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Levels of toxic and essential metals in maternal and umbilical cord blood from selected areas of South Africa—results of a pilot study†

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This pilot study uses concentrations of metals in maternal and cord blood at delivery, in seven selected geographical areas of South Africa, to determine prenatal environmental exposure to toxic metals. Samples of maternal and cord whole blood were analysed for levels of cadmium, mercury, lead, manganese, cobalt, copper, zinc, arsenic and selenium. Levels of some measured metals differed by site, indicating different environmental pollution levels in the regions selected for the study. Mercury levels were elevated in two coastal populations studied (Atlantic and Indian Ocean sites) with mothers from the Atlantic site having the highest median concentration of 1.78 μg/L ranging from 0.44 to 8.82 μg/L, which was found to be highly significant ($p < 0.001$) when compared to other sites, except the Indian Ocean site. The highest concentration of cadmium was measured in maternal blood from the Atlantic site with a median value of 0.25 μg/L (range 0.05–0.89 μg/L), and statistical significance of $p < 0.032$, when compared to all other sites studied, and $p < 0.001$ and $p < 0.004$ when compared to rural and industrial sites respectively, confounding factor for elevated cadmium levels was found to be cigarette smoking. Levels of lead were highest in the urban site, with a median value of 32.9 μg/L (range 16–81.5 μg/L), and statistically significant when compared with other sites ($p < 0.003$). Levels of selenium were highest in the Atlantic site reaching statistical significance ($p < 0.001$). All analysed metals were detected in umbilical cord blood samples and differed between sites, with mercury being highest in the Atlantic site ($p < 0.001$), lead being highest in the urban site ($p < 0.004$) and selenium in the Atlantic site ($p < 0.001$). To the best of our knowledge this pilot investigation is the first study performed in South Africa that measured multiple metals in delivering mothers and umbilical cord blood samples. These results will inform the selection of the geographical sites requiring further investigation in the main study.

Introduction

Human exposure to persistent toxic substances (PTS) in the living environment, which include toxic metals and persistent organic pollutants, can be from natural sources, anthropogenic from current or past industrial activities, and from living activities of the population. PTS have the ability to exert negative health effects that are often subtle, long-term, sometimes transgenerational and difficult to measure, even in epidemiological studies in large populations. Furthermore, the most vulnerable periods for toxic impact of pollutants on human development are the embryonic and foetal stages, followed by early childhood; most PTS are known to affect reproductive health and pregnancy outcomes, reduce disease defense mechanisms, impact on children's physical and mental development, and increase the risk of cancer.[1–3]

Several multidisciplinary international projects are currently investigating firstly, the sources and levels of PTS in people residing in different geographical regions and secondly, ascertaining the relationship between the levels of these compounds and health. For example, the Arctic Monitoring and Assessment Programme (AMAP) initiated in 1991 measured levels of multiple contaminants and studied possible health effects and birth outcomes of these in the indigenous and other populations living in the Arctic and other areas of the Northern Hemisphere.[4–6] Studies in Canada found elevated levels of methyl mercury not only in indigenous Dene and Inuit populations, but also in the general population residing in other areas of Canada.[7] Elevated levels of organochlorines and metals were also detected in human fluids such as breast milk, in populations residing in different areas within the polar region.[8–12]

At present no comprehensive data exist on the levels of contaminants in ecosystems and populations in the Southern Hemisphere. To date, in South Africa, research linking environmental exposures to human health outcomes in the general population has been scarce. A number of South African studies used animals as bio-indicators for environmental contamination; examples are vanadium levels in cattle, cadmium levels in terrestrial isopod (Porcellio laevis) and in the river crab, or the arsenic resistance in species of multi-host ticks.[13–15]

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A limited number of community based studies performed in South Africa indicate elevated environmental levels of metals that may have detrimental effects on public health. For example, environmental mercury pollution, fish contamination and health problems in the community residing in the vicinity of a non operational mercury processing plant have been reported.[16] Due to the pervasive lead contamination in the country, a high percentage of children residing in inner cities and informal settlements, as well as peri-urban and rural areas, was found to have unacceptably high blood lead levels.[17–20] Elevated levels of blood manganese have been found in school children in some areas of South Africa.[21,22]

Although a number of South African studies report on exposure to metals and possible health effects in occupationally exposed subjects, little is known about exposures of the communities residing in the vicinity of such operations.[23,24]

South Africa, the southernmost part of Africa in the Southern Hemisphere, and being both a developed and a developing country, is of particular importance to the global research in the science of environmental pollutants and human health outcomes.

