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Relationship between Zinc Concentration of Amniotic Fluid and Maternal Plasma and Adverse Pregnancy Outcomes

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ABSTRACT

Background and Objective: Zinc deficiency has been suggested as a risk factor for adverse pregnancy outcomes. Since dealing with zinc deficiency is an easy and inexpensive method, this study was conducted with the aim of investigating the relationship between adverse pregnancy outcomes and zinc concentration of amniotic fluid and maternal plasma in the second trimester and biomarkers of the first and second trimester.

Methods: This cross-sectional study was conducted on 102 pregnant mothers who were candidates for amniocentesis in Mousavi Hospital in Zanjan in 2018 through convenience sampling. Women with normal amniocentesis results were followed up until delivery in terms of adverse pregnancy outcomes (incidence of preeclampsia, intrauterine growth retardation, premature delivery, fetal death, and low birth weight) and were divided into two groups with adverse pregnancy outcomes (first group) and without adverse pregnancy outcomes (second group) and were compared in terms of zinc concentration in plasma and amniotic fluid.

Findings: The concentration of zinc in the plasma of the mothers of the first group (59.53±15.88 µg/dl) was significantly lower than that of the mothers of the second group (71.44±19.25 µg/dl) (p=0.02). However, there was no significant difference in the concentration of zinc in the amniotic fluid of the two study groups. In this study, the best cutoff point to determine people at risk of adverse pregnancy outcomes was determined to be 60.5 µg/dl.

Conclusion: Based on the results of this study, there seems to be a relationship between low zinc concentration of plasma in pregnant women and adverse outcomes.

Keywords: *Zinc, Amniocentesis, Plasma, Pregnancy Outcome, Premature Delivery, Low Birth Weight, Preeclampsia, Intrauterine Growth Retardation, Intrauterine Death*.

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Introduction

Zinc is an essential element for vital body functions including protein synthesis, cell division, and nucleic acid metabolism (1). Although severe zinc deficiency is rare in the words, mild to moderate zinc deficiency is common in pregnant and lactating women in different geographical areas (2-4). Zinc deficiency during pregnancy is a global public health problem, and it is estimated that more than 80% of pregnant women in the world do not have adequate zinc intake (1).

Zinc also plays a key role during the development of the fetus, the growth and development of the baby, and the function of the mammary gland for the synthesis and secretion of breast milk. Zinc deficiency during pregnancy and breastfeeding has harmful effects on pregnancy outcomes (5, 6). Several studies have reported multiple fetal abnormalities, fetal or neonatal death, infant growth retardation, and congenital complications during pregnancy and childbirth in connection with zinc deficiency. Although severe zinc deficiency is rare in the worlds, mild to moderate zinc deficiency is common in pregnant and lactating women in different geographic regions (4-6). Zinc deficiency during pregnancy is a global public health problem, and it is estimated that more than 80% of pregnant women in the world do not have adequate zinc intake (1).

Adverse fetal and maternal outcomes caused by zinc deficiency have been proven in animal studies, but regarding the relationship between zinc levels and fetal, neonatal, and maternal outcomes in humans, the results of studies have been contradictory (7-11). Keshavarz et al. have reported a statistically significant relationship between the decrease in plasma zinc and the incidence of preeclampsia (7). However, Wibowo et al., Gul et al. did not observe a significant relationship between these two variables (8, 9). In a study by Wang et al., a significant relationship between preterm birth and low zinc concentration of plasma in pregnant women was reported (10), while in a study by Rahman et al., this was rejected (11).

As mentioned, several studies have investigated the relationship between zinc deficiency in plasma and the occurrence of preeclampsia, but the relationship between zinc in serum and amniotic fluid on other pregnancy outcomes has been less addressed. Therefore, the present study was conducted with the aim of investigating the relationship between pregnancy outcomes and zinc levels in amniotic fluid and maternal plasma in the second trimester and the biomarkers of the first and second trimesters.

