e-ISSN: 0975-1556, p-ISSN:2820-2643
Available online on www.ijpcr.com
International Journal of Pharmaceutical and Clinical Research 2024; 16(5); 1835-1840

Original Research Article

# Observational Study Correlating Maternal Serum and Cord Blood Zinc Levels with Fetal Growth Restriction

**Kumari Shilpa[1], Pratibha Jha[2], Seema Prasad[3]**

[1]Ex. Senior Resident, Department of Obs and Gynae, DMCH, Laheriasarai, Darbhanga
[2]Senior Resident, Department of Obs and Gynae, DMCH, Laheriasarai, Darbhanga
[3]Professor & Head, Department of Obs and Gynae, DMCH, Laheriasarai, Darbhanga

**Received: 25-02-2024 / Revised: 23-03-2024 / Accepted: 25-04-2024**
**Corresponding Author: Dr. Pratibha Jha**
**Conflict of interest: Nil**

**Abstract:**

**Background:** To study maternal serum and cord blood zinc as causal factor in fetal growth restriction and to find out correlation, if any, between birth weight and maternal serum and cord blood zinc levels.

**Material and Methods:** This prospective observational study was carried out on 120 term pregnant women who attended the Department of Obstetrics and Gynaecology, at DMCH Laheriasarai, Darbhanga. of which, 60 had FGR babies and 60 had normal growth babies. Serum zinc levels were studied in these women and cord blood zinc levels in their neonates.

**Results:** After adjusting for other variables in the multivariable model we found that the mean serum zinclevel in study group women was 115.65±6.36µg/dL at term and 116.91±6.39µg/dL in late preterm neonates. Also, we found that the mean cord blood zinc levels were 136.03±9.25µg/dL in study group and135.24±4.72µg/dL in control group in term neonates while in late preterm neonates, it was 135.06±9.52µg/dL in study group and 133.18±6.58µg/dL in control group. A statistically significant positive correlation was found between birth weight of FGR babies with the maternal serum zinc levels atterm and between cord blood zinc levels and birth weight in both preterm and term neonates.

**Conclusion:** Zinc is an essential micronutrient during pregnancy and is needed for fetal development andplacental functions. Its role in fetal growth and development, need of supplementation in pregnant women needs to be studied further to demonstrate better clinical outcomes in women with growth retarded fetus.

**Keywords:** Cord blood zinc, Fetal growth restriction, late preterm neonates, maternal zinc, micronutrients, term neonates.



## Introduction

Fetal growth restriction (FGR) has been defined as the rate of fetal growth that is below the growth potential of a specific fetus as per the race and gender of fetus. FGR is a clinical definition and applies to neonates born with clinical features of malnutrition and in-utero growth retardation, irrespective of their birth weight percentile. FGRcan be a diagnosis at term and even in babies born prematurely. The incidence of FGR is approximately 5-10% of all pregnancies. [1] Fetal growth is regulated at multiple levels starting from maternal components to placenta,

environmental factors and even fetal components. The maternal- placental- fetal unit act in harmony to provide needs of fetus while supporting the physiological functions of the mother. The maternal causes of FGR include malnutrition, substance abuse and smoking, high blood pressure, chronic kidney disease, chronic anemia, advanced diabetes mellitus, hematological disease, cardiovascular disease, respiratory disease and infections. These factors hamper nutrition delivery to the fetus leading to FGR. The placental factors comprise of factors leading to chronic placental insufficiency as in placental infarcts, circumvallate placenta, chorioangiomata or velamentous cord insertion. [2]Idiopathic FGR counts for around 40% of all FGR cases. [3] One of the investigated causes behind the reduced birth weight is nutritional deficiency in the mother. Micronutrients like zinc comprise a small yet significant part to this nutrition. It is needed in general metabolism pathways and so is an important type 2 nutrient. Zinc is one of the most abundant trace element inhumans and interacts with proteins by promotingenzymatic processes where it has either catalytic or coactive or a structural role. Thus, its role becomes particularly important in period of increased metabolism as in fetal growth.

Birth weight is significant indicator of the normal growth milestones during fetal life and indetermining neonatal prognosis apart from beinga reflection of maternal health. FGR has important implications

not just for the fetus, childand adult, but also for the parents and the society. Multiple studies have been conducted to study causes of FGR [4-8] but studies on micronutrients as causal factor in FGR are rare. Keeping that in mind, the present study was undertaken to study maternal serum zinc and cord blood zinc as causal factor in fetal growth restriction.