Firstly, South Africa is rich in mineral deposits and economically important metals such as lead, manganese, platinum, chromium, vanadium and gold, are being mined extensively. The country is also a major producer of other metals such as aluminium, zinc and copper, from enriched deposits; thus the potential exists for emission of these metals into the environment. Though industries are constantly upgrading production technologies to meet global standards and to comply with environmental regulations, the use of outdated technologies in the past may have contributed to toxic metal contamination around certain industrial sites, particularly mining and smelting. South Africa is also experiencing a rise in informal mining (especially artisanal gold mining) and other uncontrolled informal industrial activities that often take place within the living environments of the communities.[25] Secondly, increased population migration and rapid urbanization, with its wide range of anthropogenic activities, may further contribute to environmental degradation and pollution. A high prevalence of infectious diseases (lung diseases, TB, HIV/AIDS) and endemic malaria present in parts of the country make South African and other populations living in the developing countries of the Southern Hemisphere more susceptible to the toxic effects of pollutants in the living environment.

Within this context and in response to the lack of comprehensive data on levels of PTS in populations residing in South Africa, a pilot project was designed and carried out under the auspices of AMAP, by the South African Medical Research Council and the University of Tromsø, Norway during 2005–2006.

Although both metals and organic persistent pollutants were measured in maternal and cord bloods in the pilot phase of the study, this paper reports on the metal results only. The results for the concurrently measured organic pollutants (polychlorinated biphenyl congeners (PCBs), pesticides and their metabolites, and perflourinated compounds) will be reported separately.

The present paper reports on the levels of cadmium (Cd), mercury (Hg), lead (Pb), manganese (Mn), cobalt (Co), copper (Cu), zinc (Zn), arsenic (As) and selenium (Se) found in maternal and umbilical cord bloods drawn from random samples of delivering women in seven selected regions of South Africa that differ in their degree of environmental pollution. Other parameters reported include socioeconomic factors of participants, self reported health status, life style, diet and birth outcomes. The manuscript that will assess in detail the placental permeability for metals measured in paired maternal-cord blood samples is in preparation.

Materials and methods

Selection of study sites

All seven study sites were purposely selected to include a range of different communities: rural, urban, industrial, fishing (situated on the Atlantic Ocean), mining, coastal endemic malaria (situated on the Indian Ocean) and inland endemic malaria. Selected sites differed in the type of environmental pollution and all had a provincial delivery hospital serving the particular community. The rural site is situated close to the Botswana border where no agricultural and industrial activities take place with no major roads or traffic in the area. The urban site is the large city of Johannesburg with extensive gold mining and other industrial activities in and surrounding areas and heavy traffic. The industrial site selected is a coal mining and stainless steel producing small town. The fishing site in the Western Cape is situated on the Atlantic Ocean is known for its fishing and fish processing industry. The mining site is a small town where extensive gold mining takes place. The coastal village on the Indian Ocean is only 8 km away from the Mozambique border and in the vicinity of the world heritage site of Kosi Bay, where only subsistence fishing is allowed. The inland site is a small town with very little industrial activity that is about 70 km away from the Indian Ocean coastal site, but also malaria endemic. The choice of two malaria endemic sites was necessary for the investigation on persistent organic pollutants which are also part of this project. Fig. 1 shows the geographical location of each study site within South Africa.

Recruitment of participants and informed consent

Ethics clearance certificate Protocol Number M040314 for the study was granted by the Committee for Research on Human Subjects of the University of the Witwatersrand, Johannesburg, South Africa. In addition, informed written consent was obtained from each participant prior to commencement of the study.

Potential participants were recruited from women who presented for delivery at the hospital. Recruitment was done by the health worker on duty and trained research assistant who briefly explained the objectives of the study and distributed a detailed information sheet about the project, written in simple language. About 95% of potential participants approached agreed to participate. Women who volunteered to participate signed an informed consent form and agreed to donate blood and urine samples before delivery and cord blood samples post-partum and they agreed to answer a socioeconomic questionnaire by interview in the language of their choice and to grant the research team access to hospital records, post-partum.

Data collection

A socioeconomic questionnaire that also included dietary, life style and self reported health status questions was administered

Fig. 1 Geographical positions of study sites within South Africa. Legend: Site 1 = Rural; Site 2 = Urban; Site 3 = Industrial; Site 4 = Atlantic Ocean; Site 5 = Mining; Site 6 = Indian Ocean; Site 7 = Inland malaria.

by trained research assistants in English or in a language of the participants' choice. After delivery, the researchers extracted records from patient hospital files that included date of delivery, weight and length of the baby, head circumference, Naegele term, Apgar score, gestational age, as well as noting any congenital malformations and birth complications as per comments of doctor or sister present at delivery.

