

Maternal Serum Zinc Level Is An Independent Factor For Infant Birth Weight, But Not For Preterm Delivery

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OBJECTIVE: To compare the maternal zinc levels in patients suffering from preterm delivery and women with term pregnancies and to assess the effect of maternal serum zinc levels on birth weight.

STUDY DESIGN: 50 preterm laboring pregnant women (mean age 23.92 ± 5.17 years) and 20 term pregnant women (mean age 26.40 ± 4.98 years) were enrolled. Serum zinc levels were measured with "flame atomic absorption technique". Gestational age, birth weight, Apgar scores of the first and fifth minutes, socioeconomic status and smoking habits were evaluated.

RESULTS: The mean value of serum zinc levels was 1.10 ± 0.23 µg/ml in the control group and 0.35 ± 0.10 µg/ml in the preterm group. Birth weight, Apgar scores of the first and fifth minutes, gestational ages and serum zinc levels were found to be significantly lower in preterm group ($p < 0.001$). Maternal serum zinc level was found to be correlated with gestational age and birth weight; however, the correlation of zinc with gestational age disappeared when regression analysis was applied and zinc was found to be an independent factor affecting birth weight. Zinc levels less than 1 µg/ml had a sensitivity of 100%, specificity of 70%, positive predictive value of 89.9% and negative predictive value of 100% for preterm labor in this study.

CONCLUSION: Maternal serum zinc level is linearly correlated with birth weight and tends to be lower in preterm deliveries, although not an independent factor.

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Key Words: Preterm delivery, Serum zinc levels, Gestational age, Birth weight

Preterm labor and delivery have been important causes of perinatal morbidity and mortality for a long time. Despite the developments in obstetrics; preterm birth constitutes approximately 10% of whole births^{1, 2} and is associated with 75% of perinatal morbidity and mortality for infants born without congenital anomalies.³

Significant improvements in survival rates for all preterm infants have been documented for the past 40 years, and have been especially important for infants born before 28 weeks; however, there is still a significant risk for mental, neurological and respiratory sequels in very preterm infants.^{4, 5} For this reason, prevention and delaying of preterm delivery have priority for obstetricians and perinatologists

Low maternal plasma or serum zinc concentrations have been reported to be associated with preterm labor and some adverse pregnancy outcomes such as abnormalities of labor, atonic bleeding and congenital malformations.⁶ A low intake of dietary zinc is suggested to be associated with an approximately twofold increase in risk of infant low birth weight and preterm delivery and a greater than threefold increase in risk of very preterm delivery.⁷ However, other trials have been unable to predict any abnormal pregnancy outcome on

the basis of serum zinc concentrations.⁸

The aim of the present study was to compare the maternal zinc levels in patients suffering from preterm delivery and women with term pregnancies and to assess the effect of maternal serum zinc levels on birth weight.

Materials and Methods

Fifty pregnant women admitted with the diagnosis of preterm labor and delivered and 20 normal term pregnant women who also delivered in the perinatology department of Dr. Zekai Tahir Burak Woman Health Training and Research Hospital between May 1999 and June 1999 and who were eligible were enrolled in this study. Women with preterm rupture of membranes, preeclampsia, abruptio placentae, placenta previa, multiple gestation, excessive or inadequate amniotic fluid volume, anomalous fetus, uterine anomaly, diabetes mellitus, asthma, drug abuse and pyelonephritis were excluded. Pregnant women whom their gestational ages were between 20-37 weeks, who had at least 3 contractions in 20 minutes according to non-stress test and who had at least 2 cm of dilatation and 80% of effacement were diagnosed as preterm labor. Ultrasonography was used to confirm the gestational age. Patients who did not deliver were excluded. The serum was collected before the administration of tocolytic agents. Pregnant women in the control group had gestational ages of 37 weeks and over, had at least 2 cm of dilatation and 80% effacement.

While choosing the patients in the study and control groups, attention was paid for them to have similar feeding habits and socio-economic status. Socio-economic status was based on the monthly income of the families.

