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Essential and non-essential trace elements among working populations in Ghana

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ABSTRACT

Background: Lead battery repair workers (LBRW) and electronic repair workers (ERW) may be exposed to inorganic components during work. This study aimed at determining essential and non-essential trace elements in male LBRW, ERW, referents and a group of female petty traders (FPT) in Kumasi (Ghana), taking into account iron status and inflammation.

Methods: Altogether 64 LBRW, 64 ERW, 65 referents and 26 FPT were investigated in this cross-sectional study. Urine, whole blood and serum were collected for determination of trace elements. C-reactive protein and ferritin were determined in serum.

Results: The LBRW had higher blood concentrations of manganese (B-Mn) and lead (B-Pb) and antimony in urine (U-Sb), and lower concentrations of cobalt in blood (B-Co). Being ERW was associated with higher concentrations of blood cadmium (B-Cd), urinary tin (U-Sn) and serum chromium (S-Cr). Concentrations of selenium (B-Se), Co and mercury (B-Hg) in whole blood and iodine in urine (U-I) were relatively high. Marginal iron status appeared to be a determinant for elevated concentrations of Co in particular, but also Mn and Cd in blood. Systemic inflammation was associated with the concentrations of copper and Se. The concentrations of Hg in whole blood were highly associated with Se and arsenic (As) in whole blood, indicating fish consumption as a common source of intake of these elements. However, Hg in whole blood was only slightly associated with Se in serum.

Conclusions: The ERW had elevated concentrations of B-Cd, S-Cr, and U-Sn, while B-Mn, B-Pb, and U-Sb concentrations were higher among the LBRW. Iron status and inflammation had substantial impact on some element concentration. This population had high concentrations of B-Se, B-Hg and B-Co and U-I.

1. Introduction

This study was carried out in Kumasi, the second most populous city in Ghana, where there has been a growth of small-scale industries, of which some are involved in the repair and recycling of electrical and electronic waste and car lead (Pb) batteries. Studies have confirmed that processing of electrical and electronic waste has the potential of releasing metals such as Pb, cadmium (Cd), chromium (Cr) and zinc (Zn) into the air and thus pose a risk to workers' health [1–6]. We have recently reported that Pb battery repair workers (LBRW) in Kumasi had elevated concentrations of Pb in blood (B-Pb) [7]. There are few studies on essential and non-essential trace elements in blood and urine collected from healthy populations in Ghana [8]. Higher concentrations of urinary Pb (U-Pb), tin (U-Sn), arsenic (U-As) and antimony (U-Sb) were measured among gold miners, in small scale artisanal gold mining communities and in electronic waste recycling workers compared to reference populations [9–11]. Urinary concentrations of arsenobetaine and dimethylarsinic acid suggested consumption of fish and shellfish to be one important source of As in the electronic waste recycling workers [11]. Seafood, and especially shellfish, are important sources for As intake in humans. The amount of As in a range of marine species is substantially higher than that of mercury (Hg) [12]. Arsenic occurs

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predominantly as organic compounds in seafood. Although rapidly excreted, it has been proposed that total As in blood (B-As) is a useful predictor of fish intake, because its concentration also reflects the consumption of lean fish [13]. Seafood also contains methyl mercury (MeHg) and the intake depends largely on the species and quantity of seafood consumed. Total Hg in whole blood (B-Hg) is an indicator for the absorbed amount in humans [12,14]. Fish is also an important source of essential trace elements, e.g. selenium (Se) [15]. The amount of selenomethionine varies substantially between fish species [16–18]. Fish also contains low molecular weight organoselenium compounds which are poorly characterized [19]. Recently selenoneine was identified in fish [20]. Iron deficiency is a worldwide prevalent deficiency state [21], which may be associated with higher concentrations of Cd, cobalt (Co) and manganese (Mn) in whole blood (B-Cd, B-Co, B-Mn) [22]. Uptake of inorganic iron (Fe) is dependent on the divalent metal transporter (DMT1) [23], that also transports divalent Mn, Cd and Co into duodenal enterocytes [24]. Export of divalent metal ions through ferroportin out of the enterocyte into the systemic circulation has been less studied. Ferroportin controls the fluxes of Fe(II) and Zn(II) entering into plasma [23]. Also Co, Cd and Mn have been suggested to be transported through ferroportin [25–28]. Ferroportin is regulated by the hormone hepcidin, and its synthesis is increased during systemic inflammation [23]. It is assumed that hepcidin mediates anaemia observed in chronic inflammatory diseases [29]. Whether lower grade inflammation has an impact on the status of other essential and non-essential trace elements is less known. This study was carried out at Suame Magazine, Asafo Fitam and Bantama, all suburbs of the Kumasi metropolis of Ghana. The aim was to assess the extent of exposure to inorganic components in LBRW and electronic repair workers (ERW), by taking into account the effects of trace element concentrations related to consumption of seafood, marginal Fe status and systemic inflammation. A further aim was to fill a knowledge gap with respect to levels of essential and non-essential trace elements in a population from Ghana.

2. Material and methods

2.1. Study design and subjects

Altogether four different groups of subjects were invited to participate in this cross-sectional study. These were male LBRW, ERW and referents. In addition, a group of female petty traders (FPT) was included.The main criterion for inclusion was at least one year of employment at the workplace, or for FPT vendoring within a close vicinity of the workplaces of interest. Subjects who were on sick leave or otherwise absent from work were not included in the study. The age among the participants was restricted to between 18 and 50 years.Eligible for inclusion were workers from two small scale Pb battery workshop sites at Suame Magazine and Asafo Fitam. Altogether 92 LBRW were approached for participation in the study to reach the target of 64 participating LBRW. Their job functions included charging of Pb batteries, breaking of batteries to replace damaged batteries and repair of Pb plates and replacing Pb terminals of the battery by welding. They did not use gloves or any personal respiratory protection during repair work. During the full-shift working period the workers typically did the same repair work for about six hours (depending on the amount of work available), otherwise they stayed outside the workshop area. Altogether 21 different electronic workshops in Bantama were approached to reach the target of including 64 ERW. In total, 85 ERW were asked to participate in order to include this target number. The main job tasks of the ERW were dismantling, soldering and welding and finally reassembly of electronic equipment (e.g. televisions, radios, video players and computers).

