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Association of Maternal Serum Zinc Level with Preterm Prelabor Rupture of Membranes

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Abstract

Background: *A number of micronutrients are known to serve as antioxidants or essential cofactors for antioxidant enzymes. One of this necessary micronutrient is zinc, which has a very important role in normal embryogenesis, intrauterine growth and helps the mother during labour. The aim of this study was to determine the association of maternal serum zinc level with prelabor rupture of membraness.*

Methods: *This case control study was conducted in-patient department of Obstetrics & Gynaecology of Institute of Child & Mother Health (ICMH), Matuail, Dhaka, from January 2021 to December 2021. A total of 80 pregnant women with singleton pregnancy were selected. Among them 40 pregnant women with gestational age 28 to ≤36 weeks with preterm prelabor rupture of membranes were considered as case and rest 40 pregnant women with gestational age 37 to 40 weeks with term labor were considered as control.*

Results: *It is observed that 77.5% patients were 21–30 years in case and 65.0% in control. The mean age was 23.6±3.72 years in case and 22.88±2.85 years in control. Majority were primi gravida (82.5% vs 75.7%). Mean gestational age was 33.38±1.51 vs 38.95*±0.99 weeks ($p<0.05$). Mean BMI was 24.23±1.91 vs 24.92±1.59 kg/m². Serum zinc <70 µg/dl had 2.83 times increased risk for preterm PROM (95% CI 0.90–9.11).

Conclusion: *In conclusion based on the results presented in this study, we found that low serum zinc level is associated with preterm prelabor rupture of membranes.*

Keywords: *Zinc, preterm prelabor rupture of membranes, Micronutrient deficiency, Pregnancy outcome.*

1. Introduction

Term prelabor rupture of membraness (PROM), whereby the amniotic sac or "bag of waters" opens before the onset of labor, occurs in approximately 8.0% to 10.0% of term pregnancies, defined as 37 or more completed weeks of gestation [1].

The fetal membranes is composed of the inner amnion and the outer chorion. At term, the amnion is a tough and firm but pliable membranes.

This innermost avascular fetal membranes is contiguous with amniotic fluid and occupies a role of incredible importance in human pregnancy. The

amnion is primarily responsible for the tensile strength of the fetal membranes; therefore, the proper development of its structural components that prevent rupture or tearing is essential for a successful pregnancy outcome [2].

Worldwide, there is a slight difference in the prevalence of prelabor rupture of membraness and this could be due to the difference in the population studied. The incidence of PROM ranges from about 5% to 10% of all deliveries, and PPROM occurs in approximately 3.0% of all pregnancies. Approximately 70.0% of cases of PROM occur in pregnancies at term, but in referral centers more than 50% of cases may occur in preterm pregnancies. PROM is the cause of about one third of all preterm births [3].

It has no known etiology but, sub clinical infection has been postulated [4]. Other workers suggested that the rupture of membranes is related to factors other than infection, membranes dysfunction on a molecular level, collagen destruction, and programmed cell death in fetal membraness [5]. The risk factors of PROM include prior preterm birth, cigarette smoking, polyhydramnios, urinary and sexually transmitted infection, prior PROM, work during pregnancy, low Body Mass Index, bleeding, low socioeconomic status [6]. The investigators showed that those who had abortion were 3.06 times more likely to develop prelabor rupture of membraness with Odds ratio=3.06 with 95%CI: 1.39, 6.71. History of caesarean section also showed a significant association with the OR=3.15 with 95%CI: 1.05, 9.46. Furthermore, abnormal vaginal discharge in the index pregnancy was also significantly associated risk factor with OR= 3.31 with 95%CI: 1.67, 6.56. Several researchers Choudhary et al., Emechebe et al., Tarek et al., found sexual intercourse during late pregnancy to be a risk factor to develop PROM. PROM is a significant cause of perinatal morbidity and mortality [7, 8, 9]. The burden of PROM extends from maternal and neonatal morbidity and mortality to broader economic losses for the nation, including costs related to medications, hospitalization, work absenteeism, and healthcare professional expenses [10]. Assefa et al., obtained in their study that a woman with prelabor rupture of membraness is at risk of intra-amniotic infection, postpartum infection, endometritis, and death [6]. A neonate born from prelabor rupture of membraness mother is at high risk of respiratory distress syndrome, sepsis, intraventricular hemorrhage and death. Among maternal risks, infection of the amniotic cavity is the most frequent complication following PROM. Endometritis and abruptio placenta varied from 2 to 29.0% and 15–25.0% of cases respectively. Uncommon but serious complications of PROM managed conservatively include retained placenta and hemorrhage requiring dilation and curettage 12.0%, maternal sepsis 0.8%, and 0.14% maternal death [2].

