Levels of Silicon in Maternal, Cord, and Newborn Serum and Their Relation With Those of Zinc and Copper

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ABSTRACT

Background: Evidence of silicon's importance to health has been gradually accumulating. Nevertheless, there are few studies comparing serum silicon levels in newborns with maternal levels. Likewise, little is known concerning the inter-relation between silicon and other trace elements.
Objective: The present study evaluated maternal and newborn levels of serum silicon and their relation to those of zinc and copper.
Methods: We measured serum silicon, copper, and zinc in 66 pregnant women, in the umbilical cord of their infants, and in 44 newborns, by atomic absorption spectrophotometry. All the samples were from fasted subjects.
Results: Serum silicon level in term newborns (20.6 ± 13.2 μmol/L) was significantly higher than in umbilical cord (8.9 ± 3.5 μmol/L; $P < 0.0001$). Mean serum silicon level in maternal vein (7.7 ± 3.4 μmol/L) was lower than that in umbilical cord, although differences were not significant. We also found higher levels of zinc ($P = 0.008$) and lower levels of copper ($P < 0.0001$) in cord blood compared with maternal blood. Umbilical venous/maternal venous level ratios of zinc, copper, and silicon were 1.5 ± 0.5, 0.2 ± 0.1, and 1.3 ± 0.7, respectively. There was a positive correlation between silicon and zinc levels ($r = 0.32$), and a negative correlation between copper and zinc levels ($r = -0.35$).
Conclusions: It seems that there is a positive gradient of silicon from the mother to her fetus. Silicon levels were higher in newborn than in cord blood, and correlated significantly with that of zinc but not copper. Additional investigations are needed to further define the role of silicon and its interaction with other trace elements during the perinatal period.

Key Words: neonatal nutrition, pregnancy, prenatal nutrition, trace elements

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What Is Known

- Evidence of silicon's importance in bone metabolism has gradually been accumulating. Data on silicon status in pregnant women and newborns are scarce.
- Previous studies found higher silicon levels in preterm than term infants and in children than in adults.
- Zinc levels in cord blood are higher than that in maternal blood and copper levels are lower.

What Is New

- There is a positive gradient of silicon from the mother to her fetus (ratio: 1.34).
- Silicon levels were lower in cord blood than in full-term newborns.
- Serum silicon levels correlated significantly with zinc but not with copper levels.

Evidence of silicon's importance to health, especially its role in bone metabolism, has gradually been accumulating. Serum silicon (Si) level in maternal and cord blood has received little attention. In adults, the main sources of Si are high-fiber foods, drinking water, mineral water, coffee, and beer (1). The sources of Si in the infant diet are not well known but may include breast milk, infant formulas, water, grain, and vegetables (2). Dietary Si is hydrolyzed in the gastrointestinal tract to soluble orthosilicic acid, $Si(OH)_4$, and approximately 40% is absorbed (1). Data on the bioavailability of Si from foods are scarce. The kidney is the major route of Si excretion. Si is found in all tissues, and at especially high level in connective tissue, including bone, tendons, ligaments, and cartilage (3). In animals, dietary Si deficiency can cause growth retardation, and bone and cartilage defects. In humans, higher dietary Si intake correlates positively with bone health, particularly bone mineral density (4). No recommended daily intake for Si has, however, been established (5).

The positive effect of Si on bone may be due to its role in the synthesis and stabilization of type I collagen and in the cellular differentiation of osteoblast-like cells (6,7). In fact, Si may be required for the activity of prolyl hydroxylase, which is involved in the posttranslational modification of collagen, and may play a role in glycosaminoglycan formation (8). Si interacts with other trace elements such as copper (Cu), magnesium, and zinc (Zn) (9,10), necessary for bone mineralization and growth (11). The serum silicon content decreases with age (12,13). Two studies that compared Si levels in pregnant women with age-matched nonpregnant

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women have shown different results (12,14). We found only 1 previous study (15) relating serum Si levels in umbilical cord with maternal levels. The authors of these 3 studies (12,14,15) also found higher level of Si in newborns compared with their mothers and in young children compared with adults. Likewise, there is little information on the inter-relationship between Si and other trace elements such as Zn and copper during the perinatal period. The present study evaluated maternal-fetal levels of serum Si and their relation to those of Zn and Cu.

MATERIALS AND METHODS

In a cross-sectional study, we measured serum Si, Cu, and Zn in pregnant women, in the umbilical cord of their infants (mother-newborn couples), and in another independent group of full-term newborns ages 2 to 3 days.

