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COAGULATION PROFILE IN DIFFERENT TRIMESTERS AMONG PREGNANT WOMEN IN AL-BAHA: SAUDI ARABIA

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***Abstract*:**

Physiological alterations occur in the coagulation and fibrinolytic systems of pregnant women compared to that of healthy non-pregnant women which is associated with a shortened in the prothrombin time (PT) and the activated partial thromboplastin time (APTT) leading to a hypercoagulable state particularly during the third trimester which protect pregnant women from probable excessive bleeding at the delivery and post-partum periods. Our study aimed to identify alterations in the coagulation profile of pregnant women throughout their pregnancy compared to non-pregnant women. ***Method:*** *analytical cross-sectional study at Antenatal Care (ANC) Clinic of the Baljurashi Maternity and Children's Hospital; Al-Baha; Saudi Arabia Coagulation profile of 75 healthy pregnant women and 50 healthy non-pregnant women were studied.* ***Results****: The mean age ± Standard deviation (SD) was found to be 25.12 ± 3.65 years for the pregnant women and 26 ± 4.3 years for the non-pregnant women. The mean value of platelet in non- pregnant women were (280 ± 10.14 × 10^3/ml) and in pregnant women in the 1st (272.55 ± 11.56 × 10^3/ml), 2nd (254. 35 ± 14.01 × 10^3/ml), and 3rd (237.50 ± 12.29 × 10^3/ml) trimesters. the mean values of prothrombin time was significantly decreased compared to non-pregnant women and as the pregnancy progress through different trimester with reported values of 10.8±0.68, 10.3±0.74, 10.1±0.65 and 9.5±0.59 seconds respectively (P=0.001). Similarly, values of INR showed significant decrease with values 0.87±0.05, 0.86±0.08, 0.83±0.06 and 0.80±0.07 respectively (P=0.001).*

Conclusions*: pregnancy shortens the coagulation profile with a resultant of a transient hypercoagulable state.*

Recommendation*: trimester-specific coagulation profile assessment are essential for the accurate judgment of haemostatic status during pregnancy.*

Keywords*: Pregnant women, puerperium, Coagulation profiles, Activated Partial Thromboplastin, Prothrombin Time, Thrombocytopenia, Al-Baha; Saudi Arabia*

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INTRODUCTION:

Normal pregnancy is associated with physiological alterations in the coagulation and fibrinolytic systems that result in a hypercoagulable and hypofibrinolytic state that serves to protect the mother from bleeding complications at the time of placental separation [1-3]. Pregnancy is typically divided into three trimesters, each lasting about three months. Each trimester comes with its own set of changes and developments for both the mother and the growing fetus. Pregnant women during the trimesters of pregnancy often experience an increase in several clotting factors, such as fibrinogen, factors VII, VIII, IX, and X. These changes are meant to prepare the body for potential blood loss during childbirth with decreased levels of natural anticoagulants such as antithrombin III and protein S this reduction helps to maintain a balance between clotting and preventing excessive bleeding. Again during pregnancy there is an increase in fibrinolytic activity, which is important in preventing excessive clot formation [4-10].

Despite the increased levels of clotting factors, some coagulation tests, such as the activated partial thromboplastin time (aPTT) and prothrombin time (PT), may be slightly prolonged during pregnancy due to changes in the concentration of certain clotting factors. While the number of platelets usually remains stable or slightly decreases during pregnancy, their function may be altered, potentially becoming more adhesive. Thrombocytopenia is the most common haemostatic abnormality observed in late pregnancy [11-17].

It's essential to note that these changes are part of the normal physiological adaptations during pregnancy and are generally not indicative of any pathology. However, they can pose a challenge in diagnosing and managing thrombotic or bleeding disorders in pregnant individuals because the interpretation of coagulation tests can be different compared to non-pregnant individuals. Therefore, it's essential for pregnant women to receive proper prenatal care and for healthcare providers to monitor their coagulation profile regularly to ensure a safe pregnancy and delivery and to detect any abnormalities that might require intervention, especially in individuals with additional risk factors like a history of blood clotting disorders or immobility [18-22]. Any concerns or deviations from the expected changes may prompt further investigation or management by healthcare providers. The current study designed to assess certain coagulation parameters such as PT, INR, APTT, and platelet count in healthy pregnant women throughout their trimesters of pregnancy and compare them to non- pregnant women.

MATERIALS & METHODS:

Study Area, Design, and Period:

A hospital- based comparative and analytical cross-sectional study was conducted at Antenatal Care (ANC) Clinic of the Baljurashi Maternity and Children's Hospital; Al-Baha; Saudi Arabia over a period of three months from February to April 2023. The hospital serves as the tertiary referral hospital for Baljurashi and its related areas and is one of the largest healthcare facility in Al-Baha.

