IJCRT.ORG ISSN : 2320-2882

INTERNATIONAL JOURNAL OF CREATIVE RESEARCH THOUGHTS (IJCRT)

An International Open Access, Peer-reviewed, Refereed Journal

# STUDY OF DIFFERENTIAL DIAGNOSIS OF DISSEMINATED INTRAVASCULAR COAGULATION BY HEMATOLOGICAL AND COAGULATION TESTS.

Authors: Dr. Manan Bhensdadiya[1], Dr. Shrenik Sheth[2] , Dr. Stuti Ankleswaria[3], Dr. R. K. Tandon[4]

[1] Resident, Department of Pathology, Shrimati Bhikhiben Kanjibhai Shah Medical Institute and Research Centre, Sumandeep Vidyapeeth.

[2] Resident, Department of Pathology, Shrimati Bhikhiben Kanjibhai Shah Medical Institute and Research Centre, Sumandeep Vidyapeeth.

[3] Resident, Department of Pathology, Shrimati Bhikhiben Kanjibhai Shah Medical Institute and Research Centre, Sumandeep Vidyapeeth.

[4]Head, Department of Pathology, Shrimati Bhikhiben Kanjibhai Shah Medical Institute and Research Centre, Sumandeep Vidyapeeth.

**ABSTRACT:**

**INTRODUCTION:** The International Society on Thrombosis and Hemostasis gives the following definition for DIC: "An acquired syndrome characterized by the intravascular activation of coagulation with loss of localization arising from different causes. It can originate from and cause damage to the microvasculature, which if sufficiently severe can produce organ dysfunction". Disseminated intravascular coagulation (DIC) is a relatively commonly suspected complication in myriad clinical situations in hospital settings (ICU)[1].

**METHOD:** The present study "Differential diagnosis of Disseminated Intravascular Coagulation by hematological and coagulation tests" was conducted in our institution.

Total 100 cases of patients admitted in ICU wards of Medicine, Pediatrics and Obstetrics and Gynecology were studied.

**RESULT:** Hematological and coagulation profile in 100 cases of patients with thrombocytopenia, <150/cmm or >25% decrease from baseline were studied. Out of 100 cases 85 cases show coagulation disorder with DIC, 5 cases show normal coagulation profile with Hemolytic uremic syndrome - Thrombotic thrombocytopenic purpura (HUS-TTP), and remaining 10 cases were of only thrombocytopenia.

**CONCLUSION:** D Dimer is >0.5 ug/dl in 100% of cases, so it can be used as more specific test when both platelet count and PT are deranged to confirm diagnosis of DIC.

The combination of platelet count and PT help discriminate between TTP-HUS and DIC.

**KEY WORDS:** Disseminated Intravascular Coagulation, Hematological abnormalities

## Introduction:

The International Society on Thrombosis and Hemostasis gives the following definition for DIC:"An acquired syndrome characterized by the intravascular activation of coagulation with loss of localization arising from different causes.It can originate from and cause damage to the microvasculature, which if sufficiently severe, can produce organ dysfunction. Disseminated intravascular coagulation (DIC) is a relatively commonly suspected complication in myriad clinical situations in hospital settings (ICU)[1].

DIC is characterised by intravascular fibrin formation and disturbance of the microvasculature[2]. It is a complex disorder with multiple interactions involving hemostasis, fibrinolysis and inflammation.

The coagulation system in the body consists of clotting and fibrolytic mechanisms. The function of the former is to prevent excessive blood loss, whereas the latter is to ensure circulation within the vasculature. Following an insult the activated coagulation cascade adequately balances the naturally occurring anti-coagulant systems and the fibrinolytic system (which generates plasmin) to maintain a normal circulation.

In DIC, there is widespread activation of the blood coagulation system leading to excessive generation and disseminated deposition of fibrin clots in small and midsize vessels which alters the microcirculation leading to ischemic necrosis in various organs resulting in organ failure. There can be concomitant consumption of platelets and coagulation factors resulting in serious hemorrhagic complications which sometimes may be the most striking clinical presentation. Hence a patient with DIC can present as thrombotic and bleeding problem simultaneously[3].

DIC is not a specific illness, rather it is complication or an effect of the progression of other illnesses. Such conditions include the following-sepsis and severe infection, trauma, malignancy, obstetric complications, transfusion reactions, but it is most commonly observed in severe sepsis, septic shock and trauma – more than half the cases of DIC.

