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ASCORBIC ACID LEVELS IN PPROM AND ITS MATERNAL AND PERINATAL OUTCOME

Obstetrics and Gynaecology

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ABSTRACT

Background: Preterm prelabour rupture of membranes is the spontaneous rupture of fetal membranes before 37 completed weeks of gestation and before onset of labour. It complicates approximately 1-5 % of all pregnancies and contributes to one- third of preterm births.
The biochemical mechanism in membrane rupture is disturbances in collagen structure and increased oxidative stress. Vitamin C deficiency during pregnancy leads to abnormal collagen formation leading to preterm, prelabour rupture of membranes and complications.
This study was undertaken to establish the relation between maternal plasma vitamin C concentration in women with PPROM and women without PPROM and to correlate the neonatal morbidity and mortality.
MATERIALS AND METHODS: This case control study was conducted in Department of Obstetrics and Gynaecology, J.J.M Medical College, Davangere. 120 patients were studied, 60 were in study group (patients admitted to labour room with h/o PPROM) and 60 in the control group (patients admitted to labour room at term for delivery). Fasting blood sample was taken to measure the plasma vitamin C levels in both the groups.
RESULTS: Plasma vitamin C levels were low in PPROM patients and the concentration decreased as the pregnancy advanced, this proves linear relationship between plasma vitamin C levels and PPROM. The results of this study showed decreased plasma vitamin C levels leading to PPROM, preterm deliveries, increased NICU admissions, increased perinatal morbidity, mortality, maternal anaemia in study group than in control group.
CONCLUSION: As vitamin C deficiency during pregnancy leads to PPROM, it's supplementation during pregnancy along with iron and calcium in second and third trimester should be made mandatory

KEYWORDS

PPROM, Vitamin C, Collagen metabolism

INTRODUCTION

Preterm prelabour rupture of membranes is the spontaneous rupture of fetal membranes before 37 completed weeks of gestation and before the onset of true labour.[1] It complicates 1-5 % of pregnancies and contributes to one- third of preterm births[2].

The main biochemical mechanism in membrane rupture is disturbances in collagen metabolism. Vitamin C is water soluble micro nutrient involved in the collagen synthesis. It acts as an enzyme cofactor to the enzymes lysyl hydroxylase and prolyl hydroxylase, which are required for the synthesis of hydroxylysine and hydroxyproline during hydroxylation of collagen. Collagen requires hydroxylysine and hydroxyproline bridges across the triple helix to provide stability to it.

Vitamin C also down regulates metalloproteinase-2 and collagenase, which hamper the collagen production. It also acts as an antioxidant which blocks the damaging effects of oxidative stress. It has been shown by cell culture studies that the synthesis and deposition of the amniochorionic matrix is dependent on the presence of vitamin C. Hence vitamin C deficiency during pregnancy leads to abnormal collagen formation which is unable to provide the mechanical strength and ruptures the membranes prematurely leading to associated complications[3].

Aetiology for such abnormal rupture of membranes are predisposing factors like:

1) Lower genital tract infection

Microorganisms ascend to the membranes, causes weakening of the membranes by protease, collagenase, elastase, prostaglandin cascade leading to chorioamnionitis and PPROM. Inflammatory response enhances the amnion destruction by producing cytokines, interleukins 1 and 6, tumour necrosis factor-α and MMPs.

Organisms involved are Group B streptococcus, Chlamydia, Escherichia coli, Trichomonas vaginalis, Bacterial vaginosis, Mycoplasma, Staphylococcus and Enterococcus

2) Nutritional deficiency- deficiency of ascorbic acid, zinc, and vitamin E, copper leads to defective membranes. Woods et al (2001) proposed the role of deficiency of vitamin C and vitamin E in the causation of PPROM by reactive oxygen species.[4]

Other factors are cervical incompetence Polyhydramnios, Multiple pregnancy and Smoking.

