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Original Research Article

"A STUDY ON COAGULATION AND FIBRINOLYTIC PARAMETERS IN OBSTETRICS CASES WITH SEPSIS"

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ABSTRACT:

Background: Sepsis is becoming the leading cause of mortality and morbidity these days in the intensive care units. Sepsis during pregnancy and postpartum period is a cause of concern. Maternal sepsis is considered the direct cause of maternal death worldwide.

OBJECTIVE: To study the correlation of coagulation and fibrinolytic parameters in the diagnosed obstetric patients with sepsis.

Material & Methods: Study Design: Case – control study. **Study area:** Department of Pathology, N. S.C. B medical college, Jabalpur.**Study Period:**March 2015 – March 2017.(2 years).**Study population:** Cases being Obstetric cases diagnosed with sepsis and admitted in the various Intensive care Units of department of Obstetrics and Gynaecology, Medicine,Surgery and Anesthesia. The controls were normal healthy obstetric cases with no inherited coagulation or bleeding disorder.**Sample size:** 200 study subjects (100 cases and 100 controls) were included in our study.**Sampling method:** Simple Random sampling method.**STATISTICAL ANALYSIS:** Chi square test, t test , frequency and percentage were used as statistical methods for analysis of data .Statistical software used for the analysis of the data was – SPSS.

Results: Prothrombin time of 17sec to 20sec and >20 sec exhibit 3.67 times and 5.78 times respectively more likely to exhibit DIC when compared to prothrombin time of 14sec to 17sec.APTT with prolonged time shows 1.91 times more to exhibit DIC when compared to APTT normal.**CONCLUSION:**Sepsis is an important cause of death in the gravida. Early recognition of sepsis may prevent maternal and fetal complications. Implementation of evidence-based diagnostic and treatment strategies can reduce the overall risk of death in pregnant patients with severe sepsis.

Key words: sepsis, prothrombin time, coagulation and fibrinolytic parameters

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INTRODUCTION:

Sepsis is becoming the leading cause of mortality and morbidity these days in the intensive care units. Sepsis during pregnancy and postpartum period is a cause of concern. Maternal sepsis is considered the direct cause of maternal death worldwide. In India according to the WHO update 15% of the maternal mortality is due to sepsis.

Maternal sepsis is the term used for sepsis developed during pregnancy. Puerperal sepsis is the term given to the infection developed during childbirth and within 42 days of delivery. In India, sepsis is the second most common cause of maternalmortality after hemorrhage. Sepsis is divided into Severe Inflammatory Response Syndrome (SIRS), severe sepsis and septic shock.

There are various risk factors which lead to sepsis in obstetrics like cesarean section, multiple cervical examinations, unskilled birth attendants, anemia, age of the mother, primi-gravida, high risk pregnancy, intrauterine fetal deaths, abruptio placenta, etc. These factors are predisposing feature for infections. Majority of the cases were negative for blood cultures.

During pregnancy a lot of changes take place in the maternal body. There are a lot of changes in the hematological, coagulation and fibrinolytic parameters. There is decrease in platelet count due to hemodilution. The prothrombin time (PT) is same as normal with small changes in activated partial thromboplastin time (aPTT).The fibrinolytic parameter D-dimer is increased postpartum. It is seen that various hormonal changes during pregnancy play an important role in infections. There are also studies which denote that placenta acts an activated coagulation system.

Sepsis leads to release of endotoxins which initiate a cascade of events. Sepsis is the most common clinical condition associated with Disseminated Intravascular Coagulation (DIC).The principal mediator of activation of coagulation appears to be interleukin-6, and it is the pivotal mediator of the dysregulation of the physiologic anticoagulation pathways and the fibrinolytic defect. Effects of the above processes cause microcirculation failure culminating in DIC and multiorgan failure. In pregnancy, all the above pathological processes take place.

Maternal body undergoes various changes during pregnancy leading to placental abruption, chorioamnionitis, intrauterine fetal death, endometritis, UTI, mastitis, etc. There are various studies which indicate that it is not necessary for blood culture to be positive for sepsis. Sepsis is one of the main causes leading to DIC, a consumptive coagulopathy.

The transmission of infecting organism is categorized into nosocomial, exogenous, and endogenous. Aseptic precautions advances in investigation tools and the use of antibiotics have played a major role in reducing the incidence of puerperal sepsis.

OBJECTIVE: To study the correlation of coagulation and fibrinolytic parameters in the diagnosed obstetric patients with sepsis.

