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Assessment of Hemostasis Status in Non-pregnant vs Pregnant Indian Women: A Comparative Analysis

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ABSTRACT

background: Pregnancy induces a hypercoagulable state, likely as an adaptive response to sustain placental function and mitigate excessive bleeding during childbirth, but it may elevate the risk of thromboembolism in predisposed women. This study evaluated hemostatic parameters across different trimesters in normal pregnancies and compared them with those in non-pregnant women.

Methods: This prospective cross-sectional study involved 148 participants. The control group of 37 non-pregnant women was matched with 37 pregnant women in each trimester (1st, 2nd, and 3rd trimesters). Hemostatic parameters assessed included prothrombin time (PT), activated partial thromboplastin time (aPTT), platelet count (PLT), and fibrinogen (Fb). Data were expressed as means and standard deviations, and statistical analyses were conducted using Student's t-test and ANOVA, with SPSS software version 19. A p-value of <0.05 was deemed significant.

Results: The PT showed a significant reduction in the third trimester compared to non-pregnant controls, with a gradual decline from the first to the third trimester. The aPTT was significantly lower across all trimesters compared to non-pregnant controls. PLT significantly decreased in the second and third trimesters compared to controls. Fb levels significantly increased in all trimesters relative to non-pregnant controls.

Conclusion: The findings suggest that normal pregnant Indian women exhibit changes in the coagulation system indicative of a persistent low-grade intravascular coagulation process, particularly in the third trimester. Consequently, coagulation studies are recommended for all pregnant women, especially those at risk for hypercoagulable states.

Key-words: Hemostasis, Pregnancy, Platelet, Fibrinogen, Multifaceted process

INTRODUCTION

Hemostasis is a multifaceted process involving numerous interactions characterized by positive and negative feedback mechanisms, incorporating blood vessels, platelets, coagulation factors, inhibitors, and fibrinolysis to uphold vascular integrity.

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Significant alterations occur within the TF pathway and the broader hemostatic system during a normal pregnancy. These changes are generally understood to prepare the body for the hemostatic demands of childbirth, with the system reverting to its non-pregnant state around four weeks post-delivery [1].

Pregnancy leads to an elevation in levels of coagulation factors I, VII, IX, X, and XII, creating a hypercoagulable state. This heightened coagulability during pregnancy, corroborated by thromboelastography, is primarily attributed to increased production of factor VII and fibrinogen (Fb). Virchow's Triad, encompassing increased venous stasis, coagulability factors, and endothelial damage, promotes thrombus formation during

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pregnancy. The likelihood of thromboembolism is quintupled during pregnancy [2-5].

A study conducted in Western India indicated that the incidence of thromboembolism in pregnant Indian women is comparable to that in Western populations [6]. However, limited research has been conducted in India to evaluate the relationship between coagulation parameters and different pregnancy trimesters, or the balance between coagulation and fibrinolysis during a typical pregnancy [7,8]. Additionally, existing literature is predominantly based on studies involving African, European, or other Asian populations. To our knowledge, no established reference ranges exist for the coagulation profile of normal pregnant women in India. Consequently, while interpreting the coagulation profiles of pregnant women across different trimesters, the hemostatic ranges for non-pregnant women are often used. This study was proposed to evaluate the impact of normal, uncomplicated pregnancy on selected coagulation parameters.

MATERIALS AND METHODS

Study Design- This prospective cross-sectional study was carried out and included 148 participants in total.

Inclusion Criteria- 37 normal pregnant women, serving as controls, were matched with 37 pregnant women in each trimester (1st, 2nd, and 3rd trimesters). The participants were non-smokers. Subjects were recruited from both outpatient and inpatient departments.

Exclusion Criteria- Individuals with coagulopathy or on medications affecting coagulation profiles, such as aspirin and clopidogrel, were excluded. Additionally, women with obesity (BMI >40), liver and kidney diseases, or other conditions potentially impacting coagulation parameters were not included.

