RESEARCH ARTICLE

A multilateral investigation of the effects of zinc level on pregnancy

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Background: The relationship between maternal zinc level and birth weight, birth week, delivery type, gestation, maternal age, etc., contribute to diagnosis and clinical follow-up.

Method: Multivariate investigated for data of 275 patients were obtained during their pregnancy periods until birth. 3 cc blood samples were centrifuged for 15 minutes at 2500 g within a period of 30 minutes and were stored at -80°C until the time of analysis. The zinc levels of the patients were found to be within the range of 49–129 $\mu\text{g/dL}$. Patients were divided into 8 groups according to their zinc levels (49–59, 60–69, ..., 120–129) and the relationships of zinc level with the parameters related to the mode of delivery, week of delivery, birth weight, age, early membrane rupture, live-stillbirth, and gravid were statistically analyzed to determine differences between the groups.

Results: There was a significant difference between the live births and stillbirths with a 95% confidence level regarding the zinc level. The zinc level affected the live-stillbirth status; patients with a zinc level of 49–59 $\mu\text{g/dL}$ had stillbirths, the live birth rate for 59–69 $\mu\text{g/dL}$ was approximately 50%, whereas it was approximately 88% for in the patients with a zinc level of 109–119 $\mu\text{g/dL}$. All patients with a zinc level of 119 $\mu\text{g/dL}$ and above had live births.

Conclusion: Based on the results of this study, it is suggested that zinc supplementation may be an appropriate treatment for the pregnant women with low zinc levels to provide the realization of live births.

KEYWORDS

early membrane rupture, pregnancy, small for gestational age, zinc

1 | INTRODUCTION

Zinc is an important enzyme involved in the realization of biological events. It is a necessary mineral for maintenance and repair of cells. Activation of the enzyme is needed for the regulation of gene expression and cell renewal.¹ Zinc has a role in the functioning of more than 200 metalloenzymes, in carbohydrate and protein metabolism, in nucleic acid synthesis, and antioxidant functions.² Severe zinc deficiency causes impaired body growth, deficiencies in sexual and bone maturation together with impaired immune system. Severe zinc deficiency develops

slowly. Acute deficiency is largely preventable by providing adequate zinc intake.³ Insufficient vitamin and mineral intake during pregnancy may lead to clinical or subclinical effects, anemia, hypertension, labor complications, and even death in the fetus and the mother.⁴ In the fetus, it may also lead to abortions, preterm delivery, IUGR (intrauterine growth retardation), congenital malformation, deterioration of the immune system, and abnormal organ development.⁵ Zinc is essential for normal fetal growth and development.⁶ Zinc intake is highly important during pregnancy, when cell production is extremely rapid.⁷ Pregnant women are vulnerable to low zinc state due to their additional zinc requirements

TABLE 1 Descriptive statistics for live-stillbirth status according to zinc levels

Parameters	Live-stillbirth results			Sig.
	Live birth	Stillbirth	No delivery	
$49 \leq x < 59$	6	1	6	0.42
$59 \leq x < 69$	22	4	6	0.49
$69 \leq x < 79$	39	1	11	0.378
$79 \leq x < 89$	49	4	10	0.481
$89 \leq x < 99$	41	2	10	0.403
$99 \leq x < 109$	38	0	4	0.688
$109 \leq x < 119$	16	0	1	0.996
$119 \leq x < 129$	4	0	0	
Total	215	12	48	

associated with pregnancy, fetal growth, and development; late pregnancy is the period when zinc is most needed.⁸ While the daily zinc requirement in non-pregnant women in the United States is 8 mg, it is recommended to be increased to 11 mg during pregnancy.⁹ Most of the zinc taken with food accumulates in the fetus and the uterus. Various studies have shown that there is no significant difference in maternal zinc absorption when compared to non-pregnant women.¹⁰ Investigators have found that zinc deficiency in the early pregnancy period resulted in miscarriage, preterm birth, and neural tube defects.¹¹

In this study, which multilaterally investigated the effects of zinc level on pregnancy, pregnant women were grouped into 8 groups according to their zinc levels, from the lowest zinc level to the highest, ranging from 49 to 129 in 10-unit increments. The delivery methods, delivery weeks, birth weights, ages, early membrane ruptures (EMRs), live-stillbirth ratios, and gravidas of each group were determined; the interactions between zinc levels and these parameters were investigated; the clinical conditions that could be caused by zinc deficiency were determined, and suggestions were made.

