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CAN ZINC AND MAGNESIUM DEFICIENCY LEAD TO LOW BIRTH WEIGHT?

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ABSTRACT

Low birth weight babies (LBW) are a source of genuine concern and worry not only to clinicians but also to society at large. Developing countries like India suffer from a huge burden of malnourished mothers with numerous complications like preterm labour, small for date and pre-term babies. Nutritional factors are implicated in the pathogenesis of low birth weight babies. This study aims to evaluate association between important microelements like magnesium, zinc with low birth weight of infants. In our study we found that Magnesium and Zinc level was significantly low in TLBW infants when compared to TNBW infants, p value <0.005. We found a strong positive correlation between cord blood magnesium level ($r= 0.369$, $p < 0.005$) with the birth weight of term babies. There was a positive but weak correlation between cord blood zinc level and birth weight ($r=0.178$, $p = 0.077$). These findings suggest that zinc and magnesium have a significant impact on the growth and development of foetus and on the action of anabolic hormones. It also indicates that lower level of Mg, Zn hamper the growth and development of foetus. These findings can hypothesize that lower zinc and magnesium level, which can indicate maternal malnutrition and which can causes impairment in the action of the anabolic hormone, insulin and thus contributes to low birth weight.

Introduction:

The term low birth weight (LBW) infants include those infants whose birth weight is less or equal to 2500g (1). It may be either small for gestational age (SGA) or preterm. Low birth weight leads to neonatal morbidity, subsequent retardation of growth and development and also early onset of adulthood diseases and mortality (2). India alone accounts for 40 percent of the incidence of low birth weight babies in the developing world. In Indian population, about 26.6% of total delivery occur as low birth weight babies and may represent an important predisposing factor for type 2 diabetes (T2D) and the metabolic syndrome later in life (3, 4). Although there are several factors for low birth weight, but proper diet and nutritional care of mothers along with adequate rest during pregnancy are most important among them (5). Magnesium deficiency in pregnant mother frequently occurs because of inadequate or low intake of magnesium. Magnesium deficiency during pregnancy can induce not only maternal and fetal nutritional problems at birth but also consequences like diabetes, obesity that might last in offspring throughout life (3). Magnesium level is known to indicate malnutrition(6). Magnesium (Mg^{+2}) has an important role in the action of anabolic hormones (7-9).

Zinc, is an essential micro element, a component of many enzymes, needed for the growth of infant during and/or after pregnancy and metabolism of infant or mother. Abnormal serum Zn concentrations in pregnant women have been associated with a number of maternal and foetal complications which includes low birth weight, adverse outcomes of pregnancy and increased risk of infections during (10-13). Zinc participates in metabolic pathways (14). This element has been associated with the interaction between hormones and their receptors and to the improvement in the post-receptor stimulus (15).

Lower consumption of dietary zinc and low serum zinc levels were associated with an increased prevalence of coronary artery disease and diabetes and several of their associated risk factors including hypertension, hypertriglyceridemia in urban subjects (16-21). With this in mind this study was designed to evaluate any differences between birth weight, cord blood magnesium and zinc concentrations between cases and controls to study any correlation.

Materials and Methods:

INCLUSION AND EXCLUSION CRITERIA

For this study, infants of both the genders who had completed 37 weeks of gestation and who were born out of uncomplicated pregnancy were included.

Pre-term infants, those born out of complicated pregnancies, and those born to mothers with history of medications (like beta blockers, corticosteroids, etc), addiction (to smoking, alcohol, etc) were excluded from the study. Infants with congenital anomalies and birth asphyxia were also excluded from the study.

Term low birth weight infant (TLBW) (of weight 2500 gm or less) were taken as case and term normal birth weight baby (TNBW) (birth weight more than 2500 gm) as control during the study. Overall exclusion criteria for control group were same as those used for case selection procedure.

STUDY DESIGN AND SAMPLE SIZE

This study was a non-interventional, observational, hospital based study.

50 healthy term infants, whose body weight was more than 2500gm, were taken in the control group and 50 term infants having birth weight 2500 gm or less were taken in the case group.

As the participants attend the hospital OPD from a large rural base, they were expected to have approximately similar ethnicity, socioeconomic status and dietary habits.

The study followed the guidelines of the Helsinki declaration of 2009 (22) and was approved by the Institutional Ethics Committee. Informed consent was taken from every subject.

SAMPLE COLLECTION AND STORAGE

Umbilical cord blood samples from all of the subjects (cases and controls) were collected in 2 vials (fluoride-oxalate tube and plain tube). Blood in the fluoride-oxalate tube was used for the estimation of glucose while blood in plain tube was allowed to clot and serum was separated by centrifugation at 2500 rpm for 5 min at $4^{o}C$ for the estimation of insulin, zinc and magnesium. Serum samples for the measurement of Insulin were stored at $-20^{o}C$ till estimation. Samples were thawed to room temperature before every assay, and repeated thaw was avoided.

