

Association Between Zinc Level and Prelabour Rupture of Membranes

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Abstract

Background: Assessment of micronutrients in pregnant women particularly ZINC and whether its concentration is different between term and preterm birth is important to optimize the normal pregnancy and to reduce the incidence of pregnancy complications, especially preterm labour and pre labour rupture of membrane. **Objectives:** Assessment of correlation between maternal serum ZINC level and the prelabour rupture of membrane in both preterm and term pregnant women. **Study Design:** Case control study. **Materials and Methods:** A case control study performed in Al-Imamain Al- Kadhmain Medical City/Obstetrics and Gynecology department from 1st of February to 1st of November 2019, Including 400 pregnant women their gestational age ranged between (24 to 42) divided in to 4 group: group A, group B, group C, group D which all undergo serum Zinc level measurement. **Result:** The mean $\pm$ SD of serum ZINC in group A which include the preterm prom, which is less than the control group (B) preterm intact membranes which, and the mean $\pm$ SD of serum zinc of group (C) which include the term prelabour rupture of membranes which is less than group (D) which is the control group of group (C) term intact membranes. This study shows significant relationship between ZINC deficiency and prelabour rupture of membrane in both term and preterm pregnant women at a P value < 0.001 and <0.001 respectively, also this study show inverse relationship between serum zinc and increasing parity, maternal age, vaginal infection, and BMI. **Conclusion:** Pregnant women with prelabour rupture of membranes whether term or preterm tend to have lower Zinc level. Increasing maternal age, increasing parity, high BMI, vaginal infection are associated with low Zinc.

Keywords: Premature preterm rupture of membrane, preterm labor, s.zinc

INTRODUCTION

Pre labour premature rupture of membranes is important cause of preterm deliveries, perinatal and neonatal mortality which is account one-third of preterm births. Preterm newborns contribute to only 8- 10% of live births but responsible for 90% of neonatal mortality.^[1]

Preterm infants are mainly complicated with difficult respiration, poor feeding, impaired body temperature regulation and increase risk of infection.^[1,2]

Preterm premature rupture of membranes (PPROM) is a subtypes of preterm labour which affects 3- 4.5% of all pregnancies globally and between 60% - 80% of the affected pregnant will deliver within 7 days and 75% within 2 weeks of PPRM^[3]

Cause of prelabour rupture of membranes may lead to physiologic weak of the membranes associated with uterine contractions and Intra amniotic infection is commonly associated with PPRM^[4]

The risk factors for PPRM include a history Of PPRM, cervical incompetence, antepartum homarrage, multiple pregnancies, connective tissue disorders, poor education, smoking, and illicit drug use.^[5]

Reduction in the intake of nutrients, such as thiamin, riboflavin, vitamin A, C, and E, copper, and zinc, is

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associated with preterm birth and higher risk of PPRM.^[6] This results from nutrient-deficiency problem that predispose women to develop abnormal collagen structure.^[7]

By gaining the knowledge about the exact role of micronutrients in the pregnancy, better nutrient approach of pregnancy would be achieved to optimize the normal pregnancy and to decrease the pregnancy complications, in particular the preterm labour and prelabour rupture of membranes. Since preterm fetal membranes are very strong, the PPRM should be a result of an internal pathology and/or external factors^[5]

According to the recent studies, rupture membranes is related to biochemical collagen disruption in the extracellular matrix of the chorion and amnion with apoptosis in thr membranes.

The disruption of collagen is primarily a result of successive activities of a number of matrix metalloproteinase (MMPs) and tissue- specific inhibitors.

The MMPs have been identified within human and some other species. They belong to a large multi gene family of zinc-dependent, photolytic enzymes with more than 26 known species, and specific structure and several properties.^[8]

Zinc is found to be an essential trace mineral second to iron, it has a vital role in protein synthesis and metabolism, DNA metabolism, and cell membrane stabilization.^[9]

Zinc play role in cell division,differentiation, DNA synthesis, regulation of gene expression,activity of insulin-like growth factors,regulation of apoptosis and promoting normal embryogenesis^[10]

Oysters, Red meat, poultry, beans, nuts, certain seafood, whole grains, fortified breakfast cereals, and dairy products are rich with Zinc while vegetable, fruits, tea, coffee, rice, and bread have iow Zinc.

