High prevalence of chemical and microbiological drinking water contaminants in households with infants enrolled in a birth cohort — Piura, Peru, 2016

Miranda J. Delahoy PhD[1], Sydney Hubbard MPH[1], Mia Mattioli PhD[1], Carlos Culquichicón MD[1,2,3], Jackie Knee PhD[4], Joe Brown PhD[5], Lilia Cabrera RN[6], Dana Boyd Barr PhD[1], P. Barry Ryan PhD[1], Andres G. Lescano PhD[2], Robert H. Gilman MD[7], Karen Levy PhD[1,8*]

Author Affiliations: (1) Gangarosa Department of Environmental Health, Rollins School of Public Health, Emory University, Atlanta, Georgia, United States, (2) Emerge, Emerging Diseases and Climate Change Research Unit, School of Public Health and Administration, Universidad Peruana Cayetano Heredia, Lima, Peru, (3) School of Health Sciences, Universidad Nacional de Piura, Piura, Peru (4) Disease Control Department, London School of Hygiene & Tropical Medicine, London, United Kingdom (5) Department of Environmental Sciences and Engineering, Gillings School of Global Public Health, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina, United States (6) Asociación Benéfica PRISMA, Lima, Peru, (7) Johns Hopkins Bloomberg School of Public Health, Baltimore, Maryland, United States, (8) Department of Environmental and Occupational Health Sciences, School of Public Health, University of Washington, Seattle, Washington, United States

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* Department of Environmental and Occupational Health Sciences, School of Public Health, University of Washington, 3980 15th Avenue NE, Seattle, Washington, USA; klevyx@uw.edu; 206-543-4341.

ABSTRACT

Chemical and microbiological drinking water contaminants pose risks to child health but are not often evaluated concurrently. At two consecutive visits to 96 households in Piura, Peru, we collected drinking water samples, administered health and exposure questionnaires, and collected infant stool samples. Standard methods were used to quantify heavy metals/metalloids, pesticides, and *Escherichia coli* concentrations in water samples. Stool samples were assayed for bacterial, viral, and parasitic enteropathogens. The primary drinking water source was indoor piped water for 70 of 96 households (73%); 36 households (38%) stored drinking water from the primary source in containers in the home. We found high prevalence of chemical and microbiological contaminants in household drinking water samples: arsenic was detected in 50% of 96 samples, ≥ 1 pesticide was detected in 65% of 92 samples, and *E. coli* was detected in 37% of 319 samples. Drinking water samples that had been stored in containers had higher odds of *E. coli* detection (adjusted odds ratio [aOR]: 4.50; 95% CI: 2.04–9.95) and pesticide detection (OR: 6.55; 95% CI: 2.05–21.0) compared with samples collected directly from a tap. Most infants (68%) had ≥ 1 enteropathogen detected in their stool. Higher odds of enteropathogen infection at the second visit were observed among infants from households where pesticides were detected in drinking water at the first visit (aOR: 2.93; 95% CI: 1.13–7.61). Results show concurrent risks of exposure to microbiological and chemical contaminants in drinking water in a low-income setting, despite high access to piped drinking water.

INTRODUCTION

Drinking water contamination poses several acute and long-term risks to child health. Nearly half a million global diarrheal deaths can be attributed to insufficient access to safe drinking water annually.[1] Drinking water contaminated by human or animal feces may contain enteropathogens that can cause acute or persistent diarrhea, lead to long-term shortfalls in physical growth and cognitive development, and inhibit oral vaccine response.[2–4] Children exposed to heavy metals/metalloids (HMM) and pesticides in drinking water, especially during critical developmental periods, may experience reductions in immune

function and cognitive development.[5–7] Yet such toxic drinking water contaminants have largely been studied in isolation from microbiological contaminants, despite the potential for both types of agents to alter immune responses and the incidence or severity of pathogen infections.[8] In low- and middle-income settings, microbial contamination of drinking water has been extensively studied, but less attention has been given to chemical contamination.[9]

