Assessment of von Willbrand Factor antigen level among 3rd trimester pregnant women

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Abstract

Background: Healthy pregnancy is usually associated with vast changes in blood clotting (hemostasis) and these changes are related to physiological adaptation, which ensures the blood stoppage when there is injury or during placenta separation. However, these changes may predispose them to thromboembolism during pregnancy and the Delivery period. The objective of this study was to assess the changes that occur in hemostatic parameters in third trimester pregnant women, especially von Willbrand Factor. This study was performed at Zytona Hospital, Khartoum State, Sudan.

Materials and Methods: Thirty samples from the study group (pregnant) women and twenty from the control group (non-pregnant) women were randomly selected and verbal agreement was done. The age of the pregnant group were ranged from 17-39 to years, whereas the age of the non-pregnant group were ranged from 17 to 45 years. Blood samples collected in a trisodium citrate anticoagulant tube were taken from each woman. The von Willbrand Factor antigen was determined using a fully automated STA compact max analyzer.

Results: The results were analyzed using the SPSS program. For the pregnant group, the analysis showed a mean age of 26.97 with SD of ±6.14. The mean weight of the test group was 64.57 with SD of ±5.59. The mean value of von Willbrand factor was 172.77, show significant. In the control group, the analysis showed an age of 25.75 with SD of ±6.62. The mean weight of 61.2 with SD of ±7.71. The value of von Willbrand Factor was 92.75, which is insignificant.

Conclusion: In summary we concluded that according to our result there is association between plasma vwf level, pregnant and age, but the result show no significant association between vwf and Weight in the test group. But in control group was insignificant and showed no association with the parameters.

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1.1 Introduction

Hemostasis is a process in which blood loss or bleeding is stopped in the cooperation of multi-systems like endothelial, platelets, coagulation factors and fibrinolytic system; all these has work together to protect women from blood loss during miscarriage or childbirth. Normal pregnancy may occur in changes in the tissue factor pathway and lead to thrombosis or some other problems. (1,2,3)

Pregnancy is a risk factor for venous thrombosis and thromboembolism during normal pregnancy is 6 times higher than in the general female population of child-bearing age. Venous thromboembolism is the most common cause of maternal morbidity and mortality. (4,5)

A Study done by Abdel Galil et al showed significant elevation of plasma in the third trimester of pregnancy. (6) Another study done by Afnan Hashim in 2014 showed that there is a significant association between pregnancy and plasma VWF levels. (7)

Another study done by Daniella N. Drury Stewart et al in November 2014 They concluded that VWF:Ag is significantly increased during pregnancy." (8)

A Similar study done by Jill M jonsen et al, They concluded their study found VWF antigen and FVIII concentrate levels were all increased (significant) in the third trimester. (9)

2. Methodology

2.1. Study Design

Hospital based (cross sectional study).

2.2. Study area and period

This study was done during 2019 from March to June at Zytona hospital.

2.3. Study population

Sudanese pregnant Women from third trimester at different age and weight were recruited to participate in this study as well as non-pregnant women were enrolled as non-pregnant women (control group).

2.4. Inclusion criteria

All third trimester pregnant women.

2.5. Exclusion criteria

Pregnant with any disease or Drugs associated with a change in vWF level.

2.6. Sample size

The sample was collected from 30 third trimester pregnant women as (cases) and 20 normal individual non pregnant as (control).

2.7. Data collection

A questionnaire was filled for each patient by direct interviewing.

2.8. Ethical consideration

All patients were informed about the aim of the study and they gave their consent.

2.9. Method of blood sample collection

About 2.7ml of venous blood sample were collected using vacationer tube which contain 0.38% tri –sodium citrate and gently mixed and then separated immediately at 4500 rpm for 15 min after which platelet poor plasma (ppp) was collected in plain container and stored at -20 ˚C until analysis.

