

MATERNAL SERUM ZINC CONCENTRATION IN GRAVIDAE SUFFERING FROM PRE-ECLAMPSIA

Dr. Muhammad Ashraf
Associate Professor of Biochemistry,
Punjab Medical College, Faisalabad.

Dr. Muhammad Nasarullah
Assistant Professor of Biochemistry,
K.E. Medical College, Lahore

Dr. Abdul Salam (Rtd)
Professor of Biochemistry,
K.E. Medical College, Lahore.

Dr. Riffat Khurshid
Assistant Professor of Biochemistry,
Rawalpindi Medical College, Rawalpindi

Dr. Zamir Ahmed
Professor of Biochemistry
Services Institute of Medical Sciences Lahore

ABSTRACT

Zinc is one of the most intensively investigated mineral during pregnancy. **OBJECTIVE:** To find out the relationship of maternal serum zinc with pre-eclampsia PERIOD 1989 to 1991. **SETTING** Lady Willington Hospital, Lahore, King Edward Medical College, Lahore, Metallurgy Department PCSIR, Lahore. **MATERIALS AND METHODS:** In this prospective study 218 pregnant women were randomly registered during their 1st trimester and followed up till delivery. A group of 46 women remained normal throughout pregnancy and they delivered normal babies by spontaneous vaginal deliveries. Ten women suffered from pre-eclampsia. They were considered as study subjects. Three blood samples were drawn from all subjects each by the end of 1st, 2nd and 3rd trimesters. Serum zinc was analyzed by atomic absorption spectrophotometer. **RESULTS:** Serum zinc levels (Mean \pm SD μ g/dl) in normal gravidae by the end of 1st, 2nd and 3rd trimester were 76.57 ± 10.76 , 61.98 ± 7.97 and 51.17 ± 8.61 while in pre-eclamptic gravidae, 64.60 ± 7.71 , 50.30 ± 6.50 and 25.30 ± 8.97 μ g/dl respectively. The pre-eclamptic women had significantly lower ($P < 0.001$) levels of serum zinc throughout gestation as compared to normal gravidae. **CONCLUSION:** Low maternal serum zinc levels may have some association with pre-eclampsia.

KEYWORDS: Pre-eclampsia, Maternal Serum zinc

CORRESPONDENCE: Dr. Muhammad Ashraf, Associate Professor of Biochemistry, Punjab Medical College, Faisalabad. E-mail: apmcfds@gmail.com

INTRODUCTION

It is known that maternal serum zinc decreases with the advancement of human pregnancy^{1,2,3}. Zinc is required for DNA replication, transcription and cellular replication as it is the metallic component of various related enzymes i.e. DNA polymerase, RNA polymerase

and thymidine Kinase⁴. Essentiality of zinc during pregnancy is evident. In zinc deficient animals and women poor outcome of pregnancy is observed^{5,6,7}. Pre-eclampsia is a multi system disorder involving placenta, liver, kidney, blood, neurological and cardiovascular systems. It is characterized by hypertension associated with

proteinuria in pregnant women which were normal prior to gestation⁸. The Incidence of pre-eclampsia is about 05% of the total pregnancies and is higher in primigravidae. Pre-eclampsia is established when diastolic blood pressure >90 mmHg or the increase is >15 mmHg over that of pre-pregnancy level or systolic blood pressure 140 mmHg or the increase is >30 mmHg over pre-pregnancy level and proteinuria >0.3 gm/24 hours. Both maternal and fetal morbidity and mortality are more likely to occur with early onset of the disease. Cerebral haemorrhage and adult respiratory distress are common causes of death in pre-eclampsia⁹. The dietary requirement of zinc is increased during pregnancy¹⁰ and various feto-maternal complications are observed in zinc deficient pregnant animals. This study was therefore designed to find out possible association of maternal serum zinc levels with the toxemia of pregnancy i.e. pregnancy induced hypertension and pre-eclampsia.

MATERIALS AND METHODS

A total of 218 pregnant women during their 1st trimester were registered at Lady Willington Hospital, Lahore. Among these, 46 subjects remained normal throughout the course of pregnancy and they delivered normal babies by spontaneous vaginal deliveries. These 46 subjects were considered as control. Among the registered subjects 10 women developed pre-eclampsia and these were considered as study subjects. From ante-cubital vein 05 ml blood was drawn by the end of each trimester. Serum was separated and analysed immediately for total serum proteins¹² and serum albumin¹³. Serum for analysis of zinc were stored at -20°C in metal free plastic tubes. Zinc was analysed by atomic absorption spectrophotometer¹⁴. Statistical analysis of the two groups was done by "t" test using the standard error of the difference¹⁵.