Zinc requirements for pregnant women have been estimated from the amount of zinc accumulated in maternal and embryonic/fetal tissues.^[11]

100 mg of total zinc in pregnant women are devided to: 57% in the fetus, 6.5% to placenta, <1% to the amniotic fluid, 24% to the uterus, 5% to the mammary tissue, and 6.5% to the maternal blood volume. This additional zinc gained for pregnancy represents 5%–7% of the whole body zinc in non-pregnant woman.^[12,13] The aim of study is to assessment of correlation between maternal serum ZINC level and the prelabour rupture of membrane in both preterm and term pregnant women.

MATERIALS AND METHODS

It is a case control prospective study include 400 pregnant women with singleton viable embryo,the gestational age range from 24 - 42 weeks of gestation according to last menstrual period and early ultrasound (11_14) weeks,their age ranged (16_40) years old.this study conducted at outpatient clinic at Al. Imamma in Al Kathumaainm Medical CITY, verbal consent was obtained from all laydes included in the study.

The study began in February 2019 and concluded towards the end of October 2019, the Iraqi Board and council of Obstetrics and Gynecology approved the study. In 15-1-2019, no. 112

Table 1: Significant difference between group A and group B regarding age,parity,BMI and gestational age

Parameter		Preterm prelabour ruptured membrane N=100	Preterm intact membrane N=100	P value
		Mean±SD	Mean±SD	
Age (yr)		29.14±7.54	28.72±7.25	0.688*
Gestational Age (wk)		30.85±3.59	30.52±3.51	0.512*
Body mass index (kg/m²)		26.31±4.06	25.78±4.35	0.374*
		N (%)	N (%)	
Parity	0	14	14	0.982**
	1	17	18	
	2	30	27	
	3	16	15	
	≥4	23	26	

Table 2: Shows Significantly lower Zinc level in group of women with prelabour rupture of membranes wether term or preterm compared with those with intact membrane since the P value <0.001*

Parameter	Preterm prelabour ruptured membrane n = 100	Preterm intact membrane n = 100	P value	Term prelabour ruptured membrane n = 100	Term intact membrane n = 100	P value
	Mean±SD	Mean±SD		Mean±SD	Mean±SD	
Zn (µ/dl)	61.75±6.9	95.08±13.0	<0.001	62.82±6.5	94.02±10.4	<0.001*

Table 3: Shows that 1 shows that there is no significant difference between group C and group D regarding age, parity, BMI and gestational age

Parameter	Term prelabour ruptured membrane N=100		Term intact membrane N=100		P value
	Mean±SD		Mean±SD		
Age (yr)	29.11±7.47		28.8±7.22		0.766*
Gestational Age (wk)	38.66±1.27		38.84±1.46		0.353*
Body mass index (kg/m ²)	26.26±4.05		25.88±4.37		0.524*
	N (%)		N (%)		
Parity	0	22	14		0.253**
	1	18	17		
	2	21	27		
	3	21	15		
	≥4	18	27		

Table 4: Shows no significant difference in presence and absence of infection by bacterial vaginosis between group with prelabour rupture of membrane whether term or preterm as the P value 0.137 and 0.657 respectively

Parameter		Term prelabour ruptured membrane N=100 N (%)	Term intact membrane N=100 N (%)	P value	Preterm prelabour ruptured membrane N=100 N (%)	preterm intact membrane N=100 N (%)	p_value
Infection	Absent	61 (61.0)	73 (73.0)	0.137	63 (63.0)	67 (67.0)	0.657
Bacterial vaginosis	Present	39 (39.0)	27 (27.0)		37 (37.0)	33 (33.0)	

All patient sent for, Complete blood count (WBC), CRP to exclude chorioamnionites, GUE with exclusion of patient who had urinary tract infection, and vaginal swab for detection of vaginal infection including bacterial vaginosis. Obstetric ultrasound done to all patient for viability, gestational age, amniotic fluid index. Finally, all patient sent for serum ZINC, and comparison done between the four groups. 2.5. Sample Collection and Preparation of Blood Samples of ZINC Measurement: The test were done in Al-Imamain Medical City laboratory, all specimens labeled by the name along with date and time of collection. A 5 millimeters of blood obtained from the forearm vein using disposable plastic syringe, the delivered blood kept in plastic tube without anticoagulant, the sample left at room temperature for 15 minutes, then the sample centrifuged to obtain the serum which stored by freezing it at 20C.