2.10. Estimation of Vwf: Ag

2.10.1. Test Principle

This assay is based on the change in turbidity of a microparticle suspension that is measured by photometry. A suspension of latex microplates, coated by covalent bonding with antibodies specific for VWF, is mixed with the test plasma whose VWF antigen level is to be assayed. An antigen-antibody reaction takes place, leading to an agglutination of the latex microparticles which induces an increase in turbidity of the reaction medium. This increase in turbidity is reflected by an increase in absorbance, the latter being measured photometrically. The increase in absorbance is a function of the VWF level present in the test sample.

2.10.2. Method

Referred to the "Standard Operating Procedures" of the instrument for full details on how to proceed from this point. The VWF:Ag assay of the plasma to be tested is automatically carried out by the analyzer at 540 nm as soon as the samples have been loaded.

2.11. Data analysis

Data were collected manually in a master sheet and analysis was performed using computerized SPSS program.

3. Result

3.1.Von willbrand factor

Von willbrand factor in the pregnant group showed minimum value as 77% and maximum value as 364%, with a mean of 172.77 above the normal range of VWF which is 50-160%. In the control group the minimum VWF was 59% and the maximum 135% with a mean value of 92.75, with in the normal range. **Fig. (1,2)** and **Table. (I,II)** may clearly explain the effect of von willbrand factor.

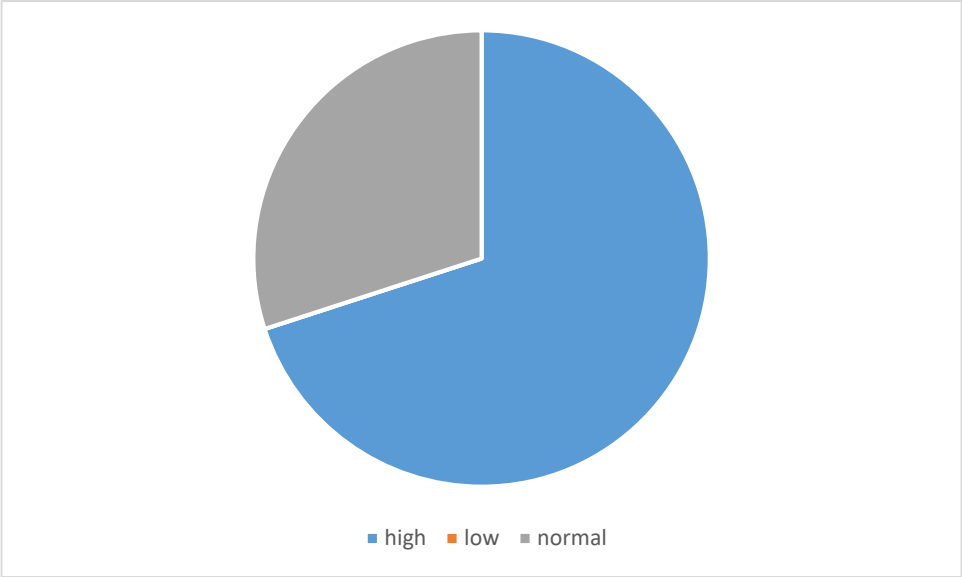

Fig. (1) The case of group.

