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# Fluoride exposure from groundwater as reflected by urinary fluoride and children's dental fluorosis in the Main Ethiopian Rift Valley

Tewodros Rango [a,*], Avner Vengosh [a], Marc Jeuland [b,g], Redda Tekle-Haimanot [c], Erika Weinthal [d], Julia Kravchenko [e], Christopher Paul [d], Peter McCornick [f]

[a] Division of Earth and Ocean Sciences, Nicholas School of the Environment, Duke University, Durham, NC, USA
[b] Sanford School of Public Policy and Duke Global Health Institute, Duke University, Durham, NC, USA
[c] Addis Ababa University, Faculty of Medicine, Addis Ababa, Ethiopia
[d] Division of Environmental Sciences and Policy, Nicholas School of the Environment, Duke University, Durham, NC, USA
[e] Duke University Medical Center, Department of Surgery, Division of Surgical Science, Duke University, Durham, NC, USA
[f] International Water Management Institute, Colombo, Sri Lanka
[g] Institute of Water Policy, National University of Singapore, Singapore

## HIGHLIGHTS

- The majority of children in the study have severe dental fluorosis (DF).
- The relationship between $F^-$ in water, urine, and DF is positive and non-linear.
- DF and urinary $F^-$ were variable in children exposed to similar groundwater sources.
- Urinary $F^-$ tests serve as an effective tool for monitoring defluoridation program.

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## ABSTRACT

This cross-sectional study explores the relationships between children's $F^-$ exposure from drinking groundwater and urinary $F^-$ concentrations, combined with dental fluorosis (DF) in the Main Ethiopian Rift (MER) Valley. We examined the DF prevalence and severity among 491 children (10 to 15 years old) who are life-long residents of 33 rural communities in which groundwater concentrations of $F^-$ cover a wide range. A subset of 156 children was selected for urinary $F^-$ measurements. Our results showed that the mean $F^-$ concentrations in groundwater were 8.5 ± 4.1 mg/L (range: 1.1–18 mg/L), while those in urine were 12.1 ± 7.3 mg/L (range: 1.1–39.8 mg/L). The prevalence of mild, moderate, and severe DF in children's teeth was 17%, 29%, and 45%, respectively, and the majority (90%; n = 140) of the children had urinary $F^-$ concentrations above 3 mg/L. Below this level most of the teeth showed mild forms of DF. The exposure–response relationship between $F^-$ and DF was positive and non-linear, with DF severity tending to level off above a $F^-$ threshold of ~6 mg/L, most likely due to the fact that at ~6 mg/L the enamel is damaged as much as it can be clinically observed in most children. We also observed differential prevalence (and severity) of DF and urinary concentration, across children exposed to similar $F^-$ concentrations in water, which highlights the importance of individual-specific factors in addition to the $F^-$ levels in drinking water. Finally, we investigated urinary $F^-$ in children from communities where defluoridation remediation was taking place. The lower $F^-$ concentration measured in urine of this population demonstrates the capacity of the urinary $F^-$ method as an effective monitoring and evaluation tool for assessing the outcome of successful $F^-$ mitigation strategy in relatively short time (months) in areas affected with severe fluorosis.



## 1. Introduction

Globally, an estimated 200 million people are exposed to high concentrations of naturally occurring fluoride ($F^-$) that exceeds the World Health Organization (WHO) guideline of 1.5 mg/L in drinking water (Ayoob and Gupta, 2006; WHO, 2006). This high exposure to $F^-$ leads to fluorosis – in its dental and skeletal forms – and is endemic in

* Corresponding author at: Division of Earth and Ocean Sciences, Nicholas School of the Environment, 205 Old Chemistry Building, Box 90227, Duke University, Durham, NC 27708, USA. Tel.: +1 919 949 8783.
*E-mail address:* tg67@duke.edu (T. Rango).

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at least 25 countries, including India, China, Mexico, Brazil, Saudi Arabia, United States (U.S.), Uganda, Tanzania, and Ethiopia (WHO, 2006; Amini et al., 2008). High-risk areas are mostly located in arid and semi-arid regions that are characterized by a rapid rate of chemical weathering of geological materials, such as the East African Rift System (EARS).

