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Tubal Ectopic Pregnancy and Variation in Platelet Parameters: A Six Years Study in Rural Population of Central India

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ABSTRACT

OBJECTIVE: *The aim of our study was evaluate alteration of various platelet parameters such as platelet count, mean platelet volume (MPV) and platelet distribution width (PDW) in tubal ectopic pregnancy in rural population of central India.*

METHOD: *This was a retrospective study carried out during period of January 2010 to December 2015. Total 107 cases of tubal ectopic pregnancy evaluated in comparison to same number of patient as a control. During this period hemoglobin level and platelet parameters (platelet count, MPV and PDW) were analyzed.*

RESULT: *In our study we found significant decrease in mean hemoglobin level. The platelet counts were not that much affected. There was significant decrease in MPV ($p < 0.001$) and increase in PDW ($p = 0.012$) as compared to control. We also compare these parameters in ruptured versus non-ruptured ectopic pregnancy in which once again we found statistically significant decrease in MPV($p < 0.001$) and increase in PDW ($p = 0.009$).*

CONCLUSION: *This study was mostly focused on rural population of central India where the rapid diagnostic tests are sometimes are unavailable. Hence decrease in trend in MPV and increase in PDW can be used as a tool to diagnose ectopic pregnancy.*

Keywords: *Mean platelet volume, platelet distribution width, platelet parameters, Tubal ectopic pregnancy.*

INTRODUCTION

Ectopic pregnancy is defined when implantation of the embryo occurs outside the uterine cavity. The overall incidence rate of ectopic pregnancies is about 1- 2%. [1] The implantation can be in fallopian tube(s), abdominal cavity and/ or ovaries. Among them tubal pregnancies is the most commons site. [2] It causes not only fetal wastage but also increased chances of morbidity and mortality, and compromises future fertility of the patient. [3] Diagnosis of ectopic pregnancy is difficult task for the clinician. Trans-vaginal ultrasonography is the only diagnostic test when there is suspicion of ectopic pregnancy in clinically stable patient. [4]

Definitive risk factor for ectopic pregnancy has not been identified till date. But few authors are classified them as low, moderate and risk high

type. Of which previous ectopic pregnancy, tubal surgery or ligation, tubal pathology, in- utero diethylstilbestrol exposure and intrauterine device are the high risk factors. [5] As the age advances there is loss of myoelectrical activity of fallopian tube. Also there is tubal ciliary dysfunction and defective tubal transport which can lead to early implantation of the fertilized ovum ultimately leading to ectopic pregnancy. [1],[6] Organic structural changes in the fallopian tube are also the leading cause for ectopic pregnancy. [2],[7] These changes are due to congenital abnormal-lities or pelvic inflammatory diseases resulting in either obstruction or impairment of tubal motility which may play a very important role in development of ectopic pregnancy. [2],[7]

Human chorionic gonadotropin (β hCG) is the only biomarker use routinely in clinical practice for rapid diagnosis of ectopic pregnancy. But it has its limited usefulness therefore β hCG level require close follow up. Other biomarkers such as Creatinine kinase, Progesterone, Inhibin A, Estradiol, Relaxin and CA 125 are currently been investigated as diagnostic marker for rapid and more accurate diagnosis of EP. [8] So, as there are limited rapid noninvasive test for the diagnosis of ectopic pregnancy we have to rely mostly on β hCG and ultrasonography which is the most important tool for the diagnosis till date. But it needs a very close follow up and repeated visits.[9]

Generally hematological parameters of an individual reflect their health conditions. It is postulated that the hematological indices if evaluated well then they can predict the outcome of the pregnancy. [1] The platelets and platelet derived factors play a very important role in thrombosis, angiogenesis, inflammation and immunity.[10] In ectopic pregnancy some inflam-matory cytokines are increased both at implant-ation sites as well as in systemic circulation. In ectopic pregnancy platelet aggregation is increased with decreased number in circulation along with that, the life span of the platelets is also reduced and there is also increase in the mean platelet volume (MPV). [1]

In the present study we have analyzed the correlation of platelet parameter which include Platelet counts, Mean Platelet Volume (MPV) and Platelet Distribution Width (PDW) in the diagnosed patients of ectopic pregnancy as compared to healthy pregnant women as control over the period of five years.

MATRIAL AND METHODS

Present study is a retrospective study carried out in Department of Pathology of teaching hospital in central India which mainly provides health care to the rural population. The study was conducted over a period of five years from January 2011 to December 2015. Over this five year we found 107 women with conclusive pathological diagnosis of total ectopic pregnancy. Out of these cases 48 cases were of ruptured EP and 59 presented as unruptured EP. We also included age matched 107 women with history of 6-8 weeks of healthy, intrauterine gestations which were confirmed by an ultrasound examination with positive fetal heart sounds as control group. The complete demographic and clinical details of these patients were noted down from the Hospital Information System. The females with chronic inflammatory disorders were excluded from the control group.

The venous blood was drawn from each subject. Blood was collected in EDTA-containing sterile tubes and shifted to the laboratory. The complete blood counts, platelet parameters including Mean platelet volume(MPV) and platelet distribution width(PDW) were determined using an automated hematology analyzer (Beckmann Coulter, Act Diff 2) immediately to minimize the potential influence of Eethylenediaminet-etraacetic acid [EDTA]) on the MPV. Simultaneously the peripheral blood smear examination was also done to provide visual confirmation of the automated result.

