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Study on role of ascorbic acid levels in PPROM and its maternal and perinatal outcome

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Abstract
Background: Preterm premature rupture of membranes (PPROM) complicates 1–5% of all pregnancies and is the major contributory factor for perinatal morbidity and mortality. Micronutrient deficiency (vitamin C) is associated with increased risk of PPROM. This study was conducted to establish the association between maternal plasma vitamin C concentration in women with PPROM and women without PPROM and to study the difference in maternal morbidity, neonatal morbidity, and mortality.
Objectives
1. Establish the association between maternal plasma vitamin C concentration in women with PPROM and women without PPROM.
2. Study the association of anemia in vitamin C deficient patients with PPROM
3. Study the difference in maternal and perinatal morbidity and mortality in both the groups

Methods: This case controlstudy was conducted in Department of Obstetrics and Gynecology, EPIONE Hera Hospitals100 patients were studied, 50 were in study group (patients admitted to labour room with h/o PPROM) and 50 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 anemia 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
Premature rupture of membrane (PROM) is the rupture of the chorioamniotic membrane and leakage of the amniotic fluid before delivery contractions [1]. PROM is the commonest cause of premature delivery. Recent studies have reported that with occurrence rates of 6 to 19%, PROM is the leading cause of mortality in the prenatal period [2]. Preterm PROM (PPROM), which leads to PROM before the 37th week of pregnancy, is responsible for 40 to 50% preterm deliveries and necessitates hospitalization in the neonatal intensive care unit (NICU) [3].
Various causes have so far been propounded for PPROM – with a sizable bulk of evidence relating it to biochemical processes such as disorders of collagen synthesis in the extra-cellular matrix of amnion and chorion and planned death of cells in fetal tissues. It is suspected that mediators released from stretching membrane or infection and activation of destructive enzymes in the matrix lead to the rupture of the uterus or amniotic membranes [4]. One of the factors involved in the activation of membrane destruction is the activity of reactive oxygen species (ROS). Because antioxidants suppress ROS by their chemical characteristic, consumption of materials like ascorbic acid or vitamin C is effective in the stability of the membrane and prevention of PROM and PPROM [5]. Epidemiological studies, linking clinical conditions known to produce ROS or reduce antioxidant protection to PPROM.
support this hypothesis [6]. Further evidence in this field comes courtesy of *in vitro* studies in which membrane segments exposed to ROS exhibited tissue changes consistent with PPROM [6]. Also, excessive collagen degradation in chorioamnion and amniotic samples from PPROM patients has been previously demonstrated [6]. Vitamin C, in addition to its antioxidant role, not only is an important factor in the synthesis of collagen but also controls the expression of type

IV collagen gene [7, 8]. This assumption is in agreement with findings like the increased likelihood of PPROM as a consequence of smoking, which is a source of ROS [9]. Maintaining cellular integrity in a normal pregnancy needs the inhibition of peroxidation reactions, which is important to protect proteins, enzymes, and cells from destruction by peroxides [10]. Antioxidant defense mechanisms contain both enzymes such as superoxide dismutase and free radical scavengers such as vitamin C. Because vitamin C is not synthesized in humans, its consumption is necessary for the prevention of scurvy, which accompanies weakness of the collagen system. Vitamin C is the cofactor for enzymes like lysyl hydroxylase and prolyl hydroxylase, enzymes that are very important for making hydroxylysine and hydroxyproline, which play a crucial role in the stability of the structure of collagen triple helix [11].

Predicting the probability of PROM and PPROM is of vital importance. Therefore, researchers have devised and assessed a vast array of clinical and paraclinical methods in search of an optimal modality. One of these methods is measuring the estriol level in serum or saliva. This assumption is based on the increase in the mother's estriol [12]. Estriol appears in the 9th week of pregnancy and rises gradually with the growth of the fetus. This increase is accompanied by a rise in steron and estradiol levels; however, estriol continues to increase until delivery – while steron and estradiol exhibit no clear changes after the 34th week of pregnancy [13].

