

Short Research Article

Cardiovascular Risk in Women with Adverse Pregnancy Outcomes

ABSTRACT

Aims: Identify cardiovascular risk factors and to estimate the risk of cardiovascular events in women presenting with APO.

Study design: Cross-sectional study

Place and Duration of Study: Two maternity wards in Lubumbashi (University Clinics of Lubumbashi and Jason Sendwe Provincial General Reference Hospital), between August 2023 and February 2024.

Methodology: We included 125 women with adverse pregnancy outcomes (APO). The participants were residents of Lubumbashi and provided informed consent for the study. Excluded were those with incomplete clinical or biological data due to refusal to participate or death, and those with known cardiovascular diseases. Clinical examination included detailed anamnesis, medical history, blood pressure monitoring, and anthropometric measurements. Blood samples were collected for lipid, glucose, and C-reactive protein (CRP) analysis. Calculation and classification of cardiovascular risk were done according to the summation score and the 30-year Framingham score. The test t was used to compare scores between different APOs, with a p-value < 0.05 considered significant.

Results: We selected 125 women aged 30 ± 6 years and found an hospital prevalence of APO equal to 17.8%. High hs-CRP (85.6%), dyslipidemia (49.2%), obesity/overweight (41.6%) and arterial hypertension (22.4%) were identified as cardiovascular risks. According to the summation method, overall cardiovascular risk was high (≥ 3 risk factors) in 21.5% of women. Applying the 30-year Framingham score the risk was moderate in 27.2%. This risk was even greater in the presence of hypertensive pregnancy disorder ($10,4 \pm 0,7$ vs $6,6 \pm 0,7$; $p=0,001$) or low birth weight ($18,0 \pm 7,1$ vs $9,0 \pm 0,5$; $p=0,004$).

Conclusion: The study highlighted the association of cardiovascular risk factors with adverse pregnancy outcomes and estimated that the risk of cardiovascular events was either high or moderate, depending on the method used.

Keywords: Adverse Pregnancy Outcome, Postpartum, Cardiovascular Health, Sub-Saharan Africa

1. INTRODUCTION

It has been shown that, from menarche to menopause, in addition to traditional cardiovascular risk factors, there are some others specific to women, such as adverse pregnancy outcomes (APO). These include hypertensive disorders of pregnancy, gestational diabetes, preterm birth, intrauterine growth retardation, macrosomia, placenta abruptio, low birth weight, miscarriage and stillbirth. Approximately 15 to 30% of pregnancies have an unfavorable outcome, particularly black people, or in the context of poverty and low level of education [1–5].

Although the link between cardiovascular disease (CVD) and APO is well established, in many medical facilities, cardiovascular risk factors are not systematically sought in pregnant women, contributing to persistent morbidity and mortality [6]. And yet, early recognition and follow-up can significantly modify cardiovascular risk even six months after an APO [7,8].

In DRC, adverse pregnancy outcome is not uncommon. Previous studies reported some prevalences: preeclampsia 4,8% [9] in utero foetal death 4% [10], macrosomia 5,7% [11], intrauterine growth retardation 10% [12], low birth weight 6,7% [13], preterm delivery 4,19% [14].

In this context, we undertook this study to identify the traditional risk factors associated with APO and to estimate global cardiovascular risk.

2. MATERIAL AND METHODS

2.1 Participants and Procedure

We conducted a cross-sectional study over an 11-month period (August 2023 to February 2024) in the maternity wards of the University Clinics of Lubumbashi and Sendwe Hospital. The study targeted women who had adverse pregnancy outcomes (APO). Simple random probability sampling was used. Inclusion criteria included women with APO residing in Lubumbashi who gave informed consent. Exclusion criteria were women for whom it was impossible to collect the necessary parameters, those refusing to participate, cases of death, and women with known cardiovascular diseases.

After delivery, participants were informed of the study objectives and signed an informed consent. Each received a unique identification code. A clinical examination including a detailed medical history and physical examination was performed. Venous blood samples were taken for analysis of lipids, lipoproteins, glucose, and highly sensitive CRP.