The present study was undertaken to establish the relationship between maternal plasma vitamin C concentration in women with PPROM and women without PPROM and to correlate the neonatal morbidity, mortality.

AIMS AND OBJECTIVES

1. Establish the association between maternal plasma vitamin C concentration in women with PPROM and women without PPROM.
2. Study the association of anaemia in vitamin C deficient patients with PPROM
3. Study the perinatal morbidity and mortality in both the groups

MATERIALS AND METHODS

This case control study was conducted in Department of Obstetrics and Gynaecology, J.J.M Medical College, Davangere. Data was collected from the patients admitted in hospitals attached to it, Bapuji Hospital, Chigateri General Hospital, Women and Child Health Hospital, Davangere.

120 patients were studied, 60 were in study group (patients admitted to labour room with h/o PPROM) and 60 in the control group (patients admitted to labour room at term for delivery). Fasting blood sample was taken to measure the plasma vitamin C levels in both the groups.

INCLUSION CRITERIA

Women with h/o PPROM, who are willing to participate in the study and have given consent for the study.

EXCLUSION CRITERIA: Women with

1. Gestational Diabetes Mellitus
2. Urinary and respiratory tract infections
3. Vaginal infection
4 Polyhydramnios
5. Smoker
6. Evidence of chorioamnionitis in present pregnancy.

PROCEDURE OF THE STUDY-

All subjects fulfilling the eligibility criteria were counselled and an informed consent was taken .All the women then underwent a detailed history and clinical examination in which temperature, pulse rate, respiratory rate and blood pressure at admission was recorded followed by obstetric findings. Per speculum examination was done for presence of leaking, foul smelling discharge, colour of discharge if it is clear or meconium stained.

Per vaginal examination was done to assess Bishop Score, stage of labour, the presence or absence of the membranes and pelvic assessment.

On admission, the study women were started on prophylactic antibiotics as per hospital protocol. Fasting blood samples were taken for the estimation of plasma vitamin C concentration.

INVESTIGATIONS

Complete blood picture, blood group, VDRL, HIV, Hep-B antigen, random blood glucose levels, and urine routine examination.

Specific to PPROM were:

1. Plasma ascorbic acid
2 ml of maternal fasting venous blood samples were collected in plain vial to estimate ascorbic acid. Ascorbic acid is estimated in plasma by spectrophotometry method. Normal level of ascorbic acid is 0.6-1.2 mg/dl.

Mode of delivery and maternal and fetal outcomes were noted.

STATISTICALANALYSIS

Qualitative data was represented in the form of frequency and percentage. Association between qualitative variables was assessed by Chi Square test with continuity correction for 2 x 2 tables and Fisher's exact test for all 2 x 2 tables where P value of chi square test was not valid due to small counts.

Mean & SD value was calculated for continuous variables. Means between two groups were analysed by using Student's t test unpaired. A P value of <0.05 was considered statistically significant.IBM SPSS Version 22 for windows was used to do statistical analysis.

RESULTS

The mean gestational age is 33.67 ± 2.06 weeks in the study group and 39.07 ±1.13 weeks in the control group, p value <0.000, highly significant

PLASMA VITAMIN C LEVELS

Table 1: Mean Plasma Vitamin C Levels

Plasma vitamin C(mg/dl)				
Groups	**N**	**Mean**	**Std. Deviation**	**Unpaired t test**
Study Group	**60**	**0.61**	**0.32**	**P<0.000, HS**
Control group	**60**	**1.14**	**0.62**	

The mean vitamin C levels in study group is 0.61 ± 0.32 and control group is 1.14 ± 0.62, p value <0.000, highly significant. (Table 1).

