

## Plasma Concentrations of Fe, Cu, Mn, and Cr of Maternal and Umbilical Cord Blood during Pregnancy

Jong-Im Lee, Hyeon-Sook Lim<sup>†</sup> and Young-Sook Cho<sup>\*</sup>

Department of Food and Nutrition, Chonnam National University, Home Ecology Research Institute,  
Gwangju 500-757, Korea

<sup>\*</sup>Division of Food Science, Sunchon National University, Sunchon 540-742, Korea

### Abstract

Anemia is prevalent among pregnant women in Korea, and Fe deficiency anemia is a major nutritional problem throughout the world. Because studies of Cu, Mn, and Cr levels excluding Fe are rare, we were interested in changes in the nutritional status of these trace minerals and their relationship to hematogenesis. Accordingly, we determined the changes in plasma Fe, Cu, Mn, and Cr concentrations of maternal and umbilical cord blood during pregnancy, and evaluated the relationships between them at different time points during pregnancy. A total of 81 women participated in the study: 26 subjects in the first trimester, 23 in the second, and 32 in the third trimester. Plasma Fe levels were lower significantly ( $p < 0.05$ ) in the third trimester. Plasma Cu level ( $\mu\text{g/dL}$ ) in each trimester were  $86.6 \pm 13.8$ ,  $111.6 \pm 27.9$ , and  $114.0 \pm 29.7$ , respectively; with significant increases ( $p < 0.05$ ) in the second and third trimester. Plasma Mn concentrations ( $\text{pg/dL}$ ) in each trimester were  $212.6 \pm 89.0$ ,  $234.0 \pm 140.0$ , and  $240.3 \pm 166.0$ , respectively and tended to increase, though not significantly, as the pregnancies progressed. The plasma concentrations of Cr ( $\text{pg/dL}$ ) in each trimester were  $3.7 \pm 2.0$ ,  $3.1 \pm 1.0$ , and  $2.4 \pm 1.2$ , respectively; and was significantly lower ( $p < 0.05$ ) in the third trimester. In umbilical cord blood, the plasma level of Fe was  $194.8 \pm 74.6 \mu\text{g/dL}$ , Cu was  $57.5 \pm 10.9 \mu\text{g/dL}$ , Mn was  $482.4 \pm 111.1 \text{ pg/dL}$ , and Cr was  $9.3 \pm 2.8 \text{ pg/dL}$ . Plasma concentrations of Fe, Cu, Mn, and Cr of cord blood were 300%, 50%, 200%, and 370% as compared to those of maternal blood in the third trimester. These results suggest that an active transport mechanism for the transport of Fe, Mn, and Cr from mother to fetus may exist, whereas, for Cu, the placenta appears to have a blocking effect on the transport from mother to baby.

**Key words:** Cu, Mn, Cr, cord blood

### INTRODUCTION

Trace minerals are known to serve many essential roles in human metabolism even though very small concentrations are found in the human body (1). Despite their essential roles in fetal development, there are few studies evaluating trace mineral status in pregnant women (2,3).

Iron (Fe) and copper (Cu) exist as components of several metabolic enzymes in humans (4,5). Together with Fe, Cu serves essential functions in hematogenesis by assisting in the absorption of iron, facilitating the synthesis of heme and globin, and in controlling the release and storage of Fe in the liver. Cu deficiency, therefore, may cause anemia (5). Maternal iron deficiency during pregnancy is common, but Cu deficiency is not. Plasma Cu concentrations increase in pregnant women to about twice those in non-pregnant women (6). Plasma Cu levels in maternal blood are about five times higher than in umbilical cord blood (6).

Manganese (Mn) exists as a constituent of several metal-

loenzymes and functions as a cofactor in the activation of other enzymes (7). Mn may interfere with Fe absorption because they have similar physicochemical properties and share the same pathway of absorption (8). It has been shown that Mn concentration of cord blood and newborn's blood are higher than those of maternal blood (9). In animal studies, Mn deficiency is characterized by lack of coordination, disturbed equilibrium, and retraction of the head (10).

