

Original article:

Study of correlation of changes in D-DIMER levels and coagulation profile with the development of coagulation disorders

¹Dr Gurpreet Singh , ²Dr Mahima Sharma , ³Dr R K Chrungoo , ⁴Dr. Arvind Kharjuria

¹Ex-resident, Department of Pathology , Acharya Shri Chander college of Medical Sciences (ASCOMS) and Hospital, Sidhra, Jammu.

²Associate Professor, Department of Pathology , ASCOMS and Hospital, Sidhra, Jammu

³Professor, Department of Surgery , ASCOMS and Hospital, Sidhra, Jammu

⁴ Professor and Head , Department of Pathology , ASCOMS and Hospital, Sidhra, Jammu.

Corresponding author: Dr Mahima Sharma

ABSTRACT:

INTRODUCTION: D-DIMER has been regarded as one of the most useful parameters to evaluate the hyperfibrinolytic state, especially for the diagnosis of various conditions like DIC, DVT, PE. Numerous studies have also shown the investigative role of D-DIMER in various conditions. Based on this background, the present work was planned to study and correlate changes in D-DIMER levels and coagulation profile with the development of coagulation disorders .

MATERIAL AND METHODS: The study was conducted for a period of two years and all the subjects were recruited from Department of surgery ASCOMS hospital, which is a tertiary care hospital. The post surgical subjects were recruited into the study group based on the inclusion and exclusion criteria after informed consent was given by the patient.

Results: Preoperatively none of the patients showed positive D-Dimer test. Overall 89.3percent of patients had positive test at some point of time postoperatively. 88.6 Percent of patients had a positive D-Dimer test on the third postoperative day and 90 Percent of patients had a positive D-Dimer test on seventh postoperative day. Thus the test has a tendency to be positive in the postoperative period.

CONCLUSION: In conclusion our study demonstrates that the changes that occur in postoperative period in coagulation and fibrinolysis in a major surgery may predispose the patients to increased risk of venous thromboembolism. D-Dimer generation was increased postoperatively in all the surgical groups. The combination of changes in D-Dimer, PT, PTT and platelet counts after surgery confirms the hypercoagulable state and hence the risk for postoperative DVT and related complications.

INTRODUCTION

D-DIMER has been regarded as one of the most useful parameters to evaluate the hyperfibrinolytic state, especially for the diagnosis of various conditions like DIC, DVT, PE. Numerous studies have also shown the investigative role of D-DIMER in various conditions. The most frequently used serum D-DIMER assays are based on the use of polyclonal antibodies. Methods to measure D-DIMER using latex agglutination are now widely used for the diagnosis of DIC, DVT, PE. Recent refinements in assay technologies has made it much easier to measure D-DIMER from blood plasma. ¹ Based on this background, the present work was planned to study and correlate changes in D-DIMER levels and coagulation profile with the development of coagulation disorders .

MATERIAL AND METHODS:

The study was conducted for a period of two years and all the subjects were recruited from Department of surgery ASCOMS hospital, which is a tertiary care hospital.

The post surgical subjects were recruited into the study group based on the inclusion and exclusion criteria after informed consent is given by the patient.

Inclusion criteria:

1. Age between 18-55 years.
2. Post operative cases would be recruited

Exclusion criteria:

1. Existing coagulopathy.
2. Patients on anticoagulant therapy.
3. Patients on hormone replacement therapy.
4. Previous surgery.

Blood sample for the coagulation profile, which include assessment of prothrombin time (PT), partial thromboplastin time (PTT), D-Dimer assay, platelet count, were collected preoperatively followed by 3rd and 7th post operative day. Their age, detailed history and physical examination were recorded carefully in the proforma which was specially prepared for this purpose. Besides the clinical examination, laboratory investigations were carried out in order to construct a base line for detecting changes in these parameters following operative trauma. Routine investigations comprising of hemoglobin estimation, total leukocyte count, differential leukocyte count and urine examination were carried out in all patients.

