MEDICAL SCIENCES

ESTIMATION OF HEMATOLOGICAL PARAMETERS AND VITAMIN D LEVEL AMONG SUDANESE WOMEN WITH HYPERTENSIVE PREGNANCY

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Abstract

Background:

Hypertension is the most common medical disorder occurring during pregnancy; also it is the leading cause of maternal and fetal morbidity. This study aimed to estimate PT, APTT, D-dimer, protein C, protein S, and vitamin D levels among Sudanese Women with hypertensive Disorders of Pregnancy.

Materials and methods:

This was a case-control hospital-based study conducted at the Omdurman Maternity Hospital Laboratory in Khartoum, Sudan, between January and March 2023. The study population included all patients diagnosed with hypertensive disorders of pregnancy at the hospital, while, healthy women were included as a control group. PT, APTT, protein-C, protein-S, D dimer, folate, serum ferritin, and Vitamin D levels were conducted using a coagulometer analyzer (RT 2220) and the ELISA (direct) technique. SPSS version 23 statistical software was used for statistical analysis.

Results:

The results revealed that; in the case group; the mean of age was (30.8±6.9), 20% of the participants had a history of abortion for one time, 26.7% had pregnancy for the first time, 50% were diagnosed with preeclampsia, 50% were diagnosed with eclampsia, 63% had a family history of hypertension. Insignificant differences in the results of PT and APTT, D dimer, and ferritin levels. Significant decrease in protein C and protein S folate levels, vitamin D levels, and all the parameters negatively correlated with age.

Conclusion:

In conclusion, our study on hypertensive pregnant women highlights critical findings regarding hemostatic and nutritional factors. While we observed insignificant differences in prothrombin time (PT), activated partial thromboplastin time (APTT), D-dimer, and ferritin levels, the significant decrease in protein C and protein S levels, as well as folate and vitamin D levels, warrant attention.

Keywords: hypertension, pregnancy, D-dimer, Ferritin, vitamin D.

Introduction:

Hypertension is characterized as a medical condition where arterial blood pressure exceeds 140 over 90 mmHg [1]. This prevalent condition results in a sustained high force of blood against artery walls, potentially leading to serious health issues such as heart disease [2,3,4]. Additionally, high blood pressure can complicate both delivery and postpartum recovery. Notably, hypertensive disorders during pregnancy are frequently preventable and manageable. In the United States, high blood pressure affects approximately one in every 12 to 17 pregnancies among women aged 20 to 44 [5], prompting the American Heart Association and the European Society of Cardiology to revise guidelines to recognize these disorders as significant risk factors for cardiovascular disease in women [5,6]. In Sudan, the prevalence of hypertension exceeds 34%, aligning with recent studies indicating rates between 35.2% and 41.0% among the general population [7,8]. A particularly high prevalence of 41.0% has been observed among females in Eastern Sudan [8]. Furthermore, Sudanese women often experience high parity, with many having five or more deliveries at a young age, typically before 35 years [9]. The Activated Partial Thromboplastin Time (APTT) test assesses the activity of endogenous blood coagulation, focusing on factors

IX, XI, and XII, and is crucial for monitoring heparin therapy [10,11]. In cases of pregnancy-induced hypertension, there is an exacerbation of a hypercoagulable state due to endothelial injury [12]. Protein C is a vitamin K-dependent glycoprotein with a molecular weight of 62 kD, synthesized by the liver in its zymogen form. It becomes activated upon binding to the thrombin-thrombomodulin complex, with protein S serving as a cofactor. As a natural anticoagulant, a deficiency in protein C, whether homozygous or heterozygous, increases the risk of thrombosis, particularly venous thromboembolism, and can lead to conditions such as myocardial infarction, deep venous thrombosis, pulmonary embolism, or stroke [13]. Deficiencies in protein C and protein S are inherited as autosomal dominanttraits and are commonly associated with recurrent venous thromboembolism, often resulting from heterozygous missense mutations. Ferritin, on the other hand, serves as the primary iron storage protein in the body, consisting of an apo protein shell with a molecular weight of 480,000 that encases a core of iron in the form of ferric hydroxy-phosphate, potentially containing up to 4,500 iron atoms. While ferritin is soluble, it can degrade into the insoluble form known as haemosiderin, which accumulates in lysosomes and is recognized as 'stainable iron' by pathologists and hematologists. Typically, the body stores approximately 1 g of iron in men and less in women, primarily in the form of ferritin; however, with increased iron overload, the amount stored as haemosiderin rises. Human ferritin comprises two subunit types: H and L. The H subunits, weighing 21,000, are found in more acidic isoforms in various tissues, including the heart and red blood cells, while the L subunits, with a molecular weight of 19,000, are predominant in the more basic isoforms located in theliver, spleen, and placenta. The variation in the H to L subunit ratio accounts for the charge heterogeneity of ferritin, which can be effectively demonstrated through isoelectric focusing. Notably, the isoelectric point of ferritin remains largely unaffected by its iron content, which varies across different tissues [14].