Chromium (Cr) is an essential element for potentiating insulin action, thereby effecting carbohydrate, protein, and lipid metabolism (11). Cr transport interferes with Fe absorption by binding to transferrin competitively with Fe, resulting in a reduction in total iron binding capacity (12). Since maternal Cr nutrition during pregnancy is frequently inadequate, Cr deficiency may be a cause of glucose intolerance during pregnancy (13). However, it is commonly believed that serum Cr concentrations do not predict glucose tolerance during pregnancy (14).

<sup>†</sup>Corresponding author. E-mail: limhs@chonnam.ac.kr  
Phone: +82-62-530-1332. Fax: +82-62-530-1339

Korean studies of trace minerals have primarily focused on Fe (15-19). There is a high prevalence of anemia in pregnant women in Korea (20,21), and Fe deficiency anemia is a major nutritional problem throughout the world. Because studies of Cu, Mn, and Cr status, but not Fe, are rare, we were interested in changes in maternal status for those nutrients and their impact on hematogenesis.

In this study, we determined the changes in plasma Fe, Cu, Mn, and Cr concentrations in maternal and umbilical cord blood during pregnancy, and analyzed the relationships between their concentrations during the last trimester of pregnancy.

## MATERIALS AND METHODS

### Subjects

The subjects of this study were recruited from among pregnant women who visited E hospital in Gwangju for prenatal care from January to August 1997. A total of 81 women voluntarily participated: 26 women were in the first trimester of their pregnancies, 23 in the second trimester, and 32 in the third trimester.

### General characteristics of the subjects

A questionnaire was used to determine anthropometric and demographic characteristics, including general health, of each subject. Height was measured to the nearest 0.5 cm using a linear height scale. Subjects were weighed at the time of delivery, and pre-pregnancy weights were collected by recall. Weight gain was calculated as the difference between pre-pregnancy weight and weight at delivery. Weight gain data were only obtained from the 32 subjects participating during the third trimester of pregnancy.

### Blood collection and biochemical assessments

Maternal blood samples were collected from the subjects during the first (8~13 wk), second (17~26 wk), and third trimester (28~40 wk) of pregnancy cross-sectionally. Umbilical cord blood samples were obtained from the 32 subjects participating during the third trimester of pregnancy. Plasma Fe concentration were analyzed with a commercial kit (Shinyang Chemical Co., Seoul, Korea). Cu, Mn, and Cr concentrations in plasma were analyzed using an Atomic Absorption Spectrometer (AI-1000/2000, AURORA Instruments LTD., Canada) (22).

### Statistical analysis

Data were statistically analyzed using SAS software (23). All data were expressed as mean  $\pm$  standard deviation. Statistically significant differences were accepted at  $p < 0.05$  by the General Linear Model (GLM). Student's *t*-test was used evaluate differences in micronutrient levels between maternal blood at the third trimester of pregnancy and um-

bilical cord blood. Pearson's correlation coefficients were calculated to identify interactions among plasma trace minerals in maternal and umbilical cord blood.

## RESULTS AND DISCUSSION

### General characteristics of the subjects

General characteristics of the subjects were the same as previously reported (19). The mean age of the subjects was  $27.8 \pm 2.8$  years. The subject's education, occupation, and family income indicated that they were in the urban middle class. Weight gain was  $13.0 \pm 2.8$  kg during pregnancy. The mean birth weight and height of newborns was  $3,250 \pm 280$  g and  $49.9 \pm 1.4$  cm, respectively.

### Changes in plasma Fe, Cu, Mn, and Cr concentrations during pregnancy

As shown in Table 1 and Fig. 1, plasma Fe concentrations ( $\mu\text{g/dL}$ ) in the 1<sup>st</sup>, 2<sup>nd</sup>, and 3<sup>rd</sup> trimesters were  $93.1 \pm 36.1$ ,  $89.2 \pm 36.7$ , and  $64.0 \pm 59.4$ , respectively. Plasma Fe concentrations were lower significantly ( $p < 0.05$ ) in the third trimester. Carriaga et al. (24) reported that the Fe concentrations of American pregnant women decreased from  $73.3 \mu\text{g/dL}$  during the 28<sup>th</sup>~32<sup>nd</sup> week to  $68.3 \mu\text{g/dL}$  during the 36<sup>th</sup>~40<sup>th</sup> week of pregnancy.

