

## ASSOCIATION OF ASCORBIC ACID CONCENTRATION AND PRETERM PREMATURE RUPTURE OF MEMBRANE

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### Abstract

**Background:** Premature rupture of membranes (PROM) is the rupture of amniotic membranes before labor begins, and when membranes rupture occurs before 37 weeks of gestation, it is known as preterm PROM (PPROM). It is known to complicate around 3% of preterm pregnancies and is responsible for 40% to 75% of neonatal deaths. It is suggested that vitamin C status plays a role in reducing the incidence of PPRM. The study aims to establish the association between maternal plasma vitamin C concentration among women with PPRM and women without PPRM.

**Subjects and Methods:** A prospective cohort study was done at Al Basrah Teaching Hospital for maternity and children over the period from January 1st, 2023, to December 31st, 2023. The study included 34 cases of PPRM, which were matched for gestational age with 28 controls. The data were collected from women who were included in the study through a well-formed questionnaire. Then 5 cc of blood was drawn from each woman to measure the Hb, WBC, and vitamin C levels.

**Results:** The vitamin C level was lower among cases ( $7.22 \pm 4.66$ ) than controls ( $14.23 \pm 5.29$ ) with a P-value of 0.001. Urinary tract infection was also higher among cases ( $p$ -value=0.001). Women with caesarean sections had a lower level of vitamin C ( $6.23 \pm 2.8$ ) in comparison to women with vaginal delivery ( $11.63 \pm 6.05$ ), and those with postpartum haemorrhage had a lower level of vitamin C ( $7.25 \pm 4.91$ ). however, only the mode of delivery had a statistically significant level ( $p$ -value of 0.001).

**Conclusion:** A lower level of vitamin C was noticed among women with PPRM in comparison to healthy women. A higher incidence of postpartum haemorrhage (PPH) and neonatal complications was noticed among those with PROM and vitamin C deficiency.

**Keywords:** Preterm, PROM, vitamin C, pregnancy.

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### Introduction

Premature rupture of membranes (PROM) is the rupture of amniotic membranes before labor begins. When membranes rupture occurs before 37 weeks of gestation, it is known as preterm PROM (PPROM). (1)

PROM is known to complicate around 3% of preterm pregnancies, 10% of term pregnancies, and 11% of preterm deliveries. It is also responsible for causing 40% to 75% of neonatal deaths in the United States(2).

Preterm PROM appears in 1%–3% of all pregnancies and one-third of preterm deliveries and thus is a leading cause of perinatal morbidity and mortality. (3, 4)

Humans cannot internally produce vitamin C, thus the consumption of fruits and vegetables in our diets represents the only source of vitamin C. Notably, an array of sources rich in vitamin C includes citrus fruits, berries, tomatoes, potatoes, and verdant leafy vegetables (5).

For individuals aged 19 and above, the Recommended Dietary Allowance (RDA) is 90 mg per day for men and 75

mg for women. However, during pregnancy and lactation, these figures rise to 85 mg and 120 mg per day, respectively. (6)

Serum ascorbic acid levels of more than 11 micromoles/L are considered sufficient, but this usually reflects a recent dietary intake. For this, the measurement of leukocyte ascorbic acid levels is more accurate, but testing is not widely available. The average plasma level of vitamin C in a healthy adult population is between 40 and 65  $\mu\text{M/L}$ . (5, 7)

There are several risk factors for vitamin C deficiency, these include inadequate nutritional intake, limited socioeconomic resources, advanced age, male gender, excessive alcohol consumption, tobacco use, and severe mental health disorders.(8)

Direct supplementation, ranging from 500 mg to 1000 mg per day for adults. The goal of this supplementation is to be maintained for about a month or until the clinical symptoms have completely resolved. Along with informing the patient about lifestyle adjustments to ensure a consistent intake of the vitamin. The constitutional symptoms tend to show signs of improvement within a day after initiating supplementation, while spontaneous bleeding issues often resolve over several days to weeks.(9)

The adequacy of vitamin C status has been suggested to play a role in reducing the incidence of PPRM. This may be attributed to the involvement of vitamin C in collagen metabolism and the importance of collagen in maintaining the mechanical strength of the chorioamnionitis membranes throughout gestation( 10)

The current recommended dietary allowance for vitamin C does not adequately consider the metabolic adjustments that occur during pregnancy. Altered patterns of collagen synthesis and reduced vitamin C concentrations at week 28 of gestation have been associated with the subsequent occurrence of preterm PROM. (11,12).