Material & Methods:

Study Design: Case – control study.

Study area: Department of Pathology, N. S.C. B medical college, Jabalpur.

Study Period: March 2015 – March 2017.(2 years).

Study population: Cases being Obstetric cases diagnosed with sepsis and admitted in the various Intensive care Units of department of Obstetrics and Gynaecology, Medicine,

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Surgery and Anesthesia. The controls were normal healthy obstetric cases with no inherited coagulation or bleeding disorder.

Sample size: 200 study subjects (100 cases and 100 controls) were included in our study.

Sampling method: Simple Random sampling method.

Ethical consideration: Institutional Ethical committee permission was taken prior to the commencement of the study.

Study tools and Data collection procedure:

Step-1:

- All the Obstetric patients admitted in the I.C.U. diagnosed with sepsis were identified and were the cases for the study.
- The normal healthy obstetric patients were taken as controls. It was made sure that they had no history of inherited coagulation or bleeding disorder.

Step-2:

- Written consent was taken from the patient prior to enrolling in the study

Step-3:

- A pre structured proforma was used to collect base line data.
- Detailed History , General Examination and Systemic Examination was done.

Step 4: Collection of patient's blood sample and analysis of the blood sample

Step 5: Collection of data and analysis

- Descriptive data was be collected and studied accordingly.
- Significant statistical test was applied

Samples to be collected in

1. **EDTA vial**- for platelet count, peripheral smear
2. **Tri Sodium Citrate**- For coagulation studies and D-Dimer
3. **Plain vial**- for Biochemistry investigations, like Liver Function Tests , Renal Function Tests .

THE TESTS PERFORMED

1. CBC WITH EXAMINATION OF PERIPHERAL BLOOD SMEAR
2. PLATELET COUNT
3. PROTHROMBIN TIME (PT)
4. ACTIVATED PARTIAL THROMBOPLASTIN TIME (aPTT)
5. D- Dimer

BIOCHEMISTRY INVESTIGATIONS: The Biochemistry investigations were analysed by automated biochemical analyser Randox which analyses all the tests of biochemistry. Liver Function Tests, Renal function Tests were performed to see MODS. The samples of the patients were collected in plain vial.

STATISTICAL ANALYSIS: Chi square test, t test , frequency and percentage were used as statistical methods for analysis of data .Statistical software used for the analysis of the data was – SPSS.

Observations & Results:

In the recent study being a case control study, 100 cases and 100 controls were taken. The cases being pregnant females already diagnosed with sepsis falling in the criteria of sepsis admitted in the intensive care units of various departments chiefly, obstetrics and gynecology

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department, medicine, anesthesia and surgery. The controls being normal obstetric patients which included 50 ANC patients and 50 post-natal patients. The cases as well as controls had no inherited coagulation defect or bleeding disorder.

Table 1: Age wise distribution of the study participants

Age group (in years)	Case	Control
<20	19	28
20-30	72	54
>30	09	18
Total	100	100

Pearson chi square value = 7.2948P value = .026058 (Significant.)

Table 2: BOOKED AND UNBOOKED PATIENTS

Being a tertiary care hospital, of the obstetric patients diagnosed with sepsis were referred from the nearby primary health care hospitals, villages and in and around.

	No. of Patients
Booked Cases	**26**
Unbooked Cases	**74**
Total	**100**

Table 3: HEMOGLOBIN LEVELS

Hemoglobin levels of both case and control were done

Hb	Case	Control	Row Total
≤7	39	9	60
7-9.9	31	10	51
10-10.9	16	35	41
≥ 11	14	46	48
TOTAL	100	100	200

The chi –square statistics is 53.6512. The p-value is <0.00001 .The result is significant at p< .05

Table 4: PERCENTAGE OF PATIENTS WITH THROMBOCYTOPENIA

Platelet count (in /mm3)	Case	Control
>1,50,000	33	89
1,00,000-1,50,000	09	11
50,000-1,00,000	26	0
<50,000	32	0
Total	100	100

Table 5: PATIENTS WITH DERANGED PROTHROMBIN TIME

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Prothrombin time of all the cases and control was done and graded as 0->14 seconds , 1 - >14seconds but <20 seconds, 2 - > 20 seconds.