Table 2: Plasma Vitamin C Levels In Study And Control Group

Plasma vitamin C(mg/dl)	Study Group		Control Group		Total
	No of cases	Percent	No of cases	Percent	
< 0.6	30	50	10	16.7	40
0.6 - 2.0	30	50.0	44	73.3	74
> 2.0	0	0.0	6	10.0	6
Total	60	100	60	100	120
Chi Square test P< 0.000, Highly Significant					

In the control group, out of 60 cases, plasma vitamin C levels than 0.6 mg/dl was seen in 10 cases (16.7%), 0.6-2.0 mg/dl in 44 cases (73.3%) and more than 2.0 mg/dl in 6 cases (10%), p value <0.000, highly significant.(table 2)

Table 3:plasma Vitamin C Levels In Relation To Gestational Age In Study Group

Plasma vitamin C(mg/dl)	Gestational age(wks)			Total
	28 - 32	32 - 34	34-36	
<0.6	8	10	12	30
0.6 - 2.0	10	4	16	30
Total	18	14	28	60
Chi Square test P<0.186, Not Sig				

In the study group, the plasma vitamin C levels in very early preterm pregnancy was <0.6 mg/dl in 8 cases and 0.6-2.0 mg/dl in 10 cases. In early preterm pregnancy, the levels were <0.6 mg/dl in 10 cases, 0.6-2.0 mg/dl in 4 cases. In late preterm pregnancy, the levels were < 0.6 mg/dl in 12 cases and 0.6 -2.0 mg/dl in 16 cases.(table 3)

The mean hemoglobin level was 10.11± 1.55 g/dl in the study group and 11.04 ± 1.59 in the control group, p value <0.002, highly significant.

Out of 60 cases in the study group 39 cases (65%) had anaemia, among them severe anaemia cases were 5 (8.33%), moderate anaemia cases were 10 (16.66%) and mild anaemia cases were 24 (40%). Out of 60 cases of control group 21 (35%) had anaemia, among them severe anaemia cases were 2 (3.33%), moderate anaemia cases were 4 (6.66%) and mild anaemia cases were 15 (25%).

Vitamin C supplementation in pregnancy leads to increased absorption of iron and prevention of anaemia. Lower levels of plasma vitamin C were associated with lower levels of hemoglobin, showing a linear relationship. In the study group 39 out of 60 cases had anaemia, whereas in the control group 21 out 60 cases had anaemia inferring the linear relationship between decreased plasma vitamin C levels and anaemia

Admission to NICU was accounted as perinatal morbidity due to different causes. Among 60 babies of study group 39 were admitted to NICU and among 60 babies of control group 6 babies were admitted to NICU, p value < 0.09 not significant.

In the study group, out of 60 babies, 21 babies (35%) were not admitted to NICU, 15 babies (25%) were admitted to NICU for 1-5 days, 5 babies (8.3%) were admitted to NICU for 6-10 days, 10 babies (16.7%) were admitted to NICU for 11-15 days, 8 babies (13.3%) were admitted to NICU for 16-20 days, 1 baby was admitted to NICU for 27 days. 9 babies were admitted in view of very low birth weight, 10 babies were admitted in view of low birth weight, 16 babies were admitted in view of respiratory distress syndrome, 1 baby was admitted in view of birth asphyxia due to abruptio placenta, 2 baby were admitted in view of transient tachypnea of new-born, 1 baby was admitted in view of early onset sepsis. Out of 60 babies in the study group, 9 babies having very low birth weight (1-1.5 kg) and 30 babies having low birth weight (1.5-2.5 kg) were admitted to NICU.

In the control group, out of 60 babies, 54 babies (90%) were not admitted to NICU, 6 babies (10%) were admitted to NICU for 1-5 days, p value <0.09, not significant. 4 babies were admitted in view of meconium aspiration syndrome, 1 baby in view of transient tachypnoea of new-born and 1 baby in view of birth asphyxia due to abruption placenta.

Duration of NICU admission in relation to the PPROM and duration of leak showed no significance, p value <0.858. Duration of leak and had no significance when compared to the gestational age, p value < 0.699, not significant.