## Material and Methods

This prospective observational study was carried out on pregnant women who attended the Department of Obstetrics and Gynaecology, DMCH Laheriasarai, Darbhanga, Bihar. after obtaining their informed and written consent. 120 women were included in the study, 60 cases and 60 controls. Women at term with clinical or sonographic diagnosis of FGR were considered as cases. Controls were taken from normal healthy women at term similar to cases but carrying normal growth babies. Women with PIHand chronic hypertension, had history of alcoholuse or smoking or use of any supplements apart from iron, calcium and folic acid, women with antepartum infections, with APH, PROM, prolonged labour, history of blood transfusions in current pregnancy, uterine malformation and with any systemic disease were excluded from the study. Gestational age was calculated from first day of last menstrual period and was confirmed by first trimester scan, if available. Women with difference of 2cm or more between period of gestation and symphysio-fundal height were clinically diagnosed as Fetal Growth Restriction or women diagnosed with FGR babies on color Doppler velocimetery even in absence of any clinical difference in SFH, were included as cases in the study. 6ml venous blood samples of study subjects were collected in red vaccutainers and labelled by name and Hospital Registration Number of patient. 6ml cord blood samples from placental end of umbilical cord of neonates of study subjects were also collected in red vaccutainers at the time of delivery and labelled by name and Hospital Registration Number of patient. Serum was separated by centrifugation and stored at -20ºc till analysis. Samples were analyzed for zinc levels using colorimetric kit. [9]

## Statistical Analysis

At the end of the study, all the data was compiled and analysed by using Student t-test for quantitative variables and Chi-square test for qualitative variables. A p value of <0.05 was considered statistically significant. Statistical package for Social Sciences (SPSS) version 21.0

was used for statistical analysis. Correlation Coefficient was calculated to deduce correlation between the variables.

## Results

Majority of women belonged to 21-25years age group i.e 50% in both study and control group.

Majority women belonged to upper lower socioeconomic status in both groups. It was found that majority patients were nulliparous in both the groups. The educational levels between study and control population was similar.

The mean pre-pregnancy weight was similar in both groups.

**Table 1: Demographic parameters**

| | Study group | Control group | P value |
|---|---|---|---|
| Mean age | 23.85±4.45yrs | 23.48±3.64yrs | 0.664 |
| Mean caloric intake (kcal) | 2359.83±76.74 | 2336.67±55.13 | 0.325 |
| Mean BMI (kg/m$^2$) | 21.35±0.82 | 21.5±0.79 | 0.304 |

The mean abdominal girth was found to be more in control group. The difference between the two groups was statistically significant (p value <0.0001) Majority of the women in study group (57.14%) had difference of 2-4cm between gestation age and symphysiofundal height in the study group. Of these, 4.76% women had SFH difference more than 4cm and 21.43%women had a difference of less than 2cm while in control group, 41.18%women had less than 2cm difference between SFH and gestational age (p<0.0001).

**Table 2: Comparative birth weight between the two groups**

| | Term | | Late preterm | |
|---|---|---|---|---|
| **Birth weight(kg)** | **Study Group (n=42)** | **Control Group (n=51)** | **Study group (n=18)** | **Control group (n=9)** |
| <1.8 | 2 (4.76%) | 0 (0%) | 3 (16.67%) | 0 (0%) |
| 1.8-1.99 | 2 (4.76%) | 0 (0%) | 4 (22.22%) | 0(0%) |
| 2-2.499 | 38 (90.48%) | 0 (0%) | 11 (61.11%) | 2 (22.22%) |
| >=2.5 | 0 (0%) | 51 (100%) | 0 (0%) | 7 (77.78%) |
| Mean ± SD | 2.18 ± 0.21 | 2± 0.27 | 1.95±0.21 | 2.58±0.23 |
| P value | <0.0001 | | 0.0002 | |

Of the study group subjects, only 5% underwent cesarean section, all due to fetal distress.

**Table 3: Mode of delivery**

| Mode of delivery | Study group(n=60) | Control group(n=60) | P value |
|---|---|---|---|
| LSCS | 3 (5%) | 0 (0%) | 0.244 |
| Vaginal delivery | 57 (95%) | 60 (100%) | |

NICU admissions were significantly more in study group while there were no NICU admissions in controlgroup and 25% of admitted neonates expired in NICU

**Table 4: NICU admission and outcome**

| NICU admission | Study Group(n=42) | Control Group(n=51) | P value |
|---|---|---|---|
| No | 38 (90.48%) | 51 (100%) | 0.038 |
| Yes | 4 (9.52%) | 0 (0%) | |
| OUTCOME | | | |
| Discharged | 3 (75%) | 0 (0%) | |
| Expired | 1 (25%) | 0 (0%) | |

The difference between the serum zinc values in study group and control group was found to be statisticallynon-significant at both late preterm and term gestation. (Reference range for serum zinc at biochemistry lab DMCH was 60-120µg/dl). Also, the difference between cord blood level of zinc in both the groups at late preterm and term gestation was not statistically significant.

