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Pediatrics

EFFECT OF ZINC SUPPLEMENTATION IN LOW BIRTH WEIGHT BABIES

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ABSTRACT

Background- Zinc is known to play a critical role in normal growth and development. Low birth weight babies (LBW) with low serum zinc levels and have higher rates of morbidity and mortality from infectious diseases because of impaired immunity and are at increased risk of growth failure.

Objectives- This study was undertaken to assess zinc deficiency status in LBW babies and the effect of zinc supplementation on them. This was a hospital based, Prospective randomized control study.

Methods- A total of 100 LBW babies delivered at Shri B M Patil Medical College, Hospital & Research Centre or delivered at outside hospital & referred to our hospital were included in the study. Quantitative analysis of serum zinc level in LBW babies was made and Cases were supplemented orally with 10mg of elemental zinc per day for 3 months.

Results- zinc supplementation especially among Low Birth Weight babies has significant benefit on their growth and is found effective to enhance the growth in early months of life, particularly weight and linear growth.

Conclusion – Because LBW is a major pediatric problem, accounting for approximately 30% of all live births in developing country like India. Serum Zinc level in LBW babies in our study was low. Zinc supplementation in them was found to be effective to enhance the growth and decrease morbidity and mortality in them.

KEYWORDS : Zinc, Low birth weight, Growth, Supplementation

INTRODUCTION

Zinc is vital micronutrient next only to iron. Zinc is known to play a critical role as a cofactor for numerous enzyme functions, protein synthesis, nucleic acid metabolism, gene expression and immune regulation. This element therefore is essential for normal growth and development.

Low birth weight (LBW) infants (infants weighing < 2500 g at birth irrespective of gestational age) have higher rates of morbidity and mortality from infectious diseases because of impaired immunity and are at increased risk of growth failure. Studies have demonstrated low zinc status in LBW infants. And it has been shown that low maternal serum zinc level during pregnancy may be associated with an increased risk of LBW, also zinc supplementation during pregnancy has resulted in reduction of health risk of these infants.

Reduced level of zinc in LBW infants, might well account for the increased morbidity and growth failure in such infants.

A study by Freil which was performed on chilean infants that were born small for gestational age (mean birth weight ,2300 g ; mean length at birth, 47 cm).They were randomly assigned to a test group receiving 3 mg of elemental zinc per day (mean total zinc intake, 1.5- 1.8 zinc per kg per day) or to a placebo group (mean zinc intake ~0.7 mg of zinc per kg per day) for 6 months. Supplemented group demonstrated improved growth, significantly greater weight for age and length for age than the placebo group[1].

Studies on zinc supplementation to LBW infants from birth through 6 months of age are very few. However studies of shorter duration on very LBW infants and also on children in older age groups have shown varying results. Similar placebo controlled studies conducted by Shrivastava[2] et al on malnourished children aged 8 to 24 months showed that children supplemented with zinc for 3 months had a significant weight gain ($P < 0.001$).

Another study made by Rafael Jimenez[3], Mayder Martinez University of Santiago has shown increase in linear growth and weight gain with zinc supplementation. A double blind longitudinal study of a cohort of 163 infants was carried out. Infants were put into two groups, the supplemented group with 87 infants received a dose of 10 mg /day of zinc sulphate solution and non supplemented group with 76 infants received a dose of 10ml/day physiologic solution without zinc. This showed infants supplemented with 10 mg/day increase in weight.

A fourth study by Lira[4] et al. on low birth weight full-term infants in northeast Brazil demonstrates an effect on growth of 1 or 5 mg of zinc/d supplementation during the first 26 week of life, although an effect is found on weight gain with 5 mg of zinc/d between 17 and 26 weeks.

In addition, zinc requirements of LBW infants are high because of their immature gastro intestinal tract, which leads to high endogenous losses and decreased absorption, an extended period of rapid growth, and low body stores of zinc. Thus zinc supplementation is started at birth in these infants, its sustained impact will continue in the weaning period.

There are few other studies showing zinc supplementation from birth to 2 months of age has been effective in improving weight gain in LBW infants. These findings indicate that zinc supplement could have important implications for child health and survival programs in developing countries with high incidence of LBW.

