SYSTEMATIC REVIEW

Neonatal Zinc Supplementation for Prevention of Mortality and Morbidity in Breastfed Low Birth Weight Infants: *Systematic Review of Randomized Controlled Trials*

ANJANA GULANI, SHINJINI BHATNAGAR* AND HPS SACHDEV

*From the Department of Pediatrics and Clinical Epidemiology, Sitaram Bhartia Institute of Science and Research, B-16 Qutab Institutional Area; and *Centre for Diarrheal Diseases Research and Nutrition, Division of Gastroenterology, Hepatology and Nutrition, Department of Pediatrics, All India Institute of Medical Sciences, Ansari Nagar, New Delhi, India.*

Correspondence to: Prof HPS Sachdev, E-6/12 Vasant Vihar, New Delhi 110 057, India. hpssachdev@gmail.com

Objectives: To evaluate whether zinc supplements prevent mortality and morbidity in breastfed low birth weight infants.

Methods: All randomized or qausi–randomized trials with individual or cluster allocation and using concurrent controls were included. Study population included LBW infants irrespective of gestational status who were exclusively or predominantly breastfed at the initiation of intervention. Intervention comprised zinc salts given as tablets or syrups orally to provide at least 1 RDA of elemental zinc for at least a period of 14 days, introduced within one month of birth. Electronic databases were searched irrespective of language and publication status.

Findings: Three trials from developing countries met the inclusion criteria. Limited data did not indicate a reduced risk of mortality (1 trial, RR=1.11; 95% CI 0.57 to 2.18 at one year), hospitalization rate (1 trial, odds ratio 1.10; 95% CI 0.87 to 1.39), acute respiratory infection (1 trial), or diarrhea (2 trials). However, the trial reporting on mortality was not adequately powered for evaluating this outcome. There was no evidence of an increase in weight (3 trials) or height (2 trials) at either 6 months or one year of age, or of an increased risk of vomiting following zinc supplementation. Serum zinc levels at the end of intervention were significantly higher in the supplemented group (2 trials).

Conclusions: In view of no convincing evidence of benefits from the limited data available, currently there is no justification for recommending routine zinc supplementation for breastfed LBW newborns in developing countries.

Key words: *Breastfed, Low birth weight, Morbidity, Mortality, Neonate, Zinc.*

Observational data indicates that higher dietary zinc may be required to meet the daily requirements of low birth weight breastfed infants [1-5]. In view of the important role of zinc in immune function, it is conceivable that zinc supplementation in LBW breastfed infants may prevent infectious morbidity and related mortality. To inform policy, we conducted a systematic review of randomized controlled trials to evaluate the effect of zinc supplementation on mortality and morbidity in breastfed low birth weight infants.

METHODS

Types of trials: All randomized or qausi–randomized trials with individual or cluster allocation and using concurrent controls. Trials employing a factorial design with multiple intervention groups were eligible for inclusion.

Participants: Low birth weight infants (birth weight less than 2500 grams) irrespective of gestational status who were exclusively or predominantly breastfed at the initiation of intervention. Exclusive breast-feeding was defined as no feed other than breastmilk. Predominant breastfeeding was defined as taking only water or multivitamins or medicines other than breastfeeds.

Intervention: Zinc salts given as tablets or syrups orally to provide at least 1 RDA of elemental zinc [6,

7] for at least a period of 14 days and introduced within one month of birth. Trials providing additional supplements (for example, vitamin A, micronutrient mixtures, iron) were considered if the only difference between the two comparison arms was zinc supplement. The comparison groups included no intervention or placebo.

Outcome measures

Primary: We examined all cause mortality in the child at two time points: during infancy, in the period between initiation of intervention and the last follow-up until the age of one year; and during the neonatal period between initiation of intervention and the last follow-up until the age of one month.

Secondary: In the period between initiation of intervention and the last follow-up until the age of one year we measured cause specific mortality due to diarrhea, acute respiratory infections and causes other than these (as defined by the authors, irrespective of ascribing a single or multiple causes of death), severity of morbidities as assessed by clinic or hospital visits or hospitalizations (as defined by the authors of the trials) and morbidities because of sepsis including probable or culture proven bacterial sepsis, acute respiratory infection or respiratory difficulty, diarrhea, meningitis, ear infections, cough or running nose, fever or severe malnutrition (severe wasting, and pedal edema or kwashiorkor). We also measured weight and height at the end of intervention and adverse effects including vomiting.

