

ORIGINAL ARTICLE

Birth Weight and Early Neonatal Outcome in Infants Born to Malnourished Pregnant Women given Multimicronutrient Supplementation: A Comparative Study.

R. Chakrabarti, SP Goel, K Dubey*.

Abstract

Objective: To study the effect of multimicronutrient supplementation to malnourished pregnant women on the birth weight and early neonatal outcome.

Design: Randomized control trial

Settings: Department of Pediatrics & Gynecology and Obstetrics, LLRM Medical College, Meerut.

Methods and Materials: 350 pregnant women carrying singleton pregnancy, any gravidity with body mass index (BMI) < 21, and hemoglobin between 7 – 9 gm/dl without established risk factors were enrolled in the study at 20 weeks of pregnancy. They were divided into 3 groups. First group was given multi micronutrient supplement from 20 weeks to term, second group from 20 weeks to 30 weeks, and the third was given placebo tablets. At the time of delivery, birth weights, neonatal anthropometry, were recorded and the babies were followed up for 7 days for complication. All the recorded data was analyzed using Chi-square test.

Results: An increase of birth weight by 185 gm was found in that group who were supplemented for longest period than the placebo group and difference in the birth weight among any 1st and any of the other 2 groups were statistically significant ($p=.001$ in 1st and 3rd, 0.1 in 2nd and 3rd, 0.02 in 1st and 2nd group). The number of sick neonates was significantly increased in placebo group (40.58%) as compared to the two supplemented groups (20.58% and 23.81 % respectively).

Conclusion: Based on the result of above study it can be said that multi-micronutrient supplementation to malnourished women reduces the risk of Low birth weight (LBW) and early neonatal morbidity.

Key Words: Birth weight, Malnutrition, Pregnant women, Multi-micronutrient, Neonate.

Introduction

In India, incidence of low birth weight (LBW) (those with a birth weight of less than 2500 g) is 30%. Two-third of them are due to intrauterine growth retardation (IUGR). This precipitates mortality and morbidity not only during neonatal period but also in infancy and childhood (1). It has also been demonstrated that babies who are small or disproportionate at birth have increased risk of developing coronary heart disease, non insulin dependent diabetes mellitus (NIDDM), and hypertension during adult life(2). One of the easiest methods to increase birth weight is to improve the nutritional status of the expectant mothers of India where most of the pregnant ladies are undernourished. It now appears that several nutrient factors including both the macronutrients and micronutrients may be deficient in mothers and children of developing countries which can have adverse effects on the mothers also like anemia, hypertension, complications of labor (more oxidative stress) and even death. Moreover, the available scientific evidence indicates that intrauterine nutritional status of infant has a profound and persistent influence on physical growth, immune

competence, and neurological and cognitive functions (5). So the current study was carried out with the objectives of comparing the birth weight and early neonatal outcome (during the first week of life) in neonates born to malnourished women administered micronutrient supplementation vs. placebo.

Methods and Materials

The placebo controlled randomized study was conducted in the Department of Pediatrics in association with the department of Obstetrics and Gynecology at LLRM Medical College and associated SVBP Hospital, Meerut, from June 2005 to July 2006. The participants were randomized by simple random sampling to receive micronutrient supplementation long term (20 weeks-term), short term (20-30 weeks of gestation), or placebo(20 weeks-term). 350 women in the age group 19-35 years of any gravidity with 18- 20 weeks pregnancy [by calculating from the first day of last menstrual period (LMP)], carrying a singleton pregnancy having a body mass index (BMI) of less than 21.0 and/or hemoglobin percentage 7-9 g/dL and planning to deliver their babies in his hospital were considered for enrollment after informed signed consent. 83 women did not turn up and thus 257 women were finally included and randomized with 90 women in Group 1, 80 women in group2 and 87 women in Group 3. Women with an established medical risk factor and which would reduce or increase birth weight of the neonate, were excluded from the initial sample. The procedure followed in the present study was in accordance with the ethical standards of the institutional ethical committee and with the Helsinki declaration of 1964 as revised in 2004 and was commenced after getting the approval of the institutional ethical committee.

