MICRO LABS LIMITED

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# GYNAE SPECTRUM

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Gynae Spectrum
Volume 5|Issue 35|2024

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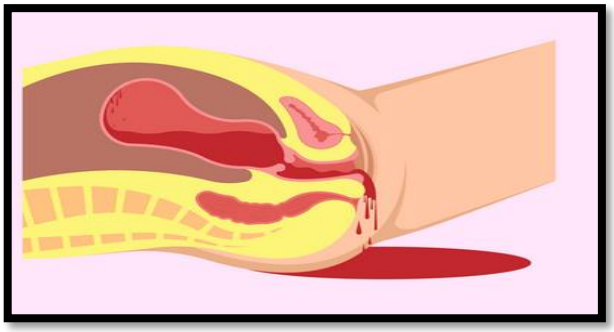
# Investigation of prenatal fibrinogen in evaluating the risk of postpartum hemorrhage

## Introduction



Postpartum hemorrhage is defined as blood loss of approximately 500 ml following child birth, accounting for 27% of maternal deaths worldwide. The World Health Organization (WHO) has released and updated several evidence-informed guidelines for the prevention and treatment of postpartum hemorrhage.[1] Postpartum hemorrhage (PPH) is a major complication of child birth, leading to significant maternal mortality and morbidity. Effective detection and treatment of PPH are often limited in primary healthcare setting due to inadequate screening and treatment equipment. Prenatal fibrinogen (FIB) levels have been implicated in PPH outcomes, but their precise relationship with PPH remains unclear.[2] This study aimed to investigate the association between prenatal FIB levels and PPH severity, providing potential diagnostic markers for clinical practice.

## Methods

This was a retrospective cohort study conducted on patients diagnosed with varying severity of PPH. Key indicators assessed included maternal age, gestational age, bleeding volume, and laboratory tests. Prenatal FIB levels measured within 3 days before delivery using ACL-TOP700 automatic hemagglutination analyser. Patients were categorized based on FIB levels into two groups, low FIB (<4g/L) and normal (≥4 g/L) and PPH severity patients were divided into 4 groups, no PPH (less than 500mL), PPH (500–1000mL), severe PPH (over 1000mL) and refractory PPH. Statistical analyses was conducted to evaluate results.

## Results

Of the 128 samples analysed, 38 (30%) patients were non-severe PPH (500–1000mL), 66 (51%) developed severe PPH, and 7 (5%) had refractory PPH, while 24 patients had no PPH. Further in terms of delivery modes, 70 patients underwent cesarean section, 57 cases of vaginal delivery, and seven cases of critical bleeding underwent interventional surgery. Prenatal FIB levels averaged 3.15g/L in the low FIB group and 4.94g/L in the normal FIB group. The average blood loss in the lower FIB group (<4g/L) was 1,316.36 mL, while the higher FIB group (≥4g/L) had 932.26 mL, with a p-value of 0.020. The mean FIB values in non-PPH, PPH, severe PPH, and refractory PPH were 4.5088, 4.3761, 3.9959, and 3.3771, respectively. Prenatal FIB levels were inversely correlated with blood loss severity. Correlation between prenatal FIB and the amount of PPH was presented in figure 1 where (A) indicated the amount of blood loss had decline trend as there was an increase in prenatal FIB and (B) indicated mean

value of blood loss at each phases of prenatal FIB. ROC curve analysis demonstrated that prenatal FIB levels could predict severe PPH with an AUC of 0.613 (P= 0.027).