**Table 5: Zinc levels (µg/dL)**

| | >37weeks | | 34-37weeks | |
|---|---|---|---|---|
| Serum zinc levels (µg/dL) (Maternal) | Study Group (n=42) | Control Group(n=51) | Study group (n=18) | Control group (n=9) |
| 60-120 | 35 (83.33%) | 45 (88.24%) | 13 (72.22%) | 8 (88.89%) |
| >120 | 7 (16.67%) | 6 (11.76%) | 5 (27.78% | 1 (11.11%) |
| Mean ± SD | 115.65 ± 6.36 | 2 6.16 | 116.91±6.39 | 114.6±6.52 |
| P value | 0.497 | | 0.628 | |
| Cord blood Zinc | | | | |
| >120 | 42 (100%) | 51 (100%) | 18 (100%) | 9 (100%) |
| Mean±SD | 136.03±9.25 | 135.24±4.72 | 135.06±9.52 | 133.18±6.58 |
| P value | 0.616 | | 0.602 | |

It was observed that, in the study group, there was statistically significant correlation betweenmaternal serum zinc levels and birth weight at term, such that increase in birth weight was observed with increase in maternal serum zinc levels but birth weight decreased with increasing serum zinc levels in control group. However, thiscorrelation between them was statistically non- significant. No statistically significant correlation was demonstrated between maternal serum zinc levels and birth weight in the control group. Statistically significant correlation of cord bloodzinc with the birth weight was demonstrated in the late preterm study group and the term study group.

**Table 6: Correlation of Zinc with birth weight**

| | Maternal | | Cord blood | |
|---|---|---|---|---|
| | Study group | Control group | Study group | Control group |
| 34-37 weeks | | | | |
| Correlation coefficient | 0.394 | 0.306 | 0.611 | 0.096 |
| P value | 0.107 | 0.437 | 0.008* | 0.843 |
| >37 weeks | | | | |
| Correlation coefficient | 0.350 | -0.271 | 0.361 | 0.048 |
| P value | 0.024* | 0.055 | 0.019* | 0.739 |

Spearman rank correlation coefficient (*) indicates significant

## Discussion

Micronutrients play a small yet pivot role incellular growth and differentiation. The present study was conducted to study maternal serum zinc level as causal factor in fetal growth restriction and to find out correlation, if any, between birth weight and maternal serum levels of zinc so as to influence prevention and treatment through micronutrient supplementation or avoiding these micronutrients during antenatal period. FGR is more prevalent in teenage pregnancy as well as in elderly gravida but in the present studymajority of women (50%) in the study group were in age group 21-25years. This was similar to the findings by Roberfroid et al [10] and Ab- Bakari-Rwebembra et al. [11] However,

the mean age was higher in studies by Melda Amalia et al [12]and Tsuzuki et al. [13] this can be accounted tocultural differences in age of marriage around the world. Fetal growth restriction is more commonly seen in nulliparous women. The majority of the women (55%) in the present study were nulliparous. This was in concordance with study conducted by Bermudez et al [14] in which 54.5% women were nulliparous.

Lower socioeconomic status is considered a risk factor for FGR. Majority of the women (76.66%)in present study belonged to lower socioeconomic status based on Modified Kuppuswamy Scale. The findings were similar as in study by Manandhar T Prasad et al [15] where 63.3% women belonged to lower socioeconomicclass and Muhammad T et al. [16]

Symphysio-Fundal height is considered a simple, safe, cheap and reasonable clinical parameter for timely diagnosis of FGR babies. The difference between SFH (cm) and gestational age in weeks more than 2cm is considered FGR, though severe FGR is found with difference of more than 4- 6cm. Here, 38.1% of women were showing no discrepancy or <2cm discrepancy in SFH but were diagnosed to have FGR fetus on Doppler studies. Table 7 shows comparative results with Manandhar T et al.