Sampling procedures

For each mother, 30 ml of blood was drawn by venous puncture into 3 Vacutainer tubes before delivery, and umbilical cord blood was collected after delivery by a nursing sister, using the sterile Vacutainer disposable system. Metal-free vessels were used throughout and great care was taken to prevent contamination of samples during collection and fractionation. All samples were stored at −20 °C and shipped in a frozen state to the University of Tromsø, Norway, from where samples were transferred in a frozen state to the analytical laboratories. Measurements of metal content in whole blood were performed by the National Institute for Occupational Health (NIOH), Oslo, Norway.

Analytical methods

Samples of maternal and cord whole blood were analysed for levels of Cd, Hg, Pb, Mn, Co, Cu, Zn, As and Se. Mn, Cu, Zn and Se are considered to be essential metals, but are known to be toxic at elevated levels. Chemical analyses were performed using the inductively coupled plasma-mass spectrometry (ICP-MS) technique. The required contamination elimination procedures and validation of results by using certified standards were applied throughout the analyses.

Sample preparation

For the measurements of elements in whole blood, 1.5 mL of 65% ultrapure nitric acid (Chemscan Ltd., Elverum, Norway) was added to 1 mL of whole blood in a polypropylene digestion tube. The mixture was digested by heating the tube at 95 °C for 1 hour. The acid homogenization procedure using nitric acid was performed in covered tubes at ambient pressure, and is a well accepted and verified procedure for whole blood, with no losses of *e.g.* Se or Hg. These procedures have been carefully studied and are used extensively at NIOH, as well as by many other international laboratories.

The digest was cooled to room temperature and 200 μL of an internal standard solution containing ^{72}Ge for ^{75}As and $^{77,78,82}Se$, ^{115}In for ^{114}Cd, ^{204}Tl for $^{206,207,208}Pb$ and $^{200,201,202}Hg$, ^{60}Ni for ^{55}Mn, ^{59}Co, $^{63,65}Cu$ and $^{64,66,68}Zn$ was added and diluted to a final volume of 10 mL with ultrapure water.

Instrumental measurements

The digested blood was analysed by using an Element 2 mass spectrometer (Thermo Electron, Bremen, Germany) calibrated with the whole blood matched standard solutions. The instrument was programmed to determine Cd by use of the $^{114}Cd^+$ ion with automatic mass correction caused by the $^{114}Sn^+$ ionic interference. Since the molybdenum (Mo) concentration in whole blood is around 1ng/mL or lower, any mass interference at $^{114}Cd^+$ from the $^{98}Mo^{16}O^+$ was not considered to contribute to the overall signal. The following mass resolutions were used; low for Cd, Hg, Pb, medium for Mn, Cu, Zn and high for As and Se. The detection limits (three times standard deviation of all blank samples) for metals in whole blood were as follows: As: 0.09 μg/L, Cd: 0.01 μg/L, Co: 0.07 μg/L, Cu: 1 μg/L, Hg: 0,1 μg/L, Mn: 0.3 μg/L, Pb: 0.1 μg/L, Se: 1 μg/L, Zn: 20 μg/L. One aliquot of each blood sample was analysed in triplicate. Seronorm ™ Trace Elements (Sero Ltd., Billingstad, Norway) human whole blood quality control materials were used for quality assurance of all element measurements; after every ten blood samples analysed, a quality control sample at two different concentration levels was also analysed.

The NIOH laboratory participates in the Wadsworth Center-New York State Department of Health Proficiency (USA) trace element testing schemes for whole blood and urine, with consistently acceptable results and no indication of any systematic biases.

Statistical analysis

Statistical analyses were conducted using the statistical STATA package, version 10 (Stata10 2007).[26]

Descriptive statistics were calculated for metals, including median, first and third quartiles. Comparisons between different sites were made using Kruskal Wallis test and Dunn test for multiple comparisons. A p value of less than 0.05 indicated a significant difference.

Results

The pilot study took place in seven selected sites during 2005–2006, and the analytical work was completed by mid 2007. In the tables that follow, study sites are referred to according to their characteristics and presented in a particular order: rural, urban, industrial, Atlantic Ocean, mining, Indian Ocean malaria and inland malaria. In total, 96 women participated in the pilot study, 12 women each at five sites, with 20 and 16 women at rural and urban sites respectively.

