

A comparative study of FDPs and D-dimers in Intrauterine fetal Death

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Ninety subjects were included in the present study and were divided into three groups. Group A included 30 pregnant females with normal pregnancy as control from 20 weeks of gestation onward. Group B included 30 pregnant females with intrauterine fetal death < 20 weeks duration and Group C included 30 pregnant females with IUFD > 2 weeks duration. FDPs and D-dimers were performed by commercially available kits. Results were analysed by using chi-square (χ^2) test and level of significance was done. FDPs and D-dimers were significantly increased in females of IUFD in groups B and C.

Key words: FDPs, D-dimers, Intrauterine fetal death

The pregnancy leads to a change in both coagulation cascade and fibrinolytic system. It is a hypercoagulable state and presents unique triggering mechanism for DIC. There is a haemostatic alteration with intrauterine retention of dead fetus¹.

Intrauterine fetal death (IUFD) refers when there is death of fetus at any time before birth. It is usually applied to an antepartum death after the first trimester, but more often after mid-pregnancy (20 weeks)². Following intrauterine death, thromboplastic substances may be released into the maternal circulation. These fetal products may precipitate intravascular coagulation³.

There is a consumptive coagulopathy with a haemorrhagic picture and increase in soluble fibrin monomer complexes as well as cross linked fibrin oligomers⁴. IUFD is related to intravascular coagulation and increase in FDPs⁵. When there is IUFD, there is a state of chronic consumptive coagulopathy with a prolonged prothrombin time (PT) due to release of thromboplastic substances that initiate DIC. There is also release of plasminogen activators along with these tissue factors. These lead to activation of plasminogen into plasmin, which when acts on fibrinogen brings about fibrinogenolysis. During release any one process may take the upper hand and hence a state of DIC or fibrinogenolysis may initiate accordingly⁶.

When there is retention of fetus after intrauterine death, it leads to significant alterations in coagulation system⁷. IUFD leads to a wide spectrum of haemostatic disturbances ranging from an increase in platelet count and a raised level of FDPs and fibrin monomers, depending upon the duration of retention of dead fetus⁸. Plasma D-dimer are the specific derivatives of cross-linked fibrin, which are produced when fibrin is degraded by plasmin and concentrations are raised by thrombolysis⁹. Plasma D-dimer represents a significant advance over current and historical FDP assays. Firstly it identifies specifically, the presence of cross-linked fibrin derivatives without interference from fibrinogen and non-cross-linked fibrin, and therefore, identifies intravascular thrombosis and fibrinolysis as distinct from fibrinogenolysis. Because of high specificity of D-dimer, the monoclonal antibody can

be used with plasma samples, thereby differentiating fibrinolysis from fibrinogenolysis and conferring an advantage over most standard assays for FDP¹⁰.

D-dimer is a test that directly addresses both thrombin and plasmin generation i.e. generation of thrombin resulting in a cross-linked fibrin clot and of plasmin resulting in a lysis of a cross-linked fibrin clot¹¹. The occurrence of increased levels of D-dimer during pregnancy is indicative of a compensated, low grade intravascular coagulation state, which may be more pronounced in patients with complicated pregnancy¹². The use of a rapid and sensitive D-dimer test for diagnosis and during the treatment of disseminated intravascular coagulation (DIC) and thrombolytic therapy, may give a better understanding of the formation and dissolution of fibrin in thrombotic disease¹³. Detection of fragment DD, therefore offers a unique advantage over other laboratory tests for DIC, because it addresses both dimensions of DIC¹¹.

The purpose of the present study is to compare the role of FDPs and D-dimer levels as an indicator of DIC and fibrinogenolysis

Patients and methods:

Ninety subjects were included in this study and were divided into three groups.

Group A: Pregnant women with normal pregnancy as control

Group B: Pregnant females with IUFD <2 weeks duration.

Group C: Pregnant females with IUFD >2weeks duration
Seven milliliter of venous blood was collected and was divided as follows:

3ml citrated blood with 1:9 ratio for D-dimers.

2ml of blood was transferred to tube containing antibirinolytic agent for FDPs.

Results were analyzed by using chi-dquare (χ^2) test and level of significance was done¹⁴.

Results:

Results and level of significance of different groups are given in tables 1 and 2.

Table 1: FDPs in subjects of IUFD & control group

FDPs ($\mu\text{g/ml}$)	Group A (Control)	Group B (IUFD within 2 weeks)	Group C (IUFD>2 weeks)
<5	20(66.7%)	14(46.7%)	07(23.3%)
>5 <40	08(26.7%)	13(43.3%)	16(53.3%)
>40	02(6.6%)	03(10%)	07(23.4%)
Total	30(100%)	30(100%)	30(100%)

Table 2: D-dimers in subjects of IUFD & control group

D-dimer (ng/ml)	Group A (Control)	Group B (IUFD within 2 weeks)	Group C (IUFD>2 weeks)
<250	08(26.7%)	-	-
250-500	19(63.3%)	06(20%)	-
500-1000	02(6.7%)	14(46.7%)	01(3.3%)
1000-2000	01(3.3%)	06(20%)	13(53.4%)
Total	30(100%)	30(100%)	30(100%)

Statistical Analysis: A vs B $p>0.05$ (S) A vs C $P<0.01$ (HS)
 $P<0.01$ (HS)

Discussion:

Fibrinogen Degradation Products (FDPs)

FDPs were found to be increased in females of IUFD >2 weeks duration (group C) as compared to control group (A) and difference was found to be significant ($p<0.05$) statistically. The present study is in favour of the results of Strauss (1997)⁷, Duchnski (1993)⁸ and Gilbert (1985)⁴ who also observed increased FDPs levels in females of IUFD. These increased FDPs may be due to enhanced fibrinolysis.

D-dimers:

D-dimers were found to be significantly increased ($p<0.01$) in females of IUFD within 2 weeks duration (group B) and more than 2 weeks duration (group C) as compared to control group (A). This study is consistent with the results of Falanga & Rickles (1999)¹⁵, Wintrobe (2003)¹⁶, Levi & Ten (1999)¹⁷, Carey & Rodgers (1998)¹⁸ and Duchnski (1993)⁸, who also observed raised levels of D-dimers in females in IUFD within 2 weeks and more than 2 weeks duration while comparing with control subjects. These increased levels of D-dimers may be due to enhanced fibrinolysis. Fibrinolysis may be due to activation of plasmin which when acts on fibrinogen brings about degradation of products causing increased levels of fibrin monomers.

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