Seventy-nine subjects working within the same geographical location as the LBRW and ERW were invited to participate in the study as referents based on the assumption that they belong to the same socio-demographic level as the target groups. As 14 subjects declined to participate, 65 referents were examined. They were recruited from the immediate environs of the workshops where the ERW and LBRW were employed. Their work included selling items such as automobile spare parts and engineering materials (excluding Pb batteries) or selling (but not repairing) used electronic equipment such as televisions, radios, compact disks etc. The FPT comprised women selling goods within the close vicinity of the working environments of the workshops where the LBRW and ERW were employed. Altogether, 52 subjects were invited, of whom 26 agreed to participate in the study. Subjects with known chronic diseases, such as cancer, heart diseases and diabetes, were not considered for inclusion. Subjects known to abuse drugs or alcohol were also excluded. Since malaria is widespread in Ghana, only subjects with active malaria at the time of the examinations were excluded. Two FPT indicated that they were diabetic, and were thus excluded.

This study was approved by the School of Medical Sciences, Kwame Nkrumah University of Science and Technology/Komfo Anokye Teaching Hospital Committee on Human Research Publication and Ethics. The study was also approved by the Regional Committee for Medical Research Ethics of Northern Norway (code 2011/729). An informed written consent was obtained from all participants.

2.2. Examinations

The participants were admitted to a place separated from the workplace for health examinations. Biological samples were collected by authorized health staff after instructions of the procedure. Blood samples were collected on the day when they brought with them from home a first voided morning urine sample. In order to record background variables, exposure and potential confounders (e.g. job history, years of formal education, medical history, alcohol consumption) of importance for the interpretation of the results, a self-administered questionnaire was used. Also pregnancy related information was recorded for the FPT. The answers were filled in by each participant, but the completeness of the answers were checked by the investigator.

2.3. Collection of biological samples

Whole blood was collected from the cubital vein in 5 mL plastic vacutainer tubes with lithium-heparin (Zhejiang Kangshi Medical Devices Co., Ltd, China) after cleaning of the skin with deionised water and ethanol. Whole blood for harvesting of serum was collected in 5 mL vacutainers without additives (Vacuette®, Greiner Labortechnik, Gmbh, Austria). After sampling, the tubes rested for 30 min before centrifugation for 10 min at 1500*g*. Serum was pipetted off into 1.0 mL cryotubes (Sarstedt AG, Numbrecht, Germany). The first voided morning urine sample was collected in a 10 mL Sarstedt polypropylene (PP) tube (Sarstedt AG, Numbrecht, Germany). The urine samples were transferred to a 5 mL PP tube (Greiner Bio-one, CELLSTAR®, UK) for storage. The biological samples were frozen immediately after collection and kept at −20 °C at the Komfo Anokye Teaching Hospital (KATH), Kumasi. The samples were transported to the National Institute of Occupational Health, Norway (NIOH) for long term storage at −20 °C.

Table 1
Background data of lead battery repair workers (LBRW), electronic repair workers (ERW), referents and female petty traders (FPT) under study.
[b]Geometric mean.

	LBRW (N = 64) AM[a](min-max)	ERW (N = 64) AM (min-max)	Referents (N = 65) AM (min-max)	FPT (N = 26) AM (min-max)
Age (years)	31.8 (20–49)	32.6 (18–50)	30.2 (18–50)	34.2 (20–49)
BMI (kg/m^2)	23.3 (17.3–31.1)	22.8 (17.9–29.4)	23.0 (16.5–31.5)	28.2 (16.2–40.0)
Work-years	11.4 (1–30)	10.8 (2–30)	8.9 (1–30)	6.2 (1–20)
Current smokers (in%)	3.1	0	1.6	0
Alcohol users (in %)	15.6	23.4	20.3	4.0
S-ferritin (μg/L)[b]	111 (15–426)	129 (22–796)	134 (16–714)	33 (2–189)
S-CRP ≥ 5 mg/L (in%)	9.4	7.8	7.9	12.0

[a]Arithmetic mean.
[b]Geometric mean.

2.4. Measurements of trace elements in biological samples

The biological samples were analysed for the content of trace elements at NIOH. Whole blood (1 mL) and serum (0.5 mL) samples were prepared by adding 2 and 1 mL of 65% ultrapure nitric acid, respectively. After heating to 90 °C for 90 min in a laboratory oven and cooling to room temperature, the samples were diluted to 14 mL (whole blood) and 7 mL (serum) with deionized (DI) water. Urine specimens were heated for one hour at 80 °C in a laboratory oven prior to analysis in order to prevent laboratory acquired infections and to dissolve urine precipitates.

The analyses were performed by inductively coupled plasma sector-field mass spectrometry (ICP-SF-MS) using an Element 2 mass spectrometer (Thermo Electron, Bremen, Germany) calibrated with whole blood, serum and urine matrix matched standard solutions. For the quality control (QC) Seronorm Trace Elements Whole Blood L-1 (LOT: 1103128) and L-2 (LOT: MR9067x), Seronorm Trace Elements Serum L-1 (LOT: 0903106) and L-2 (LOT: 0903107) and Seronorm Trace Elements Urine L-1 (LOT: 1011644) and L-2 (LOT: 1011645) reference materials (Sero AS, Billingstad, Norway) were used. The results obtained for the elements in the Seronorm™ Quality Assurance materials were within the producer's recommended reference ranges.

