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ORIGINAL ARTICLE

Ascorbic Acid Concentration and Preterm Premature Rupture of Membranes

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Abstract

Introduction 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.

Methods A prospective study was conducted where 40 women (20 in each study and control group) with singleton pregnancies between 28 and 37 weeks gestation were recruited. Women with anemia, diabetes, UTI, RTI, vaginal infection, bleeding, h/o PPROM in previous pregnancy, polyhydramnios, and smoker were excluded from the study. Maternal plasma vitamin C levels were measured.

Results 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. There was a significant difference in maternal morbidity, neonatal morbidity, and mortality.

Conclusion Ascorbic acid concentration was low in women with PPROM. Thus, vitamin C supplementation should be made mandatory along with iron and calcium to antenatal women to avoid the complications of PPROM.

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Introduction

Preterm premature rupture of membranes (PPROM) complicates 1–3 % of all pregnancies and is the major contributory factor for perinatal morbidity and mortality. Approximately, 40 % of preterm births are associated with PPROM [1, 2].

The cause of PPROM is unknown but the pathophysiology appears to be multifactorial. Recent evidence suggests that membrane rupture is also related to biochemical processes such as abnormalities in collagen structure and formation as well as increased oxidative stress [3].

Micronutrient deficiency that leads to abnormal collagen structure has been associated with increased risk of PPROM [3, 4]. The micronutrient vitamin C is an effective water soluble antioxidant that scavenges several reactive oxygen species, thus reducing oxidative stress. It also acts as an enzymatic cofactor to the enzymes lysyl hydroxylase and prolyl hydroxylase, which is required for synthesis of hydroxyproline and hydroxylysine. Collagen requires hydroxyproline bridges across the triple helix to provide stability to it. Ascorbic acid also causes downregulation of the metalloproteinase-2 and biosynthesis of collagen where it is required for the formation of triple helical structure of collagen.

Thus, ascorbic acid participates in the equilibrium between synthesis and degradation of collagen and this may be critical in reducing the occurrence of preterm PROM [5, 6].

Daily supplementation of 100 mg/day vitamin C after 20 weeks gestation effectively reduces the incidence of PROM [7].

We conducted a study to compare the serum vitamin C levels in women with preterm PROM and women without PPROM.

Objective

To establish the association between maternal plasma vitamin C concentration in women with PPROM and women without PPROM and also to study the difference in maternal & perinatal morbidity and mortality in both the groups.

Methods

Prospective randomised study was conducted in our institution for a period of 1 year from Dec 2011 to 2012, where 40 women with singleton pregnancies between 28 and 37 weeks were recruited.

Study group included 20 antenatal women with history of PPROM and fulfilled the inclusion and exclusion criteria.

Control group also included 20 pregnant women without PPROM following every recorded case of PPROM and matched for gestational age.

Inclusion criteria

Women who were willing to participate in the study and gave written consent to complete the study.

Exclusion criteria

Women with anemia, diabetes, UTI, RTI, vaginal infection, polyhydramnios, smoker, h/o PPROM in previous pregnancy, and evidence of chorioamnionitis in current pregnancy were excluded from the study.

A general physical and abdominal examination was done. Sterile per speculum examination along with nitrazine test and ferning test was carried out to confirm PPROM. Vaginal swab culture was obtained.

After 6–8 h fasting, maternal 5 ml venous blood samples were collected in EDTA vial to estimate vitamin C concentration from both the groups. Vitamin C cut off limit taken as 0.6 mg/dl [8], and all the patients were followed till the delivery.

Results

There were no statistically significant difference in age and parity among both the groups. 50 % versus 60 % of women belonged to 20–25 years of age in study and control groups, respectively (Table 1).

65 % women in study group compared to 50 % in control group were multigravidas (Table 2).

Majority (30 %) of women reported within 6–12 h of rupture of membranes (Table 3).

Ascorbic acid levels were low in women with PPROM. There was a statistically significant difference in vitamin C levels in both the groups, and the mean was 0.41 ± 0.08 versus 0.84 ± 0.19 mg/dl in controls (*t* test .000 SS). There is a linear decline in Plasma vitamin C levels as the pregnancy advances (Fig. 1).

