Serum Zinc, Copper, and Selenium Concentrations in Healthy Mothers During Pregnancy, Puerperium, and Lactation: A Longitudinal Study

Pirjo Anttila, S. Salmela, J. Lehto, and O. Simell

Children's Hospital and Institute of Public Health, University of Helsinki, SF-00290 Helsinki, Finland

Zinc deficiency is clearly teratogenic in animals (1). The catabolism of maternal tissues during pregnancy, however, seems to protect the fetus from the teratogenic effects of hypozincemia (2). In humans, most evidence suggesting the importance of zinc during pregnancy comes from patients with acrodermatitis enteropathica, an inherited severe zinc deficiency state. These patients have spontaneous abortions and malformed fetuses unless properly supplemented with zinc (3). Much less is known of the possible teratogenicity of copper deficiency (1). Deficiency of selenium, a third trace element, the availability of which in nutrition has been frequently questioned, has been connected with cardiomyopathy (4) and possibly with atherosclerosis (5) but not with teratogenicity.

Serum zinc concentrations diminish during pregnancy (6,7). Moderate decrease is obviously physiological and explainable by hemodilution after the fourteenth week of gestation (8). At the beginning of pregnancy, however, the decrease must be related to other physiological factors (7). Low zinc concentrations in serum leukocytes and placental tissues have been reported in preeclamptic women (9,10), in mothers delivering prematurely (11), and in mothers delivering small-for-date babies (8).

Copper levels increase during pregnancy and correlate with ceruloplasmin levels (8). In preeclamptic mothers, placental copper concentration was high (10) and serum copper lower than in controls (9). No data exist on serum selenium levels in pregnant and lactating women.

Fasting serum zinc concentrations are slightly lower in Finns compared with inhabitants of many other countries (12). Serum copper values in Finns are in the range reported from other countries, but serum selenium tends to
be lower (13) because of the low selenium content of the soil (14). Owing to the low serum zinc and selenium values in healthy subjects in Finland and the deleterious effects of hypozincemia during organogenesis, we longitudinally followed concentrations of zinc, copper, and selenium in healthy Finnish women during early pregnancy, organogenesis, later pregnancy, puerperium, and lactation. The values were correlated with changes in the carrier proteins albumin and ceruloplasmin and with other data about the mothers, including smoking.

MATERIAL AND METHODS

Healthy Finnish pregnant women from the urban Helsinki area were contacted during their first visit to the regional maternity care unit. Of 69 volunteer mothers, 65 (aged 20–41 years; mean ± SD, 29.1 ± 4.7 years) were able to give a blood sample each month. All of these were included in the study. Iron supplement was given to 29 women in daily doses of 36 to 200 mg Fe²⁺. Three spontaneous abortions occurred because of ovum abortivum. Two of these mothers participated in the study during subsequent normal pregnancies. Blood samples were also taken from eight mothers during delivery, from 53 mothers within the first 5 postpartal days and 1 month after delivery. Samples were also taken 2, 3, and 6 months after delivery from those lactating: 33 at 3 months, and 19 at 6 months. The pregnancy studied was the first in 14 mothers, second in 26 mothers, third in 17 mothers, fourth in eight mothers, and sixth in two mothers (mean of parity 2.4; SD 1.1).

Blood samples were taken after an overnight fast, and special care was taken to avoid external contamination with zinc. Serum zinc and copper concentrations were measured by atomic absorption spectrometry utilizing the flame technique (Perkin-Elmer, Model 300). The measurement was performed by single-dilution method (15). The variation coefficients of the measurements were 11% for zinc and 6% for copper. Serum selenium concentrations were determined by atomic absorption spectrometry using the graphite furnace technique (Perkin-Elmer, Model 5000) with Ni(NO₃)₂ as matrix modifier (16). Serum albumin was measured with an immunoturbidometric method using commercial albumin antiserum (Albumin Antiserum Reagent, Orion, Espoo, Finland) (17). For serum ceruloplasmin analysis, a commercial immunodiffusion method (NOR-Partigen, Boehringer Institute, Marburg, F.R.G.) was used.

Statistical analyses were made using BMDP software (18). Those employed were the Wilcoxon signed-rank test between pairs, correlation analysis, and analysis of variance for repeated measurements.

Informed consent was obtained from mothers. The Ethics Committee of the Health Care Unit of the City of Helsinki approved the study.
RESULTS

Serum Zinc and Albumin

Serum zinc concentration decreased significantly (in mean by 40%) during pregnancy, and a significant rise occurred during the first postpartum month (Fig. 1). The further increase in serum zinc between the first and sixth month of lactation was also significant. Women who received iron supplementation during pregnancy (29 mothers; see Methods) failed to differ from those not supplemented. The age of the mother correlated negatively with the first trimester serum zinc ($p = 0.04; r = -0.259$). The effect of the age of the mother on serum zinc concentration during pregnancy was significant ($p = 0.017$) (analysis of variance). Parity correlated negatively with serum zinc during the third trimester of pregnancy ($p = 0.012; r = -0.311$). Smoking had no influence on serum zinc values. The length of gestation at delivery and the weight of the baby did not correlate significantly with serum zinc.