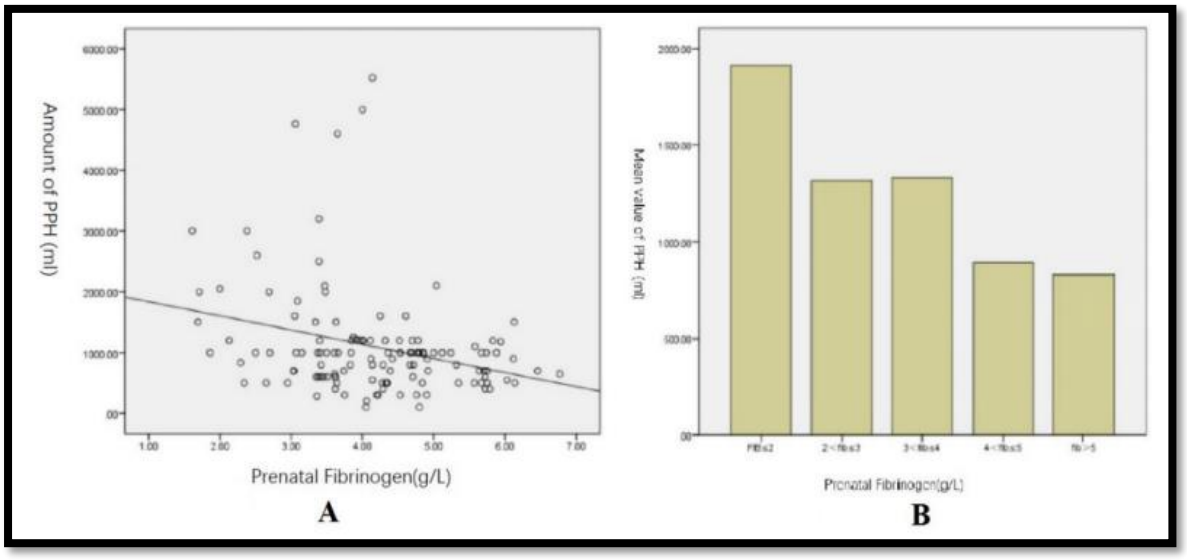



**Figure 1. (A) Scatter diagram showing prenatal fibrinogen concentration and volume of blood loss. (B) Prenatal fibrinogen subsection and the mean value of blood loss**

## Discussion

This study highlighted the significant role of prenatal FIB in predicting PPH severity. Lower prenatal FIB levels were associated with increased bleeding volumes, indicating that FIB could serve as a crucial biomarker for assessing PPH risk. This study results align with the previous research that highlighted the importance of fibrinogen in coagulation and PPH management.[2] For instance, Cortet et al. found that decreased plasma FIB levels were linked to severe postpartum bleeding, which supported the present study results showing that patients with lower FIB levels experienced higher volumes of blood loss.[3] Notably, gestational diabetes mellitus was identified as a protective factor against PPH, potentially due to hyperglycemia induced thrombotic changes.

## Conclusion

Prenatal FIB levels were significantly associated with PPH severity. Low FIB levels predict a higher risk of severe bleeding, emphasizing the need for early detection and management. Prenatal FIB assessment should be integrated into clinical practice to improve PPH outcomes.

**Prenatal fibrinogen was significantly related to thrombin time, which may be an independent factor to predict the coagulation state of prenatal pregnancy.**

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# Evaluation of Relationship Between Endometriosis and Pelvic Inflammatory Diseases

## Introduction

**Mendelian randomization supports a potential causal relationship between endometriosis and an increased risk of pelvic inflammatory diseases.**

Pelvic inflammatory disease (PID) is an infection affecting the endometrium, fallopian tubes, ovaries, and pelvic peritoneum, often presenting with pelvic pain, abnormal vaginal discharge, fever, chills, and painful urination.[1] The cause of PID varies, with Chlamydia trachomatis (CT), Neisseria gonorrhoeae (GC), Trichomonas vaginalis (TV), Mycoplasma genitalium (MG), and other bacterial vaginosis–associated bacteria (BVAB) isolated from the lower genital tract of women diagnosed with acute PID.[2] In 2013-2014, there were 110,000 cases of PID among women aged 18-44, posing a significant healthcare concern with high treatment costs. Endometriosis, a condition where tissue similar to the uterine lining grows outside the uterus, was associated with symptoms that overlap with PID and has been linked to various diseases. Previous studies have indicated a potential connection between endometriosis and PID, but traditional observational studies were limited by reverse causality and residual confounding.[1] This study aimed to explore two-sample Mendelian randomization (MR) approach to evaluate the causal relationship between endometriosis and pelvic inflammatory diseases (PID).