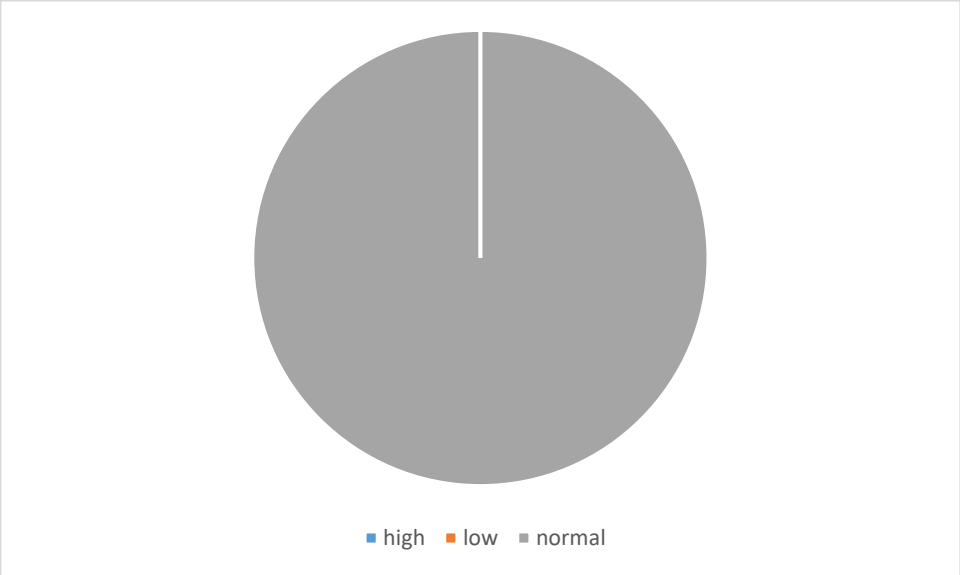

Fig. (2) The control of group.

Table. I. Test group

Parameter	Mean	Minimum	Maximum	STD
Age	26.97	17	39	6.14
Weight\Kg	64.57	52	77	5.59
VWF %	172.77	77	364	68.68

Table. II. Control group

Parameter	Mean	Minimum	Maximum	STD
Age	25.75	17	45	6.62
Weight\Kg	61.2	50	79	7.71
VWF %	92.75	59	135	20.22

3.2. Age of Test and Control groups

The age of test group were between 17-39 years. It mean the minimum value of test group was 17 years and maximum value 39 years old. While the mean value as 26.97 in pregnant group, compared with 17 years as minimum value, 45 years old maximum value, and 25.75 as a mean value in the control group group. As you can see **Fig. (3,4)** and **Table. (I,II)** previous section.

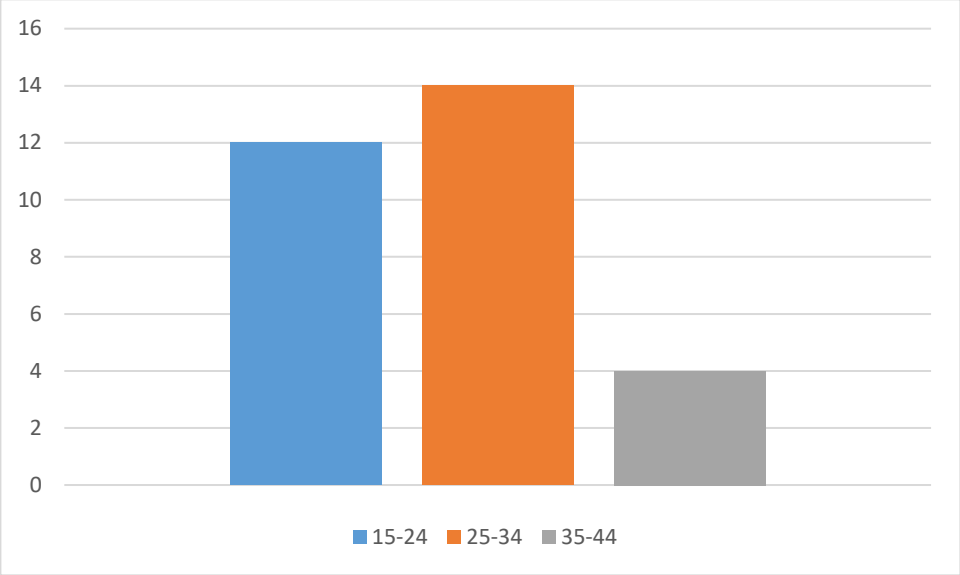

Fig. (3) The age of test group.