Plasma Cu concentrations ( $\mu\text{g/dL}$ ) in each trimester were  $86.6 \pm 13.8$ ,  $111.6 \pm 27.9$ , and  $114.0 \pm 29.7$ , respectively; and were significantly higher ( $p < 0.05$ ) during the second and third trimesters than the first. Since there is no pre-pregnancy data in this study, it is not possible to evaluate early changes in pregnancy. However, plasma Cu levels increased substantially during the second half of pregnancy. Ha and Na (25) found that plasma Cu levels were  $72.9 \mu\text{g/dL}$  in women of child-bearing age,  $123.8 \mu\text{g/dL}$  during early pregnancy, and  $143.3 \mu\text{g/dL}$  during late pregnancy, suggesting that plasma Cu concentrations begin to increase in early pregnancy and increase more rapidly in late pregnancy. Martin-Lagos et al. (26) reported that plasma Cu levels ( $\mu\text{g/dL}$ ) of Spanish pregnant women were 105.3, 161.6, and 168.9 in each trimester, respectively, which supports our finding of increased Cu during the second

**Table 1.** Plasma Fe, Cu, Mn and Cr concentrations of maternal blood during pregnancy

	Pregnancy (trimester)		
	First (n = 26)	Second (n = 23)	Third (n = 32)
Fe ( $\mu\text{g/dL}$ )	$93.1 \pm 36.1^{1)a2}$	$89.2 \pm 36.7^a$	$64.0 \pm 59.4^b$
Cu ( $\mu\text{g/dL}$ )	$86.6 \pm 13.8^b$	$111.6 \pm 27.9^a$	$114.0 \pm 29.7^a$
Mn ( $\text{pg/dL}$ )	$212.6 \pm 89.0^a$	$234.0 \pm 140.0^a$	$240.3 \pm 166.0^a$
Cr ( $\text{pg/dL}$ )	$3.7 \pm 2.0^a$	$3.1 \pm 1.0^{ab}$	$2.4 \pm 1.2^b$

<sup>1)</sup>Values are mean  $\pm$  standard deviation.

<sup>2)</sup>Values with different superscripts(s) in a row are significantly different among trimesters ( $p < 0.05$ ).