Laboratory testing for DIC is nearly always urgent and requires frequent repetitions to establish the diagnosis as well as to monitor the impact of interventions. Patients with DIC can present with a wide range of abnormalities in their laboratory values.

The most frequent laboratory abnormalities reported for diagnosis of DIC are[1]:

1. Low platelet count

2. Prolonged clotting times (aPTT and PT)

3. Low serum fibrinogen

4. Elevated D-dimer

5. Microangiopathic pathology (schistocytes) on peripheral smears

Current strategies, chiefly the International Society on Thrombosis and Hemostasis (ISTH) scoring algorithm assess multiple hemostatic and coagulation parameters to achieve adequate sensitivity and specificity of tests. This scoring system takes into account prothrombin time (PT), fibrinogen levels, levels of fibrin-related marker and platelet count.

DIC is a dynamic process and thus interpreting a series of laboratory tests over time is more relevant than looking at a single set of results. The results need to be interpreted in close collusion with the clinical data, including the primary diagnosis, presence of bleeding and/or thrombosis, and therapies administered - especially blood product support.

## AIMS AND OBJECTIVES:

1) To study hematological and coagulation parameters of patients by a combination of following tests -

- Platelet count
- PT
- aPTT
- D dimer
- Fibrinogen

2) To study the clinical conditions associated with DIC.

3) To prevent the patients from complications of DIC by its early detection.

4) To study differential diagnosis of DIC by hematological and coagulation tests.

## MATERIAL AND METHODS:

The present study "Differential diagnosis of Disseminated Intravascular Coagulation by hematological and coagulation tests" was conducted in our institution.

Total 100 cases of patients admitted in ICU wards of Medicine, Pediatrics and Obstetrics and Gynecology were studied.

**Type of study:** Prospective study

**Inclusion criteria:** Coagulation profile and peripheral smear examination records in central Hematology laboratory of patients with the clinical diagnosis of DIC or TTP-HUS and subjects with only thrombocytopenia.

**Exclusion criteria:** Patients having normal platelet count.

**Statistical analysis:** Data collected was analysed statistically using percentage and frequency distribution and was presented in the form of tables, charts and graphs.

## OBSERVATIONS AND RESULTS:

Hematological and coagulation profile in 100 cases of patients with thrombocytopenia, <150/cmm or >25% decrease from baseline were studied. Out of 100 cases 85 cases show coagulation disorder with DIC, 5 cases show normal coagulation profile with Hemolytic uremic syndrome - Thrombotic thrombocytopenic purpura (HUS-TTP), and remaining 10 cases were of only thrombocytopenia.

**Table 1: Division according to type of DIC**

| | | No. of cases (%) |
|---|---|---|
| 1 | Coagulation abnormality with overt DIC | 53 (62.3%) |
| 2 | Coagulation abnormality with non overt DIC | 32 (37.6%) |
| | Total | 85 |