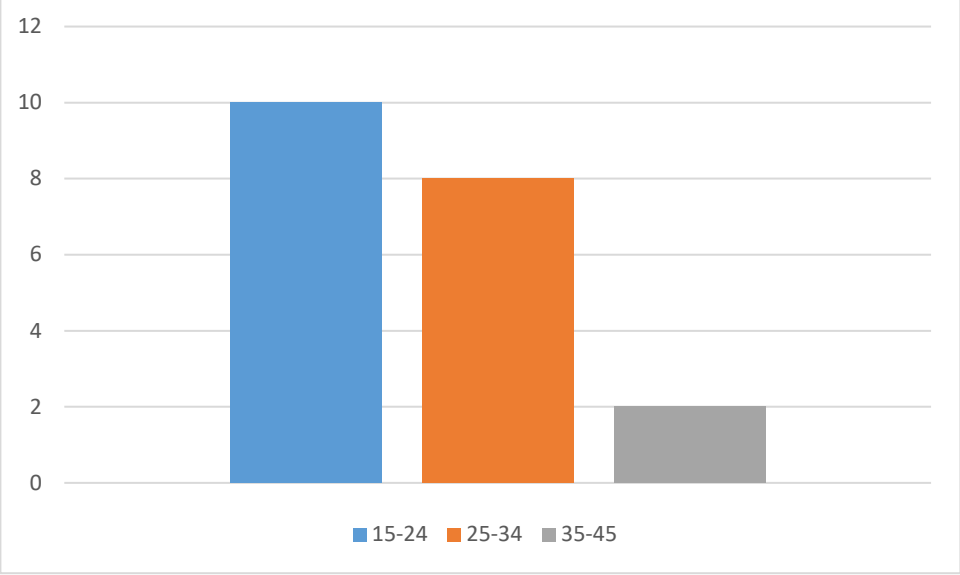

Fig. (4) The age of control group.

3.3. weight of test and control groups

The weight of test group showed minimum value of 52 Kg, maximum value of 77 Kg and mean value as 64.57 Kg in the pregnant group, whereas the control group showed 50 Kg as minimum value, 79 Kg maximum value and 61.2 Kg mean value. Although the weight showed no association with the VWF both test and control groups. As explained **Fig.** (5,6) and **Table.** (I,II).

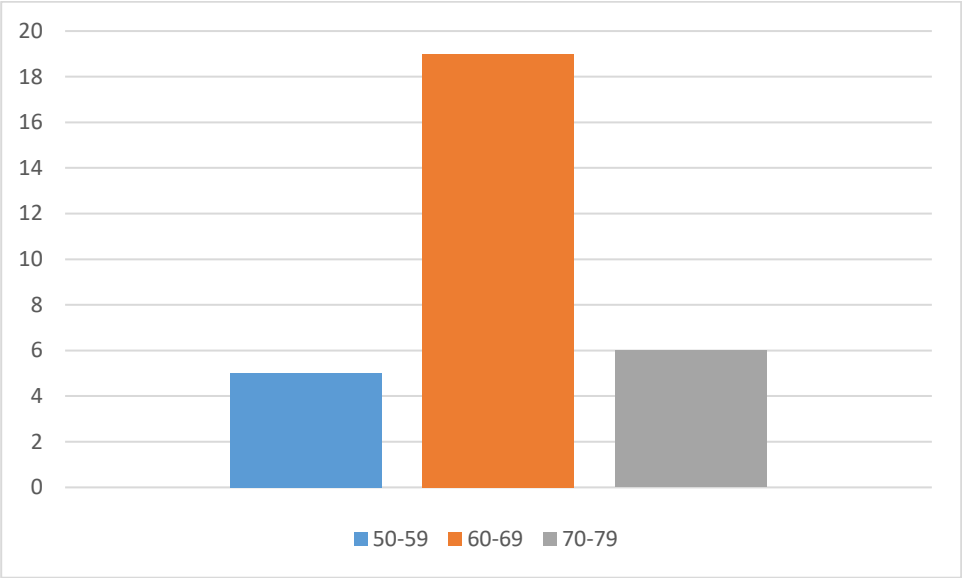

Fig. (5) the weight of test group.