Table 1 Age distribution

Age group (years)	Study group	Control group
20–25	10 (50 %)	12 (60 %)
26–31	10 (50 %)	7 (35 %)
32–37	0	1 (5 %)
Total	20	20

Table 2 Parity distribution

Parity	Study group	Control group
Primigravida	7 (35 %)	10 (50 %)
Multigravida	13 (65 %)	10 (50 %)
Total	20	20

Table 3 Duration of rupture of membranes

Duration (hrs)	Study group ($n = 20$)
<6	1 (5 %)
6–12	6 (30 %)
12–24	5 (25 %)
24–48	5 (25 %)
>48	3 (15 %)

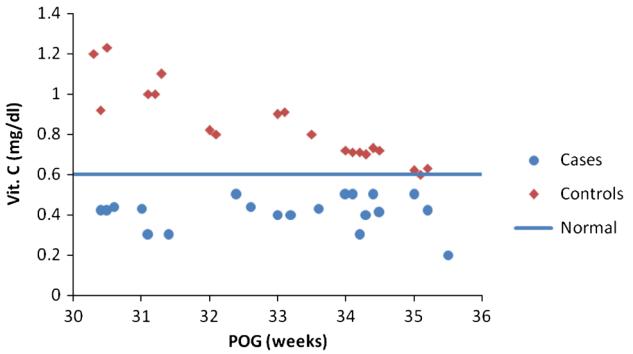

Fig. 1 Comparison of vitamin C levels at different POG in both the groups

Table 4 Relation of vitamin C and duration of PPROM in both the groups

Duration of PPROM	Plasma vitamin C levels
<48 h	0.2–0.5 mg/dl
>48 h	0.1 mg/dl

Inverse relationship was observed between duration of PPROM and vitamin C levels (Table 4).

There was a significant difference in the mode of deliveries, and 55 % of women underwent LSCS in the study group VS 20 % in the control group (Pearson Chi-square test 0.022 SS). Maternal morbidity was increased in the study group as three (15 %) women had wound dehiscence and prolonged hospital stay. NICU stay beyond 24 h was 60 % versus 15 % in the study and control groups, respectively. Early neonatal deaths were more in the study group 25 % probably due to prematurity and low birth weight (Table 5).

Discussion

The main cause of PROM with different pathologies is disorder in collagen metabolism. Reduction in collagen content of membranes decreases their stability and causes rupture of membranes. Vitamin C supplementation during pregnancy can prevent PROM as it regulates the metabolism of membrane's collagen and augment their resistance.

Table 5 Maternal and fetal outcome in both the groups

	Study group	Control group
Mode of deliveries		
LSCS	11 (55 %)	4 (20) %
NVD	09 (45 %)	16 (80) %
Wound dehiscence	3 (15 %)	0
NICU admissions	12 (60 %)	3 (15 %)
Mean NICU (days)	9.42 ± 4.89	6.33 ± 3.1
Early neonatal death	5 (25 %)	2 (10 %)

The association between vitamin C and the preventable devastating consequences of preterm PROM and prematurity encouraged us to study the plasma levels of ascorbic acid in women with and without rupture of membranes. This may be necessary to develop health strategies aimed at improving outcome by predicting and preventing PPROM.

Osakhuwuomwan JA et al. [8] reported that plasma vitamin c decreases with increasing gestational age, and its levels were low in women with PPROM compared to the women without PPROM 0.53 ± 0.05 versus 0.58 ± 0.05 mg/dl. Our study also observed a decreasing trend of vitamin C as the pregnancy advances and vitamin C levels in women with PPROM and without PPROM was 0.41 ± 0.08 versus 0.84 ± 0.19 mg/dl.

Barett BM et al. [9] conducted a study and concluded that PROM patients had lower ratios of ascorbic acid in amniotic fluid than controls and lower ratios of amniotic fluid to serum ascorbic acid ($p < 0.0001$). Our study also showed lower ascorbic acid concentration in PROM women compared to the controls (0.41 ± 0.08 Vs 0.84 ± 0.19).

Tejero E et al. [10] and Awolelu CO et al. [11] concluded no significant difference in the study and the control groups, which is contradictory to our study.

Mehrangiz et al. [12] reported that vitamin c supplementation prevents early rise of serum estriol, and its levels were low in women without PROM as compared to women receiving placebo ($p = 0.044$).

Conclusion

Vitamin C concentrations were low in PPROM patients, and also its concentration declines as the pregnancy advances. However, large multicenter clinical trials are required to further test this association of ascorbic acid and PPROM. Vitamin C supplementation should be made

mandatory along with iron and calcium to antenatal women to avoid the preventable complications of PPROM.

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