Detection limits (DL) for elements in whole blood were 0.28 (B-As), 0.12 (B-Cd), 0.047 (B-Co), 3.5 (copper, B-Cu), 0.13 (B-Hg), 0.30 (B-Mn), 0.071 (molybdenum, B-Mo), 0.20 (B-Pb), 1.3 (B-Se), and 4.3 (B-Zn) μg/L. The corresponding DLs for elements in serum were 0.041 (S-As), 0.025 (S-Co), 2.7 (S-Cu), 0.058 (S-Hg), 0.19 (S-Mn), 0.16 (S-Mo), 0.051 (S-Pb), 0.92 (S-Se), and 3.1 (S-Zn) μg/L. The DLs for the measured elements in urine were 0.037 (U-As), 5.5 (bromine, U-Br), 0.017 (U-Co), 0.056 (U-Cr), 0.16 (U-Cu), 1.4 (U-Fe), 0.074 (U-Hg), 1.2 (U-I), 0.064 (U-Mo), 0.69 (nickel, U-Ni), 0.018 (U-Sb), 0.13 (U-Se), 0.029 (U-Sn), 0.009 (vanadium, U-V), 0.033 (tungsten, U-W) and 13 (U-Zn) μg/L.

The following trace elements were also determined, but their concentrations are not reported since a substantial fraction of the measurements were below DL. The DLs and the number of measurements < DL (shown in brackets) were; B-Bi (bismuth, 0.034; 213) B-Cr (0.79; 124), B-Ni (1.0; 68), B-Sn (0.40; 190), B-U (uranium, 0.091; 218), B-V (0.066; 94), B-W (0.023; 151), S-Bi (0.0072; 185), S-Cd (0.035; 191), S-Cr (0.60; 122), S-Ni (0.80; 110), S-Sn (0.15; 183), S-U (0.0031; 200), S-V (0.077; 158), S-W (0.036; 204), U-Bi (0.002; 73), U-Cd 0.056; 133), U-Mn (0.051; 148), U-Pb (0.46; 82), U-Ti (titanium, 0.39; 102) and U-U (0.011; 122) μg/L. Data on S-Cr, S-Ni and U-Pb are, however, reported due to the substantial differences in values < DL between groups.Urinary creatinine (cr.) was measured with a SFA-200 flow injection analyzer (Burkard Scientific Ltd., Uxbridge, UK) according to the Jaffé reaction. Fifteen participants had urinary cr. below 0.20 g/L. Their urinary measurements were not considered in the statistical analysis.

2.5. Measurements of ferritin and C-reactive protein in serum

Serum ferritin (S-ferritin) was measured by a Cobas 8000 Modular analyzer with reagents from Roche Diagnostics (Mannheim, Germany). The analytical coefficient of variation (CV) was < 4%. Serum C-reactive protein (S-CRP) was measured by a Cobas 8000 Modular analyzer with reagents from Roche Diagnostics (Mannheim, Germany). The analytical CV was < 3.5%.

2.6. Statistical analysis

The trace element concentrations had generally skewed distributions. In order to achieve a normal distribution, these variables were log-transformed and geometric means (GM) are presented. Differences between groups were assessed with analysis of variance (ANOVA), and least significant differences were calculated and compared, in order to separate the groups that differed when more than two groups were compared. In a few cases (S-Cr, S-Ni, U-Pb) where many values were < DL, the Kruskal-Wallis test was used to assess differences between groups and Mann-Whitney *U* test to assess which groups differed from each other. Median values are reported for these concentrations. Multiple linear regression analysis (backward procedure) was also applied to assess associations between specific element concentrations as dependent variables and a set of independent variables, including sex (1/0), being a LBRW (1/0), being an ERW (1/0), S-ferritin (lg), S-CRP > 5 mg/L (1/0), age, body mass index (BMI), alcohol use (1/0), and being active smoker (1/0). Finally, univariate associations were assessed by least square regression analysis giving Pearson's correlation coefficient as the measure of association. A two-tailed p-value < 0.05 was considered to be of statistical significance. Statistical calculations were performed with SPSS, version 24.

3. Results

Three subjects were active smokers and 39 participants reported to consume alcohol (Table 1). The 19 participants with S-CRP ≥ 5 mg/L had GM S-CRP of 10.5 mg/L (range 5–57). The group of FPT had significantly lower S-ferritin compared to the other groups. The concentrations of elements in whole blood, serum and urine are presented in Tables 2 and 3. LBRW had significantly higher B-Pb, S-Pb, U-Pb and U-Sb and significantly lower B-Co than all other groups. ERW had significantly higher S-Mn and S-Cr than all other groups. The concentrations of B-Cu, S-Cu, S-Co, U-Co, U-I and S-Se were significantly higher while B-As, B-Pb, S-Pb and B-Se were significantly lower among FPT compared to all other groups. The GM concentrations of B-Se, S-Se, B-Hg, B-Co and U-I among all participants combined were 252 μg/L, 113 μg/L, 3.8 μg/L, 1.9 μg/L and 238 μg/g cr., respectively.

Multiple linear regression analysis including all participants was

Table 2
The geometric mean (GM) concentrations (in μg/L) of trace elements in whole blood and serum among lead battery repair workers (LBRW), electronic repair workers (ERW), referents and female petty traders (FPT).