RESULTS

The level of maternal serum zinc, total proteins and albumin in normal gravidae and pre-eclamptic subjects along with their comparison is shown in the Tables I, II and III.

TABLE-I: Levels (mean ± S.D.) of serum zinc, total protein and albumin in normal gravidae.

Serum level	Ist Term n=46	2 nd Term n=46	3 rd Term n=46
Zinc ug/d	76.57±10.76	61.98±7.97	51.17±8.61
Total protein g/dl	06.05± 0.24	05.84±0.22	05.76 ± .25
Albumin g/dl	03.94± 0.24	03.70±0.16	03.60± .19

TABLE-II: Levels (mean ± S.D.) of serum zinc, total protein and albumin in pre-eclamptic gravidae.

Serum level	Ist Term n=10	2 nd Term n=10	3 rd Term n=10
Zinc ug/d	64.6 ± 7.71	50.3 ± 6.50	25.3±8.97
Total protein g/dl	6.02 ± 0.19	5.77 ± 0.10	4.52 ± 0.31
Albumin g/dl	3.93 ± 0.15	3.60 ± 0.15	2.18 ± 0.23

TABLE-III: Comparison of serum zinc in normal and pre-eclamptic gravidae.

Terms	X1-X2	S.E.of diff.	t. value	p.value	Significance
1 st	11.97	3.60	3.33	p<0.01	S
2 nd	11.68	2.71	4.31	p<0.001	H.S.
3 rd	25.87	3.03	8.54	p<0.001	H.S.

Abbreviations:

Trim: Trimester, X1: mean of normal gravidae. X2: mean of pre-eclamptic gravidae. SE.diff: standard error of difference. S.D: Standard deviation. S: significant. H: highly, µg: microgram, g: gram, n: number of subjects, >: equal to or greater. >: greater than.

The decrease in maternal serum zinc levels in pre-eclamptic gravidae is highly significant during 2nd and 3rd trimesters as compared to the normal gravidae.

DISCUSSION

There is progressive decline in the level of serum zinc from 1st trimester to the 3rd trimester both in normal and the pre-eclamptic gravidae. The progressive hypozincemia of pregnancy is due to plasma expansion¹⁶, enhanced endogenous steroid production¹⁷ and fetal uptake of zinc from maternal plasma¹⁸. The levels of serum zinc in each trimester among pre-eclamptic gravidae is significantly lower than the normal gravidae. The more rapid decline of serum zinc in pre-eclamptic women may be due to hypoalbuminemia resulting from albuminuria. About 65% serum zinc is bound to albumin⁰⁷. The loss of albumin bound zinc is a major cause of gross hypozincemia in pre-eclamptic gravidae. Secondly fetal uptake of zinc is one of the causes of maternal hypozincemia. In this study significantly higher birth weight babies were delivered by pre-eclamptic mothers than the normal gravidae. So the relatively increased uptake of zinc by high birth weight babies belonging to pre-eclamptic mothers may be a cause of more rapid hypozincemia. Such type of findings are also reported in other studies¹⁹.

The effects of hypozincemia on pre-eclampsia has not yet established. Some investigators have hypothesized a relationship between zinc and prostaglandin utilization in the development of pregnancy induced hypertension²⁰. However others have suggested that marginal zinc deficiency state and low dietary protein might confer an increased sensitivity to cadmium toxicity, sodium retention, altered catecholamine metabolism, increased rennin activity and resultant hypertension²¹. Most of the subjects in this study belong to low socioeconomic class. Their dietary intake of protein was inadequate than the Recommended Dietary Allowance. Low protein intake alongwith hypozincemia may aggravate the toxic effects of cadmium resulting in hypertension. Zinc is metallic component of the enzyme superoxide dismutase⁷, which causes protection from damage by the free radicals. Recent studies show beneficial effects of supplementing antioxidants to pre-eclamptic gravidae²². So hypozincemia suppressing the activity of superoxide dismutase may be a precipitating factor of

pre-eclampsia. However further studies are required to find out the effects of hypozincemia on pre-eclampsia.