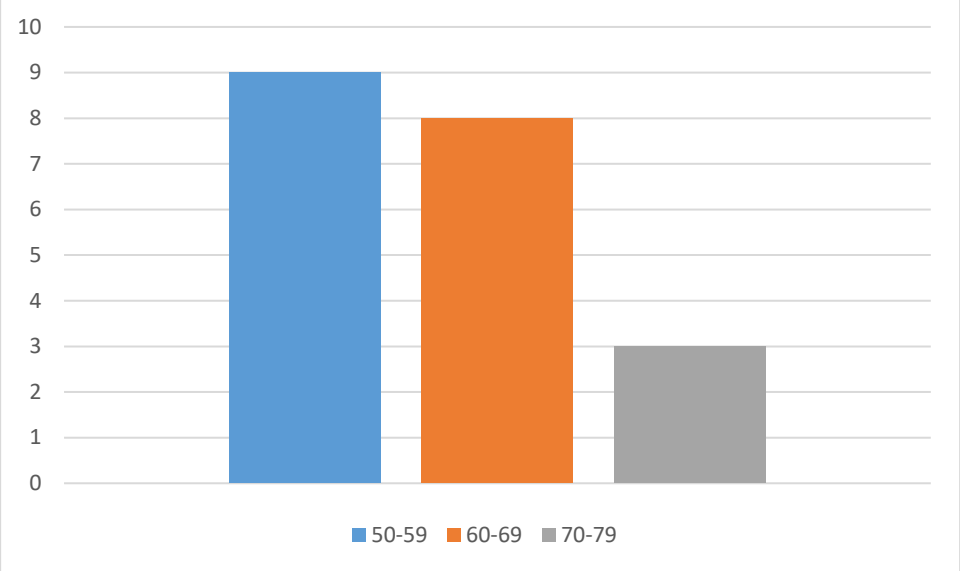

Fig. (6) the weight of control group.

3.4. Correlation

The result of correlation in our study showed significant association between plasma vwf level and age (p-value=0.004) but the result show no significant association between vwf and weight (P-value=0.063), while the control group showed no association between Vwf, age and weight. **Table.** (7,8).

Table (III): Study group of VWF and Ag

Parameter		AGE	VWF
AGE	Pearson Correlation	1	.508(**)
	Sig. (2-tailed)	.	.004
	N	30	30
	Pearson Correlation	.508(**)	1
	Sig. (2-tailed)	.004	.
	N	30	30

** Correlation is significant at the 0.01 level (2-tailed).

Table (IV): Study group of Vwf and Weight

Parameter		VWF	WEIGHT
VWF	Pearson Correlation	1	.343
	Sig. (2-tailed)	.	.063
	N	30	30

Table (V): Control of Vwf and Age

Parameter		AGE	VWF
AGE	Pearson Correlation	1	.365
	Sig. (2-tailed)	.	.113
	N	20	20
VWF	Pearson Correlation	.365	1
	Sig. (2-tailed)	.113	.
	N	20	20

Table (VI): Control group of Vwf and Weight

Parameter		WT	VWF
WT	Pearson Correlation	1	.399
	Sig. (2-tailed)	.	.082
	N	20	20
VWF	Pearson Correlation	.399	1
	Sig. (2-tailed)	.082	.
	N	20	20

4. Discussion

Normal pregnancy is accompanied by changes in the coagulation and fibrinolytic systems. These include a decrease in platelet count, increases in a number of clotting factors, a decrease in protein S levels, a significant fall in the activity of activated protein C and inhibition of fibrinolysis. These changes may be important for reducing intrapartum blood loss, but they determine an increased risk of thromboembolism during pregnancy and puerperium.