**Table 7: Symphysio-Fundal Height**

| SFH difference | Present study (study group) | Manandhar T et al[15] |
|---|---|---|
| No difference | 16.67% | 8.33% |
| <2cm | 21.43% | 11.66% |
| 2-4cm | 57.14% | 50% |
| >4cm | 4.76% | 30% |

FGR babies are more prone to intranatal hypoxia and are unable to bear stress of normal labour and so land up in cesarean sections and this is more commonly seen in severe type of FGR. However, majority of the women in present study delivered vaginally as majority of the study group women in present studyhad neonates with mild FGR. Table 8 shows comparative distribution between various studies.

**Table 8: Mode of delivery**

| Mode of delivery | Present study | Manandhar T et al[15] | Jaafar et al[17] |
|---|---|---|---|
| LSCS | 5% | 61.66% | 54% |
| NVD | 95% | 38.32% | 46% |

FGR is characterised usually by low birth weight. The mean birth weight in study group of present study was lower than in studies by Bermudez et al [11], Villar et al [7] & Jaafar et al. [10] The differences in mean birth weight of present study to other studies could be attributed to the fact that average birth weight in India is lower than western countries. Table 9 shows that the mean serum zinc level in women with FGR babies was 115.65±6.36µg/dL and in women with normal growth babies was 113.92± 6.16µg/dL and this was statistically non-significant. This was in agreement with study by Srivastava et al [20] where also no difference was seen between the two groups. This was discordant to studies conducted by Suman et al [18] and Jyotsna S et al. [19] We conclude that there might be a threshold of serum zinc level below which there can be association betweenoccurance of FGR and maternal serum zinc levels and in present study serum zinc in both the groups were found to be in normal range. Also, other unknown underlying factors might coexist in etiology of FGR. The mean serum zinc level was found higher in study group (116.91±6.39µg/dL) women between 34-37weeks of gestation compared to study by Elizabeth et al where it was 70.25±24.59µg/dL. This difference can be due todifference in mineral distribution and salinity depending on the geographical area In the present study, the mean cord blood levels of zinc were similar in study group (136.03±9.25µg/dL) compared to the control group (135.24± 4.72µg/dL). This was in agreement in study by Srivastava et al [20] where no statistically significant difference was observed between cord blood zinc levels in the two comparable groups. However, a statistically significant difference was observed in the groups in study by Jyotsna S et al [19] and Elizabeth et al [21]. This difference could be due to difference ingeographical area where studies were conductedand difference in food habits of the population and the difference in laboratory conditions wherethe samples have been analysed. [22]

**Table 9: Comparison of mean serum zinc level in maternal serum and cord blood**

| >37weeks | Mean maternal serum zinc level in study group (µg/dL) | Control group | P value |
|---|---|---|---|
| Present study | 115.65±6.36 | 113.92±6.16 | 0.497 |
| Suman S et al[18] | 45.96 ±15.14 | 81.33±45.96 | <0.001 |

| | | | |
|---|---|---|---|
| Jyotsna S et al[19] | 67.02±15.99 | 83.59±18.46 | <0.05 |
| Srivastava et al[20] | 6.31±5.09µg/mL | 5.67±2.49µg/mL | Non significant |
| 34-37weeks | | | |
| Present study | 116.91±6.39 | | |
| Elizabeth et al[21] | 70.25±24.59 | | |
| >37 weeks | Mean Cord blood zinc instudy group | Control group | P value |
| Present study | 136.03±9.25 | 135.24±4.72 | 0.616 |
| Jyotsna S et al[19] | 83.45±16.74 | 93.74±16.74 | <0.05 |
| Srivastava et al[20] | 7.86±8.16µg/ml | 9.46±8.35µg/ml | Non significant |
| Elizabeth et al [21] | 78.09±18.39 | 92.24±19.40 | Significant |
| 34-37 weeks | | | |
| Present study | 135.06±9.52 | | |
| Tsuzuki et al[13] | 89±14.3 | | |
| Gupta et al[22] | 46.26±22.54 | | |

## Conclusion

Idiopathic FGR is a rare entity. Zinc is an essential micronutrient during pregnancy and is needed for fetal development and placental functions. The present study shows a statistically significant correlation between maternal zinc levels and FGR in term neonates. The study had a few limitations. The dietary content of zinc was not quantified. Also, serum levels of zinc do not truly define the amount of this micronutrient in the body. Therefore, further larger scale studies are needed to explore the roleof these micronutrients in fetal growth and development, their need of supplementation in pregnant women and to demonstrate better clinical outcomes in women with growth retardedfetus.

