Available online on 25.12.2021 at http://jddtonline.info

Journal of Drug Delivery and Therapeutics

Open Access to Pharmaceutical and Medical Research

Open Access Full Text Article

Research Article

Estimation of Fibrinogen level among Sudanese women with recurrent miscarriage

Eman Ibrahim Mohamed[1], Maye M. Merghani[4], Nihad Elsadig Babiker*[,1,2,3]

[1] Faculty of Medical Laboratory Sciences, National University, Sudan

[2] Darfur University College, Sudan

[3] National Center of Neurological Sciences, Sudan

[4] Nahda College, Sudan

Article Info:

Article History:

Received 19 October 2021
Reviewed 16 December 2021
Accepted 23 December 2021
Published 25 December 2021

Cite this article as:

Mohamed EI, Merghani MM, Babiker NE, Estimation of Fibrinogen level among Sudanese women with recurrent miscarriage, Journal of Drug Delivery and Therapeutics. 2021; 11(6-S):140-144

DOI: http://dx.doi.org/10.22270/jddt.v11i6-S.5149

*Address for Correspondence:

Nihad Elsadig Babiker, Faculty of Medical Laboratory Sciences, National University, Sudan

Abstract

Background: Recurrent Spontaneous abortion (RSA) is defined as consecutive pregnancy loss before 20 weeks gestation and it has been attributed to either genetic, structural infective, endocrine, immune, or unexplained causes

Material and methods: This study was case – control study conducted at the Algophran medical laboratory, Khartoum, Sudan during the period July to November, 2021 and aimed to estimate the fibrinogen level among Sudanese women with recurrent miscarriage**.** 50 patients attending obstetrics and gynecology unit at Ibrahem Malik teaching hospital and diagnosed with recurrent spontaneous abortion during the aforementioned period were selected as cases group. In addition to that, 50 apparently healthy women with no history of abortion and without any other risk factor related to abortion were selected as control group. From each participant 5ml of venous blood samples were dispensed into sterile containers with tri-sodium citrate anticoagulant container. Fibrinogen level was estimated by using the coagulometer (Automated Bio Bas) by BioMed-Fibrinogen kite

Result: The results showed; when compared the fibrinogen level between cases and control group there was significant decreased of fibrinogen level with (P = 0.000). Also in the case group there was insignificant differences between fibrinogen level and age , number of miscarriages and the gestational age (P >0.05)

Conclusion: In the conclusion the result showed significant decreased of the fibrinogen level and insignificant differences between fibrinogen level and age, number of miscarriages and the gestational age among Sudanese women with recurrent miscarriage.

Keywords: Recurrent Miscarriage, Pregnancy, Fibrinogen, Genetic, Abortion And Endocrine

INTRODUCTION

Recurrent Spontaneous abortion (RSA) is defined as consecutive pregnancy loss before 20 weeks gestation **(**Jaslow,2010) . Historically, recurrent miscarriage has been attributed to either genetic, structural infective, endocrine, immune, or unexplained causes. Thrombophilic disorders are thought to have an influence in the cause of recurrent pregnancy loss which expand the scope of investigations and management options for recurrent miscarriage. The hazard of (RSA) after two consecutive losses is 17% to 25% and the risk of miscarrying fourth pregnancy loss after three consecutive losses is between 25% and 46%, with practically no workup or treatment, the opportunity of a successful live birth in a couple with a history of RPL and no previous live birth is 55-60%.(Asaad Mohammed, 2015)

The World Health Organization (WHO) evaluated that 21.6 million abortions occurred worldwide in 2008 and complications from these accounted for about 13% of maternal deaths (MD) (47,000 MD per year). There is also enormous disparity in the ratio of maternal deaths attributable to recurrent miscarriage per 100,000 live births in developed countries compared to developing countries: 1 vs 40/100,0005. Less developed regions of the world have the greatest risk of morbidity and mortality from recurrent miscarriage (World Health, 2004**)**

Fibrinogen is a soluble glycoprotein ' it is340kd and synthesized in the liver. It is a symmetric heterodimeric protein consist from 3 pairs of polypeptides (α -B -γ) 2. The fibrino peptide regions of fibrinogen contain several glutamate and aspartate realize a high negative charge to this region and support the solubility of fibrinogen in plasma.