Study Procedure- Participants were briefed on the study protocol, and general physical, systemic, and obstetric examinations were conducted. Six ml of blood were drawn from the antecubital vein under aseptic conditions. 4.5 mL was mixed with 0.5 mL of 3.2% trisodium citrate and centrifuged at 2500 rpm for 15 minutes to obtain platelet-poor plasma. The plasma was aspirated using a plastic Pasteur pipette and transferred to plastic tubes for the determination of prothrombin time (PT), activated partial thromboplastin time (aPTT), and fibrinogen (Fb) levels. The remaining 1.5 mL of blood was placed into an EDTA container for platelet count (PLT) determination.

Hemostatic parameters were measured in the hospital laboratory as follows:

PT: measured using the photo-optical clot detection method.

aPTT: measured using the electro-mechanical clot detection method.

PLT: measured using the cell counter (electro impedance) method.

Fb level: measured using the photo-optical clot detection method.

Statistical Analysis- Data were recorded and analyzed using the Statistical Package for the Social Sciences (SPSS) version 19.0. Statistical analyses were performed using Student's t-test and one-way analysis of variance (ANOVA). A p-value of <0.05 was considered statistically significant, while a p-value of >0.05 was considered not significant.

RESULTS

Table 1 presents the values of coagulation parameters in non-pregnant women (Group 1) compared to pregnant women in the first, second, and third trimesters. The analysis reveals that PT is relatively stable across the trimesters, with no significant differences observed between the non-pregnant group and the first trimester. However, PT decreases significantly from the second to the third trimester ($p<0.05$). In contrast, aPTT shows a decreasing trend across trimesters, with statistically significant reductions from the non-pregnant state to each trimester ($p <0.05$ for Group 1 vs. Group 2, and $p<0.01$ for Group 2 vs. Group 3, and Group 3 vs. Group 4). Platelet count decreases from the first to the second trimester and remains relatively stable after that, with significant differences between the first and second trimesters ($p<0.05$) and the second and third trimesters ($p<0.05$). Fibrinogen levels increase progressively from the first to the third trimester, with significant differences noted between each trimester ($p<0.05$ for Group 1 vs. Group 2, and $p<0.01$ for Group 2 vs. Group 3, and Group 3 vs. Group 4).

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Table 1: Coagulation profile in non-pregnant vs pregnant women in various trimesters

Parameter	Group 1: NP (Mean±SD)	Group 2: First Trim (Mean±SD)	Group 3: Second Trim (Mean±SD)	Group 4: Third Trim (Mean±SD)	p-value (Group 1 vs Group 2)	p-value (Group 2 vs Group 3)	p-value (Group 3 vs Group 4)
PT (Sec)	11.68±1.14	11.53±1.29	11.28±1.55	11.16±1.49	0.28	0.15	<0.05
aPTT (Sec)	36.15±1.90	36.00±2.20	35.60±2.05	34.85±2.60	<0.05	<0.01	<0.01
PLT (lacs/mm³)	2.31±0.32	2.25±0.23	2.19±0.20	2.22±0.18	0.31	<0.05	<0.05
Fb (g/l)	3.27±0.80	3.78±1.10	4.10±0.80	4.38±1.02	<0.05	<0.01	<0.01

Table 2 details the changes in coagulation parameters across the trimesters. PT and aPTT exhibit relatively stable trends with no significant overall changes throughout the trimesters (p=0.65 for PT and p=0.34 for aPTT). Platelet count shows a minor but not statistically significant decline overall (p=0.18). Fibrinogen levels demonstrate a progressive increase across the trimesters, although this change is not statistically significant when considering the overall trimester progression (p=0.10).

Table 2: Changes in coagulation profile with trimester progress

Parameter	First Trim (Mean±SD)	Second Trim (Mean±SD)	Third Trim (Mean±SD)	p-value (Overall)
PT (Sec)	11.49±1.28	11.29±1.56	11.13±1.49	0.65
aPTT (Sec)	35.80±2.20	35.60±2.05	34.90±2.50	0.34
PLT (lacs/mm³)	2.27±0.23	2.18±0.18	2.20±0.16	0.18
Fb (g/l)	3.85±1.06	4.12±0.74	4.38±1.00	0.10

DISCUSSION

This study aimed to investigate hemostatic variations throughout the first, second, and third trimesters of pregnancy. The hemostatic parameters compared between pregnant and non-pregnant women included PT, aPTT, PLT, and Fb. Significant decreases in PT, aPTT, and PLT were observed in the third trimester, while Fb consistently increased across all trimesters as the pregnancy progressed.