Ethical clearance was obtained from the ethics committee of Acharya Shri Chander College of Medical Sciences & Hospital, Sidhra, Jammu. The study protocol was made in accordance with the ethical guidelines of the declaration of Helsinki and written informed consent was obtained from all study subjects before recruitment.

D-DIMER ASSAY :

This test is based on the principle of agglutination. When the test sample is mixed with monoclonal Anti-D dimer antibody, cross linked fibrin degradation products in the sample bind to the coated latex particles and results in visible agglutination when the concentration is above the threshold for detection of the assay. The cross linked fibrin degradation products, D dimer, D dimer E and high molecular weight derivatives are all recognized by this reagent incorporating the monoclonal antibodies.

Assay of Platelet count:

The whole blood sample is mixed with a diluents (1 percent ammonium oxalate) in which red cells are lysed. An improved Neubauer counting chamber is filled with the mixture and the platelets are counted under the microscope.

STASTICAL TESTS APPLIED

Continuous variables are presented as mean \pm SD. Demographic data were compared using 2-tailed t tests. To look for significant differences between groups at each time point, unpaired t tests were used and for significant differences from baseline within each group, paired t tests was used. Stastical evaluations were performed using standardized software (SPSS version 1.6).A p value of less than 0.05 was considered significant. Differences between groups. (eg cholecystectomy versus hemicolectomy) were determined using unpaired Student's t-tests for demographic and baseline variables.

OBSERVATIONS

A total of seventy patients were studied who underwent routine and uncomplicated abdominal surgeries from November 2014 to October 2015, in the Department of Surgery, ASCOMS hospital, a tertiary care hospital, in Jammu. The subjects were selected in accordance with the inclusion and exclusion criteria after informed consent was given by the patient.

Table 1: Statistical analysis of changes in coagulation parameters in all patients (n=70).

| SL No | Changes in Coagulation Parameters | P value | Correlation (r) |
|-------|--|---------|-----------------|
| 1. | Prothrombin time (preop vs post op day 3) | 0.000* | 0.131 |
| 2. | Prothrombin time (preop vs post op day 7) | 0.000* | 0.129 |
| 3. | Prothrombin time (post-op day3 vs post-op day 7) | 0.009* | 0.855 |
| 4. | PTT (preop vs post op day 3) | 0.000* | 0.597 |
| 5. | PTT (preop vs post op day 7) | 0.000* | 0.528 |
| 6. | PTT (post-op day3 vs post-op day 7) | 0.001* | 0.830 |
| 7. | Platelet count(preop vs post op day 3) | 0.001* | 0.437 |
| 8. | Platelet count (preop vs post op day 7) | 0.000* | 0.351 |
| 9. | Platelet count (post-op day3 vs post-op day 7) | 0.000* | 0.758 |
| 10. | D-Dimer (preop vs post op day 3) | 0.002* | - |
| 11. | D-Dimer (preop vs post op day 7) | 0.000* | - |
| 12. | D-Dimer(post-op day3 vs post-op day 7) | 0.353 | - |

* p-value less than 0.05 is considered statistically significant

Prothrombin Time

Preoperatively PT was not prolonged in any patient studied. The mean preoperative PT was 12.23 seconds. On the third post operative day the mean value of PT was 14.52 seconds and the mean PT was 14.91 seconds. Pre and post operative values were compared for different surgical groups using paired t test and the difference was found to be statistically significant ($p < 0.05$) between pre-op and post-op (day3 and 7),and between post-op day 3and day 7.(Table 1)

Partial thromboplastin time:

Preoperatively PTT was not prolonged in any patient studied. The mean preoperative PTT was 26.64 seconds. On the third post operative day the mean value of PTT was 32.75 seconds and the mean PTT was 34.09 seconds. Pre and post operative values were compared for different surgical groups using paired t test and the difference was found to be statistically significant ($p < 0.05$) between pre-op and post-op (day3 and 7),and between post-op day 3and day 7 (table1).