Socioeconomic and housing characteristics

Socioeconomic and housing characteristics for participants at each site are summarized in Table 1 and Table 2. Questionnaire data confirmed a similar socioeconomic status of participants at

Table 1 Socioeconomic characteristics of participants by site

Statistics	Rural N = 20	Urban N = 16	Industrial N = 12	Atlantic Ocean N = 12	Mining N = 12	Indian Ocean malaria N = 12	Inland malaria N = 12
Population group % B = African Black, C = Coloured, W = White	B 100	B 94, C 6	B 92, W 8	B 27, C 73	B 100	B 100	B 100
Marital status (%) M = married, S = single L/T = living together, D = divorced	M 25, S 75	M 29, S 17, L/T 54	M 9, S 75, L/T 16	M 20, S 40, L/T 30, D 10	M 20, S 40, L/T 40	S 100	S 100
Home language (%) E = English, S = Sotho, Z = Zulu, X = Xosa, A = Afrikaans, T = Tswane, O = Other	S 50, T 50	E 27, X 7, S 7	E 11, Z 67, O = 23	E 18, A 55, X27	S 90, Z 10	Z 100	Z 100
Educational status (mean years) W = women, P = partner/husband	W 9.6, P 7.5	W 11.4, P 11	W 10.5, P 11.7	W 9.6, P 10.8	W 8.5, P 10	W 8.3, P 11.3	W 9.8, P 9.6
Mean monthly income Rand (1US$ = 7.2 R)	943 (445)	4166 (4440)	No data	3286 (2276)	2250(1838)	No data	968 (547)
Number of persons (%) employed per household	1 (55%), 2 (27%), 3 (9%)	1 (54%), 2 (38%), 3 (7%)	1 (78%), 2 (22%), 3 (9%)	1 (28%), 2 (57%), 4 (14%)	1 (85%), 3 (14%)	1 (33%), 2 (67%)	1 (100%)

Table 2 Housing characteristics of participants by site

Statistics	Rural N = 20	Urban N = 16	Industrial N = 12	Atlantic Ocean N = 12	Mining N = 12	Indian Ocean malaria N = 12	Inland malaria N = 12
Ownership %	95	19	92	80	60	100	92
Rooms	3.5	2.3	3.5	1.8	1.9	4.5	2.8
Occupancy mean (SD[a])							
Males > 15 y	1.6 (1.3)	1.4 (0.87)	1.7 (1.2)	1.4 (1)	1.4 (0.7)	2.4(1)	2.1(1.5)
Females > 15 y	1.5 (1)	1.3 (1)	2.8 (1)	2 (0.9)	1.7 (0.7)	3.4(0.81)	2.6(1.4)
Children<15 y	4 (2)	1.6 (1)	2.4 (0.8)	2.5 (1.8)	2.4 (0.8)	2.5(1.8)	4.6(1.8)
Electrified %	60	100	83	91	40	9	0
Water source %							
Tap indoor	10	88	75	55	20	0	0
Tap outdoor	70	12	25	45	80	45	42
Borehole	20					27	17
River						27	42
Somebody smoking in household %	55	18	50	73	30	22	33

[a] SD = standard deviation.

all sites. Most of the women were unemployed and relied mainly on social grants or financial support of their partner and other family members. Although cigarette smoking among residents in participants' households was reported (highest 73% in fishing Atlantic Ocean and 55% in rural sites), 56% of actual study participants from the fishing Atlantic site admitted to smoking cigarettes before and during pregnancy. Similarly, alcohol intake was reported only at the Atlantic site by 14% of women, but no participants reported the use of drugs.

The participants were also asked how they rated air quality in the vicinity of their residence and the majority (92%) at the industrial site and 50% at the mining site reported air to be highly polluted (Table 3). The most satisfied with air quality were participants from the Atlantic fishing site. Overall, participants reported to be healthy. Their dietary intake as evaluated from dietary questionnaire appeared to be sufficient and adequate, both before and during pregnancy. Attendance at antenatal clinics by participants before delivery varied from never (mining and coastal malaria) to an average of five times reported in the industrial site.

Maternal age, weight, height and parity by site

Table 4 reports on maternal age, weight, height and parity. The youngest delivering woman was 14 years old; the oldest was 41 years old. The number of children the women already had ranged from none to 6.

Short overview of birth outcomes by site

Details of birth outcomes by site are presented in Table 5. Overall birth weight of babies ranged from 1900 to 3900g, and length from 40 to 56 cm, and gestational age varied between 26 and 41 weeks. 8.3% of the total number of babies born in the study

Table 3 Self reported information on air quality, health, diet and clinic visits by site

Statistics	Rural N = 20	Urban N = 16	Industrial N = 12	Atlantic Ocean N = 12	Mining N = 12	Indian Ocean malaria N = 12	Inland malaria N = 12
Air quality							
G = good, B = bad, D/K = do not know (%)	G 35, B 35, D/K 30	G 70, B 18, D/K 12	G 0, B 92, D/K 8	G 82, B 9, D/K 10	G 40, B 50, D/K 10	G 55, B 36, D/K 9	G 42, B 42, D/K 18
Health status good (%)	75	47	83	100	60	100	83
Diet before/ during pregnancy as evaluated by researchers	Sufficient	Sufficient	Sufficient	Sufficient	Sufficient	Sufficient	Sufficient
Fresh fish intake during pregnancy Weekly %	0	69	33	33	57	18	71
Clinic visits prior to delivery	4	4	5	2	—	—	2