The World Health Organization/United Nations International Children's Emergency Fund Joint Monitoring Programme for Water Supply, Sanitation and Hygiene (WHO/UNICEF JMP) defines safely managed drinking water as water coming from an improved source (piped water, boreholes or tubewells, protected dug wells, protected springs, or rainwater) that is located on the household premises, available when needed, and free of fecal and chemical contamination.[10] Provision of improved drinking water sources may limit children's exposure to waterborne pathogens; however, these sources are not always free of contaminants.[11] Piped drinking water supplies in low- and middle-income settings often fail to meet the criteria of safely managed sources, in part because they fail to provide continuous service. Intermittent piped water service can pose challenges in maintaining water quality within a water distribution system due to intrusion into the system from changes in pressure, and within the household if water is stored for use during service cuts.[12,13]

In this study, we examine microbiological, HMM, and pesticide contamination of drinking water samples predominantly from improved sources, collected from 96 households with infants enrolled in a birth cohort in Piura, Peru. We examine water source characteristics and household-level factors associated with detection of *Escherichia coli* (as an indicator of microbiological contamination), arsenic, and pesticides in drinking water samples and examine how the presence of these agents is associated with infant enteropathogen infection, as defined by detection in fecal samples.

MATERIALS AND METHODS

Study site and enrollment

The data presented in this manuscript were collected during a household water quality sub-study of a previously established birth cohort. Midwives enrolled 327 mothers into the original birth cohort during November–December 2015 when they presented to give birth at the José Cayetano Heredia Hospital or the Santa Rosa Hospital in Piura, Peru. Inclusion criteria for the birth cohort were that mothers had to reside in the department of Piura or Tumbes and had to deliver the infant vaginally, or via Cesarean delivery for reason of cephalopelvic disproportion or prolonged labor. Exclusion criteria were lack of informed consent or plans to move residence outside of Piura or Tumbes. The birth cohort enrolled live-born infants, from whom a heel stick blood sample was collected. Therefore, infants with foot malformations, injuries, or infections were excluded. The water quality sub-study recruited a random subset of birth cohort participants available for follow-up during June–July 2016. Sub-study inclusion criteria were that the caretaker had to reside in the department of Piura and provide informed consent. There were no exclusion criteria, other than failure to meet inclusion criteria.

Sub-study participants resided in the provinces of Piura, Morropon, Paita, Sechura, and Sullana in the department of Piura (Supplemental Figure 1). The patient populations differ between the two enrollment hospitals. The José Cayetano Heredia Hospital serves patients with social security insurance, which is managed by the Peruvian Ministry of Labor and available to persons with stable employment. The Santa Rosa Hospital accepts the Peruvian Ministry of Health's universal insurance coverage: patients are generally of lower socio-economic status with unstable employment.

Study visits and sample collection

Two study visits were planned for each household when infants were approximately six months old, with the second visit ("Visit 2") occurring approximately one week (target range 4–10 days) after the first visit ("Visit 1") (Figure 1). At Visit 1, after obtaining written consent from each caretaker, trained

enumerators administered a health and exposure questionnaire, including questions on household characteristics and demographics, water source and household water treatment, and whether study infants had diarrhea in the preceding week. Diarrhea was defined as having three or more loose stools in a 24-hour period, or presence of blood in the stool, as reported by the caretaker.