Platelet count:

For the entire group the mean preoperative platelet count was 1.95 lakh. The mean value for platelet count on the 3rd postoperative day was 2.94 lakh and the mean value for the platelet count on the 7th post operative day was 3.47 lakh

D-DIMER ASSAY:

Preoperatively none of the patients showed positive D-Dimer test. Overall 89.3percent of patients had positive test at some point of time postoperatively. 88.6 Percent of patients had a positive D-Dimer test on the third postoperative day and 90 Percent of patients had a positive D-Dimer test on seventh postoperative day. Thus the test has a tendency to be positive in the postoperative period.

Table 2-D-dimer assay

| | Number of patients (%) | |
|-------------------------------------|------------------------|-------------|
| | Positive | Negative |
| (3 rd day) Postoperative | 62 (88.57) | 8 (11.43) |
| (7 th day) Postoperative | 63 (90.00) | 7 (10.00) |
| Overall postoperative | 62.5 (89.29) | 7.5 (10.72) |

DISCUSSION

D-Dimer levels have been used as a marker of intravascular clot formation, and are frequently increased after surgery or trauma and indicating the presence of intravascular clot that has undergone lysis. In the present study, D-Dimer levels were elevated in all the groups postoperatively on both day three and day seven .In the study conducted by Siemens et al (1999) in 61 patients undergoing four different types of surgery, it was shown that maximum activation of coagulation is not reached until 2 hours postoperatively and slowly decreases until normal values are reached around the fifth postoperative day.³ But the coagulation parameters in our study subjects remained elevated up to the 7th postoperative day. Similar findings were observed by Lopez et al (1997) who found elevated D-Dimer levels throughout the postoperative period in patients undergoing orthopedic and abdominal surgeries. Yet another study conducted by Umino et al (1993) demonstrated fibrin degradation products to be increased significantly after oral surgery and reach the maximum value on the 1st postoperative day. They concluded that coagulation and fibrinolysis are enhanced between the 3rd and 7th postoperative days.^{4,5} Similar findings were observed by Misaki et al (2008), who found D-Dimer and FDP to be gradually elevated at 3 days and 7 days after a major orthopedic surgery.⁶ Shinohara et al (1997) also found biphasic changes in plasma levels of FDP which peaked twice on the 1st and 7th days. This emphasizes the fact that a positive D-Dimer test indicates the occurrence of coagulation as well as fibrinolysis in the postoperative period. This test serves as a good evidence that secondary fibrinolysis was taking place in these patients.⁷ Moresco et al (2006) found an association between plasma levels of FDP in the investigation of thromboembolic disorder and suggested that the preliminary determination of FDP levels could be useful because it allows estimating the D-dimer levels before the automated systems analysis, reducing costs associated to dilutions of plasma samples. Positive evidence of D-Dimer test in high percentage of cases may be due to several factors. A change is seen to occur in surgical repair process and muscular activity, an inducer of fibrinolysis also increases during this time (Menon et al, 1967).^{8,9} Our observations in the present study demonstrated the mean prothrombin time (PT) on the third postoperative day to be 14.52 seconds and on the seventh postoperative day to be 14.91 seconds. The postoperative values were compared with the preoperative values and the difference was found to be statistically significant (p value =0.005) on all the days.

Thus this observation might reasonably be expected to occur. Because these changes were slight, they do not seem too discrepant from the previous reports which state that prothrombin time is not significantly changed .

Minor changes were observed in partial thromboplastin time (PTT). There was slight lengthening of partial thromboplastin time post operatively, but the mean value remained within the normal range. This suggested that even if coagulation occurs by intrinsic pathway, it was overshadowed by the extrinsic pathway, as revealed by the lengthening of prothrombin time. Although, when the postoperative values were compared with the preoperative values, the difference was found to be statistically significant (p value =0.005) on all the days.

CONCLUSION:

In conclusion our study demonstrates that the changes that occur in postoperative period in coagulation and fibrinolysis in a major surgery may predispose the patients to increased risk of venous thromboembolism. D-Dimer generation was increased postoperatively in all the surgical groups. The combination of changes in D-Dimer, PT, PTT and platelet counts after surgery confirms the hypercoagulable state and hence the risk for postoperative DVT and related complications.

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