Research Report

Comparison of Fibrinogen Level Changes between Pregnancy with History of Abortion and Normal Pregnancy

Perbandingan Perubahan Kadar Fibrinogen antara Kehamilan dengan Riwayat Kehamilan Aborsi dan Normal

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Abstract

Objective: To know the change of fibrinogen level in pregnancy with history of abortion and normal pregnancy on 6 - 8 weeks pregnancy and 10 - 12 weeks pregnancy.

Method: This is a comparative study analytic comparative with cross sectional method on both groups, pregnancy with history of abortion and normal pregnancy. Observe the changes of fibrinogen level on 6 - 8 weeks pregnancy and then on 10 - 12 weeks pregnancy in pregnancy with history of abortion and normal pregnancy.

Result: Comparison of mean fibrinogen level between 6 - 8 weeks pregnancy and 10 - 12 weeks pregnancy, on both group showed that the fibrinogen level in the group with history of abortion increased 9.6% and in the group of normal pregnancy increased 11.4%. The raise on both group was not significant stastistically ($p = 0.810$). The raise fibrinogen level on normal pregnancy was significant ($p < 0.001$), while on pregnancy with history of abortion is not significant ($p = 0.255$). All patterns of raise and fall on fibrinogen level on both groups were not stastistically significant ($p > 0.005$).

Conclusion: Fibrinogen level on 10 - 12 weeks pregnancy was not lower than on 6 - 8 weeks pregnancy in pregnancy with history of abortion. There was no significant raise changes in fibrinogen level on both groups.

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Keywords: abortion, fibrinogen, haemostasis, history of abortion, normal pregnancy

Abstrak

***Tujuan**: Mengetahui perubahan kadar fibrinogen pada pemeriksaan usia kehamilan 6 - 8 minggu dan usia kehamilan 10 - 12 minggu pada kehamilan dengan riwayat abortus dan kehamilan normal.*

***Metode**: Penelitian ini merupakan penelitian studi perbandingan atau perbandingan analisis dengan metode potong silang pada kedua kelompok kehamilan dengan riwayat abortus dan kehamilan normal. Penelitian ini mengamati perubahan kadar fibrinogen pada usia 6 - 8 minggu dan kemudian diperiksa kembali pada usia kehamilan 10 - 12 minggu, pada kelompok hamil dengan riwayat abortus dan kelompok hamil normal.*

***Hasil**: Perbandingan rata-rata kadar fibrinogen antara pemeriksaan pada 6 - 8 minggu dan pemeriksaan pada 10 - 12 minggu menunjukkan bahwa pada kelompok kehamilan dengan riwayat abortus meningkat sebesar 9,6%, sedangkan pada kelompok hamil normal meningkat 11,4%. Perbandingan peningkatan kadar fibrinogen pada kedua kelompok secara statistik tidak bermakna ($p = 0,810$). Terjadi peningkatan kadar fibrinogen secara signifikan pada kelompok hamil normal ($p < 0,001$), sedangkan pada kelompok dengan riwayat abortus peningkatannya tidak bermakna ($p = 0,255$). Selain itu, tidak ada perbedaan yang bermakna antara kehamilan normal dan riwayat abortus dengan kenaikan atau penurunan kadar fibrinogen ($p > 0,005$).*

***Kesimpulan**: Kadar fibrinogen pada usia 10 - 12 minggu tidak lebih rendah dibandingkan dengan usia 6 - 8 minggu. Selain itu, tidak ada perbedaan yang bermakna pada persentase peningkatan kadar fibrinogen pada kelompok hamil normal dan kelompok dengan riwayat abortus.*

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***Kata kunci**: abortus, fibrinogen, hemostasis, kehamilan normal, riwayat abortus*

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INTRODUCTION

Abortion is premature birth of pregnancy before the fetus is developed enough to be able to live outside the womb, before 20 weeks gestation, or fetal birth weight less than 500 gr. Abortion remains a major problem in obstetric care, because it is one of the highest cause related to mother and fetus mortality.[1-4]

The incidence varies from 2% to 22%. The incidence of abortion in general, for 5 - 20% of all pregnancy.[1] In Hasan Sadikin Hospital, the prevalence of abortion was recorded at 6.5 to 15%, with the mortality rate is 1 - 2%.