2. Objective

The objective of this study was to determine the association of maternal serum zinc level with preterm prelabor rupture of membranes.

3. Methodology & Materials

This case-control study was conducted in the Department of Obstetrics and Gynaecology, Institute of Child and Mother Health (ICMH), Dhaka, from January 2021 to December 2021. The study population comprised women with preterm prelabor rupture of membranes (PPROM) and women in labor at term attending the inpatient department of Obstetrics and Gynaecology, ICMH, Dhaka.

The case group included pregnant women aged 18–35 years with gestational age between 28 to 36 weeks having preterm prelabor rupture of membranes, while the control group included pregnant women aged 18–35 years at term in labor. Purposive sampling was done according to the availability of patients fulfilling the inclusion criteria, with a total of 80 participants (40 in each group) based on Abdullah and Fauzi (2010). Inclusion criteria for cases were singleton pregnancies, gestational age 28–36 weeks, spontaneous rupture of membranes before onset of labor, and not in active labor. Controls included singleton pregnancies at 37–40 weeks with regular uterine contractions, cervical dilatation ≥1 cm, effacement ≥80%, and without complications of prelabor rupture of membranes. Women with infections, multiple pregnancy, polyhydramnios, malpresentation, anemia, diabetes, hypertension, heart disease, antepartum hemorrhage, pre-eclampsia, eclampsia, fetal abnormality, uncertain gestational age, history of abdominal trauma, or cervical surgery were excluded. Data were

collected using a structured questionnaire by interview, clinical examination, and laboratory investigations. Blood samples (5 ml) were collected from the antecubital vein after at least 12 hours of fasting under aseptic precautions, allowed to clot, and centrifuged at 3000 rpm for 5 minutes. Serum was separated and stored at −20°C until analysis. Serum zinc level was determined according to the manufacturer's instruction, with values below 70 µg/dL considered deficient.

Data were analyzed using SPSS version 22. Quantitative variables were presented as mean ± SD and tested using the unpaired t-test, while qualitative data were analyzed using the Chi-square test. Odds ratio with 95% confidence interval was calculated, and $p<0.05$ was considered statistically significant. Ethical approval was obtained from the Institutional Review Board of ICMH.

4. Results

This case control study was conducted carried out to assess the association of maternal serum zinc level with preterm prelabour rupture of membranes. Total 80 patients at the department of Obstetrics & Gynaecology of Institute of Child & Mother Health (ICMH), fulfilling the inclusion and exclusion criteria among them 40 women (28-≤36 weeks) diagnosed with prelabor rupture of membranes and 40 pregnant women (37-40 weeks) diagnosed with labor as control were evaluated for serum zinc level.

