

Progress in Medical Geology

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Edited by

Motomu Ibaraki and Hiroko Mori

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PREFACE

The field of medical geology has continued to expand in interest and importance over the last several decades. This unique research field focuses on relationships between geological environments and humans, leading to both detrimental and beneficial health outcomes. Not surprisingly, the field is broad and complex, and commonly requires a broad interdisciplinary focus to address the variety of human health issues and diseases specifically related to geological materials or earth-system processes. Moreover, this field of study extends beyond simply describing the geographical incidences of disease and likely associations with geological settings to include vector-borne diseases of emerging interest to the medical community (Bowman et al., 2003).

This book provides a sample of the diversity now evident with various research topics. For example, researchers remain interested in health problems resulting from exposure to toxic minerals and lack of essential trace elements, problems with strong roots in geology, be they natural or anthropogenic. Research also extends to health problems, which could include respiratory diseases caused by chronic exposure to dust from mining or volcanic eruption; cancer, leukemia or other serious diseases related to exposure to radioactive materials or ingestion of toxic elements; and anemia, miscarriages or various health problems caused by nutrient deficiencies. Alternatively, research commonly turns up health benefits that for example are associated with hot springs and sand baths or certain health-protective effects related to natural constituents in drinking water.

The widespread opportunities in research, given the importance of human health problems influenced by various geological factors, have fostered the development of a vibrant community of scholars working in medical geology. Bunnell et al. (2007) elaborate five principal goals for research in medical geology. These include: (1) to determine the geological materials in soil and water which cause adverse health effects to living organisms, (2) to tackle the environmentally associated health problems with interdisciplinary teams, (3) to find the geological materials which bring health benefits to humans, (4) to help the public become aware of health issues related to hazardous geological materials, and (5) to

better understand relationships of environmental issues in developed as compared to developing countries. The main purpose of publishing “Progress in Medical Geology” is (1) to introduce the kinds of studies in medical geology, which best represent the core areas of this field, to communities of researchers including both graduate and undergraduate students, and (2) to provide examples of research topics that are unique in terms of their broad interdisciplinary focus.

Overall, the book includes 16 case studies contributed by researchers in science and engineering, covering broad areas of interest in medical science, neurology, and Earth sciences. Topics are organized in four chapters. The first chapter covers adverse health effects related to contaminants in water. Such contamination commonly includes naturally occurring elements associated with geologic materials, like arsenic, fluoride and uranium. The first chapter includes four papers. Papers by Godebo and others, and Hartmann and Breitstadt cover the health concerns related to children in African countries drinking water contaminated with arsenic and fluoride, respectively. Renteria-Villalobos and others, and Singh and others investigate uranium contamination in groundwater in Chihuahua, Mexico and in Punjab State, India, respectively. They provide recommendations on techniques for the purification of water contaminated by radionuclides.

The second chapter includes four papers that address relationships between natural environments and human health, including both negative and beneficial outcomes. The spectrum of topics ranges from relating seasonal influences to the incidence and etiology of hospitalization disease in Texas (by Pingitore et al.) to an examination of geomagnetic disturbances on multiple sclerosis (by Sajedi et al.), to an investigation relating heart disease and hardness of drinking water (by Horodyski) and finally to an investigation of the effects of natural treatment of geological materials in Nigeria (by Nghargbu et al.)

Chapter three includes five papers focusing on health issues associated with human activities, including coal mining and war. For the past few decades, as demands for energy have continued to increase, so too have concerns associated with human health, especially in the mining and use of coal and exposure to harmful elements from coal in power production. Health issues associated with coal mining activities are addressed in papers by Lar, and Golka and others. They examine potentially harmful elements due to mining in Nigeria, and urinary bladder cancer associated with coal miners in Germany, respectively. The paper by Riberio and

others is focused on the identification and quantification of volatile organic compounds from the self-burning of the Arroyo Galladas coal waste pile in Spain. The final two papers in this chapter are related to military service, including a historical review of research by Kalinich, and work by Shinn and others examining the long-term effects of wounds containing metal fragments.