The study aims to Establish the association between maternal plasma vitamin C concentration among women with PPRM and women without PPRM, to Study the difference in maternal and perinatal morbidity and mortality among women with PPRM and women without PPRM, and to Study the correlation of patents with

PROM with different parameters like antenatal care, social class and others.

## Method

This study was carried out as a prospective cohort study at Al Basrah Teaching Hospital for maternity and children over 12 months (From 1st of January 2023 to 31st of December 2023).

The study group was divided into case and control groups: The case group: involved 34 women with Singleton pregnancy between 28 and 37 weeks of gestation who were admitted to the obstetric ward with a history of premature rupture of the membranes. The control group: involved 28 women with Singleton pregnancy between 28 and 37 weeks of gestation who were admitted to the obstetric ward for any reason other than a history of premature rupture of membranes. Both groups were matched for gestational age the Inclusion criteria include Singleton pregnancy of apparently normal fetus with a diagnosis of PPRM and between 28 and 37 weeks of gestation .Women with medical diseases including infections, polyhydramnios, those who smoke., with a history of preterm pre-labour rupture of membranes in previous pregnancies, and Women with evidence of chorioamnionitis in the current pregnancy were excluded from the study. History taken from the patients was according to a questionnaire which included:

Patient demographics: name, age, parity, LMP, GA, occupation, educational level and address.

Patient clinical profile: past medical history (any history of diabetes or hypertension), past surgical history, drug history.

The rupture of membrane characteristic: time and duration of rupture membrane, colour, the odour of fluid leaking per vagina.

Any other associated symptoms which include: abdominal pain, fever and urinary symptoms.

past obstetrical history (history of previous rupture membranes in previous pregnancies).

Then an examination was done for each woman which included :Vital signs: temperature, blood pressure, and pulse rate were checked (to exclude signs of

chorioamnionitis). General, abdominal and obstetric examinations were done. Then Sterile per vagina speculum examination was carried out to confirm PPRM (made the patients rested supine for 20-30 minutes and pooling of fluid was noticed). The fern test was also done to detect the presence of amniotic fluid. We put a drop of fluid from the vagina onto a slide, letting it dry and then examine it under a microscope to see if there is a fern-like pattern.

Then a blood sample was taken for a complete blood count for measuring Hb, and WBC. A total of 5 ml of maternal venous blood was taken in gel tubes to measure the vitamin C level from both patients and the control groups. A general urine exam was done to check for urine albumin, pus cells and epithelial cells.

Patients group were followed up for a period (which is the time interval between ROM and onset of labour). The mother's outcome was assessed including development of chorioamnionitis, mode of delivery, and development of PPH. The neonatal outcome includes admission to the neonatal care unit and birth weight was also assessed.

Data was entered using computerized statistical software; Statistical Package for Social Sciences (SPSS) version 26 was used. The appropriate statistical tests were performed, a Chi-square test was used for categorical variables, Fisher's exact test was used when the expected variable was less than 5, and two samples of independent t-tests for the continuous variable. In all statistical analyses, the level of significance (p-value) is set at  $\leq 0.05$ .

## The result

The study included 62 women divided as 34 women in the case group and 28 women in the control group. The majority of women in both groups were between 20-29 years and there is no significant difference in the age of both groups p-value = 0.230. Regarding education, the highest percentage of women in the study had a primary school education. And there is no significant difference between the groups p-value = 0.644. The employment status shows that most women were unemployed and there is no significant difference in both groups since p-value = 0.768. In regards to parity, nearly 70.0% of women in both groups were multipara. The gestational age mean for

the case group was 33.29 weeks while for the control group 34.07 weeks but still there's no significant difference between them, p-value= 0.131.

Women were asked about their supplement intake during pregnancy, 92.2% of women in the control group mentioned supplement intake in comparison to 58.8% of women in the case group. There is a significant statistical difference since p-value=0.002. all these data are presented in Table 1.

Table 2 shows the maternal and fetal outcomes among the participant women. The highest percentage of cesarean section was noticed among women in the case group (70.6%) in comparison to 57.1% among the control group but still, there was no significant difference p-value= 0.721. Similarly for the postpartum haemorrhage, 29.4% for the case group and 7.1% for the control group. There's a significant difference between both groups p-value= 0.027. Regarding neonatal admission to the NICU, 47.1% of the case group neonates need NICU admission while only 7.1% in the control group. This difference is statistically significant since P-value =0.002.

