no link between the ABO and Rh blood groups and risk of preeclampsia<sup>[28]</sup>. According to the participants' obstetrical histories in the current study, the total number of births in the sample ranged from 0 to 13, and the majority of the APO group (79.9%) had more than three deliveries. They also had a history of preterm births (11%), abortions (76%), stillbirths (20.8%), other placental complications, and ectopic pregnancies.



According to Seyyed et al., Iranians' live birth rates are linked to CVD, which is consistent with these findings<sup>[29]</sup>. The biologic pathway could play a role in the association between parity and incident CVD in females. Incidences of CVD that persisted even after delivery can be negatively impacted by physiological changes related to pregnancy, such as weight gain, dyslipidemia, elevated plasma glucose and insulin resistance, endothelial dysfunction, inflammatory and hemostatic processes<sup>[30]</sup>. While another studies found a relatively high prevalence of miscarriage (12.1%)<sup>[31]</sup> and gestational diabetes among Saudi 51%<sup>[32]</sup> and among Kuwaiti mothers was 12.6%<sup>[33]</sup>. The possible reasons for the high prevalence of GDM in women could likely be attributed to the increasing incidence of obesity and the high prevalence of type 2 diabetes<sup>[32]</sup>. According to Ahmed et al., preeclampsia represented 54.9% of all HDP as in the current study, and the risk of prematurity was higher in women who were multigravid and those who had chronic hypertension<sup>[34]</sup>. For the prevention and treatment of cardiovascular diseases, models of cardiovascular risk such as the FRS and World Health Organization/International Society of Hypertension (WHO/ISH) models are essential. Numerous studies discovered that the WHO/ISH score underestimated Asians' risk when compared to FRS<sup>[35–37]</sup>. According to a report, the WHO/ISH model cannot categorize Malaysians as having high cardiovascular risk, but the FRS and SCORE-high models can<sup>[35]</sup>. A few Indian studies have found that the FRS risk assessment model is the best at identifying patients at high CVD risk, while the WHO and atherosclerotic cardiovascular disease (ASCVD) calculators are the worst<sup>[36–38]</sup>.

### **The Impact of Clinical and Laboratory Measurements on Cardiovascular Disease Risk Score level**

According to the findings of the current study, the blood pressure (SBP, DBP), FBS, and lipid profile of women in both study groups were significantly higher in the intermediate and high-risk categories compared to the low-risk categories ( $P < 0.01$ ). Moreover, in addition to older age and according to the results of logistic regression analysis, high SBP and high FBS make women more susceptible to be in intermediate and high risk of cardiovascular disease. Increasing SBP by 1mmHg increased the likelihood of being in the intermediate and high-risk categories by 16% and 19% respectively as compared to the low-risk group. There was a slight but significant increase in the probability of patients being in intermediate (3%) and high risk (5%) groups when they had a 1 mg/dL increase in their FBS. Additionally, having 1mg/dL lower HDL increased the probability of being in the intermediate and high-risk groups by 20% and 29% respectively. These findings were in line with earlier studies; the first was carried out in Iran by Jahangiry et al., who found that high SBP and FBS were significantly associated with an increased risk of CVD when compared to other parameters<sup>[10]</sup>. Another study by Takahashi et al. linked SBP, TC, and lower HDL concentrations in the general population to CAD risk<sup>[39]</sup>.

### **Association between adverse pregnancy outcomes and clinical and laboratory measures as risk factors of cardiovascular disorders**

The obstetrical history of women particularly gestational hypertension has consistently been associated with an increased risk of CVD and stroke<sup>[11]</sup>. The associations with CVD were progressively stronger for moderate and severe preeclampsia<sup>[11]</sup>. Prior data suggest that 20% of women with preeclampsia develop hypertension within 15 years<sup>[40]</sup>. Another study stated that women with HDP have strong risk factors for subsequent hypertension 5 years after delivery<sup>[41]</sup>. A study reported that women with a history

of stillbirth were 49% more likely to experience a cardiovascular event compared to women with no previous history, as they found that women with a history of stillbirth had an approximately 2-fold increased risk compared to women with no prior history<sup>[20]</sup>. In the present study, women with a positive history of pregnancy-induced hypertension and preeclampsia were 7.5 times more likely to be in the intermediate group than the low-risk group, while those with a positive history of stillbirth were 17.2 times more likely to be in the high-risk group compared to the low-risk group. Previous study from India suggested the association of abortions and preterm delivery with future CVDs<sup>[42]</sup>. The significant association between stillbirth and increase in CVD risk is probably due to some genetic or epigenetic characteristics and family history of CVD appear to predispose women to both pregnancy loss and CHD. Nevertheless, the pathophysiological mechanisms that connect pregnancy loss to the development of CHD have not yet been fully understood<sup>[43]</sup>.