The last chapter addresses certain societal roles for research in protecting the health of communities from both anthropogenic activities and natural hazards. Wilson investigates the impact of hydraulic fracking on communities. Martinez-Sacristan and Martinez-Mojica investigate issues related to access to safe drinking water in Columbia and also discusses social responsibility for the control of natural hazards in terms of preventative measures.

The inspiration of this book came from "*The 5th international conference on medical geology 2nd Symposium on advances in geospatial technologies for health*" convened in Arlington, Virginia, USA, between August 25-29, 2013. The editors are grateful for the opportunity to work on assembling this volume. We particularly would like to thank the reviewers who provided valuable comments and contributed to improving the quality of this publication. We also appreciate the assistance of Bruce Rogers at Ohio State University, whose editing skills enabled us to achieve the highest international standards, and proofreading help from Joshua Wu at College of Public Health, Ohio State University. The implementation of our manuscripts would not have been possible without their support. We also want to express our sincere thanks to the publisher and their technical support team who helped us to organize our book. Finally, special thanks are also due to all of the authors who took time to contribute their research.

We hope that the readers of this book will see this volume as a stepping stone for deeper understanding of human health issues related to geological environments. Furthermore, we expect that the readers will gain greater insight into the field of medical geology, which will lead to further interest in this emerging interdisciplinary field.

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CHAPTER ONE

ADVERSE HEALTH EFFECTS OF WATER CONTAMINATION

1.1

IMPACTS OF DRINKING WATER CONTAMINATION ON CHILDREN

ARSENIC OCCURRENCE AND EXPOSURE TO CHILDREN IN THE MAIN ETHIOPIAN RIFT

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Abstract

Chronic exposure to arsenic (As) in drinking water has been associated with adverse health effects in many parts of the world. This study aims to assess the relationship between arsenic (As) in drinking water and in urine samples collected from exposed children in the Main Ethiopian Rift (MER), and to compare these with As reference levels in urine established in other biomonitoring studies. The MER groundwater is used as a primary source of drinking water in the central MER and is often contaminated with As. The average As concentration in groundwater from the lacustrine sediment aquifer underlying the study locations was 25.7 ± 23.3 $\mu\text{g/L}$ (range: 1.5–73.4 $\mu\text{g/L}$; $n=67$), from which 43% of the investigated wells exceeded the World Health Organization (WHO) drinking water guideline value of 10 $\mu\text{g/L}$. The occurrence of As in the groundwater is controlled by the oxidizing state (Eh) of the groundwater in the aquifer (mean Eh = +73.3 \pm 65) and by its sodium bicarbonate (Na-HCO₃) chemical composition and high pH (>~8). These conditions lead to desorption of As from Iron (Fe) oxides and consequently result in groundwater contamination with As. Urinary As in exposed children aged 10 to 15 years ($n=164$) was significantly correlated with As concentration in drinking water ($R^2 = 0.45$, $p < 0.001$), although the majority of individuals (88%; $n=144$) had urinary As levels higher than those

measured in drinking water, suggesting possible exposure from other sources. Moreover, many of the study individuals (88%; n=144) had urinary As exceeding commonly used reference levels (e.g., the 15 µg/L level from a biomonitoring study in Germany) established in other populations from uncontaminated areas. Arsenic was also detected in cereal samples of maize, wheat, and teff (with mean values of 0.0044µg/g, 0.0044µg/g, and 0.034µg/g, respectively), which are the major cereals consumed in the MER. The health effects of As in the MER are not known at this time; future studies are therefore needed to evaluate the possibility of adverse health effects of As in this region from long-term exposure to this known contaminant.