The laboratory findings of the participants are shown in Table 3. The WBC level among the case group was higher than the control group and this difference is of statistically significant p-value=0.011. Nearly the same mean Hb level among women in both groups, p-value=0.542. The GUE was done and its results revealed that the highest percentage of UTIs among women in the case group was 94.1%. p-value= 0.001

The serum Vitamin C level shows a mean of  $7.22 \pm 4.66$  for the cases and a mean of  $14.23 \pm 5.29$  for the control group. This difference is statistically significant p-value=0.001.

The vitamin C level and its relation to the sociodemographic variables among the case group were presented in Table 4. Age shows no significant association with vitamin C level p-value=0.892. Similarly, the education and parity both had a p-value of more than 0.05. The employed women had a higher level of vitamin C in

comparison to unemployed women and this difference is of statistically significant  $p$ -value= 0.046.

Table (4): The vitamin C level and its relation to the sociodemographic variables among

## Discussion

The occurrence of premature rupture of membranes (PROM) is a complication seen in 1–5% of pregnancies, and it serves as a significant factor contributing to both perinatal morbidity and death. (13) The aetiology of premature rupture of membranes remains unclear; however, its pathophysiology is believed to include many factors. Emerging research indicates that the occurrence of membrane rupture is associated with biochemical mechanisms, including aberrations in collagen structure and synthesis and heightened levels of oxidative stress. (14) The occurrence of premature rupture of membranes is positively correlated with a deficit in the micronutrient vitamin C, as indicated by Sharma et al. (2014). (13)

The present research shows that women in the control group exhibited a notably greater proportion of supplement use, namely in the form of multivitamins containing vitamin C. Additionally, a greater proportion of women in the PROM group exhibited low levels of vitamin C. These findings suggest that vitamin C may potentially be a risk factor for PROM. According to Ghomian et al. (2013) and Sharma et al. (2014), the primary factor contributing to premature rupture of membranes across many diseases is a disruption in collagen metabolism. (13, 15) Additionally, it was said that the decrease in collagen content inside membranes leads to a decline in their stability and ultimately results in membrane rupture. Additionally, it has been shown that the administration of vitamin C during pregnancy has the potential to mitigate the occurrence of premature rupture of membranes by regulating collagen metabolism inside the membranes and enhancing their capacity for repair. (13, 15)

The study conducted by Defrin and Rasyid in 2018 revealed that the average concentrations of vitamin C in blood plasma were lower in individuals experiencing premature rupture of membranes during term pregnancy compared to those without such complications. (16)

Additionally, Osakhuwuomwan et al. (2011) found that plasma vitamin C levels were significantly lower in women diagnosed with premature rupture of membranes compared to women without PROM. (17) Additionally, Sharma et al. (2014) discovered a decrease in ascorbic acid concentration in women with premature rupture of membranes (PROM) compared to the control group. (13) The above-mentioned three studies are in line with our findings.

In contrast, Rizka (2011) conducted research using a similar study methodology and a comparable sample size. However, Rizka's findings diverged from our own, as they said that there was no statistically significant disparity in vitamin C levels between maternal plasma with premature rupture of membranes and maternal plasma without PROM. (18)

Furthermore, our study revealed decreased concentrations of vitamin C in individuals who had caesarean sections (CS), experienced postpartum haemorrhage, and had their newborns hospitalised in the neonatal intensive care unit. Our research results are inconsistent with the findings of Rumbold et al. (2015) since they concluded that their data did not provide support for the regular use of vitamin C supplementation, either alone or in conjunction with other supplements, in preventing adverse outcomes for both the foetus and the mother. (19) There is an increasing database of scholarly research that investigates the correlation between an inadequate supply of vitamin C and the likelihood of experiencing postpartum haemorrhage. (19) The structural integrity of blood vessels may be compromised, leading to an increased risk of haemorrhage in the presence of a deficit in vitamin C. (20) Furthermore, it should be noted that insufficiencies in vitamin C can hinder the proper functioning of blood coagulation mechanisms, which may result in an elevated susceptibility to bleeding and perhaps worsen the condition of postpartum haemorrhage. (21) Moreover, there is a correlation between sufficient amounts of vitamin C and enhanced uterine muscle tone. The contraction of the uterus has a vital role in the prevention and management of postpartum haemorrhage. According to Jenkins et al. (2014), a lack of vitamin C might potentially impair the contractility of the uterine muscles,

hence elevating the likelihood of experiencing extensive bleeding. (22)

The present research also emphasises the correlation between premature rupture of membranes, levels of vitamin C, and susceptibility to infections. In their study, Defrin and Rasyid (2018) observed a decrease in vitamin C levels among individuals with infections. Additionally, they discovered a correlation between lower vitamin C levels and the presence of both infection and premature rupture of membranes, which aligns with our research results. The phenomenon was elucidated via the mechanism of migration of polymorphonuclear cells rich in vitamin C to the site of infection, leading to the displacement of immature leukocytes and subsequently resulting in diminished levels of vitamin C. (16).