It play important physiological role in haemostasis. In the final step of the coagulation cascade, fibrinogen is converted to fibrin, to form a fibrin clot. The fibrin clot has fundamental role to stop bleeding at sites of blood vessel injury; it also supplies the structure for assembly and activation of the fibrinolytic proteins. Fibrinogen also plays important roles in other pathophysiological processes, apart from clot formation in the haemostatic process include infection and clot retraction. Pathophsiology by various studies, which can determine increased levels of fibrinogen lead to thrombophilia, and decreased levels of fibrinogen are associated with an increased risk of bleeding. Increased fibrinogen levels lead to thrombus formation can convert the kinetics of the coagulation cascade, resulting in increased fibrin formation, increase platelet interaction by increased binding to the glycoprotein IIb/IIIa receptor, and increasing plasma viscosity. Congenital abnormalities of fibrinogen are divided into 2 types: type I, or quantitative abnormalities afibrinogenemia and hypofibrinogenemia, and type II or qualitative abnormalities dysfibrinogenemia and hypodysfibrinogenemia.(Lang, 2009, Wang,2002)

The primary role of fibrinogen in the safety and stability of the placenta in the uterus High fibrinogen and clotting factor platelet pregnant women from bleeding ;especially bleeding caused by placental abruption. (Evron, 1985)

Some studies revealed that women with thrombophilias have 66-83% recurrence rate of fetal loss in subsequent pregnancies and also that fibrinogen deficiencies result in abortions in the early gestational period, however none of the studies have confirmed the role of fibrinogen levels in the context of recurrent miscarriage. Measuring the changed levels of fibrinogen to predict occurrence of recurrent miscarriage, could be a main direction to be followed to earn prudence into the thrombogenic possibility of this protein. Also in the Sudan no published data regarding the relation between the fibrinogen level and recurrent miscarriage for that this study designed to estimate the fibrinogen level among Sudanese women with recurrent miscarriage.

MATERIAL AND METHODS

This study was case – control study conducted at the Algophran medical laboratory, Khartoum, Sudan during the period July to November, 2021. Patients attending obese and gaina unit at Bashair teaching hospital and diagnosed with recurrent spontaneous abortion during the aforementioned period were included. In addition to that, apparently healthy women with no history of abortion and their age between 20-40years were selected as control group. Patients under anticoagulant treatment, also patients refuse to give consent, and those with previous history of abortion were not recruited as controls were excluded.From each participant 5ml of venous blood samples were dispensed into sterile containers with tri-sodium citrate anticoagulant container. Fibrinogen level was estimated by using the coagulometer (Automated Bio Bas) by BioMed-Fibrinogen kite. The data was gathered using pre-designed structural questionnaire and the SPSS16.0 statistical software (SPSS Inc., USA) was used for statistical analysis. Finally the study was licensed by the ethical committee ethical committee of national university.

RESULTS

Socio- demographic data

In the present study 50 women with recurrent miscarriages were selected as cases and apparently 50 women were selected as control group. The most affected age group was 35-40 year (40%), followed by 25-34 years (36%) and 18-24 (10%). The frequency of the miscarriage number was; more than three times about 68 % and three time about 32%. All cases their pregnancy outcome were miscarriage, and frequency of the gestational age was; more than 14 weeks about 34 %(Table1). In addition about 26 % had a history of diabetes Miletus, 5% had thyroid disease, only about 2% had a history of renal disease and 12% had family history of the genetic disease. For the risk factor only about 2% was smoker. All of the cases are taken folic acid during pregnancy and all of them were diagnosed as unexplained causes of miscarriage (table 1, 2)