Folic acid (FA), derived from the Latin term 'folium' which translates to 'leaf', is a synthetic variant of folate essential for cellular development and various biochemical processes, including demethylation reactions involved in DNA synthesis and the remethylation of homocysteine to methionine. It is commonly utilized in dietary supplements due to its stability. While folate is naturally present in foods such as dark green leafy vegetables, legumes, and oranges, many individuals fail to meet the recommended daily intake of folate through diet alone. Consequently, it is advised that women who are planning or capable of becoming pregnant take periconceptional FA supplements (400–800μg/d) to decrease the incidence of fetal neural tube defects, which are a range of congenital abnormalities that can result in death or disability [15].

Vitamin D deficiency has reached epidemic levels globally, with prevalence rates varying from 18% to 84% based on factors such as country, ethnicity, and local customs regarding clothing and diet [16]. Hypertension is the most prevalent medical issue during pregnancy, affecting 5-10% of pregnancies [17]. During pregnancy, maternal vitamin D metabolism undergoes changes,

resulting in elevated levels of both the vitamin D binding protein (VDBP) and the active metabolite, 1,25-dihydroxyvitamin D (1,25(OH)2D). Clinical research has produced inconsistent findings regarding the relationship between vitamin D levels and negative pregnancy outcomes, including preeclampsia, gestational diabetes, low birth weight, preterm labor, and cesarean delivery. There is limited data on the prevalence of vitamin D deficiency during pregnancy in India [18]. Factor I, also known as fibrinogen, is a glycoprotein that plays a crucial role in the clotting process. This soluble form is transformed into fibrin through the action of thrombin during clot formation, with Factor XIII subsequently cross-linking fibrin strands to create a stable clot. D-dimers are generated during fibrinolysis as small protein fragments (FDP). Pregnancy is one of the conditions associated with a hypercoagulation state [19].

Results:

Sixty participants were enrolled in this study, thirty as a case group and thirty as a control group. The mean age in the case group was (30.8±6.9) and in the control group was (28.9±5.5). in the case group, 20% had a history of abortion for one time, 26.7% had pregnancy for the first time, 50% were diagnosed with preeclampsia and50% were diagnosed with eclampsia, in addition, 63% had a family history of hypertension (table1) (figure 1, 2.3,4).

Hematological Result:

In this study, the results revealed that; in the case group The means of PT was (23.13±12.969) APTT was (37.77±7.776), D dimer was (1.567±3.18536), protein C levels were (97.8± 23.4), protein S was (96.5±21.1), ferritin levels were (11.57±4.739), folate levels were (12.9± 3.7), and vitamin D levels were(7.97±5.617), in the control group the mean of PT (13.40±1.037), PTT(33.47±7.021), D dimer (33.47±7.021), protein C, and protein S were (83.6±13.7) (83.7±15.5) respectively, ferritin levels were (12.77±0.817), folate levels were (33.9±2.5) and Vitamin D levels were (7.03±3.810). When comparing the means of the parameters between the case and control group there were insignificant differences in PT, PTT, D dimer, and ferritin levels with (p-value≥0.05), and a significant decrease of protein C, protein S levels, folate levels, and Vitamin D levels with (p. v< 0.05). In addition, all the parameters had a negative correlation with age.