2 | METHODS

In this study, which was carried out to multilaterally investigate the effects of zinc level on pregnancy, 326 patients, who were admitted to Ankara Yenimahalle Training and Research Hospital between October 2015 and October 2016 and who were in the 12th week of pregnancy or earlier, were included. Patients who had systemic diseases and multiple pregnancies were excluded from this study to reduce the number of factors that may affect the results of the study. 3 cc blood samples were taken from the volunteering patients who had read and signed the informed consent form to participate in the study; the samples were then taken into biochemical tubes and centrifuged for 15 minutes at 2500 g within the period of 30 minutes following the blood collection. Blood samples were stored at -80°C until the time of analysis. Data from 275 patients were obtained during their pregnancy period until birth. The zinc levels of the patients were determined by "thermo atomic absorption spectrophotometer" method, and were

found to be in a range from 49 to 129 $\mu\text{g/dL}$. Serums were diluted to 1/5 and worked. The normal range of zinc was 70-115 $\mu\text{g/dL}$. The test range was 15-250 $\mu\text{g/dL}$. The lower limit of detectable zinc level was 10 $\mu\text{g/dL}$. The investigated parameter of zinc level was evaluated in 8 groups in 10-unit increments as follows: 49-59, 60-69, 70-79, 80-89, 90-99, 100-109, 110-119, and 120-129 $\mu\text{g/dL}$. Delivery methods were categorized as abortion, normal birth, and cesarean section, history of the previous cesarean section, ectopic pregnancy, and intentional termination of pregnancy. Delivery weeks were categorized as abortion, on 24-37th weeks, on or before 37 and 41 weeks, over 41 weeks, and ectopic pregnancy. Birth weights were categorized as abortion, 2500 g and below, 2500-4000 g, 4000 g and above, ectopic pregnancy, and intentional termination of pregnancy. EMR was categorized as present and absent. Birth status was categorized as a live birth, stillbirth, and no birth. Gravid was categorized into 3 groups as 1, 2-3, 4, and over. The no birth group consisted of cases of abortion, intentional termination of pregnancy, and ectopic pregnancy.

The data of the patients involved in the study were evaluated in 8 groups according to their zinc levels. The data which was obtained from the patients for this purpose were converted into tables according to their zinc levels. The obtained data were analyzed by the SPSS 16 software package; descriptive statistics were determined, multiple comparison tests for the evaluated parameters were performed between the groups according to the zinc levels, and the significance levels with a confidence level of 95% were tested by multivariate analysis of variance (MANOVA) and were evaluated in different groups. The average age of the patients was found to be 28.3 ± 0.28 . The average level of zinc was found to be 86.4 ± 0.87 $\mu\text{g/dL}$. When the low threshold value for zinc was considered as 60 $\mu\text{g/dL}$, zinc deficiency rate in the study group was found to be 4.6%.

The results of the patient data analyzed in 8 groups according to the zinc level in terms of live-stillbirth, delivery method, delivery week, birth weight, age, EMR, and gravid were presented below. The analysis of the tabulated data can suggest that the live-stillbirth patterns differ according to the zinc level. Multivariate analysis of variance (MANOVA) analysis was used to determine whether there was a significant relationship between the patient zinc level and the live-stillbirth status among the 8 different zinc groups and the results were shown below. It was analyzed whether the delivery method changed according to the zinc level and the significance values were found to be greater than 0.05 with a confidence level of 95% in all groups; therefore it was concluded that there was no significant difference between the groups regarding the delivery methods, gestational week of delivery, birth weight, with respect to EMR, with respect to gravid, and with respect to the patient age (sig. > 0.05).

3 | RESULTS

3.1 | The effect of zinc level on live-stillbirth

Data analysis was performed in 8 sub-groups regarding zinc level with a range of 49-129 $\mu\text{g/dL}$ and for 3 sub-groups regarding live-stillbirth; the results were presented in tables (Table 1).