Zinc assay kit was Rodex. The samples thawed at room temperature when all collected, then they were diluted with deionized water, by using atomic absorption spectrophotometer.

Exclusion criteria

1. Polyhydramnios.
2. BMI under 20 kg/m²
3. Medical disease including diabetes mellitus, connective tissue disorders
4. Chorioamnionitis.

5. Urinary tract infection.
6. Uterine congenital anomalies.
7. Inflammatory bowel disease, malabsorption.
8. Vaginal bleeding
9. Smokers
10. Patient in labour (with positive uterine contraction, or cervical dilatation).

Ethical consideration

The study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki. It was carried out with patients verbal and analytical approval before sample was taken. The study protocol and the subject information and consent form were reviewed and approved by a local ethics committee according to the document number 1232 dated 5/1/2019 to get this approval.

RESULTS

Table 1 shows no significant difference between group A and group B regarding age, parity, BMI, and gestational age. Table 2 shows significantly lower Zinc level in group of women with prelabour rupture of membranes whether term or preterm compared with those with intact membrane since the *P* value <0.001*. Table 3 shows that 1 shows that there is no significant difference between group C and group D regarding age, parity, BM, and gestational age. Table 4 shows no significant difference in

Table 5: Comparism of maternal characteristic and serum zinc between the 4 groups included in the study

Parameter		Zn (μ /dl)			
		Preterm ruptured membrane N=100 Mean $\pm$ SD	Preterm intact membrane N=100 Mean $\pm$ SD	Term ruptured membrane N=100 Mean $\pm$ SD	Term intact membrane N=100 Mean $\pm$ SD
Age (yr)	<20	63.15 $\pm$ 5.71	91.43 $\pm$ 10.73	64.69 $\pm$ 4.52	97.29 $\pm$ 10.35
	20-24	58.25 $\pm$ 5.22	93.23 $\pm$ 15.08	62.15 $\pm$ 6.26	95.92 $\pm$ 11.77
	25-29	61.86 $\pm$ 9.68	99.4 $\pm$ 14.8	62.82 $\pm$ 8.03	94.8 $\pm$ 10.82
	30-34	63.81 $\pm$ 5.82	99.09 $\pm$ 12.44	65.27 $\pm$ 4.34	96.46 $\pm$ 10.79
	35-39	62.44 $\pm$ 4.79	93.25 $\pm$ 10.06	61.61 $\pm$ 6.19	91.13 $\pm$ 6.39
	$\geq$ 40	55.88 $\pm$ 5.59	84.44 $\pm$ 5.15	55.63 $\pm$ 7.52	82.89 $\pm$ 5.21
	P value	0.030	0.023	0.007	0.009
BMI (kg/m ²)	Normal (18.5-24.9)	60.8 $\pm$ 5.92	92.3 $\pm$ 12.78	63.42 $\pm$ 5.5	96.65 $\pm$ 10.82
	Overweig ht (25-29.9)	63.64 $\pm$ 6.53	98.6 $\pm$ 13.73	62.7 $\pm$ 7.29	94.87 $\pm$ 10.68
	Obese ($\geq$ 30)	58.27 $\pm$ 7.51	89.95 $\pm$ 8.62	62.38 $\pm$ 5.91	88.91 $\pm$ 7.86
	P value	0.006	0.014	0.849	0.025
Parity	Para 0	64.79 $\pm$ 5.67	98.57 $\pm$ 14.85	66.45 $\pm$ 5.26	100.0 $\pm$ 9.63
	Para 1	65.94 $\pm$ 5.41	103.28 $\pm$ 14.55	64.56 $\pm$ 6.96	100.18 $\pm$ 10.46
	Para 2	63.77 $\pm$ 3.87	98.19 $\pm$ 13.51	63.86 $\pm$ 4.33	95.67 $\pm$ 11.13
	Para 3	61.75 $\pm$ 4.09	91.87 $\pm$ 8.21	62.05 $\pm$ 3.41	92.4 $\pm$ 6.81
	Para $\geq$ 4	54.17 $\pm$ 7.63	86.15 $\pm$ 5.42	56.33 $\pm$ 7.99	86.3 $\pm$ 6.6
	P value	<0.001	<0.001	<0.001	<0.001
Infection	Absent	64.32 $\pm$ 4.89	100.7 $\pm$ 12.07	64.66 $\pm$ 6.27	97.44 $\pm$ 9.88
	Present	57.38 $\pm$ 7.67	83.67 $\pm$ 4.76	59.95 $\pm$ 5.96	84.78 $\pm$ 4.97
	P value	<0.001	<0.001	<0.001	<0.001
GA* wk	R	0.236	0.207	-0.154	-0.197
	p	0.018	0.039	0.126	0.049

