DOI: 10.7860/JCDR/2015/10449.5402

Original Article

Paediatrics Section

Study of Serum Zinc in Low Birth Weight Neonates and Its Relation with Maternal Zinc

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ABSTRACT

Objective: Assessment of serum Zinc in LBW (Low Birth Weight) and appropriate for gestational age (AGA) neonates in relation to their maternal zinc level.

Materials and Methods: A prospective study was conducted in a tertiary care teaching hospital of central India between August 2011 to July 2012. Serum samples were collected from the eligible LBW (preterm & term IUGR) and term AGA healthy neonates and their mothers for zinc level estimation. Serum zinc was measured by atomic absorption spectrophotometer. Newborn of mothers having any medical illness, on any medication, with anaemia (Hb <10 gm/dl) were excluded from the study. Neonates with any perinatal insult were also excluded.

Results: Out of 100 newborn-mother pairs enrolled in the study, 46 newborns (18 preterm and 28 term IUGR) with birth weight <2.5kg comprised the case group and rest 54 term AGA newborns (birth weight >2.5kg) were categorized as control group. Mean serum zinc level was significantly low in LBW neonates (83.45±16.74 µg/dl) in comparison to term AGA newborns (93.74±19.95 µg/dl), (p-value <0.05). Similarly, zinc level was also low in mothers of LBW babies (67.02±15.99 µg/dl) in comparison to mothers of term AGA newborns (83.59±18.46 µg/dl), (p-value < 0.05). Low maternal zinc levels were significant correlated with lower serum zinc in LBW neonates (Pearson correlation value - 0.938). However, maternal zinc levels have shown no significant correlation with neonatal serum zinc levels in term AGA (0.029).

Conclusion: LBW neonates and their mothers have significant zinc deficiency as compared to term AGA neonates and their mothers and this deficiency is correlated with zinc deficiency in mothers of these LBW neonates.

Keywords: Low birth weight, Newborn, Serum zinc, Term appropriate for gestational age

INTRODUCTION

Babies with birth weight less than 2500 gm irrespective of gestation are classified as low birth weight (LBW). These include both preterm & term small for date (IUGR). The incidence of IUGR is about 5 to 8% in developed countries while its incidence has been reported to be as high as 18 to 20% in our country [1]. Maternal micronutrient deficiency is one of the contributing factors for higher incidence of IUGR and LBW births in developing countries. Zinc deficiency is one of the most common micronutrient deficiencies in developing countries and about 82% of all pregnant women in the world suffer from zinc deficiency which can either be due to be marginal intakes or chronic infections that reduce plasma zinc concentrations [2]. Lower maternal zinc concentration can lead to reduced placental zinc transport and foetal zinc supply. Maternal zinc deficiency has been associated with poor fetal growth in both animal and human. Recent study estimated about 0.5 million maternal and child deaths annually due to zinc deficiency especially in developing countries [3].

Zinc deficiency has a negative effect on the endocrine system, leading to growth failure. Zinc has vital role in a wide range of biological activities including maintenance of cell architecture & functions, and protein synthesis, nucleic acid metabolism and immune-functions by acting as a co-factor for production of over 200 enzymes e.g. phosphatases, metalloproteinases, oxido-reducatases, and transferases [4]. Severe maternal zinc deficiency has been associated with poor fetal growth, spontaneous abortion and congenital malformation (e.g. anencephaly). Even milder forms of zinc deficiency can lead to LBW, IUGR and preterm delivery [4].

Previous studies conducted in developing as well as developed countries reported positive association between prenatal zinc supplementation and birth weight [5-7]. However, meta-analysis failed to show any association between maternal zinc level and birth weight as randomized controlled trials (RCTs) report conflicting conclusions [8]. Therefore, we conducted this study to further assess maternal zinc level and to find any correlation with maternal zinc level and birth weight. Serum zinc level in LBW neonates was also assessed and compared with that in term AGA neonates.