Recurrent miscarriage is a miscarriage incidence at least twice or more in a row at the age of less than 20 weeks gestation or fetal weight of less than 500 grams.[3,5]

The cause of abortion can not be determined with certainty, such as genetic factors, immunological, hormonal, anatomical, chronic disease, and lifestyles. The most common cause of miscarriage is chromosomal

abnormality that occurs in 50% - 80% cases.[3] This genetic disorder has no further intervention to do.

Of the many causes of abortion, hemostatic disorders recently started to get noticed. This is a good opportunity for us to know better and understand the causes of abortion. The role of investigation in an effort to find out the causes of abortion is important because it can help determine the cause and perhaps predict the occurrence of obstetric complications that may be encountered.

Fibrinogen, a major blood glycoprotein, a dimer of three polypeptide chains, Aα, Bβ, and γ. Fibrinogen is synthesized in hepatic parenchymal cells and has a half-life of 3 to 4.5 days. Fibrinogen is the primary molecule linking the activated platelets together with the glycoprotein IIb/IIIa.[3,6,7]

The success of implantation in pregnancy requires good balance between coagulation, fibrinolysis, and vascular remodeling. Thrombosis in decidual blood vessels is one of the causes of abortion, which is the excessive thrombosis in blood vessels of the placenta, placental infarction, and insufficiency uteroplasental.[8,9]

The correlation between abnormalities in blood clotting process in the case of abortion in Indonesia today is not widely studied, because the authors were interested in conducting research to determine the correlation between low levels of fibrinogen in pregnancy and abortion.

METHODS

Determining Subjects

The amount subjects in this study were to 32 people consisting of 16 pregnant patients with a history of abortion and 16 normal pregnant patients. All patients underwent blood tests to check levels of fibrinogen in the blood. In each group, the fibrinogen level was examined twice. The first examination conducted at 6 - 8 weeks of gestation, while the second inspection carried out at 10 - 12 weeks of gestation. All patients are pregnant woman firstly 6 - 8 weeks of gestational age, based on last menstrual periode, and confirm normally by ultrasound examination. For pregnancy with history of abortion, first abortion must not be a mole or blighted ova. All patient have no haemostatic disorders, and not in infection condition.

Statistical Analysis

Analysis of the data used in this study were the t test for unpaired data. If data are not normally distributed, Mann-Whitney test was used, whereas to compare the characteristics of data (data categories) used x2 (chi squared). Significance test results are determined based on the value of $p < 0.05$.

RESULT

The average age of subjects was 26.2 years in the group of pregnancies with a history of abortion, while in the normal pregnant group was 26.6 years.

Table 1. Patient's characteristics

Characteristic	Group	
	History of Abortion (n = 16)	Normal Pregnancy (n = 16)
Age (year) $\bar{x}$ (SD)	26.2 (2.9)	26.6 (4.8)
Range	21 - 30	20 - 35
Parity		
0	16	7
≥ 1	0	9

From Table 2, fibrinogen level examination conducted at 6 - 8 weeks of gestation as a measurement baseline and at 10 - 12 weeks of gestation as a second monitor. Preview inspection to I and II between the two groups of research subjects is not significant.

Table 2. Comparison of Fibrinogen Level

Examination	Fibrinogen (mg/dl) Group		T test	p
	History of Abortion (n = 16)	Normal Pregnancy (n = 16)		
6 - 8 weeks			0.418	0.679
$\bar{x}$ (SD)	451.9 (129.7)	468 (83.8)		
Range	256.2 - 788.7	284.2 - 571.1		
10 - 12 weeks			0.776	0.444
$\bar{x}$ (SD)	484.5 (146.4)	516.2 (72.6)		
Range	200.1 - 717.4	344.1 - 602.1		
Percentage of raise	9.6	11.4	0.243	0.810
p	0.255	< 0.001		

Table 3 shows that the average levels of fibrinogen in normal pregnant group, either or the first examination and second examination tended to be higher compared with pregnant groups with a history of abortion, but it did not indicate any statistically significant difference ($p > 0.05$).

Furthermore, comparison of the average fibrinogen level between the first examination and second examination showed that the group of pregnancies with a history of miscarriage increased by 9.6%, while in the normal pregnant group increased by 11.4%. Comparison of elevated levels of fibrinogen in both groups was not statistically significant ($p = 0.810$).

The comparison between the elevation level average of fibrinogen levels in normal pregnant group was statistically significant ($p < 0.001$), whereas in the group with a history of abortion did not increase significantly ($p = 0.255$).