PT, which evaluates the extrinsic coagulation pathway and is sensitive to factors VII, X, V, II, and Fb, showed a progressive decrease from the first to the third trimester, with a significant change only in the third trimester compared to controls. No significant differences were found among the PT values of the first, second, and third trimesters. The decreased PT in this study can be attributed to the activation of coagulation during pregnancy, especially in the third trimester [9]. These findings align with other studies [10].

However, Shrimala *et al.* found increased PT values in normal pregnant women compared to non-pregnant controls [11], while Chen et al. reported a significant decrease in PT in early pregnancy [12]. Contrarily, Buseri et al. and Avwioro et al. observed increased PT in Nigerian pregnant women [13,14].

aPTT, which assesses the intrinsic pathway of coagulation and is sensitive to deficiencies in factors I, II, VIII, IX, X, XI, and XII, was significantly lower in all trimesters compared to non-pregnant controls. This result is consistent with other studies [15-17]. However, no significant differences were found among the aPTT values of the first, second, and third trimesters. Similarly, Szecsi et al. found no significant differences in aPTT during various gestational weeks [18]. The decreased aPTT observed in this study may be due to the rapid activation of coagulation factors within the intrinsic pathway [9].

The study also found a gradual reduction in PLT as pregnancy progressed, with statistically significant

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differences only observed in the second and third trimesters compared to controls. No significant differences were found among the PLT values of the first, second, and third trimesters. This finding aligns with studies by James *et al.* [19], Akinbami *et al.* [20] and Ajibola *et al.* [21]. The reduction in PLT may be due to increased blood volume, enhanced platelet activation, and decreased lifespan within the uteroplacental circulation [22-24].

Fb levels showed a consistent and significant increase from the first to the third trimesters compared to non-pregnant controls, with no significant differences among the trimesters. Similar findings were reported by Olomu *et al.* [17] and Szecsi *et al.* [18]. Hammarova et al. observed significantly increased Fb levels only in the third trimester despite consistent increases in all trimesters [25]. Momodu and Ajayi found significant increases in Fb levels in all trimesters in pregnant women from Northern Nigeria compared to non-pregnant controls [26]. The increased Fb concentration during pregnancy in this study may be due to increased Fb synthesis for uteroplacental circulation or hormonal changes such as elevated progesterone levels [27].

The findings suggest that the third trimester is characterized by maximum coagulation activation, reduced fibrinolytic activity, and evident thrombocytopenia, creating a pro-coagulant state to minimize blood loss during labor. However, this situation may predispose pregnant women to conditions related to pregnancy, especially in the third trimester, as suggested by other studies [10]. The increased Fb levels may predispose pregnant women to thromboembolic events, although no actual evidence of such events was observed in this study.

This study focused on specific hemostatic parameters, excluding fibrinolytic parameters such as d-dimer and fibrin degradation products. Despite this limitation, the study provides valuable insights into the physiological changes in hemostasis in normal pregnant Indian women during different trimesters. The results underscore the need to establish reference ranges for hemostatic parameters in normal pregnant women.

CONCLUSIONS

A state of physiological low-grade intravascular coagulation characterizes normal pregnancy. PT and aPTT decrease as pregnancy progress, while fibrinogen (Fb) levels increase. These changes become particularly pronounced in the third trimester, a pro-coagulant stage. Although platelet (PLT) counts decrease during the third trimester, they do not fall to levels that would cause bleeding events. While coagulation parameter values in pregnant women are comparable to those in non-pregnant women, there are notable differences. Therefore, population studies must establish normal reference ranges for coagulation parameters in pregnant Indian women. This information would greatly assist healthcare professionals in diagnosing and treating related conditions, particularly thrombotic disorders during pregnancy.

CONTRIBUTION OF AUTHORS

Research concept- Ayushi Shrivastava, Vidushee Upadhyay
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