Table (1) Sociodemographic data of the cases

Socio-demographic		Frequency	Percent
Age	18-24	5	10.0
	25-34	18	36.0
	35-40	20	40.0
	>40	7	14.0
	Total	50	100.0
How many miscarriage	3	16	32.0
	>3	34	68.0
	Total	50	100.0
Outcome of the pregnancies	Miscarriage	50	100
At what gestational age	<6w	6	12.0
	7-10w	13	26.0
	11-14w	14	28.0
	<14w	17	34.0
	Total	50	100.0
Folic acid taken during pregnancy	Yes	49	98.0
	No	1	2.0
	Total	50	100.0
Social background of patient	No	46	92.0
	Smoking	1	2.0
	Recurrent medical drugs	3	6.0
	Total	50	100.0

Table (2): Frequency of treatment and other diseases

		Frequency	Percent
History of any diseases	DM	13	26.0
	Thyroid problem	5	10.0
	SLE	1	2.0
	Renal disease	1	2.0
	DVT/PE	1	2.0
	Obesity	8	16.0
	No	21	42.0
	Total	50	100.0
Any previous treatment taken	Yes	14	28.0
	No	36	72.0
	Total	50	100.0
Suggestion of cause	Decrease weight	1	2.0
	do not remember	1	2.0
	Endocrine	1	2.0
	Low folic acid	1	2.0
	Unknown	44	88.0
	Thyroid problems	2	4.0
	Total	50	100.0
Diagnosis of recurrent miscarriage	Un explained	50	100.0
Family history of genetics or inherited disease from (female side)	Yes	6	12.0
	No	44	88.0
	Total	50	100.0

Hematological Results

The results showed; When compared the fibrinogen level between cases and control group there was significant decreased of fibrinogen level with (P = 0.000) (table 3)(fig 1) . Also in the case group there was insignificant differences between fibrinogen level and age, number of miscarriages and the gestational age (P >0.05) (table 4, 5, 6) .

Table (3): Comparisons of fibrinogen between case and control

Parameters	Case (n=50)	Control (n=50)	P. value
Fibrinogen (mg/dl)	149.9 ± 97.1	284.3 ± 71.6	0.000*

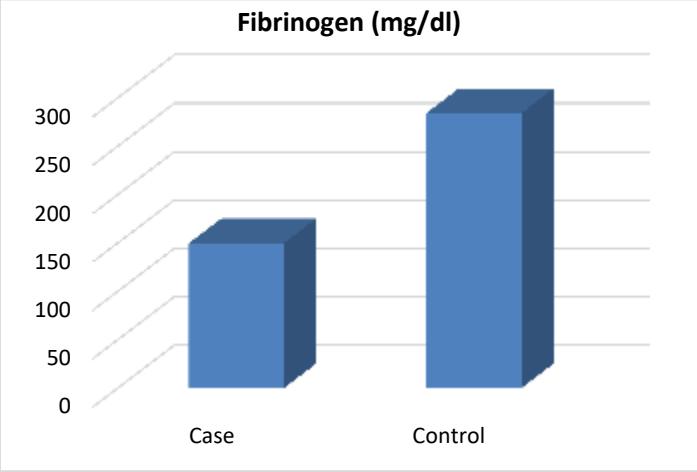

Figure (1): **Mean of fibrinogen among case and control**

Table (4): Comparisons of fibrinogen according to age of cases

Parameters	Age				P. value
	18-24(n=5)	25-34(n=18)	35-40(n=20)	>40(n=7)	
Fibrinogen (mg/dl)	160.0 ± 68	157.1 ± 125.8	141.1 ± 86.6	150.0 ± 69.2	0.959

Table (5): comparisons of fibrinogen according to frequency of miscarriage

Parameters	Frequency of miscarriage		P. values
	3 times (n=16)	>3 times (n=34)	
Fibrinogen (mg/dl)	150.1 ± 103.4	149.9 ± 95.6	0.994

