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ORIGINAL RESEARCH

Coagulation Disorders and Their Impact on Pregnancy Outcomes: A Histological Examination of Placental Pathology

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ABSTRACT

Aim: The aim of this study is to investigate the relationship between coagulation disorders and adverse pregnancy outcomes through a histological examination of placental pathology. **Material and Methods:** The study population consisted of 80 pregnant women with diagnosed coagulation disorders such as thrombophilia, antiphospholipid syndrome (APS), disseminated intravascular coagulation (DIC), and other related conditions. Participants were closely monitored throughout the pregnancy, and data collection was carried out in three main phases. The first phase involved clinical assessments**,** where regular evaluations were conducted to monitor maternal and fetal well-being. Maternal parameters such as blood pressure, hemoglobin levels, and platelet counts were measured routinely. Any antenatal complications, including preeclampsia, intrauterine growth restriction (IUGR), and preterm delivery, were recorded during these assessments. The second phase focused on the coagulation profile, where specific coagulation parameters were monitored throughout pregnancy. **Results:** The fibrinogen levels were markedly lower in the DIC group (2.2 g/L), further emphasizing the severity of the disorder (p=0.001). D-dimer levels were also significantly higher in the DIC group (1.8 mg/L), indicating increased fibrinolytic activity (p=0.005). Women with abnormal placental pathology had significantly worse outcomes. Preterm birth was notably more common in women with abnormal placentas (40%) compared to those with normal placentas (12%), with a significant p-value of 0.01. Preeclampsia was also significantly higher in the abnormal placental group (27.27%) compared to the normal group (12%) (p=0.03). IUGR occurred in 20% of women with abnormal placentas, compared to just 8% in women with normal placentas (p=0.02). NICU admissions were significantly higher in the abnormal placental group (34.54%) compared to the normal group (16%) (p=0.01). These findings highlight the strong association between placental pathology and adverse pregnancy outcomes.Vascular occlusions had the highest odds ratio (OR = 3.1), indicating that women with these placental abnormalities were over three times more likely to experience adverse pregnancy outcomes compared to those without. Villous calcifications also had a strong association with adverse outcomes (OR = 3.5). Fibrin deposition (OR = 2.3) and ischemic lesions (OR = 2.7) were also significant predictors. All of these factors had p-values < 0.05, confirming their strong association with adverse pregnancy outcomes. **Conclusion:** We concluded that a strong correlation between coagulation disorders and placental pathology, with DIC being the most severe condition in terms of coagulation abnormalities and placental damage. These placental abnormalities were significantly associated with adverse pregnancy outcomes, particularly preterm birth, preeclampsia, and IUGR.

Keywords: Coagulation Disorders, Pregnancy Outcomes Placental Pathology

INTRODUCTION

Coagulation disorders in pregnancy pose significant risks to both maternal and fetal health, influencing various aspects of pregnancy outcomes. These disorders disrupt the delicate balance between procoagulant and anticoagulant systems in the maternal body, potentially leading to severe complications. The impact of these disorders is often reflected in the placenta, an essential organ that facilitates nutrient and oxygen exchange between the mother and fetus. Placental pathology can reveal important clues about the underlying mechanisms that drive adverse pregnancy outcomes in women with coagulation disorders.[1]Pregnancy itself is a hypercoagulable state, with physiological changes in the coagulation system that are designed to prevent

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excessive bleeding during childbirth. However, in certain cases, these changes can predispose women to thrombosis and other clotting disorders. When coagulation mechanisms become dysregulated, it can lead to conditions such as thrombophilia, antiphospholipid syndrome (APS), and disseminated intravascular coagulation (DIC). These disorders are associated with a variety of adverse pregnancy outcomes, including recurrent pregnancy loss, preterm birth, intrauterine growth restriction (IUGR), and preeclampsia.[2]Thrombophilia is one of the most common coagulation disorders affecting pregnancy. It encompasses a range of inherited and acquired conditions that increase the risk of venous thromboembolism (VTE). Women with thrombophilia are at higher risk of developing blood clots, particularly in the placental vessels, which can compromise blood flow to the fetus. Reduced blood flow to the placenta can result in fetal hypoxia, growth restriction, and in severe cases, stillbirth. Furthermore, thrombophilia has been linked to an increased risk of placental abruption, a serious condition where the placenta detaches from the uterine wall, leading to heavy bleeding and premature delivery.[3]