## Methods

This study employed a two-sample MR approach using data from the Integrative Epidemiology Unit Open Genome-Wide Association Studies (GWAS) database. Genetic variants associated with endometriosis and PID were selected based on a minimum minor allele frequency greater than 0.01 in the European population. The study adhered to three core MR assumptions: the genetic variants should be related to the exposure, independent of confounding factors, and should affect the outcome only through the exposure. The inverse variance weighting (IVW) method was used to estimate the causal impact of endometriosis on PID, supplemented by MR-Egger regression and weighted median (WM) methods to address pleiotropy and assess the robustness of the findings.

## Results

From the initial 35 single nucleotide polymorphisms (SNPs) associated with endometriosis, 33 were selected after quality control measures. The MR analysis, using summary data from 2913 PID cases and 111,858 female controls, indicated a causal relationship between endometriosis and PID. The odds ratios (OR) from different methods were: IVW (OR = 1.39, $P < 1\times10^{-8}$), MR-Egger (OR = 1.41, P = 0.003), WM (OR = 1.37, $P = 1.16\times10^{-5}$), and weighted mode (OR

= 1.64, P = 0.0003). Furthermore, IVW, MR-Egger, WM, and Weighted mode all showed a limited presence of confounding factors within the data, and the intercept shows the average pleiotropic effect of genetic variation (Figure 1). Sensitivity analyses confirmed low heterogeneity and minimal pleiotropic effects, supporting the reliability of the findings.

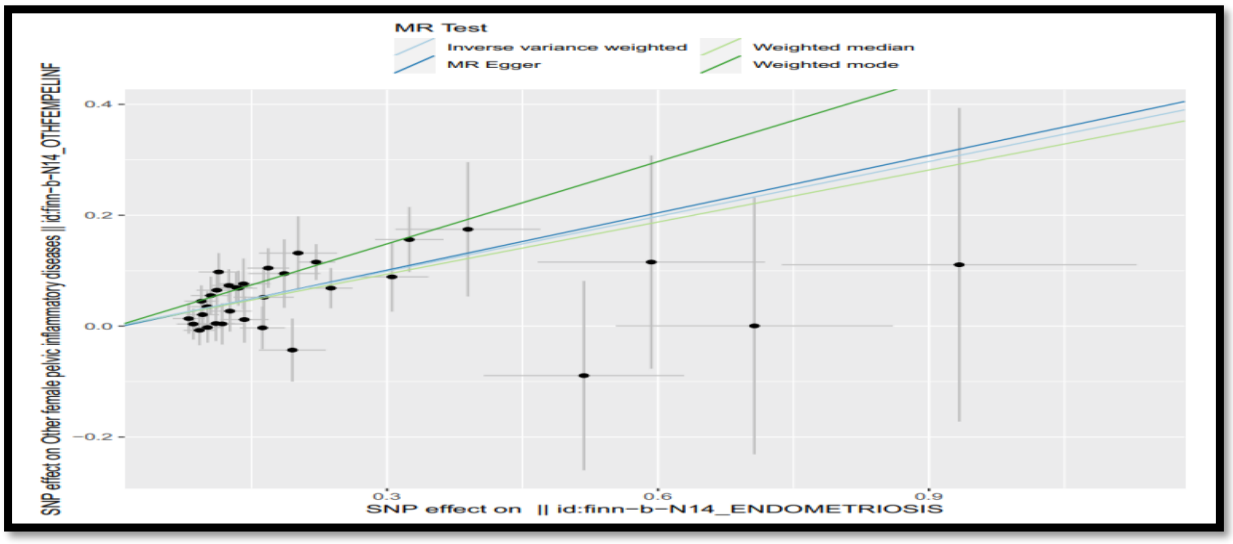


**Figure 1. Genetic association between endometriosis and pelvic inflammatory disease**

## Discussion

This study confirmed a causal relationship between endometriosis and increased risk of PID using MR analysis. The results were consistent with previous observational studies suggesting multiple pathways through which endometriosis may contribute to PID, including structural changes in pelvic organs,[3] alterations in the local microbial environment,[4] immune system dysregulation, and changes in inflammatory mediators. The robustness of MR, which minimizes confounding and reverse causality, reinforces the validity of these results. However, the study's limitation to European populations suggested the need for broader, multi-ethnic studies to generalize the findings.