REFERENCES

1. Lazebnik B, Kuhnert BR, Kuhnert MP, Thompson KL. Zinc status; Pregnancy Complications and labour abnormalities. *Am.J.Obstet Gynaecol* 1988, 158:161-66
2. Lagos G de la, Novarro AM, Terres M C, Hopez-MMC Zinc and copper concentrations in serum from Spanish women during pregnancy *Biol-Trace Elem-Res.* 1998 Jan; 61(1): 61-70.
3. Ashraf M, Salam A, Khan MN, Ahmed Z, Chaudhary Z.A. Maternal serum zinc levels in normal gravidae in relation to course and advancement of human pregnancy. *The Professional* 1999; 06(01): 133-36.
4. Chaney SG. Zinc as cofactor of enzymes. In *Biochemistry with clinical correlation* ed.05 Devlin. Wiley Lyess, 2002: 1162
5. Carey LC, Coyle P, Philcox JC, Rofe AM. Maternal ethanol exposure, low plasma zinc, increased incidence of fetal abnormalities in normal but not in metallo-thionine-null mice. *Alcohol.Clin Exp Res* 2000 Feb; 24(2): 213-9
6. Prasad AS. Zinc deficiency in women, infants and children. *J.Am. Coll Nutr* 1996. Apr 15(2): 113-20.
7. Aggett Pj. Physiology and metabolism of essential trace elements; an outline. *Clinics in endocrinology and metabolism.* 1985; 1-85.
8. Davey DA, Mac Gillivray I. The classification and definition of hypertensive disorders of pregnancy. *Am J. Obstet Gynaecol* 1988; 158: 892-8.
9. Schennan A. Pre-eclampsia and Non-proteinuric PIH. In: *Obstetric and Gynaecology* by Leusley DM and Baker PN. 2004: 179-86.
10. Toffaletti JA. Trace elements. In: *Clinical Chemistry* by Bishop MI, Foddy EP, Schoeff L. Lipincott, William and Wilkin; 2005: 370-371.
11. King JC, Determination of maternal zinc status during pregnancy. *Am J. Clin Nutr* 2000 May; 71:5) (Suppl): 1334-43.
12. Peters T JR, Biamonte ET, Protein (total) in serum, urine, CSF, Albumin in serum. In; Faulkner WR, Meites S, eds. *Selected methods in clinical chemistry*, Vol. 9. Washington, DC: American Association for clinical chemistry, 1982: 317.

13. Dumas BT, Watson wa, Biggs HG. Albumin standards and the measurement of serum albumin with bromoresol green. *Clin. Chem. Acta* 1971; 31: 87.
14. mith JC, Butrimovitz GP, Purdy WC. Direct measurement of zinc in plasma or serum by atomic absorption spectrophotometry. *Clin. Chem.* 1979; 25: 1487-89.
15. Swinscow TDV. Evaluation of the significance of the difference between the mean of two samples by "t" test. In: *Statistics at square one* by Dawson and Gordall Ltd. Mendip Press, Bath England. 1976: 36.
16. Cunningham FG, Mac Donald PC, Norman FG, et al. Maternal adaptation to pregnancy. In: *William's Obstetrics 20th ed* Prentice Hall International UK Ltd. London. 1979: 201.
17. Friedman M. and Beard RW. Plasma 11-hydroxy-corticosteroid in pregnancy and the Puerperium. *J. Obstet. Gynaecol.* 1988, 73; 123-130.
18. Swanson CA, and King JC. Zinc and pregnancy outcome. *Am J Clin Nutr.* 1987;76:763-71.
19. Xiong X, Demianczuk NN, Buekens P, Saunders LF. Association of pre-eclampsia with high birth weight for age. *Am J Obstet Gynaecol.* 2000; 183: 148-55.
20. Hunt IF, Murphy NJ, Cleaver AE. Zinc supplementation during pregnancy: effects on selected blood constituents and on progress and outcome of pregnancy in low income women of Mexican descent. *Am J Clin Nutr.* 1984; 40: 508-21.
22. Chisolm JC and HandorfCR. Zinc cadmium, metallothionein and progesteron; do they participate in etiology of pregnancy induced hypertension. *Med Hypothesis* 1985; 17:231.
23. Linder MC. Nutrition and metabolism of trace elements. In: Linder MC, Ed. 1996.
24. *Nutritional Biochemistry and Metabolism 2nd ed.* New York; Elsevier, 1991: 215-76.

**HE IS WISE WHO KNOWS THE
SOURCES OF KNOWLEDGE,
WHO KNOWNS WHO HAS WRITTEN
AND WHERE IT IS TO BE FOUND**