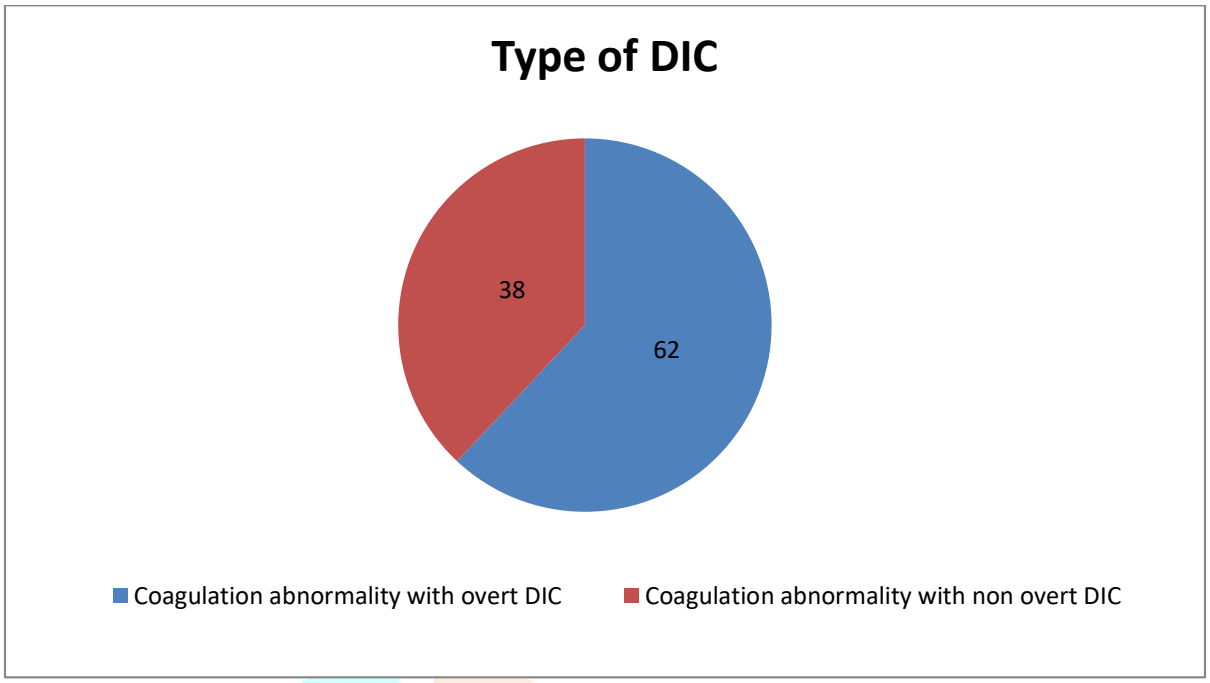


**Table 2: Other conditions causing DIC**

| Clinical condition | Frequency | Percentage |
|---|---|---|
| Septicemia | 15 | 55.5 |
| Malaria | 1 | 3.7 |
| Dengue | 4 | 14.8 |
| Liver disease (FHF, CLD) | 4 | 14.8 |
| Venomation (snake) | 3 | 11.1 |
| Total | 27 | 100% |

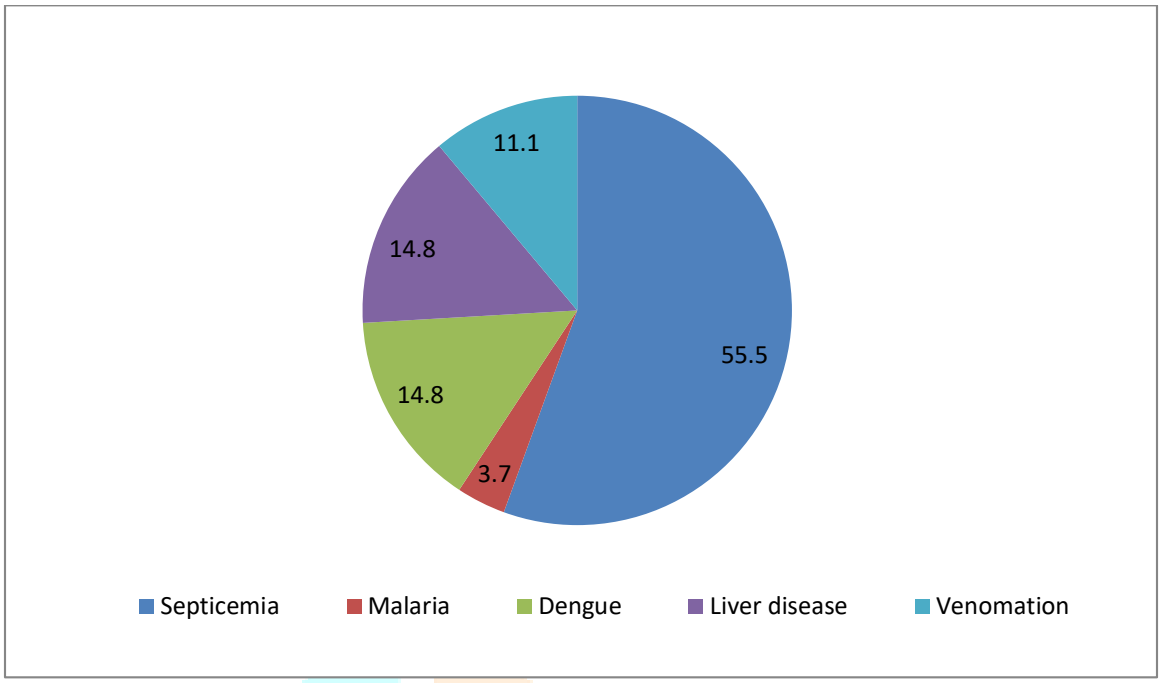


**Table 3: Distribution of Platelet count**

| Platelet count | Overt DIC | Non Overt DIC | Total |
|---|---|---|---|
| 1.5 – 1 lakhs | 4 (7.5%) | 2 (6.2%) | 6 (7%) |
| 1 lakh – 50000 | 14 (26.4%) | 11 (34.3%) | 25 (29.4%) |
| ≤50000 | 35 (66%) | 19 (59.3%) | 54 (63.5%) |
| Total | 53 | 32 | 85 |