Study Population

The study population were previous hospital records of two groups who had visited the outpatient at Baljurashi Maternity and Children's Hospital; Al-Baha; Saudi Arabia during the three-month period prior to the study.; the first group include healthy pregnant women at any gestational age who underwent prenatal tests as a routine antenatal clinic for monitoring of their pregnancy. The second group include non-pregnant women who underwent normal physical examination.

Eligibility criteria:

Hospital reports of the participants who met the following criteria were incorporated in the study such as: women in aged 18 to 45 and in pregnancy at any trimester; with no history of coagulation

disorders or of liver and kidney diseases; and drugs that disturb coagulation and fibrinolytic system.While excluding multiple pregnancies (e.g., twins, triplets) due to potential variations in coagulation profiles.

Study Sample

Among the study population, 75 healthy pregnant women and another 75 records of healthy non pregnant women who fulfilled the inclusion criteria were selected as study sample using systematic random sampling. The demographic, clinical and laboratory data were retrieved from the electronic records of Baljurashi Maternity and Children's Hospital; Al-Baha; Saudi Arabia. Data of study sample were gathered and compared between the pregnant and non-pregnant women according to their age, gestational age, and coagulation profile. The coagulation parameters were compared according to gestational trimester.

Data Collection and Laboratory processing

Assessing the coagulation profile is crucial in diagnosing and managing various bleeding or clotting disorders. Several laboratory methods are commonly used to evaluate coagulation. Following standard operating procedures (SOPs) and an aseptic technique five milliliters (mL) of venous blood was collected by qualified laboratory staff. The blood sample was divided into two test tubes. 3 ml in a tube containing 0.3 mL of the 3.2% sodium citrate. From which a platelet-poor plasma (PPP) was obtained by centrifugation at 1500 rpm for 15 minutes for analysis of coagulation profile (APTT, PT, and INR) using the HumaClot Junior coagulation analyzer (Wiesbaden, Germany).The 2 ml were contained in a tube containing an EDTA anticoagulated and mixed well for platelet parameters using Sysmex XN-3000 automated hematology analyzer (Sysmex, Kobe, Japan). The PT≥14 seconds was considered prolonged PT. INR of ≥1.3 was categorized as increased, APTT of ≥32 seconds was considered prolonged and D-Dimers of ≥0.5 was labelled as raised Similarly, the platelet count was categorized as normal ≥150x103/ul and low <150x103/ ul**.**

Data Analysis:

The data was collected in Microsoft excel and descriptive analysis was performed on all the variables of coagulation profile and were compared between healthy pregnant and non- pregnant women.

Quantitative parameters like Mean Platelet Volume (MPV), Platelet counts, Activated Partial Thromboplastin Time (APTT), Prothrombin Time (PT) and INR were presented as Mean± SD. Qualitative data was expressed as number and percentage. The final analysis was done using statistical package for social sciences (SPSS) software, version 21.0. For statistical significance, p value of less than 0.05 was considered statistically significant.

RESULTS:

One hundred twenty five laboratory records of a healthy women who attended Antenatal Care (ANC) Clinic of the Baljurashi Maternity and Children's Hospital; Al-Baha; Saudi Arabia over period of study were selected to be enrolled as study subjects. Twenty -three were excluded owing to a technical error in running samples, clerical errors, incomplete data or medical/surgical complications. The remaining data of one hundred twenty five study subjects were grouped into fifty none pregnant women as the first group which regarded as a control group. Of the reaming study subjects; seventy five pregnant women were considered as a study cases and grouped according to the trimesters depending on the gestational age in weeks ; those with gestational age of 0–13 weeks were considered as a first trimester group with 18 pregnant women , those with gestational age of 14–27 weeks were considered as a second trimester grouo with 26 pregnant women. And the third trimester group with a gestational age of ≥28 weeks; with 31 pregnant women. The mean age ± Standard deviation (SD) was found to be 25.12 ± 3.65 years for the pregnant women and 26 ± 4.3 years for the non-pregnant women. There is no significant difference in age between of pregnant and non-pregnant women (P. value 0.365) as shown in Table (1) below.