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Table 1. Comparison of Control and Preterm Delivery Groups

	CONTROL (n=20)	PRETERM (n=50)	t
	X±SD	X±SD	
Age (year)	26.40±4.98	23.92±5.17	p>0.05
Birth weight (g)	3269.50±211.12	1940.00±593.60	p<0.001
Apgar (first minute)	7.00±0.00	5.26±1.55	p<0.001
Apgar (fifth minute)	9.00±0.00	7.26±1.75	p<0.001
Gestational age (weeks)	38.20±1.11	31.61±3.35	p<0.001
Zinc (µg/ml)	1.10±0.23	0.35±0.10	p<0.001
Gravidity	1.65±0.67	1.8±1.12	p>0.05
Parity	0.65±0.67	0.56±0.81	p>0.05

t: Student's t-test for independent samples

Table 2. Comparison of mean zinc levels between extremely preterm, very preterm, preterm and term labors

	<28 weeks of gestation (n:9)	28-32 weeks of gestation (n:15)	32-37 weeks of gestation (n:26)	>37 weeks of gestation (n:20)
Zinc level (mean±SD)	0.33±1.32 ^a	0.32±0.10 ^b	0.36±0.10 ^c	1.10±0.37 ^d

Table 3. Correlation of zinc with other parameters

	Preterm Group n:50		Term Group n:20		Overall n:70	
	r	p	r	p	r	p
Birth weight	0.104	0.472	0.095	0.690	0.722	<0.0001*
Apgar 1st minute	-0.079	0.587	-0.205	0.387	-0.079	0.587
Apgar 5th minute	-0.034	0.815	-0.263	0.263	-0.034	0.815
Gestational week	0.030	0.836	0.204	0.389	0.679	<0.0001*
Maternal age	0.241	0.092	0.204	0.389	0.211	0.079
Smoking	-0.236	0.099	-0.177	0.456	-0.194	0.107
Socioeconomic status	0.230	0.109	-0.281	0.230	0.103	0.398
Gravidity	-0.127	0.380	-0.258	0.272	-0.127	0.380
Parity	-0.257	0.072	-0.258	0.272	-0.257	0.072

*: statistically significant

10 cc of peripheral venous blood was collected from each case and put in plain biochemistry tubes. Then they were centrifuged with 3000 rpm for 5 minutes to separate the serum. The serum was kept in deep freeze of -25° C until the analysis time.

Samples were analyzed in "Gulhane Military Medical Academy, Faculty of Pharmacology, Toxicology Department". Measurements were performed with double-beam atomic absorption spectrophotometer system and serum zinc levels were measured by "flame atomic absorption technique". 213.9 nanometers of wave length was used. Serum was diluted with 1% of nitric acid in appropriate conditions and each sample was measured two times with straight calibration. Air-acetylene was used for the gas medium. Every dilution was done with bidistilled deionized water. Every chemical that was used had analytic purity. Polypropylene tubes were original and used only once. The laboratory cut-

off value for serum zinc level was 1 µg/ml. the study was approved by the institution's ethical committee and all patients gave informed consent to the study.

Statistical Analysis

SPSS for Windows Release 11.01 Program was used for statistical analysis of the data. Student's t-test and Man Whitney U tests were used to compare the parameters between the groups. Pearson's correlation analysis and regression analysis were applied in order to determine the correlation of zinc with other parameters and to determine the factors that were independently affecting the birth weight and duration of pregnancy respectively. A p value less than 0.05 was assumed to be significant. To compare zinc levels in extremely preterm, very preterm, preterm and term groups Kruskal-Wallis and Man Whitney U tests were used. For this analysis level of significance was set at 0.0167.

Results

When the ages, gravidity and parity of the control and preterm groups were compared, no significant differences were found ($p=0.145$). Comparison with regard to smoking and socioeconomic status also yielded no significant difference between groups with p values of 0.381 and 0.327 respectively. Birth weight, Apgar scores of first and fifth minutes, gestational age and maternal serum zinc levels were found significantly lower in the preterm group ($p<0.001$) (Table 1).

Comparison of mean zinc levels between extremely preterm, very preterm, preterm and term labors were depicted in Table 2. The extremely preterm, very preterm and preterm groups did not differ with regard to zinc levels; however, all these three groups were found to have significantly lower serum zinc levels when compared with the term pregnancies (Table 2).

Table 3 shows the correlation of zinc with other parameters. In correlation analysis zinc was found to be associated with birth weight and gestational age. In order to determine the exact effect of zinc on these parameters, regression analysis was applied. In regression analysis, zinc was found to be an independent factor for birth weight ($\beta=0.207$, $p=0.004$); however, it was not an independent determining factor for gestational age ($\beta=0.118$, $p=0.118$).

All the patients in the preterm group had zinc levels below the cut-off value $1 \mu\text{g/ml}$. In the control term group 6 patients had zinc levels below $1 \mu\text{g/ml}$, so zinc level was found to have a sensitivity of 100%, specificity of 70%, positive predictive value of 89.9% and negative predictive value of 100% for preterm labor in this study.