Keywords: arsenic, biomarker, children, Main Ethiopian Rift

1. Introduction

Chronic exposure to As from drinking water and food sources is known to affect the health of millions of people worldwide (WHO, 2001; Chakraborti et al., 2002; Smedley and Kinniburgh, 2002; Cheng et al., 2010; Yunus, et al., 2011; Chen et al., 2011). This study focuses on the Main Ethiopian Rift (MER), which is part of the Great East African Rift System (EARS) and is a unique geological feature where active faulting has generated huge pyroclastic volcanic rocks (Chorowicz, 2005) that are reactive with local groundwater (Rango et al., 2013). The geochemical processes that control the groundwater chemistry lead to mobilization of As to the MER groundwater (Rango et al., 2013). Indeed, the interaction between low salinity water from the highlands and aquifer rocks composed of young pyroclastic volcanic sediments enriched with a variety of naturally-occurring elements releases a variety of contaminants. A large number of wells that are used for drinking water in the region have been documented to contain high levels of other types of naturally occurring contaminants with known health effects, including fluoride (F⁻) and As (Reimann et al., 2003; Rango et al., 2012, 2013, 2014).

In the MER, over ten million people depend primarily on groundwater for drinking and domestic utilization (Kloos and Tekle-Haimanot, 1999), thus the widespread presence of these toxic contaminants is of considerable concern. Recent findings from research in the region have highlighted that As concentrations exceed the current World Health Organization (WHO, 2011) guideline value of 10 µg/L for As in drinking water in many locations (Reimann et al., 2003; Rango et al., 2010, 2013). This suggests that As may pose a direct health risk to local populations, an

issue that warrants additional investigation and health effects studies.

Although recent studies in the MER (e.g., Rango et al., 2013; Merola et al., 2014) have mapped the distribution of As in groundwater wells, additional exposure from food sources is likely. This is particularly true in the MER area since local communities mainly rely on food grown locally in As-containing soils. The As in the local farming soil is mainly derived from volcanic ash that contains elevated As (Rango et al., 2013), which can be absorbed by the crops grown in the area. To better account for the total exposure to As, urine analysis can be used to estimate recent ingestion resulting from consumption of food and water sources (Hughes, 2006; Marchiset-Ferlay et al., 2012).

A previous study has attempted to evaluate long-term exposure by measuring As in toenails and found a high correlation to As in water (Merola et al., 2014). The present study further explores As content in the staple local crops and urine of individuals residing in MER rural communities. In particular, the study aims to evaluate the relationships between As concentration in MER groundwater and urinary As from exposed individuals, and compares these with reference levels established in biomonitoring studies conducted in other regions where people are not known to be exposed to environmental sources of As. This comparison is crucial for obtaining a better perspective on the source and the level of As in urine that could pose health risks, as well as for generating better hypotheses to investigate As-related health effects in the region.

2. Materials and methods

2.1. Water sampling and arsenic measurement in groundwater

The groundwater samples considered in this study comprise a subset of samples collected in previous research (Rango et al., 2013). The samples were collected during the dry season from 67 community wells in the Ziway-Shala basin of the MER (April–May 2010, March 2011, and November 2012) (Fig. 1). They were collected from active pumping wells that are primarily used for drinking water. Water was first allowed to flow for a few minutes from the wells. Prior to sampling, in situ measurements were conducted for pH, redox potential (Eh), temperature, and electrical conductivity (EC) using instruments that were calibrated daily. Water samples were then filtered in the field using 0.45 µm filters. Samples allocated for cation/trace metal analyses were filtered directly into 60ml polyethylene bottles that had been cleaned with trace metal grade ~1N

HCl and ~1N HNO₃, and then rinsed with deionized water having resistivity >18 MΩ/cm. The samples were immediately acidified with high-purity HNO₃ (Fisher Optima). Unfiltered and unacidified water samples were also collected into 60 ml and 30 ml polyethylene bottles for measurement of alkalinity (as bicarbonate (HCO₃³⁻)).

