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# Zinc Deficiency in Pregnancy and Fetal - Neonatal Outcomes and Impact of the Supplements on Pregnancy Outcomes

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## Abstract

***Introduction:***
Zinc is one of the essential elements of body which has an important role in natural growth, development, and many biological performances. Zinc deficiency is a major health problem and pregnant women are at high risk. 82% of pregnant women worldwide suffer from zinc deficiency. Zinc deficiency during pregnancy has dangerous and irreparable effects such as growth impairment, spontaneous abortion, congenital malformations, intrauterine growth retardation (IUGR), low birth weight (LBW), preeclampsia, premature labor, prolonged labor, postpartum bleeding, delayed neurobehavioral development, delayed immune system development, and leads to increase of mortality rate. Therefore, the importance of proper nutrition during pregnancy and fetal period, because of lasting effects of these periods are far more than other parts of life.
Data gathered from human studies indicate that using zinc supplements have contradictory effects on pregnancy period and growth, survival and neurobehavioral development of the embryo, but the supplements can also have beneficial effects on neonatal immune system and decrease of infants morbidity rate resulted from infectious diseases. Hence, focus on functional outcomes of using supplements such as rates of survival, congenital malformations, embryo growth, pregnancy duration, neurobehavioral development, and also considerations on the micronutrients interferences are suggested for further research.

***Keywords:***
Fetal-neonatal outcomes, Pregnancy, Zinc element.

## Introduction

Zinc is an essential element for optimal development of human body. Zinc plays an important role in cellular cohesion, natural growth and development, proper performance of immune system and increase of appetite, and is a necessary element for many vital functions of body (1-5).

During pregnancy, level of zinc in mother plays an important role in fetal-neonatal outcomes like growth, birth weight, neurobehavioral development, performance of immune system and rate of mortality (6-7) and adequate amount of zinc in pregnant women is essential for the optimum health of mother, embryo and neonatal (8). Nowadays, zinc deficiency is a major health problem (9) which pregnant women are at a higher risk (10).

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Zinc level decreases in the early pregnancy and the decrease continues up to the term period and reaches around 35% lower than non-pregnant women. Therefore, pregnant women are very susceptible for zinc deficiency, especially in the third trimester of pregnancy (11,12).

Some researches conducted in India showed that the zinc deficiency is prevalent among urban, rural and tribal pregnant women of India (13,14).

In some other researches the high prevalence of zinc deficiency among pregnant women has been reported, 64.6% (15-17), and generally, the level of zinc intake in under development countries, in which most of the population are vegetarian, is lower than normal range (11).

According to the adverse effects that insufficient zinc intake can have on health, performance and survival of embryo and neonatal, RDA has recommended daily intake of 12mg for pregnant women between 12-14 years, and 11mg for pregnant women between 19-50 years (18,19).

Generally, nutrition of mother during pregnancy is one of the main effecting factors of mortality rate around birth, and since zinc level of plasma in embryo significantly depends on zinc level of plasma in mother, zinc deficiency of mother can lead to the same in embryo and neonate, and this deficiency during pregnancy may result in serious outcomes in embryo and neonate.

Most of the findings of different studies also indicate that zinc deficiency may affect pregnancy prognosis in 82% of cases (20, 21).

Most of the researches conducted on the effect of zinc element during pregnancy on fetal- neonatal outcomes, reported contradictory results regarding the effect of this element on survival and growth of embryo and neonate, congenital malformation, duration of pregnancy, neurobehavioral and cognitive development and immune system performance. Therefore, more researches should focus on the effects of zinc deficiency and the benefits of administration of zinc supplements during pregnancy on fetal-neonatal outcomes, especially in the countries which zinc deficiency is a major health problem. Hence, according to the high prevalence of zinc deficiency among Iranian pregnant women (22,23), performing the current study is highly important and necessary.

The current study was conducted to evaluate the role of zinc deficiency during pregnancy and its' fetal-neonatal outcomes, and the benefits of zinc supplements administration during pregnancy to reduce these outcomes.