At Visit 1, to identify the primary drinking water source for each household, we asked the caretaker to identify where they would normally get water to give to the study infant (either to drink or mixed in formula). This could include water obtained directly from a tap or, when applicable, from containers of water stored in the household. If >1 L of water was available from the tap or container, it was used as the primary source. If not, enumerators asked if there was another tap or container of household drinking water that the study infant would drink, alone or mixed in formula, and this was used as the primary drinking water source. Samples collected from this source are referred to as primary drinking water samples. We obtained multiple drinking water samples from the household's primary drinking water source: 100 mL for *E. coli* testing, 15 mL for HMM testing, and 1 L for pesticide testing. After sampling the primary source, enumerators asked whether there was another source or container of household drinking water that the study infant drinks, either alone or mixed in formula. If so, 100 mL of water was collected from that tap or container for *E. coli* testing. If not, enumerators asked whether there was another source or container of water that any household member drinks, and, when applicable, collected 100 mL from that source. This process was repeated until two additional 100 mL drinking water samples beyond the primary sample were collected for *E. coli* testing (referred to as secondary/tertiary samples), or until there were no additional sources to sample. Enumerators placed numbered stickers on the water taps or containers and recorded a written description of the sources, so they could be re-sampled at Visit 2. For samples that were stored in containers in the household prior to collection, the source type (indoor, outdoor, or neighbor's piped water connection; protected well; public water basin; tanker truck or other bought/bottled water; or unprotected well) refers to the source from which the water was obtained before it was stored.

At Visit 2, enumerators administered a short health questionnaire and recorded whether study infants experienced diarrhea symptoms since the first visit, as reported by the caretaker. The drinking water taps and containers sampled at Visit 1 were reidentified and 100 mL of drinking water was collected from each for microbiological testing only. If an infant defecated during the visit, a stool sample was collected at that time. Otherwise, caretakers were given a diaper, plastic container, and gloves for collecting an infant stool sample, and enumerators retrieved the sample later that day.

Laboratory methods

Microbiological water testing

Field staff collected the primary, secondary, and tertiary water samples intended for fecal indicator bacteria testing (*E. coli* and total coliforms) in 100 mL Whirl-Pak sterile bags pre-packed with sodium thiosulfate to neutralize chlorine (Nasco, Fort Atkinson, WI, USA). Samples were transported on ice from households to the laboratory in Piura and processed the same day with the IDEXX Colilert Quanti-Tray/2000 (IDEXX Laboratories, Westbrook, ME, USA). Samples were incubated at 37°C for 24 hours, after which the most probable number (MPN) of *E. coli* and total coliforms were quantified, with a detection range of 1–2,419.6 MPN/100 mL. Field staff processed distilled water samples approximately every other day in the laboratory in Piura (N = 30, four of which were poured into a Whirl-Pak bag in the field) to serve as negative lab and field controls.

Quantification of HMM in water

Field staff collected 15 mL of water in a metal-free conical tube from the primary household drinking water source. Samples were stored in a refrigerator at 4°C for up to two months then transported to Atlanta, Georgia for processing. For inductively coupled plasma-mass spectrometry (ICP-MS) analysis, 2 mL of the water samples were prepared concurrently with three blank samples, calibration samples, National Institute of Standards and Technology reference material 1643f, and two levels of quality control samples per analytic run. To ensure dissolution of target elements and to digest organic sample constituents, samples were digested with nitric acid before dilution with a mixture of internal

144 standards (indium, iridium, lutetium, and rhodium). The digests were then analyzed via ICP-MS,
145 removing spectral interferences with a collision reaction cell. Concentrations of the target elements were
146 determined from the ratio of the instrument response to the native analyte to the response to the internal
147 standards in the sample, by comparison to the standard curve. The average lower limit of detection (LOD)
148 for all HMM across the study was 0.1 µg/L, with HMM occasionally being detected at lower levels.