All lab analyses were conducted in the analytical facilities at Duke University (USA). Concentrations of major cations of calcium (Ca²⁺), magnesium (Mg²⁺), sodium (Na⁺), and silica (SiO₂) were measured using a Fisons Spectraspan 7 direct-current plasma (DCP) spectrometer. This instrument was calibrated using solutions prepared from plasma-grade single-element standards. Major anions of chloride (Cl⁻), sulfate (SO₄²⁻), and nitrate (NO₃⁻) were analyzed using an ion chromatograph (IC). Alkalinity (as HCO₃³⁻) was measured using titration techniques to pH 4.5. Arsenic was analyzed via a VG Plasmaquad 3 inductively coupled plasma-mass spectrometer (ICP-MS) calibrated using serial dilutions according to the National Institute of Standards and Technology (NIST) 1643e standard.

2.2. Cereal sampling and arsenic analysis

A total of 23 cereal samples, including 9 maize, 7 wheat, and 7 teff samples, were collected from the MER. These cereals are the dominant crops grown locally, and all three are regularly consumed by local populations. The samples were collected and kept in plastic bags for further analysis.

For measurement of their As content, the cereal samples were ground finely, dried at 60 °C, and digested as follows: approximately 0.3 g of the sample was poured into an acid resistant Teflon tab. Then, 2-3 mL of optima nitric acid (50% HNO₃) was added to the sample and heated at 60°C. Hydrogen peroxide (0.5 - 1 mL) was periodically added to the solution until digestion was complete, that is, until a clear solution was reached for As analysis using ICP-MS.

The accuracy of the analytical procedures was verified based on analysis of appropriately certified reference materials (CRMs) using the same digestion and analytical methods. Maize CRMs were purchased from the National Research Center for Certified Reference Materials, China (NRCCRM). Mean recovery of the CRM was 86%.

2.3. Study subjects, urine sampling and arsenic analysis

Urine samples were collected from 17 communities (representing a sub-sample of the 67 groundwater wells described above) in order to cover a large range of As concentrations in the basin (e.g., 1.5 to 74 $\mu\text{g/L}$). We collected first morning void urine samples from children aged between 10 to 15 years old ($n=164$), who were enrolled in a study of urinary fluoride and dental fluorosis in the MER (Rango et al., 2014). Only permanent residents drinking water from community wells were enrolled in the study. Prior to enrollment, the subjects were informed of the study purpose and were asked if they were willing to participate in the study. The children who volunteered were then enrolled (subject to additional parental consent) in the study by coming to local clinics, schools, or other village-level meeting sites.

The urine samples were collected in acid-washed 60 ml ultra-cleaned polyethylene bottles. Quality control was conducted using freeze-dried urine reference material (SERO210705, LGC Standards, and NIST SRM 2668 low level). Repeatability of the arsenic measurements in urine was evaluated using 25 samples in a lab at the Research Triangle Institute (RTI) International (Research Triangle Park, USA). The results from these re-analyses were consistent with our measurements (the repeatability of As was 103.8%). The recovery of As in the urine samples with respect to the National Institute of Standards and Technology (NIST) standard was 105%. The detection limit for As using our methods was 0.05 $\mu\text{g/L}$.

2.4. Ethical considerations

The research design was conducted with the ethical approval (Protocol No. A0045 and A0741) of the Institutional Review Board (IRB) at Duke University. All children who agreed (with their parents) to participate were provided written informed consent prior to enrollment in the study. The anonymity of investigated subjects has been maintained.

2.5. Statistical analysis

The database construction and basic statistical analyses were conducted using Microsoft Excel 2010 and the IBM SPSS statistical package version 22.0. Descriptive analyses were carried out using medians, means, and standard deviations for continuous variables. Bivariate analyses were performed using t-tests.