Antiphospholipid syndrome (APS) is another coagulation disorder with profound implications for pregnancy outcomes. APS is an autoimmune condition characterized by the presence of antiphospholipid antibodies (aPL), which increase the risk of blood clots. Women with APS are more likely to experience recurrent pregnancy loss, preeclampsia, and IUGR. The pathophysiology of APS involves the formation of clots within the placental vasculature, leading to placental insufficiency and poor fetal growth. Additionally, APS has been associated with preterm birth due to complications arising from severe preeclampsia or placental abruption. The management of APS in pregnancy often involves the use of anticoagulant therapies to prevent clot formation and improve pregnancy outcomes.[4]

Disseminated intravascular coagulation (DIC) is a rare but life-threatening coagulation disorder that can occur during pregnancy. DIC is characterized by widespread activation of the coagulation cascade, leading to the formation of microthrombi in small blood vessels throughout the body. This excessive clotting depletes the body's clotting factors and platelets, increasing the risk of severe hemorrhage. In pregnancy, DIC is often associated with obstetric complications such as placental abruption, severe preeclampsia, and intrauterine fetal death. DIC can have devastating consequences for both the mother and the fetus, with high rates of maternal mortality and fetal loss. The management of DIC requires prompt intervention to address the underlying cause and to restore the balance of the coagulation system.[5]Placental pathology plays a crucial role in understanding the impact of coagulation disorders on pregnancy outcomes. The placenta serves as the primary interface between the mother and fetus, and any disruption in its function can lead to poor pregnancy outcomes. In cases of coagulation disorders, the placenta often shows signs of impaired blood flow, ischemia, and infarction. Fibrin deposition, vascular occlusions, and placental infarctions are common histological findings in women with coagulation disorders. These placental abnormalities can lead to decreased oxygen and nutrient supply to the fetus, resulting in growth restriction and, in severe cases, fetal demise.[6]

Fibrin deposition is a hallmark of coagulation disorders, reflecting excessive clot formation in the placental vasculature. Fibrin is a protein involved in blood clotting, and its accumulation in the placenta can block the exchange of oxygen and nutrients between the mother and fetus. Vascular occlusions, caused by the formation of blood clots in placental vessels, further exacerbate the problem by reducing blood flow to the fetus. Ischemic lesions and infarctions, which represent areas of tissue damage due to inadequate blood supply, are also commonly observed in placental samples from women with coagulation disorders. These findings suggest that impaired placental blood flow is a major contributing factor to the adverse outcomes seen in these pregnancies.[7]Preeclampsia, a hypertensive disorder of pregnancy, is another significant complication associated with coagulation disorders. Preeclampsia is characterized by high blood pressure and damage to organs such as the liver and kidneys. It often occurs in conjunction with placental abnormalities and is more common in women with thrombophilia, APS, and DIC. Preeclampsia can lead to serious complications for both the mother and fetus, including preterm birth, placental abruption, and IUGR. The exact mechanism linking coagulation disorders to preeclampsia is not fully understood, but it is believed that abnormal blood clotting in the placenta plays a key role. The management of preeclampsia in women with coagulation disorders involves close monitoring and, in severe cases, early delivery to prevent maternal and fetal morbidity and mortality.Intrauterine growth restriction (IUGR) is another common outcome in pregnancies complicated by coagulation disorders. IUGR occurs when the fetus does not receive adequate nutrients and oxygen, leading to poor fetal growth. The presence of placental abnormalities such as fibrin deposition, vascular occlusions, and infarctions contributes to the development of IUGR. In cases of severe IUGR, the fetus may need to be delivered early to prevent further complications.[8]

MATERIAL AND METHODS

This study was a prospective observational investigation conducted to explore the relationship between coagulation disorders and pregnancy outcomes through histological examination of placental pathology. The study involved 80 pregnant women diagnosed with various coagulation disorders,

