# COAGULATION PROFILE IN PATIENTS WITH INTRAUTERINE FOETAL DEATH

by

SULEKHA BHATTACHARYA,* M.B.B.S.,

B. DUBE,** M.D.,

DEVINDER SHARMA,*** M.S.

and

RAMAKANTA DUBE,**** M.D.

Since the first comprehensive study of coagulopathy associated with intrauterine death from Rh iso-sensitization by Weiner *et al.*, (1950), many women with 'dead baby syndrome' have been reported to have developed coagulation defects to varying extent (Jackson *et al.*, 1955; Frick and Mekelvey, 1955).

In view of the extreme paucity of coagulation data on such patients from our country, it was considered worthwhile to report this series.

*Material and Methods*

Six pregnant women with intrauterine foetal death, admitted at S. S. Hospital, Banaras Hindu University, Varanasi, were investigated. The coagulation data was also worked up in 15 normal control pregnant women in third trimester.

Routine haematological tests were done as described by Dacie and Lewis (1968). Coagulation tests were mostly done as described by Denson (1966). The other techniques used were: plasma fibrinogen (Quick, 1966), euglobulin lysis time (Buckell, 1958), Astrup fibrin plate lysis as described by Dacie and Lewis (1968), using bovine fibrinogen (Sigma), thrombin time (Owen *et al.*, 1969) and serum F.D.P. (Merskey *et al.*, 1969).

The values of prothrombin time, thrombin time and K.C.C.T. were expressed as ratio of the reading of the patient's sample to that of a normal healthy adult male.

*Observations*

Six cases of intrauterine foetal death were studied. Four of them belonged to the age group of 21-30 years. Out of 6 cases 3 were primigravidas, 1 was second gravida and 2 were third gravidas.

Clinical diagnosis of intrauterine foetal death in third trimester was made on grounds of loss of foetal movement, disparity between the height of fundus and period of amenorrhoea, absence of foetal heart sounds (even on auscultation by doptone) supported by radiological evidence and urinary oestriol estimation. As assessed by fundal height and loss of foetal movements, period of retention of dead foetus in utero ranged from 2-10 weeks (Table 1). Twenty-four hour urinary oestriol excretion values were low in all the patients (Table II).

*Clinical Registrar in Obstetrics & Gynaecology.

**Professor of Pathology.

***Reader in Obstetrics & Gynaecology.

****Lecturer in Pathology.

Institute of Medical Sciences, Banaras Hindu University, Varanasi, U.P.

Received for publication on 26-2-74.

TABLE I

*Period of Retention of Dead Fetus in Utero*

| Patient | Fundal height by date (in weeks) | Fundal height by size (in weeks) | Period of retention of dead fetus (in weeks) |
|---|---|---|---|
| 1 | 40 | 38 | 2 |
| 2 | 32 | 28 | 4 |
| 3 | 34 | 28 | 6 |
| 4 | 38 | 28 | 10 |
| 5 | 40 | 32 | 8 |
| 6 | 30 | 24 | 6 |

TABLE II

*Urinary Oestriol (24 hours) in Cases of Intra-uterine Death of Fetus*

| Case number | Urinary oestriol (mg.) |
|---|---|
| 1 | 4.00 |
| 2 | 3.40 |
| 3 | 2.40 |
| 4 | 3.80 |
| 5 | 2.22 |
| 6 | 1.80 |

*Coagulation studies:* The values of bleeding time, whole blood clotting time, prothrombin time, thrombin time, kaolin cephalin clotting time (K.C.C.T.), prothrombin consumption index (P.C.I.), euglobulin lysis time, platelet count, serum fibrinogen degradation products (F.D.P.) and plasma fibrinogen in individual cases, together with their mean and standard deviation in these patients and controls are depicted in scattergrams (Figs. 1 to 3).

Two of the patients showed prolonged thrombin time; after addition of equal volume of normal plasma it was not corrected at all in one and partially corrected in another. Euglobulin lysis time was reduced in both of them (100 and 110 min. respectively) and serum F.D.P. elevated

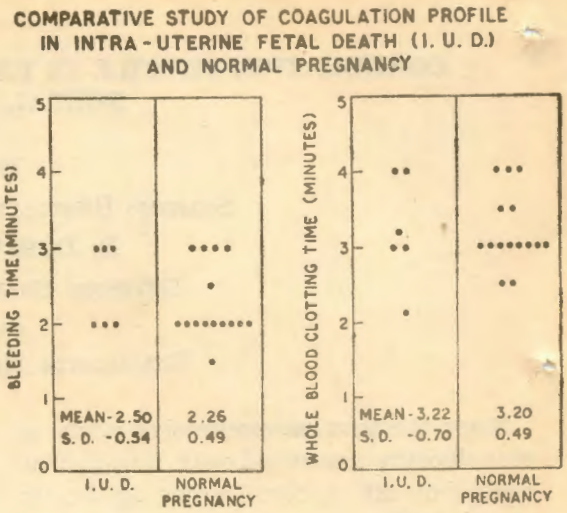


Fig. 1.