3. Results and discussion

3.1. Arsenic occurrence in MER groundwater

The concentration of As in the groundwater from wells sampled in the Ziway-Shala basin ranged from 0.4 to 190 $\mu\text{g/L}$ with a mean of $18.6 \pm 30.9 \mu\text{g/L}$ ($n=67$). The median concentration was $6.3 \mu\text{g/L}$. In 43% of these wells, the As concentration exceeded the World Health Organization recommended limit of $10 \mu\text{g/L}$ in drinking water (WHO, 2011) (Fig. 1),

The groundwater chemistry of the region is characterized by two major hydrochemical signatures. The first type is one that contains low total dissolved solids (TDS) (generally with electrical conductivity (EC) $< 400 \mu\text{S/cm}$) and high $\text{Ca}^{2+}(\text{Mg}^{2+})\text{-HCO}_3^-$ concentrations; this water originates primarily from the basaltic highlands and escarpments surrounding the Rift Valley. This type of groundwater is characterized by low concentrations of As (all $< 2 \mu\text{g/L}$; mean: $0.95 \pm 0.45 \mu\text{g/L}$; $n=11$). The second type is characterized by high TDS and $\text{Na}^+\text{-HCO}_3^-$ concentrations. This groundwater is assumed to be generated by the hydrolysis process in the aquifers within the Rift and is characterized by high concentrations of As ($21.5 \pm 32 \mu\text{g/L}$; $n=56$) and other associated contaminants such as U and F^- . The pH of the groundwater samples taken from the floor of MER ranged from near neutral to alkaline (range: 6.9-8.9), while EC varied from 248 to 3970 $\mu\text{S/cm}$ (mean: $1237 \pm 747 \mu\text{S/cm}$).

In the MER, field-based measurements of the inorganic As species predominantly contain arsenate -As(V) (over 80%) over the more toxic arsenite-As(III) species, indicating an oxidizing condition of the groundwater (Rango et al., 2013). Most wells had high levels of Eh ($> 50 \text{ mV}$; range: -146 to 229 mV ; mean: $+73 \pm 65 \text{ mV}$), although water from three wells had negative Eh (-26 , -130 and -146 mV). These results suggest that groundwater from the floor of the MER is typically under slightly to moderately oxidizing conditions.

The MER aquifer is mainly composed of rhyolitic volcanic and derived fluvio-volcano lacustrine sediments. In this aquifer, the total content of As in rhyolites and sediments was found to range between $1.1\text{-}3.5 \text{ mg/kg}$ (mean: $2.5 \pm 0.6 \text{ mg/kg}$) and $1.4\text{-}16.1 \text{ mg/kg}$ (mean: $6.6 \pm 6 \text{ mg/kg}$), respectively (Rango et al., 2013). These values correspond to As levels found in similar sediments ($5\text{-}10 \text{ mg/kg}$) from other locations (Webster, 1999; Smedley and Kinniburgh, 2002).

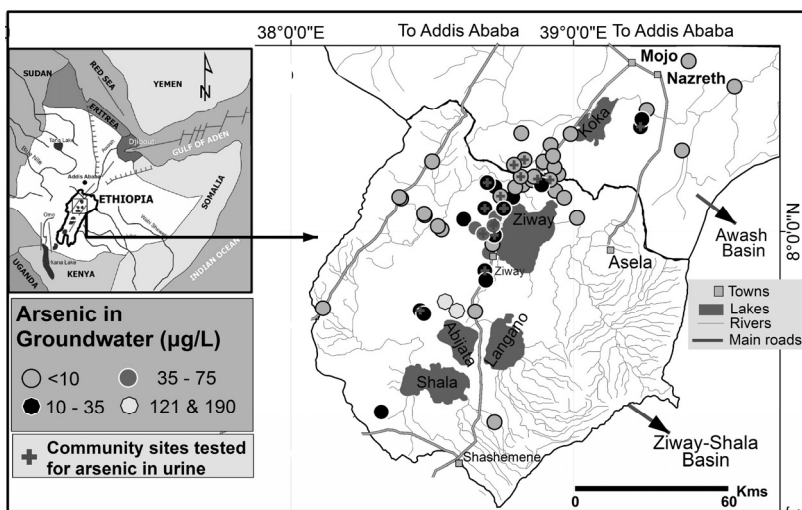


Fig. 1. Locations of groundwater sampling sites and community sites where urine samples were collected and corresponding groundwater As concentrations. The map is modified from Rango et al. (2013).