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recruited from a tertiary care hospital's obstetric unit. The study was approved by the Institutional Ethics Committee of the hospital. Informed consent was obtained from all participants before enrollment. All data were anonymized to protect patient confidentiality, and participants were informed of their right to withdraw from the study at any time.The study population consisted of 80 pregnant women with diagnosed coagulation disorders such as thrombophilia, antiphospholipid syndrome (APS), disseminated intravascular coagulation (DIC), and other related conditions. Participants were selected based on the following criteria:

Inclusion Criteria

- Pregnant women aged 18-40 years
- Singleton pregnancies
- Confirmed diagnosis of coagulation disorders
- Informed consent obtained

Exclusion Criteria

- Women with multiple pregnancies
- History of chronic hypertension or diabetes mellitus
- Previous history of placental abruption or preterm labor without coagulation disorders
- Refusal to provide informed consent

Methodology

Participants were closely monitored throughout the pregnancy, and data collection was carried out in three main phases. The first phase involved clinical assessments**,** where regular evaluations were conducted to monitor maternal and fetal well-being. Maternal parameters such as blood pressure, hemoglobin levels, and platelet counts were measured routinely. Any antenatal complications, including preeclampsia, intrauterine growth restriction (IUGR), and preterm delivery, were recorded during these assessments.The second phase focused on the coagulation profile, where specific coagulation parameters were monitored throughout pregnancy. These parameters included prothrombin time (PT), activated partial thromboplastin time (aPTT), fibrinogen levels, D-dimer, and thrombin-antithrombin complex levels. Measurements were taken at regular intervals to assess coagulation disorders' impact on pregnancy outcomes.In the third phase, a histological examination was performed after delivery. Placentas from all participants were collected and preserved in 10% formalin. Histopathological examination was conducted to evaluate the placental villi architecture, fibrin deposition, thrombi formation, signs of ischemia, infarction, calcifications, syncytial knots, intervillous hemorrhage, and intervillous thrombi.For placental sampling and histological analysis, placentas were sectioned into 3-5 mm slices and processed for paraffin embedding. Thin sections (5 µm) were stained using hematoxylin and eosin (H&E) to visualize the tissue structure. Additional stains such as Masson's trichrome and periodic acid-Schiff (PAS) were applied to assess specific abnormalities like fibrosis and glycogen deposition. The histological findings were reviewed by two independent pathologists, with particular attention to fibrin deposition within the intervillous spaces and around terminal villi, vascular occlusions, thrombi, vessel wall changes in the maternal and fetal compartments, inflammation (e.g., chorioamnionitis), and ischemic lesions such as infarcts and villous calcification.

Statistical Analysis

The collected data were analyzed using SPSS version 25.0. Descriptive statistics were employed to summarize baseline characteristics of the participants. The relationship between coagulation disorders and pregnancy outcomes (e.g., preterm birth, IUGR, preeclampsia) was analyzed using chi-square tests, t-tests, and logistic regression models. Histological findings of placental pathology were compared across different coagulation disorder groups, and p-values < 0.05 were considered statistically significant.

RESULTS

Table 1: Baseline Characteristics of Participants

This table provides a comparison of baseline characteristics across the 80 participants diagnosed with various coagulation disorders, including thrombophilia, antiphospholipid syndrome (APS), disseminated intravascular coagulation (DIC), and other disorders. The maternal age across the groups was similar, with an average of 30.5 years, and no significant differences were noted among the groups ($p=0.72$). The gestational age at delivery ranged from 36.8 to 37.5 weeks, with no statistically significant differences observed ($p=0.61$).Preterm birth rates varied across the groups, with the highest incidence in the DIC group (46.67%) and the lowest in the APS group (30%). However, the differences were not statistically significant ($p=0.39$). Similarly, the rates of preeclampsia and intrauterine growth restriction (IUGR) showed variability across the groups but were not significantly different. The DIC group showed the highest rates of preeclampsia (33.33%) and IUGR (26.67%), but the overall p-values indicated no significant differences across the groups for these outcomes.

Table 2: Coagulation Parameters by Disorder Group

Table 2 presents the coagulation profile of the participants, showing significant differences in coagulation parameters across the four disorder groups. DIC was associated with significantly prolonged prothrombin time (PT) and activated partial thromboplastin time (aPTT) compared to the other groups, indicating a more severe disruption of the coagulation pathway in this group. The fibrinogen levels were markedly lower in the DIC group (2.2 g/L), further emphasizing the severity of the disorder

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(p=0.001). D-dimer levels were also significantly higher in the DIC group (1.8 mg/L), indicating increased fibrinolytic activity (p=0.005). These findings suggest that DIC patients had more severe coagulation abnormalities compared to those with thrombophilia, APS, or other disorders.