The EARS is a unique geological feature, where active faulting has generated voluminous pyroclastic volcanic rocks (Chorowicz, 2005) that are highly reactive with local groundwater (Rango et al., 2013). This study focuses on the Main Ethiopian Rift (MER), which is located in the northern part of EARS, and where a large number of drinking water wells have been documented to contain high levels of naturally occurring contaminants such as $F^-$, arsenic (As) and uranium (U) (Reimann et al., 2003; Rango et al., 2012, 2013). Systematic water testing in the Ziway–Shala basin of the MER has shown that $F^-$ concentrations can reach up to 68 mg/L (mean: 9.4 ± 10.5 mg/L), and that $F^-$ levels in 94% of the tested wells exceeded the World Health Organization (WHO) standard of 1.5 mg/L (Rango et al., 2012). In this region, an estimated 8.5 million people mostly from rural communities are highly dependent on groundwater resources for drinking and domestic purposes and are thus at risk of fluorosis (Tekle-Haimanot et al., 1987; Tekle-Haimanot, 2005; Tekle-Haimanot and Haile, 2014).

Exposure to $F^-$ has two critical effects on the teeth. On the one hand, optimum intake of this element is critical for dental development; $F^-$ intake of 0.5–1 mg/L is recommended to achieve maximum protection against dental caries (U.S. DHHS, 1991; WHO, 2006). Indeed, fluoridation of community drinking water is considered a safe and effective means of preventing such caries and has been called one of the ten great public health achievements of the 20th century (U.S. CDC, 1999). On the other hand, excessive intake of $F^-$ from sources such as water, food and fluoride-containing dental products is known to cause dental and skeletal fluorosis (DF and SF) (WHO, 2006). DF – the focus of this study – is a condition of subsurface enamel porosity that may progress to enamel pitting, followed by total enamel loss and secondary discoloration of the enamel surface (Fejerskov et al., 1996).

The severity of DF depends on the complex interplay of exposure, duration, and timing of $F^-$ intake and ingestion (Den Besten, 1994). It is particularly acute when children are exposed to high levels of $F^-$ in early childhood (typically at ages up to 4 years) (Fomon et al., 2000; U.S. CDC, 2001; Hong et al., 2006). To achieve dental protection without compromising health, the U.S. Environmental Protection Agency (EPA) has thus specified the optimal level of 0.06 mg/kg bw/day as the No-Observed-Adverse-Effects-Level (NOAEL) (U.S. EPA, 2002). The NOAEL is an estimate of the daily $F^-$ exposure that does not lead to cosmetic DF effects (brown staining and/or pitting of enamel) among children. For a $F^-$ intake from drinking water through the consumption of 1 L/day by 12 to 14 year old children, the NOAEL corresponds to a concentration of about 1 mg/L of $F^-$ (U.S. EPA, 2002). The WHO guideline for drinking water is 1.5 mg/L, but the guidelines note that when water intakes are high, for example in arid and semi-arid settings, it may be appropriate to consider a local guideline concentration that is lower than 1.5 mg/L (WHO, 2006).

It is indisputable that $F^-$ in drinking water is the primary factor that causes DF; however, the precise exposure–response condition has not been well established, in part due to the difficulty of tracking varying exposures over long and critical periods of dental development. Previous studies, for example in the US, have demonstrated a linear dose–response relationship at low-$F^-$ intakes, i.e., mostly below 4 mg/L from drinking water (U.S. NRC, 2006). Very few studies – e.g., Ruiz-Payan et al. (2005) (covering water sources <5.7 mg/L in Mexico), Wang et al. (2012) (<11 mg/L, mostly below 7 mg/L in China), and Wondwossen et al. (2004) (including low (0.3–2.2 mg/L) and high $F^-$ (10–14 mg/L) concentrations of $F^-$ in the Ethiopian Rift Valley) – have considered the development of DF across a wide range of $F^-$ exposures in a specific geographic region. There are also challenges related to confounding by other sources of exposure: for example, existing studies from the MER have shown that food ingredients and food or beverages prepared with high $F^-$ water contribute significantly to total $F^-$ intake (Malde et al., 1997, 2003, 2004, 2011; Dessalegne and Zewege, 2013). Based on the available research evidence, the U.S. EPA established a MCLG (Maximum-Contaminant-Level Goal) threshold of 4 mg/L to protect from adverse health effects (crippling skeletal fluorosis) and a SMCL (Secondary-Maximum-Contaminant-Level) threshold of 2 mg/L of $F^-$ to protect from adverse cosmetic effects (moderate and/or severe DF) (U.S. NRC, 2006). Yet it is not clear whether the $F^-$ exposure thresholds established by the U.S. EPA, or by the WHO, are valid or applicable in other countries, with different climates, exposure sources and pathways, and population characteristics such as Ethiopia.