On ROC curve analysis the Platelet count yielded a cut off of ≤78,000/cmm, with an 87% sensitivity and 82.86% specificity. The AUC was 0.917, implying that the Platelet count has a good discriminate value for the diagnosis of DIC.

**Table 4: Distribution of Prothrombin time**

| PT normal range 11-15 seconds | Overt DIC | Non Overt DIC | Total |
|---|---|---|---|
| PT 15-18 seconds | 10 (18.8%) | 16 (50%) | 26 (30.5%) |
| PT 18-21 seconds | 15 (28.3%) | 6 (18.7%) | 21 (24.7%) |
| PT >21 seconds | 28 (52.8%) | 10 (31.2%) | 38 (44.7%) |
| Total | 53 | 32 | 85 |

On ROC curve analysis, the PT yielded a cut off of >16.5 seconds, with a 62.86% sensitivity and 77% specificity. The AUC was 0.746, implying that PT has a good discriminate value for the diagnosis of DIC.

**Table 5: Distribution of APTT**

| APTT normal range 25-35 seconds | Overt DIC | Non Overt DIC | Total |
|---|---|---|---|
| 26-40 seconds | 28 (52.8%) | 20 (62.5%) | 48 (56.4%) |
| >40 seconds | 25 (47.1%) | 12 (37.5%) | 37 (43.5%) |
| Total | 53 | 32 | 85 |

On ROC curve analysis the APTT yielded a cut off of >45.3 seconds with a 32% sensitivity and 85.7% specificity. The AUC was 0.5910, implying that the APTT has a lower sensitivity for diagnosis of DIC.

**Table 6: Distribution of Serum Fibrinogen**

| Serum Fibrinogen level | Overt DIC | Non Overt DIC | Total |
|---|---|---|---|
| 200 mg/dl – 150 mg/dl | 19 (35.8%) | 20 (62.5%) | 39 (45.8%) |
| 150 mg/dl – 100 mg/dl | 9 (16.9%) | 9 (28.1%) | 18 (21.1%) |
| <100 mg/dl | 25 (47.1%) | 3 (9.3%) | 28 (32.9%) |
| Total | 53 | 32 | 85 |

On ROC curve analysis, the fibrinogen yielded a cut off of 210 mg/dl, with 82% sensitivity and 54.29% specificity. The AUC was 0.727, implying that the fibrinogen has a lower sensitivity and specificity for the diagnosis of DIC.

**Table 7: Distribution of D Dimer**

| D Dimer level | Overt DIC | Non Overt DIC | Total |
|---|---|---|---|
| <0.5 ug/ml | 00 | 01 (3.1%) | 01 (1.1%) |
| >0.5 ug/ml - ≤4 ug/ml | 08 (15.09%) | 09 (28.1%) | 17 (20%) |
| >4 ug/ml - ≤8.2 ug/ml | 29 (54.7%) | 19 (59.3%) | 48 (56.4%) |
| >8.2 ug/ml | 16 (30.1%) | 03 (9.3%) | 19 (22.3%) |
| Total | 53 | 32 | 85 |

On ROC curve analysis, the D Dimer yielded a cut off of 6.52 ug/ml, with a 62% sensitivity and 68.57% specificity. The AUC was 0.697, implying that D Dimer alone has a lower sensitivity for the diagnosis of DIC. For an ideal test area under the ROC curve would be expected to be 1.0. Cut off value is calculated by ROC curve having maximum sensitivity and specificity.

## DISCUSSION:

### Platelet count:

Table 8: Comparision of Platelet count

| Platelet count | Present study in overt DIC | Prashant s et al.2010[4] in overt DIC |
|---|---|---|
| <1.5 lakhs/cmm | 98.2% | 100% |
| <1.0 lakhs/cmm | 93.7% | 97.2% |
| <50000/cmm | 69% | 71.8% |

Present study result of Platelet count at different cut off is comparable with Prashant s et al. study. Platelet count <50,000/cmm can be used as a cut off to differentiate patient with overt DIC from patient with Non Overt DIC.

