MEDS Basic Medicine (2024)
Clausius Scientific Press, Canada

DOI: 10.23977/medbm.2024.020212
ISSN 2616-2091 Vol. 2 Num. 2

Research on the Clinical Test Value of D-D and Coagulation Indicators in Patients with Hypertension during Pregnancy

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Keywords: D-D; Coagulation Indicators; HDCP; Diagnostic Value

Abstract: Coagulation indicators not only change within the bodies of normal pregnant women but are also closely related to various pregnancy-related diseases, such as hypertensive disorders complicating pregnancy (HDCP). HDCP is a common condition during pregnancy, which can be categorized into gestational hypertension (GH) and preeclampsia (PE), among others. In addition to posing risks to both pregnant women and their fetuses around the time of birth, HDCP can have long-term effects on the mother. Studies suggest that patients with HDCP have abnormal coagulation function, primarily due to the production of various active factors resulting from placental dysfunction in these patients. Once these active factors enter maternal circulation, they lead to small vessel spasms, endothelial cell damage, and activated coagulation responses, causing HDCP patients to experience a pathological hypercoagulable state. Therefore, analyzing coagulation indicators and D-dimer (D-D) parameters in HDCP patients with varying degrees of severity before delivery is crucial for diagnosing HDCP. Based on this, this article provides a retrospective analysis of studies on D-D and coagulation indicators in patients with hypertensive disorders during pregnancy, aimed at providing clinical support for the early prediction and treatment of high-risk perinatal women to reduce the incidence of adverse pregnancy outcomes, ultimately lowering maternal and neonatal mortality and morbidity rates.

1. Introduction

Hypertensive disorders complicating pregnancy (HDCP) is a diseases that pose a serious threat to maternal and infant health worldwide, with an incidence rate of approximately 5% to 12% among pregnant women[1]. The mortality rate associated with this condition is extremely high, around 0.042%, making it one of the leading causes of high morbidity and mortality in pregnant and perinatal populations. According to the WHO, deaths due to HDCP account for about 10% to 16% of total maternal deaths globally, with an estimated 50,000 to 60,000 cases of preeclampsia-related deaths each year[2]. Preeclampsia is a dynamic condition that can progress continuously; any form of preeclampsia can lead to severe adverse pregnancy outcomes. Therefore, timely prediction, close

monitoring of preeclampsia, and early intervention during the course of hypertensive disorders in pregnancy are crucial for reducing the risks and mortality associated with this condition[3].

It is widely recognized that patients with hypertensive disorders during pregnancy exhibit abnormal coagulation function, particularly in the late stages of pregnancy. Recent studies have indicated that many patients with adverse pregnancy outcomes related to hypertensive disorders exhibit a tendency for thrombosis[4]. Consequently, monitoring D-dimer (D-D) and coagulation parameters in these patients during pregnancy holds significant clinical importance for preventing hemorrhage during delivery and avoiding thrombus formation. Common clinical indicators used to evaluate coagulation function include prothrombin time (PT), activated partial thromboplastin time (APTT), thrombin time (TT), and plasma fibrinogen (FIB)[5]. These indicators are essential for monitoring coagulation and fibrinolytic function. Additionally, literature suggests that disturbances in coagulation and fibrinolytic systems are primary causes of hypertensive disorders in pregnancy, and changes in coagulation function may occur before the onset of clinical symptoms[6].

Based on this, this article conducts a retrospective analysis of studies on D-D and coagulation indicators in patients with hypertensive disorders during pregnancy, providing clinical assistance for early prediction and treatment of high-risk perinatal women. This analysis aims to offer a basis for clinicians to detect, diagnose, and intervene early, ultimately reducing the incidence of adverse pregnancy outcomes and further lowering maternal and neonatal mortality and morbidity rates.

2. Research Progress

In some research, the authors found the same results of D-D value and coagulation indicators in experimental groups and control groups: PT,APTT and TT were shorter in experimental groups while D-D and FIB were higher. Expect these results, their papers also had further study in different aspects.