The composition of the micronutrient tablet was as follows: Vit A - 2500 IU, B1 - mononitrate 2 mg, B2 - 2 mg, B6 - 1.5 mg, B12 - 1.5 mcg, Vit E acetate - 10 IU, Calcium D-pantothenate - 3 mg, Folic acid - 0.30 mg, Nicotinamide - 15 mg, Zinc - 7.5 mg, Manganese chloride - 1.4 mg, Copper - 2.5 mg, Phosphorus - 125 mg, Potassium - 40 mg, Chloride - 36.3 mg, Chromium - 65 mcg, Molybdenum - 25 mcg, Sodium selenate - 30 mcg, Vanadium - 10mcg, Boron - 150 mcg. Placebo tablets contained Calcium 500 mg. The supplement was taken on once daily basis at any time of the day. The tablets were given to the participants on fortnightly basis and they were asked to maintain a record of its consumption. All the participants were advised proper diet (based on Indian council of Medical Research-ICMR recommendation for pregnant women) (6) and iron and folic acid, calcium and vitamin D supplementation in usual dosages i.e. 100mg, 500 mg, 1000mg and 400IU respectively, along with routine antenatal advises, immunization and health education. At each antenatal visit, the participants were questioned regarding compliance and side effects of the drugs. Placebo group also took the tablet on once daily basis from 20 weeks till delivery. Their compliance was also monitored. Baseline data was recorded including the past obstetric history, gestational age, nutritional status of the mothers [by body mass index (BMI) and hemoglobin estimation].

Monitoring was carried out during each antenatal visit, which is fortnightly till 36 weeks and then weekly till delivery.

Neonatal details included a record of gestational age by new Ballard's score (7) and birth weight by an electronic weighing scale. The newborn was labeled as term (37- 41weeks), preterm (<37 weeks), very preterm (32 weeks), or post term (>42 weeks). All the newborns were classified for their weight for gestational age with Lubchenko's chart of intrauterine growth (8). They were followed up for 7 days for mortality and morbidity. Weight at birth of the neonates, gestational age and early neonatal outcome in different groups were compared using Chi-square test. (9)

Results

Baseline maternal characteristics in the Micronutrient Vs Placebo Supplementation Groups is depicted in Table 1. Maximum duration of supplementation was (placebo or multimicronutrient) 21.4 weeks. The compliance in 3 groups was comparable -average 68.57%. No significant adverse effect was found in association with the supplementation. Women in the 1st supplementation group gained a mean weight of 10.20±2.56 kg during pregnancy and 9.60±2.0 kg in the second supplementation group. The average gain in weight in the placebo group was 8.95±2.30 kg. Of the 257 subjects in whom supplementation/ placebo was started, the detail about the delivery was available for 245 women (12 women did not deliver their baby in this hospital and could not be traced). Of these 245 women, 87 belonged to Group I, 76 belonged to Group II and 82 belonged to Group III. Obstetric complications during or just after delivery were similar in all 3 groups. The

mean gestational age at delivery was 39.6±1.4, 39.9±1.2 and 38.8±1.9 weeks in group 1,2 and 3 respectively, the difference being statistically insignificant (p=0.992). Five babies (2, 1, 2 in the 3 groups respectively) were stillborn. Total 12 babies were born as premature (4, 3, 5 in group 1,2 and 3 respectively) (p=0.812). The incidence of small for gestational age (SGA) was 10, 14, 31 in the 3 groups respectively, the difference became statistically significant (p=0.002). The birth weight ranged from 750 g to 3500 g. The mean birth weight in the first supplementation group was 2735g as compared to 2550g in the placebo group. The mean difference was 185g and found to be significant (p = 0.001). Again mean birth weight of the 2nd supplementation group was 2610g and when compared to the placebo group was found to be insignificant (p =0.100). Mean difference between 1st and 2nd supplementation group was 125 gm which was also significant (p =0.010).