Table 4 Maternal age, weight, height and parity by site

Statistics	Rural N = 20	Urban N = 16	Industrial N = 12	Atlantic Ocean N = 12	Mining N = 12	Indian Ocean malaria N = 12	Inland malaria N = 12
Maternal mean age years (SD)	26 (6)	28 (4)	23 (6)	25 (5)	25 (8)	25(7)	22 (6)
range	16–38	21–36	16–34	20–23	14–38	17–41	17–35
Maternal mean weight (SD) Kg	67 (13)	83 (14)	79 (12)	67 (12)	75 (16)	70 (6)	69 (6)
Maternal mean height (SD) m	1.56 (0.03)	1.59 (0.06)	no data	1.68 (0.09)	no data	1.61 (0.08)	1.53 (0.07)
Parity mean (SD)	2.5 (1.6)	1 (0.5)	1.5 (0.7)	2.4 (1.8)	2 (1)	2 (2)	1 (1)

Table 5 Birth outcomes by site

Statistics	Rural N = 20	Urban N = 16	Industrial N = 12	Atlantic Ocean N = 12	Mining N = 12	Indian Ocean malaria N = 12	Inland malaria N = 12
Birth weight (g) mean (SD)	3126(379)	3170 (351)	2900 (608)	3012 (588)	3184 (444)	3238 (468)	3116 (473)
range	2260–3800	2660–3800	1900–3800	1900–3900	2090–3600	2500–4150	2200–3900
Birth length (cm) mean (SD)	49 (3)	49 (5)	49 (3)	50 (4)	51(2)	50 (3)	49 (4)
Head circumference (cm) mean (SD)	34 (1)	35 (1)	33 (3)	34 (2)	35 (2)	35 (1)	34 (2)
Gestation age (weeks) mean (SD)	40 (1)	39(2)	37 (5)	40 (1)	40 (1)	40 (1)	39 (2)
Gender: girls %	44.4	54.5	44.4	27.2	40	66.8	41.6

sample had low birth weight (LBW), below 2500g, that was directly associated with gestation age and preterm delivery due to a medical emergency. The difference in mean gestational age between the lowest (37.2 weeks at the industrial site) and the highest (39.7 at the coastal malaria Indian site) was found to be statistically significant ($p < 0.04$). Gender ratio differed by site with the lowest number of girls born at the fishing Atlantic site and highest at the coastal malaria Indian site, but did not reach statistical significance. Due to the limited number of participants in the pilot study, the statistical interpretation of gender ratio must be done with caution.

Maternal blood levels of Cd, Hg, Pb, Mn, Co, Cu, Zn, As and Se

Concentrations of the different metals in maternal blood by site are summarised in Table 6. Concentrations of Cd in maternal blood were found to be highest in the Atlantic site where the median concentration was 0.25 μg/L, range between 0.05 and 0.89 μg/L. These concentrations were also significantly higher compared to all other locations, reaching statistical significance of $p < 0.032$ overall. Notably, concentrations of Hg were also highest in mothers from the Atlantic site with a median of 1.78 μg/L, range 0.44–8.82 μg/L and overall highly significant ($p < 0.001$), except when comparing the two coastal populations at the fishing Atlantic and the coastal malaria Indian sites ($p > 0.11$). The Hg levels in the coastal malaria Indian Ocean site were found to be higher than all other sites, except the Atlantic site but were not statistically significant ($p > 0.05$). Median Pb levels were found to be highest in the urban site (32.9 μg/L; range 16.3–81.5 μg/L), significantly higher when compared to any of the other study sites ($p < 0.003$). The Mn levels were found to be similar in all study areas, with no significant differences. Concentrations of Co were found to have similar median levels, with some outliers at relatively high concentrations in the mining area. The Cu levels in whole blood were found to be higher in the inland malaria site compared to all other areas, $p < 0.032$. Levels of Zn were very similar in all sites, except for some real outliers on both high and low concentrations in the Atlantic site. The highest median concentration of As was found to be 0.74 μg/L with range 0.17–2.46 μg/L in inland malaria site, significantly different when compared to other sites ($p < 0.005$). The Se concentrations demonstrate the same pattern as the Hg levels, with highest concentrations in the Atlantic and the coastal malaria Indian Ocean sites, with significant differences between the Atlantic and all the other sites ($p < 0.001$). In addition, the coastal malaria Indian Ocean site shows a significant difference when compared to industrial and mining sites ($p < 0.001$).