Table (6): Comparisons of fibrinogen according to gestational age of miscarriage

Parameters	Gestational age of miscarriage				P. value
	<6w (n=6)	7-10w(n=13)	11-14w(n=14)	<14w(n=17)	
Fibrinogen (mg/dl)	123.2 ± 78.1	155.4 ± 110.0	116.8 ± 68.8	182.7 ± 107.9	0.260

DISCUSSION

Fibrinogen is essential for hemostasis, it is a final result of extrinsic and intrinsic pathway. Incidence of bleeding and thrombotic complications during pregnancy and postpartum, as well as an increased risk of recurrent pregnancy loss and abruptio placenta (Naz 2017, Casini 2016)

The result of this study revealed; The most affected age group was 35-40 year (40%). This result was agreed with Evans et al which reported; the miscarriage rate increases with age. (Evans,2011) . Also our results showed; the frequency of the miscarriage number was; more than three times about 68 % and three time about 32%. The Clinical researches suggest that the risk of another miscarriage after 3 consecutive pregnancy losses is 30-45%. However, without any workup or treatment, the opportiunity of a successful live birth in a couple with a history of RPL and no previous 55-60%. 70% for the couple with a history of RPL and has had at least one previous normal pregnancy (Evans ,2011) .

Regarding the causes of miscarriage the present results found; 26 % had a history of diabetes Miletus, 5% had thyroid disease, only about 2% had a history of renal disease and 12% had family history of the genetic disease. Ford and Schus et al said; diabetes mellitus, thyroid disease, and hyperprolactinemia are among the endocrinologic disorders implicated in approximately 17% to 20% of RM (Ford,2009) .

In addition our results present when compared the fibrinogen level between cases and control group there was significant decreased of fibrinogen level and insignificant differences between fibrinogen level and age, number of miscarriages and the gestational age. While **Robbi et al** study showed that levels of fibrinogen in pregnancy is increasing according to gestational age. This is consistent with studies that have already existed, stating that in pregnancy, there are some changes on the components associated with blood clotting factor. (Robbi 2011, Thornton 2010)

On the other hand Kitchens Bolton and each also concluded that women with afibrinogenemia and hipofibrinogenemia have a higher risk of experiencing abortion. Moreover Some studies reveal a link between fibrinogen levels in early pregnancy with obstetric complications at a later date (Bolton-Maggs 2006, Miesbach 2009) · indeed an increase in fibrinogen is in line with its role as a hemostatic agent, which achieved a balance of adhesion utero plasental fibrinoid layer on the fabric of the mother and fetus (Iwaki , 2002)

Athira Sasidharan tal revealed The timing of pregnancy loss is typically at approximately five to eight weeks gestation, if fibrinogen replacement therapy is not administered. Thus, as per previous reports it's a hematological emergency and should be diagnosed at the earliest in recurrent miscarriages (Athira,2021).

Finally the Royal College of Obstetricians and Gynecologists (RCOG) guideline published in 2017 provides specific guidance for the management of pregnancy and delivery. It's recommended to begin replacement therapy as early as four to five weeks of gestation and to continue throughout pregnancy till delivery. Fibrinogen should be preserved at 100 mg/dl or >50 mg/dl with frequent monitoring at every one to two weeks (Pavord, 2017)

CONCLUSION

In the conclusion the result showed significant decreased of the fibrinogen level and insignificant differences between fibrinogen level and age, number of miscarriages and the gestational age among Sudanese women with recurrent miscarriage

REFERENCES

Asaad Mohammed Ahmed Abd Allah Babker1, SalaheldeinGumaa Elzaki2, Sarah ElsiddigDafallah. 2015. An Observational Study of Causes of Recurrent Spontaneous Abortion among Sudanese Women. IJSR; 4(9):1435-1438.