TABLE 2 Descriptive statistics for delivery methods according to zinc levels

Parameters	Delivery method							Sig.
	Abortion	Vaginal delivery	Section	Have a cesarean before	Ectopic	Terminated	Total	
$49 \leq x < 59$	4	3	3	1	0	2	13	0.900
$59 \leq x < 69$	3	17	3	5	1	3	32	0.686
$69 \leq x < 79$	9	25	7	7	0	3	51	0.600
$79 \leq x < 89$	9	31	10	12	0	1	63	0.695
$89 \leq x < 99$	7	26	9	8	1	2	53	0.671
$99 \leq x < 109$	2	19	9	10	1	1	42	0.762
$109 \leq x < 119$	1	6	4	6	0	0	17	0.579
$119 \leq x < 129$	0	2	2	0	0	0	4	
Total	35	129	47	49	3	12	275	

It was analyzed whether the live-stillbirth status changed according to the zinc level. A significant difference, with a signification value greater than 0.042, and with the confidence level of 95% was found only in the 1st group in which the zinc level range was $49 \leq x < 59$. The signification value was greater than 0.05 in the other groups, and there was no significant relation.

3.2 | The effect of the zinc level on delivery method

Data analysis was performed for 8 sub-groups of zinc level in the range of 49-129 $\mu\text{g/dL}$ and for 6 sub-groups of delivery methods, and results were presented in tables (Table 2).

3.3 | The effects of zinc level on the gestational week of delivery

With the aim of investigating the relationship between zinc level and the gestational week of delivery, the descriptive analysis of gestational week of delivery according to zinc level was presented below (Table 3).

3.4 | The effect of zinc level on birth weight

With the aim of investigating the relationship between zinc level and birth weight, the descriptive analysis of birth weight according to the zinc level was presented below (Table 4).

3.5 | The effect of zinc level on EMR

With the aim of investigating the relationship between zinc level and EMR, the descriptive analysis of EMR with respect to zinc level was presented below (Table 5).

3.6 | The effect of zinc level on gravid

With the aim of investigating the relationship between zinc level and gravid, the descriptive analyzes of gravid with respect to zinc level were presented below (Table 6).

3.7 | The interaction of zinc level with age

With the aim of investigating the relationship between zinc level and the age of the patient, the descriptive analysis of the patient age with respect to zinc level was presented below (Table 7).

4 | DISCUSSION

Most of the studies on zinc use during pregnancy were not well-designed, and the study groups were small; therefore, their results were not very clear, and they could merely provide recommendations.¹²

Previous studies conducted on the effects of zinc level on pregnant women have emphasized the importance of the zinc level, and zinc supplementation has been suggested in patients when required. In the study, of a total of 275 pregnant women, 215 of them had a live birth, 12 of them had a stillbirth, and 48 of them did not have birth. Regarding the delivery method, 35 of them had an abortion, 129 of them had a normal birth, 47 of them had a cesarean section, 49 of them had a history of the previous cesarean section, 3 of them were diagnosed with ectopic pregnancy, and 12 had their pregnancies intentionally terminated. Zinc deficiency rate was 4.6% in the first trimester of pregnancy.

In this study; 9 (75%) of 12 stillbirth patients were in the 24-37th week of pregnancy, whereas 3 (25%) of them were past the 41st week of their pregnancy; however, no stillbirths were found in term pregnancies. 10 (83.3%) of the stillbirth patients were found to have a birth weight of 2500 g or less, and EMR was found in only 2 of the patients.

In a study conducted in the year 2000, it was reported that maternal age, gestational weight, parity, and gravida had minor roles in the zinc level in pregnancy.¹³

In our study, we also did not find any significant relationship between birth weight and zinc level. In 2 studies conducted on 415 pregnant women in Gaziantep, one of the cities in our country, no changes in zinc levels were found during pregnancy.¹⁴

In our study, no baby with an anomaly was identified.