2.2 Measures

The study variables included sociodemographic aspects (age, education level of husband and wife), gynecological-obstetrical history (obstetrical identity, age at menarche, adverse outcomes of previous pregnancies), medical history and comorbidities (hypertension, smoking, diabetes, overweight/obesity, dyslipidemia), clinical aspects (cardiovascular vital parameters, anthropometry, gestational age, mode of delivery, length of hospitalization), adverse pregnancy outcomes (hypertensive disorders of pregnancy, gestational diabetes, placental abruption, preterm delivery, low birth weight, macrosomia), and biological parameters (lipid profile, renal function, C-reactive protein, hemoglobin). Cardiovascular risk was calculated using the risk factor summation method and the 30-year Framingham score.

2.3 Statistical Analyses

Data were double-encoded in Excel 2021 and analyzed using Jamovi software. Descriptive statistics included frequencies for qualitative variables, means and standard deviations for normally distributed quantitative variables, and medians and quartiles for those not following a normal distribution. Inferential analysis used the chi-square test for associations between qualitative variables and the independent samples t-test to compare means of quantitative variables. A p-value <0.05 was considered statistically significant.

3. RESULTS AND DISCUSSION

3.1 Prevalence of APO

A total of 150 APO was diagnosed out of 843 deliveries, i.e. 17.8%. However, only 125 women made up the sample whose data was subsequently analyzed, because some had died, and others had known heart disease or had not given their consent to take part in the study (see Fig.1).

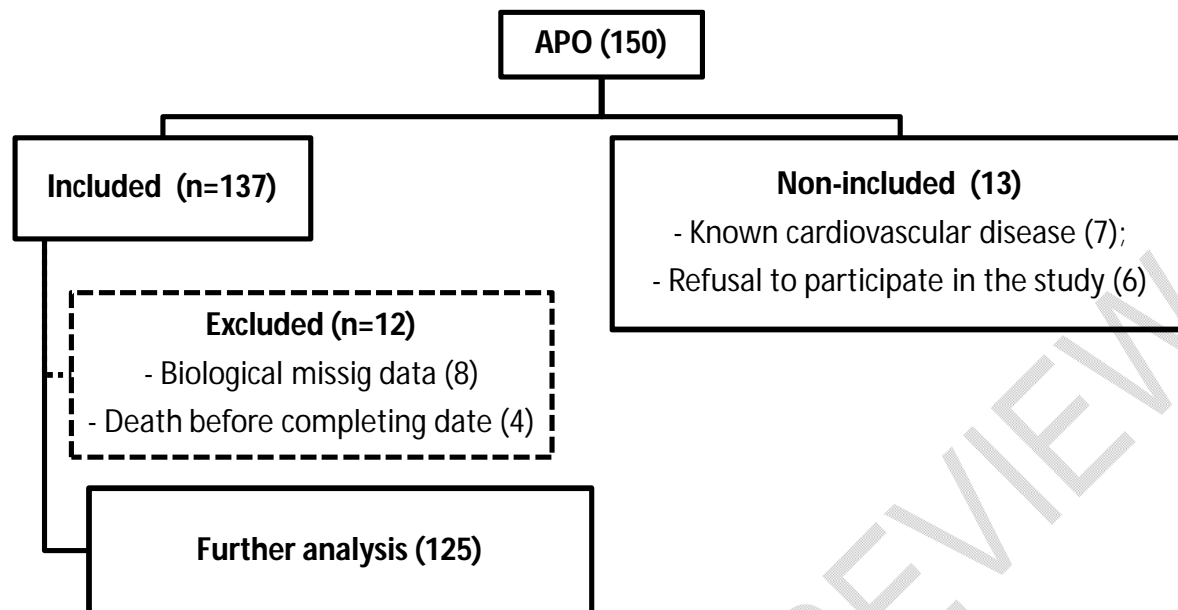


Fig. 1. Study Participant Selection Flowchart (This flowchart details the patient selection process for the cardiovascular risk assessment in women with a history of adverse pregnancy outcomes.)