### Study limitations

The sample size of participants in our study was relatively small, which led to a low percentage of placenta previa, placental abruption, and ectopic pregnancy.

### Conclusion

The current study revealed that positive history of pregnancy-induced hypertension and preeclampsia was predictor for intermediate CVD risk, while a positive history of stillbirth was predictor for high CVD risk. Older age and the overall clinical and laboratory measures were significantly higher within intermediate and high-risk categories according to Framingham Risk Score.

**Conflict of interest**      Authors declare non

### Acknowledgment

The author would like to thank Mustansiriayah University (www.uomustansiriayah.edu.iq) Baghdad, Iraq for its support in the present work and special thanks to Hameedah Hadi, Consultant in Obstetrics and Gynecology for her helping.

### References

- 1- Cosselman KE, Navas-Acien A, Kaufman JD. Environmental factors in cardiovascular disease. *Nat Rev Cardiol*. 2015;12(11):627–42.
- 2- Bansilal S, Castellano JM, Fuster V. Global burden of CVD: Focus on secondary prevention of cardiovascular disease. *Int J Cardiol* 2015;201:S1–7.
- 3- Kumar Khanal M, Ahmed AM, Moniruzzaman M, Chandra Banik P, Dhungana R, Bhandari P, et al. Total cardiovascular risk for next 10 years among rural population of Nepal using WHO/ ISH risk prediction chart. *BMC Res Notes* 2017;10:120.
- 4- Brown HL, Smith GN. Pregnancy Complications, Cardiovascular Risk Factors, and Future Heart Disease. *Obstet Gynecol Clin North Am*. 2020;47(3):487–95.
- 5- Bansal P, Chaudhary A, Wander P, Satija M, Sharma S, Girdhar S, et al. Cardiovascular Risk Assessment Using WHO/ISH Risk Prediction Charts In a Rural Area of North India. *J Res Med Dent Sci* 2016;4(2):127.
- 6- Wang J, Tan GJ, Han LN, Bai YY, He M, Liu HB. Novel biomarkers for cardiovascular risk prediction. *J Geriatr Cardiol* 2017;14:135–50.
- 7- Roth GA, Mensah GA, Johnson CO, Addolorato G, Ammirati E, Baddour LM, et al. Global Burden of Cardiovascular Diseases and Risk Factors, 1990–2019. *J Am Coll Cardiol*. 2020;76(25):2982–3021.
- 8- Cardiovascular diseases. [cited 2022 May28];Available from: [https://www.who.int/health-topics/cardiovascular-diseases#tab=tab\\_1](https://www.who.int/health-topics/cardiovascular-diseases#tab=tab_1)

