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RESEARCH ARTICLE

RELATIONSHIP BETWEEN NEONATAL LOW BIRTH WEIGHT AND MATERNAL SERUM ZINC CONCENTRATION

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ABSTRACT

Background: Low birth weight is a crucial and substantial factor contributing to infant mortality. Zinc deficiency can lead to clinically relevant disturbances in tissue functions and may affects birth weight of neonates. **Objective:** The aim of this study is to determine the relationship between maternal serum zinc concentration and the low birth weight (<2500g) of their newborns. **Design:** Cross sectional, case-control study. **Patients and methods:** A total of 70 women were enrolled in this study. Thirty five women as case and 35 women as control. Women who gave birth to low birth weight infants (< 2500g) were regarded as the case group while those who gave birth to infants with weight ≥ 2500g were regarded as the control group. Maternalserum zinc was measured by spectrophotometry method in both groups soon after delivery and the results were compared in both groups. Mothers with twin and multiple pregnancies, per-eclampsia, eclampsia, uterine and cervical abnormalities, APH, oligo and polyhydramnios were excluded from the study. **Results:** Seventy women were enrolled, 35 of them were with LBW newbornswith a mean birth weight 2385 gram of whom the serum zinc level was 63.8±23.8 µgand the other 35 were controls with a mean birth weight with a serum zinc level was 71.6±19.4. There was no significant association between low maternal serum zinc level and low birth weight. **Conclusion:** Maternal zinc concentration was shown to slightly affect birth weight but the effect did not reach a statistical significance.

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INTRODUCTION

Low birth weight (LBW) infants are defined as babies with birth weight of less than 2500 gm irrespective of gestational age. The incidence of intra uterine growth retardation (IUGR) is about 5 to 8% in developed countries while its incidence has been reported to be as high as 18 to 20% in developing countries a finding might be partly explained by the high prevalence of malnutrition and micronutrients deficiency. Zinc deficiency is on the top of these micronutrient deficiencies in developing countries and it is estimated that 82% of all pregnant women in the world have insufficient dietary zinc supply (Jyotsna *et al*., 2015; Caulfield *et al*., 1998). Zinc is a trace mineral that is essential for the activity of approximately 100 enzymes in human body that are important for normal growth and development, cellular integrity, and many biological functions, including protein synthesis and nucleic acid metabolism and its deficiency can lead to impaired growth, sexual problems and even diabetes. Zinc also required for cellular division and differentiation, and is an essential nutrient for normal embryogenesis. The adverse health effects of mild-to-moderate maternal zinc deficiency in animal studies raised concerns of similar effects in human beings and there was strong association between poor maternal zinc status and poor pregnancy outcomes on observational studies. Zinc is believed to be important for fetal growth, development, and immune function (Caulfield *et al*., 1998; Bayomy *et al*., 2017; Khoushabi *et al*., 2016; Shah and Sachdev, 2006; Alvarez *et al*., 2007). Plasma zinc concentration begins to decline in early pregnancy and continues to decline until term, when it is about 15-35% below that in non-pregnant women. This decline in zinc levels has been attributed to hemodilution, decrease in the level of zinc binding protein, hormonal changes during pregnancy, and the active transport of zinc from the mother to the fetus (Alvarez *et al*., 2007; Swanson and King, 1987). The results of many studies of association of low maternal serum zinc concentration and LBW and even the zinc supplementation trials have not produced consistent results (see below in

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discussion) so we did this study to see if there is an association between maternal serum zinc level and the LBW of the newborns in our society.

MATERIALS AND METHODS

We conducted this case-control study at AL-Zahra Teaching Hospital in Najaf /Iraq. Any newborn with a weight of <2500 g without any known underlying risk factors that could explain the reason for the LBW was regarded as a candidate for the case group and the " control " subject was enrolled when a subsequent mother delivered infant with normal birth weight (NBW) which is ≥2500g. Mother – infants pairs were included if maternal age was 17-35 years at the time of delivery with uncomplicated singleton pregnancy. Mothers who smoke or with mutiple pregnancy, pre-eclampsia, eclampsia, uterine and cervical abnormalities, antenatal bleeding, oligohydramnios, polyhydramnios and chronic illness prior to pregnancy (like hypertension, diabetes …etc.) were excluded from the study.
Blood was withdrawn from mothers in the first 5 minutes after delivery for zinc level assessment. Immediately after collection, the blood was centrifuged at 3000 rpm for 15 minutes and plasma was separated and serum zinc concentration was determined by spectrophotometer. Our laboratory reference range for normal serum zinc level was at the range of 70 – 115 µg/dl.