149 *Quantification of pesticides and herbicides in water*

150 One liter of water was collected from the primary household drinking water source in a sterilized
151 glass bottle for pesticide analysis. Samples were transported to a laboratory in Piura, where the water was
152 passed through surface modified styrene divinylbenzene solid phase extraction cartridges (Phenomenex
153 8B-S043-HCH, Torrance, CA, USA). Cartridges were stored in a sealed container with silica gel packets
154 to prevent moisture condensation until transferred to the laboratory in Atlanta, Georgia. In Atlanta, the
155 dry cartridges were eluted with ethyl acetate and methanol, then the eluate was concentrated to dryness
156 with nitrogen in a Turbovap set at 37ºC. Each dried sample was reconstituted with acetonitrile and
157 analyzed using gas chromatography-tandem mass spectrometry with isotope dilution quantification.[14]
158 Calibration samples, blanks, and quality control samples were prepared similarly but processing occurred
159 in the laboratory in Atlanta rather than in the field. Target pesticides were atrazine (LOD: 0.05 ng/L),
160 diazinon (LOD: 0.125 ng/L), chlorpyrifos (LOD: 1.25 ng/L), p,p'-dichlorodiphenyldichloroethylene (*pp*-
161 DDE; LOD: 0.05 ng/L), permethrin (LOD: 0.125 ng/L), and cypermethrin (LOD: 0.125 ng/L), chosen
162 because they are among the most widely used pesticides globally and have high potential to be present in
163 groundwater.

164 *Enteropathogen detection in stool*

165 Field staff collected stool samples (approximately 500 mg) using the OMNIgene-Gut stool
166 collection and stabilization kit (OMR-200) (Genotek, Ottawa, Canada) and stored specimens at room
167 temperature for approximately six months until processing in Atlanta. Samples were extracted using the

QIAamp PowerFecal DNA Kit (Qiagen, Hilden, Germany). Stool samples were assayed for a panel of 15 bacterial, viral, and parasitic enteropathogens using the Luminex multiplex Gastrointestinal Pathogen Panel (Thermo Fisher Scientific, Waltham, MA). Bacterial targets on this panel are *Campylobacter* spp., *Clostridium difficile* toxin A/B, *E. coli* O157, enterotoxigenic *E. coli* (heat-stable toxin or heat-labile toxin), *Salmonella* spp., shiga toxin-producing *E. coli* (shiga toxin 1 or shiga toxin 2), *Shigella* spp., *Vibrio cholerae*, and *Yersinia enterocolitica*; viral targets are adenovirus 40/41, rotavirus A, and norovirus GI/GII; protozoal targets are *Cryptosporidium* spp., *Giardia* spp., and *Entamoeba histolytica*.

Statistical analysis

Data were cleaned and analyzed using SAS 9.4 (SAS Institute, Inc., Cary, NC). We considered the univariate associations between individual enteropathogens detected in stool and caretaker-reported infant diarrhea (both collected at Visit 2) using standard logistic regression maximum likelihood methods. We also considered the associations between various household, demographic, and water characteristics and five binary outcomes: (1) whether *E. coli* was detected in household drinking water samples collected at Visit 1 and Visit 2 (including primary, secondary, and tertiary water samples collected from either a tap or stored in a container), (2) detection of *E. coli* in the subset of household drinking water samples collected at Visit 1 and Visit 2 that were stored in containers in the household, (3) arsenic concentration exceeding the WHO standard[18] of 10 μg/L in primary drinking water samples collected at Visit 1, (4) detection of any pesticide in primary drinking water samples collected at Visit 1, and (5) infant infection with any enteropathogen at Visit 2. We constructed a multivariable model for each of these binary outcomes by screening variables of interest (those included in each model's results table [Tables 2–5 and Supplemental Table 1]) using univariable logistic regression and including variables in a multivariable model if $p < 0.10$ on screening. If cell counts were < 5 for any variable, a Fisher's exact test was used. The study participant enrollment hospital and presence of refrigerator in the household were considered in each analysis as indicators of socio-economic status. We performed backward selection on multivariable models until all associations were significant at $p < 0.05$. Parameter estimates and confidence intervals

were derived by standard logistic regression maximum likelihood methods. Models evaluating *E. coli* contamination had each water sample as a unit of observation (rather than the household). Because multiple drinking water samples were collected from each household for *E. coli* testing, these models accounted for clustering at the household level (by accounting for the number of households in the degrees of freedom choice for the Taylor series variance estimation). The choice of examining presence rather than concentration of *E. coli* was based on the JMP safety standard for *E. coli* in drinking water, whereby any detectable level of *E. coli* is considered unsafe.[10] Multi-collinearity was assessed for all multivariable models using conditional indeces.[15] No conditional indices in any model were > 30, thus no multi-collinearity problems are reported.