Table (1)

Descriptive Statistics

	N	Minimum	Maximum	Mean	Std. Deviation
Case					
Age	30	18	43	30.8	6.9
Control					
Age	30	18	40	28.9	5.5

Table (2)

Comparison of PT between case and control

Parameter	Study Population		P.value
	Case (n = 30)	Control (n = 30)	0.313
PT	23.13±12.969	13.40±1.037	

Table (3)

Correlations of age with PT

	PT	Age
PT	Pearson Correlation	-.101
	p.value	.595
N	30	30

Table (4)

Comparison of APTT between case and control

Parameter	Study Population		P.value
	Case (n = 30)	Control (n = 30)	0.106
APTT	37.77±7.776	33.47±7.021	

Table (5)

Correlations of age with APTT

	APTT	Age
APTT	Pearson Correlation	-.127
	p.value	.504
N	30	30

Table (6)

Comparison of D-dimer between case and control

Parameter	Study Population		P.value
	Case (n = 30)	Control (n = 30)	0.796
D-dimer	1.567±3.18536	0.3313±0.14212	

Table (7)

Correlations of age with D-dimer

	D-dimer	Age
D-dimer	Pearson Correlation	.-.163
	p.value	.391
N	30	30

Table (8)

Comparison of protein C and protein S between case and control

Parameters	**Study population**		**P. value**
	Case (n=30)	**Control (n=30)**	
Protein C	97.8 ± 23.4	83.6 ± 13.7	0.006*
Protein S	96.5 ± 21.1	83.7 ± 15.5	0.010*

Table (9)

Comparison of Ferritin between case and control

Parameter	Study Population		P.value
	Case (n = 30)	Control (n = 30)	0.531
Ferritin	13.37±1.217	12.77±0.817	

Table (10)

Correlations of age with Ferritin

	Ferritin	Age
Ferritin	Pearson Correlation	-.121
	p.value	.525
N	30	30

Table (11)

Comparison of folate level between case and control

Parameters	**Study population**		**P. value**
	Case (n=30)	**Control (n=30)**	
Folate	12.9 ± 3.7	33.9 ± 29.5	0.001*

Table (12)

Correlations of age with Folate

	Folate	Age
Folate	Pearson Correlation	-.071
	p.value	.710
N	30	30

Table (13)

Comparison of Vitamin D between case and control

Parameter	Study Population		P.value
	Case (n = 30)	Control (n = 30)	0.009
Vit D	7.97±5.617	7.03±3.810	

Table (14)

Correlations of age with Vitamin D

	Vit-D	Age
Vit-D	Pearson Correlation	.057
	p.value	.766
N	30	30

Table (15)

Correlations of age with protein C and protein S

		Age
Protein C	Pearson Correlation	-.091
	P. value	.633
Protein S	Pearson Correlation	-.193
	P. value	.307