Findings of the study are presented by table as bellows:

Table I. *Distribution of the study patients by socio*

Socio-demographic profile	Case (n=40)		Control (n=40)		*p* value
	n	%	n	%	
Age (in years)					
≤20	5	12.5	12	30.0	
21-30	31	77.5	28	65.0	[b]0.288[ns]
>30	4	10.0	2	5.0	
Mean±SD	23.6±3.72		22.88±2.85		[a]0.334[ns]
Range (min,max)	19,34		18,30		
Monthly family income (in taka)					
Lower class (≤7,378)	14	35.0	17	42.5	[b]0.778[ns]
Lower middle class (7,379- 28,810)	21	52.5	19	47.5	
Upper middle class (28,811- 89,280)	5	12.5	4	10.0	
Educational status					
Primary	17	42.5	11	27.5	[b]0.355[ns]
Secondary	20	50.0	26	65.0	
Graduate	3	7.5	3	7.5	

-demographic profile (n=80)

s= significant

ns= not significant

[a]p value reached from Unpaired test

[b]p value reached from Chi-square test

Case= Prelabor rupture of membranes

Control= Normal pregnant women with term labour

According to Table I there was no statistically significant difference between case and control regarding age, monthly family income and educational status ($p>0.05$).

Table II. *Distribution of the study patients by obstetrical characteristics (n=80)*

Obstetrical characteristics	Case (n=40)		Control (n=40)		*p* value
	n	%	n	%	
Gravida					
Primi	33	82.5	28	75.7	[a]0.461[ns]

Multi	7	17.5	9	24.3	
Gestational age (weeks)					
Mean±SD	33.38±1.51		38.95±0.99		[b]0.001[s]
Range (min,max)	28,36		37,40		

s= significant

ns= not significant

[a]p value reached from Chi-square test

[b]p value reached from Unpaired test

The mean gestational age was 33.38±1.51 weeks in case and 38.95±0.99 weeks in control, which was matched according to selection criteria and the difference was statistically significant (p=0.001) between two groups (Table II).

Table III. *Distribution of preterm prelabor rupture of membranes according to gestational age (n=40)*

Gestational age (weeks)	Number of patient	Percentage
28-32	18	45.0
33-34	15	37.5
35-36	7	17.5

In preterm prelabor rupture of membranes, almost half (45.0%) of patients gestational age level was 28-32 weeks, followed by 15(37.5%) were 33-34 weeks and 7(117.5%) were 35-36 weeks (Table III).

Table IV. *Distribution of the study patients by BMI (n=80)*

BMI (kg/m^2)	Case (n=40)		Control (n=40)		*p* value
	n	%	n	%	
Normal (18.5-24.9)	32	80.0	25	62.5	0.083[ns]
Overweight (25.0-29.9)	8	20.0	15	37.5	
Mean±SD	24.23±1.91		24.92±1.59		0.083[ns]
Range (min,max)	18.5,28.5		19,29.9		

ns= not significant

p value reached from Unpaired test

There was no statistically significance difference in the distribution of the study patients according to BMI categories (p=0.083) and in the mean (±SD) BMI (p=0.083) between two groups patients (Table IV).

Table V. *Distribution of preterm prelabor rupture of membranes according to low level of maternal serum zinc level (n=40)*

Serum zinc level (µg/dl)	Number of patient	Percentage
30-50	24	60.0
51-69	6	15.0
70-100	10	25.0

In preterm prelabor rupture of membranes, almost three fourth (60.0%) of subjects serum zinc level was 30-50 µg/dl (Table V).

Table VI. *Odds ratio (OR) and 95 % confidence interval (CI) for preterm prelabor rupture of membranes according to serum zinc level in pregnancy (n=80)*

Serum zinc (µg/dl)	Case (n=40)		Control (n=40)		OR	*p* value
	n	%	n	%		
<70	33	82.5	25	62.5	2.83(0.90-9.11)	[a]0.045[s]
≥70	7	17.5	15	37.5		
Mean±SD	60.43±18.14		70.25±18.33			[b]0.018[s]
Range (min,max)	39,100		35,104			

s= significant

[a]p value reached from Chi-square test

[b]p value reached from Unpaired test

Majority (82.5%) patients belonged to serum zinc level <70 (µg/dl) in case and 25(62.5%) in control. The mean serum zinc was 60.43±18.14 (µg/dl) in case and 70.25±18.33 (µg/dl) in control. Serum zinc level <70 µg/dl had 2.83 times significantly (p=<0.05) increase risk to developed PROM with (95% CI 0.90 to 9.11) (Table VI).