Chen Mengdie selected 24 cases of pregnant women with gestational hypertension as the observation group, on the ohter hand, 24 healthy pregnant women from the same period were selected as the control group[7]. Both groups underwent D-D and four coagulation assays to compare the levels of related indicators. The results indicated that the observation group had higher levels of D-D and FIB, while the APTT and PT were shorter compared to the healthy group, with statistical significance ($P<0.05$). The increase of D-dimer vaule indicates that it was relatively higher in pregnant women with hypertensive diseases during the third trimester. D-dimer was a specific fibrinolytic marker, derived from plasminase-dissolved cross-linked fibrin clots, and was highly expressed in the blood of pregnant women, either because the pregnant woman was in a hypercoagulable state, or because of secondary hyperfibrinolysis, more fibrin was dissolved, increasing thrombosis[8]. Higher FIB, lower APTT and PT mean that compared with healthy pregnant women, there was no significant difference in the conversion time of fibrinogen to fibrin in pregnant women with hypertensive diseases during pregnancy, which may be related to the fibrinolytic process and the dynamic balance of anticoagulant state after receiving clinical intervention in late pregnancy[9].The fibrinogen was higher in late trimester pregnant women with hypertensive disease during pregnancy, while APTT and PT were shorter,which was consistent with the results of Tao Hong's study.

Tao Hong and his team also explored the clinical testing value of D-D and coagulation indicators in pregnant women with gestational hypertension[10]. 80 pregnant women with gestational hypertension were selected as the experimental group, and 80 normal pregnant women who came to the hospital for examination during the same period were selected as the control group. All participants underwent D-D and coagulation indicator tests, with results showing that the experimental group had shorter PT, APTT, and TT compared to the control group ($P<0.05$). FIB and

D-D levels were higher in the experimental group (P<0.05), which were the same with Chen's study. They also found that as the condition of pregnant women with gestational hypertension worsened, PT, APTT, and TT gradually shortened, while FIB and D-D levels increased, with statistically significant differences (P<0.05). Moreover, the diagnostic value of D-D combined with coagulation indicators was higher than that of single tests(AUC>0.9). This suggests that D-D and coagulation indicator testing can assist in clinically assessing the severity of gestational hypertension in pregnant women, with combined testing having greater diagnostic value than isolated tests.

There was a similar case by Ge Weiwei which mentioned that the area under the curve (AUC) for the combined detection of D-D and coagulation indicators in diagnosing gestational hypertension was greater than 0.9 as well, indicating high diagnostic value, and was superior to individual tests. They conducted a retrospective analysis of the clinical data of 68 patients with gestational hypertension, forming the research group[11**]**. An additional 30 healthy pregnant women from the hospital served as the control group. Receiver operating characteristic (ROC) curve analysis was performed to evaluate the effectiveness of D-D and coagulation indicators, both individually and in combination, in diagnosing gestational hypertension. The AUC indicated that the clinical value of combined tests was better than one single test. Their study also showed that PT, APTT, and TT levels in the research group were lower than in the control group, while FIB and D-D levels were higher in the research group, with statistical significance (P<0.05). What's more, the research group was further divided into a gestational hypertension group consisting of 26 cases, a mild preeclampsia (PE) group with 24 cases, and a severe PE group with 18 cases, to compare the D-D and coagulation indicator levels among these subgroups. In the severe PE group, PT, APTT, and TT levels were lower than those in the mild PE and gestational hypertension groups, while the mild PE group also had lower levels than the gestational hypertension group. Furthermore, FIB and D-D levels in the severe PE group were higher than in the mild PE and gestational hypertension groups, with significant differences (P<0.05).

Another paper also aimed to explore the correlation between plasma D-D levels and coagulation indicators in patients with hypertensive disorders of pregnancy (HDP), as well as their impact on pregnancy outcomes. They divided HDP patients into three groups: the gestational hypertension group, the mild preeclampsia group, and the severe preeclampsia group[12]. A control group of healthy pregnant women delivering during the same period was also selected. The coagulation function indicators, hematological parameters, and D-D levels were assessed for all four groups, followed by an evaluation of adverse pregnancy outcome rates. Results showed that compared to the control group, the three observed groups had lower levels of PT, TT and APTT, while FIB and D-D levels were higher (P<0.05). The severe preeclampsia group showed lower levels of PT, TT and APTT, with higher levels of FIB, D-D compared to the gestational hypertension and mild preeclampsia groups (P<0.05),which were just as the same outcomes as the research of Ge Weiwei. The incidence rates of adverse pregnancy outcomes were 4.34%, 14.28%, and 31.81% for the gestational hypertension, mild preeclampsia, and severe preeclampsia groups, respectively, showing a significant difference (P<0.05). This indicates that as HDP progresses, notable changes occur in coagulation indicators and D-D levels, and close monitoring of these parameters in HDP patients is essential for assessing disease progression and formulating effective treatment measures to reduce adverse pregnancy outcomes.