Four mothers developed toxemia with hypertonia, proteinuria, and edema during pregnancy. Their serum zinc was slightly higher than in other pregnant women. Three mothers with abortive ovum had serum zinc values well within the range of the others, as did the mothers treated for early uterine contractions, puerperal infections, or mastitis during lactation. Serum al-

![Graph](image-url)
Serum Zinc, Copper, and Selenium

Serum zinc correlated highly significantly with serum zinc concentrations ($p < 0.001; r = 0.669$).

Serum Copper and Ceruloplasmin

Serum copper concentration increased significantly (by 84% in the mean) during pregnancy and decreased significantly during the first postpartum month (Fig. 2). The decrease in serum copper was also significant between the first and sixth month of lactation ($p < 0.001$). The age of the mother correlated with the first ($p = 0.005; r = 0.353$); second ($p < 0.001; r = 0.413$); and third ($p = 0.041; r = 0.262$) trimester copper concentrations.

Neither the parity of the mother, nor iron supplementation, nor her smoking had any effect on copper concentration. The copper concentration during pregnancy, moreover, had no influence on the weight or gestational age of the baby delivered.

Toxemic mothers had serum copper values above those of other women, but the difference was not significant. Serum copper in mothers with abortive ovum, early uterine contractions, puerperal infections, or infections during lactation did not differ from values in mothers with uncomplicated pregnancies. There was a highly significant correlation between serum copper and ceruloplasmin during pregnancy and lactation ($p < 0.001; r = 0.761$).

![FIG. 2. Serum copper (---) and ceruloplasmin (----) concentrations during each month of pregnancy, at delivery and during lactation (means ± SEM). Increases from the first trimester to the second and from the second to the third were highly significant ($p < 0.001$). The decrease in both values during the first postpartum month was also highly significant ($p < 0.001$), as was the correlation between serum copper and ceruloplasmin ($p < 0.001; r = 0.761$).]
Serum Selenium and Albumin

Serum selenium concentration was not measured in all samples, and the results are expressed per gestational week (Fig. 3) and per trimester of pregnancy (Fig. 4). Interindividual variations of selenium were much greater than those of zinc and copper. The mean value decreased by 16% during pregnancy (p < 0.001 for means of each trimester; analysis of variance). During lactation, serum selenium increased to a higher level compared with initial values in early pregnancy (p = 0.18). Selenium concentration during pregnancy had no effect on the weight of the baby or the length of the pregnancy. Neither the age of the mother, her parity, smoking, nor iron supplementation had any effect on selenium concentrations during pregnancy.

Selenium concentrations did not differ in mothers with toxemia of pregnancy, abortive ovum, early uterine contractions, or infections occurring during puerperium or lactation. The correlation between serum selenium and albumin was significant (p < 0.001; r = 0.252).

Omphalocele and Polyhydramnios

One child in our study group was born with omphalocele. During pregnancy, the mother had continuously higher serum zinc and selenium values and lower copper concentrations than other mothers. Polyhydramnios with-
out malformation in the child occurred in one pregnancy; serum zinc, copper, and selenium were consistently lower than in all other pregnancies.

DISCUSSION

Serum zinc, copper, and selenium concentrations during lactation showed no difference in our study from levels seen in the Finnish population in previous studies (12–14). Each of these trace elements manifested its own typical changes during pregnancy, puerperium, and lactation. Almost identical physiological changes occurred also in concentrations of the proteins transporting these minerals. Albumin and ceruloplasmin concentrations of the mothers in our study were similar to those published elsewhere for pregnant women (19).

Supplementation with iron had no effect on the levels of serum zinc, copper, or selenium in our study, although in another study, iron-supplemented mothers have shown lower serum zinc concentrations than those not supplemented (6). Smoking also was without influence, but the number of smokers in our study was small, and most smokers consumed fewer than 10 cigarettes daily.

Serum zinc, copper, and selenium concentrations in toxemic mothers did not differ significantly from those in other mothers. In previous studies, preeclamptic mothers showed lower serum zinc and copper values than con-
trols (9); our toxemic mothers had an opposite tendency, exhibiting slightly elevated zinc and copper concentrations. It was interesting to note that in the single pregnancies with polyhydramnios and malformed child (omphalocele), the trace element concentrations differed from those of other pregnancies. These associations may be accidental or may be caused by abnormally functioning fetoplacental and amnionic fluid transport of such trace elements.

ACKNOWLEDGMENT

This study was supported by the Foundation for Pediatric Research, Finland, and F. Hoffmann-La Roche & Co. Ltd., Basel, Switzerland. We express our sincere thanks to Korhonen Maija, Peltonen Raili, and also to all the mothers who participated in the study.

REFERENCES