Umbilical cord blood levels of Cd, Hg, Pb, Mn, Co, Cu, Zn, As and Se

Umbilical cord blood results for all sites except rural are summarised in Table 7. All toxic metals measured were detected in umbilical cord blood. Median cord blood levels of Cd were found to be low in all sites, and highest in the urban site (0.04 μg/L), with statistical significance between sites ($p < 0.001$). The median levels of Hg were found to be lowest in urban and industrial sites (0.5 μg/L) and highest in the Atlantic site (4.6 μg/L); this result was highly significant ($p < 0.001$). The lowest median levels of Pb were measured in the inland malaria site (9 μg/L), while the highest were recorded for the urban site (23.9 μg/L); with statistical differences between the sites ($p < 0.004$). Levels of Mn in cord blood ranged from lowest (19.7 μg/L) in the urban and highest (36.6 μg/L) in the mining site; lowest levels of Co were measured in the fishing Atlantic site (0.17 μg/L) and the highest in the industrial site (0.38 μg/L), with statistical significance between sites ($p < 0.013$). No statistical differences were observed between sites for Zn and Cu in cord bloods. The lowest levels of As were measured in the urban and industrial site and the highest in the inland malaria site (0.79 μg/L), followed by the Atlantic site with no significant differences between sites. The median concentration of Se was highest in the fishing Atlantic site measuring 159 μg/L and overall highly significant ($p < 0.001$).

Discussion

Women's exposure to metals during their lifetime and during pregnancy, combined with metabolic alterations in status of essential metals such as zinc, copper, iron and selenium during this period, may mobilize metals from body stores and affect the function of placenta and foetal development.

The present pilot study found significant statistical differences in maternal blood levels between different geographical sites for cadmium, mercury, lead, copper, arsenic and selenium. When comparing umbilical cord blood metal levels between the sites, significant differences were found for cadmium, mercury, lead, cobalt and selenium. Essential metal levels measured (copper, zinc and selenium) were within normal concentrations, probably due to adequate diet and to the intake of vitamin and iron supplements, which are routinely prescribed to all pregnant women attending antenatal clinics in South Africa. It is important to mention that in South Africa staple foods are fortified with micronutrients, including folic acid, which is crucial for healthy foetal development.

As for cadmium, the median levels of this toxic metal in maternal blood and cord bloods were highest in smokers.

Table 6 Concentration of Cd, Hg, Pb, Mn, Co, Cu, Zn, As and Se in maternal blood (μg/L) by site[a]

Metals μg/L	Statistics	Rural N = 20	Urban N = 16	Industrial N = 12	Atlantic Ocean N = 12	Mining N = 12	Indian Ocean malaria N = 12	Inland malaria N = 12
Cd [b]	Median	0.10	0.15	0.10	0.25	0.13	0.16	0.12
	Range	0.05–0.25	0.06–0.48	0.05–0.50	0.05–0.89	0.06–0.39	0.06–0.46	0.04–0.26
	IQR	0.07–0.16	0.10–0.22	0.06–0.17	0.20–0.52	0.10–0.16	0.10–0.20	0.10–0.22
Hg [c]	Median	0.40	0.30	0.30	1.78	0.61	0.93	0.89
	Range	0.18–0.82	0.19–3	0.13–0.99	0.44–8.82	0.28–1.25	0.25–3.18	0.22–1.25
	IQR	0.30–0.57	0.30–0.70	0.22–0.50	0.64–2.91	0.39–0.91	0.61–1.33	0.50–1.13
Pb [b]	Median	20.9	32.9	20.7	23.7	26.4	21.9	11.5
	Range	7.4–50.3	16.3–81.5	11–32.3	10.6–38.9	6.1–161.5	8.8–29.4	6.3–49.4
	IRQ	15.2–30.4	22.5–37.8	15.7–23.6	18.1–34.2	12.5–35.2	14.7–27	9.8–19.6
Mn	Median	16.4	17.7	12.7	16	17	17.9	16.8
	Range	8.3–25.2	8.8–30.6	7.9–63.5	9.4–26.6	9.2– 36.1	8.8–24.9	12.7–22.3
	IQR	12–22	13–22.5	9.5–22.7	10.4–20.8	14.5–22.3	13.6–23.1	14.4–20.6
Co	Median	0.62	0.46	0.64	0.63	0.54	0.78	0.65
	Range	0.15–1.75	0.22–2.68	0.14–1.67	0.45–0.9	0.21–15.32	0.24–2.41	0.3–6.10
	IQR	0.34–1.05	0.26–0.94	0.28–1.36	0.54–0.85	0.36–2.41	0.27–1.16	0.4–0.96
Cu[b]	Median (SD)	1639	1600	1787	1693	1825	1784	1913
	Range	1349–1938	1329–2035	1200–2040	1279–2271	1506–2173	1500–2336	1329–2418
	IQR	1568–1687	1520–1788	1480–1964	1455–1889	1561–1992	1641–2333	1640–1913
Zn	Median	5934	5849	6098	6296	6989	6286	6465
	Range	4201–7628	3745–8075	4708–9103	2995–11349	5078–9788	4282–8719	4275–8401
	IQR	5385–6596	5100–6750	5698–6934	5415–6858	5695–8521	4503–7627	5434–7561
As[b]	Median	0.37	0.43	0.33	0.66	0.73	0.59	0.74
	Range	0.08–0.67	0.08–1.65	0.17– 0.96	0.29–2.84	0.35–3.12	0.31–1.73	0.17– 2.46
	IQR	0.25–0.56	0.16–0.88	0.22–0.53	0.36–1.51	0.39–1.37	0.37–0.95	0.34–0.94
Se [c]	Median	101	100	85	131	89	122	105
	Range	84–125	82–153	63–101	117–203	69–108	84–192	85–163
	IQR	94–108	92–111	79–95	118–151	76–101	101–151	89–144