There was one more set of date looking at the value of D-dimer and coagulation indexes in eclampsia gestational. Jing Shuhui selected 56 patients with HDCP as the HDCP group, and 50 healthy mothers as the control group[13]. The levels of D-D and coagulation indicators were compared between the two groups, and variations among different types of patients in the HDCP group were also analyzed. Furthermore, correlations between statistically significant indicators among different types of HDCP patients were assessed. The results indicated that compared to the

control group, pregnant women in the HDCP group had higher levels of D-D and FIB, while PT and APTT levels were lower (P<0.05). The D-D levels ranked from low to high were: gestational hypertension, mild preeclampsia, and severe preeclampsia. APTT ranked from high to low were: gestational hypertension, mild preeclampsia, and severe preeclampsia. Patients with gestational hypertension had lower FIB levels than those with mild and severe preeclampsia, while their antithrombin III (AT-III) and PT-INR levels were higher (P<0.05). Additionally, D-D levels in the HDCP group were negatively correlated with APTT levels (P<0.05). This suggests that testing D-D and coagulation indicators in pregnant women can aid in screening for HDCP patients, and that D-D and APTT levels significantly change with the worsening condition of HDCP patients.

Not only Xu's team worked on the adverse pregnancy outcomes, but also Tao Diandian aimed to explore abnormal maternal and infant prognosis and analyze the clinical value of D-D and four coagulation factors in late-stage hypertensive pregnancy[14]. They selected 120 patients with gestational hypertension (hypertensive group) and 120 normal pregnant women (normal group). D-D and coagulation factor levels were measured in both groups, and a correlation analysis was conducted, alongside a survey of maternal and neonatal outcomes. The results showed that the D-D and coagulation factor levels in the hypertensive group were significantly higher than those in the normal group (P<0.05). All mothers delivered successfully, and both mothers and neonates survived; however, the incidence of postpartum hemorrhage, puerperal infection, neonatal asphyxia, and macrosomia was significantly higher in the hypertensive group compared to the normal group (P<0.05). Among the 240 mothers, Spearman analysis indicated a positive correlation between D-D, coagulation factor levels, and gestational hypertension (P<0.05). Multivariate logistic regression analysis revealed that both D-D and coagulation factor levels were major contributing factors to the occurrence of gestational hypertension (P<0.05). This indicates that mothers with gestational hypertension often experience abnormal maternal and neonatal outcomes, which can increase D-D and coagulation factor expression levels, showing a correlation with the incidence of gestational hypertension.

It happened that there was another work by Chen Chunhui exploring the correlation of plasma D-D and coagulation index in gestational hypertension patients and its influence on pregnancy outcome[15]. They selected 60 pregnant women with gestational hypertension as the observational group and an additional 60 normal pregnant women during the same period were chosen as the control group for comparison. All women's plasma D-D levels were measured before delivery and on days 1, 3, and 5 postpartum, along with FIB, APTT, PT and TT levels before delivery. The correlation between plasma D-D levels and other plasma indicators (FIB, APTT, PT and TT) was analyzed, and delivery outcomes between the two groups were compared. Results indicated that compared to before delivery, the plasma D-D levels in both groups decreased from days 1 to 5 postpartum; however, levels in the observational group were consistently higher than those in the control group throughout this period. Additionally, the observational group exhibited higher plasma FIB levels and shorter APTT, PT, and TT compared to the control group (all P<0.05). Pearson correlation analysis revealed a positive correlation between plasma D-D levels and FIB levels in women with gestational hypertension (r=0.784, P<0.05), and negative correlations with APTT, TT, and PT (r=-0.823, -0.754, -0.714, P<0.05). The incidence of adverse pregnancy outcomes was significantly higher in the observational group compared to the control group (P<0.05). These findings suggest that gestational hypertension is associated with an increased risk of adverse pregnancy outcomes, adversely impacting maternal and infant health. In women with gestational hypertension, elevated plasma D-D levels correlated positively with FIB levels and negatively with APTT, TT, and PT. Monitoring changes in fibrinolytic system and coagulation function indicators can aid in identifying at-risk pregnant women, facilitating the development of effective prevention and treatment strategies to improve maternal and neonatal health outcomes.