Methods

After approval by the ethics committee of Zanjan University of Medical Sciences with ethics code IR.ZUMS.REC.1396.319, this cross-sectional study was conducted on 102 pregnant women who were candidates for amniocentesis and referred to the perinatology clinic of Zanjan in 2018. To choose the samples, all women who referred for amniocentesis (referral due to abnormal screening results of the first and second trimesters) from March 2018 till August 2018 were included in the study based on convenience sampling. Inclusion criteria were being in week 12 to 25 of pregnancy, normal amniocentesis result, age between 18 and 35 years, no history of premature birth, preeclampsia and gestational diabetes, no diabetes in current pregnancy and body mass index of 18.6 to 30. The exclusion criteria were unwillingness to continue cooperation.

The following information was collected and recorded in a checklist: items related to evaluation of zinc levels in plasma and amniotic fluid, adverse pregnancy outcomes including pre-eclampsia, intrauterine growth restriction (IUGR), preterm labor (PTL), intrauterine fetal demise (IUFD), and low birth weight (LBW), as well as participants' features such as age and body mass index.

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After explaining the implementation method and objectives of the study to the participants and ensuring them of the confidentiality of their information, a written consent for cooperation was obtained from them. The participants in this study were women who were referred for amniocentesis due to the abnormal results of the first and second trimester screenings. In these cases, according to the laboratory instructions, 1 cc of amniotic fluid sample obtained from amniocentesis and 1 cc of mother's blood sample were prepared. In this study, in order to comply with the ethical standards, no extra amount was prepared (exceeding the routine amount) and the researcher used the same sample of the amniocentesis test to perform the supplementary tests. In order to evaluate the concertation of zinc in blood and amniotic fluid, the samples that were collected during 6 months were sent to a specialized laboratory.

After announcing the results of amniocentesis, only mothers whose test results were reported as normal remained in the study and were followed up until delivery. A gynecologist and obstetrician took care of them until delivery and examined them for pre-eclampsia and premature birth, and recorded the birth weight of the baby after delivery. Finally, the participants were divided into two groups: the first group, mothers with adverse pregnancy outcomes, and the second group, mothers without adverse pregnancy outcomes. To analyze the data, descriptive statistics and t-test were used in SPSS 16. In order to evaluate the predictive power of plasma zinc level for the occurrence of adverse pregnancy outcomes, ROC curve was drawn and $p<0.05$ was considered significant.

Results

Based on the results of amniocentesis, 120 pregnant mothers were finally included in the study. According to the evaluations, 15 mothers had adverse pregnancy outcomes (group 1) and 78 had no adverse pregnancy outcomes (group 2), 27 were excluded due to not meeting the inclusion criteria. In the first group, the mean age of the mothers was 28.73±4.72, in the second group it was reported to be 28.77±4.71 years, and no statistically significant difference was observed between the two groups. Furthermore, in terms of body mass index, the participants in the two groups (first group 25.23±3.98 and second group 23.85±3.48) had no significant difference.

According to laboratory findings, blood plasma zinc in the group of mothers with adverse pregnancy outcomes (premature delivery, preeclampsia, and low birth weight) was significantly lower than that of mothers in the second group (p=0.02). However, there was no statistically significant difference in amniotic fluid zinc content in the two groups (Table 1). The evaluation of the screening power of zinc value is shown with the help of ROC curve (ROC=Receiver Operating Characteristics) (Figure 1). In this study, the best cutoff point to determine people at risk of adverse pregnancy outcomes was determined to be 60.5.

Table 1. Comparison of the mean concertation of zinc in amniotic fluid and blood plasma regarding adverse pregnancy outcomes in the two groups

Variable	Without adverse pregnancy outcome Mean±SD	With adverse pregnancy outcome Mean±SD	p-value
Level of zinc in blood plasma (µg/dl)	71.44±19.25	59.53±15.88	0.02*
Level of zinc in amniotic fluid (µg/dl)	20.66±12.22	22.20±14.19	0.96