Athira Sasidharan, Aboobacker Mohamed Rafi, Ramesh Bhaskaran, Nithya M Baiju, Susheela Jacob Innah. 2021. Successful Pregnancy in a Patient With Recurrent Pregnancy Loss Due to Afibrinogenemia Managed With Cryoprecipitate Prophylaxis in a Resource-limited Setting. Mal J Med Health Sci 17(2): 308-310

Bolton-Maggs PH. 2006. The rare coagulation disorders. Treatment of hemophilia.; 39: 1-11

Casini A, de Moerloose P.2016. Management of congenital quantitative fibrinogen disorders: a Delphi consensus. Haemophilia ; 22: 898-905. https://doi.org/10.1111/hae.13061

Evans M: Recurrent pregnancy loss. available from Huntington reproductive in California: URL: http://www.infertilityspecialist.com/recurrent_pregnancy_loss.htm (Accessed on December, 2011).

Evron, S., Anteby, S.O., Brzezinsky, A., Samueloff, A., and Eldor, A. 1985. Congenital afibrinogenemia and Recurrent early abortion: a case report. Eur. J. Obstet. Gynaecol. Reprod. Biol ;19(5), 307-311. https://doi.org/10.1016/0028-2243(85)90046-2

Ford H B, Schust D J. 2009. Recurrent Pregnancy Loss: Etiology, Diagnosis, and Therapy. Rev Obstet Gynecol; 2: 76-83

Iwaki T, Mayra J, Cooper S.2002. Fibrinogen stabilizes placental-maternal attachment during embryonic development in the mouse. Am J Path; 160: 1021-34 https://doi.org/10.1016/S0002-9440(10)64923-1

Jaslow CR, Carney JL, Kutteh WH. 2010. Diagnostic factors identified in 1020 women with two versus three or more recurrent pregnancy losses. FertilSteril ;93(4):1234-1243. https://doi.org/10.1016/j.fertnstert.2009.01.166

Lang, T., Johanning, K., Metzler, H., Piepenbrock, S., Solomon, C., Rahe-Meyer, N., Tanaka, K.A. 2009. "The effects of fibrinogen levels on thromboelastometric variables in the presence of thrombocytopenia". Anesth Analg 108 (3), 751-8.5. https://doi.org/10.1213/ane.0b013e3181966675

Miesbach W, Galankis D, Scharrer I. 2009. Treatment of patients with dysfibrinogenemia and history of abortions during pregnancy. Blood Coagul Fibrinolysis ; 5: 366-70 https://doi.org/10.1097/MBC.0b013e32832aec2b

Naz A, Biswas A, Khan TN, Goodeve A, Ahmed N, et al. 2017 Identification of novel mutations in congenital afibrinogenemia patients and molecular modelling of missense mutations in Pakistani population. Thromb J ; 15: 24 https://doi.org/10.1186/s12959-017-0143-3

Pavord S, Rayment R, Madan B, et al. Management of Inherited Bleeding Disorders in Pregnancy. Green-top Guideline No. 71. BJOG 2017; 124:e193-e263. https://doi.org/10.1111/1471-0528.14592

Robbi A. Wicaksono, Jusuf S. Effendi, Budi Handono . 2011. Comparison of Fibrinogen Level Changes between Pregnancy with History of Abortion and Normal Pregnancy. Indones J Obstet Gynecol; 35(2):53-56

Thornton P, Douglas J. 2010. Coagulation in Pregnancy. Best Practice and Research Clinical Obstetrics and Gynaecology; 24: 340 https://doi.org/10.1016/j.bpobgyn.2009.11.010

Wang, S., Retzinger, G.S.2002. Hypercoagulability during pregnancy. Lab Lines ; 8(5), 1-4.

World Health Organization (WHO). Unsafe abortion: global and regional estimates of the incidence of unsafe abortion and associated mortality in 2000, 4th edn. Geneva: WHO, 2004