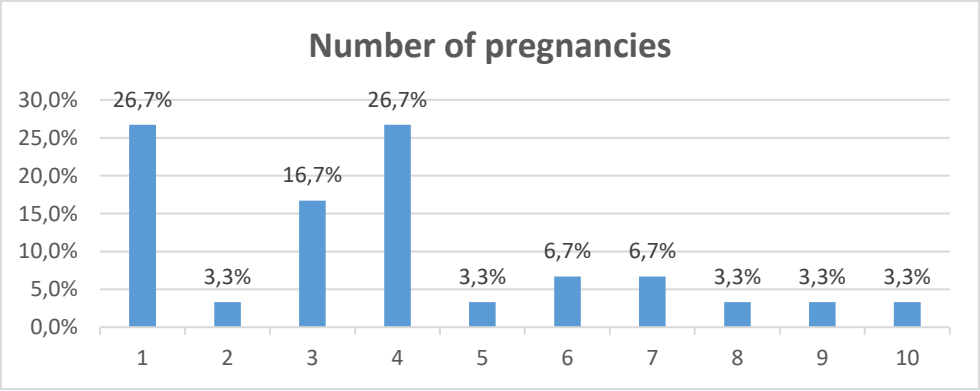

Figure (1): Distribution of number of pregnancies

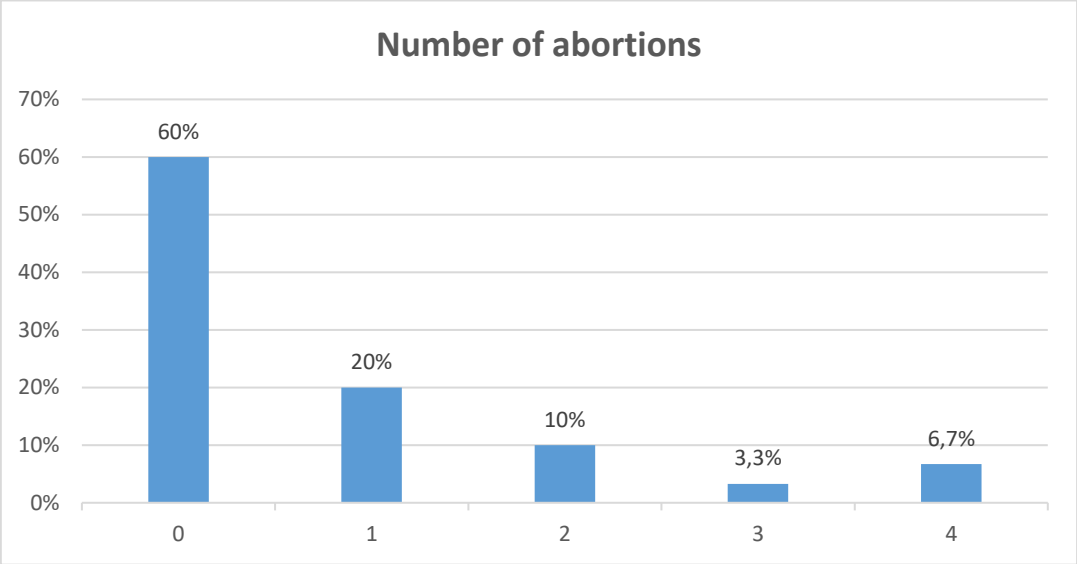

Figure (2): Distribution of abortion number

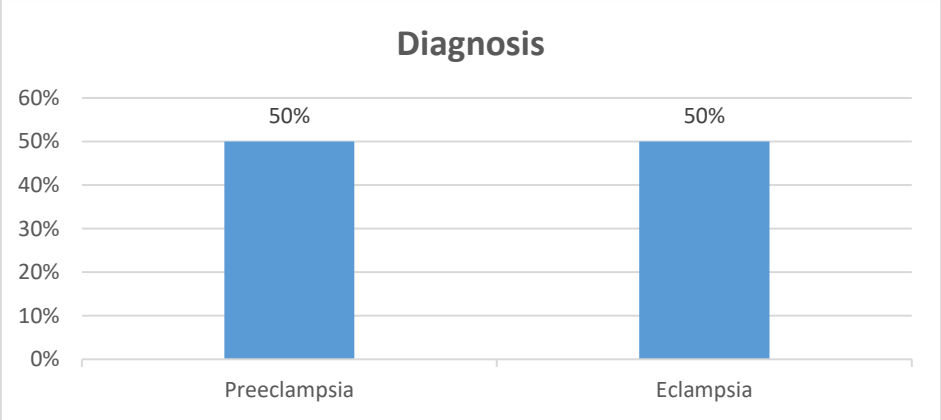

Figure (3): Distribution of Diagnosis

Discussion:

Hypertension is the most common medical disorder occurring during pregnancy, complicating 5% to 10% of all pregnancies, also it is the leading cause of maternal and fetal morbidity and mortality.[25]