Prothombin Time	Case	Control
0 – 14seconds	46	100
1 - >14seconds but <20 seconds	07	0
2 - > 20 seconds	47	0
Total	100	100

Table 6: PATIENTS WITH DERANGED aPTT

Activated partial thromboplastin time of all the cases and control was done and graded as 0- Normal , 2 – Prolonged.

aPTT	Case	Control
0 - Normal	52	100
2 – Prolonged	48	0
Total	100	100

Table 7: PATIENTS WITH RAISED D-DIMER

D-Dimer	Case	Control
0	16	58
1	28	42
2	56	0
Total	100	100

Table 8: Assessing the Risk of DIC (Binary logistic Regression)

	B	S.E	Significance	Odds Ratio	95% CI for odds ratio	
					Lower limit	Upper limit
Platelets						
>150000				1		
100000-150000	0.798	0.252	0.253	1.43	1.12	3.45
50000-100000	2.398	0.598	0.04	4.5	2.78	6.34
<50000	10.398	1.125	0.001	12.53	8.56	15.78
Prothombin Time						
14sec – 17 sec				1		
17sec – 20sec	0.789	0.445	0.02	3.67	2.56	5.45
Greater than 20 sec	1.799	0.345	0.009	5.78	2.67	7.89
D Dimer						
No increase				1		
Moderate increase	-0.598	0.490	0.123	0.918	0.67	1.34
Strong increase	-1.296	0.091	0.241	0.85	.55	1.15
APTT						
Normal				1		
Prolonged	1.398	0.917	0.004	1.91	1.34	2.98

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Regression model or predictor equation for DIC is :-

Log (p/1-p) = Constant + B platelets 100000-150000 + B Platelets 50000-100000 + B Platelets <50000 + B Prothrombin time 17sec to 20sec + B Prothrombin time >20 sec + B D Dimer moderate increase + B D Dimer strong increase + B aPTT prolonged.

Where P is the probability of DIC. Expressed in terms of the variables used in this logistic regression model

Log (p/p-1) = 5.676 + 0.798+2.398 +10.398 + 0.789 +1.799 -0.598 -1.296 +1.398

Binary logistic regression was performed to ascertain the effects of the Platlets counts , prothrombin time, D dimer and Appt on the likelihood of unsafe injection practices.

Platelets count of Less than 50000 were 12.53 times more likely to exhibit DIC while platelets count of 50000-100000 and 100000-150000 were 4.5 times and 1.43 times respectively more prone to DIC as compare to >150000 platelets.

Prothrombin time of 17sec to 20sec and >20 sec exhibit 3.67 times and 5.78 times respectively more likely to exhibit DIC when compared to prothrombin time of 14sec to 17sec.

APTT with prolonged time shows 1.91 times more to exhibit DIC when compared to APTT normal.

DISCUSSION:

In India, the maternal deaths due to sepsis were 15%. Sepsis is considered as a direct cause of maternal mortality and morbidity.In the present study, which is a case control study, 100 cases and 100 controls were taken. The cases were Obstetric females, already diagnosed with sepsis and following the sepsis criteria.

The cases which were pregnant females already with sepsis were taken. Studies showed that there are several risk factors which lead to sepsis in pregnancy the need for taking control arose because the various previous studies showed the physiological changes in hematological, coagulation and fibrinolytic parameters in pregnancy.[1-3]

In the present study, out of the 100 cases diagnosed with sepsis 19 patients were under the age of 20 years out of which 4 patients went into septic shock and 4 were patients had severe sepsis. The obstetric patients diagnosed with sepsis maximum fell within the age group of 20 to 30 years i.e; 72 cases.

Amongst the diagnosed cases of sepsis 77 patients were primigravida , out of these 6 patients developed septic shock , 11 went into severe sepsis and 18 patients developed MODS. The remaining 23 patients were multigravida of which 2 patients developed septic shock and 10 patients developed severe sepsis. In our study we found that primi gravida were more susceptible to severe sepsis and septic shock as compared to the multigravida. Our finding correlated with thestudies of Acosta et al. which stated that the primigravida were more prone to septic shock.[4]

Amongst the patients admitted to ICU maximum of the patients were diagnosed with preeclampsia (15%), 10 patients had Intra Uterine Fetal Death, 09 patients had Sickle cell Anemia, 12 Patients had severe anemia, 6 patients were diagnosed with abruption placentae , 4 patients had undergone abortion, 2 patients had HELLP syndrome . Other causes including peurperal pyrexia , mastitis, vaginal discharge , chorioamnitis, twin gestion, Rh negative blood group, Retained placenta, amniotic fluid embolism , placenta previa, ectopic pregnancy, HIV positive ,etc.