Perinatal mortality- In the study group, out of 60 babies- 54 babies (90%) were alive and 6 babies (10%) died. In the control group, out of 60 babies- 58 babies (96.7%) were alive and 2 babies (3%) died, p value <0.153, not significant. In the study group, out of 18 babies of very early preterm, 13 were alive and 5 died, cause of death was severe respiratory distress syndrome in 2 babies, very low birth weight in 2 babies and late onset sepsis in 1 baby. Among 14 babies of early preterm, all 14 were alive. Among 28 babies of late preterm, 27 were alive and 1 died due to severe respiratory distress syndrome.

The perinatal mortality was more in the very early preterm group than the early and late preterm groups. The cause of death in control group was meconium aspiration syndrome in 2 babies. This signifies the neonatal deaths were more in the study group than the control group. The perinatal mortality had no significance in relation to duration of leak, p value <0.192, not significant.

Anam Majid et al [9] inferred that vitamin C supplementation decreases the occurrence of PPROM, improves mean gestational age at delivery, neonatal Apgar score and mean birth weight.

DISCUSSION

A total of 120 patients were included in the study, 60 cases being in the study group with history of PPROM and 60 cases in control group without PPROM

The mean plasma vitamin C level in study group was 0.61 ± 0.32mg/dl and control group was 1.14 ± 0.62 mg/dl, p value <0.000, highly significant.

In the study group, out of 60 cases, plasma vitamin C levels less than 0.6 mg/dl was in 30 cases (50%) and plasma vitamin C levels ranging from 0.6-2.0 mg/dl was in 30 cases (50%), whereas in the control group, out of 60 cases, plasma vitamin C levels than 0.6 mg/dl was in 10 cases (16.7%), 0.6-2.0 mg/dl in 44 cases (73.3%) and more than 2.0 mg/dl in 6 cases (10%), p value <0.000, highly significant.

In the study group, the plasma vitamin C levels in very early preterm pregnancy was <0.6 mg/dl in 8 cases and 0.6-2.0 mg/dl in 10 cases. In early preterm pregnancy, the levels were <0.6 mg/dl in 10 cases, 0.6-2.0 mg/dl in 4 cases. In late preterm pregnancy, the levels were < 0.6 mg/dl in 12 cases and 0.6 -2.0 mg/dl in 16 cases.

Hence inferring that plasma vitamin C levels were low in the study group who had preterm prelabour rupture of membranes than the control group, and the concentration of vitamin C declines as the pregnancy advances, signifying the need for vitamin C during pregnancy to maintain the membrane stability.

Richa Sharma and Sumita Mehta[5] and Emmanuel Ajucukwu Ugwa et al[6] proved that vitamin C levels were low in the patients having PPROM than the patients delivering at term gestation.

J A Osaikhuwuomwan et al[7] and Esther Casanueva et al[8] and also demonstrated that plasma vitamin C levels decreased as the pregnancy advanced.

CONCLUSION

Although PPROM occurs due to various causes, but the ultimate mechanism which triggers the final damage is the decreased collagen content in the amniochorionic membranes leading rupture.

In this study, plasma vitamin C levels were low in PPROM patients and the concentration decreased as the pregnancy advanced, this proves the linear relationship between plasma vitamin C levels and occurrence of PPROM.

The results of this study showed decreased plasma vitamin C levels leading to the PPROM and preterm deliveries, increased NICU admissions, increased perinatal morbidity, mortality and maternal anaemia. The daily intake of vitamin C in food is very small 40- 50 mg/day. The need for vitamin C in pregnancy is increased due to increased oxidative stress, decreased dietary intake and, hemodilution. Improvement in the dietary habits and nutritional status of pregnant women helps in reducing PPROM and vitamin C supplementation in the dietary dose (100 mg/day) should be made mandatory along with iron and calcium to all antenatal women in second and third trimester to avoid the devastating and preventable complications of PPROM.

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