***p<0.05**

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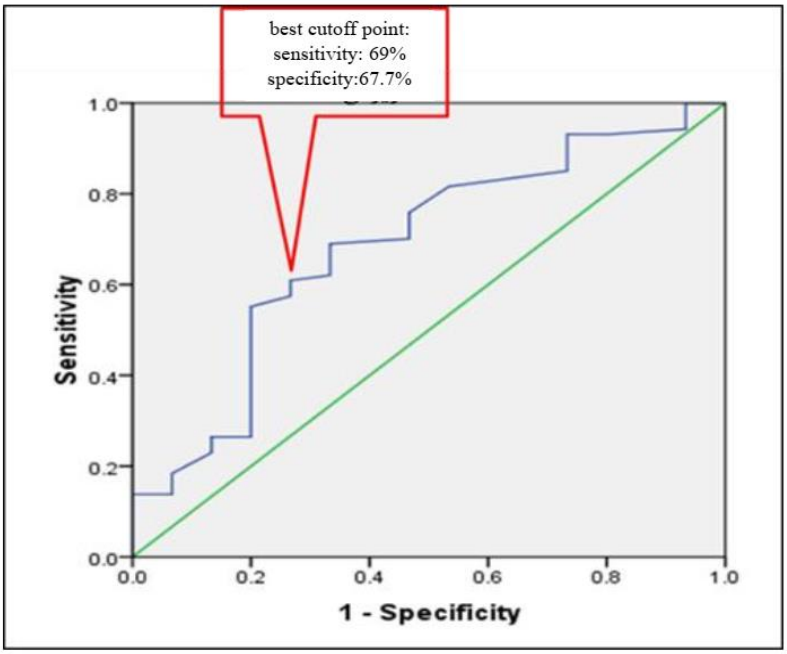

Figure 1. The ability of plasma zinc level to predict the occurrence of adverse pregnancy outcomes

Discussion

In the present study, the level of zinc in the blood plasma of mothers with adverse pregnancy outcomes was significantly lower than that of mothers without pregnancy outcomes, while no statistically significant relationship was observed between the level of zinc in amniotic fluid and pregnancy outcomes. Other studies, in line with the results of this study, have shown the relationship between plasma and various pregnancy outcomes (10, 12-14). In their study, Wang et al. showed that there is an inverse relationship between the concentration of zinc in the plasma of pregnant mothers and the increased risk of PTL complications (10). However, Rahman et al. did not report a relationship between zinc levels of maternal plasma and pregnancy outcomes (11). It seems that the reason for the discrepancy in the findings is related to the type of study design, the sample size and the difference in the study population.

In this study, there was no significant difference in the level of zinc in the two studied groups. However, Lewicka et al. showed that the decrease in zinc content in amniotic fluid can be associated with the increased risk of low birth weight and intrauterine growth delay (15). It seems that laboratory techniques in investigating zinc in amniotic fluid have a noteworthy importance in the results of different studies.

The results of the present study showed that the level of zinc in the blood plasma of pregnant women is not an acceptable criterion for predicting adverse pregnancy outcomes. However, the area under the roc curve was close to acceptable. In the study of Martadiansyah et al., it was reported that the probability of preeclampsia is 2.3 times higher in women whose serum zinc level is less than 45.5 mg/dL (16). However, in the case-control study of Gul et al., plasma level of zinc was not reported as a predictor of preeclampsia risk and no statistically significant relationship was observed (9). Studies on the level of zinc in amniotic fluid are very limited and no study was found so that we could compare it with the findings of the present study.

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One of the limitations of this study was not evaluating the confounding factors in relation to the incidence of adverse outcomes under investigation and the sampling method was convenience sampling. The small number of samples referred for amniocentesis made it impossible to use random sampling method and it was done based on convenience sampling. Conducting this investigation in future studies with a larger sample size and in similar groups is recommended.

In general, and based on the results of the present study, there seems to be a significant relationship between the plasma zinc level of pregnant women and the adverse outcomes of pregnancy. Therefore, by conducting extensive and more specialized studies, perhaps this experiment can be used for timely prediction and intervention regarding adverse pregnancy outcomes.

Conflict of interest: The authors declare that there is no conflict of interest.

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