Our previous study demonstrated that As in the form of oxyanion is released from the MER fluvio-lacustrine sediments as a result of desorption of As from hydrous metal oxides and clay minerals under alkaline pH $>\sim 8$ and oxidizing conditions (Rango et al., 2013). The hydrolysis process in the MER also generates high Na and HCO_3^- , which triggers desorption of As and other oxyanion-forming elements such as U from oxides and clay minerals.

3.2. Arsenic in drinking water, cereal, and urine samples

Drinking water is considered to be a major source of inorganic As in humans (ATSDR, 2007). The concentration of As in drinking water samples from the study wells ranged between 1.5 and 73.4 $\mu\text{g/L}$ (mean: 25.7 ± 23.3 $\mu\text{g/L}$; $n=17$), whereas the concentration of As in urine ranged between 6 and 366 $\mu\text{g/L}$ (mean: 58.3 ± 56.2 $\mu\text{g/L}$; $n=164$). Similar to other studies where water has been identified as the main source of As exposure (Calderon et al., 1999; Lindberg et al., 2006; Mandal et al., 2001; Meza et al., 2004; Sun et al., 2007; Merola et al., 2014), As concentrations in urine and drinking water were found to be positively and significantly correlated ($R^2=0.45$, $p<0.001$; Fig. 2A). Similar results were found when As

bioaccumulation in toenail samples was compared to As in drinking water (Merola et al., 2014). Despite the seemingly linear relationship, As measurements in urine were highly variable across children within a community (Fig. 2A and Table 1). In addition, large numbers of study subjects (88%; $n=144$) had higher urinary As concentrations than the respective As concentration in drinking water. The variation in urinary concentrations could be due to a variety of factors, including the possibility of significant additional exposure to As from food or other sources. In particular, there may be significant variations in children's diets and in the amounts of water they consume. We also found that mean urinary As concentrations were higher on average among male ($62.6 \pm 59.7 \mu\text{g/L}$; $n=81$) subjects than females ($54 \pm 52.5 \mu\text{g/L}$; $n=83$), but this difference was not statistically significant ($p=0.33$).

In rural communities in the MER, staple foods consist of locally grown cereals (i.e., maize, wheat, and teff 'indigenous cereal'), which likely contribute to As exposure in the population. Our analyses confirmed that all cereal samples from the MER contain As. Teff contained the highest levels on average ($0.034 \mu\text{g/g}$), whereas the lowest levels were found in maize ($0.0016 \mu\text{g/g}$) (Table 2). The As content of these cereals was below $0.034 \mu\text{g/g}$ ($n=23$), which is lower than the permissible limit for cereals in China ($0.2 \mu\text{g/g}$) (Shao et al., 2014). The average content of As in maize and wheat was similar ($0.0044 \mu\text{g/g}$), and was generally lower than global levels measured in maize ($0.01 \mu\text{g/g}$) and wheat ($0.05 \mu\text{g/g}$) samples (Adomako et al., 2011). The content of As in wheat from the MER was also lower than in wheat flour samples (0.021 – $0.054 \mu\text{g/g}$) collected from As-contaminated areas in France (Zhao et al., 2010). In the MER, the concentrations of As in cereal samples were much lower than the As concentrations measured in other areas, and thus the consumption of staple foods may not be a significant source of As exposure in the region.