Table 3. Fibrinogen Level Changes

Fibrinogen Level	Group		X_2	p
	History of Abortion (n = 16)	Normal Pregnancy (n = 16)		
Raise	13 (46.4%)	15 (53.6%)		
Fall	3 (75%)	1 (25%)		
			1.143	> 0.05

From Table 3, it appears that there was no significant difference between normal pregnancy and abortion history with the increase or decrease in fibrinogen levels ($p > 0.005$). There are 3 cases decreased fibrinogen levels in cases with a history of abortion, but all remained at normal levels fibrinogen. Similarly, in the case of normal pregnancy, there was 1 case of decreased levels of fibrinogen with the limit levels are still normal.

DISCUSSION

This study shows 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.[10]

Pregnancy-related changes in hemostasis, including the majority of the increase in clotting factors, the decline in the number of natural anticoagulants, and reduction in fibrinolytic activity. These changes produce a state body at the level of hypercoagulability.[10,11]

Fibrinogen increased according to gestational age, but from these studies, no content limits obtained improvement.[12-15] But Patrick et al. revealed that elevated levels of fibrinogen up to two times above normal may occur in pregnancy.[10]

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.[9] The role of fibrinogen is in the stabilization phase fibrinoid layer is very important in the pressed layers of trophoblast into the decidua.

Etiology of an abortion are extremely diverse and many possibilities, so that a deeper observation is needed to determine the etiology, both abortion history, as well as recurrent miscarriage.

Haematological abnormalities either acquired or inherited is one of the causes of which are sufficient counts.[3,16,17] These blood disorders such as sickle cell anemia, disfibrinogenemia, hipofibrinogenemia congenital, afibrinogenemia, Wilson's disease, and hiperhomosisteinemia may be a cause of abortion.[8]

Various studies, found no relationship between incidence of abortion, as well as recurrent miscarriage with low levels of fibrinogen. Plasma fibrinogen is a predictor of a very strong and consistent in a moment of clinical ischemia, which is mainly caused by arterial thrombosis.[18] Adhesion of platelets is the beginning of the cascade, which converts soluble fibrinogen into insoluble and cause blood clotting, platelet adhesion and aggregation is very important to prevent bleeding that causes death. Adhesion of platelets that cause atherosclerosis accelerate the formation of plaque, so that the occlusive against the distal tissue.[18-20]

Beside, there are differences in coagulation parameters between IUFD with normal pregnancies, namely platelets, PT, aPTT, TT, fibrinogen, and antitrombin III.[21,22]

Kitchens Bolton and each also concluded that women with afibrinogenemia and hipofibrinogenemia have a higher risk of experiencing abortion.[23,24]

In this study, no single case of patients experienced hipofibrinogenemia, and in its development there was no cases of abortion. There was a significant improvement in the normal pregnant group, while in the group with a history of abortion was not found significant improvement.

This study tried to reveal the possible etiology from the standpoint of blood clotting factor disorders, at the time of the incident just after 1 time abortion.

Recurrent miscarriage requires at least 2 times the incidence of abortion in a row, this may cause significant psychological effect on patient[25], and genetic problem can not be manipulated, therefore, the writer studied in patients with a history of abortion 1 time only.

Further research that can support and that are useful to know the etiology of abortion with respect to disturbances in blood clotting system, such as fibrinogen and platelet function tests is required. Some studies reveal a link between fibrinogen levels in early pregnancy with obstetric complications at a later date.

Fibrinogen levels increase with gestational age, whereas prothrombin time and overall activity of vitamin K dependent coagulation factors decrease before labor, it describes the physiological response to prevent bleeding during parturien.[13,26,27] From this, other studies can be linked later known fibrinogen level during early pregnancy, to be used as a tool in determining the risk of deadly complications during childbirth.

Vascular anomalies of the placenta can result in various pathologies of pregnancy, including first and second trimester abortion, IUGR, IUFD, preeclampsia, and bleeding post-saline.[16] Furthermore, levels of fibrinogen are associated with a disturbance stability of the placenta, may also be examined as predictors of pregnancy complications.

CONCLUSIONS AND SUGGESTION

Fibrinogen level at 10 - 12 weeks of age is not lower than the age of 6 - 8 weeks. There was no significant difference in the percentage increase in fibrinogen levels in normal pregnant group and the group with a history of abortion.

As suggestion, there should be other studies related to blood clotting factor that may be related to the etiology of abortion, and research to predict the oc-currence of obstetric complications such as IUFD, IUGR, preeclampsia, and post partum haemorrhage.

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