Ethics

Study protocols and procedures were approved by the Emory (#IRB00088348) and A.B. PRISMA (CE1157.16) Institutional Review Boards.

RESULTS

Enrollment

We enrolled 96 infants into the sub-study during June 14–July 21, 2016. Two caretakers refused or were unavailable for the second visit; 94 infants were available for follow-up and provided a stool sample at Visit 2. Follow-up visits were conducted a median of six days after the first visit (range: 4–27 days). Most follow-up visits (94%) occurred < 10 days after Visit 1.

Infant and household characteristics

The median age of the study infants was 7.0 months (range: 5.7–8.0 months) (Table 1). We enrolled a balance of infants born at the Santa Rosa (47%) and José Cayetano Heredia (53%) hospitals. Among 96 households, 69 (72%) reported that one or more animals reside in or around the household and 62 (65%) had toilets connected to piped sewerage. The primary drinking water source was piped water for

76 households (79%); among all households, 36 (38%) stored drinking water from the primary source in containers in the household. Among the 75 households using piped water as the primary drinking water source for which information on intermittent water supply was available, 39 caretakers (52%) reported that there had been a cut to their water service in the week prior to Visit 1.

All caretakers reported that their infants had been breastfed. Of the 96 infants, 90 (94%) were still being breastfed and 93 (97%) were receiving complementary solid foods at the time of the Visit 1 survey. Not all infants were regularly given drinking water. At Visit 1, caretakers of 11 study infants (11%) reported that their infants (all of whom were still breastfed) were not given any drinking water in the last week, either alone or mixed in formula.

Diarrhea and enteropathogen infections

At Visit 1, 19 of 96 caretakers (20%) reported that their infant had diarrhea in the past week; of the 94 infants with a second visit, caretakers reported that 13 (14%) had experienced diarrhea since the first visit, including seven infants whose caretakers had reported they had diarrhea at the first visit. One or more enteropathogens were detected in 64 of the 94 stool samples (68%) collected at Visit 2 (Table 1). The most prevalent pathogens in stool samples were *Salmonella* spp. (detected in 26% of samples), *Campylobacter* spp. (23%), and *Clostridium difficile* toxin A or B (23%) (Supplemental Table 2). Infants with at least one enteropathogen detected in their stool at Visit 2 had higher odds of having diarrhea symptoms reported at that time (odds ratio [OR]: 2.91; 95% CI: 0.60–14.0). *Campylobacter* spp. and enterotoxigenic *E. coli* were associated with significantly higher odds of caretaker-reported diarrhea symptoms at the time of sample collection (OR: 3.48; 95% CI: 1.03–11.8 and OR: 6.76; 95% CI: 1.53–29.8, respectively). *C. difficile* (toxin A or B) was the only enteropathogen that did not tend toward association with higher odds of concurrent caretaker-reported infant diarrhea (OR: 0.56; 95% CI: 0.11–2.72).

Drinking water contaminants in samples collected from the primary drinking water source

E. coli, arsenic, and at least one pesticide were each found in samples from all types of household primary drinking water sources collected at Visit 1 (piped drinking water, protected wells, public water basins, bought/bottled drinking water, and unprotected wells) (Figure 2). Considering these three types of contaminants, 11 of 87 households with available data (12.6%) had no contaminant detected, 35 (40.2%) had one contaminant detected, 30 (34.5%) had two types of contaminants detected, and 11 (12.6%) had all three types of contaminants detected in primary drinking water samples (Supplemental Table 3).