Oxidative stress is known as a key feature in PROM.[12] One study reported that antioxidant therapy conferred protection against hypochlorous acid-induced damage and concluded that PROM was, in part, due to ROS and antioxidant deficit, which resulted in membrane damage [14]. Vitamin supplementation, including vitamin C, can prevent oxidative stress and consequently lower the risk of PROM [14].

Objectives

1. To establish the association between maternal plasma vitamin C concentration in women with PPROM and women without PPROM.
2. To study the association of anemia in vitamin C deficient patients with PPROM
3. To study the difference in maternal and perinatal morbidity and mortality in both the groups

Materials and Methods

The proposed study was conducted in Department of Obstetrics and Gynecology, EPIONE Hera Hospitals, Hyderabad, Telangana. Hospital based case control study was conducted on 100 patients, 50 were in the study group (patients admitted to labour room with h/o PPROM) and 50 in the control group (patients admitted to labour room at term for delivery)

Inclusion criteria

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

Exclusion criteria: Women with

1. Gestational Diabetes Mellitus
2. UTI
3. RTI
4. Vaginal infection
5. Polyhydramnios
6. Smoker
7. Evidence of chorioamnionitis in present pregnancy.

Procedure of the study

All subjects fulfilling the eligibility criteria were counselled and an informed consent was taken (in the language understood by the patient and attender). All the women then underwent a detailed history and clinical examination. 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.

History

For all the patients, a detailed history was taken. The intervals between pregnancies in case of multigravidas was noted. Also, a note was made about the exact time when leaking started and first day of her last menstrual period to accurately calculate the duration of leaking and the period of gestation respectively.

Examination

A general physical examination was performed in which temperature, pulse rate, respiratory rate and blood pressure at admission was recorded. A special note was made for any evidence of fever and tachycardia at admission.

Systemic examination was done. Abdominal examination included

1. Fundal height
2. Lie, presentation, position of the fetus
3. Presence of fetal heart sound
4. Status of liquor clinically
5. Any evidence of uterine tenderness
6. Presence of uterine contractions along with duration and intensity.

Per speculum examination was done for demonstrating

1. Presence of leaking by observing pool of liquor in vagina
2. Any evidence of foul smelling discharge
3. Colour of discharge if it is clear or meconium stained.

Per vaginal examination was done to note

1. Assessment of Bishop Scoring to assess the stage of labour, with special note on the presence or absence of the membranes.
2. Pelvic assessment

Diagnosis of PPROM

Rupture of membranes was diagnosed based on history of gross vaginal fluid loss. At the same time a speculum examination was done to observe the pool of liquorin posterior fornix. In case of doubt, uitrasound examination was done for confirming the diagnosis. Finding of oligohydramnios was taken as confirmatory. All the subjects met the inclusion criteria. An informed and written consent was taken from all subjects.

A note was made for any evidence of clinical chorioamnionitis at admission.

Investigations

Investigations sent after admission included-Baseline investigations such as complete blood picture, blood group, VDRL, HIV, Hep-B antigen, random blood glucose levels, urine routine examination. Investigations specific to PPROM were:

1. Plasma ascorbic acid

Plasma Ascorbic acid: Maternal 2 ml of 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.
All the data was entered into a predesigned case proforma during the study.

Results

This case control study was conducted on 100 patients admitted in the Department of Obstetrics and Gynecology, EPIONE Hera Hospital, Hyderabad, Telangana, India.

Age distribution

Mean age distribution is 27.02 ± 3.5 9 years in the study group, whereas the mean age is 27.83 ± 3.22 years in the control group, p value <0.795 (not significant). There was no significant difference in the age distribution.
In the study group, 5 cases (10%) were in the age group of 18-20 years, 17 cases (34%) in the age group of 21-25 years, 37 cases (74%) in the age group of 26-30years, 1 case (2%) in the age group of more than 30 years. In the control group, 5 (10%) cases were in the age group of less than 20 years, 22 cases (44%) in the age group of 21-25 years, 29 cases (58%) in the age group of 26-30 years, 4 cases (8%) in the age group of 30- 40 years.