Search Strategy

The trials were identified by simultaneous searches of medical databases (till August 26, 2009) including PubMed (since 1966), EMBASE (since 1980), Cochrane Controlled Trials Register, Web of Science (WoS), Allied and Complementary Medicine (AMED) (since 1985), British Nursing Index (BNI) (since 1994) and CAB abstracts (since 1973) with no language restrictions. For PubMed the search strategy employed was: (newborn OR neonat* OR infant OR neonates OR postnatal OR post-natal) AND (low birth weight OR preterm OR small for gestational age OR premature) AND ("zinc" OR micronutrient* OR vitamin*) AND ((clinical[Title/Abstract] AND trial[Title/Abstract]) OR clinical trials[MeSH Terms] OR clinical trial[Publication Type] OR random*[Title/Abstract] OR random allocation[MeSH Terms] OR systematic OR review OR metaanalysis OR meta-analysis).

A lateral search using the related articles link in PubMed was done for selected articles. We reviewed the reference lists of identified articles and hand searched reviews, and abstracts of international micronutrient conferences of past three years. To avoid publication bias, we included published and unpublished trials. Requests for information were sent to experts and major development and aid agencies including United Nations Children's Fund (UNICEF), WHO, United States Agency for International Development, and Bill and Melinda Gates Foundation.

Data extraction and management: We extracted data in duplicate on study design, participant characteristics, interventions, and outcomes and contacted authors for additional information if required. Any discrepancies in extracted data were resolved by discussion.

Assessment of risk of bias in included studies: This was assessed in relation to sequence generation, allocation sequence concealment, blinding, incomplete outcome data assessment, selective reporting and any other bias [8].

Statistical Analysis

In factorial trials and in multi-arm designs yielding two or more intervention groups (different dosage or administration regimens) and a single control group, the data in the intervention groups, including the variation in the intervention characteristic, was to be pooled and compared against the single control group to prevent unit-of-analysis error.

Data entry and initial analysis were performed on SPSS (Version 13.0) software. Meta-analysis and meta-regression was to be performed with user written programmes on Stata (version 9.2) software. Presence of bias in the extracted data was to be evaluated by funnel plot [9]. We were to use formal statistical tests for funnel plot asymmetry (Begg's and Egger's) with the "metabias" command [10,11].

Pooled estimates (relative risk with 95% confidence intervals) of the evaluated outcome measures were calculated by the generic inverse variance method by "metan" command [10,12]. For continuous outcomes (for example, weight and height) pooled weighted mean differences (WMD) were computed using both fixed effects and random effects models. We used formal tests of heterogeneity, namely, the statistic Cochran Q and I^2 (variation in pooled estimate attributable to heterogeneity) [13]. If I^2 exceeded 25% and *P* value for Cochran Q statistic was below 0.05, then heterogeneity was to be considered substantial. In this eventuality, random effects model was to be preferred and reasons for heterogeneity were to be explored by subgroup analyses and meta-regression, if sufficient number of trials were available.

Subgroup and sensitivity analyses: We were to perform subgroup analyses only for the primary outcome, all cause mortality within one year of age, as a hypothesis generating exercise. The pre-specified subgroup analyses were to include: (*i*) dose of zinc; (*ii*) duration of supplementation; (*iii*) birth weight; (*iv*) gestational age (term gestation ≥37 weeks *versus* preterm gestation <37 weeks); (*v*) follow-up age to examine the possibility of a greater response in the first half of infancy; (*vi*) infant mortality rate in the placebo group to examine the possibility of a greater response with higher baseline mortality [lower *versus* upper half (median) of infant mortality rate in included trials]; (*vii*) Maternal zinc supplementation (yes *vs* no); and (*viii*) development status of the trial area to examine the possibility of a greater response in high-risk populations (developing *versus* developed countries). We were also to conduct a sensitivity analysis to investigate the robustness of results taking into account the trial quality components (randomization, allocation concealment, blinding and attrition). The contribution of these variables to heterogeneity was to be explored by meta-regression with the restricted maximum likelihood option [14].