	LBRW (N = 64) GM (min-max)	ERW (N = 64) GM (min-max)	Referents (N = 65) GM (min-max)	FPT (N = 26) GM (min-max)
Whole blood				
As^{**,cef}	3.5 (0.7–10)	3.6 (0.9–14)	3.8 (1.5–16)	2.5 (0.8–7.4)
Cd^{d}	0.2 (< DL-0.9)	0.3 (0.1–0.7)	0.2 (< DL-1.8)	0.3 (< DL-4.2)
Co^{***,abc}	1.2 (0.5–7.6)	2.6 (0.5–22)	2.1 (0.4–37)	2.1 (0.7–8.8)
Cu^{†**,cef}	1.0 (0.7–1.3)	1.0 (0.8–1.4)	1.0 (0.8–1.5)	1.1 (0.8–1.6)
Hg^{b}	3.6 (1.0–9.3)	3.6 (1.3–13)	4.3 (1.5–18)	3.6 (2.1–15)
Mn^{**,abef}	9.5 (3.6–24)	8.1 (3.2–39)	8.0 (2.1–17)	10.3 (2.8–37)
Mo	1.1 (0.5–3.9)	1.1 (0.5–2.2)	1.0 (0.3–4.7)	1.0 (0.5–3.2)
Pb^{***,abcef}	200 (45–1099)	97 (36–437)	102 (34–478)	54 (18–379)
Se^{***,cef}	252 (117–369)	265 (167–500)	255 (161–401)	214 (154–300)
Zn^{†,f}	7.1 (2.6–11.1)	7.1 (4.3–9.9)	7.3 (4.2–9.8)	6.6 (3.4–8.8)
Serum				
As	2.1 (0.2–8.0)	1.9 (0.6–6.1)	2.2 (0.4–13)	1.9 (0.5–8.1)
Co^{***,cef}	0.2 (0.1–0.7)	0.2 (0.1–1.2)	0.2 (0.1–1.6)	0.5 (0.1–7.2)
Cr$^{¶,\#\#\#,ade}$	< DL (< DL-15)	0.7 (< DL-6.6)	< DL (< DL-1.4)	< DL (< DL-15)
Cu^{†***,cef}	1.1 (0.5–2.4)	1.1 (0.7–1.9)	1.0 (0.7–2.0)	1.5 (0.8–6.7)
Hg	0.7 (0.2–1.7)	0.7 (0.3–2.0)	0.8 (0.3–2.9)	0.8 (0.4–15)
Mn^{***,ade}	0.8 (0.5–3.0)	1.0 (0.5–2.1)	0.8 (0.5–2.5)	0.8 (0.5–3.0)
Mo	1.5 (0.8–5.3)	1.5 (0.6–3.1)	1.4 (0.4–5.4)	1.3 (0.6–4.2)
Ni$^{¶,\#,bd}$	< DL (< DL-114)	0.9 (< DL-4.5)	< DL (< DL-20)	< DL (< DL-6.3)
Pb^{***,abcef}	1.2 (0.1–28)	0.5 (0.1–9.4)	0.4 (0.1–4.2)	0.3 (0.1–3.4)
Se^{**,cdef}	112 (88–178)	108 (75–153)	115 (86–183)	124 (87–159)
Zn^{†,a}	0.9 (0.6–1.2)	0.8 (0.6–1.2)	0.8 (0.6–1.2)	0.8 (0.5–1.0)

†mg/L; ¶Median; $P_{ANOVA:}$ *** < 0.001; ** < 0.001; * < 0.05. $P\text{-}_{Kruskal\text{-}Wallis:}$ $^{\#}$ < 0.05; $^{\#\#\#}$ < 0.001; $^{a}p < 0.05$ between LBRW and ERW; $^{b}p < 0.05$ between LBRW and referents; $^{c}p < 0.05$ between LBRW and females; $^{d}p < 0.05$ between ERW and referents; $^{e}p < 0.05$ ERW and females; $^{f}p < 0.05$ between referents and females.

Table 3
The geometric mean (GM) concentrations (in μg/g creatinine) of trace elements in urine among lead battery repair workers (LBRW), electronic repair workers (ERW), referents and female petty traders (FPT).

	LBRW (N = 64) GM (min-max)	ERW (N = 64) GM (min-max)	Referents (N = 65) GM (min-max)	FPT (N = 26) GM (min-max)
As^{a}	75 (4.7–559)	101 (27–551)	82 (21–391)	85 (33–251)
Br$^{\dagger f}$	3.7 (1.0–13)	3.5 (1.2–13)	3.1 (0.89–16)	4.5 (2.4–10.1)
Co^{**,cef}	0.59 (0.07–5.8)	0.61 (0.20–3.8)	0.61 (0.14–12)	1.5 (0.42–36.9)
Cr	0.25 (< DL-6.4)	0.23 (< DL-1.0)	0.28 (< DL-7.6)	0.34 (0.13–3.1)
Cu	13 (2.4–80)	13 (5.4–142)	14 (3.9–136)	14 (9.0–86)
Fe^{f}	6.0 (< DL-157)	6.6 (< DL-147)	5.3 (< DL-450)	11 (< DL-210)
Hg^{cf}	0.22 (< DL-4.2)	0.27 (< DL-2.6)	0.26 (< DL-1.2)	0.42 (< DL-6.9)
I^{**,bcef}	208 (80–621)	231 (110–695)	253 (84–613)	328 (162–1221)
Mo	96 (16–1401)	87 (7–590)	118 (10–931)	75 (26–223)
Ni	3.1 (< DL-25)	2.9 (< DL-10)	2.9 (< DL-46)	3.6 (< DL-37)
Pb$^{¶,\#,bc}$	1.8 (< DL-46)	1.1 (< DL-24)	0.6 (< DL-6.1)	0.6 (< DL-2.3)
Sb^{***,abc}	0.75 (0.05–17)	0.16 (0.03–7.6)	0.18 (< DL-2.0)	0.16 (0.06–0.73)
Se^{**,ac}	24 (8.0–92)	32 (15–86)	28 (9.0–89)	35 (24–62)
Sn^{***,a}	0.24 (< DL-20)	0.62 (< DL-9.1)	0.32 (< DL-8.1)	0.36 (0.11–1.9)
V^{*,bc}	0.07 (0.02–0.35)	0.09 (0.03–0.31)	0.09 (0.01–3.2)	0.12 (0.03–1.2)
W	0.14 (< DL-6.2)	0.12 (< DL-2.3)	0.14 (< DL-1.8)	0.13 (< DL-0.49)
Zn^{ab}	178 (30–647)	234 (35–1525)	232 (54–980)	243 (65–430)