MATERIALS AND METHODS

This prospective study was conducted in a tertiary care teaching hospital of central India between August 2011 and July 2012, after obtaining approval from the institutional ethics committee. Written consent was obtained from the mothers as well as the fathers or legal guardians of the eligible newborns. Assuming the ratio of controls to cases as 0.8, the permissible sample size calculated was 28 cases and 23 controls.

Healthy LBW (birth weight less than 2.5 kg, either preterm or IUGR) newborns and their mothers were enrolled as cases while term AGA newborns (birth weight more than 2.5 kg) and their mothers included in control group. Newborn of mothers having any medical illness, severe malnutrition, anemia (Hb less than 10 gm/dl), diabetes mellitus, hypertension, preeclampsia, eclampsia, parathyroid, thyroid, bone and gastrointestinal disorders or mothers receiving drugs (e.g. diuretics, anticoagulants, anticonvulsants, antidiabetics) were excluded from the study. Similarly, neonates with history of perinatal insult or requiring admission in neonatal intensive care unit due to any reason were also excluded.

Blood samples (2 ml) were obtained from a peripheral vein of mothers and their newborn within 24 h of delivery; samples were collected in a sterile container and labelled. Then samples were centrifuged at 3000 rpm for 20 min and supernatant serum was collected in a separate sterile polyethylene container and was stored at -20°C

	LBW (n=46)	Term AGA (n=54)	Total (n=100)
Sex of the Baby			
F	16 (35%)	30 (55%)	46 (46%)
M	30 (65%)	24 (45%)	54 (54%)
Total	46	54	100
Age of the Mother			
20-24	32 (69.5%)	36 (66.6%)	68 (68%)
25-39	13 (28.2%)	15 (27.7%)	28 (28%)
30-34	1 (2.1%)	1 (1.8%)	2 (2%)
>34	0	2 (3.7%)	2 (%)

[Table/Fig-1]: Demographic profile of study population

Serum Zinc (in µg/dL)	Neonates		Mothers	
	LBW (n=46)	Term AGA (n=54)	LBW (n=46)	Term AGA (n=54)
Mean ± SD	83.45± 16.74	93.74± 19.95	67.02 ± 15.99	83.59 ± 18.46
Range	55-130	50-155	40-112	46-140
95% CI	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	

[Table/Fig-2]: Serum zinc levels in study population

until analysis. Serum zinc was measured by atomic absorption spectrometer [3]. Difference between two means was evaluated by students t-test by calculating the standard of error of difference. p value less than 0.05 was considered significant.

RESULTS

Total 100 newborn-mother pairs were enrolled in the study as per our inclusion criteria. Out of 100 cases, 46 newborns with birth weight <2.5kg were enrolled in the study group (18 preterm and 28 term IUGR) and rest 54 term AGA newborns (birth weight >2.5kg) were categorized as control group. Demographic profile of babies and their mothers has been shown in [Table/Fig-1]. Mean birth weight was 2.13±0.90 kg in LBW babies white it was 3.04±1.30 kg in term AGA newborns.

Serum zinc levels in study population are given in [Table/Fig-2]. Mean neonatal serum zinc level in the study group (83.45±16.74 µg/dl) was comparatively lower than in control group (93.74±19.95 µg/dl), which was statistically significant (p-value <0.05). Mean maternal serum zinc level was also lower in study group (67.02±15.99µg/dl) than in control group (83.59±18.46µg/dl), which was statistically significant (p-value <0.05).

DISCUSSION

Pregnant women are very susceptible to zinc deficiency, especially in developing countries and an Indian study reported 73.5% Zn deficiency among rural pregnant women [9]. This zinc deficiency can be due to expanded blood volume, increased demands and poor intake or bio-absorption. Zinc deficiency during pregnancy is shown to be associated with various feto-maternal complications including spontaneous abortion, congenital malformations, IUGR, and preterm births [2-4]. In the present study, we observed lower serum zinc level in LBW babies than in term AGA babies. Elizabeth et al., [10] also found lower cord serum zinc level in both preterm and term LBW neonates as compared to term AGA neonates. In our study, we found that serum zinc level of mothers of LBW newborns was also significantly low and this deficiency was correlated with zinc deficiency in their neonates. This is in collaboration with the study by Ashraf et al., [11], where they found lower serum zinc in mothers of SGA neonates as compared to serum zinc in mothers of AGA neonates. They also showed that zinc level has positive correlation with birth weight and LBW babies had lower levels of zinc, which might be an independent factor influencing the birth weight.