Statistical analysis: This was done by using SPSS (statistical package for social sciences) version 20 in which we use independent sample T-test for numerical data and Chi square test for categorical data. P value of <0.05 was regarded as significant.

RESULTS

A total of 70 infants were enrolled in this study during the study period, of whom 35 had LBW and the others were with NBW. The characteristics of mothers of these infantsare shown in Table (1) below which shows no statistically significant differences in regard to maternal age, gestational age or number of gravida or parity. The mean of maternal serum zinc in the LBW group was 63.8µg/dL. Which was not significantly different from that of the NBW group (71.6 µg/dL)as shown in Table 2 together with the mean infants weight in both studied groups. The effect of gender on birth weight also studied and there was no significant statistical difference between male and female gender regarding their effects on birth weight as shown in Table (3). The only significant finding in association with low birth weight was the history of giving birth to low birth weight babies as shown in Table (4)

DISCUSSION

IUGR which is manifested as LBW or SFA (small for gestational age) is associated with higher infant morbidity and mortality and is associated with increased risk for development of cardiovascular and metabolic diseases in later adulthood. Thus it is of vast importance to study the etiology of IUGR in order to control those occurrences (Wang *et al*., ?). Serum zinc level and its relation to LBW is one of the most frequently studied subject in this regard and it is beyond dispute that zinc deficiency can lead to fetal-growth retardation and malformations in animal models but in humans, such effects are not clear and studies did not reach to a consensus in this regard (Tamura *et al*., 2000).

Table 1. Maternal characteristics of both studied groups

Variables	Infant <2.5 kg	Infant ≥2.5 kg	P value
Age of mother	25.08± 6.28	22.88 ± 5	0.110
Gestational age	37.6 ± 0.9	37.9 ± 1.1	0.203
Gravida	2.3±1	1.7±1	0.108
Para	1.2±1	1±1	0.151
Infant weight	2385gm±96gm	3342gm±152gm	<0.001

Table 2. Mean infants weight and mean maternal serum zinc level and their standard deviations of both groups

Variable	Infant <2.5 kg	Infant ≥2.5 kg	P value
Infant weight	2385gm±96gm	3342gm±152gm	<0.001
Zinc level	63.8 ± 23.8	71.6 ± 19.4	0.519

Table 3. Gender of the newborns and its relation to birth weight in both groups

		Infant weight		P value
		<2.5 Kg	≥ 2.5 Kg	
Infant gender	male	20(57.1%)	24(68.6%)	0.322
	female	15(42.9%)	11(31.4%)	
Total		35(100%)	35(100%)	

Table 4. History of low birth weight and its relation to birth weight in both groups

		Infant weight		P value
		<2.5 Kg	≥ 2.5 Kg	
History of low birth weight	Yes	14	5	0.016
		73.7%	26.3%	
	No	21	30	
		41.2%	58.8%	
Total		35	35	
		50.0%	50.0%	

The results of experimental studies conducted in animal models have motivated concern about the potential health effects of mild-to-moderate maternal zinc deficiency. Observational studies in human populations have produced strong associations between poor maternal zinc status and various indicators of poor pregnancy outcome (Caulfield *et al*., 1998). As mentioned above and in a lot of studies the maternal serum zinc decline with advancement of pregnancy due to reasons mentioned in the same statement above but the direct effect of low serum zinc on fetal growth and its relation to LBW is not that clear. A study held by Fosmire *et al*. (1977) on rats demonstrated that a very small daily supply of zinc (at a level equivalent to 2 mg/day in humans) can prevent the development of congenital anomaliesin rats exposed to sever zinc deficiency because at early pregnancy the demand for zinc is very small so this may explain why congenital anomalies are not prevalent in zinc deficient populations in contrast to findings in experimental animals which are exposed to severe state of zinc deficiency and deliberately fed zinc deficient diet.