5. Discussions

This case control study was carried out with an aim to estimate serum zinc level among preterm prelabor rupture of membranes and pregnant women in labor with term gestational period and also to find out the association of serum zinc level between preterm prelabor rupture of membranes with pregnant women in labor at term. A total of 80 pregnant women with singleton pregnancy attending in the in-patient department of obstetrics and Gynaecology of Institute of Child & Mother Health (ICMH), Dhaka, during January 2021 to December 2021 were included in this study. Among them 40 pregnant women with gestational age 28 to ≤36 weeks as preterm prelabor rupture of membranes was considered as case and rest 40 pregnant women with gestational age 37 to 40 weeks ass term labor was considered as control. Patients with preterm prelabor rupture of membranes, gestational age 28 to 36 weeks singleton pregnancies and patients not in active labour were enrolled as case. Singleton pregnancy, gestational age 37 to 40 weeks, regular uterine contraction documented by uterine palpation generally ≥1 in 10 minutes and dilatation and effacement of cervix were enrolled as control. Multiple pregnancy, polyhidramnios, malpresentatios, pregnancy with anemia, diabetes mellitus, hypertension, heart disease, antepartum hemorrhage, history of abdominal trauma, history of cervical surgery and women with ante partum hemorrhage and with infection were excluded from the study. All selected patients were perform Zinc level before delivery. Maternal Serum Zinc level was compared between preterm prelabor rupture of membranes and pregnant women at term in labor. The present study findings were discussed and compared with previously published relevant studies.

In this present study, 77.5% of patients belonged to age 21–30 years in the case group and 65.0% in the control group. The mean age was 23.6±3.72 years in cases and 22.88±2.85 years in controls, showing no significant difference (p>0.05). Ernita et al., found the mean age of patients with prelabor rupture of membranes to be 27.47±4.71 years and 28.00±4.99 years in normal pregnancies, with no significant difference (p>0.05) [11]. Rahmanian et al., observed the highest PROM rate among women aged 26–35 years, with decreased risk beyond 35 years [12,13,14]. Mahmoodi et al., reported that abnormal labor and high-risk outcomes increase in older women due to higher rates of comorbidities [15]. Comparable findings were also noted by Assefa et al., and Rahmanian et al., [6, 12].

In this study, 52.5% of patients had lower middle-class income (7,379–28,810 taka) in the case group and 47.5% in control. Half (50.0%) of patients had secondary education in cases and 65.0% in controls, with no significant difference (p>0.05). Assefa et al., reported that most participants had education beyond secondary level [6]. Sheeraz et al., found low antenatal care, education, and socioeconomic status among PROM patients [16]. Gabbe et al., listed risk factors for PROM as prior preterm birth, infection, smoking, low BMI, bleeding, and low socioeconomic status [17].

In this study, 82.5% were primigravida in cases and 75.7% in controls, with no significant difference (p>0.05). Ernita et al., and Svigos et al., also found no relationship between parity and PROM (p>0.05) [11, 18]. Rahmanian et al., reported that PROM was not significantly higher among nulliparas [12].

The mean gestational age was 33.38±1.51 weeks in cases and 38.95±0.99 weeks in controls (p<0.05). Among preterm PROM cases, 45.0% were 28–32 weeks, 37.5% were 33–34 weeks, and 17.5% were 35–36 weeks.

Regarding BMI, 80.0% of cases and 62.5% of controls had BMI 18.5–24.9 kg/m². The mean BMI was 24.23±1.91 vs. 24.92±1.59 kg/m² (p>0.05). Ernita et al., also found no BMI difference between PROM and normal pregnancies (p>0.05) [11].

However, earlier studies reported BMI <20 as a risk factor for PROM [19, 20]. Underweight women may face complications including PROM, anemia, preterm delivery, and low birth weight [21, 22, 23, 24]. Rahmanian et al., found no significant BMI effect on PROM, likely due to smaller sample size [12].