presence and absence of infection by bacterial vaginosis between group with prelabour rupture of membrane whether term or preterm as the P value 0.137 and 0.657, respectively. Table 5 shows comparism of maternal characteristic and serum zinc between the 4 groups included in the study.

The study show that low level of zinc was more in patient more than 40 years also show that zinc deficiency is more in those with BMI more than 30, significant decrease in the mean Zinc level in women with parity $\geq$ 4 in all subgroups. There is significantly lower level of Zinc in patient with vaginal infection by bacterial vaginosis compared to absence in all subgroup. And gestational age there is a negative correlation between the gestational age and mean serum Zinc in all subgroups

DISCUSSION

In this study evaluation of the correlation of maternal serum Zinc status and prelabour rupture of membranes at preterm and term pregnancy has been under taken, demonstration a significant relationship between ZINC deficiency and prelabour rupture of membranes in both preterm and term pregnant women as Mean $\pm$ SD in Preterm ruptured membrane, in Preterm intact membrane, in term ruptured membrane, in term intact membrane with significant association, and there was no significant

difference between both preterm prom and term promas the mean and SD of preterm prom, and the mean and SD of term prom were virtually the same.

The study of (Bakhshandeh Nosrat Dr, *et al.*, -2005)^[14] they noticed a significant relationship between decreased plasma Zinc and premature rupture of membranes in both term and preterm pregnancies this agreed with current results.

The study of (Muh. Nadir Abdullah, Moh. Fauzi, *et al.*, 2010)^[15] found that pregnant women at term who had prelabour rupture of membranes, had significantly lower serum zinc in comparison to their control group, this finding support our data

Mojgan Rahmanian, (*et al.*, 2014)^[16] found lower serum zinc levels in premature rupture of membranes in the study group more than the control group, but the deficiency was not statistically significant, and this deficiency was physiological, meaning that it is not a cause of prom. this particular result is inconsistent with this study

In this study there was lower serum zinc presenting by the age of 40 in all study groups, but this deficiency is statistically significant as the P value were (0.030, 0.023, 0.007, 0.009) in group

A, B, C, D respectively. but this result is not supported by the result of Kaliki Hymavathi Reddy, (*et al.*, 2015)^[17] who

demonstrate maternal age is of no significance in zinc deficiency

Regarding parity in this study a statistically significant lower zinc values are found by increasing parity in preterm prom, preterm not prom and term prom at a P values <0.001, <0.001, <0.001, <0.001 respectively, and this result is agreed upon by Kaliki Hymavathi Reddy, et..al, 2015, in his study, because of increase Zinc consumption. And in Sikorski R, (et..al, 1990)^[18] who studied the zinc status in premature rupture of membranes at term pregnancy.

This study observed that zinc levels were significantly lower in prelabour ROM. The study of Ian Darnton-Hill, 2013^[19] shows that zinc supplementation reduced the incidence or severity of maternal infections, which are known risk factors for premature birth.

Regarding BMI, there was a significant zinc deficiency in all Study group patients who had high BMI and this result is supported by Rebecca L. Wilson, et...2018^[20] who conclude maternal trace mineral early in pregnancy associated with pregnancy outcome, and there is association between decrease Zinc and increase BMI, and this advocates our finding.

Our study showed that there is significant zinc deficiency, which is consistent with Taiwo Olagoke Dunsin 2016^[21] notice that an increase in BMI resulted in lower ZINC levels.

CONCLUSION

It can conclude that pregnant women with prelabour rupture of membranes whether term or preterm tend to have lower Zinc level. Also, increasing maternal age, increasing parity, high BMI, and vaginal infection are associated with low Zinc level.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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