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RAISED D-DIMER LEVELS BEFORE DELIVERY AS AN EFFECTIVE PREDICTOR OF POSTPARTUM HEMORRHAGE.

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ABSTRACT:

INTRODUCTION: The most common cause of maternal morbidity & death is postpartum hemorrhage (PPH). Secondary coagulopathy as a result of PPH or its treatment is frequently overestimated, & as a result, it goes untreated, potentially leading to even more severe PPH. D-dimer is a minor protein product that is detected in very small concentrations in the bloodstream due to endogenous fibrinolysis.DD level is elevated during pregnancy progressively. Its increased level can positively be correlated with venous thromboembolism. This has been investigated in previous researches but the observation of high DD levels at the time of admission for delivery & increased incidence of PPH in such women has not been investigated previously. **PATIENTS & METHODS:** 162 women with PPH who delivered at term vaginally or by caesarean section after uncomplicated pregnancies were included in the research.

RESULTS: Among all women having marked elevation (>500ng/ml) of DD before delivery, 64.1% had developed PPH which was significant. While only 35.8%. of women with normal DD levels had developed PPH.**CONCLUSION:** DD (D-Dimmer) levels tend to increase progressively during pregnancy but how it increases the incidence of postpartum hemorrhage in patient was not well known. DD level is one of the clinical parameter associated with coagulation & fibrinolysis. This research was conducted to conclude the association of raised DD (D-Dimmer) level at the time of delivery along with demographic factors of women with higher incidence of postpartum hemorrhage.

KEY WORDS: DD (D-Dimmer) (DD), postpartum hemorrhage (PPH),women & children hospital(WCH) Body mass index(BMI), antithrombin(AT), caesarean section(c-section),venous thromboembolism(VTE)

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INTRODUCTION

PPH (postpartum hemorrhage) is still the largest cause of maternal death & morbidity in the world[1]. While the majority of fatalities occur in low-resource nations, PPH is becoming more common in wealthy countries[2]. The presence of coagulopathy, particularly low fibrinogen concentrations, is one of the early signs of severity that predicts a bad result in PPH. [3] Placenta previa, prior PPH, Asian ethnicity, anemia, & preeclampsia are all established risk factors for PPH. coagulation profile of mother & profiles of fibrinolysis have recently been studied to see if they might predict severe postpartum hemorrhage. Although there has been a link between a reductions in fibrinogen in the early stages of PPH & the severity of the condition there

have been few research on the prediction of PPH before birth. D-dimer is a minor protein product that is produced in very small concentrations in the bloodstream due to endogenous fibrinolysis [4,5.] In a normal hemostatic process, the development of bodily lump of accumulated platelets on the place of damage includes development of a physical lump of gathered platelets, which is more become stable by fibrin protein, which is formed close by in reaction to damage by the coagulation cascades. [1] The cascade of coagulation is accelerated even further, culminating in the formation of thrombin, an enzyme which separates fibrinopeptides A & B as of fibrinogen to produce fibrin monomers.[2]

Thrombin activates factor XIII, that catalyses cross-linking among D-domains of neighbouring fibrin monomers, stabilising the polymer of fibrin. The initiation of cascade of coagulation, which is essential for formation of a clot of fibrin, which is followed by the initiation of the fibrinolytic scheme, that includes breakdown of fibrin (fibrinolysis) and subsequent dissolution of the fibrin clot to produce D-dimers. [3] D-dimers are cross-linked fibrin breakdown protein products seen in trace amounts in the blood of most healthy persons, on the order of 100–200 ng/mL.[2]

Intravascular coagulation and thrombotic disease are evidenced by increased D-dimer content in the blood, that is independent confirmation of continuing fibrin lysis (VTE). The lack of D-dimers in blood plasma rules out the development of intravascular clots, but high plasma D-dimers suggests that the thrombotic / fibrinolytic progression is still going on.[2]

A normal or negative (lower level) D-dimer test can rule out the presence of a serious intravascular thrombotic condition, while a positive (higher level) result can suggest the presence of an acute illness involving abnormal clot formation, such as venous thromboembolism (VTE). This test, on the other hand, is unable to pinpoint the location and/or cause of an unusual blood clot[6].

High D-dimer plasma levels have been recorded during normal pregnancy, with levels rising proportionally with gestational age as a result of better maternal coagulation and increased synthesis of intrinsic and extrinsic coagulation factors.[7,8]

Furthermore, D-dimer levels were considerably greater in pregnant women with severe illnesses such as diabetes, preeclampsia, and abruption placentae[9,10]. Lower antithrombin activity and fibrinogen levels, as well as higher D-dimer levels, were all independent risk factors for PPH in late pregnancy.

The current research is aimed to evaluate the value of plasma level of D-dimer at the time of delivery in normal & uncomplicated term pregnancies in women attending the Women & Children Hospital Abbottabad Pakistan. To our knowledge, this research is the first of its type to be performed among Pakistani women.