In this present study it was observed that 82.5% patients belonged to serum zinc level <70 (µg/dl) in case and 62.5% in control. The mean serum zinc was 60.43±18.14 (µg/dl) in case and 70.25±18.33 (µg/dl) in control. The mean serum zinc difference was significantly ($p<0.05$) lower in case. In preterm prelabor rupture of membranes groups, almost three fourth (60.0%) of subjects serum zinc level was 30-50 µg/dl. On the other hand serum zinc level <70 µg/dl had 2.83 times significantly ($p<0.05$) increase risk to developed PROM with (95% CI 0.90 to 9.11). Previous studies have shown that the maternal zinc level in women with PROM and preterm labour is significantly lower than in women without such complications [25, 26]. Supplementation studies, however, do not confirm these associations reported by Sikorski et al [26]. Sikorsi et al., proved the difference in the level of prelabor rupture of membranes between mothers with low zinc status compared to the control group ($p<0.05$) [26]. Weiss et al., concluded that low zinc levels will cause preterm birth [27]. The exact mechanism of action for proper zinc supplementation in pregnancy outcome is not yet fully known. Zinc is very important for growth, the beneficial effects of zinc on growth may be due to the direct role of zinc in protein synthesis and nucleic acid metabolism. Zinc causes antibacterial properties of amniotic fluid, so that the decrease in maternal zinc status during pregnancy can also cause a decrease in zinc availability for the fetus and placenta, then affect the ongoing extracellular matrix restructuring process in the chorionic amnion membranes and cause weakening of membranes strength and integrity and ultimately increase risk prelabor rupture of membranes. Ernita et al., study concluded that there is no difference in serum zinc levels in prelabor rupture of membranes and normal pregnancies, this might be caused by imperfect zinc absorption [11]. Where zinc is the most trace found in the human body besides iron. Iron inhibits absorbing zinc when both are given in inorganic forms. The interaction of zinc and iron first occurs in the intestine. Zinc competes with iron to be absorbed in the intestine. Rahmanian et al., study showed that the serum zinc concentration is lower in pregnant women with and without PROM than non-pregnant women [12]. The decline in the zinc level has been attributed to haemodilution, decrease in the level of zinc binding protein, hormonal changes during pregnancy and active transport of zinc from the mother to the foetus [28]. All of the aforementioned factors diminish the validity of using serum zinc level as an indicator of zinc nutriture during pregnancy [29]. Sikorski et al., Shah and Sachdev, studies showed a connection between reduced maternal serum zinc concentration during pregnancy or at delivery and a 3.5 to 7-fold increase in the risk of PROM [26, 30]. In addition, research has shown that subnormal tissue zinc content, and milder forms of zinc deficiency during pregnancy may cause PROM at term and preterm labour as well as inefficient uterine contraction [25,26, 31, 32, 33]. The lower maternal serum zinc concentration may inhibit immunological competence in both mother and foetus and therefore increase the risk of amniotic infection and onset of PROM. The above studies findings are comparable with the present study [31].

6. Limitations of the Study

The study population was selected from one selected hospital in Dhaka city, so that the results of the study may not be reflect the exact picture of the country. The present study was conducted at a very short period of time. Small sample size was also a limitation of the present study. Therefore, in future further study may be under taken with large sample size. This study did not adjust for maternal insufficiency of other micronutrients, which also elevate the risk of PPROM. Many lifestyle factors and nutritional status that influence PPROM are not considered in this study. Limited resources and facilities.

7. Recommendations

To undertake further prospective study with a larger sample size to find out the validity of the findings of the present study. Other risk factors of PPROM should be evaluated. Multi-centric studies may be undertaken to conclude the role of maternal serum zinc level in determining PPROM.

8. Conclusion

This study results showed that low serum zinc level is significantly associated with preterm prelabor

rupture of membranes. Therefore, this study conclude that low serum zinc level can be considered as a risk factor for the development of PPROM.

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CONFLICTS OF INTEREST

There are no conflicts of interest.

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