## References


1. Bamfo J K, Odibo AO. Diagnosis and management of Fetal Growth Restriction. J Pregnancy 2011; 2011:640715.
2. Manandhar T, Prashad B, Nath Pal M. Risk Factors for Intrauterine Growth Restriction and its Neonatal Outcome. Gynaecol Obstet 2018; 8:1000464.
3. Militello M, Pappalardo E M, Ermito S et al. Obstetric Management of IUGR. J PrenatMed 2009;3(1):6-9.
4. Asta A, Brunelli V, Prefumo F, Frusca T, Lees C. Early onset fetal growth restriction. Matern Health Neonatol Perinatol 2017; 3: 2.
5. Burton G, Jauniaux E. Pathophysiology of placental- derived fetal growth restriction. AJOG 2018; 218: S745-S761.
6. Wang H, Hu YF, Hao JH, Chen YH, Su PY, Wang Y, et al. Maternal zinc deficiency during pregnancy elevates the risks of fetal growth restriction: a population-based birth cohort study. Scientific Rep 2015; 5:1-11.
7. Villar J, Carroli G, Wojdyla D, Abalos E, Giordano D, Ba'aqeel H, et al. Preeclampsia, gestational hypertension, and intrauterine growth restriction related or independent conditions? AJOG 2006;194(4):921-31.
8. Peter S, Michael Y, Bernstein. Etiologies of fetal growth restriction. Clinical obstetrics and gynaecology 1997;40(4):723-29.
9. Beckett JM, Hartley TF, Ball MJ. Evaluationof the randox colorimetric serum copper and zinc assays against atomic absorption spectroscopy. Ann Clin Biochem 2009; 46:322-6.
10. Roberfroid D, Huybregts L, Lanou H, Henry MC, Meda N, Menten J et al. Effects ofmaternal multiple micronutrient supplementation on fetal growth: a double- blind randomized controlled trial in rural Burkina Faso. Am J Clin Nutr 2008; 88 (5): 1330-40.
11. Ab-Bakari-Rwebembera, Munubhi EKD, Manji KP, Mpembeni R, Philip J. Relationship between infant birth weight≤2000g and maternal zinc levels at Muhimbili national hospital, Dar Es Salaam, Tanzania. J Trop Pediatrics 2005; 52:2:118- 125.
12. Amalia M, Yusrawati, Rita RS. Differences of zinc and copper levels in placenta blood normal neonates and intrauterine growth restriction. J. Midwifery 2018;3(2):19-26.
13. Tsuzuki S, Morimoto N, Hosokawa S, Matsushita T. Associations of maternal and neonatal serum trace element concentrations with neonatal birth weight. PLoS ONE2013;8(9):1-4.
14. Bermudez L, Vicent CG, Lopez J, Torro MI, Lurbe E.Assessment of ten trace elements in umbilical cord blood and maternal blood: association with birth weight. J. Transl Med 20 15;13(291):1-8.
15. Manandhar T, Prashad B, Nath Pal M. Risk Factors for Intrauterine Growth Restriction and its Neonatal Outcome. Gynaecol Obstet 2018; 8:1000464.
16. Muhammad T, Khattak AA, Rehman S, Khan MA, KhanA, Khan MA. Maternal factorsassociated with intrauterine growth restriction. J Ayub Med Coll.2010;22(4):64- 69.
17. Jaafar Z A, Salman D A, Obeid R Z. Role of maternal and fetal serum zinc levels in low birth weight. J Pharm Sci & Res 2018;10(8): 2115-118.
18. Suman S, Saini S, Gupta RC. Association of zinc, copper and iron levels with birth weight.

Int Multispec J Hlth 2015; 1:1-6.
19. Jyotsana S, Agrawal A, Kumar A. Study of serum zinc in low-birth-weight neonates and its relationship with maternal zinc. J Clin Diagn Res 2015; 9:1-3.
20. Shivaprasad B, Sharma DK. To compare the perinatal outcome of IUGR infants with abnormal and normal antenatal umbilical artery doppler flow in the immediate neonatal period. Int J Reprod, Contracep, Obstet Gynecol 2017 :6.
21. Elizabeth KE, Krishnan V, Vijaykumar T. Umbilical cord blood nutrients in low-birth-weight babies in relation to birth weight and gestational age. Indian J Med Res 2008;128-133.
22. Gupta N, Bansal S, Gupta M, Nadda A. A comparative study of serum zinc levels in small for gestational age babies andappropriate for gestational age babies in a tertiary hospital, Punjab. J Family Med Prim Care.2020;9:933-7.