MATERIALS & METHODS:

The research was conducted at the Women & Children Hospital Abbottabad's Department of Obstetrics & Gynecology, a tertiary care facility. The research procedure was approved by the institution's Ethical Committee, & each participant gave written informed permission. Women who were pregnant with a singleton at full term (37 weeks gestation) were included in the research. Women who had medical difficulties during pregnancy, such as hypertension, diabetes, or coagulation issues, were excluded from the research. The research took place over the course of six months, from November 2020 to April 2021, & total of 1800 participants remained enrolled. At the time of admission for delivery, the DD level was measured. Data on demographic variables including as age, gestational age, parity, & delivery method was also gathered.

RESULTS:

During 6 months period of research, a total of 1800 patients undergoing vaginal deliveries or C- sections were analyzed. Out of these, 162 (9%) patients developed PPH (table 1). A total of 112(69%) patients were between 20 to 30 years age group & only 50(30.8%) patients were of 31 to 40years of age. Only 28(17.2%) patients delivering at <37 weeks gestation had postpartum hemorrhage while 82.7% of patients having PPH delivered at >37weeks gestation.

There were 40(24.6%) patients who were primi gravida & 122 (75.3%) were multiparous. In 33.9% of patients, the BMI was 20 to 25 & in 66% of patients of PPH, BMI was more than 26 showing obesity as an independent risk factor for PPH.

In 64.1% patients of PPH, the measured DD (D-Dimmer) level was >500ng/ml & it was <500ng/ml in 58(35.8%) patients showing that raised level of DD (D-Dimmer) at the time of delivery makes it a significant risk factor for postpartum hemorrhage

Table 1: Frequency of PPH in study population(n=1800)

Parameter	Frequency (no of patients)	Percentage
Patients with PPH	162	9%
Patients with no PPH	1638	91%

Table 2: Characteristics of patients with PPH(n=162)

Parameter		**Frequency**	**Percentage**
Age	20 to 30 years (n=)	112	69.1%
	31 to 40 years (n=60)	50	30.8%
Gestational age	<37 weeks gestation	28	17.2%
	>37 weeks gestation	134	82.7%
Parity	Primiparous	40	24.6%
	Multiparous	122	75.3%
BMI	20-25	55	33.9%
	>26	107	66%
D-dimer level	<500ng/ml	58	35.8%
	>500ng/ml	104	64.1%

DISCUSSION

The occurrence of D-dimer as a fibrinolysis indicator implies a considerable rise in fibrinolytic organization activity, likely to equilibrium the rises in coagulation issues found in usual gravidity, which results in a low incidence of venous thromboembolism.[11-15]

24 The occurrence of an intravascular thrombus & the natural elimination (fibrinolysis) of the thrombus are both reflected by a high D-dimer level in a patient's plasma. [16-23]

According to prior reports, D-dimer levels rise to 600 ng/ml throughout the 2nd& 3rd trimesters of gravidity, according to several research. [24,25,26-29.] According to previous research, D-dimer testing is a feasible screening tool for removing VTE in non-pregnant people. For the diagnosis of acute VTE in non-pregnant persons, it has a high sensitivity, middling specificity, and a high negative predictive value.[30] D-dimer concentrations in pregnant women, on the other hand, enlarged gradually throughout the gravidity & rise on the 1st postpartum period.[31]

During pregnancy and puerperium, most healthy pregnant women have higher D-dimer readings than the typical reference range.[32] According to a prospective research, 84% of women had normal D-dimer in the first trimester, 33% in the second trimester, and just 1% in the third trimester, implying that D-dimer has no practical diagnostic relevance for VTE if the abnormal threshold is utilised.[33]

Previous research has also shown that a physiologic adaptation to the hyper consumption of fibrinogen that occurs during pregnancy, as evidenced by higher D-dimer levels in pregnant women than in non-pregnant women[20], may be a physiologic adaptation to the hyper consumption of fibrinogen that occurs during pregnancy. Reduced AT activity, combined with an increased D-dimer level, has been evaluated as an independent risk factor for PPH, with both of these factors indicating improved coagulation. Because AT is the most significant anti-coagulation molecule in the circulating blood, interacting 1:1 with thrombin, reduced AT activity might indicate excessive thrombin production. In the presence of thrombin, blood coagulates. As a result of the increased coagulation[22], both the decreased AT activity & the greater D-dimer level occur.

Our research demonstrated that higher D-dimer level (>500ng/ml) in late gestation was an independent risk factor for PPH, being an indirect evidence of enhanced coagulation, as highlighted by previous studies[22]. In our research population, demographic risk factors for PPH were a BMI of >26 & multiparity as also reported previously by several studies [14–19].

CONCLUSION

In our research, 64.1 percent of women with PPH had DD levels greater than 500ng/ml, whereas only 35% of patients with PPH had DD levels less than 500ng/ml, indicating that a high DD level in late pregnancy is an independent risk factor for PPH. Before a more logical conclusion can be formed, additional research including other diagnostic factors, as well as large population-based studies are required.

ETHICS APPROVAL: The ERC gave ethical review approval

CONSENT TO PARTICIPATE: written and verbal consent was taken from subjects and next of kin

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