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Research Article

Effect of Maternal Zinc Deficiency in Neonates

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Abstract: ***Introduction:*** Zinc is an essential element for the body. Zinc deficiency poses a significant health risk, particularly for pregnant women and newborns. ***Objective:*** The aim of the current study was to evaluate the outcome of low zinc levels during pregnancy on newborn babies. ***Methodology:*** This prospective study was conducted in the Department of Obstetrics and Gynecology at BSMMU from January 2012 to December 2013. Blood samples were collected from low birth weight (LBW) neonates (including both preterm and term IUGR) and from healthy term appropriate for gestational age (AGA) neonates, along with their mothers. Zinc levels were measured using an atomic absorption spectrophotometer. ***Results:*** A total of 115 newborns with a birth weight under 2.5 kg were classified as low birth weight (LBW), while 135 newborns over 2.5 kg were categorised as AGA. LBW neonates had a lower mean zinc level (83.55 ± 16.64 µg/dL) than AGA newborns (93.74 ± 19.95 µg/dL), with a p-value under 0.05. Mothers of LBW infants also showed lower zinc levels (66.02 ± 16.99 µg/dL) compared to those of AGA newborns (73.59 ± 28.46 µg/dL), also with a p-value under 0.05. ***Conclusions:*** The current study provided evidence for the outcome of zinc deficiency during pregnancy among neonates. Only zinc supplement intake cannot affect the birth weight. Other factors also have an impact on neonatal outcome.
Keywords: Low birth weight, Newborn, Zinc deficiency, AGA, Zinc level.

INTRODUCTION

Fetal growth restriction (FGR), which is characterized by low birth weight (LBW) or being small for gestational age (SGA), is associated with increased rates of infant mortality and morbidity [1, 2]. Research by Barker and colleagues revealed a strong correlation between FGR and a heightened risk of developing cardiovascular diseases in adulthood [3, 4]. Since then, many epidemiological studies have demonstrated a link between FGR and an increased risk of adult onset of both metabolic and non-metabolic diseases [5, 6]. Therefore, understanding the etiology and underlying mechanisms of FGR is a significant concern. Zinc (Zn) is a crucial structural component that plays an essential role in cell growth, development, and differentiation [7]. Studies have shown that maternal zinc deficiency during pregnancy is associated with negative pregnancy outcomes, including miscarriage, preterm delivery, stillbirth, and fetal neural tube defects [8-11]. A meta-analysis found that multinutrient supplementation, including zinc during pregnancy, can enhance birth length, even after accounting for factors such as maternal height, pre-pregnancy weight, and parity [12]. Additionally, reviews indicated that prenatal zinc supplementation significantly reduces the incidence of preterm birth [13-15]. Several small epidemiological studies have also investigated the relationship between maternal zinc status during pregnancy and birth weight [16, 17]. Zinc deficiency adversely affects the endocrine system, which can result in growth failure. Zinc plays a crucial role in various biological functions, including maintaining cell structure and function, protein synthesis, nucleic acid metabolism, and immune functions. It acts as a co-factor for the production of over 200 enzymes, such as phosphatases, metalloproteinases, oxidoreductases, and transferases. Severe maternal zinc deficiency has been linked to poor fetal growth, spontaneous abortion, and congenital malformations, including anencephaly. Even mild zinc deficiency can lead to low birth weight (LBW), intrauterine growth restriction (IUGR), and preterm delivery [18]. Research conducted in both developing and developed countries has shown a positive association between prenatal zinc supplementation and birth weight [19-21]. However, meta-analyses have not found a consistent link between maternal zinc levels and birth weight, as randomized controlled trials (RCTs) yield conflicting results [22]. The objective of this study was to find the effect of zinc deficiency in newborns during pregnancy. Ethical clearance and written consent were assured before the study.

Objectives

- *General objective:* The primary aim of this study was to evaluate the outcome of maternal zinc deficiency.
- *Specific objective:* This study is targeted to find the effect of poor zinc levels in the maternal phase on neonates.