## Conclusion

This study demonstrated that endometriosis was a significant risk factor for PID, highlighting a potential causal relationship. These insights enhance the understanding of the underlying mechanisms connecting endometriosis and PID and pave the way for improved clinical diagnosis and prevention strategies.

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# Effectiveness of a 12- month early postnatal lifestyle intervention program in women with gestational diabetes mellitus

## Introduction

**Early postnatal lifestyle intervention program reduces the long-term risk of diabetes in this high-risk population.**

Gestational diabetes mellitus (GDM) is a condition of hyperglycemia (fasting plasma glucose ≥ 5.1 mmol/L, 1 h ≥ 10 mmol/L, 2 h ≥ 8.5 mmol/L during a 75 g oral glucose tolerance test according to IADPSG/WHO criteria) that is diagnosed first during pregnancy.[1] Women with gestational diabetes mellitus (GDM) have a 7- to 10-fold higher risk of developing diabetes mellitus (DM) later in life. High prevalence of GDM, diabetes progression in women with GDM and obesity among women at the reproductive age, promoting weight loss is an important strategy to prevent obesity after pregnancy11 and reduce the risk for diabetes progression among women with GDM. Effective interventions are essential to mitigate this risk. Evidence shows that lifestyle interventions can reduce diabetes incidence by up to 58% and sustain the effect for up to 20 years.[2] This study aimed to evaluate the feasibility and effectiveness of a 12-month lifestyle intervention program for women with GDM.

## Methods

This prospective randomized intervention study which included 103 women aged 18-50 who had GDM during their most recent pregnancy. Participants were randomized in a 1:1 ratio to standard care group or a lifestyle intervention group. The intervention included dietary and physical activity counselling, with an initial two-month core intervention period followed by ten months of maintenance. The primary outcome was the proportion of women achieving their body weight goals. Secondary outcomes included changes in body composition, glycemic status, dietary habits, and physical activity, presence of dyslipidemia and percentage achieving lifestyle goal.

## Results

Out of 103 women who started the study, 79 completed it. In the intervention group, 57.5% achieved their weight targets compared to 46.2% in the standard care group, though the

difference was not statistically significant (Figure 1). Women in the intervention group showed greater reductions in body weight, energy intake, and improvements in dietary habits. Mean (SD) body weight decreased in the lifestyle intervention group by 0.93 (4.68) kg and in the standard care group by 0.1 (3.12) kg (P= 0.326). In addition, women in the lifestyle intervention group significantly reduced energy intake by 497.6 kcal/day compared to the standard care group, in which it was reduced by 222.0 kcal/day (P= 0.007). Additionally, the lifestyle intervention group's mean (SD) daily consumption of fruits and vegetables increased by 23.9 (158.9) g, while the standard care group's intake decreased by 17.9 (139.2) g (P=0.84). However, there were no significant differences in biochemical parameters between the groups. Stratified analysis indicated that overweight/obese women in the intervention group had more significant reductions in body composition, while lean women had better cardiometabolic profiles.