Table 3: Histological Findings of Placental Pathology

This table highlights the placental abnormalities observed across the different coagulation disorder groups. Fibrin deposition, a marker of abnormal blood clotting, was highest in the DIC group (66.67%), followed by APS (45%) and thrombophilia (40%), with significant differences across the groups (p=0.03). Similarly, vascular occlusions, which are indicative of impaired blood flow to the placenta, were most frequent in the DIC group (73.33%) and significantly higher compared to other groups (p=0.02).Ischemic lesions, which represent tissue damage due to inadequate blood supply, were also more common in the DIC group (53.33%) compared to other groups, with a significant p-value of 0.04. Villous calcifications, a sign of placental aging and poor fetal oxygenation, were most prevalent in the DIC group (53.33%) and showed a statistically significant difference among the groups (p=0.01). Overall, these histological findings suggest that DIC is associated with more severe placental pathology compared to the other coagulation disorders.

Table 4: Pregnancy Outcomes in Relation to Placental Pathology

Table 4 compares pregnancy outcomes between women with normal and abnormal placental pathology. Women with abnormal placental pathology had significantly worse outcomes. Preterm birth was notably more common in women with abnormal placentas (40%) compared to those with normal placentas (12%), with a significant p-value of 0.01. Preeclampsia was also significantly higher in the abnormal placental group (27.27%) compared to the normal group (12%) (p=0.03). IUGR occurred in 20% of women with abnormal placentas, compared to just 8% in women with normal placentas (p=0.02). NICU admissions were significantly higher in the abnormal placental group (34.54%) compared to the normal group (16%) (p=0.01). These findings highlight the strong association between placental pathology and adverse pregnancy outcomes.

Table 5: Logistic Regression Analysis of Predictors for Adverse Pregnancy Outcomes

This table shows the results of a logistic regression analysis, identifying key predictors for adverse pregnancy outcomes. Fibrin deposition, vascular occlusions, ischemic lesions, and villous calcifications were all significant predictors of adverse outcomes. Vascular occlusions had the highest odds ratio (OR = 3.1), indicating that women with these placental abnormalities were over three times more likely to experience adverse pregnancy outcomes compared to those without. Villous calcifications also had a strong association with adverse outcomes (OR = 3.5). Fibrin deposition (OR = 2.3) and ischemic lesions (OR = 2.7) were also significant predictors. All of these factors had p-values < 0.05, confirming their strong association with adverse pregnancy outcomes. These findings suggest that placental abnormalities are significant risk factors for complications such as preterm birth, preeclampsia, and IUGR.

Table 1: Baseline Characteristics of Participants

Characteristics	Total (n=80)	Thrombophilia (n=30)	APS (n=20)	DIC (n=15)	Other Disorders (n=15)	p-value
Maternal Age (years)	30.5 ± 5.6	30.2 ± 5.4	31.1 ± 5.9	30.0 ± 5.3	30.7 ± 5.8	0.72
Gestational Age at Delivery (weeks)	37.2 ± 2.4	36.8 ± 2.6	37.4 ± 2.2	37.0 ± 2.5	37.5 ± 2.3	0.61
Preterm Birth (%)	28 (35%)	12 (40%)	6 (30%)	7 (46.67%)	5 (33.33%)	0.39
Preeclampsia (%)	18 (22.5%)	8 (26.67%)	3 (15%)	5 (33.33%)	3 (20%)	0.42
IUGR (%)	14 (17.5%)	6 (20%)	3 (15%)	4 (26.67%)	2 (13.33%)	0.38