METHODOLOGY

This prospective study included 250 patients who gave birth to healthy neonates with LBW (birth weight less than 2.5 kg, either preterm or IUGR) and appropriate for gestational age (AGA) newborns (birth weight more than 2.5 kg) who visited the Department of Obstetrics and Gynecology, BSMMU, Dhaka, Bangladesh, from January 2012 to December 2013. The LBW newborns and their mothers, who were aged 20 years old or more, were divided into a case group consisting of 115 people, and AGA newborns were counted as a control group consisting of 135 people.

- *Inclusion criteria:* The study enrolled healthy low birth weight (LBW) newborns (defined as birth weight less than 2.5 kg, whether preterm or due to intrauterine growth restriction) and their mothers as the case group. In contrast, term appropriate for gestational age (AGA) newborns (with a birth weight greater than 2.5 kg) and their mothers, were included in the control group.
- *Exclusion criteria:* Newborns from mothers with any medical illnesses, severe malnutrition, anemia (hemoglobin less than 10 gm/dl), diabetes mellitus, hypertension, preeclampsia, eclampsia, parathyroid or thyroid disorders, bone and gastrointestinal disorders, or those receiving certain medications (such as diuretics, anticoagulants, anticonvulsants, or antidiabetics) were excluded from the study. Additionally, neonates with a history of perinatal complications or those requiring admission to the neonatal intensive care unit for any reason were also excluded.

Blood samples (2 ml) were collected from a peripheral vein of both mothers and their newborns within 24 hours of delivery. The difference between the two means was evaluated using the Student's t-test, with the standard error of the difference calculated. A p-value of less than 0.05 was considered significant. The hospital authority gave ethical clearance and well-informed written consent was ensured before the study.

RESULT

Majority of study participant mothers were in the age group between 20–24 years. Of the 110 LBW, 65% were males and 35% were females. Where, out of 135 AGA, the males and females were 45% and 55%, respectively as shown in Table 1. Out of 110 cases, 58 (64.4%) had the habit of SLT use, while out of 140 controls, 32 (26.7%) had this habit [Table 1]. There were 0 participants in LBW group who were aged more than 34 years. Number of participants with higher parity is higher in LBW group compared to AGA group. According to Table 2, the mean neonatal zinc level in the study group was 83.45 ± 16.74 µg/dl, which was significantly lower than the control group, which had a mean level of 93.74 ± 19.95 µg/dl (p-value < 0.05). Additionally, the mean maternal zinc level in the study group was 67.02 ± 15.99 µg/dl, compared to 83.59 ± 18.46 µg/dl in the control group, also showing a statistically significant difference (p-value < 0.05).

Table-1: Basic Characteristics of Study Population (n=250).

Variables		LBW (n=115)	Term AGA (n=135)
Sex of the Baby	F	40 (35%)	30 (55%)
	M	75 (65%)	24 (45%)
Age of the mother	20-24	79 (69%)	89 (66%)
	25-39	32 (28%)	36 (27%)
	30-34	4 (3%)	3 (2%)
	>34	0	7 (5%)
Parity	1	39 (34%)	70 (52%)
	≥2	76 (66%)	65 (48%)

Table 2: Zinc Levels in Study Population (n=250)

Zinc (in pg/dL)	Neonates		Mothers	
	LBW (n=115)	Term AGA (n=135)	LBW (n=115)	Term AGA (n=135)
Mean ± SD	83.55± 16.64	93.74± 19.95	66.02 ± 16.99	73.59 ± 28.46
Range	55-130	50-155	40-112	46 ¯ 140
95% Cl	78.61 - 88.29	88.42 to 99.06	62.4 to 71.64	78.67 to 88.51
p-value	<0.05		<0.05	