Table 1: Age distribution according to the study groups

Age (years)	Study groups		P-value
	Cases/ N (%)	Control/ N (%)	
Mean age ± Standard deviation (SD)	25 ± 5.6	26 ± 4.3	0.365
18-28	38(50.7 %)	35(46.7%)	
29-39	27(36 %)	27(36%)	
40-50	10(13.3 %)	13(17.3%0	

Platelets Counts among Study Participants:

As shown in Fig.(1) below the mean value of platelet in non- pregnant women were (280 ± 10.14 × 10^3/ml) and in pregnant women in the 1st (272.55 ± 11.56 × 10^3/ml), 2nd (254. 35 ± 14.01 × 10^3/ml), and 3rd (237.50 ± 12.29 × 10^3/ml) trimesters. The mean platelet decreases significantly in different trimester when compared with non-pregnant women (P=0.014).

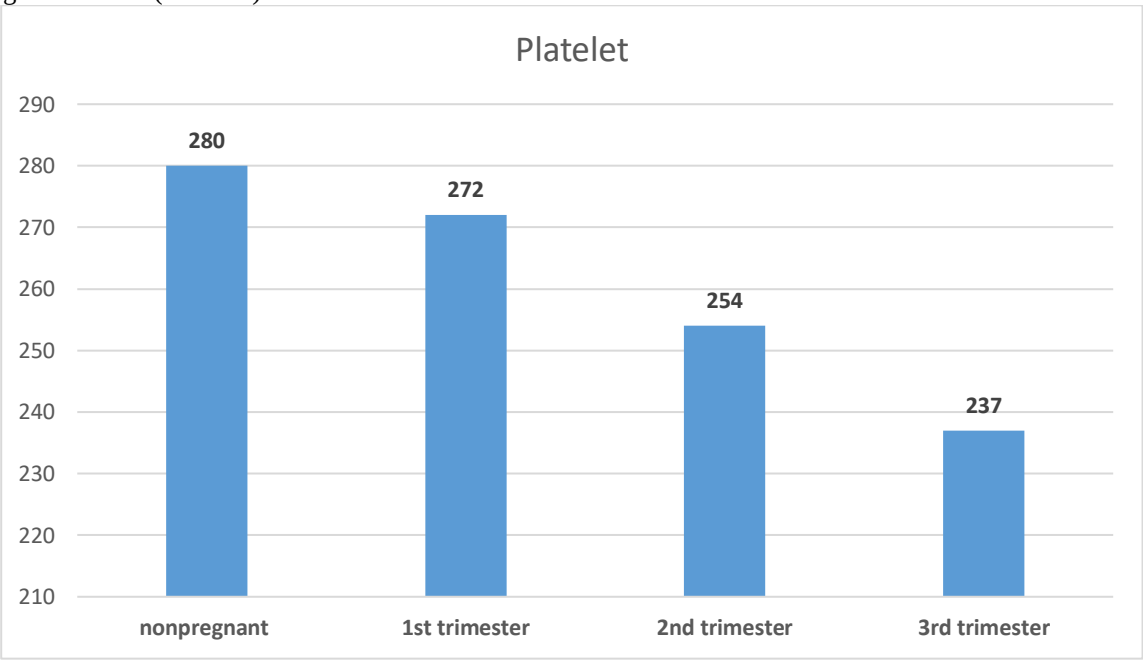

Fig. 1: Platelets Counts among Study Participants

Changes of Coagulation profile of Study Subjects.

Table (2) below show reported values of coagulation profile in our study, the mean values of prothrombin time was significantly decreased compared to non-pregnant women and as the pregnancy progress through different trimester with reported values of 10.8±0.68, 10.3±0.74, 10.1±0.65 and 9.5±0.59 seconds respectively (P=0.001). Similarly, values of INR showed significant decrease with values 0.87±0.05, 0.86±0.08, 0.83±0.06 and 0.80±0.07 respectively (P=0.001). However, APTT recorded no significant differences among different study groups (P=0.325).

Table 2: Coagulation Profile of the study population

Parameter	Non-Pregnant (n=50)	Pregnant according to trimester			P-value
		First (n=35)	Second (n=35)	Third (n=35)	
PT (second) Range (min-max)	10.8±0.68 9.40-13.10	10.3±0.74 9.40-13.00	10.1±0.65 9.00-12.60	9.5±0.59 8.70-12.30	0.001
APTT (second) Range (min-max)	33.68±0.58 30.20-40.70	31.4±5.1 27.20-39.10	30.9±5.0 27.60-39.10	30.4±4.6 25.20-44.50	0.325
INR Range *(min-max)*	0.87±0.05 0.72-0.91	0.86±0.08 0.71-1.00	0.83±0.06 0.74-0.92	0.80±0.07 0.72-0.95	0.001

PT: Prothrombin Time. INR: International Normalized Ratio. APTT: Activated Partial Thromboplastin Time. All values were tabulated as mean ±SD. P<0.05: Significant, P>0.05: Not significant.