ESTIMATION OF TEST PARAMETERS:

ESTIMATION OF FASTING BLOOD GLUCOSE:

Quantitative estimation of blood glucose was done by Glucose oxidase / Peroxidase method (23) from the separated plasma by using the autoanalyzer ERBA XL 600. Internal quality control was performed simultaneously. All test reagents are supplied by Span Diagnostics Ltd. India and the quality control materials (Level 1 and 2) were supplied by Bio-Rad laboratories, USA.

ESTIMATION OF SERUM MAGNESIUM:

Principle: Magnesium ions react with Calmagite in alkaline medium to produce a red complex that was measured photometrically at 532 nm. The intensity of color produced is directly proportional to magnesium concentration (24).

ESTIMATION OF SERUM ZINC:

Principle: Serum zinc was estimated by Nitro-PAPS (pyridylazo-N-propyl-N-sulfopropylamino-Phenol) method. The intensity of color was measured photometrically at 570 nm which is directly proportional to zinc concentration (25).

STATISTICAL CALCULATIONS:

Pearson's bivariate correlation study was performed for any correlation between the parameters within a group. Student's't' test is used to compare means between two groups. Significance was considered at 95% confidence interval ($p<0.05$) for all statistical analysis. All statistical analyses were done using SPSS software v16.0 for Windows.

Result and discussion:

This study aims to evaluate any correlation between nutritional factors as reflected by serum zinc and magnesium levels and glucose tolerance as reflected by insulin resistance with the birth weight of term infants.

The Mean and SD of cord blood Magnesium was 0.75 + 0.26 mmol/L and 0.55 + 0.12 mmol/L in the control and case groups. Mean and SD of cord blood zinc level was 76.94 + 29.20 and 61.14 + 21.63 µgm/dl in the two groups.

Table: 1, Mean and SD of different studied parameter in our study group and comparison between them

	Control Group	Case Group	"p" value
Cord blood Magnesium (mmol/L)	0.75 + 0.26	0.55 + 0.12	<0.005
Cord Blood Zinc (µgm/dl)	76.94 + 29.20	61.14 + 21.63	<0.005

In this study, it was found that cord blood magnesium is lower in low birth weight babies in comparison to normal birth weight babies. Mean and SD of Magnesium in this study, was 0.75 + 0.26 mmol/L in control group and 0.55 + 0.12 mmol/L in case group, p < 0.005. Cord blood Zinc was also lower (mean 61.14 + 21.63 µgm/dl) in low birth weight babies than normal birth weight babies (mean zinc level 76.94 + 29.26 µgm/dl), p < 0.005.

Kaushabi et al (2016) demonstrated that the except magnesium, the profile of other biochemical variables like zinc in the umbilical cord blood of the neonates with normal birth weight (NBW) were significantly higher than in the umbilical cord blood of neonates with low birth weight (LBW). Which suggests that maternal serum zinc concentration influenced the birth weight of neonates as outcome of pregnancy (25). Gomez et al (2015) in their study found that Zn-level of preterm subgroup was significantly lower compared to control group (p=0.001)(26). Bogden et al (1978) in their study had found that there was no statistically significant difference in the cord blood magnesium level in low birth weight and normal birth weight term babies (27).

In our study we found that the mean level of both zinc and magnesium was lower in the cord blood of TLBW infants, when compared to TNBW infants. This though agrees with the previous studies when we compare the cord blood zinc level. But the finding of lower cord blood magnesium in the cord blood of TLBW infants is in contrast with the finding of Bodgen et al.

Gomez et al (2015) in their study had found statistically significant low positive correlation between Zn-levels and birth weight (rho=0.283; p=0.005) (26). Akman et al (2006) on the other hand found that Zn deficiency was not observed to be a risk factor for low birth weight (28). So the results for cord blood zinc level and birth weight was conflicting. Bogden et al (1978) didn't find any correlation between cord blood magnesium levels and birth weight (27). Sherwani et al (1998) in their study found a negative correlation between birth weight and Mg levels (29). Takaya et al (2004) found that magnesium was significantly correlated with the birth weight (P < .001) (30). So there was no definitive co-relation between magnesium and birth weight on comparing these studies.

On performing Pearson's bivariate correlation analysis, we found that there is a strong positive correlation between cord blood magnesium level and birth weight (r=0.369, p<0.005). We also found that there was a positive but weak correlation between cord blood zinc level and birth weight (r=o.178, p =0.077). We also found that cord blood zinc and magnesium levels were positively correlated with birth weight.

Table 2: showing correlation of various study parameters with birth weight.

BIRTH WEIGHT	Magnesium	Zinc
	r=0.369, p <0.005	r=0.178, p=0.077

CONCLUSION:

The associations derived from this study indicate that lower levels of Zinc and Magnesium can indicate maternal malnutrition. They are contributory to the hampered growth of the foetus. This may be one reason for the causation of low birth weight and subsequent complications. Prospective studies with large sample population are necessary to confirm the findings of this study for better understanding of the pathogenesis of low birth weight and to understand if zinc and magnesium supplementation can prevent intrauterine growth retardation, and to open up more avenues for study and management and prevention of low birth weight.

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CONFLICT OF INTEREST

None

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