3.2 General Characteristics of the Study Population

The average age of women was 30 ± 6 years, ranging from 18 to 45 years. Over half of them, 56.0 %, had completed secondary school and at least a quarter (27.2%) had already suffered from hypertensive disorders during previous pregnancy (Table 1).

Mean body mass index was 24.9 ± 4.6 kg/m². At least a quarter of them (28 %) were overweight, and 13% obese. Dyslipidaemia (especially hypercholesterolemia), and high hsCRP were present in respectively 49.6%, and 85.6% (Table 1).

Further analysis showed that high blood pressure was significantly associated with maternal APO ($p=0.033$) and obesity with abortion ($p=0.036$) (Table 1).

Hypertensive disorders of pregnancy were frequent with preeclampsia being the most common (52%). Gestational diabetes was quite rare (3,2%). On the foetal side, we found mostly foetal death in utero (33.6%) and prematurity (21,6%) (Table 1).

Table 1. Baseline characteristics (This table outlines the general demographics, obstetric background, and cardiovascular risk profile of women with a history of adverse pregnancy outcomes.)

Parameters	Count or Mean \pm SD	Percentage or Range
Age (year)	30 \pm 6	18 – 45
Secondary level of education	70	56,0
Previous APO		
Hypertensive disorders of pregnancy	34	27,2
Previous foetal APO	71	56,8

Foetal death in utero	28	22,4
BMI		
Overweight	35	28,0
Obesity	17	13,6
Lipogram		
Dyslipidaemia		
Total cholesterol (mg/dL)	62	49,6
HDL (mg/dL)	159,5 ± 43,7	[89 - 282]
LDL mg/dL	54,4 ± 16,1	[28 - 98]
Triglycerides (mg/dL)	80,9 ± 29,9	[30 - 195]
	114,0 ± 43,5	[29 - 256]
Inflammation		
Hs-CRP (mg/dL)	107	85,6
	2,9(8,7)	[0,2 - 20]
Actual APO		
Hypertensive disorders of pregnancy		
Preeclampsia	65	52,0
Eclampsia	29	23,2
Gestational hypertension	10	8,0
Superimposed preeclampsia	25	20,0
Placenta abruptio	8	6,4
Gestational diabetes	4	3,2
Foetal death in utero	42	33,6
Prematurity	27	21,6
Macrosomia	23	18,4
Abortion	12	9,6
Low birth weight	4	3,2

3.3 Cardiovascular Risk Factors and Cardiovascular Risk Assessment

High hsCRP was the most prevalent risk factor (85.6%) followed by dyslipidaemia (49,6%) and overweight/obesity (42%). Smoking and diabetes were fairly rare. Using the cardiovascular risk factor summation method, 16.8 % of women were at high risk, i.e. had at least 3 risk factors present. The mean Framingham score over 30 years was 9 ± 6 %, and 27.2% of women had a moderate risk (Table 2).

In further analysis, we found that the presence of hypertensive pregnancy disorder conferred an increased 30-year Framingham score (10.4 ± 0.7 vs 6.6 ± 0.7 ; $p=0.001$) as did having a low birth weight (18.0 ± 7.1 vs 9.0 ± 0.5 ; $p=0.004$) as shown in Table 3.