Table 2: Coagulation Parameters by Disorder Group

Coagulation Parameter	Thrombophilia (n=30)	APS (n=20)	DIC (n=15)	Other Disorders (n=15)	p-value
PT (seconds)	12.5 ± 1.1	12.8 ± 1.2	14.1 ± 1.5	12.6 ± 1.3	0.004
aPTT (seconds)	30.2 ± 2.4	32.0 ± 2.8	36.5 ± 3.2	30.5 ± 2.6	0.002
Fibrinogen (g/L)	3.5 ± 0.6	3.4 ± 0.5	2.2 ± 0.4	3.3 ± 0.5	0.001
D-dimer (mg/L)	1.1 ± 0.2	1.3 ± 0.3	1.8 ± 0.4	1.2 ± 0.3	0.005

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Table 3: Histological Findings of Placental Pathology

Histological Findings	Thrombophilia (n=30)	APS (n=20)	DIC (n=15)	Other Disorders (n=15)	p-value
Fibrin Deposition (%)	12 (40%)	9 (45%)	10 (66.67%)	5 (33.33%)	0.03
Vascular Occlusions (%)	10 (33.33%)	10 (50%)	11 73.33%)	4 (26.67%)	0.02
Ischemic Lesions (%)	9 (30%)	8 (40%)	8 (53.33%)	4 (26.67%)	0.04
Villous Calcifications (%)	8 (26.67%)	6 (30%)	8 (53.33%)	3 (20%)	0.01

Table 4: Pregnancy Outcomes in Relation to Placental Pathology

Pregnancy Outcome	Normal Placenta (n=25)	Abnormal Placenta (n=55)	p-value
Preterm Birth (%)	3 (12%)	22 (40%)	0.01
Preeclampsia (%)	3 (12%)	15 (27.27%)	0.03
IUGR (%)	2 (8%)	11 (20%)	0.02
NICU Admission (%)	4 (16%)	19 (34.54%)	0.01

Table 5: Logistic Regression Analysis of Predictors for Adverse Pregnancy Outcomes

Predictor Variable	Odds Ratio (OR)	95% Confidence Interval (CI)	p-value
Fibrin Deposition	2.3	1.4 - 3.8	0.02
Vascular Occlusions	3.1	1.8 - 5.2	0.01
Ischemic Lesions	2.7	1.5 - 4.6	0.03
Villous Calcifications	3.5	2.1 - 5.8	0.01

DISCUSSION

The baseline characteristics of participants across the four coagulation disorder groups showed no significant differences in maternal age and gestational age at delivery. This finding aligns with studies by Dekker et al. (2020) and Rigo et al. (2021), which also reported no substantial variations in maternal age among women with different types of thrombophilia and APS.[2,3] The preterm birth rates, while highest in the DIC group (46.67%), were not significantly different across the groups, consistent with Kupferminc et al. (2020), who found that thrombophilia and APS are not always directly associated with preterm birth, but the severity of coagulation dysregulation, especially in DIC, can be a stronger predictor.4

The DIC group showed the highest rates of preeclampsia and IUGR, but these differences were not statistically significant, which contrasts with the findings of Hemmings et al. (2019), who demonstrated a stronger association between APS and preeclampsia, suggesting that the small sample size in this study may limit statistical power.[6] However, it is notable that the trends in IUGR and preeclampsia prevalence reflect a similar pattern to other studies, where DIC and APS are commonly implicated in these outcomes due to impaired placental blood flow.

The coagulation profile of the participants demonstrated significant differences, with DIC being associated with the most severe coagulation abnormalities. Prolonged PT and aPTT, along with lower fibrinogen levels in the DIC group, align with the known pathophysiology of DIC, where widespread clotting and consumption of clotting factors occur. These results are consistent with the work of Lockwood (2021), who highlighted the hypercoagulable state in DIC, leading to both clot formation and increased risk of hemorrhage.[5]

Elevated D-dimer levels in the DIC group further indicate increased fibrinolytic activity, a hallmark of DIC, as noted by Cerneca et al. (2019). This finding underscores the systemic involvement of coagulation pathways in DIC, leading to severe disruptions in hemostasis.[7] These coagulation abnormalities were less pronounced in thrombophilia and APS, but still present, suggesting milder yet clinically significant disruptions in coagulation.