Among these 240 cases, 200 neonates could be followed up during early neonatal period (first week). Details of early neonatal morbidity is shown in Table 2. Out of these 200 neonates 68 were in the 1st micronutrient group, 63 were in 2nd group and 69 in the placebo group. Morbidity (total sick neonates) was recorded in 57/200 (28.5%) neonates during the first week of life. Among these sepsis was the commonest sickness. The difference in the total number of sick neonates is significant among 1st and 3rd and 2nd and 3rd group (p=0.030), but the difference between 1st and 2nd group was not significant (P=0.400) and also, except sepsis, for all other sickness, the difference among the 3 groups were not statistically significant.

Table I. Baseline Maternal Characteristics in the Micronutrient Vs Placebo Supplementation Groups

Maternal parameters	Group I Multi - micronutrient (20 weeks to term)	Group II Milti - micronutrient (20 to 30 weeks)	Group III Placebo
No. of subjects	90	80	87
Maternal age (Years)	24.5± 2.4	24.1± 3	24.4 ± 2.8
Family income/ month (Rs.)	4550±1490	4200±1200	4300±1110
Enrolment weight (Kg.)	43.9±3.1	44.4±2.8	46.0±2.1
Height (Cm)	153.0±2.7	152.4±3.1	150.8±3.4
BMI	18.7±1.8	18.2±2.4	19.1±2.0
Hemoglobin (gm/dl)	9.5±1.3	9.0±1.0	9.2±2.1
Primigravida	60(66.6%)	58(72.5%)	52(59.7%)
Slum residence	66(73.3%)	60(75.0%)	66(75.8%)
Illiterate	36 (40.0%)	35(43.75%)	29(33.3%)
Domestic physical activity	88(97.7%)	77(96.2%)	80(92.0%)
Previous low birth weight	21(23.3%)	17(21.25%)	12(13.7%)
BMI(<21)	86(96.0%)	78(98.0%)	84(96.0%)

Table 2: Illness in the Early Neonatal Period (Number of Neonates = 200)

Illness	Group 1 Multi- micronutrient (20 weeks to term) (n=68)	Group2 Multi - micronutrient (20 to 30 weeks) (n=63)	Group 3 Placebo (n=69)	Total (n=200)
Number of sick neonates	14 (20.58%)	15 (23.81%)	28 (40.58%)	57 (28.5%)
Sepsis	6 (8.82%)	7 (11.11%)	14 (20.29%)	27 (13.5%)
Jaundice	3 (4.41%)	4 (6.35%)	5 (7.24%)	12 (6.0%)
Convulsion	2 (2.94%)	2 (3.17%)	4 (5.79%)	8 (4.0%)
Hemorrhagic disease of newborn	1 (1.47%)	1 (1.59%)	2 (2.90%)	4 (2.0%)
Hypoglycemia	2 (2.94%)	1(1.59%)	3 (4.34%)	6 (3.0%)

Discussion

Maternal nutrition is a critical determinant of the outcome of pregnancy. Deficiencies of micronutrients like vitamin A, folic acid, iron and zinc are widely prevalent in population of developing countries,(10) which has been shown to increase the risk of low birth weight (LBW), pregnancy complications and birth defect.

In the previous studies like Mexico Study (11,12) , Nepal study (13-15), it was found, though multimicronutrient supplementation improves maternal health and replenishes the deficit, it hardly affects birth weight. In these cases selection of study subjects did not stress upon maternal malnutrition probably for this reason failed to show any positive result. But in an Indian study (3), China study (16) it was found that multimicronutrient supplementation to malnourished mother, improved birth weight significantly. This Indian Study (3) also showed that the supplementation reduces metabolic complications of neonates. Another study done in Delhi (17) also corroborated this finding. But that study failed to show the optimum time period of supplementation. Tanzania Study (4) again showed that micronutrient supplementation improves birth weight of babies born to HIV-affected mothers. In our study we provided malnourished pregnant ladies, a multi-micronutrient supplement, that contained 20 micronutrients of which 12 were suggested by World Health Organization/United Nations Children's Fund (WHO/UNICEF) expert group (18-20) and 8 additional micronutrients. These included pantothenic acid, manganese, phosphorus, potassium, chlorine, chromium, molybdenum and vanadium which have a close proximity to the USA/Canadian Recommended daily allowances (RDA) references (21,22) for each nutrient. The supplementation was given from mid-second trimester to 3rd trimester of pregnancy as maternal malnutrition gets precipitated during this time.