Table 2. Cardiovascular risk factors and cardiovascular risk assessment

Cardiovascular risk assessment	Count (n=125)	Percentage (%)
Cardiovascular risk factors		
Hypertension	28	22,4
Tobacco	1	0,8
Obesity	17	13,6
Overweight	35	28,0
Dyslipidaemia	62	49,6
High hs-CRP	107	85,6
Diabetes	0	0,0
Overall cardiovascular risk		
Summation score		

Low (0 or 1 CVRF)	53	42,4
Moderate (2 CVRF)	51	40,8
High (3 CVRF or more)	21	16,8
Framingham score 30 years		
Low (<12%)	91	72,8
Moderate (12 - 40%)	34	27,2
High (> 40%)	0	0,0

Table 3: Comparison of Score Averages Between Different APOs

APOs	Summation score		Framingham's 30-year score		
	N	Average \pm SD	p-value	Average \pm SD	p-value
Hypertensive Disorders of Pregnancy					
Yes	87	1.8 \pm 0.1	0.255	10.4 \pm 0.7	0.001
No	38	1.6 \pm 0.1		6.6 \pm 0.7	
Gestational diabetes					
Yes	4	2.3 \pm 0.7	0.239	8.0 \pm 1.1	0.692
No	121	1.7 \pm 0.1		9.0 \pm 0.5	
Placental abruption					
Yes	8	1.8 \pm 0.3	0.924	8.1 \pm 1.3	0.609
No	117	1.7 \pm 0.1		9.3 \pm 0.6	
Preterm delivery					
Yes	27	1.8 \pm 0.2	0.712	7.9 \pm 1.1	0.212
No	98	1.7 \pm 0.1		9.6 \pm 0.7	
Abortion					
Yes	12	1.9 \pm 0.4	0.434	8.2 \pm 1.8	0.539
No	113	1.7 \pm 0.1		9.4 \pm 0.6	
In utero foetal death					
Yes	42	1.9 \pm 0.1	0.161	9.4 \pm 1.0	0.860
No	83	1.7 \pm 0.1		9.2 \pm 0.7	
Low birth weight					
Yes	4	2.5 \pm 0.7	0.082	18.0 \pm 7.1	0.004
No	121	1.7 \pm 0.1		9.0 \pm 0.5	
Macrosomia					
Yes	23	1.8 \pm 0.2	0.539	9.5 \pm 1.1	0.843
No	102	1.7 \pm 0.1		9.2 \pm 0.7	

4. DISCUSSION

To our knowledge, this is the first study to date carried out in Lubumbashi (DRC) to highlight the link between APO and cardiovascular risk. The aim of this study was to identify cardiovascular risk factors and estimate the future risk of a cardiovascular event in women presenting APO. Indeed, cardiovascular risk factors such as hypertension, obesity/overweight, dyslipidaemia and inflammation were associated with APO. Moreover, moderate-to-high risk of future cardiovascular event was found in at least 16%.

APO are largely reported worldwide with a prevalence even higher than ours: 30% in the Swedish study [15], 39% in southern Ethiopia hospitals [16] et 35,6% in USA [17]. We may believe that our medical data management system is not as efficient as that of more developed countries, and that the prevalence of

APO in our study is underestimated. This is all the truer as it is in the black race and when living conditions are unfavourable that APO are more likely to occur.

Hypertension was present as a risk factor in 22.4% of cases, and it's certainly no coincidence that hypertensive disorders of pregnancy were also the most important APO reported. Murray Horwitz [17] reported a prevalence of 18.4% that is close to our result. However, a lower prevalence (1.3%) can be found elsewhere, such as in the UK (1,3%) [18]. Our high prevalence of arterial hypertension as a risk factor associated with APO may be related to the black race of our patients and probably to the overweight/obesity noted in most of them.

In fact, obesity and overweight accounted for more than 40% in this study. This is much higher than the 23.6% found by AAM Djelantik in the Netherlands in 2013 [19] and less than 64% in South Africa, 65% in Mexico and 55 to 63% in the USA [20].

This phenomenon, observed almost everywhere in the world, is the result of urbanisation, combined with a sedentary lifestyle and the consumption of high-energy supermarket foods. And in our environment, women in general and pregnant women in particular are not very keen on sport. Nor are there any precise recommendations during prenatal consultations on what exactly women should do to avoid putting on too much weight.

Almost half of our patients had dyslipidaemia, whether related to total cholesterol, HDL, LDL or triglycerides. There is growing evidence of a link between dyslipidaemia and adverse pregnancy outcomes [21–23]. It has also been shown that lipids increase with gestational age and should therefore be monitored, particularly because of the risk of macrosomia [24].