†mg/g creatinine; ¶Median; $P_{ANOVA:}$ *** < 0.001; ** < 0.01; * < 0.05.$^{\#}P\text{-}_{Kruskal\text{-}Wallis}$ < 0.01; ^{a} $p < 0.05$ between LBRW and ERW; $^{b}p < 0.05$ between LBRW and referents; $^{c}p < 0.05$ between LBRW and females; $^{d}p < 0.05$ between ERW and referents; $^{e}p < 0.05$ ERW and females; $^{f}p < 0.05$ between referents and females.

Table 4
Results from multiple linear regression analysis (backwards procedure) including all participants. Presented are the respective β-coefficients that were of statistical significance, multiple r and the corresponding p-values.

	Sex	Ferritin	CRP	Alco	Smoke	ERW	LBRW	Age	BMI	Mult r
Whole blood										
As	0.20***			0.08*					0.01*	0.30***
Cd		−0.21***	0.16**		0.35**	0.10**				0.40***
Co		−0.19**					−0.28***		−0.02**	0.40***
Cu	−0.03*		0.07***						0.003*	0.44***
Hg	0.14*			0.14***		−0.09*	−0.09*	0.005*	0.01**	0.42***
Mn		−0.17***					0.06*	0.003*		0.40***
Pb	0.27***						0.30***			0.55***
Se	0.10***		−0.05*	0.04**					0.006***	0.44***
Zn	0.04*									0.15*
Serum										
Cu	−0.15***		0.10***	0.04*						0.46***
Mn				0.06*		0.11***				0.37**
Pb	0.25**						0.45***			0.50***
Se			−0.04**			−0.02*			0.003***	0.33***
Zn		0.03*	−0.03*			−0.02*	0.02*			0.23**
As				0.11*	−0.32*				0.01*	0.24**
Co		−0.56***								0.71***
Hg				0.12**		−0.09*	−0.09*	0.006***		0.36***
Urine										
Cr	−0.21*								−0.02*	0.21*
Se	−0.13*					0.09**				0.26**
Zn							−0.12*			0.17*
As						0.10*				0.15*
Co		−0.50***						−0.007*		0.49***
Hg	−0.23*									0.17*
Ni		−0.19**							−0.02**	0.30***
Sb							0.65***			0.56***
Sn						0.34***			−0.02*	0.33***

*** p < 0.001.
** p < 0.01.
* p < 0.05.

used to assess several factors simultaneously (Table 4). Being LBRW was associated with higher concentrations of B-Mn, B-Pb, S-Pb, U-Pb and U-Sb and lower B-Co. Being ERW was associated with higher concentrations of U-As, B-Cd, S-Mn and U-Sn. Several element concentrations were associated with being FPT. S-ferritin concentrations were negatively associated with B-Cd, B-Co, S-Co, U-Co and B-Mn. The highest S-Co concentrations were associated with having low S-ferritin concentrations (Fig. 1). This was also observed for B-Co (Fig. 2, panel A) and U-Co (Fig. 2, panel B). Also the concentrations of B-Mn (Fig. 3, panel A) and B-Cd (Fig. 3, panel B) were highest among subjects with the lowest concentrations of S-ferritin. When excluding 13 subjects with S-ferritin below the normal range according to the reference range of the laboratory, indicative of Fe deficiency, the remaining subjects in the low S-ferritin group still had significantly higher concentrations of S-Co and U-Co compared to the group with S-ferritin from 66 to 99 µg/L (results not tabulated). Subjects having S-CRP ≥ 5 mg/L had higher GM (95% CI) concentrations of S-Cu (1.37 mg/L (1.24-1.51) vs. 1.08 (1.04-1.12); p < 0.001) and B-Cu (1162 µg/L (1091–1241) vs. 994 (976–1012); p < 0.001) than subjects having S-CRP < 5 mg/L, while B-Se (255 µg/L (248–262) vs 225 (207–246); p = 0.01) and S-Se (114 µg/L (112–116) vs. 103 (96–109); p = 0.005) were lower (not tabulated). The GM (95% CI) B-Mn concentration of the LBRW was higher than the other subjects combined (9.6 µg/L (8.7-10.5) vs 8.3 (7.9-8.8); p = 0.01) after adjusting for S-ferritin and age. B-Pb was significantly associated with B-Mn (Pearson's r = 0.54, p < 0.001) among the LBRW, but not among the non-LBRW combined. Fig. 4 shows that the GM concentrations of B-Mn was highest among the third of LBRW with the highest B-Pb concentrations after adjusting for S-ferritin and age. The GM (95% CI) concentration of B-Co was lower among the LBRW when compared to the non-LBRW combined (1.2 µg/L (1.0-1.5) vs 2.3 (2.0-2.6); p < 0.001) after adjusting for S-ferritin and