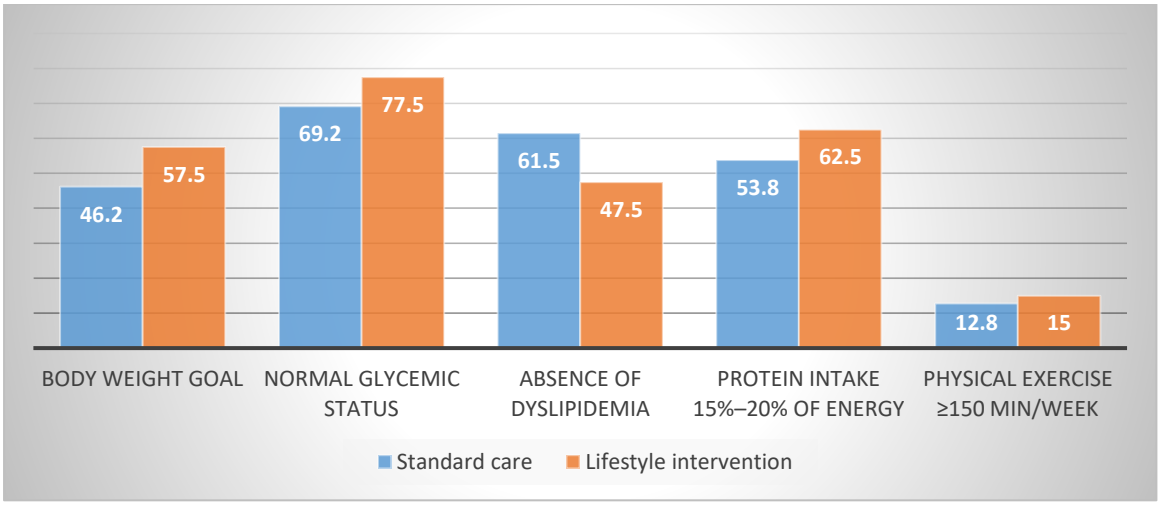


**Figure 1. Results of primary and secondary outcomes**

## Discussion

The study demonstrated the feasibility and acceptability of an early postpartum lifestyle intervention for women with GDM. The present study indicated that an early lifestyle intervention may help women with GDM lose weight after giving birth and so avoid the weight retention that was linked to a decreased chance of developing diabetes.[2] A study has reported that there was an increase in number of normal weight individual becoming diabetes in Asian, which may relate to a lower beta cell capacity compared with Caucasians.[3] Despite the COVID-19 pandemic's impact on recruitment and study conditions, the intervention group achieved comparable results to more intensive programs. Differences in baseline BMI influenced the intervention's effectiveness, suggesting tailored approaches may be necessary.

## Conclusion

An early postpartum lifestyle intervention promoted weight loss and healthier lifestyles in women with GDM, particularly in overweight and obese individuals. This approach may reduce the risk of developing diabetes, highlighting the importance of early intervention and continuous support to sustain long-term health benefits.

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# Case report on spontaneous uterine rupture complicated by bilateral pulmonary emboli

## Introduction

Spontaneous uterine rupture in an unscarred uterus is a rare event which can lead to maternal and fetal morbidity and mortality. The prevalence of rupture of unscarred uteri was 0.0175% to 0.005% of pregnancies.[1] The most prevalent risk factors for uterine rupture, according to the literature, were scarring of the uterus following a prior caesarean section (CS) and prostaglandin-induced labour induction.[2] The incidence of massive thrombo-emboli during pregnancy and labour is about 1 in 100-3000 pregnancies. In conditions of uterine rupture, patients suffer from hemorrhage and require large blood transfusions. This report described a case of patient with uterine rupture following failed induction of labour at term complicated by massive bilateral pulmonary embolism (PE).

## Case presentation

A 32 years old female, G1P0, underwent induction of labor at 40w4d for gestational hypertension. Patient was GBS positive in which gynaecological history showed a HPV16 positive Pap smear with no intraepithelial lesion. While patient was in labor, developed a fever to 38.3°C and fetal tachycardia of 180 bpm for over 10 h with minimal variability, concerning for chorioamnionitis. Cesarean delivery (CD) was recommended for arrest of dilation and category 2 tracing remote from delivery. Fetal bradycardia of 50 bpm was seen prior to administration of spinal anaesthesia promoting an emergency CD. Hemoperitoneum was noted in the peritoneal cavity. Later a live male baby weighing 3720 g was delivered via a low-transverse uterine incision. Apgar scores was 2 at 1 min and 8 at 5 min. The uterus was exteriorized for repair where there was an 8 cm vertical defect approximately 4 cm left of the midline, consistent with uterine rupture of an unknown duration. The ruptured site was repaired using locked suture of 0 Monocryl. Following surgery, the patient had a tachycardia of 132 bpm and was hypoxic, requiring 4-6 L of extra oxygen through a nasal cannula due to a spO2 of 80–90%. After a complicated delivery, based on the abnormal vital signs, the differential diagnoses included intra-abdominal hemorrhage, pulmonary edema, PE, peripartum cardiomyopathy, sepsis, or transfusion reaction. Computerized tomography of arteriogram showed extensive bilateral PE with flattening intraventricular septum consistent with right cardiac dysfunction. On echocardiogram, right ventricle was almost akinetic. Patient