TABLE 3 Descriptive statistics for gestational week of delivery according to zinc level

Parameters	Gestational week of delivery						Total	Sig.
	Abortion	24-37 wk	Between 37 and 41 wk	41 wk and over	Ectopic	Terminated		
49 ≤ x < 59	4	3	1	3	0	2	13	0.786
59 ≤ x < 69	3	7	15	3	1	3	32	0.945
69 ≤ x < 79	9	9	26	4	0	3	51	0.819
79 ≤ x < 89	9	12	30	11	0	1	63	0.979
89 ≤ x < 99	7	13	23	7	1	2	53	0.667
99 ≤ x < 109	3	10	20	7	1	1	42	0.525
109 ≤ x < 119	2	5	9	1	0	0	17	0.302
119 ≤ x < 129	0	1	3	0	0	0	4	
Total	37	60	127	36	3	12	275	

TABLE 4 Descriptive statistics for birth weight according to zinc level

Parameters	Birth weight						Total	Sig.
	Abortion	2500 g and below	2500-4000 g	4000 g and over	Ectopic	Terminated		
49 ≤ x < 59	4	2	5	0	0	2	13	0.985
59 ≤ x < 69	3	5	19	1	1	3	32	0.637
69 ≤ x < 79	9	5	30	4	0	3	51	0.581
79 ≤ x < 89	9	7	42	4	0	1	63	0.847
89 ≤ x < 99	7	4	34	5	1	2	53	0.469
99 ≤ x < 109	2	1	33	4	1	1	42	0.374
109 ≤ x < 119	1	3	11	2	0	0	17	0.645
119 ≤ x < 129	0	1	3	0	0	0	4	
Total	35	28	177	20	3	12	275	

TABLE 5 The Descriptive statistics for EMR according to zinc level

Parameters	EMR		Total	Sig.
	(+)	(-)		
49 ≤ x < 59	12	1	13	0.819
59 ≤ x < 69	26	6	32	0.859
69 ≤ x < 79	43	8	51	0.933
79 ≤ x < 89	55	8	63	0.785
89 ≤ x < 99	47	6	53	0.675
99 ≤ x < 109	38	4	42	0.571
109 ≤ x < 119	15	2	17	0.470
119 ≤ x < 129	3	1	4	
Total	239	36	275	

EMR, early membrane rupture.

When the effect of the zinc level on live-stillbirth status was evaluated, it was found that patients with a zinc level of 49-59 µg/dL had stillbirths. The live birth rate was 50% in the patients with a zinc level of 59-69 µg/dL, 55% in the patients with a zinc level of 69-79 µg/dL,

TABLE 6 Descriptive statistics for gravid with respect to zinc level

Parameters	Gravid			Total	Sig.
	1	2 and 3	4 and over		
49 ≤ x < 59	5	6	2	13	0.659
59 ≤ x < 69	12	14	6	32	0.320
69 ≤ x < 79	14	30	7	51	0.171
79 ≤ x < 89	17	42	4	63	0.302
89 ≤ x < 99	18	32	3	53	0.320
99 ≤ x < 109	11	30	1	42	0.501
109 ≤ x < 119	8	7	2	17	0.652
119 ≤ x < 129	3	1	0	4	
Total	88	162	25	275	

60% in the patients with a zinc level between 79-89 µg/dL and 89-99 µg/dL, 81% in the patients with a zinc level of 99-109 µg/dL, and 88% in the patients with a zinc level of 109-119 µg/dL, approximately. All of the patients with a zinc level of 119 µg/dL and above had live births.

TABLE 7 Descriptive statistics for the patient according to zinc level

Zinc range	Values about the age of the patients				Sig.
	Count patient	Average	Minimum	Maximum	
$49 \leq x < 59$	13	28,92	19	37	0.408
$59 \leq x < 69$	32	27,94	19	37	0.574
$69 \leq x < 79$	51	27,94	19	37	0.817
$79 \leq x < 89$	63	28,52	19	39	0.580
$89 \leq x < 99$	53	27,23	18	37	0.890
$99 \leq x < 109$	42	29,59	21	38	0.308
$109 \leq x < 119$	17	29,0	19	37	0.474
$119 \leq x < 129$	4	25,5	23	30	
Total	275				

Even though mathematical differences were determined regarding zinc levels between the delivery methods, gestational weeks of delivery, birth weights, EMRs, gravidas, and ages of the patients in the groups (8 groups), and these differences were not found to be statistically significant.

Based on the results of the statistical analyzes obtained in this study, it is suggested that zinc supplementation may be an appropriate treatment for the pregnant women with low zinc levels to provide the realization of live births.

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How to cite this article: Özgan Çelikel Ö, Doğan Ö, Aksoy N. A multilateral investigation of the effects of zinc level on pregnancy. *J Clin Lab Anal*. 2018;32:e22398. <https://doi.org/10.1002/jcla.22398>