E. coli detection in primary, secondary, and tertiary drinking water samples

We collected and tested 347 household drinking water samples from 96 households for *E. coli*, and additionally tested 30 negative controls for *E. coli* and total coliforms. None of the negative controls had detectable *E. coli*; however, two of these samples had low levels of total coliforms detected (< 4 total coliforms per 100 mL). The 28 household drinking water samples processed for *E. coli* on the two days when coliforms were detected in the negative controls were excluded. Ultimately, *E. coli* analyses were conducted on 319 household drinking water samples: 91 primary drinking water samples, 102 additional secondary/tertiary drinking water samples collected during Visit 1, and 126 drinking water samples (61 primary and 65 secondary/tertiary) collected during Visit 2 (Figure 1).

The source type of 230 of the 319 drinking water samples evaluated for *E. coli* (72.1%) was a piped water connection (Table 2). Overall, 221 of the 319 samples (69.3%) had been stored in containers in the household. Storage time for 173 of 221 stored samples (78.3%) was ≤ 2 days (Supplemental Table 1).

Overall, 118 of 319 household drinking water samples collected for microbiological testing (37.0%) had detectable *E. coli* (concentration range: 1–1,299.7 MPN/100 mL; median concentration: 10.6 MPN/100 mL) (Figure 2). Factors significantly positively associated with *E. coli* detection in household drinking water samples were presence of animals in or around the household (adjusted odds ratio [aOR]: 2.37; 95% CI: 1.09–5.13) and household storage of water (aOR: 4.50; 95% CI: 2.04–9.95); having a toilet

connected to the sewerage system was protective against *E. coli* detection in household drinking water samples (aOR: 0.45; 95% CI: 0.21–0.95) (Table 2).

E. coli detection in stored primary, secondary, and tertiary drinking water samples

We also evaluated factors associated with *E. coli* detection among the subset of 221 water samples (collected from 80 households) that had been stored in containers in the household prior to collection. Stored water samples from households with at least one animal residing in or around the household had triple the odds of *E. coli* detection (aOR: 3.02; 95% CI: 1.24–7.33) and water stored in containers on the ground (as opposed to on a table or countertop) had quadruple the odds of *E. coli* detection (aOR: 4.16; 95% CI: 2.17–7.95); water samples stored in covered containers had lower odds of *E. coli* detection compared with samples from uncovered containers (aOR: 0.26; 95% CI: 0.10–0.67) (Supplemental Table 1).

HMM detection in primary drinking water samples

Of the 96 primary drinking water samples, the source of 70 (72.9%) was an indoor piped water connection. Half (50.0%) of the 96 primary samples had detectable levels of arsenic (concentration range: 0.01–15.1 µg/L), two samples (2.1%) had detectable lead levels (2.31–2.78 µg/L), and one sample (1.0%) had detectable chromium (1.84 µg/L); cadmium was not detected in any sample (Figure 2).

Of the 48 drinking water samples with detectable arsenic, 24 (50.0%) had an arsenic concentration exceeding the WHO standard of 10 µg/L. All 24 were collected from households enrolled from the Santa Rosa hospital. Factors positively associated with arsenic contamination exceeding 10 µg/L in drinking water samples included piped drinking water source (OR: 3.67; 95% CI: 0.78–17.1; referent: non-piped water source) and caretaker-reported insecticide use in the home (OR 3.55; 95% CI: 1.35–9.31) (Table 3). As only two variables (enrollment hospital and household insecticide use) met the criterion for inclusion in a multivariable model and all positive samples were collected from households enrolled from the same hospital, multivariable modeling was not conducted.