This is a Hospital based cross sectional study conducted in Al zytona Hospital in Khartoum State, Sudan, from March to June 2019. To reveal hemostatic changes in health pregnant women in von willbrand factor compared with non-pregnant women.

The patients were lies in average of ages between 15-24 years, 25-34 years and 35-45 years both case and control groups with percentage 44%, 44% and 12% respectively**(Fig 3,4)**. As well As the average weight of both case and control groups was 50-59 kg, 60-69 kg, and 70-79 kg with percentage of 28%, 54% and 18% Respectively(**Fig 5,6**). Also look **(Table I,II)** represent case and control groups respectively. While the values of VWF in both groups Test and Control was 172.77 and 92.75 respectively. As you can see (**Fig 1,2)** and (**Table I,II)**.

In the present study there is increased von willbrand factor level during normal pregnancy when compared with age matched control groups of non-pregnancies which was normal the von willbrand factor level. This increase may be because of change in haemostatic balance in the direction of Hypercoagulability in which increase concentration of all clotting factors except XI, XIII or The hormones which are necessary for the maintenance of pregnancy i.e. estrogen and progesterone increase several folds and these especially estrogen stimulate hepatocytes thereby increasing the production of virtually all coagulation factors. Progesterone has been found to increase decidual tissue factor. However, most of these changes in blood coagulation create a state of hypercoagulability which protects the pregnant women from haemorrhage during pregnancy and delivery but predisposes them to thromboembolism.

The result of our study showed significant association between plasma vwf level and age (p-value=0.004) but the result show no significant association between vwf and weight (P-value=0.063). Which agrees with Abdel Galil M. et.all who found In the third trimester of pregnancy, there was significant elevation of plasma fibrinogen, 55%; factor VIII activities, 64%; factor VIII:ristocetin cofactor, 44% ; factor VWF antigen, 49%. Also our results agrees with Brenner B in 2004 who found that in normal pregnancy, there is a marked increase in the procoagulant activity in maternal blood characterized by elevation of factors VII, X, VIII, fibrinogen and von Willebrand factor, which is maximal around term. Overall, there is a 4- to 10-fold increased thrombotic risk throughout gestation and the postpartum period (Brenner B. 2004). Also our study agree with Another study done by Daniella N. Drury Stewart et.all in November 2014. Stated “We measured VWF antigen (VWF:Ag) in samples collected from 46 women during pregnancy and at non-pregnant baseline. 1st trimester samples 9.3±3.4, 2nd trimester samples

21.9±2.3, and 3rd trimester samples 35.2±2.7. They cocluded VWF:Ag is significantly increased during pregnancy."

We agree Similar study done by Jill M jonsen et.all show significant increase of von willbrand factor in third trimester of pregnancy. Also we agree with MG Conlan who found that VWF level increases with age (Conlan MG, et al 1993). But we disagree study done by Afnan Hashim in 2014 reveal no significant association between vwf and age. Also we disagree another study done by Sánchez-Luceros A et all they stated "The von Willebrand factor increased markedly from non-pregnant values up to the end of early puerperium (P <0.0001), while factor VIII only showed a slight increase. Factor VIII and von Willebrand factor activity remained within the normal range for non-pregnant women.

5.1 Conclusion

In summary we conclude that according to our result there is association between plasma vwf level and age, but the result show no significant association between vwf and Weight.

5.2 Recommendations

❖ Further studies with large sample size should be carried out in vWF
among pregnant Women to provide more definitive information about its effect
❖ Further studies must be done in the other coagulation parameter and endothelial marker to evaluate its changes in Pregnant Women.
❖ More intensive study must be done in all trimester.
❖ Study the activity of coagulation parameter in three trimester.

❖Prenatal medical care is the medical and nursing care recommended for women during pregnancy. The aim of good prenatal care is prevention, early identification, and treatment of any medical complications.