### Prothrombin time:

Table 9: Comparision of PT

| PT | Present study in overt DIC | Prashant s et al.2010[4] in overt DIC |
|---|---|---|
| >15 seconds | 86.2% | 81.7% |
| >18 seconds | 74.2% | 65.5% |
| >21 seconds | 48.5% | 38.0% |

Present study result of raised PT is comparable with Prashant s et al 2010. Prolonged PT is consistent finding in patients with overt DIC.

**APTT:**

Table 10: Comparision of APTT

| APTT | Present study in Overt DIC | Vani Chandrashekhar at el. 2011[5] study in overt DIC |
|---|---|---|
| >40 seconds | 41.43% | 82% |

In present study APTT is raised in 41.43% of patients (37 out of 85 cases) of total cases.

Vani Chandrasekhar et al. 2011[5] study of 50 cases, APTT was raised in 82% of patients (41 out of 50).

Findings of present study of raised APTT do not match with Vani Chandrasekhar et al.2011 study. As in present study 32 cases were of Non Overt DIC and APTT is raised in only 37.5% (12 out of 32) of patients with Non overt DIC. However APTT is raised in 47.1% 25 out of 53 of patients with overt DIC. So less number of patients with raised APTT seen in present study. However raised APTT is seen in significant number of patients with overt DIC.

**Serum Fibrinogen:**

Table 11: Comparision of Serum Fibrinogen

| Serum Fibrinogen | Present study in overt DIC | Prashant s et al.2010[4] |
|---|---|---|
| <200 mg/dl | 70.28% | 68.3% |
| <150 mg/dl | 35.8% | 39.2% |
| <100 mg/dl | 47.1% | 44.8% |

Present study result of reduced serum fibrinogen is comparable with Prashant s et al 2010. Reduced serum fibrinogen is consistent finding in patients with overt DIC.

## SUMMARY AND CONCLUSION:

- In this prospective study, Hematological and coagulation parameters in 100 patients admitted in ICU wards were studied to differentiate between DIC and TTP-HUS and study the usefulness of different laboratory parameters in rapidly distinguishing DIC from other causes.
- Out of 100 cases studied, 85 were of DIC 5 were of HUS -TTP and 10 were only cases with thrombocytopenia.
- Out of 85 cases of DIC, 53 were of Overt DIC and 32 were of Non-Overt DIC.
- Platelet count was decreased (<1.5 lacs/cmm) in 98.2% of patients with Overt DIC.
- PT was raised (15 seconds) in 86.2% of patients with Overt DIC.

- APTT was raised (>40 seconds) in 48.5% of patients with Overt DIC.
- Serum fibrinogen was decreased in 26% of patients with Overt DIC.
- D Dimer was increased in 100% of patients with Overt DIC.
- Platelet count PT and D Dimer were significantly altered in more than 50% of cases with overt DIC.
- There is no single test which can diagnose Overt DIC.
- Combination of tests is more useful in diagnosis of Overt DIC.
- Under ROC curve analysis platelet count and PT both have a highest sensitivity and specificity, so both can be used as an initial screening test in appropriate clinical context.
- D Dimer is >0.5 ug/dl in 100% of cases so it can be used as more specific test when both platelet count and PT are deranged to confirm diagnosis of Overt DIC.
- The combination of platelet count and PT help discriminate between TTP-HUS and DIC.

**REFERENCES:**

1) Wintrobe's Clinical Hematology 14 edition, 3780-3863

2) Hoffbrand's Essential Haematology, 297-300

3) Levi M, Toh CH, Thachil J, Watson HG. Guidelines for the diagnosis and management of disseminated intravascular coagulation. British Committee for Standards in Haematology. Br J Haematol. 2009:145:24-33.

4) Prashant Sharma et al, Limited utility of a Rapid Quantitative Enzyme linked Flurescent Assay for the D Dimer in diagnosis of overt Disseminated Intravascular Coagulation, Clinical and Applied Thrombosis/ hemostasis 16(6) 609-613.

5) Vani Chandrashekhar et al, DIC score statistical relationship with PT,APTT and simplified scoring system with combination of PT and APTT, International Scholarly research Network, ISRN He autology volume 2012, Article ID 579420.