Subjects

We studied an incidental sample of healthy women with singleton low-risk pregnancies and their newborns, who met the following criteria:

Inclusion criteria: Adult women with 37 to 41 weeks of a normal pregnancy with 1 fetus attended by the Obstetric Services of either Hospital Universitario de Canarias, Tenerife, Spain (HUC) or Centre Hospitalier Universitaire de Tivoli, La Louvière, Belgium (CHUT).

Exclusion criteria: Any obstetric or medical complication during pregnancy; noxious habits (smoking, alcoholism, drug abuse); unconventional diets, Si, Zn, and Cu supplements; preterm delivery; intrauterine growth restriction; perinatal asphyxia; infants with congenital anomalies; or early postnatal medical complications.

Of the pregnant women meeting the study criteria, 66 consented to participate with their offspring.

To determine possible changes in trace element levels in the first few days after birth, we also studied these levels in another group of 44 full-term healthy infants ages 2 to 3 days, breast-fed ad libitum, who met the same criteria.

Blood samples from both groups (mother-newborn couples and newborns ages 2–3 days) were collected in similar proportions at the 2 participating centers (HUC and CHUT).

The following data were recorded: maternal age, parity, birthweight, gestational age (GA), and sex.

The present study was approved by the Research Ethics Committee of CHUT, La Louvière, Belgium and the Research Ethics Committee of HUC, Tenerife, Spain. Written informed consent was obtained from the mothers.

Collection of Samples and Laboratory Analyses

We collected 66 paired maternal and cord blood samples (4–5 mL) from fasting (7–8 hours) mothers' antecubital vein during the first stage of labor and from the umbilical vein (UV). In 29 cases, umbilical artery (UA) blood was also sampled. In addition, 44 fasting (5–6 hours) venous blood samples (2–3 mL) from full-term newborns ages 2 to 3 days were collected.

Blood samples in disposable polypropylene tubes were centrifuged at 3000*g* for 10 minutes at 4°C. The serum were immediately stored at −40°C until use.

No glassware was used. Before use all plastic tubes were washed with 0.2% trace elements quality nitric acid in 0.1% Triton X-100 solution and then dried at 50°C. Serum Zn, Cu, and Si were measured by atomic absorption spectrophotometry (AAS) in the Clinical Chemistry Department, University Hospital Freiburg, Germany. All samples were assayed in duplicate.

Measurement of Trace Elements

Flame AAS and graphite furnace AAS were used to prevent interferences with Si and carry over during analysis.

Serum Zn and Cu levels were determined by routine flame AAS (PerkinElmer Model Analyst 100 spectrometer) performed in acetylene-air flame. Single element hollow cathode lamp (PerkinElmer) was used with resonance lines at 324.8 and 213.9 nm for Cu and Zn, respectively. Standard solutions (1000 mg/L; Merck, Darmstadt, Germany) were diluted with high-purity water. They were run in the range 6.9 to 31.5 and 8.4 to 40.2 μmol/L for Cu and Zn, respectively. Accuracy and precision of the analytical procedures were assessed using certified control material. Intra-assay CVs were 1.3% and 1.6% for Cu and 1.3% and 1.7 % for Zn. Inter-assay CVs for Cu and Zn were 2.1% and 3.5% and 2.0% and 2.5%, respectively. Details of the entire analytical procedure for the determination of Si have been described previously (13). A PerkinElmer model 4110 ZL Zeeman atomic absorption spectrometer equipped with a transverse heated graphite atomizer and a PE AS-72 autosampler (PerkinElmer Instruments GmbH, Rodgau-Juegesheim, Germany) was used. The silicon standard of 1000 mg/L in water (N9303799) from PerkinElmer (PerkinElmer Instruments GmbH) was used by the standard addition technique. The detection limit was 0.53 μmol/L and the limit of quantification was set at 1.78 μmol/L. Intra-assay CVs were 4.0% and 4.7%. Interassay CVs were 4.2% and 5.0%.

Statistical Analysis

The assumption of normality was tested using Kolmogorov-Smirnov test. We used unpaired Student *t* test, paired *t* test, and Pearson correlation coefficient, when appropriate. Statistical significance was defined as a P value <0.05. We used SPSS v.17 (SPSS, Chicago, IL).

RESULTS

Table 1 shows clinical characteristics of mothers and newborns. Levels of Si, Zn, and Cu are reported in Table 2. In some cases, the amount of blood samples was too low to complete all the analyses and missing values were not substituted.