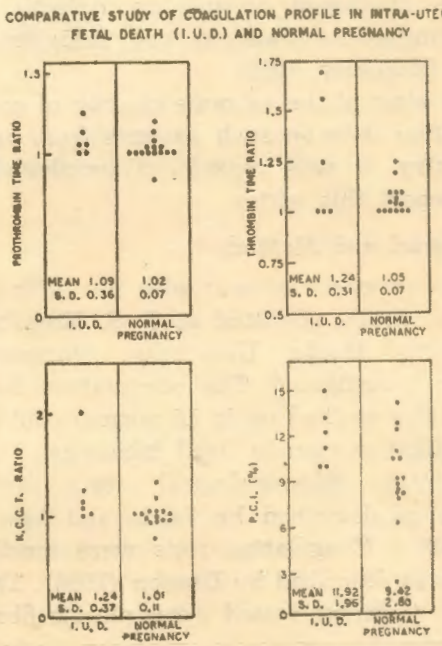


Fig. 2.

in one. Plasma fibrinogen in them was 220 mg% and 240 mg%, respectively.

On statistical comparison of cases of intrauterine foetal death with normal pregnancy there was no significant diffe-

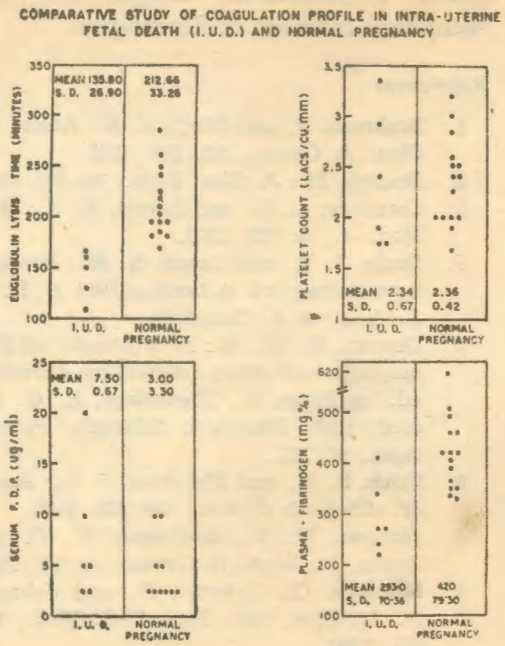


Fig. 3.

rence in bleeding time, whole blood clotting time, prothrombin time, thrombin time, K.C.C.T. and platelet count but there was significant decrease in euglobulin lysis time ($t = 2.623$; $p<0.02$) and in plasma fibrinogen ($t = 3.43$; $p<0.001$).

*Discussion*

Six pregnant women with retention of dead foetus in utero for a varying period from 2 to 10 weeks were studied. Induction of labour with "syntocinon" and artificial rupture of membranes was successful in 5 of them; in the remaining one hysterotomy had to be done. None of these patients showed any bleeding diathesis before, during or after induction of labour or hysterotomy.

The study of coagulation profile, however, revealed clotting abnormalities, though of mild degree, in 3 of these patients. In 2 of them plasma fibrinogen level was significantly reduced (lower than control mean minus 2 S.D.), with prolongation of thrombin time and acceleration of euglobulin lysis. One of them had elevated serum F.D.P. levels.

The exact frequency of bleeding diathesis or coagulopathy in cases with retention of a dead foetus is difficult to assess. Weiner *et al.*, (1950) noted that 3 of the 15 Rh negative women with this syndrome developed a haemorrhagic state. Pritchard and Ratnoff (1955) in a study of 31 patients noted bleeding manifestations in 1 patient prior to delivery and in 2 others immediately postpartum. Hypofibrinogenemia was found not only in the 3 patients but in 5 additional patients who had no bleeding diathesis. It is thus evident that coagulopathy is more common than clinical bleeding in this syndrome.