However, some other authors had different opinions, even completely the opposite view compared with the studies above. He Wenyang selected 88 pregnant women diagnosed with gestational hypertension as the gestational hypertension group[16]. Another 88 healthy pregnant women who underwent prenatal inspections at the same hospital served as the control group. Both groups were tested for D-D, PT, and APTT, among other indicators, to determine their diagnostic value. Results indicated that the plasma D-D content was higher in the gestational hypertension group compared to the control group ($P<0.05$). It is because that during the formation of pregnancy hypertension, under the action of thrombin, plasma fibrinogen decomposes into fibrin monomer and combines to form a polymer, resulting in an increase in D-dimer content. Current studies have shown that the increase of D-dimer content can cause placental ischemia and hypoxia and enhance local cellular immune response, destroy cell structure and affect its function, and cause lipid peroxidation and free radical mass release, thus leading to the occurrence of pregnational hypertension[17].The PT and APTT levels were also elevated in the hypertensive group ($P<0.05$). This indicated that pregnant women with hypertension during pregnancy were accompanied by abnormal coagulation indexes. At the same time, the content of PT and APTT could promote the adhesion and aggregation of platelets, lead to the abnormality of glycoprotein synthesis intermediates, cause the acceleration of cell division, inhibit the delay of cell apoptosis and antioxidant effect, and induce the occurrence of hypertension during pregnancy[18]**.**Spearman analysis among the 176 pregnant women confirmed a correlation between plasma D-D, PT, APTT, and gestational hypertension ($P<0.05$). Multiple linear regression analysis indicated that plasma D-D, PT, and APTT were significant factors leading to the occurrence of gestational hypertension ($P<0.05$). The ROC curve showed that the area under the curve for the combined detection of plasma D-D, PT, and APTT for identifying gestational hypertension was 0.867. This demonstrates that patients with gestational hypertension often exhibit abnormalities in D-D and coagulation indicators, highlighting the value of testing these markers in identifying pregnant women with gestational hypertension early.

Huang Haochuan not only worked on gestational hypertension, but he also focused on gestational diabetes mellitus (GDM)[19]. The participants were divied into three groups: pregnant women with GDM for the observation group, hypertensive disorders of pregnancy for the study group, and normal pregnant women during the same period served as the reference group. All three groups underwent tests for coagulation factors, thrombotic parameters, and D-D levels, allowing for comparison of results. Findings indicated no statistical significance in the coagulation factor comparisons among the three groups ($P>0.05$). Compared to the reference group, the study group showed significant decreases in fibrin degradation products (FDP) and D-D levels, along with a notable increase in plasminogen (PLG) levels. Conversely, in comparison to the observation group, the study group exhibited significantly elevated PLG levels, while decreasing FDP, antithrombin (AT), and D-D levels ($P<0.05$). This suggests that the relevant indicators in patients with gestational diabetes mellitus and hypertensive disorders differ significantly from those in normal pregnant women and possess distinct specificity, thus could serve as clinical diagnostic standards.

3. Conclusion

HDCP is a common condition during pregnancy, characterized by new-onset hypertension after 20 weeks of gestation, which may or may not be accompanied by proteinuria, or involve any significant organ or system complications[20]. As the second leading cause of maternal mortality globally, HDCP not only results in adverse pregnancy outcomes for both the mother and fetus but is also considered a risk factor for long-term thrombotic and cardiovascular diseases in women[21]. The pathogenesis of HDCP is highly complex, featuring interactions among multiple factors and mechanisms, particularly in the case of PE[22]. Research suggests that abnormalities in the

coagulation system of pregnant women may be linked to the development of HDCP[23]. In light of this, this article provides a retrospective analysis of studies on D-D and coagulation indicators in patients with pregnancy-induced hypertension, aiming to offer clinical support for the early prediction and treatment of high-risk pregnancies during the perinatal period. This could help reduce the incidence of adverse pregnancy outcomes and ultimately lower maternal and neonatal mortality and morbidity rates.

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