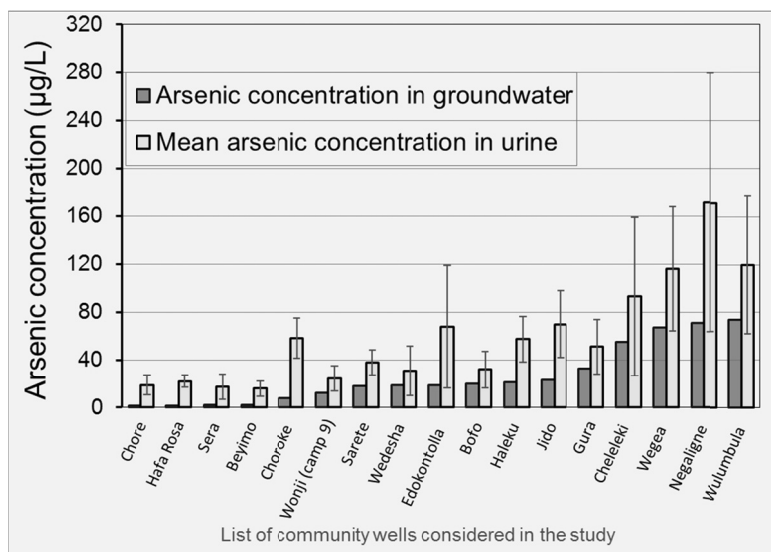
Protein consumption of fish, which is another internationally known source of As, is not common in the MER population, and thus no significant As exposure is expected from fish. Arsenic in fish is predominantly present in the organic non-toxic As species such as arsenobetaine (Cullen and Reimer, 1989; Heinrich-Ramm et al., 2002; Navas-Acien et al., 2011).

Table 1. Water quality parameters, including As in drinking water samples and in the urine of children consuming water from the respective community-level groundwater sources.

Community wells	Field parameters in water						Arsenic in drinking water (µg/L)	Arsenic in urine (µg/L)				Number of subjects
	N	E	pH	Eh	EC	T (°C)	TDS	Min	Max	Mean±SD	Median	
Chore	8.18	38.92	7.93	+90	816	27.6	715	10.1	37.6	18.9±8.1	18.5	9
Hafa Rosa	8.26	38.83	7.89	-	569	27.4	546	16.7	32.1	22.1±5.3	22.1	7
Sera	8.20	38.81	8.24	-	461	25.3	446	6.00	37.0	17.4±10.3	11.7	9
Beyimo	8.24	38.79	7.92	-	486	27.5	454	7.20	25.5	15.9±6.5	16.1	8
Choroke	8.13	38.74	8.5	-	1286	25.8	835	38.3	87.0	58.2±16.7	61	10
Wonji (Camp 9)	8.37	39.24	7.28	+131	1417	27.6	1130	12.3	10.0	24.6±10.5	25.5	14
Sarete	8.08	38.69	8.1	+17	1100	33.7	805	18.3	14.8	37.6±10.5	40.6	10
Wedesha	8.17	38.69	8.22	+148	782	25.6	660	18.6	94.3	30.9±20.6	24.2	8
Edokontolla	7.99	38.72	8.11	+42	1710	25.7	1532	19.0	9.54	67.6±51.4	36.5	11
Bofo	8.19	38.87	8.42	+75	719	26.6	652	20.3	7.50	31.8±15.2	30.2	13
Haleku	7.86	38.69	8.18	+30	998	29.6	843	21.0	26.0	57.3±19.1	52.8	12
Jido	7.72	38.46	8.47	+50	1288	26.9	1112	23.0	37.3	69.8±27.8	61.9	10
Gura	8.08	38.75	8.35	-	1530	28.3	1376	33.0	30.0	51.1±22.9	45	6
Cheleleki-1	8.08	38.75	8.29	+113	1829	26.9	1691	55.0	34.7	93.0±66.0	65.4	12
Wegea	7.99	38.68	8.77	+64	2429	27.3	1746	67.0	59.3	115.8±51.8	107.1	7
Negaligne	8.02	38.72	8.57	-	1036	27.4	1423	71.0	46.6	171.5±108	142.1	9
Wulumbula	8.03	38.72	6.86	+55	1945	26.2	1786	73.4	57.0	119.7±57.9	101.7	9

Table 2. Statistical distribution of As concentration ($\mu\text{g/g}$ dry basis) in cereal samples in the MER.

