Disseminated intravascular coagulation in obstetrics
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Abstract
Disseminated Intravascular Coagulation (DIC) is an acute emergency characterized by inappropriate activation of coagulation and fibrinolytic system and manifested by severe bleeding. DIC is always a secondary phenomenon and often encountered in obstetric practice. Common condition predisposing to DIC include abruptio placentae, amniotic fluid embolism, sepsis, sever pre-eclampsia and eclampsia. Diagnosis is often made from clinical manifestation and estimation of coagulation profile though histological diagnosis of fibrin deposits is the definitive feature of DIC. Basic principles of management include understanding the pathophysiology, elimination of underlying cause and replacement of lost blood and specific components.

Key words
Disseminated Intravascular Coagulation, intrinsic and extrinsic system, replasement therapy, Fibrinolysis

Disseminated intravascular coagulation in obstetrics

Definition
Disseminated Intravascular Coagulation (DIC) is a pathologic condition associated with inappropriate activation of coagulation and fibrinolytic system that result in a tendency towards hypercoagulability but paradoxically result in sever bleeding. DIC is always a secondary phenomenon and not a disease entity in its own rights.

Incidence
The incidence of DIC in obstetrical patients is difficult to ascertain owing to the wide variation of precipitating events and the exceedingly complex range of clinical manifestations. Obstetric related DIC is encountered in 1 in 500 deliveries for the severe type of DIC and more commonly for milder forms.

Pathogenesis
The coagulation system is divided into intrinsic and extrinsic systems. The intrinsic system contains all the intravascular components required to activate thrombin by sequential activation of factors XII, XI, IX, X, V, and II (prothrombin). The extrinsic system is initially activated by tissue thromboplastin, leading to sequential activation of factors VII, X, Vi and prothrombin. Both the intrinsic and extrinsic pathways converge to activate factor X. Factor X subsequently reacts with activated factor V in the presence of calcium and converts prothrombin to thrombin. Thrombin is a proteolytic enzyme responsible for splitting fibrinogen chains into fibrinopeptides, leading to the formation of fibrin monomer. This central enzyme is capable of activating factor XIII to stabilize the newly formed fibrin clot and will enhance the activity of factors V and V11. DIC occurs when monocytes and endothelial cells are injured by toxic substances elaborated in the course of certain diseases that generate tissue factor activating the coagulation cascade. There is an unregulated explosive generation of thrombin that deplete clotting factor and platelets and activate the fibrinolytic systems. Secondary to clot lysis an anticoagulant effect results in erythrocyte fragmentation, haemorrhage, tissue hypoxia and anaemia. It is the generation of free thrombin and plasmin in the circulation that is responsible for the thrombotic and haemorrhagic manifestation respectively. Functional healthy endothelium concentrates antithrombin molecule on its surface and express thrombomodulin molecules. If thrombin is generated next to healthy endothelium it is neutralized by antithrombin or bind to thrombomodulin which alters its
property that it is no longer capable of converting fibrinogen to fibrin. Instead, thrombomodulin bound thrombin activate the natural anticoagulant protein C system. DIC occurs when this antagonist systems of coagulation and anticoagulation are not balanced. Figure-1 depicts the disease process of DIC.

Disseminated intravascular coagulation

Most common obstetric conditions associated with DIC are
• Abruptio placentae
• Amniotic fluid embolism
• Septic abortion
• Intrauterine infection
• Retained dead fetus in utero
• Hydatidiform mole
• Placenta accreta
• Pre-eclampsia and eclampsia
• Prolonged shock from any cause

Mechanism of DIC in specific obstetric conditions

Placental Abruption
• Liberation of tissue thromboplastin and
• Intrauterine consumption of fibrinogen and clotting factors in retro placental clot -leads to activation of extrinsic system.

Retained dead fetus
• Liberation of tissue thromboplastin from non viable tissue

Amniotic fluid embolism
• Liberation of tissue thromboplastin,
• intrinsic procoagulant property of fluid and
• associated hypotension, hypoxaemia and tissue acidosis encourage coagulation factors

Pre-eclampsia and eclampsia
• It is postulated that the abnormality may reflect platelet adherence to exposed collagen at the sites of damaged endothelium.
• This condition is associated with chronic coagulation abnormalities that lead to thrombocytopenia and elevation of Fibrin

Degradation Product
• Septic abortion
• release of tissue thromboplastin
• release of bacterial endotoxin

Clinical findings
It relates primarily to haemorrhage, anaeimia and ischaemia. Patients generally have frank bleeding or a tendency to bleed from mucous membranes, intravenous line sites and surgical incisions. Abnormal bruising, purpura, petechiae and ecchymosis frequently are noted. There may be haematemesis, haematuria and vaginal bleeding. The quality and character of bleeding are directly related to severity of the disease process.