The primary constraint of this investigation is the limited sample size, resulting from the unavailability of vitamin C testing within the hospital context. This restriction has the potential to impact the statistical power of significance. A further constraint pertains to the reliance on one-time measurement of vitamin C levels without sufficient subsequent monitoring.

## Conclusion

In conclusion, Women with PROM have a significantly lower intake of supplements and a lower vitamin C level than women with no PROM, and a lower level of vitamin C was noticed among those who underwent C-sections. A higher incidence of PPH and neonatal complications is associated with a lower mean of vitamin C. WBC count and abnormal GUE was significantly higher among the cases in comparison with control.

## Reference

1. Waters TP, Mercer B. Preterm PROM: Prediction, Prevention, Principles. *Clinical Obstetrics and Gynecology*. 2011;54(2).
2. Diriba TD. Incidence, the maternal and perinatal outcome of premature rupture of fetal membrane cases in Jimma University Teaching Hospital, South west Ethiopia. *EC Gynaecol*. 2017;5:163-72.
3. Tchirikov M, Schlabritz-Loutsevitch N, Maher J, Buchmann J, Naberezhnev Y, Winarno AS, et al. Mid-trimester preterm premature rupture of membranes (PPROM): etiology, diagnosis, classification, international recommendations of treatment options and outcome. *J Perinat Med*. 2018;46(5):465-88.
4. Simhan HN, Canavan TP. Preterm premature rupture of membranes: diagnosis, evaluation and management strategies. *Bjog*. 2005;112 Suppl 1:32-7.
5. Abdullah M, Jamil RT, Attia FN. Vitamin C (Ascorbic Acid). StatPearls. Treasure Island (FL) ineligible companies. Disclosure: Radia Jamil declares no relevant financial relationships with ineligible companies. Disclosure: Fibi Attia declares no relevant financial relationships with ineligible companies.: StatPearls Publishing Copyright © 2023, StatPearls Publishing LLC.; 2023.
6. The Nutrition Source: Harvard T.H. Chan School of Public Health; 2022 [Available from: <https://www.hsph.harvard.edu/nutritionsource/vitamin-c/#:~:text=RDA%3A%20The%20Recommended%20Dietary%20Allowance,RDA%20is%20suggested%20for%20smokers>].
7. Doseděl M, Jirkovský E, Macáková K, Krčmová LK, Javorská L, Pourová J, et al. Vitamin C-Sources, Physiological Role, Kinetics, Deficiency, Use, Toxicity, and Determination. *Nutrients*. 2021;13(2).
8. Krečak I, Babić G, Skelin M. Scurvy. *Acta Dermatovenerol Croat*. 2022;30(1):59-60.
9. Maxfield L CJ. Vitamin C Deficiency: StatPearls Publishing; 2022 [Available from: <https://www.ncbi.nlm.nih.gov/books/NBK493187/>].
10. Majid A, Rahim F, Majid M, Jamal T. EFFECTIVENESS OF VITAMIN C IN PREVENTING PRE - LABOUR RUPTURE OF CHORIO- AMNIOTIC MEMBRANES IN PREGNANCY IN WOMEN HAVING HISTORY OF PROM IN PREVIOUS