Zinc is one of the numerous trace elements which are known to have a significant role in the growth and development of an infant. In fact its role has been attributed right from antenatal period, as deficiency of this micronutrient can have a crucial bearing upon the health of the newborn. Prasad defined the role of zinc in human nutrition in 1991. It was the observation linking increased susceptibility to infectious diseases and nutritional zinc deficiency which lead to the increased interest in the importance of this trace element.[5]

Zinc is required for functioning of over 200 enzymes and hence likely to affect a number of various systems in the human body. Severe to moderate zinc deficiency has been found to cause oxidative damage to proteins, lipids and DNA in rats' testes[6] which may be due to iron accumulation or a reduction in zinc dependent antioxidant processes.

MATERIALS AND METHODS

100 Low birth weight babies delivered at Shri B M Patil Medical College, Hospital & Research centre and delivered at outside hospital & referred to our hospital between November 2014 to August 2015. It is a randomized control trial.

After taking written informed consent from the parents and fulfilling inclusion and exclusion criteria of neonates were included in the study.

LBW babies were randomly assigned into two groups, case group (n=50) and control group(n=50). The study was approved by ethical committee of BLDE University. After taking written consent, history and examination 3 ml of blood was collected in plain vial was sent to

department of biochemistry BLDEA's Shri B M Patil Medical college.Serum was separated from the whole blood and investigated for zinc level by Zinc Kit, Colorimetric method[30].Out of total 100 samples only 60 were done done by colorimetric method. Due to non availability of Zinc kit remaining 40 blood samples for Zn analysis were done by atomic absorption spectrophotometry[31](AAS) at Karnataka University, Dharwad.

Cases were supplemented with 10mg of elemental zinc for 3 months.

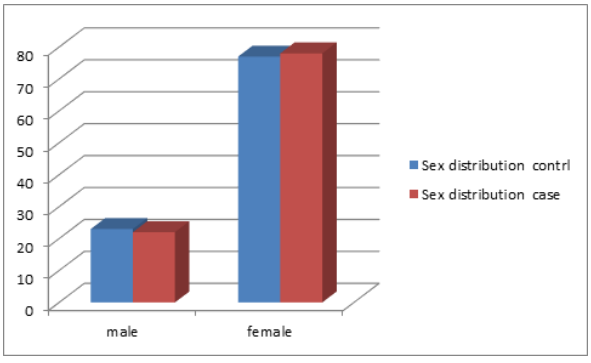
Anthropometry measurement of each baby was done at 0, 1 and 3 months . Weight was measured on a electronic weighing scale, length was measured with infantometer and HC with non stretchable tape.

Follow up was done for all 100 LBW babies till 3 months age. And each follow-up visit, infant weight,length and HC were measured. Cases (50) with Zinc supplementation were compared with control group(n=50) not supplemented with zinc, for difference in the growth, development and morbidity and mortality in these groups. Z score statistical analysis will used to compare the difference in the serum zinc level ,and difference in their growth and development, of Zinc supplemented and control LBW babies at the end of the study period.

RESULTS

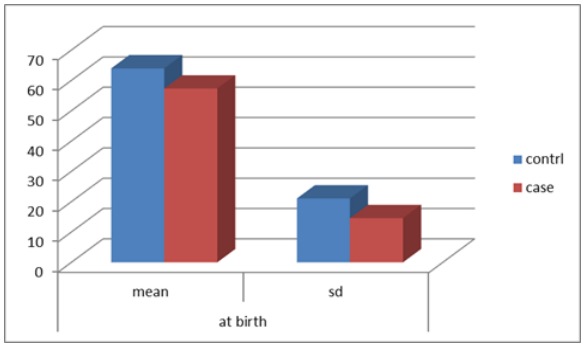
Graph 1. Shows sex distribution

	control	case
male	23	22
female	77	78



Graph 2. Shows serum Zn at birth

	mean	Std deviatoin
control	63.952	21.05144563
case	57.3	14.56729633

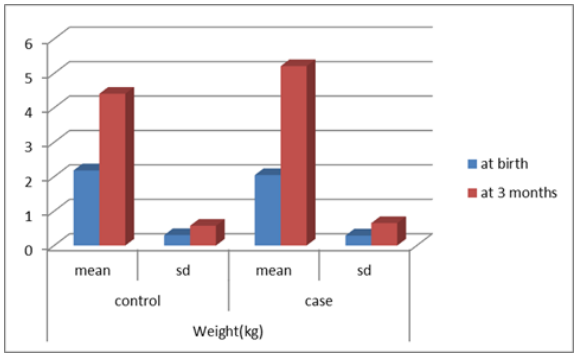


Anthropometry measurement of 50 cases and 50 control were taken at birth and at 3months followup. The cases supplemented with zinc and control group were comparable for weight, length, HC, and male/female ratio(Graph 1)

Serum zinc levels(Graph 2) were in lower limit of normal range. After supplementation weight, height and head circumference were comparable in both groups. Significant differences in weight gain and increment in length were found in first and second follow up between two groups. Reduction of morbidity was seen in zinc supplemented group with no apparent infection and hospitilisation. No serious No serious adverse effect was noted related to supplementation therapy.