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The 100 cases of obstetrics which were diagnosed with sepsis were further divided into Systemic inflammatory response syndrome (SIRS), severe sepsis and septic shock on the basis of the definition given by ACCP/SCCM and Levy et al [5]. In the present study, 8 cases had septic shock and 39 patients had severe sepsis. The remaining patients had Severe Inflammatory Response Syndrome (SIRS). Patients with severe sepsis were also diagnosed with MODS. The finding was consistent with the study by Acosta et al [4].

The Complete Blood Count (CBC) of the cases and controls were done along with the examination of the peripheral smear. Out of the 100 cases 39 obstetric patients and 09 controls had Hemoglobin of less than 7g/dl and were diagnosed as severe anemia. 31 cases and 10 controls had the hemoglobin in the range of 7-9.9 g/dl.

The CBC of patients (done by automated cell counter) of the patients with sepsis were examined, out of which maximum patients had T.L.C greater than 20,000, with greater than 80% neutrophils. But on peripheral smear maximum patients showed toxic changes in neutrophils and immature band form greater than 10%. The cytoplasm of the neutrophils showed vacuolations , indicating septicemia. This was consistent with the criteria for diagnosis of sepsis given by Levy et al [5].

In100 pregnant patients with sepsis, 58 patients had platelet counts less than 1,00,000/mm3 out of which 43 patients had Disseminated Intravascular Coagulation . That is, along with thrombocytopenia the other coagulation (PT, aPTT) and fibrinolytic parameters (D-Dimer) were deranged . Our findings correlated with the studies of Thatchil and Toh.(6)

Out of 100 cases, 09 patients had a platelet count of the range 1,00,000- 1,50,000/mm3 and none of the patients had abnormality in PT and aPTT. D- Dimer was moderately raised in 02 of the patients who were postpartum. It wasseen in studies that in pregnancy, at peripartum the D- Dimer levels are raised moderately from 4 to 10 folds and come to normal in 4 to 6 weeks postpartum. [7,8]

Out of the 100 cases diagnosed with sepsis 47 patients had disseminated intravascular coagulation. The patients had undergone with the tests for coagulation and fibrinolysis Prothrombin Time (PT), Activated Partial Thromboplastin Time (aPTT) and D-Dimer and all the tests were found deranged.Out of the 100 patients and 100 controls, we did not find cases of isolated prolonged PT. But there were 2 cases of prolonged aPTT as the patients were on Heparin. PT was found prolonged in 54 cases. Out of which 7 cases had PT in the range of 14 To 20 seconds. The normal Prothrombin Time being 14sesconds.

However, the values of D-Dimer showed marked variations both in cases and controls. In the present study we had divided the values of D- Dimer into no increase (i.e 0-0.8 mug/dl) , moderate increase (0.8 to 4 mug/dl) and strong increase as (> 4mug/dl) The values of D-Dimer were raised in post-partum period in maximum patients. (Post-partum controls also showed increase in D-Dimer.

This finding was consistent with the previous studies showing the Post-partum increase in D-dimer levels in normal pregnancy. [6-8]there were 32 patients diagnosed with sepsis, severe sepsis and septic shock who had Disseminated Intravascular Coagulation and had severe thrombocytopenia i.e, platetet counts less than 50,000/mm3 and the D- Dimer levels were strongly increased along with significant prolongation of PT and aPTT. This showed a strong correlation between severe thrombocytopenia and DIC. According to the studies by Klein et

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al the D-dimer assay alone is not reliable for predicting the possibility of DIC in pregnant patients [8] our observations was consistent with the study.

In the present study, out of the 100 diagnosed cases of sepsis 47 cases were of DIC (47%). Our hospital being a Tertiary care hospital, receives a lot of referral cases from the surrounding primary health care center and neighboring villages Platelets count of Less than 50,000 were 12.53 times more likely to exhibit DIC while platelets count of 50000-100000 and 100000-150000 were 4.5 times and 1.43 times respectively more prone to DIC as compare to >150000 platelets.Prothrombin time of 17sec to 20sec and >20 sec exhibit 3.67 times and 5.78 times respectively more likely to exhibit DIC when compared to prothrombin time of 14sec to 17sec. aPTT with prolonged time shows 1.91 times more to exhibit DIC when compared to aPTT normal.

CONCLUSION:

Sepsis is an important cause of death in the gravida. Early recognition of sepsis may prevent maternal and fetal complications. Implementation of evidence-based diagnostic and treatment strategies can reduce the overall risk of death in pregnant patients with severe sepsis.

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