In this paper, we describe the results of an exposure–response study of the effects of $F^-$ that was conducted in the MER. The study builds on prior work in the same region that considered the relationship between $F^-$ in groundwater and DF (Rango et al., 2012), by more carefully: 1) specifying the full range of $F^-$ concentrations in groundwater encountered in this region; 2) restricting the sample to the specific age range (10 and 15 years) of children; 3) limiting threats related to confounding by including only individuals who are life-long residents of rural communities in which the primary community drinking water supplies were installed before the children were born; and 4) generating new data on urinary $F^-$ concentration and establishing their relationship with exposures to $F^-$ in groundwater and DF severity. Due to the temporal stability and spatial variability in $F^-$ levels across communities (ranging from 1.1 to 18 mg/L) in these sources, the study of this population provides us a unique opportunity to make inferences about the relationship between exposure and health effects over a wide range of $F^-$ concentrations. Working with this population, we investigated whether there might be thresholds for drinking water $F^-$ concentrations for either minimal or severe DF.

Our study contributes to a relatively limited literature that examines the relationship between $F^-$ levels measured in drinking water and urine among a subset of study subjects and is one of the only ones to consider such a wide range of $F^-$ exposures. In the human body, approximately 99% of the $F^-$ is stored in calcified tissues (i.e., bones and teeth) (Whitford, 1996). Roughly 30–50% of the $F^-$ absorbed every day by young to middle-aged adults is assimilated within 24 h by calcified tissues as compared to about 80% by young children, and the remainder is predominantly excreted in the urine (Ekstrand et al., 1994; Whitford, 1996). Prolonged exposure to steady and high concentrations of $F^-$ can yield urinary $F^-$ excretion above 80% of the total $F^-$ intake, particularly when mineralized tissues are close to saturation with $F^-$ (Myers, 1978). Based on this premise, we supplemented analyses of drinking water and DF examinations with measures of urinary $F^-$ concentrations, in order to more adequately monitor recent $F^-$ exposure (Whitford, 1994; Singh et al., 2007; Srikanth et al., 2013). We also evaluated urinary $F^-$ concentrations in a community with an active pilot defluoridation intervention to provide an initial understanding of the short-term effect of defluoridation on this biomarker. To date, studies have largely been conducted in areas with either exclusively low (e.g., Czarnowski et al., 1996 (<1.2 mg/L); Heintze et al., 1998 (<1.3 mg/L); Villa et al., 2000 (<0.6 mg/L); Forte et al., 2008 (<1.5 mg/L); Zohouri and Rugg-gunn, 2000 (<0.4 mg/L); Ding et al., 2011 (<3 mg/L); Zohouri et al., 2013 (<1.06 mg/L)) or high $F^-$ in drinking water (e.g., Ruiz-Payan et al., 2005 (up to 5.7 mg/L); Wang et al., 2012 (mostly below 7 mg/L)).

The present study thus provides more comprehensive evidence on the effects of a wide range of exposures to $F^-$ on DF than the majority of existing studies. The study population from the MER was found to be an ideal research group for these exposure–response investigations because of the relatively homogeneity of the population being studied (in terms of diet, ethnicity, and rural location), its high reliance on specific groundwater sources for drinking water in which concentrations of $F^-$ are temporally stable, and the low potential for confounding given the limited ingestion of other products containing $F^-$ such as industrial (e.g., processed diet and soft drinks) or topical products (e.g., toothpaste). Finally, our analyses also consider the role of potential