References

1. Buseri F, Jeremiah Z, Kalio F. Influence of pregnancy and gestation period on some coagulation parameters among Nigerian antenatal women. Res J Med Sci. 2008;2(6):275-81.
2. Sengupta BS, Chattopadyay SK, Thornton HG, Sengupte PS. Obstetrics for Post graduates & Practitioners Aspects of Fetal and Maternal Medicine 1st Edition 1999, BI Churchill Livingstone Pvt. LTD.
3. Agarwal S. Asha Buradkar. Coagulation studies in toxaemias of pregnancy. Journal of Obstetrics and Gynaecology of India. 1978:992-6.
4. Hellgren M, editor Hemostasis during normal pregnancy and puerperium. Seminars in thrombosis and hemostasis; 2003: Copyright© 2003 by Thieme Medical Publishers, Inc., 333 Seventh Avenue, New ….
5. James AH, Bushnell CD, Jamison MG, Myers ER. Incidence and risk factors for stroke in pregnancy and the puerperium. Obstetrics & Gynecology. 2005;106(3):509-16.
6. Dati F, Pelzer H, Wagner C, editors. Relevance of markers of hemostasis activation in obstetrics/gynecology and pediatrics. Seminars in thrombosis and hemostasis; 1998: Copyright© 1998 by Thieme Medical Publishers, Inc.
7. McCrae KR. Thrombocytopenia in pregnancy: differential diagnosis, pathogenesis, and management. Blood reviews. 2003;17(1):7-14.
8. Boehlen F, Hohlfeld P, Extermann P, Perneger TV, De Moerloose P. Platelet count at term pregnancy: a reappraisal of the threshold. Obstetrics & Gynecology. 2000;95(1):29-33.
9. Wallenburg H, Kessel P. Platelet lifespan in normal pregnancy as determined by a nonradioisotopic technique. BJOG: An International Journal of Obstetrics & Gynaecology. 1978;85(1):33-6.
10. Shirish MK. Essentials of Haematology. Jaypee Brothers. 2013.
11. Franchini M, Lippi G. The role of von Willebrand factor in hemorrhagic and thrombotic disorders. Critical reviews in clinical laboratory sciences. 2007;44(2):115-49.
12. Hillman RS, Ault KA, Leporrier M, Rinder HM. Hematology in Clinical Practice, Fifth Edition: McGraw-Hill Education; 2010.
13. Shehan CL. The Wiley Blackwell Encyclopedia of Family Studies, 4 Volume Set: John Wiley & Sons; 2016.
14. Heijdra JM, Cnossen MH, Leebeek FW. Current and emerging options for the management of inherited von Willebrand disease. Drugs. 2017;77(14):1531-47.
15. Polin RA, Fox WW, Abman SH. Fetal and Neonatal Physiology: Expert Consult-Online and Print: Elsevier Health Sciences; 2011.
16. Mustafa AHA. Measurement of Plasma Von Willebrand Factor Antigen Level among pregnant Sudanese Ladies in Third Trimester: Sudan University of Science & Technology; 2018.
17. Vazquez JC. Constipation, haemorrhoids, and heartburn in pregnancy. BMJ clinical evidence. 2010;2010.
18. Waters TR, MacDonald LA, Hudock SD, Goddard DE. Provisional recommended weight limits for manual lifting during pregnancy. Human factors. 2014;56(1):203-14.
19. Dowswell T, Carroli G, Duley L, Gates S, Gülmezoglu AM, Khan-Neelofur D, et al. Alternative versus standard packages of antenatal care for low-risk pregnancy. Cochrane Database of Systematic Reviews. 2015(7).