Si and Cu levels and Si/Zn ratio and Cu/Zn ratio in term newborn veins were significantly higher than that in umbilical cord vein. In contrast, Zn levels in UV were significantly higher than that

TABLE 1. Clinical characteristics of mothers and newborns

Mother-newborn couples	
Mothers (n = 66)	
Age, yr	28.9 ± 5.7
Primiparous/multiparous, n/n	26/40
Newborns at birth (cord blood) (n = 66)	
Male/female, n/n	34/32
GA at birth, wk	39.5 ± 1.2
Weight, g	3367 ± 475
Newborns (2–3 days postdelivery) (n = 44)	
Maternal age, yr	29.1 ± 6.6
Primiparous/multiparous mothers, n/n	16/28
Male/female, n/n	24/20
GA at birth, wk	39.9 ± 1.2
Weight, g	3427 ± 568

Data are expressed as mean ± standard deviation or absolute numbers (n). GA = gestational age.

TABLE 2. Serum Si, Zn, and Cu concentrations in pregnant women, in the umbilical cord of their infants and in term newborns at 2– to 3 days of life

	Maternal vein (MV) mean ± SD, n	Umbilical vein (UV) mean ± SD, n	Umbilical artery (UA) mean ± SD, n	Newborn vein (NV) mean ± SD, n	Umbilical vein-newborn vein comparisons	Umbilical vein-maternal vein comparisons
Si, μmol/L	7.7 ± 3.4, 56	8.9 ± 3.5, 47	12.7 ± 8.8, 29	20.6 ± 13.2, 43	t (47,45) = 5.61 $P < 0.0001$	t (37) = 1.60 p n.s.
Zn, μmol/L	23.7 ± 13.3, 66	30.0 ± 9.6, 53	23.7 ± 5.0, 23	28.8 ± 8.5, 26	t (77) = 0.95 p n.s.	t (52) = 3.38 $P < 0.0010$
Cu, μmol/L	31.3 ± 7.5, 64	4.9 ± 3.4, 48	7.1 ± 3.0, 20	7.7 ± 3.1, 19	t (65) = 3.15 $P < 0.0002$	t (46) = 22.70 $P < 0.0001$
Si/Zn ratio	0.4 ± 0.2, 55	0.3 ± 0.1, 46	0.4 ± 0.2, 23	0.6 ± 0.2, 26	t (37,75) = 5.60 $P < 0.0001$	t (36) = 1.73 p n.s.
Cu/Zn ratio	1.7 ± 0.9, 63	0.2 ± 0.2, 48	0.3 ± 0.2, 19	0.3 ± 0.1, 19	t (65) = 2.53 $P < 0.0140$	t (46) = 11.32 $P < 0.0001$

Data are expressed as mean ± standard deviation.
Cu = copper; n = specimens evaluated for each variable; SD = standard deviation; Si = silicon; Zn = zinc.

in maternal veins, and both Cu levels and Cu/Zn ratio were significantly lower (Table 2).

Si, Cu, and Zn in the UA samples showed significant correlation with UV values (Fig. 1).

When all the data were considered (regardless of whether the samples were from the UA or UV of the same newborn), mean levels of Si and Cu in UA were 43% and 45% higher respectively than that in UV. Regarding Zn, the mean levels in UA were 27% lower than that in UV.

Umbilical venous/maternal venous ratios of Zn, Cu, and Si were 1.48 ± 0.54 (n = 52), 0.15 ± 0.10 (n = 46), and 1.34 ± 0.72 (n = 37), respectively.

Table 3A shows correlation coefficients of Cu, Zn, Cu/Zn, and Si/Zn ratios, between maternal and umbilical cord samples. There was no significant correlation between silicon levels in umbilical cord and maternal vein.

Considering all maternal and UV blood samples, we found a positive correlation between Si and Zn, and a negative correlation between Cu and Zn (Table 3B). There was also a positive correlation between Si and Zn in newborn blood samples ($r = 0.436$, n = 26, $P = 0.026$). There was no significant correlation between serum Si and Cu levels in any of the study groups (Table 3B).

Maternal age showed a positive correlation with umbilical Cu/Zn ratio ($r = 0.53$, n = 48, $P < 0.001$), and with maternal vein Cu/Zn and Si/Zn ratios ($r = 0.33$, n = 63, $P = 0.01$ and $r = 0.28$, n = 55, $P = 0.04$, respectively).

GA correlated with UV Cu ($r = 0.31$, n = 48, $P = 0.03$), and Cu/Zn ratio ($r = 0.31$, n = 48, $P = 0.03$), and with newborn Zn and Cu ($r = 0.41$, n = 26, $P = 0.04$ and $r = 0.59$, n = 19, $P = 0.01$, respectively). Serum Si levels showed no correlation with GA.