Graph 3. Shows weight at birth and 3 month

	Weight(kg)			
	control		case	
	mean	sd	mean	sd
at birth	2.1822	0.304183685	2.04782	0.2901043
at 3 months	4.411	0.574418073	5.2122	0.6527127

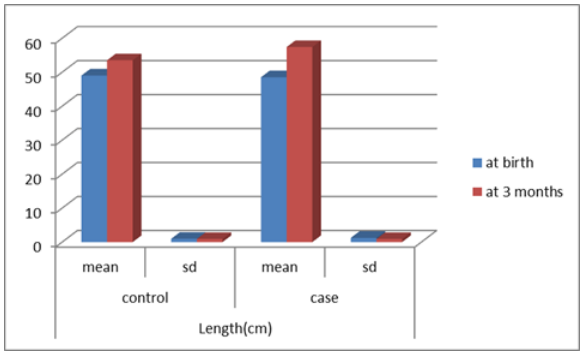


In our study growth parameter i.e weight of cases supplemented with zinc were significantly higher than the control group not supplemented with zinc.

This was stastistically significant with p value of 0.009(<0.05)

Graph 4.Shows length at birth and at 3 month

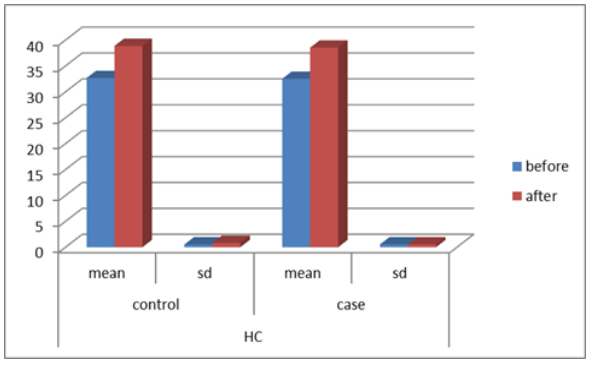
	Length(cm)			
	control		case	
	mean	sd	mean	sd
at birth	49.006	0.974032225	48.508	1.2494636
at 3 months	53.516	0.917040493	57.412	0.9252997



The length velocity in the case group supplemented with zinc were significantly higher compared to control group not supplemented with zinc. This was stastically significant with the p value 0.003(<0.05) .

Graph 5. shows HC at birth and at 3months

	Control		case	
	mean	Sd	mean	sd
at birth	32.65	0.523820346	32.502	0.5497643
At 3 mth	38.856	0.828118103	38.524	0.5434433



In our study head circumference increased in both the groups but difference was not stastically significant with the p value 0.599(>0.05)

DISCUSSION

During this study 100 LBW neonates were randomly assigned into two groups, case and control group. In both groups serum zinc level estimation was done by colorimeric[30] and atomic absorption spectrophotometry[31](AAS) methods. Case group were supplemented with 10 mg of elemental zinc for 2 months and control group not supplemented. Follow up is done for 3 months and reassessed for anthropometric parameters to see for weight gain and increase in linear growth. Cases with zinc supplementation are compared with control group not supplemented with zinc for difference in growth, development and morbidity and mortality in these groups.

In our study we observed decreased serum zinc levels in study group and at follow up we observed remarkable and significant weight gain and increased length in case group supplemented with zinc compared to control group.

These findings were compared with following studies done by Castillo- Duran et al[34] and TV Ramkumar[35] et al.

Table 1. shows anthropomery parameters after zinc supplementation in present study and compared with following studies.

	Present study	TV Ramkumar[35] et al	Castillo-Duran[34] et al
Weight	Significant Weight gain	Increased	Increased
Length	Increased	Increased	Increased
Serum zinc level	Low (mean 57.3)	Low	Low
HC	No significant change	Not significant	No significant change

Table 2. shows changes in weight after supplementation in case and control group

Weight(g)	Case	Control	P value
Present study(at birth)	1510+_860	1800+_400	
Present study(after supplementation)	5210+_200	4100+_180	**0.009**
TV Ramkumar[35] et al(at birth)	1310+_185	1268+_197	
TV Ramkumar et al(after supplementation)	4120+_635	3404+_802	**0.003**

Present study showed significant increase in weight in case group supplemented with zinc compared to control group not supplemented with zinc. Castillo-Duran[34] et al and TV Ramkumar[35] et al also showed the same results.