Zinc deficiency during pregnancy may lead to growth retardation in infants by affecting the development of body's immune system. It has been shown to regulate IGF-I activity in formation of osteoblasts and thus it particularly regulates the bone growth. Many enzymes and growth hormones, which play important role in post-natal growth, require zinc during pregnancy e.g. placental alkaline phosphatase which stimulates DNA synthesis and cell proliferation in pregnancy [12]. Our study results are in collaboration with the results of many studies conducted in different parts of the world which showed positive association with maternal zinc status and birth weight [4-7,13-16]. Rwebembera et al., reported that mothers with low zinc levels were 2.6 times more likely to have LBW babies than those with normal zinc levels, and newborns with low zinc levels were 2.8 times more at risk of being LBW [14]. A recent study showed that more number of normal birth weight babies delivered by the mothers receiving zinc supplementation than by the mothers who did not receive zinc supplementation during pregnancy [16]. Another study recently showed significant difference in plasma cord zinc levels between low and normal birth weight babies [17].

Still, the effect of prenatal zinc supplementation on birth weight is controversial as RCTs report conflicting conclusions and a recent meta-analysis as well as a Cochrane review failed to any significant association between prenatal zinc supplementation and delivery of low birth weight babies [8,18]. Although, a reduction in preterm birth was seen in zinc supplemented group as compared to non-supplemented mothers. One possible reason for the discrepancy between the conclusion of our study as well as other observational studies and two meta-analyses might be risk of potential confounding bias in observational studies. Secondly, lack of consistent growth effect in intervention trials could be due to participant non-compliance, inherent risk in field settings. The other reason might be related to the bioavailability of the zinc supplement as absorption of zinc can be inhibited by iron and phytates and adequate zinc level to promote birth weight could not be achieved.

Also, interpretation of the measurement is difficult as plasma zinc concentration, commonly used indicator of zinc status, declines in proportion to the increase in plasma volume during pregnancy. Lastly, supplementation might only be effective among those suffering from zinc deficiency, and therefore, population-level effects might not capture improvements among this subgroup. A recent study showed that the zinc levels decreased with increase in the parity of women [19]. Therefore, parity of the women should also be taken into account while studying the effects of prenatal zinc supplementation.

Our study was an observation study with small number of cases and we did not study the effect of maternal zinc supplementation on birth weight. Birth weight depends on many other factors also such as gender, gravida and parity of the mother, race, BMI, and maternal weight gain during pregnancy [17]. We could not take into account all these factors and multiple regression analyses should have been performed to control for all of these variables before blaming zinc deficiency for LBW. Although, with these limitations, we successfully demonstrated a positive association between lower maternal zinc level and lower birth weight. Future studies can be planned to answer questions such as ideal dosage, time of initiation and duration of zinc supplementation, and type or mode of supplementation.

CONCLUSION

In this prospective observation study, we showed that low birth weight neonates have significant zinc deficiency as compared to term AGA neonates. Also, the mothers of LBW newborns have lower serum zinc levels that the mothers of the AGA newborns and lower maternal serum zinc level was positively correlated with lower birth weight.