The placental histopathology in women with DIC showed the most severe abnormalities, with significantly higher fibrin deposition, vascular occlusions, ischemic lesions, and villous calcifications compared to other groups. This is consistent with the findings of Sibai (2019), who reported that placental pathology in DIC is marked by extensive fibrin deposition and thrombosis, which impair placental function and contribute to poor pregnancy outcomes.[1]

Vascular occlusions were also significantly more frequent in the DIC group, which aligns with studies by Dekker et al. (2020), where placental thrombi were frequently observed in cases of severe preeclampsia and IUGR.[2] The increased prevalence of ischemic lesions and villous calcifications in the DIC group further supports the conclusion that DIC causes widespread placental damage, similar to the findings in studies by Kupferminc et al. (2020), who observed these abnormalities in women with APS and severe placental insufficiency.[4]

Women with abnormal placental pathology had significantly worse pregnancy outcomes, with higher rates of preterm birth, preeclampsia, and IUGR. These findings are consistent with Hemmings et al. (2019), who identified placental abnormalities such as fibrin deposition and ischemic lesions as significant

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contributors to preterm birth and IUGR in women with APS and thrombophilia.[6]

Preterm birth was significantly more common in women with abnormal placental pathology (40%) compared to those with normal placentas (12%). This finding is supported by Lockwood (2021), who demonstrated that placental dysfunction, particularly in the context of APS and DIC, often necessitates early delivery to prevent further complications.[5]

Similarly, the higher rates of NICU admissions among women with abnormal placentas (34.54%) compared to those with normal placentas (16%) align with studies by Cerneca et al. (2019), who found that placental insufficiency resulting from coagulation disorders significantly increases the likelihood of neonatal complications, including preterm birth and low birth weight.[7]

Logistic regression analysis revealed that fibrin deposition, vascular occlusions, ischemic lesions, and villous calcifications were significant predictors of adverse pregnancy outcomes. Vascular occlusions had the highest odds ratio (OR = 3.1), indicating that women with these placental abnormalities were over three times more likely to experience adverse outcomes. These findings are consistent with the work of Kupferminc et al. (2020), who demonstrated that vascular occlusions and thrombi within the placenta are strong predictors of complications such as IUGR and preterm birth.[4]

Villous calcifications were also identified as a significant predictor of adverse outcomes (OR = 3.5), which corroborates the findings of Rigo et al. (2021), who reported that calcifications in the placenta are often a sign of chronic placental insufficiency, leading to fetal growth restriction and preeclampsia.[3]

CONCLUSION

We concluded that a strong correlation between coagulation disorders and placental pathology, with DIC being the most severe condition in terms of coagulation abnormalities and placental damage. These placental abnormalities were significantly associated with adverse pregnancy outcomes, particularly preterm birth, preeclampsia, and IUGR. The logistic regression analysis further confirmed that specific placental pathologies, such as fibrin deposition and vascular occlusions, are strong predictors of adverse pregnancy outcomes.

REFERENCES

1. Sibai BM. Etiology and management of postpartum hemorrhage: A review. Am J Obstet Gynecol. 2019;220(4):339-50.
2. Dekker GA, Sibai BM. Etiology and pathogenesis of preeclampsia: Current concepts. Am J Obstet Gynecol. 2020;203(6):613-9.
3. Rigo J, Szendei G, Fekete S. Thrombophilia and severe preeclampsia: Clinical importance of the factor V Leiden mutation. J Thromb Haemost. 2021;19(7):1849-56.
4. Kupferminc MJ, Eldor A, Steinman N, Many A, Bar-Am A, Jaffa A, et al. Increased frequency of genetic thrombophilia in women with complications of pregnancy. N Engl J Med. 2020;340(1):9-13.
5. Lockwood CJ. Mechanisms of abnormal coagulation and thrombosis during pregnancy. Obstet Gynecol Clin North Am. 2021;48(1):1-14.
6. Hemmings DG, Williams SJ, Davidge ST. Increased vascular resistance in the placenta and pregnancy complications associated with coagulation disorders. Placenta. 2020;92(5):49-56.
7. Cerneca F, Simeoni V, Ricci G. Hemostasis in pregnancy: Hypercoagulability and associated complications. J Matern Fetal Neonatal Med. 2019;32(18):3127-35.
8. Brenner B, Lanir N. Coagulation disorders and preeclampsia: Pathophysiological mechanisms and clinical implications. Thromb Res. 2019;178(1):115-20.