First and foremost malnourished women were identified properly as they are at risk for producing a LBW and SGA babies. Another approach available for increasing micronutrient intake include dietary modification which was taken in Pune Study (23) but as the malnourished ladies have less inclination and reach to micronutrient rich foods and to change their habit might take more time, we have tried medical intervention which provided a rapid improvement in the nutritional status of the target groups. In this study, almost all the enrolled subjects were having regular antenatal checkups and dietary counseling, birth weight was available in 68.57% of the enrolled pregnancies. This follow-up loss is also consistent with the previous studies. (11-14) Birth weight exceeded by 185 gm in the micronutrient supplementation group who were supplemented for the longest time compared to the placebo. Even by adjusting maternal parity, gestational age and fetal gender, birth weight increased significantly if the duration of multi-micronutrient supplementation was more and specifically continued during 3rd trimester (as the difference in weight between placebo group and 2nd group was not significant). So duration of supplementation and specific time frame appear to decrease the incidence of low birth weight (LBW). There was also statistically significant decrease in SGA. These observations go in favor of the micronutrient supplementation, which also act as antioxidants (6, 23). But we found no significant decrease of prematurity by this supplementation. We studied the early neonatal morbidity in the micronutrient supplementation group as compared to the placebo. The difference in number of sick neonates in 1st and 3rd group and 2nd and 3rd group was statistically significant. But the difference in 1st and 2nd group was not significant. That means though 2nd trimester supplementation does not improve birth weight much it builds up immunity to developing fetus as incidence of sepsis was almost double in non

supplemented group. So it appears that multi-micronutrient supplementation to pregnant women does reduce the risk of SGA and the incidence of neonatal illnesses. The increase in birth weight in the supplementation group is related to the duration of the micronutrient supplementation but irrespective of the duration of supplementation, early neonatal morbidity is reduced in the micronutrient group.

Conclusion

It can be concluded that, dietary improvement and a small intervention like providing one multi-micronutrient tablet per day to identified malnourished women can take us a long way towards improving birth weight, decreasing neonatal morbidity and thus attaining the national goal of decreased infant mortality rate. More studies on a large scale by considering other determinants are required before national recommendations can be made.

Acknowledgement

We acknowledge the cooperation of all the pregnant ladies and all the departmental staff without whose help this study would not be successful.

Contributors

RC was involved in designing the study, collection and analysis of data and preparation of the manuscript, SPG was involved with the designing the study, analysis of the data and results and reviewing of the manuscript, KD was involved in designing the study, collection of data and taking gynecological decision, and preparing the manuscript.

Funding: None.

Competing Interest: None.

References:

1. Fact sheet-NFHS-3. National Family Health Survey (NFHS-III), available on: URL: <http://www.nfhsindia.org>. Accessed on May 10, 2007.
2. Barker DJP. Mothers, Babies and health in later life. 2nd edition Churchill Livingstone, Edinburgh, U.K.1998.
3. Shah D, Sachdev HP. Maternal micronutrients and fetal outcome. *Indian J Pediatr* [serial online] 2004 [cited 2007 Jun 17];71:985-990. Available from: <http://www.ijppediatricsindia.org/text.asp?2004/71/11/985/13528>
4. Fawzi WF, Msamanga G, Spiegelman D, Urassa E, McGrath N, Mwakagile D et al. Randomized trial of effects of vitamin A supplements on pregnancy outcomes and T cell counts in HIV-1 infected women in Tanzania. *Lancet* 1998; 351: 1477-1482.
5. Udipi SA, Ghugre P, Antony U. Nutrition in pregnancy and lactation. *J Ind Med Assoc* 2000; 98:548-57.
6. Indian Council of medicine Research recommended dietary intakes for Indians, ICMR, New Delhi, India (1987).
7. Ballard JL, Khoury JC, Wedicgk et al. New Ballard Scores expanded to include extremely premature infants. *J Pediatr*. 1991; 119: 417-23.
8. J.P.Cloherty, E.C.Eichenwald, A.R.Stark: Manual of Neonatal Care ; 5th Edition: 116f : Lippincott Williams & Wilkins. 2003.
9. Fisher.R.A.& Yates.F, Statistical table for biological ,agricultural and medical research,6th edition, Longman Group Ltd.London,1974.
10. Singh M. Care of the Newborn, 6th ed.23-232 ,New Delhi: Sagar publications; 2004.
11. Ramakrishnan U, Manjrekar R, Rivera J et al. Micronutrients and pregnancy outcome. A Review of