Discussion

Today it is well known that the role of micronutrients is vital for cell growth and differentiation⁹ and zinc is one of these vital elements. Approximately 300 enzymes need zinc for their activities. Zinc is needed for DNA synthesis, cell division and protein synthesis.¹⁰ Hundreds of different nucleoproteins containing zinc play role in gene expressions of some proteins.¹⁰ It is an important co-factor of the major enzymes in collagen synthesis.¹¹ All nuclear receptors of steroids contain zinc.¹² Zinc deficiency affects the proliferation and maturation of lymphocytes negatively which are important for immunity¹⁰ and has negative effect on androgen, estrogen, progesterone, prostaglandin metabolisms and male fertility.¹² Zinc deficiency is also suggested to cause spontaneous abortion, preeclampsia, intrauterine growth retardation¹² and that low maternal zinc levels play an important role in preterm labor etiology.^{7, 13-19}

Controversy on zinc to be an etiologic factor for preterm births still exists as different researchers reported different results. In this study zinc was found to be significantly lower

in patients suffering from preterm delivery when compared with patients that delivered at term. It was found to be correlated with gestational age at delivery and birth weight; however, it was not an independent factor for preterm birth alone. On the other hand maternal serum zinc level was found to be linearly associated with birth weight and an independent factor that could be relied on to increase birth weight of the infant.

Scholl et al. indicated that low zinc intake in early pregnancy increases very preterm delivery (smaller than 33 weeks) three folds.⁷ Prasad and his colleagues also reported parallel results.¹⁰ In a study, performed by Garg et al., 200 mg zinc sulfate (45 mg of elemental zinc) was given to 106 pregnant in different trimesters since their pregnancies were confirmed, while no zinc supplementation was given to 62 control group pregnant. As a result, it has been found that the zinc supplemented group (especially longer than three months) had higher gestational ages at birth.²⁰ Cherry et al. also reported a lower rate of preterm delivery in zinc supplemented women with normal body weight at delivery and a longer gestation duration in zinc-supplemented multiparas.²¹ However, many other trials did not demonstrate a preventive effect of zinc supplementation on preterm delivery.^{6, 22, 23} In the present study we also found that maternal serum zinc level does not affect gestational age at delivery.

In their study, using plasma zinc to indicate zinc status, Negggers et al.¹⁵ reported that maternal serum zinc was significantly related to birth weight after various independent determinants of birth weight were controlled for and suggested that maternal serum zinc concentration measured early in pregnancy could be used to identify those women at higher risk of giving birth to a low-birth-weight infant.¹⁵ The same investigator reported that serum zinc concentrations measured at approximately 16 (early) and 32 weeks (later) in gestation were both found to be significant predictors of birth weight.¹⁴ In their study they showed that even after controlling for gestational age at birth and other determinants of birth weight, for each microgram/dl increase in serum zinc early and later in pregnancy, birth weight increased by 5.8 and 8.6 g, respectively.¹⁴ Goldenberg et al. in their zinc supplementation study, showed statistically significant birth weight increases in infants of women with body mass index less than 26 kg/m^2 although there were no statistically significant differences in preterm deliveries (defined as <37 or <33 weeks) between supplemented and non-supplemented groups.²⁴ The results of these studies are parallel to our findings. On the other hand results of 8 trials, from published and unpublished studies were summarized in a recent study²⁵ and no effect of maternal zinc supplementation during pregnancy on birth size was found except for a small reduction in low birth weight incidence in Chile.²⁶

In addition, zinc levels less than $1 \mu\text{g/ml}$ were found to have high sensitivity, specificity, positive predictive and ne-

gative predictive values for preterm delivery in this study. Although not an independently affecting factor, zinc level determination may be used to predict which patients are under risk of preterm delivery. However, larger series are needed to clarify this issue.

As mentioned before results are very contradictory. One of the main reasons for these contradictions may be the way that the zinc is measured as zinc concentrations can be measured in different ways. In this study flame atomic absorption technique was used to measure serum zinc levels. Another reason may be related to the insensitivity of plasma zinc values.²³

Today the public health justification for including zinc as an antenatal supplement to improve birth weight remains unclear and there is no consensus all around the world about the amount of zinc supplementation needed.²⁷

In conclusion trials on assessment of any association between zinc and preterm birth and birth weight show mixed results. In the present study zinc was found to be linearly related to infant birth weight and tend to be significantly lower in patients suffering from preterm deliveries. Measurement of maternal serum zinc levels may be beneficial in prediction of patients that are under risk of preterm delivery.

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