Pesticide detection in primary drinking water samples

Results of pesticide detection in drinking water were available for most of the 96 samples collected from primary drinking water sources: missingness varied by pesticide but was < 6% for each target (Figure 2). At least one pesticide was detected in 60 samples collected from the primary drinking water source from 92 households with available data (65%). Atrazine, a commonly used herbicide that is relatively soluble in water, was most commonly detected (48% of samples; concentration range: 0.06–29.4 µg/L); chlorpyrifos, an organophosphate insecticide, was detected in 15% of samples (range: 3.71–21.4 µg/L); *pp*-DDE, a degradate of the insecticide dichlorodiphenyltrichloroethane (DDT), was detected in 14% (range: 0.36–2.15 µg/L); and cypermethrin, a pyrethroid insecticide was detected in 12% (range: 1.19–9.71 µg/L). No drinking water sample had detectable diazinon or permethrin.

In univariable analyses, there were higher odds of pesticide detection in drinking water samples that had been stored in containers in the household (OR 6.55; 95% CI: 2.05–21.0) (Table 4). Enrollees from the Santa Rosa hospital tended to have lower odds of pesticide detection in water compared with enrollees from the José Cayetano Heredia hospital (OR 0.46; 95% CI: 0.19–1.09), and odds of detecting a pesticide in drinking water tended to be higher when the mother or father of the study infant worked in agriculture (OR: 2.67; 95% CI: 0.70–10.2). Only drinking water storage met screening criteria for inclusion in a multivariable model; thus, no adjusted estimates are presented.

Characteristics associated with enteropathogen infection

In the multivariable model examining factors associated with infant enteropathogen infection, infants from households that had a primary drinking water sample that was positive for any pesticide/herbicide (measured at Visit 1) had higher odds of having an enteropathogen infection at Visit 2 (aOR: 2.93; 95% CI: 1.13–7.61) and infants given drinking water in the week prior to the Visit 1 survey had higher odds of enteropathogen infection at Visit 2, compared with those not given drinking water (aOR: 4.36; 95% CI: 1.11–17.1) (Table 5).

DISCUSSION

In this study we combined chemical and microbiological methods to test drinking water samples collected from 96 households with infants in Piura, Peru, in addition to testing infant stools for enteropathogen virulence genes. Most water samples came from households using a piped water supply and nearly all samples were from households that had access to improved drinking water sources, yet we found widespread chemical and microbiological drinking water contamination, especially among water samples that had been stored in the household. *E. coli*, arsenic, and at least one pesticide were each found in all types of drinking water sources we collected and 47% of households had multiple types of contaminants detected in samples collected from the primary drinking water source. Our results point to the concurrent risks of microbiological, HMM, and pesticide exposures in a low-income setting with high access to piped water and suggest that safer drinking water storage may reduce health risks.

Higher odds of enteropathogen infection at Visit 2 were observed among infants from households where pesticides were detected in drinking water at Visit 1. Pesticide exposure may affect human immune response, although epidemiologic data on this association are sparse.[16] It is possible there were unmeasured factors associated with both enteropathogen exposure and pesticide prevalence. Insecticides may be used in the region due to concern about dengue, which is endemic in the region.[17,18] This study highlights a need for further research on pesticides in drinking water and child immune response.

While we found higher odds of enteropathogen infection among infants residing in households where a pesticide was detected in the primary drinking water sample, an association between *E. coli* detection in drinking water and subsequent enteropathogen infection was not observed. Possible reasons for the lack of association include (1) inadequate sample size to assess this association, (2) infants not consistently drinking the water that was sampled, (3) inability of an indicator organism to establish risk of pathogen contamination of water, or (4) other predominant enteropathogen transmission pathways than drinking water, such as ingestion of pathogens present on hands.[19,20]

There were 11 breastfed infants who were not given drinking water during the week before the Visit 1 survey. These infants had significantly lower odds of enteropathogen infection the following week, suggesting that consumption of drinking water may be a risk for infant enteropathogen infection and breastfeeding may be protective. This risk of pathogen exposure via drinking water might have been missed if the only exposure considered had been presence of indicator bacteria in household drinking water, and water consumption habits were not evaluated.