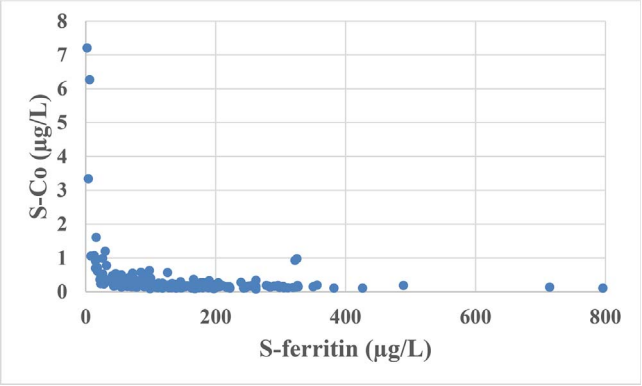
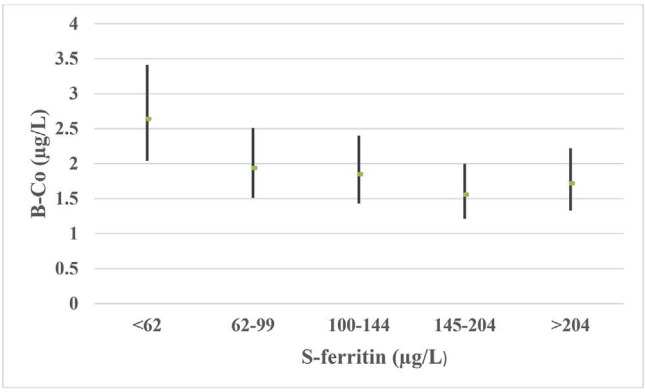


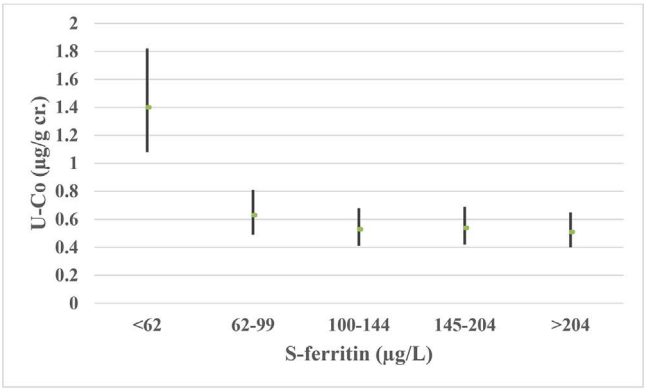
Fig. 1. The association between cobalt and ferritin in serum among all participants.

Panel A



p<0.05; between <62 and 145-204; between <62 and >204

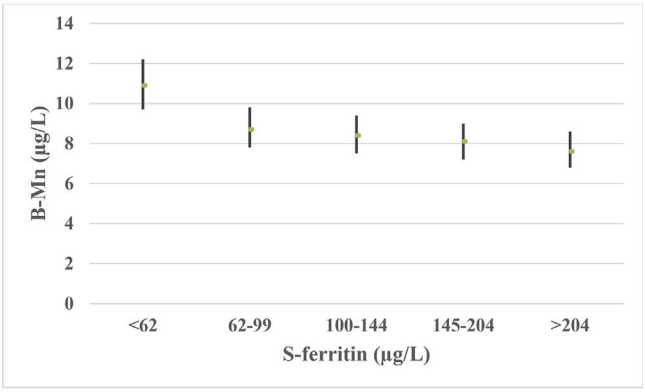
Panel B



p<0.05; between <62 and 62-99; between <62 and 100-144; between <62 and 145-204; between <62 and >204

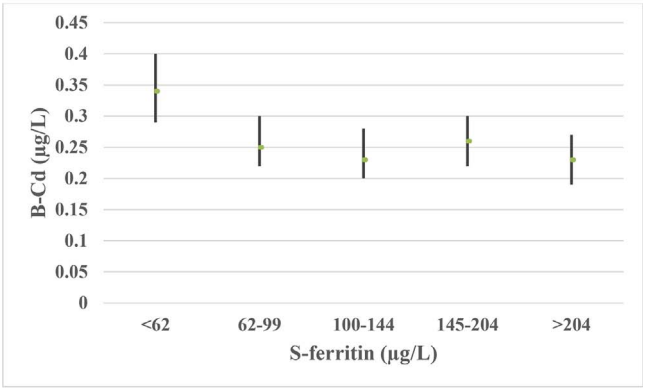
Fig. 2. The GM (and 95% CI) concentrations of cobalt in whole blood (adjusted for being LBRW and BMI) (Panel A) and urine (adjusted for age) (Panel B) according to the serum ferritin concentrations stratified into five equally large groups.

Panel A



p<0.05; between <62 and 62-99; between <62 and 100-144; between <62 and 145-204; between <62 and >204

Panel B



p<0.05; between <62 and 62-99; between <62 and 100-144; between <62 and 145-204; between <62 and >204

Fig. 3. The GM (and 95% CI) concentrations of manganese (adjusted for age and being LBRW) (Panel A) and cadmium (adjusted for being ERW, smoker and S-CRP ≥ 5 mg/L) (Panel B) in whole blood according to the serum ferritin concentrations stratified into five equally large groups.

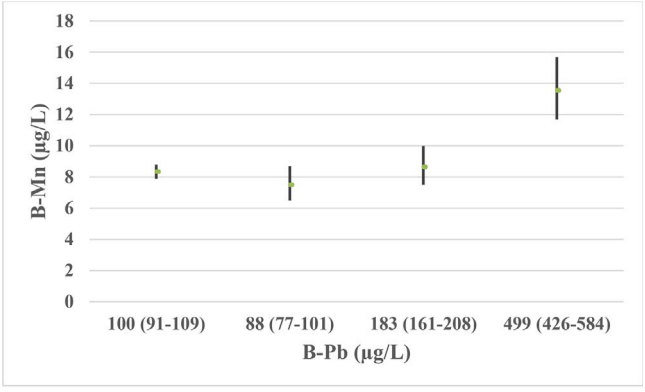
BMI. No statistically significant association was observed between B-Co and B-Pb.