**This case evaluated a potential connection between uterine ruptures, hemorrhage, and multiple, large pulmonary emboli.**

was started with intravenous heparin therapy and underwent emergency thrombolysis and inferior vena cava (IVC) filter placement. Transthoracic echocardiogram showed severely dilated right ventricle and hypokinesis. An emergency pulmonary embolectomy was performed and implantation of an extracorporeal right ventricular assist device (RVAD) and rigid sternal fixation was done. Acute thrombi damaged the whole left branch pulmonary artery and the intermediate branch leading to the middle and lower lobes after the primary pulmonary artery was severe and removed (Figure 1). Additionally, smaller thrombi in the upper and lobe segmental arteries were also removed. Cardiopulmonary bypass was weaned, and as the patient had very little cardiac ejection RVAD was initiated. An IVC filter was placed. After the therapy with the medications, patient was clinically stable and provided counselling on the increased risk of recurrent spontaneous uterine rupture, and an etonogestrel implant was placed for contraception.

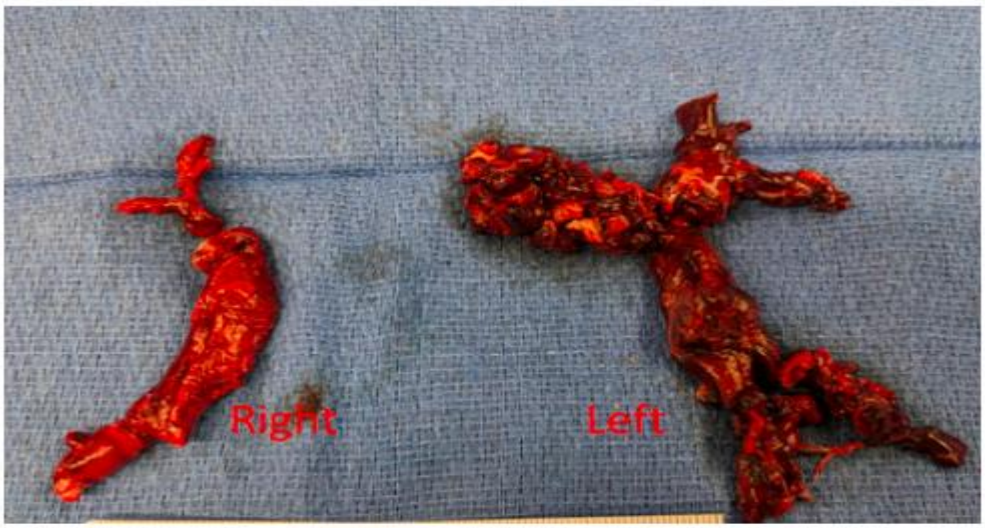


**Figure 1. Pulmonary emboli that was removed from the intermediate branch to the middle and lower lobes.**

## Discussion

This case report showed that combination of uterine rupture and thromboembolic events was a rare occurrence, particularly for patients with no history of uterine surgery. The etiology for uterine rupture in this case might be due to prolonged administration of oxytocin causing acquired weakness. It may also be due to connective tissue disorder linked to the VUS (variant of uncertain significance) due to the patient experiencing two organ defects.[1] Previous study has reported top three surgical interventions associated with uterine wall disruption were cesarean section (67.92%), dilation and curettage (28.30%), and myomectomy (9.43%).[3] As there were limited similar cases on spontaneous uterine rupture complicated by massive PE, it reflected the need to further understand the complication and potential etiologies and biological causes for this rare but life-threatening phenomenon.[1]

## Conclusion

This case reports highlighted the importance of potential connection between uterine ruptures, hemorrhage, and multiple, large pulmonary emboli. Further research should be carried to identify risk factors and biologic causes for these rare but life-threatening complications.

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