RESULTS

Using the search strategy, 12 potentially eligible reports were identified [15-26]. Amongst these, 9 reports [15-23] were excluded for various reasons (***Web Fig.* 1**). The remaining 3 reports [24-26] provided data on 3 trials satisfying the inclusion criteria. The baseline characteristics of the included trials, all from developing countries [27] and the notable individual study specific features are summarized in ***Web Table* I** and ***Web Annexure***. ***Web Table* II** summarizes the assessed risk of bias in the included studies. In 2 trials, no risk of bias was evident; while in the third trial; intention to treat analysis was not performed. Data was insufficient to calculate the routine measures of publication bias (Begg-Mazumdar bias and Horbold-Egger bias statistics).

Assessment of heterogeneity: As the search retrieved only 3 trials with information on outcomes of interest being available in even lesser trials, the estimate of I^2 statistic should not be considered to be robust (***Table* I**). Most of the evaluated outcomes suggested evidence of significant heterogeneity (I^2 or Cochran Q statistics). We therefore preferred to use the random effects model estimates.

Primary Outcomes

Infant mortality: Only one trial reported on the number of infant deaths [26]. Of the 1026 infants randomized in each group, there were 21 deaths in the supplemented and 19 deaths in the placebo groups. The relative risk of mortality with zinc supplementation group was 1.11 (95% CI 0.57 to 2.18) at one year.

Neonatal mortality: No trial reported on the number of neonatal deaths.

Secondary outcomes

Cause specific mortality: The only trial [26] with information on deaths did not report on cause specific mortality.

Severity of morbidities: Only one trial [26] reported on hospitalization rate as number/1000 child-years of follow up (189.9 in zinc supplemented and 175.3 in placebo groups, respectively). The odds ratio for hospitalization with zinc supplementation was 1.10 (95% CI 0.87 to 1.39). No trial had reported upon clinic or hospital visits.

Acute respiratory infection (ARI) or respiratory difficulty: One trial reported [26] on ARI at 3, 6, 9