This was a case-control hospital-based study conducted at the laboratory of the Omdurman maternity hospital - Khartoum, Sudan during the period January 2023 to March 2023, and aimed to estimate PT, APTT, D-dimer, protein C, protein S, and Vitamin D Levels among Sudanese Women with Hypertensive Disorders of pregnancy the results revealed that; in the case group; the mean of age was (30.8±6.9), 20% of the participants had a history of abortion for one time, 26.7% had pregnancy for the first time, 50% were diagnosed with preeclampsia, 50% were diagnosed with eclampsia, 63% had a family history of hypertension; this was agreed with those Tian ML, et al who reported the mean of age was (28.18±4.7) years. However, they contrast with findings from Shi P et al., which indicated that women aged 40 and above were the most affected group, with the risk of chronic hypertension.[26, 27] Also, Xiong, et al found in their study; that a highly participants had a history of abortion.[27] and Dumitrascu-Biris et al. mentioned that women who exhibited significant susceptibility to elevated blood pressure during the first trimester faced a greater risk of developing severe hypertension compared to those who maintained normal blood pressure, with a difference of 95%. [28]. Hinkosa et al. also found in their study that there was a significant correlation between hypertensive disorders of pregnancy and a family history of hypertension, with 63.3% of cases showing this association.[29] In the present study, there were insignificant differences in the results of PT and APTT, this finding agreed with Onisai et al., who observed no change in PT and APTT in their study.[30], and disagreed with FitzGerald et al. who found that APTT was prolonged in 32% of cases. [31] Regarding other coagulation parameters, D-dimer protein C and protein S, there were insignificant differences in D dimer and a significant decrease in protein C and protein S levels, in contrast to Kearon C et al results, who mentioned; D- dimer values were significantly increased throughout pregnancy. Overall, women with confirmed DVT had higher D-dimer levels than women without DVT [32], also Mohamedain et al reported D-dimer levels are often elevated in pregnancy in the absence of DVT. [32] However, Su, Y et al and Singh MD et al found there is a deficit in the protein C and protein S,a and often associated with an increased incidence of thrombotic disorders. [33, 34] In addition Ray JG et al study showed the levels of free and bound protein S decline in pregnancy

and the level of functional protein S remains at 40-50% of normal until the first few days after delivery.[35] On the other hand, Wei SQ et al mentioned that there are major changes in the levels of protein C in normal pregnancy or in the postpartum period, preeclampsia is associated with decreased levels of protein C but not with a further decrease in protein S level.[36] Also, this study showed insignificant differences in the ferritin levels and a significant decrease in folate levels, vitamin D levels, and all the parameters negatively correlated with age. These results consented with Eriksson L, et study which reported; that women of childbearing age (18–44 years) had a lower folate intake despite increasing intake of fruit and vegetables [36]. Also Social styrelsen et, al found there was a significant decrease in folate levels about 15% of women reported the use of folic acid supplements during early pregnancy in 2012, compared to about 1% in 1999 [37].

For the ferritin levels in this study, the results varied from others, Siddika A et, al revealed that ferritin serum levels in the second and third trimesters were significantly different [38]. Lao TT et, al and Irshad G et, al found that; ferritin serum level decreased consistently in the second trimester, up to 50% of the normal range, this change is caused by hemodilution and iron mobilization from the storage to fulfill the increasing iron need in pregnancy [39, 40]. Finally, Vitamin D results in the present study concurred with Wei, FAudibert et al who found, that 39% of women were vitamin D deficient, and there was a strong positive correlation with hypertensive pregnancy. [41],, also Rao it observed that the serum Vitamin D levels were significantly low with an increase in blood pressure, and the negative correlation between serum vitamin D and blood pressure moved the cases from the mild to the severe hypertension group. [42]

Conclusion:

In conclusion, our study on hypertensive pregnant women highlights critical findings regarding hemostatic and nutritional factors. While we observed insignificant differences in prothrombin time (PT), activated partialthromboplastin time (APTT), D-dimer, and ferritin levels, the significant decrease in protein C and protein S levels, as well as folate and vitamin D levels, warrants attention. These findings suggest a potential impairment in the coagulation pathway and nutritional deficiencies that could contribute to the complications associated with hypertension during pregnancy. The stability of PT and APTT indicates that conventional coagulation tests may not fully reflect the underlying hemostatic challenges faced by these patients. Therefore, monitoring protein C and S levels, along with folate and vitamin D status, may be crucial for better understanding the thrombotic risk and overall health of hypertensive pregnant women. Future research should aim to explore the clinical implications of these deficiencies and consider targeted interventions to improve maternal and fetal outcomes.

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