**Zinc Deficiency Consequences and Outcomes**

*Congenital Malformation:* Some researches have indicated the teratogenic effects of zinc deficiency on animals, especially on their nervous system, and some other studies have underlined the importance of anti-teratogenic role of zinc element on animals (24,25).

Human researches have also reported that zinc deficiency leads to the spontaneous abortion and congenital malformation (22, 26, 27).

Considering the necessity of zinc in the absorption, synthesis and biological activity of Folate, zinc deficiency of embryo may lead to the Folate deficiency and finally results in NTDs and other disorders of embryo(28-30).

For the first time, a recent study has expressed the role of zinc on the etiology of cleft lip and cleft palate (31).

The number of studies conducted on the effect of zinc supplements on reducing the congenital malformations is inadequate.

Results of a study showed that the incidence of cleft lip and cleft palate in the children whose mothers had taken zinc supplements during pregnancy was lower than that of children whose mothers had taken placebo (1.8% vs. 0%) (25,32).

According to the available data it cannot be concluded that zinc deficiency alone is teratogenic in human, therefore it can be said that the effectiveness of zinc supplements in prevention of embryopathy is unknown. But considering the great importance of zinc deficiency in the etiology of congenital malformations, more clinical trial researches are needed to answer these questions (33).

**Embryo Growth and Pregnancy Duration**

Many researches indicate the relation between the amount of nutritional zinc, the level of zinc in mother`s plasma, and the animal neonate weight at birth (34, 35). Researches on animals have shown that micronutritions regulate the activity of IGF-I in the formation of osteoblasts and bone development.

Some findings of human studies indicate that the low level of zinc has no effect on the weigh at birth and head circumference. But other researches have shown the relation between zinc deficiency and decrease of head circumference, low weight at birth, delivery of SGA neonate and prenatal weak results. (25,36,37)

In human studies, the reason of delay in neonate growth, resulted from zinc deficiency during pregnancy, was reported to be the effect of this micronutrition on immune system development.

Zinc is an essential element for the function of many enzymes and growth hormones during pregnancy, therefore it can play an important role on growth. For example, during pregnancy, placental alkaline phosphatase needs zinc to induce DNA synthesis and cell proliferation. (36)

Some randomized clinical trials in developed countries showed that intake of zinc supplements has benefits such as decrease of low weight at birth and premature birth. But generally, available studies do not support beneficial effects of zinc supplements on embryo growth and pregnancy duration (19,25,33,34).

**Growth after Birth**

Experiences obtained from animal studies indicate that growth disorders related to the embryonic zinc deficiency also continue in neonatal period (33). But in some human studies, in the first 6 months of birth no difference was observed in growth level of infants whose mothers had taken zinc supplement (17,37).

The available studies indicate that more studies are needed in this field.

**Neurobehavioral Development, Cognitive Function**

Experimental studies on animals show that zinc has significant effect on brain development and proper function of central nervous system and the relation between zinc deficiency and delay in development of brain function has been proven. It has been demonstrated that zinc deficiency results in nervous disorders in early stage of pregnancy and in further stages, it causes brain functional disorders, behavioral abnormalities, and also has negative effects on nervous system development (4,17,33).

The human experimental data which relate the effect of prenatal zinc deficiency to the developmental nervous changes in children are rare.

Some studies have reported a relation between zinc intake during pregnancy and improvement of neurobehavioral development in embryo, increase of developed skills, and movement and development of motor activities in infants and toddlers.

But the results of some other studies show that intake of zinc supplement during pregnancy has no positive effect on developmental consequences and different abilities like auditory, visual senses and memory scores. (9,17,19,25,33,38,39)

Therefore, to approve the effect of zinc supplements intake on motor and cognitive development, conducting clinical trials is necessary, especially on populations with zinc deficiency.