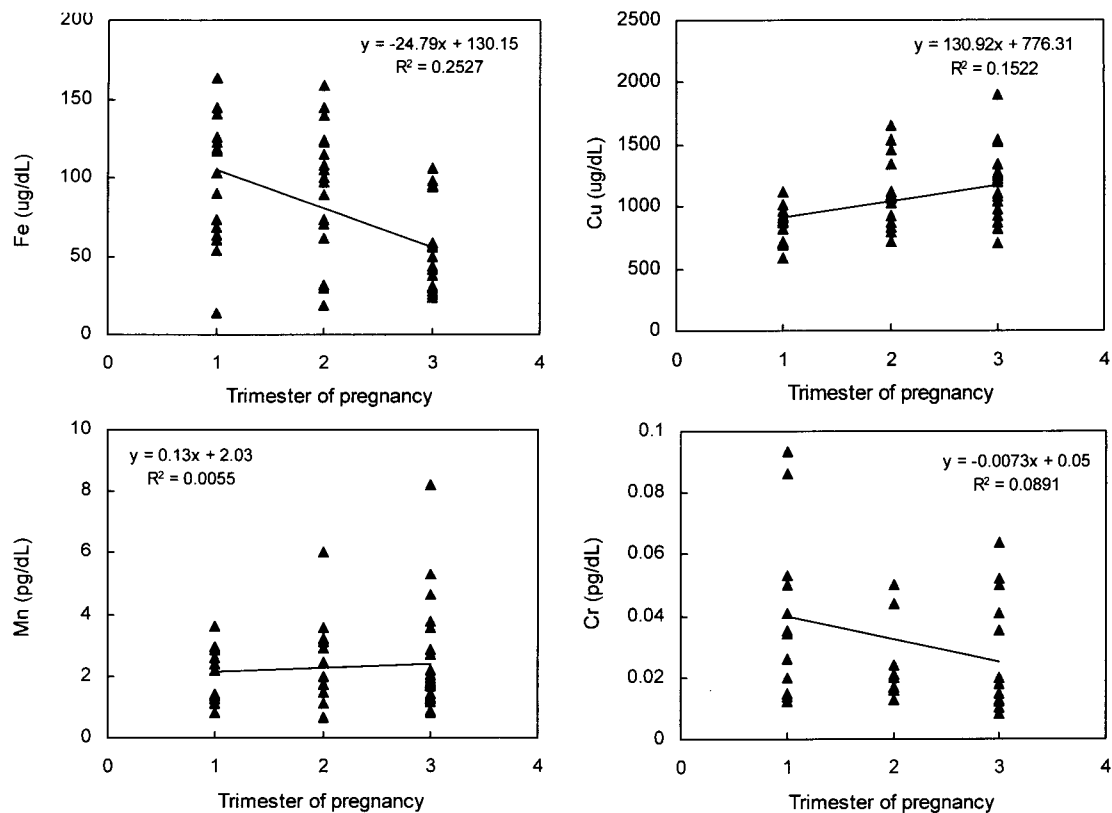


Fig. 1. Change in maternal plasma Fe, Cu, Mn, and Cr concentrations during pregnancy.

trimester, and remaining stable through the third trimester. All of these results were also in agreement with the hypothesis described by Speich (27), stating that the increase of maternal Cu levels during pregnancy are the result of mobilization of Cu stored in the liver and other tissues. The fact that 90% of the subjects in the study were taking supplemental Fe after the 20th week of their pregnancies suggests that the amount of Cu absorbed was less than usual. The duration of iron supplementation was  $113.0 \pm 28.0$  days and the dosage averaged  $42.6 \pm 12.5$  mg/day.

Plasma Mn concentrations (pg/dL) in each trimester were  $212.6 \pm 89.0$ ,  $234.0 \pm 140.0$ , and  $240.3 \pm 166.0$ , respectively, which tended to increase with time, but were not statistically significant. Tholin et al. (28) reported that plasma Mn in Spanish pregnant women increased from 154 pg/dL in the first trimester of pregnancy to 190 pg/dL and 230 pg/dL in the second and third trimesters, respectively; which is consistent with the results of Favier (29) and Spencer (30). The combined results of the above three studies (28-30) provide convincing evidence that Fe deficiency results in Mn mobilization from storage sites, much the same as with Cu.

Plasma concentrations of Cr (pg/dL) in each trimester were  $3.7 \pm 2.0$ ,  $3.1 \pm 1.0$ , and  $2.4 \pm 1.2$ , respectively and was ( $p < 0.05$ ) significantly lower in the third trimester than the first. Anderson et al. (11) reported that plasma Cr con-

centrations decreased during pregnancy, which is in agreement with our results. Because it has been suggested that inadequate maternal Cr status in late pregnancy might induce glucose intolerance (13), the relationship of Cr nutrition and glucose intolerance during pregnancy deserves further investigation.

Since we did not collect dietary intakes data for these four elements, it is not possible to account for the influence of dietary changes on their status during pregnancy. However, it is not reasonable to assume that the intakes of Cu and Cr changed conversely during pregnancy; in other words, that Cu intake was greatly increased while Cr intake simultaneously decreased substantially enough to raise or reduce plasma levels oppositely. While not conclusive, these results suggest that changes in plasma concentrations of these elements resulted from metabolic alterations such as mobilization, storage, distribution or excretion.

#### Correlations among plasma Fe, Cu, Cr, and Mn levels in each trimester

In the first and second trimesters there were no correlations among the maternal plasma concentrations of the four trace minerals. However, in the third trimester, there was a significant negative correlation between the maternal plasma Fe and Cu concentrations ( $r = -0.5478$ ,  $p < 0.01$ )

(Fig. 2); perhaps suggesting that the decrease in maternal plasma Fe levels induced the release of stored Cu (27).