There were no significant correlations between birthweight and Zn, Si, and Cu levels. We also found no significant differences according to mother's parity, infant sex, or sample origin (HUC vs CHUT).

DISCUSSION

Data on Si status in pregnant women and newborns are sparse and, to our knowledge, there is only 1 previous study (15) relating serum Si levels, in human umbilical cord, with maternal levels. The present study was undertaken to clarify this issue and to investigate a possible relation between silicon and other trace elements in the earliest perinatal period of extrauterine life.

In a previous study (12), serum silicon levels were 18.4 ± 9.2 μmol/L for a group of 11 children younger than 1 year old, 4.5 ± 2.6 μmol/L for 34 adult nonpregnant women and 1.5 ± 0.4 μmol/L for 28 pregnant women. Unanian (16) reported Si levels in cord blood samples obtained from term (14 μmol/L) and preterm newborns (19 μmol/L), but not maternal blood samples. In a recent study Jugdaohsingh et al (15) found that serum Si levels in 14 umbilical cord vein samples (6.0 ± 6.8 μmol/L) and in 5 umbilical cord artery samples (7.8 ± 5.1 μmol/L) were higher than those in 14 maternal vein samples (3.2 ± 2.6 μmol/L), although the differences were not significant.

Our study with a higher sample size of mother-newborn couples, compared with Jugdaohsingh study (15), and also including newborns 2 to 3 days postdelivery, showed higher Si levels after 2 to 3 days in term newborn than in umbilical cord and maternal blood. We also found a significant correlation between Si and Zn. Fetal/maternal ratio of Si was 1.34. All samples were obtained from fasted subjects from Belgium and Spain. Although some dietary differences may exist, the levels of the 3 trace elements analyzed did not differ significantly according to the country of origin.

There is some discrepancy between studies evaluating serum Si levels in pregnant women. In the present study, serum Si values in 56 pregnant women were higher than those reported by Van Dyck et al (12) and Jugdaohsingh et al (15), but lower than those of 354 nonpregnant women reported by Bisse et al (13). Van Dyck et al (12) also found lower serum Si in 28 pregnant women than in 34 nonpregnant women, although silicon levels in the pregnant women

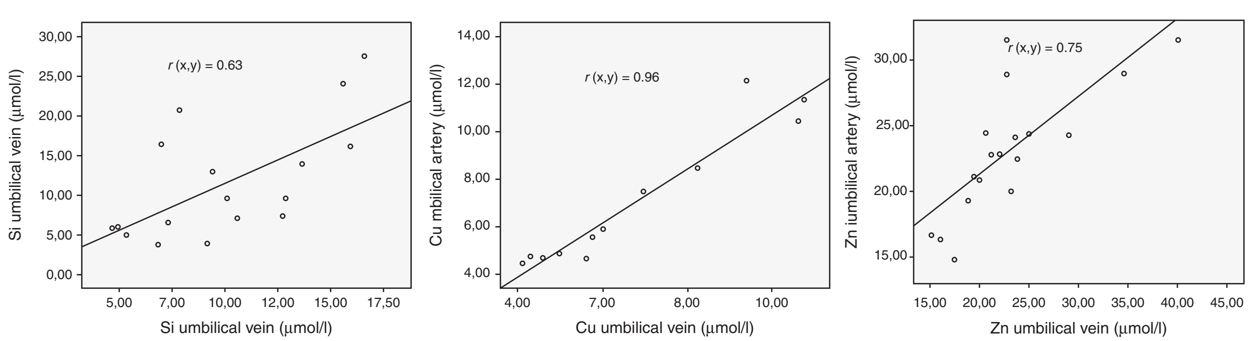

FIGURE 1. Scatterplots of the relations between serum Si, Cu, and Zn levels in newborn umbilical artery and umbilical vein samples.

TABLE 3. (A) Correlations between concentrations of the same trace elements studied, in maternal vein and in umbilical vein serum. (B) Correlations between the different trace elements studied

	r	N	*P*
(A)			
Zn in MV and Zn in UV	0.33	53	0.015
Cu in MV and Cu in UV	0.35	47	0.014
Si/Zn ratio in MV and Si/Zn in UV	0.70	36	0.0001
Cu/Zn ratio in MV and Cu/Zn in UV	0.70	46	0.0001
(B)			
Si and Zn (MV + UV)	0.32	102	0.001
Si and Zn (MV)	0.31	56	0.021
Si and Zn (UV)	0.28	46	0.06
Cu and Zn (MV + UV)	−0.35	112	0.0001
Cu and Zn (MV)	−0.34	64	0.006
Cu and Zn (UV)	−0.42	48	0.003

Cu = copper; MV = maternal vein; Si = silicon; UV = umbilical vein; Zn = zinc.