Recently, attentions have been drawn to the relation between micronutrients deficiency and early cognitive development derived from the role of micronutrients in physiological processes, and zinc is one of the micronutrients which are related to the cognitive processes of infants and children. Studies on animals have shown that zinc has an important role in cognitive functions and memory, and zinc supplements, before and after birth, may improve cognitive developments. Although human studies have indicated that zinc deficiency may affect early motor development in children, evidences are not decisive to show any relation between zinc deficiency and cognitive development (4,9,40).

**Infection and Immunity**

Zinc has a significant role in health, structure and function of organs and tissues, also the immune system. Some of the studies have indicated that zinc is an essential element for phagocytosis and bactericidal activity of macrophages and also cellular and humoral lymphocytes functions. Hence, immune system is highly sensitive to the zinc level deficiencies and lack of zinc may cause negative effects on the immune system of the embryo. In the studies conducted on animals, it was shown that zinc deficiency results in decrease of immunity, thymus activity, loss of T cells function, reduction of spleen and thymus size, disorder in mitogenic response of lymphocytes and platelets formation rate, and decrease of immunoglobulin concentration. Decrease in lymphocytes is associated with decrease of T lymphocytes activity and natural killer cells, and also increase of B lymphocytes (1,2,33,38,41).

Despite the important role of zinc in the immune system function, the effects of zinc deficiency on the immune system of infants have not been investigated yet.

In some researches, the relation between level of zinc deficiency during pregnancy and mortality rate resulted from infectious diseases in LBW infants has been indicated. Several studies performed to evaluate the effect of zinc supplements consumption before birth on pregnancy consequences, indicated no effect on decrease of neonatal sepsis. But in some other researches, the results indicated that in neonates with maternal consumption of zinc, the risk of acute diarrhea, dysentery, bloody diarrhea and impetigo was reduced (17,32,38).

Totally, the performed trials in under development countries reported the improvement in the performance of immune system and decrease in the rate of diarrhea and respiratory diseases in the neonates whose mothers had consumed zinc supplements, and also indicated that effects of the supplement would remain after birth on the efficiency of immune system. It seems that consumption of zinc supplements in mothers causes increase of immunity level of neonates and decrease of morbidity rate resulted from infectious diseases. Nevertheless, more researches in this area are needed (33,42).

**Serious Potential Effects**

Before administration of a micronutrient, safety considerations, such as results of the micronutrient interference with other important micronutrients and vitamins should be considered. Because, fluctuation in the level of a micronutrient may make changes in the metabolism of another micronutrient and consequently affect health. For example, zinc has interferences with ferrous, copper and vitamin A.

Unfortunately this important topic has not been considered in the performed studies on intake of zinc supplements. It is recommended to observe the safety considerations in the further studies, especially at the clinical level (11,39).

**Conclusion**

Adequate amount of nutrients is essential for the mother, embryo and neonate health. Inadequate intake of vitamins and minerals

may have negative effects on the health and function of the mother and embryo. Micronutrients deficiency is one of the main problems of women in reproducing age in under development countries and zinc deficiency is one of the most prevalent ones.

According to the above mentioned studies, zinc deficiency can make disorders in growth and nervous, physical, behavioral and cognitive development, immune system function, congenital malformations, spontaneous abortion, IUGR (intrauterine growth retardation), preeclampsia, premature rupture of membrane, premature birth, LBW (low birth weight), disruption in delivery, prolonged labor and bleeding after delivery. These effects may finally lead to increase in mortality rate of mothers, embryos and neonates. Therefore, zinc plays an important role during pregnancy and embryonic period, and has high efficiency at fertilization and during pregnancy period.

Also, according to the data obtained from human studies, the effect of zinc supplement consumption on survival, congenital malformations, embryo growth, pregnancy duration, neurobehavioral development is contradictory. But zinc supplement consumption of mother has beneficial effects on the immune system of the neonate and decrease of morbidity rate of neonates resulted from infectious diseases.

According to all the mentioned topics, more researches should be conducted on the effects of zinc supplements consumption during pregnancy or enrichment of foods with micronutrients, and they should be done according to safety considerations, especially about micronutrients interferences.

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