The available literature including the isolated case reports, indicates that the degree of coagulopathy and haemorrhagic manifestations depend to some extent on the period of retention of dead fetus (Weiner *et al.*, 1950; Reid, *et al.*, 1953; Schneider, 1953 and Pritchard and Ratnoff 1955). The 3 cases in the present series with varying degree of coagulopathy, had retained the dead fetus for 10, 8 and 6 weeks, respectively. In the other 3 cases without coagulopathy, the period of retention was 2, 4 and 6 weeks, respectively.

The laboratory data in the different series suggest consumption of fibrinogen by a relatively low grade intravascular coagulation (Weiner *et al*, 1950; Reid *et al.*, 1953; Schneider, 1953 and Pritchard and Ratnoff, 1955). This is also supported by rise of plasma fibrinogen following a short course of intravenous heparin therapy in one case of retained dead foetus (Phillips and Sciarra, 1965).

The increase in permeability of amnio-

tic membranes in dead fetus (Courtney and Boxall, 1971) may facilitate the escape of liquor causing amniotic fluid infusion or escape of thromboplastic material liberated from necrotic placenta and decidual tissue into maternal circulation causing consumption coagulopathy. The other mechanism for this type of coagulopathy may be the fibrin deposition in the intervillous spaces of placenta (Stouffer and Ashworth, 1958; Peterbeak and Hill 1971).

Though hyperfibrinolysis has been emphasized occasionally the general opinion is that fibrinolytic system is not of primary importance for hypofibrinogenemia (Brakman and King, 1965; Phillips and Sciarra, 1965). The mild increase of fibrinolysis as noticed by us is probably secondary to intravascular coagulation.

*Summary*

Six pregnant women with intrauterine foetal death for 2 to 10 week's period were investigated. None of them exhibited any haemorrhagic diathesis. However coagulation changes, though of mild degree, were revealed in 3 of them. Two patients showed prolonged thrombin time, reduced plasma fibrinogen and shortened euglobulin lysis time; one of them had elevated serum level of fibrinogen/fibrin degradation products. Statistically significant reduction of plasma fibrinogen and euglobulin lysis time was noticeable in the group of these 6 patients when compared to 15 normal pregnant women in third trimester. The coagulation disturbance in these patients is likely caused by low grade intravascular coagulation with secondary increase of fibrinolysis.

*References*

1. Brakman, P. and King, A. E.: Amer. Jr. Obst. & Gynec., 92: 221, 1965.
2. Buckell, M.: J. Clin. Path., 11: 403, 1958.
3. Courtney, L. D. and Boxall, R. R.: Brit. Med. J., 4: 492, 1971.
4. Dacie, J. V. and Lewis, S. M.: Practical haematology, ed. 4, London 1968, E. L. B. S. & J. & A Churchill.
5. Denson, K. W. E.: In treatment of Haemophilia and other coagulation disorders. ed. by Biggs, R., Macfarlane, R. G. Oxford, 1966, Blackwell Scientific Publications. p. 337.
6. Frick, P. G. and Mekelvey, J. L.: Amer. Jr. Obst. & Gynec., 70: 328, 1955.
7. Jackson, D. P., Hartmann, R. C. and Busby, J.: Obst. & Gynec., 5: 223, 1955.
8. Merskey, C., Lalezari, P. and Johnson, A. J.: Proc. Soc. Exp. Biol. Med., 131: 871, 1969.
9. Owen, C. A. Jr., Bowie, E. J. W., Didisheim, P. and Thompson, J. R.: The diagnosis of bleeding disorders. ed. 1, London 1969. J. & A. Churchill Ltd., p. 89.
10. Peterbeck, R. and Hill, J. R.: Amer. Jr. Obst. & Gynec., 110: 123, 1971.
11. Phillips, L. L. and Sciarra, J. J.: Amer. Jr. Obst. & Gynec., 92: 1161, 1965.
12. Pritchard, J. A. and Ratnoff, O. D.: Surg. Gynec. & Obst., 101: 467, 1955.
13. Quick, A. J.: Haemorrhagic diseases and thrombosis. Philadelphia, 1966, Lea & Febiger, p. 410.
14. Reid, D. E., Weiner, A. E., Roby, C. C., Diamond, L. K.: Amer. Jr. Obst. & Gynec., 66: 500, 1953.
15. Schneider, C. L.: Amer. Acad. Obst. & Gynec., 1: 321, 1953.
16. Stouffer, J. G. and Ashworth, C. J.: Amer. Jr. Obst. & Gynec., 75: 407, 1958.
17. Weiner, A. E., Reid, D. E. and Roby, C. C.: Amer. Jr. Obst. & Gynec., 60: 1015, 1950.