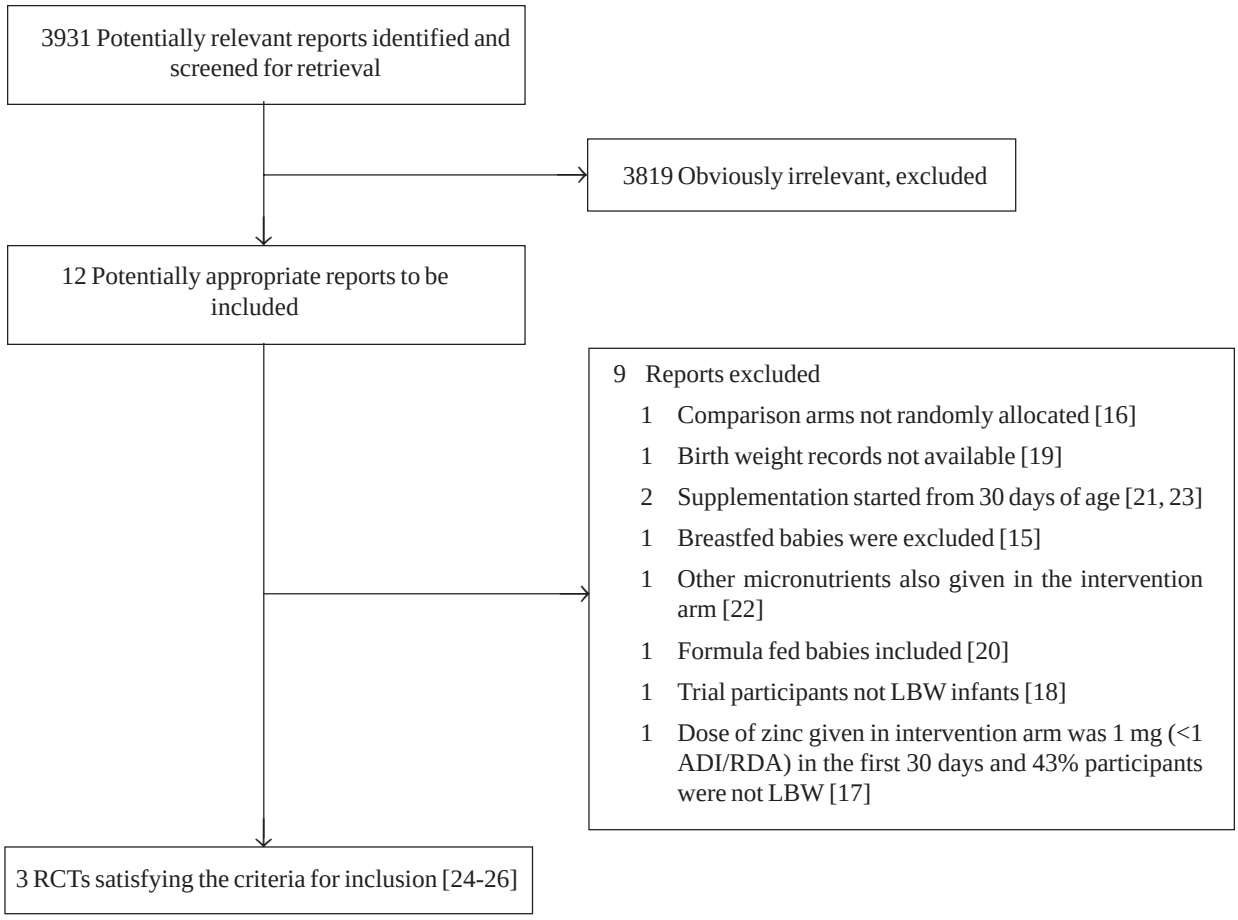

FIG. 1 *Flow chart depicting the trial flow for selection of randomized control trials included in the systematic review.*

and 12 months as morbidity recall within the past 24 hours or within the past 7 days. There was no evidence of reduced ARI with zinc supplementation for both these measures at any time point of evaluation. The pooled relative risk (random effects model) of reported ARI within 7 days was 1.13 (95% CI 0.98 to 1.3) till one year of age and 1.13 (95% CI 0.96 to 1.34) till 6 months of age.

Diarrhea: Two trials from India [25,26] had reported on diarrhea. There was no evidence of a reduced risk of diarrhea with zinc supplementation (***Table* I**). The trial from Kolkata, India [25] had only reported on the number of diarrheal episodes without adjustment for individuals having more than one episode. On replacing the number of diarrheal episodes with the number of individuals developing diarrhea in this trial [25], there was no evidence of a reduced risk of diarrhea (RR 0.97; 95% CI 0.90 to 1.04). The Kolkata trial [25] had also reported on the proportion of days ill with diarrhea/child/year, which was comparable during the exclusive breast feeding period (zinc *vs* placebo 3.7 *vs* 4.0; $P>0.05$) but significantly lower in the zinc supplemented group during the post breastfeeding period (6.6 *vs* 10.2; $P<0.0001$).

Other morbidities: No trial reported morbidities other than diarrhea and ARI.

Growth: Three trials provided information on weight. There was no evidence of a greater weight for age z scores following zinc supplementation either at 6 months or one year of age (***Table* I**). Two trials [25,26] provided information on height. There was no evidence of a greater height (cm) following zinc supplementation either at 6 months or one year of age (***Table* I**).

Adverse effects: Only one trial had reported on adverse effects [26]. There was no evidence of an increase in vomiting following zinc supplementation. The pooled relative risk (random effects model) of vomiting with zinc supplementation was 1.06 (95% CI 0.88 to 1.28) till one year of age and 1.17 (95% CI 0.91 to 1.51) till 6 months of age.

Serum zinc levels: Two trials [24, 26] had evaluated serum zinc levels at the end of the trial. Data were available from 387 participants (186 in zinc group and 201 in placebo group). The serum zinc levels (μg/dL) were significantly higher following zinc supplementation (***Table* I**).

Exploratory subgroup and meta-regression analyses were not feasible because outcomes were reported in a small number (one to three) of trials.

DISCUSSION

There was no convincing evidence of benefit following zinc supplementation in breastfed LBW infants. Limited data from 1 to 3 trials did not indicate a reduced risk of mortality (1 trial), hospitalization rate (1 trial), acute respiratory infection (1 trial), or diarrhea (2 trials). However, the trial reporting on mortality was not adequately powered for evaluating this outcome. There was no evidence of an increase in weight (3 trials) or height (2 trials) at either 6 months or one year of age or of an increased risk of vomiting following zinc supplementation. Serum zinc levels at the end of intervention were significantly higher in the supplemented group (2 trials) indicating successful absorption of the micronutrient.

Following limitations merit consideration. First, only three trials satisfied the inclusion criteria and inferences on some outcomes were based on 1 or 2 trials only. The only trial reporting on mortality was not adequately powered to evaluate this outcome. Second, all trials were conducted in developing countries and two were from India, which limits the generalization of findings to other regions in developing countries and developed nations. Third, the possibility of publication bias and predictors for heterogeneity could not be explored due to the small number of trials. Fourth, information on exclusive or predominant breast feeding status was available only at the time of initiation of the study but not in a longitudinal manner till the end of the intervention.