Literature *Jutr Res* 1999; 17:103-59.

12. Ramakrishnan U, Gonzalez-Cossio T, Neufield LM et al. Multiple micronutrient supplementation during pregnancy does not lead to greater infant size than does iron-only supplementation: a randomized controlled trial in a semi-urban community in Mexico. *Am J Clin Nutr* 2003; 77: 720-5.

13. Christian P, Khattry SK, Katz J et al. Effects of alternative maternal micronutrient supplements on low birth weight in rural Nepal: double blind randomized community trial. *BMJ* 2003; 326: 571-6.

14. Christian P, S.C. LeClerq, S.R.Shrestha, Khattry SK. Antenatal supplementation with micronutrients and biochemical indicators of status and subclinical infection in rural Nepal. *Am.J. Clinical Nutrition* 2006,83:788-94.

15. West KP Jr, Katz J, Khattry, P.Christian. The NNIPS-2 study group (1999) double blind, cluster randomized trial of low dose supplementation with Vit A or B-carotene on mortality related to pregnancy in Nepal. *BMJ* 1999; 318: 570-5.

16. Effect of micronutrients supplementation on the health of pregnancies and the growth and development of fetus and children—study by National Institute for Nutrition and Food Safety, (The second prize winner literature of Chinese Medical Association for science and Technology in 2002) Chinese Center for Disease Control and Prevention available at URL <http://www.chinacdc.net.cn/n272562/n276719> accessed on 14th June,2007.

17. Ray M. Birth weight and early neonatal outcome in infants born to malnourished pregnant women given multimicronutrient supplementation –a double blind randomized control trial.-2002-2003. Post graduate thesis submitted for MD Pediatrics 2004 at University College of Medical Science and Guru Tej Bahadur Hospital, New Delhi.

18. Kant AK, Consumption of energy dense, nutrient poor foods by adult Americans: nutrition and health implications. The third National Health and Nutrition Examination Survey, 1988-1994. *Am J Clin Nutr* 2000; 72: 929-36.

19. UNICEF Composition of a micronutrient supplement to be used in pilot programmes among pregnant women in developing countries (1999).

20. WHO requirements of Ascorbic Acid, Vit D, Vit B-12, folate and iron. *World Health Organ Tech Rep Ser* 1972; 452.

21. A National Collaboration Study of identification of high risk families, mothers and outcome of their offspring with particular reference to the problem of maternal nutrition, low birth weight, perinatal and infant morbidity and mortality in rural and urban slum communities. An ICMR Task Force study, Indian Council of Medical Research, New Delhi, 1990.

22. National Research Council. Recommended Dietary Allowances. Washington DC: national academy Press, 1989.

23. Kinare, A. S., Natekar, A. S., Chinchwadkar, M. C., Yajnik, C. S., Coyaji, K. J., Fall, C. H. D. & Howe, D. T. (2000) Low mid-pregnancy placental volume in rural Indian women: a cause for low birth weight? (The Pune Maternal Nutrition and Fetal Growth Study). *Am. J. Obstet. Gynecol.* 182: 443-448

E-published: November 2008

From: Department of Pediatrics & Gynaecology*, LLRM Medical College & SVBP Hospital, Meerut.

Address for Correspondence: R. Chakrabarti, Dept of Pediatrics and Neonatology, LLRM Medical College, Meerut. E-mail: dr_raktima@yahoo.com