[a] IQR = inter-quartile range (25–75). [b] Statistically significant differences ($p < 0.05$). [c] $p < 0.001$.

Table 7 Concentration of Cd, Hg, Pb, Mn, Co, Cu, Zn, As, Se in umbilical cord blood (μg/L) by site[a]

Metals μg/L	Statistics	Urban N = 16	Industrial N = 8	Atlantic Ocean N = 12	Mining N = 12	Indian Ocean malaria N = 12	Inland malaria N = 7
Cd [c]	Median	0.04	0.01	0.03	0.01	0.01	0.01
	Range	0.01–0.1	0–0.01	0.01–0.32	0–0.13	0.01–0.02	0–0.1
	IQR	0.02–0.1	0.01–0.01	0.02–0.05	0.01–0.02	0.01–0.02	0.01–0.02
Hg [c]	Median	0.5	0.5	4.6	0.7	1.7	1.5
	Range	0.1–5.4	0.2–1.1	1–9.7	0.5–2.3	0.5–6.4	0.3–2.4
	IQR	0.3–2.0	0.3–0.8	1.4–6.3	0.6–1.3	1.1–3.3	1.0–2.2
Pb[b]	Median	24	15	15	21	14	9
	Range	15–87	10–21	7.7–37	1.4–95	5.6–28	5–14
	IQR	18–28	11–17	11–22	8–34	10–19	5–12
Mn	Median	19.7	34.5	33	36.6	35.9	34.6
	Range	7.2–69	29.7–53.6	16.8–80.7	11–59	20–59	19–61
	IQR	15.8–53.2	30.4–39.9	27.2–45.2	27–45.2	27.7–47	31.1–44.4
Co[b]	Median	0.34	0.38	0.17	0.33	0.23	0.33
	Range	0.07–0.85	0.16–0.97	0.41–0.31	0.11–9.4	0.07–0.66	0.17–1.47
	IQR	0.17–0.42	0.27–0.85	0.08–0.19	0.19–1.39	0.16–0.47	0.21–0.4
Cu	Median	641	618	668	637	668	724
	Range	384–1165	532–698	543–931	511–1413	578–870	588–842
	IQR	487–699	551–682	611–702	526–727	641–710	653–842
Zn	Median	2338	2237	2708	2285	2717	2499
	Range	1558–4738	1684–3637	2357–4018	1926–2883	1969–4685	2190–3493
	IQR	1797–4441	1909–2752	2545–3615	2070–2511	2158–3131	2293–2715
As	Median	0.41	0.37	0.57	0.49	0.48	0.79
	Range	0.09–1.26	0.2–0.89	0.13–2.44	0.16–2.84	0.13–1.21	0.09–1.95
	IQR	0.26–0.90	0.22–0.49	0.35–1.3	0.3–1.0	0.34–0.73	0.16–0.82
Se[c]	Median	99	89	159	98	141	131
	Range	79–182.	65–96	128–202	50–113	83–188	103–170
	IQR	83–106	83–93	134–187	83–104	116–158	111–166

[a] Note—no cord blood results for rural site available IQR = inter-quartile range (25–75). [b] Statistically significant differences ($p < 0.05$). [c] $p < 0.001$.