Gestational Age: The mean gestational age is 34.33 ± 3.06 weeks in the study group and 40 .07 ± 1.23 weeks in the control group, p value <0.000, highly significant.

Gravida score

Table 1: Gravida score

Gravida	Study Group		Control Group		Total
	No of cases	Percent	No of cases	Percent	
Primigravida	24	48%	20	40%	44
Multigravida	26	52%	30	60%	56
Total	50	100%	50	100	100
Chi Square test P< 0.722, Not Sig					

Primigravida were 24 cases (48%) in the study group and 20 cases (40%) inthe control group. Multi gravidae were 26 cases (52%) in the study group and 30 cases (60%) in the control group.

Plasma vitamin C levels

Table 2: Mean plasma vitamin C levels

Plasma vitamin C(mg/dl)				
Groups	N	Mean	Std. Deviation	Unpaired t test
Study Group	50	0.60	0.30	P<0.000, HS
Control group	50	1.12	0.60	

The mean vitamin C levels in study group is 0.50 ± 0.30 and control group is 1.12 ± 0.60, p value <0.000, highly significant.
In the study group, out of 50 cases, plasma vitamin C levels less than 0.6mg/dl was seen in 25 cases (50%) and in the range of 0.6-2.0 mg/dl in 25 cases (50%).
In the control group, out of 50 cases, plasma vitamin C levels than 0.6 mg/dl was seen in 10 cases (20%), 0.6-2.0 mg/dl in 38 cases (76%) and more than 2.0 mg/dl in 2 cases (4%), p value <0.000, highly significant.

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	3	10	12	25
0.6 - 2.0	10	4	11	25
Total	13	14	23	50
Chi Square test	P<0.133, Not Sig			

In the study group, the plasma vitamin C levels in very early preterm pregnancy was<0.6 mg/dl in 3 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 11 cases.

Hemoglobin distribution

Table 4: Mean hemoglobin levels

Hemoglobin (g/dl)				
Groups	N	Mean	Std. Deviation	Unpaired t test
Study Group	50	10.2	1.8	P<0.002, HS
Control group	50	11.4	1.2	

Mean hemoglobin level is 10.2 gm/dl in the study group and 11.4 gm/dl in the control group, p value <0.002, highly significant. Mean hemoglobin distribution in the study group, among the primigravida was 9.27 ± 1.35gm/dl and multigravida was 8.74 ± 1.23 gm/dl, p value < 0.205 not significant. Mean hemoglobin distribution in the control group, among the primigravida was 10.05± 1.61 gm/dl and multigravida was 9.55 ± 1.43 gm/dl, p value<0.126, not significant.
In the control group, among the primigravida, there was 1 case of severe anemia and 5 cases of mild anemia. Among the multigravida there was 1 case of severe anemia, 4 cases of moderate anemia and 10 cases of mild anemia, p value <0.330, not significant.

Table 5: Relationship of hemoglobin levels and plasma vitamin C levels

Hemoglobin (g/dl)	Plasma vitamin C(mg/dl)					
	Study Group			Control Group		
	< 0.6	0.6 - 2.0	> 2	< 0.6	0.6 - 2.0	> 2
Severe	4	1	0	0	1	1
Moderate	7	3	0	0	3	1
Mild	12	12	0	2	13	0
Total	23	16	0	2	17	2
Chi Square Test	P>0.05, Not Sig			P>0.05, Not Sig		