- PREGNANCIES. Journal of Postgraduate Medical Institute. 2015;29(3).
11. Casanueva E, Ripoll C, Tolentino M, Morales RM, Pfeffer F, Vilchis P, et al. Vitamin C supplementation to prevent premature rupture of the chorioamniotic membranes: a randomized trial. *The American journal of clinical nutrition*. 2005;81(4):859-63.
  12. Woods Jr JR, Plessinger MA, Miller RK. Vitamins C and E: missing links in preventing preterm premature rupture of membranes? *American journal of obstetrics and gynecology*. 2001;185(1):5-10.
  13. Sharma R, Mehta S. Ascorbic Acid concentration and preterm premature rupture of membranes. *J Obstet Gynaecol India*. 2014;64(6):417-420.
  14. Menon R, Richardson LS. Preterm prelabor rupture of the membranes: A disease of the fetal membranes. *Seminars in perinatology*. 2017;41(7), 409–419.
  15. Ghomian N, Hafizi L, Takhti Z. The role of vitamin C in prevention of preterm premature rupture of membranes. *Iran Red Crescent Med J*. 2013;15(2):113-116.
  16. Defrin D, Rasyid R. Differences in Blood Plasma Levels of Vitamin C in Term Pregnancy with Premature Rupture Of Membranes and Blood Plasma Levels of Vitamin C in Term Pregnancy Without Premature Rupture Of Membranes *Andalas Obstetrics And Gynecology Journal*. 2018;2(2):101–108.
  17. Osaikhuwuomwen JA, Okpere EE, Okonkwo CA, et al. Plasma vitamin C levels and risk of preterm prelabour rupture of membrane. *Arch Gynecol Obstet*. 2011;284(4):595.
  18. Rizka Sarah. “Vitamin C Level in Pregnant Women with Premature Rupture of the Membrane (PROM) and in Women with Normal Pregnancy.” *Indonesian Journal of Obstetrics and Gynecology*. 2011; 35(4): 173-175.
  19. Rumbold A, Ota E, Nagata C, Shahrook S, Crowther CA. Vitamin C supplementation in pregnancy. *Cochrane Database Syst Rev*. 2015;2015(9):CD004072.
  20. Maxfield L, Daley SF, Crane JS. Vitamin C Deficiency. In: *StatPearls [Internet]*. Treasure Island (FL): StatPearls Publishing; 2023 [Cited 19 November 2023]. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK493187/>
  21. Mohammed BM, Sanford KW, Fisher BJ, et al. Impact of high dose vitamin C on platelet function. *World J Crit Care Med*. 2017;6(1):37-47.
  22. Jenkins J, Rowland M, Van Doren E. Uterotonic agents and oxytocinergic receptors in the human uterus. *Am J Obstet Gynecol*. 2014;210(5):497-507.

**Table (1): The socio-demographic characteristics of the participants**

Variables		Case group (N=34)	Control group (N=28)	p-value
Age	Mean ±SD	27.17± 5.31	25.57 ± 5.02	0.230
	< 20	1 (2.9)	2 (7.1)	
	20-29	21 (61.8)	22 (78.6)	
	30-39	12 (35.3)	4 (14.3)	
Education	Primary	22 (64.7)	18(64.3)	0.644
	Secondary	^ (23.5)	£(14.3)	
	College and higher education	£ (11.8)	¶ (21.4)	
Employment status	Unemployed	30 (88.2)	24 (85.7)	0.768
	Employed	4 (11.8)	4 (14.3)	
Parity	Nullipara	10 (29.4)	8 (28.6)	0.942
	Multipara	24 (70.6)	20 (71.4)	
Gestational age	Mean ±SD	33.29±2.1	34.07± 1.8	0.131
Supplement intake	Yes	∫ (58.8)	∫∫ (92.9)	0.002
	No	∫£ (41.2)	∫ (7.1)	
Total		∫£ (100.0)	∫∫ (100.0)	∫∫

**Table (2): The maternal and fetal outcomes among the participant women**

Variables		Case group (N=34)	Control group (N=28)	p-value
Mode of delivery	vaginal delivery	10 (29.4)	12 (42.9)	0.721
	cesarian section	24 (70.6)	16 (57.1)	
Postpartum haemorrhage	Yes	10 (29.4)	2(7.1)	0.027
	No	24 (70.6)	26 (92.9)	
Neonatal admission to NICU	Yes	16 (47.1)	2 (7.1)	0.002
	No	18 (52.9)	26 (92.9)	

**Table (3): The laboratory findings of the participants.**

Variables		Case group (N=34)	Control group (N=28)	p-value
WBC	Mean ±SD	12.47± 3.29	10.49±2.44	0.011
Hb	Mean ±SD	10.34 ±1.08	10.09 ±1.4	0.542
GUE	Normal	2 (5.9)	22 (78.6)	0.001
	Abnormal	32 (94.1)	6 (21.4)	
Vitamin C level	Mean ±SD	7.22 ± 4.66	14.23±5.29	0.001
	Normal	10 (29.4)	24 (85.7)	
	Low	24 (70.6)	4 (14.3)	

**the case group.**

Variables		Case group (N=34)	p-value
		Mean ±SD	
Age	< 20	7.8 ± 3.2	0.892
	20-29	7.9 ± 4.7	
	30-39	7.6 ± 4.6	
Education	Primary	8.29 ± 4.98	0.443
	Secondary	7.46 ± 4.1	
	College and higher education	9.68 ± 8.1	
Employment status	Unemployed	7.2 ± 4.3	0.046
	Employed	12.2 ± 5.2	
Parity	Nullipara	8.85 ± 4.72	0.415
	Multipara	7.39 ± 4.66	