However, lower cadmium levels measured in the respective cord bloods may indicate a limited transfer from mother to foetus. This may be of clinical significance, as cadmium has been shown to cause fetotoxic and embrogenic effects in animal studies and has been found to accumulate in the placenta of smoking mothers.[27,28] Animal experiments have also shown that the protective capacity of the placenta against exposure to Cd is at its strongest during the last trimester of pregnancy, combined with the alteration in the deposition and transportation of zinc and copper.[29,30] During pregnancy these alterations are thought to be mediated by metallothioneins (MT) that bind cadmium to decrease its toxicity.[31] When compared with other studies in the Arctic region, levels of cadmium in South African non-smoking delivering women were found to be very similar.[32,33]

Mercury is a toxic metal that has been identified as a priority contaminant in the circumpolar north (AMAP 2003) and was detected in more than 97% of maternal blood and cord blood samples in the recent study.[33] Concentrations of mercury in umbilical cord blood in our study were found to be almost double when compared to maternal levels at delivery at all sites. The mercury level ratio of cord blood to maternal blood was 2.58 and 1.82 in participants from Atlantic and Indian Ocean coastal populations, respectively. This is of concern as recent studies confirm loss of IQ in children prenatally exposed to mercury, even at very low concentrations.[34] A number of studies have found a direct correlation between blood mercury levels and frequent consumption of fish and other mercury contaminated traditional foods. This is the case for general populations and not only pregnant women. In our study sample, it was found that fish consumption was very low, even in participants residing in coastal areas, where levels of mercury were found to be highest when compared with other sites. In South Africa, other environmental sources such as informal gold mining in the region and the effect of global climate change may be main contributors of increased blood mercury levels. Globally it is estimated that mercury levels will continue to increase for at least the next decade.[35]

The neurotoxic effects of lead, particularly to foetus and children, are well documented.[36] Lead has an ability to freely cross the placental barrier but generally its concentrations in cord blood are slightly lower than in maternal blood. In the present study the highest median levels in both compartments were found in participants from the urban area of Johannesburg. Recent research suggests that there is no safe level of lead and the action level in children should be reduced from the current 100 μg/L to 20 μg/L.[37] Overall levels of lead in maternal and cord blood at delivery were found to be similar to those other industrialised countries in the north, but relatively lower than levels reported in rural, industrial and urban regions of China.[33,38]

Although no data on levels of lead in pregnant South African women exist, lead levels in South African school children have been extensively studied over time.[19,20] A study performed in 2002 found that about 35% of 7 year old schoolchildren in urban areas and approximately 6% in rural areas were found to have blood lead levels equal or above action levels of 100 μg/L. Main confounding factors were the proximity to busy roads and the use of lead in paint in old dwelling and schools, and informal industrial activities and pica. It should be noted that lead was removed from South African petrol only in the beginning of 2007 and the ban on the addition of lead to paint is still to be legislated. Other

developing countries also reported elevated blood levels of lead in young children: rural children in Philippines; children residing in industrial areas of Mumbai and Delhi in India; Karachi in Pakistan and Jakarta.[39–42] At this stage, the possibility of further exposure to lead after birth, especially in socioeconomically disadvantaged populations, not only in South Africa but also in other developing countries, cannot be ruled out.[43]

In contrast to cadmium, mercury and lead discussed above, manganese is an essential trace metal and both deficiency and excess of manganese are toxic to humans. Like lead and mercury, manganese is a neurotoxic metal able to easily cross the blood-brain barrier. In the present study, we found both median levels of manganese in blood samples from delivering women and in cord blood to be above what is considered to be a normal levels (above 14 μg/L) for all sites.[44] It is widely believed that blood manganese levels in pregnant women and neonates are higher than the normally accepted levels for populations due to a compromised processing mechanism, which requires further investigation.[45] A South African study of schoolchildren showed that manganese blood levels were elevated in 14% of children living in Johannesburg (where manganese containing the methyl-cyclopentadienyl manganese tricarbonyl compound (MMT) was introduced to petrol to replace lead, 24 months before the survey) and low in other sites.[21,22]

Concentrations of arsenic were found to be similar at all sites but highest in the inland malaria site. Unconfirmed sources of arsenic may be from the local water as there is no known mining activity at this particular site. Concentrations of cobalt and selenium were found to be within normal limits at all sites.

In summary, this pilot study is the first study performed in South Africa that concurrently measured a broad spectrum of metals in delivering mothers and their newborns in different geographical areas. This study confirmed the ability of toxic metals to permeate the placental barrier (manuscript in preparation). An obvious limitation is the small number of subjects studied in this pilot phase. The results emphasize the need for a main study aimed at indentifying risk factors associated with prenatal exposure to metals and other persistent pollutants in key South African settings, thus contributing to national and international databases and scientific knowledge.

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