### Comparison of plasma Fe, Cu, Mn, and Cr levels in umbilical cord blood with those from maternal plasma during the third trimester

In umbilical cord blood, the plasma Fe level was  $194.8 \pm 74.6 \mu\text{g/dL}$ , Cu was  $57.5 \pm 10.9 \mu\text{g/dL}$ , Mn was  $482.4 \pm 111.1 \text{ pg/dL}$ , and Cr was  $9.3 \pm 2.8 \text{ pg/dL}$ . The Fe level was close to the values of  $181.3 \sim 188.8 \mu\text{g/dL}$  previously reported in Korea (31,32) and  $208 \mu\text{g/dL}$  in America (33). The Cu level was similar to  $50.2 \mu\text{g/dL}$ , reported from Spanish pregnant women (34), but higher than the  $39.8 \mu\text{g/dL}$  from Indian pregnant women (35) and  $31 \mu\text{g/dL}$  from pregnant women in Bangladesh (36).

Fig. 3 shows that the plasma Fe levels of umbilical cord blood were about three times higher than those in maternal blood. On the other hand, Cu levels of cord blood were about 50% of those in maternal blood. The result agrees with the theory that the placenta might have a blocking effect on the transfer of Cu from mother to baby (9). The placental and cord blood concentrations of Cu were not significantly different, which indicates that the increase in maternal blood is not of placental origin (37). Mn concentrations of cord blood were approximately two fold higher than maternal blood. Krachler et al. (9) found that the Mn concentrations of cord blood was about 150% of that in maternal blood, and Spencer (30) reported that they were three to four times higher. These results indicate that an active transport mechanism for Mn might exist in the placenta (9). Plasma Cr concentrations from cord blood were 3.7 times higher than those of maternal blood, which also implies that the placenta might be capable of transferring large amounts of Cr from mother to fetus, and supports the theory that maternal Cr is depleted during pregnancy (38).

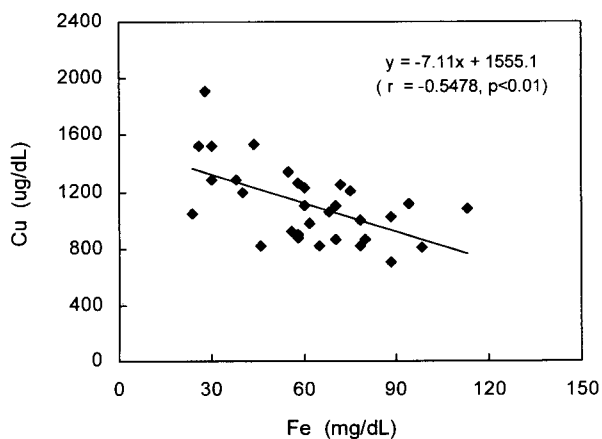


Fig. 2. Correlation between maternal plasma concentrations of Fe and Cu in the third trimester of pregnancy.

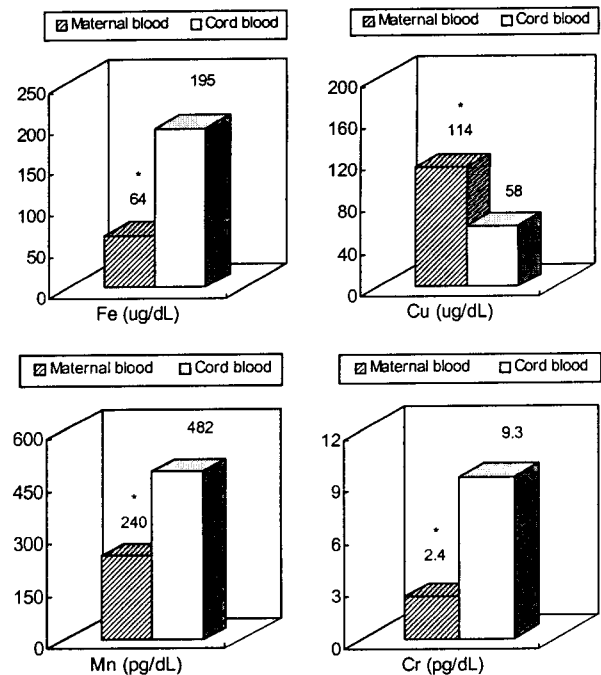


Fig. 3. Comparison of plasma Fe, Cu, Mn, and Cr concentrations between maternal blood at the third trimester of pregnancy and cord blood. \*Values are significantly different by t-test at  $p < 0.05$ .