- 9- Groenewegen KA, Den Ruijter HM, Pasterkamp G, Polak JF, Bots ML, Peters SAE. Vascular age to determine cardiovascular disease risk: A systematic review of its concepts, definitions, and clinical applications. *Eur. J. Prev. Cardiol.* 2016;23(3):264–74.
- 10- Jahangiry L, Farhangi MA, Rezaei F. Framingham risk score for estimation of 10-years of cardiovascular diseases risk in patients with metabolic syndrome. *J Heal Popul Nutr* 2017;36(1):36.
- 11- Parikh NI, Gonzalez JM, Anderson CAM, Judd SE, Rexrode KM, Hlatky MA, et al. Adverse Pregnancy Outcomes and Cardiovascular Disease Risk: Unique Opportunities for Cardiovascular Disease Prevention in Women: A Scientific Statement From the American Heart Association. *Circulation* 2021;143(18):E902–16.
- 12- Park K, Minissian MB, Wei J, Saade GR, Smith GN. Contemporary clinical updates on the prevention of future cardiovascular disease in women who experience adverse pregnancy outcomes. *Clin Cardiol* 2020;43(6):553–9.
- 13- Wu P, Mamas MA, Gulati M. Pregnancy As a Predictor of Maternal Cardiovascular Disease: The Era of CardioObstetrics. *J Women's Heal* 2019;28(8):1037–50.
- 14- Sharma G, Zakaria S, Michos ED, Bhatt AB, Lundberg GP, Florio KL, et al. Improving Cardiovascular Workforce Competencies in Cardio-Obstetrics: Current Challenges and Future Directions. *J Am Heart Assoc* 2020;9(12):15569.
- 15- World Medical Association. Ethical Principles for Medical Research Involving Human Subjects. *Eur J Emerg Med* 2001;8(3):221–3.
- 16- Abdulaali AR, Abdulridha MK, Sameh I, Al-turfi HH. Effect of Vitamin D3 Supplement on Biochemical Markers and Blood Pressure Reading in Hypertensive patients as A secondary Prevention. *Al Mustansiriyah J Pharm Sci* 2018;18(2):24–32.
- 17- Clinical Biochemistry / Lipids - SPINREACT. [cited 2022 Jun 13];Available from: <https://www.spinreact.com/en/products-list/clinical-biochemistry/lipids.html>
- 18- Rodondi N, Locatelli I, Aujesky D, Butler J, Vittinghoff E, Simonsick E, et al. Framingham Risk Score and Alternatives for Prediction of Coronary Heart Disease in Older Adults. *PLoS One* 2012;7(3):e34287.
- 19- Jahangiry L, Farhangi MA, Rezaei F. Framingham risk score for estimation of 10-years of cardiovascular diseases risk in patients with metabolic syndrome. *J Heal Popul Nutr* 2017;36(1):1–6.
- 20- Grandi SM, Filion KB, Yoon S, Ayele HT, Doyle CM, Hutcheon JA, et al. Cardiovascular Disease-Related Morbidity and Mortality in Women With a History of Pregnancy Complications. *Circulation*. 2019;139(8):1069–79.
- 21- Niran Kamel WM, Wasan Munim, Alaa Raheem Kareem, Mustafa Rasool Hussein Aal-Saleh, Mohammed Luay Subhi, Sarah Abdulkareem Ali Al-Dujaili. Lipid Profile Changes in Pregnant Women with Pre-Eclampsia and Their Correlation with Severity of Pre-Eclampsia. *Al Mustansiriyah J Pharm Sci* 2020;20(3):105–13.
- 22- Minhas AS, Ying W, Ogunwole SM, Miller M, Zakaria S, Vaught AJ, et al. The Association of Adverse Pregnancy Outcomes and Cardiovascular Disease: Current Knowledge and Future Directions. *Curr Treat Options Cardiovasc Med* 2020;22(12):61.
- 23- Stuart JJ, Tanz LJ, Cook NR, Spiegelman D, Missmer SA, Rimm EB, et al. Hypertensive Disorders of Pregnancy and 10-Year