In the study group, number of cases of anemia with plasma vitamin C levels <0.6 mg/dl were 23 cases, among them severe anemia were 4 cases, moderate anemia were 7 cases and mild anemia were 12 cases. Number of cases of anemia with plasma vitamin C levels 0.6-2.0 mg/dl were 16, among them severe anemia was 1 case, moderate anemia were 3 cases, mild anemia were 12 cases, p value >0.05, not significant.
In the control group, number of cases of anemia with plasma vitamin C levels <0.6 mg/dl were 2 and both had mild anemia. Number of cases of anemia with plasma vitamin C levels 0.6-2.0 mg/dl were 17, among them severe anemia was 1 case, moderate anemia were 3 cases and mild anemia cases were 13. Number of cases of anemia with plasma vitamin C >2 mg/dl were 2, among them severe anemia case was 1 and other was moderate anemia,

p value > 0.05, not significant.

Distribution of birth weight

The mean birth weight in the study group is 1.96 ± 0.37 kg, whereas 2.97 ±

Table 6: Distribution of birth weight

Birth weight (kg)	Study Group		Control Group		Total
	No of cases	Percent	No of cases	Percent	
< 1.0	0	0	0	0	0
1-1.5	9	18	0	0.0	9
1.5 - 2.5	41	82.0	3	6.0	44
> 2.5	0	0.0	47	94.0	47
Total	50	100	50	100	100
Chi Square test P< 0.000, Highly Sig					

In the study group, out of 50 babies, 9 babies (18%) had birth weight in the range of 1-1.5 kg (very low birth weight), 41 babies (82%) in the range of 1.5-2.5 kg (low birth weight).

In the control group, out of 50 babies, 3 babies (6%) had birth weight in the range of 1.5-2.5 kg (low birth weight) and 47 babies (94%) in the range of >2.5 kg. 0.30 in the control group, p value <0.000, highly significant.

Distribution of birth weight according to gestational age

In the study group, 8 babies had birth weight in the range of 1-1.5 kg (very low birth weight) in very early preterm (28-32 weeks), 1 baby of birth weight in the range of 1-1.5 kg (very low birth weight) in early preterm (32-34 weeks). 10 babies had birth weight in the range of 1.5-2.5 kg (low birth weight) in very early preterm (28-32 weeks), 13 babies had birth weight in the range of 1.5- 2.5 kg (low birth weight) in early preterm and 28 babies of birth weight in the range of 1.5-2.5 kg (low birth weight) in late preterm (34-36 weeks).

In the study group, out of 50 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. Out of 39 babies, very low birth weight were 9,low birth weight were 11, respiratory distress syndrome were 16, birth asphyxia due to abruption placenta was 1, transient tachypnea of newborn was 1, early onset sepsis was 1.

In the control group, out of 50 babies, 44 babies (88%) were not admitted to NICU, 5 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 newborn and 1 baby in view of birth asphyxia due to abruption placenta.

Number of babies admitted to NICU for 1-5 days were 15(14 cases had leak for duration of less than 24 hours and 1 case had leak for duration of more than 24 hours), 5 babies (5 cases had leak for duration of less than 24 hours) were admitted to NICU for 6- 10 days, 10 babies (9 cases had leak for duration of less than 24 hours and 1 case had leak for duration of more than 24 hours) were admitted for 11-15 days,8 babies (8 cases had leak for duration of less than 24 hours) were admitted to NICU for 16- 20 days.

Perinatal morbidity in relation to birth weight in study Group

Out of 50 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. Among very low birth weight 3 babies were admitted to NICU for 11-15 days, 6 babies were admitted to NICU for 16-20 days. Among 30 low birth weight 15 babies were admitted to NICU for 1- 5 days, 5 babies were admitted to NICU for 6- 10 days, 7 babies were admitted to NICU for 11-15 days, 2 babies were admitted to NICU for 16-20 days, 1 baby was admitted to NICU for 27 days.

Perinatal morbidity in relation to birth weight relationship of duration of leak and gestational age in study group

In the study group, out of 50 cases duration of leak within 24 hours was in 47 cases, among those 11 cases were very early preterm, 13 cases early preterm and 28 cases were late preterm. Duration of leak was more than 24 hours in 2 cases, among those 1 is very early preterm and 1 case is late preterm.