### REFERENCES

- Gopalan C. 1995. Micronutrient deficiencies: public health implications. *Indian J Pediatr* 62: 157-167.
- Arnaud J, Preziosi P, Mashako L, Galan P, Nsibu C, Favier A, Kapongo C, Hercberg S. 1994. Serum trace elements in Zairian mothers and their newborns. *Eur J Clin Nutr* 48: 341-348.
- Hambidge KM. 1985. Trace minerals and fetal development. *Curr Con Concepts Nutr* 14: 73-82.
- Skikne B, Baynes RD. 1994. Iron absorption. In *Iron Metabolism in Health and Disease*. Brock JH, Halliday JW, Pippard MJ, Powell LW, eds. WB Saunders, London. p 151-187.
- Tumulund JR. 1994. Copper. In *Modern nutrition in health and disease*. Shils ME, ed. Lea and Febiger, Philadelphia. p 231-241.
- Vir SC, Love AH, Thompson W. 1981. Serum and hair concentrations of copper during pregnancy. *Am J Clin Nutr* 34: 2382-2388.
- Hurley LS, Keen CL. 1987. Manganese. In *Trace Elements in Human Health and Animal Nutrition*. Underwood E, Metz W, eds. Academic Press, New York. p 185-223.
- Rossander-Hulten L, Brune M, Sandstrom B, Lonnerdal B. 1991. Competitive inhibition of iron absorption by manganese and zinc in humans. *Am J Clin Nutr* 54: 152-256.
- Krachler M, Rossipal E, Micetic-Turk D. 1999. Trace element transfer from the mother to the newborn: investigations on triplets of colostrum, maternal and umbilical cord sera. *Eur J Clin Nutr* 53: 486-494.
- Keen CL, Bell JG, Lonnerdal B. 1986. The effect of age on manganese uptake and retention from milk and infant formulas in rats. *J Nutr* 116: 395-402.
- Anderson RA. 1986. Chromium metabolism and its role in disease processes man. *Clin Physiol Biochem* 4: 31-41.

