Zinc deficiency is common in young infants in the developing world and is associated with reduced immunocompetence and increased rates of serious diseases(1). Low zinc concentrations have been observed in the cord blood of low birthweight (LBW) newborn babies (<2500 g) and birthweight has been shown to be highly correlated with cord zinc concentration in India(2,3). For several reasons, preterm infants have relatively high zinc dietary requirements and face special challenges to meet them. About 60% of fetal zinc is acquired during the third trimester of pregnancy, when fetal weight increases three-fold. Preterm infants (<37 weeks gestation) have lower zinc reserves than term infants and because of immaturity, they may be less efficient at absorbing and retaining zinc for growth(4). Zinc deficiency has a negative effect on the endocrine system, leading to growth failure, among other clinical manifestations. Zinc plays an important role in gene transcription and is also one of the most prevalent trace elements in the brain(5).

**Effect of Oral Zinc Supplementation on the Growth of Preterm Infants**

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**Objective:** To compare the effect of oral zinc supplementation on growth of preterm infants.

**Design:** Randomized controlled trial.

**Setting:** Dhaka Shisu Hospital (Tertiary care hospital).

**Subjects:** 100 appropriate for date preterm infants weighing between 1000 to 2500g were randomized to receive zinc and multivitamin supplement (Group I; n=50) or only multivitamin supplement (Group II).

**Intervention:** Zinc supplementation was given 2mg/kg/day for 6 weeks along with multivitamin in Group I and only multivitamin to Group II.

**Primary outcome variable:** Increment of weight and length.

**Results:** At enrollment, serum zinc (62.1±12.4μg/dL in Group I and 63.1±14.6μg/dL in Group II) and hemoglobin levels (14.9±2.4g/dL in Group I and 14.4±1.7g/dL in Group II) were almost similar in both groups. Serum zinc levels were in lower limit of normal range. After supplementation, serum zinc and hemoglobin levels were significantly higher in Group I (105±16.5μg/dL) than Group II (82.2±17.4μg/dL) (P<0.05). Weight, length and head circumference were comparable in both groups at enrollment. Significant differences in weight gain and increment in length were found in first and second follow up between two groups but OFC increments were not significant (P>0.05). Reduction of morbidity was apparent in zinc supplemented group. No serious adverse effect was noted related to supplementation therapy.

**Conclusion:** Zinc supplementation for preterm low birth weight babies is found effective to enhance the growth in early months of life.

**Key words:** Infants, Preterm, Supplementation, Zinc.

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Zinc supplementation has been shown to reduce the rates of diarrhea and pneumonia, and to enhance physical growth of young infants (6). Several studies conducted in various parts of the world have shown beneficial effect of zinc supplementation in early growth of preterm babies (7,8). No study has been conducted in Bangladesh to evaluate the effect of zinc on growth of preterm babies. We conducted this study to evaluate the efficacy of oral zinc on growth of preterm infants.

**METHODS**

This randomized controlled trial was conducted in the Neonatal Special Care unit of Dhaka Shishu (Children) Hospital between January 2006 and May 2007. According to the incidence of low birthweight, the assumed targeted proportion was 0.03 (UNICEF, 2005) (9), the degree of accuracy was 0.05 and with 5% level of significance, the targeted sample size was 323 for population size equal or more than 10,000. However, during the study period of 16 months, there were only 160 population cases, and the estimated sample size was 107. As seven cases were not enrolled due to their parent’s unwillingness to participate in the study, 100 cases were included and randomized to supplemented group (n=50) and control group (n=50). Randomization was done by lottery method of selection cards, which were equal in number for each group in sealed opaque envelopes. Principal investigator and data analyzer were blinded to the allocation of the treatment groups.

We included preterm infants below 37 weeks, weighing 1000 g to <2500 g and appropriate for gestational age. Those with major birth defect or congenital deformities, unstable vital signs, or with parents unwilling to participate, were excluded. The study protocol was approved by ethical review committee of Dhaka Shishu Hospital. Informed written consent was obtained from the parents before enrollment of the patient in the study.

Immediately after registration of the patient, detailed history was taken from mothers or relatives and physical examination was performed. Gestational age was determined by maternal record and by New Ballard Score system. Before intervention weight was measured by an electronic weighing scale (Scale–Tronix Pediatric Scale, USA), which was accurate to 5g and was calibrated before each measurement. Weighing was carried out with the baby nude and before feeding. Occipito–frontal circumference (OFC) was measured with a non-elastic standard plastic measuring tape (1cm wide) to the nearest 1mm. Baseline serum zinc level and hemoglobin estimation were done in both the groups, before giving supplementation, within 7-21 days of postnatal age. Determination of serum zinc concentration was carried out in the laboratory of chemistry division of Atomic Energy Centre, Ramna, Dhaka, Bangladesh. Serum zinc level was measured by flame atomic absorption spectrophotometry method. At the same time, blood sample was sent for hemoglobin estimation and hemoglobin level was assayed within half an hour of blood collection, using the cyanmethemoglobin method.

When the neonates were 7 to 21 days old, before discharge from the hospital, mother was given two bottles of supplement containing zinc and instructed to feed her baby at a dose of 2 mg/kg/day orally with other multivitamins for 6 weeks (Group I). Control group (Group II) was instructed to take only the multivitamins (0.3mL daily, each mL containing vitamin A 1500 IU, vitamin D 300 IU, thiamin hydrochloride 0.48mg, riboflavin 0.3mg, pyridoxine hydrochloride 0.3mg, nicotinamide 3mg, calcium D pantothenate 1.5mg and ascorbic acid 15mg) for the same duration. Mothers were advised to attend the follow up clinic after six weeks. Information was obtained about diarrhea, respiratory illness, presence of fever or vomiting, pattern of feeding during these six weeks. Anthropometric measurements were also recorded.

Blood samples for serum zinc and hemoglobin estimation were obtained again from the babies of both the groups. Mothers of both the groups were advised to visit again after six weeks. This time no zinc supplementation was given but iron supplementation was added at a dose of 2.5 mg/kg/day along with multivitamin. During the second follow up, anthropometric measurements and related history were obtained again.

Statistical analyses were done by SPSS. Independent samples t test and Chi-square test were