In a study done by Castillo-Duran MD[34] the z scores for weight by groups showed better catchup growth in supplemented group(S) than in placebo group(P).Group S, -2.05+/_0.52 to -0.24+/_0.64; group P , -2.06+/_0.48 to -1.07+/_0.61.These differences were significant (p value<0.003) after 2 months of supplementation.

Table 3 shows changes in length after supplementation

Length(cm)	Case	Control	P value
Present study(at birth)	48.0 +/_1.6	49+/_1.2	
Present study(after supplementation)	56+/_2.2	52+/_2.3	0.003
TV Ramkumar[35] et al(at enrollment)	43.8+/_2.4	42.8+/_2.3	
TV Ramkumar(after supplementation)	55.9+/_2.4	50.7+/_3.9	0.001

Present study shows significant increase in length in zinc supplemented group compared to control group with p value0.003 (<0.05). It was also same in other studies by TV Ramkumar[35] et al,Castillo-Duran[34] et al, Diaz- Gomez[36] et al and Friel[1] JK et al. Castillo-Duran[34]et al study showed length were identical at birth, but at 6 months were 64.9+/-1.8cm versus 63.4+/_3.5cm for supplemented and placebo group respectively with p value<0.01.

Table 4. shows changes in HC after supplementation

HC(cm)	Case	Control	P value
Present study(at birth)	29+/_1.4	29.2+/_1.2	
Present study(after supplementation)	36+/_2.4	36+/_2.46	0.599
TV Ramkumar et al(at birth)	30.9+/_1.7	30.9+/_2.2	
TV Ramkumar et al(after supplementation)	37.5+/_1.7	36.1+/_2.2	0.008

In our study HC increased in both groups. The difference was not stastistically significant.

But TV Ramkumar[35] et al showed significant increase in HC post supplementation with zinc.

Diaz-Gomez[36] et al and Lind[37] et al also showed no significant increase in HC.

The present study demonstrated that LBW infants who were exclusively breastfed and supplemented with zinc for 60 days had significantly higher weight, length at follow up after 3 months after birth per compared to those who had not received zinc.

Zinc supplementation to LBW babies for 3 months resulted in improved weight gain, linear growth. There were no significant side effects of the supplements. These findings could have important implications for the child health survival program in developing countries with high incidence of LBW babies and preterm low birth infants.

The strength of this study includes its randomized, open label and minor differences in initial anthropometric status. The groups were similar at baseline, thus any differences in study outcomes were likely due to the supplements that are provided.

Follow up between the two groups was observed. Compliance with supplementation was good.

Limitations of the study include sample size is small, this cannot be applied in community based study. Larger sample size may confirm our findings. Follow up serum sinc level estimation could not be done , though not able to do ten cases serum zinc estimation were done post supplementation which showed higher serum zinc level. If this can be extrapolated to rest of the sample size.

Dose of zinc supplemented 10mg elemental zinc/day. taken is arbitrary, but 7 followup samples serum zinc level showed signicant improvement in serum zinc level post supplementation. Probably 10 mg/day elemental zinc is approved for LBW babies as supplement.

Baseline serum zinc levels were seen in both groups. Altigani[38], *et al* reported serum zinc concentration approximately 65µg/dL in low birth weight babies in their study. Itabashi[39], *et al* found mean serum zinc concentration 54+_ 14.4µg/ dL in their study. Our findings corroborated the findings of these studies.

There were no significant difference in weight, length and head circumference at enrollment But a significant difference were found at 6 weeks and 12 weeks follow up ($p < 0.05$).

This is understandable as zinc has profound role on cellular growth and proliferation and performs various metabolic functions.

Castilo-Duran[34], *et al* demonstrated improved growth of LBW babies in their study, significantly greater weight for age and length for age were found in zinc supplemented group. Lira[4], *et al* found the growth was enhanced in low birth weight babies by giving 10mg zinc. Osendarp[40], *et al* found similar results.

Head circumference was increased in both groups after supplementation. The difference was not statistically significant. This results was consistent with Lind[37], *et al* and Diaz- Gomez[36] *et al.*

Mortality pattern of both the groups were observed and significant difference in morbidity was found between two groups. Our findings are comparable with these studies.

Thus zinc supplementation should be recommended along with other vitamins and minerals for all low birth weight infants for their optimal growth and development.

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