CRP was elevated in the majority of cases (85.6%). In our study, we looked for it as a cardiovascular risk factor. High levels of hsCRP are associated with an increased risk of cardiovascular events such as myocardial infarction and strokes[25]. Inflammation plays a crucial role in the development and progression of atherosclerosis, a key process in CVD. The measurement of hsCRP thus allows for the evaluation of cardiovascular risk in addition to traditional risk factors[25].

It is also considered a useful parameter for assessing the severity of the clinical risk of pre-eclampsia in patients with a BMI of less than 25 kg/m² in the 3rd trimester [26].

It has also been suggested that an elevated CRP postpartum could serve as a guide for interventional studies aimed at reducing cardiovascular morbidity in women with metabolic syndrome, particularly after pre-eclampsia or gestational hypertension [27].

As regards cardiovascular risk, we found an average risk of 9.24% using the Framingham score over 30 years. A median of 2.2% was found by calculating for the same Framingham score the risk of more than 4273 women who had previously (2-7 years) suffered from gestational diabetes, and 1.8% of these women had a high risk. Gestational diabetes, hypertensive disorders during pregnancy and premature delivery were associated with a higher risk [28].

5. CONCLUSION

The study demonstrated the existence of cardiovascular risk factors in women with adverse pregnancy outcomes in Lubumbashi. The risk to which these factors expose these women is real. These results underline the importance of early and systematic management of cardiovascular risk factors in women with adverse pregnancy outcomes, in order to prevent the onset of cardiovascular disease in the long term. A multidisciplinary approach and studies, involving obstetricians, cardiologists and nephrologists, seem essential to improve the long-term follow-up of this category of women.

Further work is needed to develop reliable analytical methods for assessing cardiovascular risk.

CONSENT (WHERE EVER APPLICABLE)

All authors declare that 'written informed consent was obtained from the patient (or other approved parties) for publication of this study. A copy of the written consent is available for review by the Editorial office/Chief Editor/Editorial Board members of this journal.'

ETHICAL APPROVAL (WHERE EVER APPLICABLE)

All authors hereby declare that all experiments have been examined and approved by the appropriate ethics committee and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki. Throughout our study, we complied strictly with ethical rules. Before collecting the data, we had obtained authorization from the UNILU ethics committee under number 001/2024, and the data collection form in support of this, we took into account free and voluntary participation in the study, and a form was drawn up beforehand to obtain the informed consent of the participants.

DISCLAIMER (ARTIFICIAL INTELLIGENCE)

The authors state that no artificial intelligence technology, such as major language models or image text generators, was used in the writing or revision of this manuscript.