DISCUSSION:

The coagulation system is a complex phenomenon affected by many factors physiological, lifestyle and environmental of these pregnancy is by far the most important one. During pregnancy, the coagulation system experiences significant alterations, these changes help in keeping placental function during pregnancy, protects from fetal hemorrhage during delivery, but at the same time predisposes to thromboembolism. Thrombophilia predisposes a woman to an increased risk of developing both early and late complications in pregnancy. This includes recurrent miscarriages and late placental vascular-mediated problems (fetal loss, preeclampsia, placental abruption, and intrauterine growth restriction. [23-27]. PT/INR detects disorders of the extrinsic and common coagulation pathways. Abnormal result is usually seen when factor I, II, V, VII, X are deficient while the aPTT looks for abnormalities of the intrinsic and common coagulation pathways. It monitors the activities of FI, II, V, VIII, IX, X, XI, XII11. Although routine coagulation profile parameters such as activated partial thromboplastin time (aPTT) and prothrombin time (PT/INR) mainly were used in monitoring anticoagulants such as heparin and warfarin respectively, but can give a clue for predicting the bleeding, thrombotic or cardiovascular risk in many conditions such as pregnancy . Due to physiological modifications during pregnancy, coagulation factors fail to be produced properly leading to a decrease in PT and Aptt.

Mean age of the study participant was found to be among pregnant women 25 ± 5.6 years and among non-pregnant women was found to be 26± 4.3 years and p value was 0.365 (>0.05). There was no significant difference between the age of study group which can be suitable to be used as cases and controls. In this cross sectional study assessment of the PT, APTT , INR levels and Platelet count of seventy five pregnant women during their different trimesters of pregnancy and fifty non pregnant women was done. PT mirrors extrinsic coagulation pathway. The mean values of prothrombin time was significantly decreased compared to non-pregnant women and as the pregnancy progress through different trimester with reported values of 10.8±0.68, 10.3±0.74, 10.1±0.65 and 9.5±0.59 seconds respectively (P=0.001). The reference intervals of PT were 11.90–13.85 s, 10.41–14.04 s, 9.70–12.64 s, and 9.20–11.95 s in the non-pregnant, first-trimester, second-trimester, and third-trimester groups, respectively. Variability in PT results among various studies may be related to the sensitivities of the reagents (thromboplastin) and techniques used (concentration of citrate anticoagulation, and method of analysis). For these reasons international normalized ratio (INR) come in use. In our study values of INR showed significant decrease among non- pregnant women compared to pregnant women in their different trimester (0.87±0.05, 0.86±0.08, 0.83±0.06 and 0.80±0.07 respectively (P=0.001). This is in agreement with many related studies [28-32]. APTT mainly mirrors intrinsic coagulation pathway. Due to the hypercoagulable state during pregnancy may lead to the decreasing trend of APTT with the gestational age. However, APTT among our study group recorded no significant differences among different study groups (P=0.325) [33-36].The

platelets count tends to fall progressively during normal pregnancy, although it usually remains within normal limits. In some pregnant women (5–10%), the count may reach levels of <150 × 10^9 cells/l at the third trimester in the absence of any pathological alteration this may be due to haemodilution with raised platelet activation, and reduced lifespan of platelets specially in late trimesters . Therefore a pregnant women woman is not considered to be thrombocytopenic until the platelet count is less than 100 × 10^3/ml. Our study revealed that the mean value of platelet among non-pregnant and pregnant women were (280 ± 10.14 × 10^3/ml) and254 ± 15.94 × 10^3/ml) respectively i.e the platelet counts in nonpregnant women were significantly higher than that of the pregnant women. These confirms the findings by many other studies [8, 15, 16]

CONCLUSION:

Our study has concluded that pregnancy shortens the coagulation profile with a resultant of a transient hypercoagulable state. This benefits in preventing excessive maternal bleeding during pregnancy and delivery. Therefore, timely assessment of coagulation profile is encouraged to monitor pregnancy and prevent associated hemorrhagic complications.

Recommendation: trimester-specific coagulation profile assessment are essential for the accurate judgment of haemostatic status during pregnancy**.** Thus, it is important to do PT, INR, APTT and platelet count to every pregnant women as a routine test to improve pregnancy outcome. In addition, there is lack of research on hematologic changes during pregnancy in Al-Baha, Saudi Arabia.so it is advice to direct researches to deal with this topic.

Limitations of the study*:* The limitations of our study should be addressed including a single center study with a small sample size.

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