The following criterion for data inclusion deserves elucidation: (*i*) The intervention was evaluated in LBW breastfed infants to guide policy formulation by the WHO for optimal feeding of LBW infants in developing countries. LBW newborns comprise a heterogeneous population of preterm and small for gestational age (SGA) newborns that are physiologically different. Preterm infants are likely to have higher zinc deficit and dietary requirements as nearly 60% fetal zinc is acquired during third trimester of pregnancy. It is therefore conceivable that the response to zinc supplementation may be variable amongst preterm and SGA babies. It would therefore have been ideal to evaluate the effect of

TABLE I SUMMARY OF POOLED ESTIMATES FOR VARIOUS OUTCOME MEASURES

Outcome	No. of trials	Random effects model RR/WMD^ (95% CI); *P* value	Fixed effects model RR/WMD^ (95% CI); *P* value	Tests for heterogeneity I^2 (%); Q (*P* value)
Diarrhea till 1 year	2	0.87 (0.65, 1.16); 0.337	0.96 (0.89, 1.03); 0.211	70.1; 3.34 (0.067)
Diarrhea till 1 year*	2	0.97 (0.90, 1.04); 0.375	0.97 (0.90, 1.04); 0.375	0.0; 0.10 (0.751)
Weight (z scores) at 6 mo^	3	0.13 (-0.18, 0.45); 0.412	-0.01 (-0.10, 0.08); 0.868	64.4; 5.62 (0.06)
Weight (z scores) at 1 year^	3	0.42 (-0.20, 1.04); 0.183	0.01 (-0.08, 0.10); 0.801	90.6; 21.6 (<0.001)
Length (cm) at 6 mo^	2	-0.21 (-0.41, 0.00); 0.052	-0.21 (-0.41, 0.00); 0.052	0.0; 0.48 (0.487)
Length (cm) at 1 year^	3	0.48 (-1.47, 2.43); 0.629	-0.09 (-0.32, 0.15); 0.487	90.1; 20.3 (<0.001)
Serum zinc (microgram/dL)	2	18.45 (2.39, 34.52); 0.024	15.58 (11.41, 19.75); <0.001	92.1; 12.7 (<0.001)

* *With number of children instead of number of episodes for the Sur, et al. [34] trial.*

intervention in relation to gestation and growth retardation. However, most of the relevant trials have not segregated the data into preterm and/or growth retarded babies. Also in the context of developing guidelines in resource starved countries, the only practical option is categorization as LBW rather than SGA and/or preterm because gestation is difficult to determine with accuracy. Further, nearly 70% of LBW babies in developing countries are SGA unlike in the developed world where the bulk of LBW babies are preterms [1]. Thus we feel that our study criteria are apt to feed the policy requirement. (*ii*) The type of intervention was defined as zinc salts given as tablets or syrups orally to provide at least 1 RDA of elemental zinc for at least a period of 14 days introduced within one month of birth. The RDAs for zinc in low birth weight breast fed infants have not been defined [6, 7]. However, the suggested average dietary intakes (ADI, which are invariably lower than RDA) for infants in the age group of 0 to 6 months are 2 mg(6) and it is believed that the requirements would be higher in LBW infants. We therefore used the conservative cut-off of 2 mg elemental zinc intake to define the RDA in LBW newborns.

One trial [17] had provided information on mortality but was excluded because the zinc dose was 1 mg (<1 ADI/RDA) in the first 30 days of life and 43% of the participants were full-term small for gestational age but not low birth weight (>2500 grams). We could not include the data relevant to our systematic review from this trial because the report did not present disaggregated results for LBW infants. Also, despite supplementation commencing at 15 days of age, effect on mortality was reported at 1 to 9 months of age. In this factorial design trial, the multivariate analysis using Cox regression (5 deaths in 581 zinc supplemented participants *versus* 15 deaths in 573 participants not receiving zinc) yielded a relative risk of 0.32 (95% CI 0.12 to 0.89; *P*=0.028). Stratified results for low birth weight participants were not available. On including this trial also in the pooled estimates, there was no evidence of a reduced risk of mortality in infancy (***Web Fig*** 1); the pooled RR was 0.63 (95% CI 0.19 to 2.13; *P*=0.458; I^2=75.5% with *P*= 0.043 for heterogeneity) by random effects model and 0.76 (95% CI 0.43 to 1.32; *P*=0.324) by fixed effects model.