DISCUSSION

Pregnant women are particularly prone to zinc deficiency, especially in developing countries. An Indian study revealed that 73.5% of rural pregnant women suffered from zinc deficiency [23]. This deficiency can arise from various factors, including increased blood volume, heightened nutritional demands, and poor intake or absorption of zinc. Zinc deficiency during pregnancy is linked to a range of feto-maternal complications, such as spontaneous abortion, congenital malformations, intrauterine growth restriction (IUGR), and preterm births [24, 25, 18]. In this study, the serum zinc levels were lower in low birth weight (LBW) babies compared to term appropriate-for-gestational-age (AGA) babies. Similar findings were reported by Elizabeth et al., [26] who noted lower cord serum zinc levels in both preterm and term LBW neonates when compared to term AGA neonates. Additionally, it is found that the serum zinc levels in mothers of LBW newborns were significantly lower, and this deficiency correlated with zinc deficiency in their infants. This aligns with the study conducted by Ashraf et al., [27] which found that mothers of small-for-gestational-age (SGA) neonates had lower serum zinc levels compared to mothers of AGA neonates. They also demonstrated a positive correlation between zinc levels and birth weight, suggesting that lower zinc levels could be an independent factor influencing birth weight.

Zinc deficiency during pregnancy can lead to growth retardation in infants by negatively impacting the development of the immune system. It has been demonstrated that zinc regulates IGF-I activity in the formation of osteoblasts, which is crucial for bone growth. Many enzymes and growth hormones that are essential for post-natal growth depend on zinc during pregnancy. For example, placental alkaline phosphatase stimulates DNA synthesis and cell proliferation [28]. Current study aligns with numerous research studies conducted worldwide that have shown a positive association between maternal zinc status and birth weight [18-21, 29-32]. Rwebembera et al. reported that mothers with low zinc levels were 2.6 times more likely to have low birth weight (LBW) babies than those with normal zinc levels. Additionally, newborns with low zinc levels faced a 2.8 times higher risk of being LBW [30]. A recent study indicated that a greater number of normal birth weight babies were born to mothers who received zinc supplementation compared to those who did not [32]. Another study highlighted maternal characteristics, food and nutrition intake, and environmental effects on babies' birth weight [33]. However, the effects of prenatal zinc supplementation on birth weight remain controversial, as randomized controlled trials (RCTs) have produced conflicting results. A recent meta-analysis and a Cochrane review found no significant association between prenatal zinc supplementation and the delivery of low birth weight babies [22, 34]. Nevertheless, a reduction in preterm births was observed in the group that received zinc supplementation compared to those who did not. One possible reason for the discrepancies between our study and other observational studies, as well as the two meta-analyses, could be potential confounding biases in observational research. Additionally, the lack of consistent growth effects in intervention trials may arise from participant noncompliance and inherent risks in field settings. The issue might also relate to the bioavailability of zinc supplements since absorption can be inhibited by iron and phytates, preventing adequate zinc levels from being achieved to promote birth weight. Furthermore, interpreting plasma zinc concentration—commonly used as an indicator of zinc status—can be challenging, as it declines in proportion to the increase in plasma volume during pregnancy. Lastly, supplementation may only be effective for those suffering from zinc deficiency, which means that population-level effects may not adequately reflect improvements in this specific subgroup. Recent studies have shown the parity of women, multinutrient intake, and infection in mothers, suggesting that the number of pregnancies should also be considered when studying the effects of prenatal zinc supplementation [35].

On the other hand, the relationship between maternal zinc deficiency during pregnancy and the risks of low birth weight (LBW) and small for gestational age (SGA) infants remains unclear. An earlier study indicated that there is a threshold level of zinc below which the prevalence of LBW infants increases [17]. In contrast, two recent reports found no significant association between maternal zinc levels during pregnancy and the incidence of LBW and SGA infants [36].

CONCLUSION

In this prospective observational study, it was found that low birth weight (LBW) neonates have a significant deficiency of zinc compared to term appropriate-for-gestational-age (AGA) neonates. Additionally, the mothers of LBW newborns had lower serum zinc levels than the mothers of AGA newborns. There was also a positive correlation between lower maternal serum zinc levels and lower birth weight.

Limitations of the study

A large population and long study duration may affect the overall outcome of the study. Also, the effect of zinc intake on birth weight was not accounted.

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