REFERENCES

[1] Singh M. Disorders of weight and gestation. In Singh M, ed. Care of the Newborn. 7th ed. New Delhi: Sagar publication; 2010: p 234-53.
[2] Caulfield LE, Zavaleta N, Shankar AH, Merialdi M. Potential contribution of maternal zinc supplementation during pregnancy to maternal and child survival. *Am J Clin Nutr.* 1998;68:499S-508S.
[3] Black RE, Allen LH, Bhutta ZA, Caulfield LE, de Onis M, Ezzati M, et al. Maternal and child undernutrition: global and regional exposures and health consequences. *Lancet.* 2008;371:243-60.
[4] Aydemir F, Cavdar AO, Soylemez F, Cengiz B. Plasma zinc levels during pregnancy and its relationship to maternal and neonatal characteristics: a longitudinal study. *Biol Trace Elem Res*. 2003;91:193-202.
[5] Garg HK, Singhal KC, Arshad Z. A study of the effect of oral zinc supplementation during pregnancy on pregnancy outcome. *Indian J Physiol Pharmacol.* 1993;37:276-84.
[6] Goldenberg RL, Tamura T, Neggers Y, Cooper RL, Johnston KE, Du Bard MB, et al. The effect of zinc supplementation on pregnancy outcome. *JAMA.* 1995;274:463-68.
[7] Castillo-Duran C, Marin VB, Alcazar LS, Iturralde H, Ruz M. Controlled trial of zinc supplementation in Chilean pregnant adolescents. *Nutr Res.* 2001;21:715-24.
[8] Mori R, Ota E, Middleton P, Tobe-Gai R, Mahomed K, Bhutta ZA. Zinc supplementation for improving pregnancy and infant outcome. *Cochrane Database of Systematic Reviews*. 2012, Issue 7. Art. No.: CD000230. DOI: 10.1002/14651858.CD000230.pub4.
[9] Pathak P, Kapil U, Kapoor SK, Saxena R, Kumar A, Gupta N, et al. Prevalence of multiple micronutrient deficiencies amongst pregnant women in a rural area of Haryana. *Indian J Pediatr.* 2004;71:1007-14.
[10] Elizabeth KE, Krishnan V, Vijayakumar T. Umbilical cord blood nutrients in low birth weight babies in relation to birth weight & gestational age. *Indian J Med Res.* 2008;128:128–33.
[11] Ashraf M, Ahmad Z, Khan MN, Khawaja TF, Khan MA, Salam A. Relationship of maternal serum zinc levels to the birth weight of the infants. *Professional Med J.* 2005;12:336-39.
[12] Domenech E, Diaz-Gomez NM, Barroso F, Cortabarria C. Zinc and perinatal growth. *Early Hum Dev.* 2001;65(Suppl):S111-17.
[13] Cavdar AO, Soylemez FB, Cengiz B, Aydemir F. Zinc status during pregnancy: a longitudinal study. *J Trace Elem Exp Med.* 2003;16:175-79.
[14] Rwebembera AA, Munubhi EK, Manji KP, Mpembeni R, Philip J. Relationship between infant birth weight ≤2000 g and maternal zinc levels at Muhimbili National Hospital, Dar Es Salaam, Tanzania. *J Trop Pediatr.* 2006;52:118-25.
[15] Danesh A, Janghorbani M, Mohammadi B. Effects of zinc supplementation during pregnancy on pregnancy outcome in women with history of preterm delivery: a double-blind randomized, placebo-controlled trial. *J Matern Fetal Neonatal Med.* 2010;23:403-08.
[16] Naher K, Nahar K, Aziz MA, Hossain A, Rahman R, Yasmin N. Maternal serum zinc level and its relation with neonatal birth weight. *Mymensingh Med J.* 2012;21:588-93.
[17] Nazari M, Zainiyah SY, Lye MS, Zalilah MS, Heidarzadeh M. Comparison of maternal characteristics in low birth weight and normal birth weight infants. *East Mediterr Health J.* 2013;19:775-81.
[18] Chaffee BW, King JC. Effect of Zinc Supplementation on Pregnancy and Infant Outcomes: A Systematic Review. *Paediatr Perinat Epidemiol.* 2012;26:118–37.
[19] Paul S, Prashant A, Chitra TR, Suma MN, Vishwanath P, Devaki RN. The micronutrient levels in the third trimester of pregnancy and assessment of the neonatal outcome: a pilot study. *J Clin Diagn Res*. 2013;7:1572-75.

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FINANCIAL OR OTHER COMPETING INTERESTS: None.

Date of Submission: **Jul 01, 2014**
Date of Peer Review: **Aug 25, 2014**
Date of Acceptance: **Sep 05, 2014**
Date of Publishing: **Jan 01, 2015**