REFERENCES

1. Bilano VL, Ota E, Ganchimeg T, Mori R, Souza JP. Risk factors of pre-eclampsia/eclampsia and its adverse outcomes in low-and middle-income countries: a WHO secondary analysis. *PloS One* 2014;9:e91198.
2. Breathett K, Muhlestein D, Foraker R, Gulati M. Differences in Preeclampsia Rates Between African American and Caucasian Women: Trends from the National Hospital Discharge Survey. *J Womens Health* 2014;23:886–93. <https://doi.org/10.1089/jwh.2014.4749>.
3. Caleyachetty R, Echouffo-Tcheugui JB, Muennig P, Zhu W, Muntner P, Shimbo D. Association between cumulative social risk and ideal cardiovascular health in US adults: NHANES 1999–2006. *Int J Cardiol* 2015;191:296–300.
4. Lane-Cordova AD, Khan SS, Grobman WA, Greenland P, Shah SJ. Long-term cardiovascular risks associated with adverse pregnancy outcomes: JACC review topic of the week. *J Am Coll Cardiol* 2019;73:2106–16.
5. O'Kelly AC, Michos ED, Shufelt CL, Vermunt JV, Minissian MB, Quesada O, et al. Pregnancy and Reproductive Risk Factors for Cardiovascular Disease in Women. *CircRes* 2022;130:652–72. <https://doi.org/10.1161/CIRCRESAHA.121.319895>.
6. Gogineni VSM, Manfrini D, Aroda SH, Zhang Y, Nelson DS, Egerman R, et al. Variations in Awareness of Association Between Adverse Pregnancy Outcomes and Cardiovascular Risk by Specialty. *CardiolTher* 2021;10:577–92. <https://doi.org/10.1007/s40119-021-00220-y>.
7. Gladstone RA, Pudwell J, Pal RS, Smith GN. Referral to cardiology following postpartum cardiovascular risk screening at the maternal health clinic in Kingston, Ontario. *Can J Cardiol* 2019;35:761–9.
8. Ivey SL, Hanley HR, Taylor C, Stock E, Vora N, Woo J, et al. Early identification and treatment of women's cardiovascular risk factors prevents cardiovascular disease, saves lives, and protects future generations: Policy recommendations and take action plan utilizing policy levers. *Clin Cardiol* 2022;45:1100–6. <https://doi.org/10.1002/clc.23921>.
9. Yves II, Mjumbe CK, Michel KN, Didier ML, Christian KN, Patrick KM, et al. Hypertensive Pathologies in Peripartum: Complications and Maternal and Neonatal Outcome. *Open J ObstetGynecol* 2020;10:311.
10. Mpoy CW, Katembo BM, Misumba WK, Kinenkinda XK. Étude de la mort fœtale in utero à Lubumbashi, République Démocratique du Congo. *Rev Infirm Congo* 2022;6:21–7.
11. Luhete PK, Mukuku O, Kiopin PM, Tambwe AM, Kayamba PK. Fetal macrosomia in Lubumbashi: risk factors and maternal and perinatal prognosis. *Pan Afr Med J* 2016;23:166–166.