12. Ani M, Moshtaghi AA. 1992. The effect of chromium on parameters related to iron metabolism. *Biol Trace Elem Res* 32: 57-64.
13. Hambidge KM, Rodgerson DO. 1969. Comparison of hair chromium levels of nulliparous and parous women. *Am J Obstet Gynecol* 103: 320-321.
14. Gunton JE, Hams G, Hitchman R, McElduff A. 2001. Serum chromium does not predict glucose tolerance in late pregnancy. *Am J Clin Nutr* 73: 99-104.
15. Kim EK, Lee KH. 1998. Assessment of the intake and availability of dietary iron and nutrition knowledge in pregnant women. *Korean J Community Nutrition* 3: 53-61.
16. Kye SH, Paik HY. 1993. Iron nutriture and related dietary factors in apparently healthy young Korean women (1): Comparison and evaluation of blood biochemical indices for assessment of iron nutritional status. *Korean J Nutrition* 26: 692-702.
17. Nam HS, Ly SY. 1992. A survey on iron intakes and nutritional status of female college students of Chungnam National University. *Korean J Nutrition* 25: 404-412.
18. Lee JI, Lim HS. 2001. A longitudinal study in maternal iron and folate status during and after pregnancy in Korean women. *Korean J Community Nutrition* 6: 182-191.
19. Lee JI, Lim HS. 2001. Iron status of pregnant women and evaluation of cut-off levels of Hb, Hct, TIBC, sTfR, sTfR: ferritin ratio for assessment of iron deficiency. *Korean J Human Ecology* 4: 36-45.
20. Chang NS, Kang MH, Paik HY, Kim IH, Cho YW, Park SC, Shin YW. 1993. Serum folate and iron levels of pregnant, lactating, and non-pregnant, non-lactating women. *Korean J Nutrition* 26: 67-75.
21. Yu KH, Yoon JS. 2000. Comparison and evaluation of hematological indices for assessment of iron nutritional status in Korean pregnant women (III). *Korean J Nutr* 33: 532-539.
22. Maret S, Henkin RI. 1971. Simultaneous direct estimation by atomic absorption spectrophotometry of Cu and Zn in serum, urine and cerebrospinal fluid. *Clin Chem* 17: 369-372.
23. Song MS, Lee YC, Cho SS, Kim BC. 1992. *SAS's Guide*. Chayu Academy Press, Seoul.
24. Carriaga MT, Skikne BS, Finley B, Cutler B, Cook JD. 1991. Serum transferrin receptor for the detection of iron deficiency in pregnancy. *Am J Clin Nutr* 54: 1077-1081.
25. Ha EJ, Na HB. 1993. The study on concentration of plasma zinc and copper of nonpregnant and pregnant women in Korea. *Korean J Nutrition* 26: 347-356.
26. Martin-Lagos F, Navarro-Alarcon M, Terres-Martos C, Lopez-Garcia de la Serrana H, Perez-Valero V, Lopez-Martinez MC. 1998. Zinc and copper concentration in serum from Spanish women during pregnancy. *Biol Trace Elem Res* 61: 61-70.
27. Speich M. 1990. Copper in the normal and diabetic pregnancy and in the perinatal period. *Rev Fr Gynecol Obstet* 85: 34-39.
28. Tholin K, Sandstrom B, Palm R, Hallmans G. 1995. Changes in blood manganese levels during pregnancy in iron supplemented and non supplemented women. *J Trace Elem Med Biol* 9: 13-17.
29. Favier A, Ruffieux D. 1983. Physiological variations of serum levels of copper, zinc, iron and manganese. *Biomed Pharmacother* 37: 462-466.
30. Spencer A. 1999. Whole blood manganese levels in pregnancy and the neonate. *Nutrition* 15: 731-734.
31. Kim DK. 1979. Serum iron, TIBC, and transferrin saturation in cord blood of newborns and normal pregnancy. *Ph.D Dissertation*. Department of Obstetrics & Gynecology, Chosun National University, Medical College.
32. Park DM. 1983. Evaluation by plasma ferritin assay of the influence of maternal and newborn's iron stores. *Ph.D Dissertation*. Department of Obstetrics and Gynecology, Seoul National University, Medical College.
33. Maria JG, Rosa MO, Olga M. 1993. Relationship between iron status in pregnant women and their newborn babies- Investigation in a Spanish population. *Acta Obstet Gynecol Scand* 72: 534-537.
34. Casanova Bellido M, Moreno Vazquez AM, Ferriz Mas B, Casas Roman M, Rico de Cos S, Tapia Barrios JM. 1996. Copper in the neonatal period. Maternal-fetal relations. *An Esp Pediatr* 44: 145-148.
35. Algerwie MH, Khatri PC. 1998. Serum copper in newborns and their mothers. *Indian J Pediatr* 65: 899-903.
36. Iqbal AS, Shahidullah M, Islam MN, Akhter S, Banu S. 2001. Serum zinc and copper levels in the maternal blood and cord blood of neonates. *Indian J Pediatr* 68: 523-526.
37. Fattah MM, Ibrahim FK, Ramadan MA, Sammour MB. 1976. Ceruloplasmin and copper level in maternal and cord blood in the placenta in normal pregnancy and in pre-eclampsia. *Acta Obstet Gynecol Scand* 55: 383-390.
38. Wallach S, Verch RL. 1984. Placental transport of chromium. *J Am Coll Nutr* 3: 69-74.

(Received April 17, 2002; Accepted June 11, 2002)