The reference range for MPV was between 7.2 to 11.7 fL and PDW was 10- 17.9% Statistical

analysis was done with help of SPSS.18 software (Chicago, IL, USA). Mean and standard deviations were used to compare the data. Significance was defined as p value less than 0.05. ($p<0.05$) Analysis of variance (ANOVA) was done to compare platelet parameters between two groups.

RESULTS

In the present study we found the mean age of the patients with EP was 31 ± 5.08 years. Mean hemoglobin level of control group was 11.7 ± 1.15 gm/dl and of EP patients was 10 ± 1.81 gm/dl the difference was found to be statistically significant ($p<0.001$). The various platelet parameters were compared between EP and control group as shown in table no.1.

The mean platelet counts was 238 ± 82 /mm^3 and 255 ± 75 /mm^3 mean platelet volume (MPV) was 8 ± 1.37 and 9.41 ± 1.14, platelet distribution width (PDW) was 16 ± 2.22 and 15.2 ± 2.4 in ectopic pregnancy patients and control group respectively. Hemoglobin percentage and MPV were found high statistically significant ($p<0.001$). Difference between PDW was also significant.($p=0.009$)

We also compared the hemoglobin level, Platelet count, MPV and PDW between ruptured and unruptured EP cases as shown in table no.2. In which once again we found the mean age, hemoglobin percentage MPV and PDW statistically significant ($p < 0.05$).

The platelet counts were lower but not statistically significant but as compared to control in ectopic pregnancy. But contrary to this when we compared platelet counts in ruptured versus non ruptured tubal ectopic pregnancy which was slightly higher side than the ruptured and statistically non significant.

Table No 1: Comparison in between platelet parameters of tubal ectopic pregnancies with control.

	Ectopic pregnancy (n=107)	Control (n=107)	P value
Hb(gm/dl)	10 ± 1.81	11.7 ± 1.15	< 0.001
Platelets(/mm3)	238 ± 82	255 ± 75	0.115
MPV(fL)	8 ± 1.37	9.41 ± 1.14	<0.001
PDW	16 ± 2.22	15.2 ± 2.4	0.012

Table No 2: Comparison of platelet parameters in between ruptured and non-ruptured tubal ectopic pregnancies with control.

	Ruptured TEP (n=48)	Non- Ruptured TEP (n=59)	Control (n=107)	P value
Hb(gm/dl)	9.5 ± 1.61	10.06 ± 1.93	11.7 ± 1.15	<0.001
Platelets(/mm3)	248 ± 84	230 ± 80	255 ± 75	0.146
MPV	8.01 ± 1.23	8.62 ± 1.42	9.41 ± 1.14	<0.001
PDW	16.3 ± 1.97	16.05 ± 2.42	15.2 ± 2.4	0.009

DISCUSSION

The combination of the defective tubal transport of the fertilized ovum and the micro-environmental changes of tubal lumen can cause early implantation of fertilized ovum before it enters into the uterine cavity which may ultimately lead to ectopic pregnancy. [1] If it is not detected early it can lead to tubal rupture and can be a main cause of maternal mortality. As our set up is in predominantly rural part of central India most of the people are unaware of this condition. The prevalence of EP ranges from 6- 16 % [11] and it can be 7.06 per 1000 deliveries or 1 per 141 deliveries. [12] Gaddagi et al. [13] and Porwal S et al. [14] showed that the incidence can be 1 per 399 to 2.46 per 1000 deliveries. The mortality

rate of EP has been reduced from 0.5 to 1.15 per 100 maternal deaths due to rapid diagnosis of EP. [15] The combination ultrasonography findings and serum β hCG level can help in rapid diagnosis. But in rural set up these rapid tests cannot be always available so we require few alternative methods to diagnose or to atleast give hint towards the diagnosis of ectopic pregnancy.

Normally the platelets are present in inactive form and when there is injury to the endothelial wall they become activated and play important role in inflammation, angiogenesis, repair and regeneration of the tissue. [16] When the platelets become activated there are some morphological alterations in activated platelets, they become larger and there are formation of pseudopodia as result of which there is alteration in MPV and PDW. [11] According to the duration of pregnancy, the platelet indices can vary. There can be a compensatory increase in MPV and PDW levels during pregnancy because of dilutional thrombocytopenia. [18] Large platelets get consumed at high grade inflammatory conditions or sites because of these can directly lead to decreased in MPV level. [19]

In present study we found that the mean Hb level females with EP was lower as compared to the control group which can be due to rupture or hemorrhage (Table 1). When we compared the platelet parameters of EP with control group, platelet count don't show any significant alteration but MPV was low as compared to the control group and was statistically significant ($p<0.001$) (Table no.1) There was increase in the PDW of EP cases as compared to control group and it was also statistically significant ($p = 0.012$) (Table no.1). That means MPV have a significant decrease and PDW have significant rise in EP as compared to normal pregnancies. We also compared the platelet parameters in ruptured as well non ruptured EP in which we found the MPV was slightly decreased and PDW was slightly increased in ruptured EP as compared to non- ruptured EP.

CONCLUSION

In present study we found there is decrease in MPV and increase in level of PDW. Therefore we propose that on repeated hematological investigation if we found such trend of decrease in MPV and increase in PDW then it can help us in a suspecting the diagnosis of ectopic pregnancy especially in rural set up where facilities of rapid diagnostic tests, imaging and availability of radiologist may not be there

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