Perinatal moratlity in relation to duration of leak

In the study group total perinatal mortality is 6 cases, among those 5 cases had leak for a duration of less than 24 hours and 1 case had leak for a duration of more than 24 hours p value < 0.192, not significant.

In the study group, out of 50 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. The cause of death in study group was severe respiratory distress syndrome in 3 babies, very low birth weight in 2 babies and late onset sepsis in 1 baby. The cause of death in control group was meconium aspiration syndrome in 2 babies.

In the study group, out of 50 babies 54 were alive and 6 died. Among 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.

In the study group, perinatal moratality was 6, 4 out of 9 in the birth weight range of 1-1.5 kg and 2 out of 51 in the birth weight range of 1.5-2.5 kg, p value <0.002, highly significant.

Discussion

The present study was conducted in the Department of Obstetrics and Gynecology, J J M Medical College Davangere during the period of 1st October 2017 to 31st August 2019 In the study group, 5 cases (10%) were in the age group of 18-20 years, 17 cases (34%) in the age group of 21-25 years, 37 cases (74%) in the age group of 26-30years, 1 case (2%) in the age group of more than 30 years. In the control group, 5 (10%) cases were in the age group of less than 20 years, 22 cases (44%) in the age group of 21-25 years, 29 cases (58%) in the age group of 26-30 years, 4 cases (8%) in the age group of 30- 40 years.

Mean age distribution is 27.02 ± 3.5 9 years in the study group, whereas the mean age is 27.83 ± 3.22 years in the control group, p value <0.795 (not significant). There was no significant difference in the age distribution.

The mean gestational age is 34.33 ± 3.06 weeks in the study group and 40 .07 ± 1.23 weeks in the control group, p value <0.000, highly significant.

The mean vitamin C levels in study group is 0.50 ± 0.30 and control group is 1.12 ± 0.60, p value <0.000, highly significant.

In the study group, out of 50 cases, plasma vitamin C levels less than 0.6mg/dl was seen in 25 cases (50%) and in the range of 0.6-2.0 mg/dl in 25 cases (50%). In the control group, out of 50 cases, plasma vitamin C levels than 0.6 mg/dl was seen in 10

cases (20%), 0.6-2.0 mg/dl in 38 cases (76%) and more than 2.0 mg/dl in 2 cases (4%), 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 3 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 11 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 *et al.* [5] and Emmanuel Ajucukwu *et al.* [31] proved that vitamin C levels were low in the patients having PPROM than the patients delivering at term gestation. JA Osaikhuwuomwan *et al.* [21] and Esther Casanueva *et al.* [22] demonstrated that plasma vitamin C levels decreased as the pregnancy advanced. In the study group, number of cases of anemia with plasma vitamin C levels <0.6 mg/dl were 23 cases, among them severe anemia were 4 cases, moderate anemia were 7 cases and mild anemia were 12 cases. Number of cases of anemia with plasma vitamin C levels 0.6-2.0 mg/dl were 16, among them severe anemia was 1 case, moderate anemia were 3 cases, mild anemia were 12 cases, p value >0.05, not significant.

In the control group, number of cases of anemia with plasma vitamin C levels <0.6 mg/dl were 2 and both had mild anemia. Number of cases of anemia with plasma vitamin C levels 0.6-2.0 mg/dl were 17, among them severe anemia was 1 case, moderate anemia were 3 cases and mild anemia cases were 13. Number of cases of anemia with plasma vitamin C >2 mg/dl were 2, among them severe anemia case was 1 and other was moderate anemia, p value > 0.05, not significant. This signifies that anemia was more prevalent in the study group when compared to the control group. Mean hemoglobin distribution was more in the primigravidae than the multi gravidae in both study and control group. In the study group 39 out of 60 cases had anemia, whereas in the control group 21 out 60 cases had anemia, inferring the linear relationship between decreased plasma vitamin C levels and anemia. Vitamin C supplementation in pregnancy leads to increased absorption of iron and prevention of anemia and its further complications.