It could be postulated that beneficial effects were not evident because the intervention may not have led to an increase in zinc nutriture of the participants. However, a significant increase of serum zinc in subgroups of two trials refutes this hypothesis. Further, as per the inclusion criteria the participants had received at least one recommended ADI per day.

All the reviewed evidence pertains to developing countries, and is primarily from populations at risk of developing zinc deficiency. In view of no convincing evidence of benefits from the limited data available currently, there is no justification for recommending routine zinc supplementation for breastfed low birth weight newborns in these populations. Future research and trials on this subject should examine: outcomes in more settings in Asia and Africa; and should be adequately powered to estimate mortality. These trials should also record feeding status of participants and record causes of death and morbidities other than diarrhea and ARI.

Contributors: AG prepared the protocol, applied the search strategy, retrieved the articles, and extracted data. HPSS developed the idea for review, finalized the protocol and search strategy, confirmed the extracted data, and did the statistical analysis. SB prepared and finalized the protocol. All authors contributed to the drafting of the final version of the paper. AG and HPSS will act as joint guarantors.

Funding: Department of Child and Adolescent Health and Development, World Health Organization and Sitaram Bhartia Institute of Science and Research, B-16 Qutab Institutional Area, New Delhi, India. The funding sources had no involvement in the study or the decision to publish the manuscript.

Competing interest: None stated.

REFERENCES

1. Sachdev HPS, Shah D. Epidemiology of maternal and fetal malnutrition in South Asia. *In*: Bhutta ZA, editor. Oxford: Perinatal and Newborn Care in South Asia. Ed.: Oxford University Press. 2007. p. 75-105.
2. Singh PP, Khushlani K, Veerwal PC, Gupta RC. Maternal hypozincemia and low-birth-weight infants. Clin Chem. 1987;33:1950.
3. Goel R, Misra PK. Study of plasma zinc in neonates and their mothers. Indian Pediatr. 1982;19:611-4.
4. Jeswani RM, Vani SN. A study of serum zinc levels in cord blood of neonates and their mothers. Indian J Pediatr. 1991;58:683-6.
5. Bhandari N, Taneja S, Mazumder S, Bahl R, Fontaine O, Bhan MK; Zinc Study Group. Adding zinc to supplemental iron and folic acid does not affect mortality and severe morbidity in young children. J Nutr. 2007;137: 112-7.
6. Dietary reference intakes for Vitamin A, Vitamin K,