Essentials of diagnosis
• History of recent bleeding diathesis, especially concurrent with some obstetric condition.
• Clinical evidence of multiple bleeding points associated with purpura and petechiae on physical examination.
• Laboratory findings classically include thrombocytopenia, hypofibrinogenemia, and elevated prothrombin time.

Histologic diagnosis of fibrin deposits is the definitive feature of DIC. There are a host of indirect tests. Laboratory findings in DIC are described in Table I.

<table>
<thead>
<tr>
<th>Test</th>
<th>Result</th>
</tr>
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<tbody>
<tr>
<td>Partial thromboplastin time</td>
<td>prolonged in 40-50 %</td>
</tr>
<tr>
<td>Prothrombin</td>
<td>prolonged in 50-75 %</td>
</tr>
<tr>
<td>Platelet count</td>
<td>decreased in 90 %</td>
</tr>
<tr>
<td>Thrombin Time</td>
<td>prolonged in 80 %</td>
</tr>
<tr>
<td>Fibrinogen</td>
<td>decreased in 90 %</td>
</tr>
<tr>
<td>Fibrinogen</td>
<td>decreased in 90 %</td>
</tr>
<tr>
<td>Fibrin degradation products</td>
<td>elevated in 85-100 %</td>
</tr>
<tr>
<td>values greater than 40 microgram / ml</td>
<td></td>
</tr>
<tr>
<td>suggestive of DIC</td>
<td></td>
</tr>
<tr>
<td>Protamine procoagulant test</td>
<td>positive</td>
</tr>
<tr>
<td>Blood smear</td>
<td>Schistocytes in 40%</td>
</tr>
</tbody>
</table>
Clot observation test (Weiner)
It is an useful bedside test. It can be repeated at intervals. 5ml of venous blood is placed in a 15 ml dry test tube and kept at 37°C. Usually blood clot forms within 6-12 minutes. This test provides a rough idea of blood fibrinogen level. If the clotting time is less than 6 minutes, fibrinogen level is more than 150 mg percent. If no clot forms within 30 minutes, the fibrinogen level is probably less than 100 mg percent

Newer tests
• O-dimer-This neoantigen is formed as a result of plasmin digestion of cross linked fibrin. This test is specific for FOP and abnormal in 90% cases-
• Antithrombin III level -abnormal in 89% cases. Fibrinopeptide A-abnormal in 75% cases

Spectrum of severity of DIC
DIC is an acute emergency and there is chances of rapid progression from stage 1 to stage 3 if appropriate measures are not taken. There is a great spectrum of manifestation of ranging from a compensated state with no clinical feature but evidence of increased production and breakdown of coagulation factors to the condition of massive uncontrollable Haemorrhage.

Management of DIC
The clinical condition demands urgent management and there is no time to wait for the results of coagulation factor assays.

Basic principles of management
• Understanding pathophysiology
• Eliminate underlying cause
• Use perinatal team approach for support of patient and family

Procedures
• Stabilize vital signs
• Maintain adequate urinary output
• Institute and maintain appropriate blood component therapy to replace consumable, blood clotting factors and platelets

Replacement therapy - Plasma substitutes
There is much controversy to use plasma substitute to give to any bleeding patient. The choice lies between simple crystalloids such as Hartmann's solution and artificial colloids such as dextran or preparation of human albumin (albuminoids). If crystalloids are used two to three times the volume of estimated blood loss should be administered. Problem with use of colloids are that dextran adversely alter platelet function, may cause pseudoagglutination and interfere with subsequent blood grouping and cross matching. It is also associated with anaphylactoid reactions and contraindicated in the pregnant women.

Use of whole blood and component
Whole fresh blood is advocated but it should be screened for Hepatitis and HIV. Sometimes it may be waste of vitally needed components required for patients with isolated deficiency. The use of fresh frozen plasma (FFP) followed by bank red cells will provide all component except platelets. It is to mention that-FFP Contains all the coagulation fractions present in plasma obtained from whole blood within 6 hours of donation. Plasma protein fraction (albumin) does not
contain carry risk of transmitting infection. Cryoprecipitate is richer in fibrinogen than FFP but lacks antithrombin III which is consumed in obstetric hemorrhage. Concentrated platelets may be given in addition to FFP to achieve homeostasis\(^1\). Red cell transfusion -stored bank blood is deficient in labile clotting factor (factor V, VIII and platelets). It is advisable to transfuse IU of FFP for every 4-6 U of bank red cell administered. Administration of Heparin is controversial in acute DIC. It is beneficial in patients when progressive thrombin formation occurs or with large thrombosis. The recommended dose is 100 unit/kg subcutaneous every 4 to 6 hours\(^1\).

**Conclusion**

As DIC is always a secondary phenomenon the mainstay of management is therefore to remove the initiating stimulus if possible. The mortality reported in patients with DIC range between 50-85 percent and the wide variation reflects the mortality of the underlying disorder. The major determinant of the survival is prompt identification of the underlying trigger, elimination of the cause and appropriate management.

**References**