The U-Hg concentrations were low, indicating that B-Hg to a large extent reflects MeHg exposure and thus the intake of products of marine origin. Concentrations of B-Hg were highly correlated with concentrations of B-Se and B-As (Table 5). It is noteworthy that the correlation between B-Hg and S-Se was low (Pearson's r = 0.14, p = 0.04). Fig. 5 shows the GM (95% CI) concentrations of B-Se and S-Se according to the concentrations of B-Hg stratified into five equally large sized groups. There is an increase in B-Se concentrations according to increasing B-Hg levels, while the concentrations of S-Se are similar across all B-Hg strata.

4. Discussion

This is, to our knowledge, the largest study of essential and non-essential trace element concentrations in biological fluids collected from a population in Ghana. The concentrations of B-Se, U-I and B-Co were high, and also B-Hg was higher than e.g. in most European countries. The LBRW had higher concentrations of B-Mn, B-Pb, S-Pb, U-Pb and U-Sb and lower concentrations of B-Co, while the ERW had higher concentrations of B-Cd, S-Cr, S-Mn, U-As and U-Sn and possibly S-Ni compared to the other groups. Iron deficiency was an important determinant for the measured concentrations of Co, Mn and Cd. Subjects with CRP ≥ 5 mg/L had higher B-Cu and S-Cu and lower B-Se and S-Se concentrations. The concentrations of B-Hg were highly associated with B-Se and B-As, indicating fish consumption as a common source of intake.

The LBRW had higher concentrations of B-Pb, S-Pb, U-Pb and U-Sb. Lead and Sb are main metal constituents in car Pb batteries [30,31].



p<0.05; between426-584 and 161-208; between 426-584 and 77-101; between 426-584 and 91-109

Fig. 4. The GM (and 95% CI) concentrations of B-Mn in referents (left) and LBRW according to their concentration of B-Pb stratified into three equally large sized groups adjusted for S-ferritin and age.

Table 5
Associations between the concentrations of mercury, arsenic and selenium in urine, whole blood and serum among all participants.

	B-Hg	B-As	B-Se	S-Hg	S-As	S-Se	U-Hg	U-As
B-Hg	–							
B-As	0.54***	–						
B-Se	0.50***	0.45***	–					
S-Hg	0.88***	0.46***	0.31***	–				
S-As	0.44***	0.86***	0.29***	0.42***	–			
S-Se	0.14*	0.14*	0.33***	0.26***	0.19**	–		
U-Hg	0.37***	0.08	0.04	0.44***	0.08	0.04	–	
U-As	0.31***	0.46***	0.14	0.28***	0.56***	0.01	0.23**	–
U-Se	0.12	0.09	0.10	0.15*	0.16*	0.16*	0.47***	0.52***

*** $p < 0.001$.
** $p < 0.01$.
* $p < 0.05$.

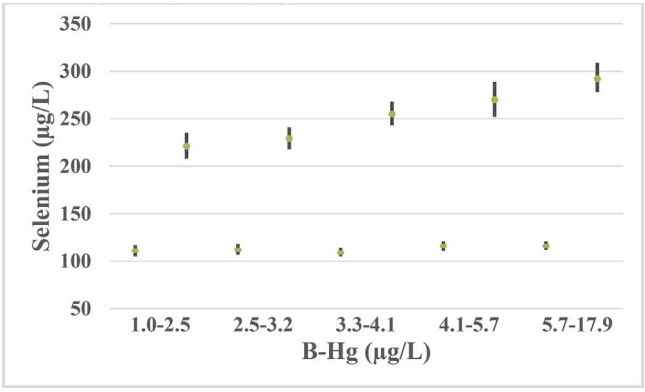


Fig. 5. The GM (and 95% CI) concentrations of B-Se (•) and S-Se (−) stratified according to the concentrations of B-Hg among all participants into five equally large sized groups.

Furthermore, LBRW with B-Pb > 294 µg/L had higher concentrations of B-Mn. Several studies have reported higher B-Mn in Pb exposed populations [32–34]. It has been proposed that increased synthesis of protoporphyrin in erythrocyte precursors induced by Pb exposure also results in increased erythrocyte uptake of Mn [32]. The B-Co concentrations were around 50% of that of the other groups, although U-Co and S-Co were comparable to that of the referents. Lower B-Co in a Pb exposed population has also been reported [34], but mechanisms are not known.

Regression analysis showed that ERW had higher concentrations of B-Cd, S-Mn U-As and U-Sn. It is plausible that the slightly higher concentrations of Cd and Sn may be related to soldering during repair made by the ERW [35–37]. The slightly higher S-Mn, S-Cr and S-Ni may point to welding as another source of work-related exposure [38]. Also concentrations of U-As were higher. This has been reported during E-waste recycling in Ghana, but fish consumption was suggested to be a cause for increased U-As [11]. The higher U-As may be difficult to interpret as the concentrations of B-As and S-As were similar among the four groups under study, and U-As is related to consumption of fish and seafood. The GM B-Hg concentration of 3.9 µg/L is higher than GM concentrations of 0.83 and 0.58 µg/L in US and German populations [39,40], but similar to the GM of 3.9 µg/L measured among Korean men [41]. Fish consumption in Korea is high. The mean per capita fish consumption in Ghana is estimated at about 26 kg [42]. The U-Hg concentrations are low, suggesting low exposure to inorganic mercury, e.g. from dental amalgam or illegal gold mining. Thus, it is likely that B-Hg mainly reflects MeHg in this population. Around 24% of the values were above human biomonitoring I (HBM I) value of 5 µg/L where no effect is anticipated. One value was higher than the HBM II value of 15 µg/L, where an increased risk of effect is assumed [43]. Concentrations of B-Se (GM = 252 µg/L) were substantially higher, while concentrations of S-Se (GM = 113 µg/L) were moderately higher among all participants than results from a pooled data analysis of 75 studies showing GM concentrations of 121 and 91 µg/L of B-Se and S-Se, respectively [44]. The S-Se concentrations increased only slightly according to the level of B-Hg among all participants, although fish is regarded as one important Se source for humans [45,46]. A recent study determined the mean Se content of numerous fish species to be 0.32 mg/kg [47].