The coefficients displayed correspond to analyses of MV and UV together, only MV and only UV.

were far lower than those found in our study. In contrast, in studies conducted by another research group (14,15), no differences in serum Si between 14 pregnant and 17 nonpregnant women were found. These discrepancies may be due to different analytical techniques and sample sizes, but further research is needed to explain these findings.

Correlation coefficients for Cu and Zn distributions between maternal and UVs were weak but still significant positive correlations were established. Most interestingly, we found highly significant correlations between maternal and umbilical Si/Zn, and Cu/Zn ratios, suggesting that ratios of these trace elements may be reliable parameters, rather than individual levels of trace elements, for investigating the strength and direction of association between fetal and maternal trace element distribution.

Coinciding with Jugdaohsingh et al (15), we found lower mean Si levels in maternal vein compared with umbilical cord values, although differences were not significant. Umbilical venous/maternal venous ratio of Si was 1.34 ± 0.72, indicating an ascending gradient from mother to fetus. Two Si transporters in plants have been identified (17,18). Recently, Garneau et al (19) identified Si transport systems in mammals for the first time. They show that the human aquaglyceroporins can act as silicon transporters in both *Xenopus laevis* oocytes and HEK-293 cells, and propose a transport model for silicon movement by water channels. Considering that the placenta has a modulating effect on the rate of transfer of trace elements (20,21), it is conceivable that Si crosses the placenta by diffusion, under physiological conditions.

The absence of significant Si-Cu correlation in our study suggests that Si and Cu establish their physiological value independently. This is supported by the considerable difference in fetal:maternal ratio (1.34 ± 0.72 vs 0.15 ± 0.10). The positive correlation between Si and Zn rules out a competitive interaction. The mechanisms by which Si may affect Zn metabolism have not yet been elucidated. Our findings suggest that Si and Zn transport is probably activated by the placenta.

The observed values for serum Cu in healthy pregnant women and their infants in the present study closely approximate those described by other authors (21,22). Higher values of maternal Cu are described compared with the usual values in nonpregnant women (23), which may suggest a mobilization of Cu during pregnancy.

Serum Zn levels in maternal and umbilical cord samples in the present study are similar to those found by Galinier et al (24) in France, but higher than those reported by Al-Saleh et al (22) in Kuwait, Krachler et al (23) in Slovenia, and Osada et al (25) in Japan. These differences may be attributed to variations in the type of diet (20).

As previously reported, the present study demonstrated higher levels of Zn (22,23,26), lower levels of Cu (22), and lower Cu/Zn ratio in cord blood compared with maternal blood. The fact that Zn levels in UV blood were significantly higher than that in maternal blood may indicate the existence of an active transport mechanism for the transfer of Zn from mother to fetus. Zn transporters have been identified at the apical membrane of the placental syncytiotrophoblast indicating a fundamental role in the transfer of Zn to the fetus (27). Other authors have also found low levels of Cu in newborn blood, increasing with age (28). The present study showed a negative correlation between serum Zn and Cu (in both maternal and UVs), as could be expected given the well-known antagonism between these 2 elements.

As previously reported (24), a positive significant correlation was observed between GA and serum Cu in UV. The levels of the elements studied, however, did not correlate with birthweight.

In agreement with other authors (25), mean levels of Zn in umbilical cord arterial blood were lower than those in venous blood, which suggests that Zn is constantly supplied to the fetus and consumed during normal growth at the end of pregnancy. In contrast, the higher mean level of Si and Cu in UA blood, compared to UV blood, may indicate that these trace elements can pass through the UA to the placenta to maintain homeostasis. This is substantiated by the strong correlations between UA and UV trace element levels. Similar findings have also been previously published by Jugdaohsingh et al (15) who reported higher Si levels in UA compared with UV, and by Rossipal et al (21) who have shown that Cu, Li, Zn, and Mo may be excreted via the arterial route into the placenta.

The main limitation of the present study is that the levels of serum silicon, copper, and zinc could not be measured in the same children in umbilical cord blood and at 2 days of life. Longitudinal studies are needed to know changes in silicon levels from birth onward and better define the physiological role of silicon in this period of life.

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