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Review Article

DIC-A Nightmare in Obstetrics

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Abstract

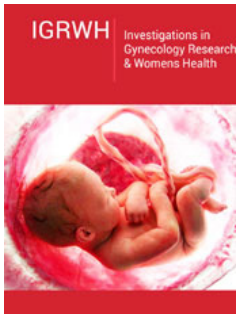
Disseminated Intravascular Coagulation (DIC), the most catastrophic obstetric acute emergency, is characterized by an inappropriate activation of coagulation & fibrinolytic system triggered by conditions like abruptio placentae & amniotic fluid embolism (release of thromboplastin intravascularly) or by diffuse endothelial damage as a result of pre-eclampsia. Clinical manifestation of severe bleeding and damaged coagulation profile are hallmarks of diagnosis, although histopathological demonstration of fibrin deposits is the pathognomonic feature of DIC. Understanding the basic pathophysiology, tackling the underlying etiological factor and replacement of the lost blood and specific components cover the principles of management of this condition.

Keywords: DIC; FFP; Thromboplastin coagulation failure; Coagulopathy

Abbreviations

DIC: Disseminated Intravascular Coagulation; HELLP: Hemolysis Elevated Liver Enzymes and Low Platelets Syndrome; IUFD: Intrauterine Fetal Death; FDP: Fibrin Degradation Products; FFP: Fresh Frozen Plasma; ISTH: International Society for Thrombosis and Hemostasis; AFE: Amniotic Fluid Embolism

ISSN: 2577-2015



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Submission: October 10, 2020
Published: March 29, 2021

Volume 4 - Issue 1

How to cite this article: Jayati Nath. DIC-A Nightmare in Obstetrics. Invest Gynecol Res Women's Health. 4(1). IGRWH. 000580. 2021.
DOI: 10.31031/IGRWH.2021.04.000580

Introduction

Disseminated Intravascular Coagulation (DIC) is a syndrome which is triggered by the activation of both the coagulation & the fibrinolytic systems, often secondary to an underlying obstetric phenomenon eg. pre-eclampsia, eclampsia, HELLP syndrome, placental abruption, Intrauterine Fetal Death (IUFD) of usually more than 4 weeks duration, massive or incompatible blood transfusion, induced septic abortion or massive tissue injury, hydatidiform mole, amniotic fluid embolism etc [1-3]. Generally, in most cases, the end-stage of DIC can be prevented by timely diagnosis and management of the underlying etiological condition and aggressive resuscitation [4].

Otherwise also known as 'Consumption Coagulopathy', the basic pathophysiology is widespread intravascular fibrin formation in response to excessive blood protease activity which overcomes the natural anticoagulant mechanism of the body. Thereafter, the exposure of the blood to phospholipids released from the damaged tissue, hemolysis & endothelial damage act as the triggering factors to the development of DIC [2].

DIC is almost never primary, but usually is secondary to some other stimulating factor of the coagulation activity by release of pro-coagulant substances into the bloodstream. DIC stimulates the process of fibrinolysis & the resultant Fibrin Degradation Products (FDPs) interfere with the formation of firm fibrin clots which results in a vicious cycle resulting in further catastrophic bleeding. FDPs, apart from the above, also interfere with the normal myometrial function & cardiac function & may themselves aggravate both hemorrhage & shock [3].

The Pathophysiological Basis of DIC

Normally the hemostatic equilibrium of the body is maintained by a fine balance of fibrinolysis & coagulation systems. The activation of the coagulation cascade produces thrombin which converts fibrinogen to fibrin, the stable fibrin clot being the final product of hemostasis. The fibrinolytic system then breaks down fibrinogen and fibrin. This activation of the fibrinolytic system generates plasmin in the presence of thrombin responsible for lysis of fibrin clots learning formation of polypeptides called Fibrin Degradation Products (FDPs). The equilibrium between coagulation & fibrinolysis is dysregulated in DIC. The main mediator of this is release of a transmembrane glycoprotein called Tissue Factor (TF). This is released

in response to exposure to cytokines especially IL-1, TNF (tumour necrosis factor) & endotoxin [4].

In sepsis, this is the main mediator for developing DIC. Gram negative sepsis triggers DIC by release of endotoxin. When exposed to blood and platelets, Tissue Factor binds with activated factor VIIa, forming the extrinsic tenase complex which activates factor IX & X formimg IXa & Xa leading to the common coagulation pathway & subsequent formation of thrombin & fibrin [5]. Excess activation of coagulation cascade leads to excess circulating thrombin resulting in elevated fibrinogen levels thereby multiple fibrin clots are formed in the circulation. These trap the platelets to become larger clots resulting in microvascular and macrovascular thrombosis. These clots are lodged in the microcirculation, large blood vessels & all the organs causing ischemia, impaired organ perfusion & end-organ-damage which are the hallmarks of DIC. The previous nomenclature of 'consumption coagulopathy' is justified by the fact that coagulation inhibitors are consumed in the process. Decrease in the inhibitor level allows more clotting leading to a positive feedback loop whereby increased clotting leads to more clotting & a vicious cycle ensues.

Simultaneously, thrombocytopenia ensues due to entrapment & consumption of platelets. Clotting factors are also consumed up due to formation of multiple clots which results in the catastrophic bleeding so very characteristics of DIC. At the same time, the excess circulating thrombin helps in the conversion of plasminogen to plasmin resulting in fibrinolysis. This breakdown of the clots leads to excess in Fibrin Degradation Products (FDPs) which, due to their powerful anti-coagulant properties, contribute to bleeding. The excess plasmin also activates the complement &kinin systems which produce the clinical symptoms of DIC namely hypotension, shock & increased vascular permeability. Therefore, the acute catastrophic variant of DIC is considered to be an extreme expression of the intravascular coagulation process with complete breakdown of the normal homeostatic equilibrium.