In contrast to S-Se, B-Se increased substantially by increasing B-Hg (Fig. 5). These results could suggest that participants consuming more marine food tend to accumulate Se in the cellular blood compartment, predominantly containing erythrocytes. A recent study of a fish- eating population in Japan reported that selenoneine was highly concentrated in the blood cellular fraction, and that selenoine was higly correlated with MeHg in that fraction [48]. One study of rats reported that selenomethionine was not taken up [49]. The selenomethionine and selenoneine content varies substantially between fish species [16–18,20]. Fish is likely also to contain low molecular mass organoselenium species other than selenoamino acids [19]. Plasma Se may be a marker of selenomethionine content in food or Se-enriched yeast supplement, but not other forms of Se [50].

The occurrence of selenosis was studied among inhabitants of the Brazilian Amazon [51]. Their median B-Se and S-Se concentrations of 228 and 135 µg/L, respectively, are similar to concentrations measured in the present study. No evidence of selenosis was observed in that study, suggesting that no toxic effects of Se among the participants of the present study can be expected. This is also in accordance with previous evaluations [52].

Although less known, studies have shown associations between fish consumption and B-As [13,46]. It is therefore no surprise that B-Se, B-Hg and B-As were highly significantly correlated in the present study. Arsenic occurs predominantly as various organic As compounds in seafood, and arsenobetaine has been shown to be the main As compound in fish [16].

Iron status is commonly assessed by measuring serum ferritin concentrations [53].However, serum ferritin may increase during inflammation, but no significant difference was observed between participants of this study having S-CRP ≥ 5 mg/L or lower than 5 mg/L (GM127 µg/L vs 105 µg/L; p = 0.51). Twenty percent of FPT and 3.1% of male participants had S-ferritin values indicating Fe deficiency. The concentrations of B-Co, B-Cd, B-Mn, U-Co and S-Co were significantly higher among participants in the lowest S-ferritin quintile. When excluding participants with Fe deficiency, S-Co and U-Co (but not B-Cd and B-Mn) were still significantly higher among the remaining participants in the lowest S-ferritin quintile. This suggests that Fe deficiency is not required for increased Co uptake. A previous study showed higher B-Co, B-Cd and B-Mn in Fe deficient humans [22]. The most efficient transport by human DMT1 was observed for Cd (II) followed by Fe (II), Co (II) and Mn (II) [24]. Thus, results from the present study are in accordance with experimental data. The main control point of gastrointestinal absorption of Fe is ferroportin that is responsible for the export of Fe out of the intestinal cells [23]. Ferroportin expression also stimulated the efflux of Co, but not Cd and Mn [27], although ferroportin as Mn exporter has been proposed [26]. Ferroportin is regulated by hepcidin. IL-6 is an important inducer of both hepcidin and the CRP gene during inflammation, and CRP is a marker of systemic inflammation [54,55]. Having S-CRP ≥ 5 mg/L had no impact on the concentrations of Cd, Mn or Co, but these subjects had higher B-Cu and S-Cu. Associations between S-CRP and S-Cu have been shown previously [56,57]. The enhanced amount of S-Cu during inflammation may be due to increased liver ceruloplasmin synthesis and release [56]. Lower S-Se and B-Se were also observed among subjects with S-CRP ≥ 5 mg/L, also in agreement with previous studies [58]. It has been suggested that an acute inflammatory response does not affect the erythrocyte concentrations of Cu and Se [59]. Thus, it is possible that the alterations observed in B-Se and B-Cu are not alterations in the blood cellular compartment, but related to altered serum

concentrations.

The I intake is regarded as adequate when the population median U-I concentration is from 100 to 199 μg/L [60]. The median concentration of U-I among the participants in this study was 225 μg/L, indicating a higher intake than recommended. Low I intake during pregancy has been associated with cognitive impairment in the offspring [60]. It is therefore important to emphasize that the FPT, aged 20–49, had median U-I of 231 μg/L, which is regarded adequate for pregnant women [61]. Excess I intake may cause thyroid diseases or extrathyroid diseases, but reported effects vary substantially in relation to ingested amounts [62]. Normal B-Co values are below 0.5 μg/L [63]. The average among all participants of this

study was, in contrast, 1.9 μg/L. No dietary data were available. It is therefore difficult to assess causes for these higher B-Co concentrations. High Co exposure is associated with a range of systemic effects, e.g. erythropoietic actions, goiter or neurotoxic effects. However, no signs of Co toxicity was observed in healthy volunteers at sustained B-Co concentrations of 10–70 μg/L for 90 days [64]. Significant systemic effects is not likely to occur below B-Co of 300 μg/L in healthy individuals [65].

In summary, both ERW and LBRW had increased concentrations of some elements in biological fluids. This studied population had high concentrations of U-I, B-Se, B-Hg and B- Co, which should be elucidated in further studies. Iron status and inflammation had substantial impact on some trace element concentrations.

Conflict of interest

The authors declare to have no conflict of interests.

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