- Cardiovascular Risk Prediction. *J Am Coll Cardiol* 2018;72(11):1252–63.
- 24- Melchiorre K, Sutherland GR, Liberati M, Thilaganathan B. Preeclampsia Is Associated With Persistent Postpartum Cardiovascular Impairment. *Hypertension*. 2011;58(4):709–15.
- 25- Markovitz AR, Stuart JJ, Horn J, Williams PL, Rimm EB, Missmer SA, et al. Does pregnancy complication history improve cardiovascular disease risk prediction? Findings from the HUNT study in Norway. *Eur Heart J*. 2019;40(14):1113–20.
- 26- Athukorala C, Rumbold AR, Willson KJ, Crowther CA. The risk of adverse pregnancy outcomes in women who are overweight or obese. *BMC Pregnancy Childbirth* 2010;10(1):56.
- 27- Phaloprakarn C, Tangjitgamol S. Maternal ABO blood group and adverse pregnancy outcomes. *J Perinatol* 2013 332 2012;33(2):107–11.
- 28- Aghasadeghi F, Saadat M. Association between ABO and Rh blood groups and risk of preeclampsia: A case-control study from Iran. *Open Access Maced J Med Sci* 2017;5(2):173–6.
- 29- Moazzeni SS, Toreyhi H, Asgari S, Azizi F, Tehrani FR, Hadaegh F. Number of parity/live birth(s) and cardiovascular disease among Iranian women and men: results of over 15 years of follow-up. *BMC Pregnancy Childbirth*. 2021;21(1):28.
- 30- Ogunmoroti O, Osibogun O, Kolade OB, Ying W, Sharma G, Vaidya D, et al. Multiparity is associated with poorer cardiovascular health among women from the Multi-Ethnic Study of Atherosclerosis. *Am J Obstet Gynecol* 2019;221(6):631.e1-631.e16.
- 31- Dallak FH, Gosadi IM, Haidar WN, Durayb AA, Alomaish AR, Alshamakhi AH, et al. Prevalence of adverse birth outcomes and associated factors in Jazan, Saudi Arabia: A cross-sectional study. *Medicine (Baltimore)* 2022;101(41):e31119.
- 32- Alfadhli EM, Osman EN, Basri TH, Mansuri NS, Youssef MH, Assaaedi SA, et al. Gestational diabetes among Saudi women: prevalence, risk factors and pregnancy outcomes. *Ann Saudi Med*. 2015;35(3):222–30.
- 33- Groof Z, Garashi G, Husain H, Owayed S, AlBader S, Mouhsen H, et al. Prevalence, Risk Factors, and Fetomaternal Outcomes of Gestational Diabetes Mellitus in Kuwait: A Cross-Sectional Study. *J Diabetes Res*. 2019;2019:1–7.
- 34- Subki AH, Algethami MR, Baabdullah WM, Alnefaie MN, Alzanbagi MA, Alsolami RM, et al. Prevalence, Risk Factors, and Fetal and Maternal Outcomes of Hypertensive Disorders of Pregnancy: A Retrospective Study in Western Saudi Arabia. *Oman Med J*. 2018;33(5):409–15.
- 35- Selvarajah S, Kaur G, Haniff J, Cheong KC, Hiong TG, van der Graaf Y, et al. Comparison of the Framingham Risk Score, SCORE and WHO/ISH cardiovascular risk prediction models in an Asian population. *Int J Cardiol* 2014;176(1):211–8.
- 36- Bansal M, Kasliwal RR, Trehan N. Relationship between different cardiovascular risk scores and measures of subclinical atherosclerosis in an Indian population. *Indian Heart J* 2015;67(4):332–40.
- 37- Bansal M, Kasliwal RR, Trehan N. Comparative accuracy of different risk scores in assessing cardiovascular risk in Indians: A study in patients with first myocardial infarction. *Indian Heart J* 2014;66(6):580–6.
- 38- Garg N, Muduli SK, Kapoor A, Tewari S, Kumar S, Khanna R, et al. Comparison of different cardiovascular risk score calculators for cardiovascular risk prediction and guideline recommended statin uses.

- Indian Heart J. 2017;69(4):458–63.
- 39- Takahashi MM, de Oliveira EP, de Carvalho ALR, de Souza Dantas LA, Burini FHP, Portero-McLellan KC, et al. Metabolic syndrome and dietary components are associated with coronary artery disease risk score in free-living adults: a cross-sectional study. *Diabetol Metab Syndr* 2011; 3(1):7.
- 40- Groenhof TKJ, Zoet GA, Franx A, Gansevoort RT, Bots ML, Groen H, et al. Trajectory of Cardiovascular Risk Factors After Hypertensive Disorders of Pregnancy. *Hypertension*. 2019;73 (1):171–8.
- 41- Mito A, Arata N, Qiu D, Sakamoto N, Murashima A, Ichihara A, et al. Hypertensive disorders of pregnancy: a strong risk factor for subsequent hypertension 5 years after delivery. *Hypertens Res*. 2018;41(2):141–6.
- 42- Garre I, Nemani L, Nallagasu R. Association of Pregnancy-Related Factors and Cardiovascular Disease in the Long Term. *Indian J Cardiovasc Dis Women WINCARS*. 2018;03 (02/03):184–8.
- 43- Asgharvahedi F, Gholizadeh L, Siabani S. The risk of cardiovascular disease in women with a history of miscarriage and/or stillbirth. *Health Care Women Int* 2019;40(10):1117–31.