Recently, there have been new assumptions & interpretations of the pathophysiology of DIC. Animal model studies of sepsis & DIC have demonstrated a highly expressed receptor on the hepatocytes surface called the Ashwell-Morell receptor which is responsible for thrombocytopenia in bacteremia and septicemia caused by streptococcus pneumoniae [6]. The hemorrhage observed in DIC maybe secondary to increased thrombosis with loss of mechanical vascular barrier. This new discovery can pave ways in devising novel approaches in reducing the morbidity & mortality associated with DIC [6].

Clinical Features of DIC

Directly proportional to the degree of imbalance in the hemostasis equilibrium & the underlying etiological factor, the commonest features of DIC are bleeding which might range from oozing from puncture sites-in skin or veins, petichiae, ecchymoses to severe hemorrhage from genito-urinary tract, gastro-intestinal tract, lung or into the central nervous system. The state of hypercoagulability of DIC usually manifests as occlusion of microcirculatory vessels resulting in multiple organ failure, as well as thrombosis of large vessels & cerebral thromboembolism. Patients with acute severe DIC might present with hemodynamic instability and complications like hypovolemia and shock. DIC is a condition with very high morbidity and mortality ranging from 30-85% depending on the severity of the condition and the underlying pathology [7,8].

Diagnosis of DIC

No single test is diagnostic of DIC. Clinical signs & symptoms along with laboratory abnormalities of coagulation or thrombocytopenia form the basis of diagnosing DIC [1]. Coagulation tests including APTT, PT, TT (Thrombin Time) & markers of the Fibrin Degradation Product (FDP), d-Dimer, platelet count & peripheral blood smear analysis are the corner stones for the same. These tests need to be repeated over a period of 6-8 hours because mild abnormality detected early on in the disease process may dramatically change with severity and progress of the disease [2].

The most common findings are prolonged PT and/or APTT, low platelet counts (<100,000/mm^3) or a rapid decline in platelet numbers (decrescendo thrombocytopenia) & elevated FDPs and d-Dimers [3]. Severe DIC is associated with low anti-thrombin-III or plasminogen activity usually < 60% of the normal [7].

International Society for Thrombosis and Hemostastic (ISTH) Scoring system for DIC [7,8]

The test results are scored as follows:

a) Platelet count

i. >100 X 10^9/L=0

ii. <100 X 10^9/L=1

iii. <50 X 10^9/L=2

b) Elevated fibrin marker (D-dimer, FDP)

i. no increase=0

ii. moderate increase=2

iii. strong increase=3

c) Prolonged PT:

i. <3 sec=0

ii. >3sec but < 6sec=1

iii. >6sec=2

d) Fibrinogen level:

i. >1 g/L = 0

ii. <1 g/L = 1

e) Calculate Total score: (1+2+3+4)

i. ≥ 5 --> overt DIC (repeat score daily)

ii. ≤ 5 --> non-overt DIC (repeat next 1-2 days)

Management of Severe Hemorrhage in DIC

An acutely bleeding obstetric patient is an acute emergency warranting a team effort of obstetrician, anesthesiologist, hematologist, physician, nursing and paramedical staff in all maternity units [9]. It is of utmost importance to locate and deal the source of bleeding, often an unsuspected uterine or genital laceration leading to hypovolemic shock & DIC resulting in hemostatic failure and prolonged hemorrhage. The management of hemorrhage is same whether the bleeding is initiated or augmented by a failure in the coagulation system. Prompt and adequate fluid replacement is imperative to be done at a war-footing so as to avoid renal shutdown and acute kidney injury [10,11].

Effective circulation, when restored, without too much delay, the FDPs in the circulation will be cleared by the liver mainly which will aid in restoration of normal hemostasis. Simple crystalloids eg. Hartmann's solution or Ringer's Lactate and artificial colloids eg. Dextran, Hydroxyethyl starch and Gelatin solution or Human albumin may be used for restoring the circulation. Two or three times of the estimated blood loss should be transfused as crystalloids as these stay in the vascular compartments for a shorter time than colloids when the rental function is maintained [12]. The best way to deal with hypovolemic shock initially is by transfusing simple balanced salt solutions (crystalloids) followed by red cells & Fresh Frozen Plasma (FFP) [11,12]. Some researchers advocate the use of a derivative of bovine gelatin polygeline (Hemaccel) as a first-line fluid replacement therapy as it does not interfere with platelet function or subsequent blood grouping and cross matching. It is seen to improved renal function when administered in hypovolemic shock [11].

Blood and Component Therapy in DIC

Whole blood, especially freshly collected, has been the treatment of choice in coagulation failure associated with obstetric disorders. Fresh Frozen Plasma (FFP) contains all the coagulation factors present in plasma when obtained within 6 hours of donation. Cryoprecipitate, though richer in fibrinogen than FFP, lacks AT (anti-thrombin), which is rapidly consumed in obstetric hemorrhage associated with DIC (24) Platelet concentrate also is useful in dealing with the thrombocytopenia of DIC.

Conclusion

The main determinant of survival from DIC of obstetric cause is prompt and timely identification of the underlying etiological trigger, elimination of the same and aggressive management with crystalloids, colloids, fresh whole blood, blood components eg. FFP, cryoprecipitate and platelet concentrate which can halt the ongoing process of consumption coagulopathy. In the absence of blood components immediately, fresh whole blood transfusion should be ordered which can be lifesaving for the patient with DIC.

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