Arsenic, Boron, Chromium, Copper, Iodine, Iron, Manganese, Molybdenum, Nickel, Silicon, Vanadium, and Zinc. A Report of the Panel on Micronutrients, Subcommittees on Upper Reference Levels of Nutrients and of Interpretation and Uses of Dietary Reference Intakes, and the Standing Committee on the Scientific Evaluation of Dietary Reference Intakes, Food and Nutrition Board, Institute of Medicine. Zinc. National Academy Press, Washington, DC, 2001 p 442-501. Available from: www.nap.edu/openbook.php?record_id=10026 & page=442. Accessed on December 2, 2009.
7. Hotz C. Dietary indicators for assessing the adequacy of population zinc intakes. Food Nutr Bull. 2007;28:S430-48.
8. Higgins JPT, Altman DG on behalf of the Cochrane Statistical Methods Group and the Cochrane Bias Methods Group. Assessing risk of bias in included studies. *In*: Higgins JPT, Green S, eds. Cochrane Handbook for Systematic Reviews of Interventions. New Jersey: John Wiley & Sons Inc. 2008. p.187-241.
9. Sterne JAC, Egger M, Smith GD. Investigating and dealing with publication and other biases. *In*: Egger M, Smith GD, Altman DG, eds. Systematic Reviews in Health Care: Meta-analysis in Context. London: BMJ Books. 2001. p. 189-208.
10. Sterne JAC, Bradburn MJ, Egger M. Meta-analysis in STATA ™. *In*: Egger M, Smith GD, Altman DG editors. Systematic Reviews in Health Care: Meta-analysis in Context. London: BMJ Books. 2001. p.347-369.
11. Steichen TJ, Egger M, Sterne JAC. sbe19.1: Tests for publication bias in meta-analysis. Stata Technical Bulletin. 1998;44:3-4.
12. Harris R, Bradburn MJ, Deeks J, Harbord R, Altman D, Steichen T, *et al*. Stata Version 9 Update (Distribution Date February 19, 2007) for the Stata User Written Programme sbe24 (Bradburn MJ, Deeks JJ, Altman D. sbe24: metan - an alternative meta-analysis command. Stata Technical Bulletin 1999; 44: 4-15). Available from: http://fmwww. bc.edu/RePEc/bocode/m. Accessed on March 24, 2007.
13. Higgins JPT, Thompson SG. Quantifying heterogeneity in a meta-analysis. Stat Med. 2002;21:1539-58.
14. Harbord R, Steichen T, Sharp SJ. 2004. "metareg: update to Stata module to perform meta-analysis regression" (Sharp SJ. sbe23: Meta-analysis regression. Stata Technical Bulletin 1998; 42: 16-22). Statistical Software Components S4446201, Boston College Department of Economics, revised 02 Feb 2005. Available from: http://ideas.repec.org/c/boc/bocode/s446201.html. Accessed March 15, 2007.
15. Friel JK, Andrews WL, Matthew JD, Long DR, Cornel AM, Cox M, *et al*. Zinc supplementation in very-low-birth-weight infants. J Pediatr Gastroenterol Nutr. 1993;17:97-104.
16. Ashworth A, Morris SS, Lira PI, Grantham-McGregor SM. Zinc supplementation, mental development and behaviour in low birth weight term infants in northeast Brazil. Eur J Clin Nutr. 1998;52:223-7.
17. Sazawal S, Black RE, Menon VP, Dinghra P, Caulfield LE, Dhingra U, *et al*. Zinc supplementation in infants born small for gestational age reduces mortality: a prospective, randomized, controlled trial. Pediatrics. 2001;108:1280-6.
18. Castillo-Durán C, Perales CG, Hertrampf ED, Marín VB, Rivera FA, Icaza G. Effect of zinc supplementation on development and growth of Chilean infants. J Pediatr. 2001;138:229-35.
19. Osendarp SJM, Santosham M, Black RE, Wahed MA, van Raaij JMA, Fuchs GJ. Effect of zinc supplementation between 1 and 6 mo of life on growth and morbidity of Bangladeshi infants in urban slums. Am J Clin Nutr. 2002;76:1401-8.
20. Díaz-Gómez NM, Doménech E, Barroso F, Castells S, Cortabarria C, Jiménez A. The effect of zinc supplementation on linear growth, body composition, and growth factors in preterm infants. Pediatrics. 2003;111:1002-9.
21. Black MM, Sazawal S, Black RE, Khosla S, Kumar J, Menon V. Cognitive and motor development among small-for-gestational-age infants: impact of zinc supplementation, birth weight, and caregiving practices. Pediatrics. 2004;113:1297-1305.
22. Loui A, Raab A, Wagner M, Weigel H, Grüters-Kieslich A, Brätter P, *et al*. Nutrition of very low birth weight infants fed human milk with or without supplemental trace elements: a randomized controlled trial. J Pediatr Gastroenterol Nutr. 2004;39:346-53.
23. Jimenez R, Martinez M, Penalver R. Effect of zinc on growth and development of children with low birth weight. Colombia Medica. 2007;38:6-13.
24. Castillo-Duran C, Rodriguez A, Venegas G, Alvarez P, Icaza G. Zinc supplementation and growth of infants born small for gestational age. J Pediatr. 1995;127:206-11.
25. Sur D, Gupta DN, Mondal SK, Ghosh S, Manna B, Rajendran K, *et al*. Impact of zinc supplementation on diarrheal morbidity and growth pattern of low birth weight infants in Kolkata, India: a randomized, double-blind, placebo-controlled, community-based study. Pediatrics. 2003;112:1327-32.
26. Taneja S, Bhandari N, Rongsen-Chandola T, Mahalanabis D, Fontaine O, Bhan MK. Effect of zinc supplementation on morbidity and growth in hospital-born, low-birth-weight infants. Am J Clin Nutr. 2009;90:385-91.
27. Human Development Report 2009, United Nations Development Programme. Available from: http://hdr.undp.org/en/media/HDR_2009_EN_Complete.pdf. Accessed on November 26, 2009.