Cereals	N	min	max	mean \pm SD
Maize	9	0.0016	0.0080	0.0044 \pm 0.0017
Wheat	7	0.0019	0.0082	0.0044 \pm 0.0023
Teff	7	0.0101	0.0770	0.0338 \pm 0.0255

**Fig. 2.** The relationship between: A) individual-level (for children aged 10 to 15 years old) and B) community-level drinking water and urinary concentrations of As. Error bars are standard deviations of the average As concentrations in each community.

We compared the concentration of As in urine with reference values measured in healthy populations in other locations lacking known exposure to As risks, as well as to international standards. A reference value of 15 $\mu\text{g/L}$ of As was established as a benchmark concentration based on 4741 urine samples in a human biomonitoring study from Germany (Wilhelm et al., 2004, 2005). A similar reference value of 16.7 $\mu\text{g/L}$ was reported based on urine sampling from individuals in areas of Lombardy, Italy (Reimann and Caritat, 1998). Other international As reference values generally lie below 50 $\mu\text{g/L}$, as reported by the National Research Council (NRC, 1999). Turning to exposure standards, the

American Conference of Governmental Industrial Hygienists (ACGIH) provides an occupational Biologic Effect Index (BEI) of 35 µg/L for inorganic As plus its metabolites in urine (ACGIH, 2001). Notably, our study found a high proportion of individuals (88%; n=144) with urinary As above the 15 µg/L reference level obtained in the German study, while 57.3% (n=94) and 39% (n=64) of the study subjects had As above 35µg/L (the BEI value) and 50 µg/L, respectively.

While we found As concentrations reaching 74 µg/L in drinking water and up to 366 µg/L in urine, no symptoms of As toxicity (e.g., skin lesions) were observed during field examinations of this sample population of children enrolled in this study.

In studies from West Bengal and Bangladesh, As skin lesions have been found among adults when the As concentrations in drinking water exceed 300 µg/L and when urinary concentrations ranged between 10 and 3147 µg/L (mean: 180 µg/L; n=9700) and 24 to 3086 µg/L (mean: 495 µg/L; n=1000), respectively (Chowdhury et al., 2000). Considering that some individuals in the study showed higher urinary As relative to the reference ranges, they may be subclinically affected. Emerging evidence indicates the potential for adverse health effects from inorganic As exposure at relatively low exposure levels common to populations worldwide, including an increased risk of cancer, cardiovascular and respiratory conditions, and diabetes mellitus (Ettinger et al., 2009; European Food Safety Authority, 2009; Karagas et al., 2001; Leonardi et al., 2012; Navas-Acien et al., 2011; Soheli et al., 2009). Chen et al. (2011) and Zheng et al. (2013) have reported As exposure and its association with proteinuria in chronic kidney disease patients. Similarly, Hsueh et al. (2009) demonstrated a link between increased urinary As and decreased glomerular filtration rate. In their study, the concentration of As in drinking water ranged from below detection up to 4 µg/L (average of 0.7 µg/L), and total urinary As levels (~ the majority had below 100 µg/g) were comparable with the As concentrations in our work.

Limitation: Due to time and logistical constraints, we obtained no data on intake (amount) of As in the drinking water and cereals to establish the relationships between total As intake and excretion. We also obtained only early morning spot urine samples, rather than excretion over a 24-hour period urine, which provides a more reliable estimate of As exposure than spot urine.

Conclusion

A number of drinking water wells from the MER region in Ethiopia had As concentrations that exceed the WHO drinking water guideline value of 10 µg/L. We found moderate associations between As in drinking water and urine samples. The majority of the children had urinary As concentrations above those in the drinking water, and urine samples from populations drinking from the same wells were highly variable, suggesting the possibility of different levels of water consumption and additional As intake from diets. Our data show that locally-grown cereals, which are important dietary staples in the region, had variable levels of As. Although early manifestation of As exposure was not observed in the study children, persistent long-term As exposure may potentially cause adverse health effects later in life. There is thus a need for additional studies of the potential health effects of As in the MER, in order to better understand the health effects of arsenic toxicity at low levels and to determine whether alternative sources of water or As mitigation techniques are needed.

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