In the control group, number of anemia cases with plasma vitamin C levels <0.6 mg/dl were 2 and both had mild anemia. Number of cases of anemia with plasma vitamin C levels 0.6-2.0 mg/dl were 17, among them severe anemia was 1 case, moderate anemia were 3 cases and mild anemia cases were 13. Number of cases of anemia with plasma vitamin C >2 mg/dl were 2, among them was severe anemia and other was moderate anemia, p value > 0.05, not significant. The number of cases of anemia were more in study group than control group, and lower levels of plasma vitamin C were associated with lower levels of hemoglobin, showing a linear relationship.

The mean birth weight was 1.96 ± 0.37 kg in the study group and 2.97 ± 0.30 kg in the control group, p value <0.000, highly significant. Babies in the study group had birth weight in the range of 1-1.5 kg (very low birth weight) to 1.5- 2.5kg (low birth weight), whereas the babies in control group had birth weight in the range of 1.5-2.5 kg (low birth weight) to normal birth weight. This signifies that as the gestational age increased the birth weight increased.

Admission to NICU was accounted as perinatal morbidity due to different causes. Out of 50 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. Among very low birth weight 3 babies were admitted to NICU for 11-15 days, 6 babies were admitted to NICU for 16-20 days. Among 30 low birth weight 15 babies were admitted to NICU for 1- 5 days, 5 babies were admitted to NICU for 6- 10 days, 7 babies were admitted to NICU for 11-15 days, 2 babies were admitted to NICU for 16-20 days, 1 baby was admitted to NICU for 27 days. In the study group, out of 50 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. The cause of death in study group was severe respiratory distress syndrome in 3 babies, very low birth weight in 2 babies and late onset sepsis in 1 baby. The cause of death in control group was meconium aspiration syndrome in 2 babies.

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.

In the study group, out of 50 babies 54 were alive and 6 died. Among 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.

In the study group, perinatal moratality was 6, 4 out of 9 in the birth weight range of 1-1.5 kg and 2 out of 51 in the birth weight range of 1.5-2.5 kg, p value <0.002, highly significant. 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.

Ascorbic acid levels were low in women with PPROM 0.41 ± 0.08 versus 0.84 ± 0.19 mg/dl. There is a linear decline in plasma vitamin C levels as the pregnancy advances. Inverse relationship was observed between duration of rupture of membranes and vitamin C levels in a study by Richa sharma *et al.* [19]

A recent study demonstrated that plasma vitamin C was lower in women with PPROM; it concluded that a low plasma vitamin C concentration might be an associated risk factor for PPROM. [17] Nayereh Ghomian, Leili Hafizi *et al.* [7] and Anam Majid *et al.* [29] inferred that vitamin C supplementation decreases the occurrence of PPROM, improves mean gestational age at delivery, neonatal apgar score and mean birth weight at delivery. In 2003, Tejero *et al.* [23] measured the concentration of vitamin C in leukocytes and found lower levels in the PROM patients than in the control group. Also, Plessinger *et al.* [24] argued that foods were not substantial enough resources to provide the appropriate level of vitamins C and E, required for the prevention of PPROM, and suggested food supplements to compensate for such insufficiencies. Borna *et al.* [25] studied 60 patients and observed that vitamin C, accompanied by vitamin E, increased the latency period. In 2003, Siega-Riz *et al.* [26] suggested that vitamin C be incorporated in the protocol for pregnant women. In contrast to these findings and what is expected theoretically, Spinnato JR *et al.* [27] reported that supplementation of vitamins C and E in a combination dose might be associated with a higher risk of PPROM and PROM.

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 also associated with maternal anemia. 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, hemodilution. Improvement in the dietary habits and nutritional status of pregnant women helps in reducing PPROM. 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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