Our study showed no significant association between maternal serum zinc level and birth weight although the level of serum zinc in the LBW group was lower than that of average birth weight group but this difference was statistically insignificant. The low normal level of serum zinc in mothers of NBW infants and the low difference between the two studied groups may be due to the effect of hemodilution and increased fetal uptake of zinc in third trimester in both groups. Our finding of no significant association between maternal serum zinc level and LBW did not differ from a lot of studies held in different parts of the world including societies with poor and good standards of living (see below). A lot of studies done in developed countries (Crosby et al., 1977; Meadows et al., 1983; Simmer, 1985; Neggers, 1990) and developing countries (Jyotsna *et al*., 2015; Singh *et al*., 1987; Mbofung and Subbarau, 1990; Jeswani and Vani, 1991) demonstrated a significant association between maternal low serum zinc level and giving birth to LBW infants.

While a study done by Tamura *et al* (Fosmire *et al*., 1977) on 3448 pregnant women (which is one of the largest studies in this regard) with a low income in US beside a lot of studies done in both developed (Wasowicz *et al*., 1993; Wolfe *et al*., 1994; McMichael *et al*., 1982) and developing (Adeniyi, 1987) countries failed to demonstrate such a significant association. To complicate the situation further, even zinc supplemental studies failed to demonstrate a consistent effect on fetal birth weight. Studies held in developed countries (Goldenberg *et al*., 1995; Simmer *et al*., 1991) and developing countries (Garg *et al*., 1993) showed positive effect of zinc supplementation on prevention of LBW while no such effects observed in other studies that are also held in developed (Hunt *et al*., 1984; Hunt *et al*., 1985; Ross *et al*., 1985; Cherry *et al*., 1989; Mahomed *et al*., 1989; Robertson *et al*., 1991; Jonsson *et al*., 1996) and developing countries (Hafeez *et al*., 2005; Osendarp *et al*., 2000; Nossier *et al*., 2015; Caulfield *et al*., 1999). King attributed this contradictory results to "an incorrect assessment of the predictor variable, maternal zinc status, and a failure to determine the independent effect of zinc on fetal growth after other factors that influence birth weight were controlled for" (King, 2000). Although it is clear that experiments held on animals demonstrated a clear association of low maternal serum zinc with congenital anomalies and fetal growth retardation when the animals fed with low zinc diet at beginning of pregnancy, Lowe *et al* emphasized on the importance of change in zinc homeostasis in humans whom already has low zinc intake and low serum zinc before conception and the adaptation that occurs in zinc absorption and metabolism during pregnancy and tried to reproduce the same environment in rats and started feeding them low zinc diet 6 weeks before conception and the rats gave birth to pups without congenital anomalies and they were with average birth weight. They proposed that there must be an increment in the turnover rate of the exchangeable zinc between plasma and body tissues when dietary zinc intake is marginal during pregnancy so even when the maternal serum zinc level is low the fetus got adequate amount of zinc that is essential for organogenesis and growthon expense of maternal tissue stores (liver and bone) (Lowe *et al*., 1999). These changes had been confirmed to occur in humans by Fung *et al* (1997) and Donagelo *et al*. (2005). This may explain in part the findings of non significant association of low maternal serum zinc with LBW and in part it may be due to that the measurement during labor does not reflect the previous maternal serum zinc where the infant can get enough zinc for proper growth by active zinc transport mechanism from plasma to placenta (and then to fetus) in periods when the maternal serum zinc or zinc supplements were not that deficient. We find a significant association between low birth weight and history of giving birth to LBW in previous parity (P value 0.016). This finding is in accordance with that of Bakketeig *et al*. (1993) and Panarettoetal (2006) with two and a half increase in the relative risk for such a history in Bakketeig study. This finding might reflect a presence of an unidentified risk factors in those ladies that require further investigations to discover them in order to control their effects if possible.

Conclusion

Although this study revealed that the effect of low maternal serum zinc on fetal birth weight did not reach a statistical significance further study that involves more frequent and more strict follow up of maternal zinc during pregnancy is needed to reach a more solid statement about its relation to LBW at least in our society.

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