12. Moyambe JNT, Bernard P, Khang'Mate F, Nkoy AMTA, Mukalenge FC, Makanda D, et al. Etude des facteurs de risque du retard de croissance intra-utérin à Lubumbashi. *Pan Afr Med J* 2013;14.
13. Luhete PK, Mukuku O, Kayamba PKM. Etude du faible poids de naissance associé à l'âge maternel et la parité dans une population couple mère-enfant suivi à Lubumbashi. *Pan Afr Med J* 2015;20.
14. Christian KN, Kitoko HT, Balthazar MB, Roger TM, Patrick MK, Yves II, et al. Accouchement prématuré aux cliniques universitaires de Lubumbashi de 2011-2019: fréquence et prise en charge. *J Med Res Health Sci* 2023;6:2457–70.
15. Crump C, Sundquist J, McLaughlin MA, Dolan SM, Govindarajulu U, Sieh W, et al. Adverse pregnancy outcomes and long term risk of ischemic heart disease in mothers: national cohort and co-sibling study. *Bmj* 2023;380.
16. Yimer NB, Gedefaw A, Tenaw Z, Liben ML, Meikena HK, Amano A, et al. Adverse obstetric outcomes in public hospitals of southern Ethiopia: the role of parity. *J Matern-Fetal Neonatal Med Off J Eur Assoc Perinat Med Fed Asia Ocean Perinat Soc Int Soc Perinat Obstet* 2022;35:1915–22. <https://doi.org/10.1080/14767058.2020.1774542>.
17. Murray Horwitz ME, Fisher MA, Prifti CA, Rich-Edwards JW, Yarrington CD, White KO, et al. Primary Care-Based Cardiovascular Disease Risk Management After Adverse Pregnancy Outcomes: a Narrative Review. *J Gen Intern Med* 2022;37:912–21. <https://doi.org/10.1007/s11606-021-07149-x>.
18. Panaitescu AM, Syngelaki A, Prodan N, Akolekar R, Nicolaides KH. Chronic hypertension and adverse pregnancy outcome: a cohort study. *Ultrasound ObstetGynecol Off J Int Soc Ultrasound ObstetGynecol* 2017;50:228–35. <https://doi.org/10.1002/uog.17493>.
19. Djelantik AA, Kunst AE, van der Wal MF, Smit HA, Vrijkotte TG. Contribution of Overweight and Obesity to the Occurrence of Adverse Pregnancy Outcomes in a Multiethnic Cohort: Population Attributive Fractions for Amsterdam. *ObstetAnesth Dig* 2013;33:43–5.
20. Langlely-Evans SC, Pearce J, Ellis S. Overweight, obesity and excessive weight gain in pregnancy as risk factors for adverse pregnancy outcomes: A narrative review. *J Hum Nutr Diet* 2022;35:250–64. <https://doi.org/10.1111/jhn.12999>.
21. Gademan MGJ, Vermeulen M, Oostvogels AJJM, Roseboom TJ, Visscher TLS, van Eijsden M, et al. Maternal prepregnancy BMI and lipid profile during early pregnancy are independently associated with offspring's body composition at age 5-6 years: the ABCD study. *PLoS One* 2014;9:e94594. <https://doi.org/10.1371/journal.pone.0094594>.
22. Jin W-Y, Lin S-L, Hou R-L, Chen X-Y, Han T, Jin Y, et al. Associations between maternal lipid profile and pregnancy complications and perinatal outcomes: a population-based study from China. *BMC Pregnancy Childbirth* 2016;16:60. <https://doi.org/10.1186/s12884-016-0852-9>.
23. Wang J, Moore D, Subramanian A, Cheng KK, Toulis KA, Qiu X, et al. Gestational dyslipidaemia and adverse birthweight outcomes: a systematic review and meta-analysis. *Obes Rev* 2018;19:1256–68. <https://doi.org/10.1111/obr.12693>.
24. Zheng W, Zhang L, Tian Z, Zhang L, Liang X, Li G. Establishing reference ranges of serum lipid level during pregnancy and evaluating its association with perinatal outcomes: A cohort study. *Int J GynaecolObstet Off Organ Int Fed GynaecolObstet* 2022;156:361–9. <https://doi.org/10.1002/ijgo.13636>.
25. Ridker PM. From C-Reactive Protein to Interleukin-6 to Interleukin-1. *Circ Res* 2016. <https://doi.org/10.1161/CIRCRESAHA.115.306656>.
26. Ertas IE, Kahyaoglu S, Yilmaz B, Ozel M, Sut N, Guven MA, et al. Association of maternal serum high sensitive C-reactive protein level with body mass index and severity of pre-eclampsia at third trimester. *J ObstetGynaecol Res* 2010;36:970–7. <https://doi.org/10.1111/j.1447-0756.2010.01279.x>.
27. Osofi AO, Page ST, Richardson BA, Guthrie BL, Kinuthia J, Polyak SJ, et al. Postpartum metabolic syndrome and high-sensitivity C-reactive protein after gestational hypertension and pre-eclampsia. *Int J GynaecolObstet Off Organ Int Fed GynaecolObstet* 2020;151:443–9. <https://doi.org/10.1002/ijgo.13352>.
28. Venkatesh KK, Khan SS, Yee LM, Wu J, McNeil R, Greenland P, et al. Adverse Pregnancy Outcomes and Predicted 30-Year Risk of Maternal Cardiovascular Disease 2-7 Years After Delivery. *ObstetGynecol* 2024. <https://doi.org/10.1097/AOG.0000000000005569>.

ABBREVIATIONS

APO: Adverse Pregnancy Outcome

BMI: body mass index
CVD: Cardiovascular Disease
CVRF: Cardiovascular Risk Factor
DRC: Democratic Republic of Congo
HDL: High-Density Lipoprotein
hs-CRP: High-sensitivity C-Reactive Protein
LDL: Low-Density Lipoprotein
mg/dL: Milligrams per deciliter
SD: Standard Deviation

UNDER PEER REVIEW