20. Hurt KJ, Guile MW, Bienstock JL, Fox HE, Wallach EE. The Johns Hopkins manual of gynecology and obstetrics: Lippincott Williams & Wilkins; 2012.
21. Ota E, Hori H, Mori R, Tobe-Gai R, Farrar D. Antenatal dietary education and supplementation to increase energy and protein intake. Cochrane database of systematic reviews. 2015(6).
22. Klusmann A, Heinrich B, StÖpler H, GÄrtner J, Mayatepek E, Von Kries R. A decreasing rate of neural tube defects following the recommendations for periconceptional folic acid supplementation. Acta Paediatrica. 2005;94(11):1538-42.
23. Stevenson RE, Allen WP, Pai GS, Best R, Seaver LH, Dean J, et al. Decline in prevalence of neural tube defects in a high-risk region of the United States. PEDIATRICS-SPRINGFIELD-. 2000;106(4; PART 1):677-83.
24. Guesnet P, Alessandri J-M. Docosahexaenoic acid (DHA) and the developing central nervous system (CNS)–implications for dietary recommendations. Biochimie. 2011;93(1):7-12.
25. Salem Jr N, Litman B, Kim HY, Gawrisch K. Mechanisms of action of docosahexaenoic acid in the nervous system. Lipids. 2001;36(9):945-59.
26. Kuoppala T, Tuimala R, Parviainen M, Koskinen T, Ala-Houhala M. Serum levels of vitamin D metabolites, calcium, phosphorus, magnesium and alkaline phosphatase in Finnish women throughout pregnancy and in cord serum at delivery. Human nutrition Clinical nutrition. 1986;40(4):287-93.
27. Rumbold A, Ota E, Hori H, Miyazaki C, Crowther CA. Vitamin E supplementation in pregnancy. Cochrane Database of Systematic Reviews. 2015(9).
28. Peña-Rosas JP, De-Regil LM, Garcia-Casal MN, Dowswell T. Daily oral iron supplementation during pregnancy. Cochrane database of systematic reviews. 2015(7).
29. Stassen Berger K. The developing person through the life span: New York Bedford, Freeman and Worth; 2005.
30. Tam C, Erebara A, Einarson A. Food-borne illnesses during pregnancy: prevention and treatment. Canadian Family Physician. 2010;56(4):341-3.
31. Jahanfar S, Jaafar SH. Effects of restricted caffeine intake by mother on fetal, neonatal and pregnancy outcomes. Cochrane database of systematic reviews. 2015(6).
32. Thangaratinam S, Rogozińska E, Jolly K, Glinkowski S, Duda W, Borowiack E, et al. Interventions to reduce or prevent obesity in pregnant women: a systematic review. NIHR Health Technology Assessment programme: Executive Summaries: NIHR Journals Library; 2012.
33. Cunningham F, Leveno K, Bloom S, Spong CY, Dashe J. Williams obstetrics, 24e: Mcgraw-hill; 2014.
34. McCall CA, Grimes DA, Lyerly AD. "Therapeutic" bed rest in pregnancy: unethical and unsupported by data. Obstetrics & Gynecology. 2013;121(6):1305-8.
35. Davies GA, Wolfe LA, Mottola MF, MacKinnon C, Arsenault M-Y, Bartellas E, et al. Exercise in pregnancy and the postpartum period. Journal of obstetrics and gynaecology Canada: JOGC= Journal d'obstetrique et gynecologie du Canada: JOGC. 2003;25(6):516-29.
36. Hunter W. Signs and symptoms.
37. Åstedt B, Hägerstrand I, Lecander I. Cellular localisation in placenta of placental type plasminogen activator inhibitor. Thrombosis and haemostasis. 1986;56(01):063-5.
38. Francalanci I, Comeglio P, Liotta AA, Cellai A, Fedi S, Parretti E, et al. D-dimer plasma levels during normal pregnancy measured by specific ELISA. International Journal of Clinical and Laboratory Research. 1997;27(1):65-7.

39. Ifeanyi OE, Uzoma OG. An update on Anaemia, Iron, Folic acid and Vitamin B 12 in Pregnancy and Postpartum. Int J Curr Res Med Sci. 2018;4(5):62-70.
40. Lakshmi B, Indumathi T, Ravi N. An hybrid approach for prediction based health monitoring in pregnant women. Procedia Technology. 2016;24:1635-42.