Most enteropathogens were associated with elevated odds of caretaker-reported infant diarrhea, although we had a limited sample size to evaluate these associations, and few met the threshold of statistical significance. There was a high prevalence of *Clostridium difficile* (toxins A and B) in stool samples (23%); this was the one enteropathogen that did not tend toward association with higher odds of caretaker-reported infant diarrhea (OR: 0.56; 95% CI: 0.11–2.72). Little is known about infant response to *C. difficile* colonization, and clinical disease associated with these toxins may be rare in this age group, as receptor sites for the toxins are not fully developed in infants.[21–23] Infants with *Campylobacter* spp. virulence genes detected in their stool at Visit 2 had higher odds of having diarrhea reported at that time. *Campylobacter* was the leading pathogen to which diarrhea cases in infants (0–11 months) were attributed in a study conducted in Loreto, Peru.[24] Previous research in Peru suggests that the presence of chickens in the household, which was common in this study, may be a risk factor for childhood *Campylobacter* infections.[25]

The high prevalence of arsenic in household drinking water samples in this study was alarming, especially given the high detection in a piped water system and the percentage of all primary drinking water samples (25%) exceeding the WHO arsenic standard. Previous research has identified a high prevalence of arsenic in groundwater and surface water in Peru.[26,27] Potential sources of arsenic include natural deposits, mining activities, or arsenical pesticide production.[26] Few studies have considered arsenic in drinking water samples collected in Peruvian households.[28,29] Addressing arsenic contamination of drinking water can be challenging: mitigation efforts may include switching water sources, which can

have unintended consequences on child health if other drinking water contaminants are not considered when such changes are made.[30] Point-of-use water filters could be a method of reducing arsenic concentrations in drinking water to safe levels;[31] filters can also be useful against microbiological contaminants.

All 24 drinking water samples with arsenic concentration ≥ 10 µg/L came from households where the study infant's mother gave birth at the Santa Rosa hospital, whose patients generally have unstable employment and lower socio-economic status, thus arsenic exposure is affecting a particularly vulnerable group of mothers and children. It is possible that the households in the Santa Rosa cohort share a common water provider or section of the water distribution system, although such information was not collected for this analysis and the 24 households were geographically dispersed throughout the study area.

While the JMP has identified arsenic as a high-priority chemical parameter for water quality testing during household surveys, it states that the highest concern for global water quality is fecal contamination. Arsenic testing was implemented in only three of 29 countries that had national water quality household surveys during 2012–2020,[32] suggesting arsenic exposure is understudied globally, likely leading to underestimation and underappreciation of exposure risks. Exposure to HMM in drinking water, such as arsenic, may inhibit cognitive development in children.[33,34] Arsenic exposure in utero has also been associated with worse birth outcomes and infant mortality.[33]

Reported use of insecticides in the home was associated with increased odds of arsenic concentration ≥ 10 µg/L in samples collected from primary drinking water sources. Although the use of arsenic-based pesticides has declined since the introduction of DDT,[35] it is possible that insecticides containing arsenic are contaminating drinking water, although our results do not establish a causal link, and pesticides containing arsenic are more likely used for agriculture rather than in the home. In contrast to arsenic detection, pesticide detection in drinking water tended to be lower among households where the mother gave birth at the Santa Rosa hospital. Better understanding of how and where in the water

distribution system or household contamination is occurring, and how this varies across settings, is needed to design and enact meaningful interventions.

E. coli was detected in 37% of household drinking water samples, even though the water source type (prior to storage, when applicable) for nearly all was an improved drinking water source (316 of 319 samples), with the majority coming from a piped distribution system. This highlights that improved drinking water sources that are not safely managed (e.g., intermittently available or not safely stored) are prone to contamination. Odds of *E. coli* detection in drinking water were higher for households that kept animals in or around the home. While improved sanitation may limit exposure to human feces, there may be residual animal feces contamination in households where animal waste is not contained. Fecal indicator organisms such as *E. coli* cannot discern whether microbiological water contamination was a result of human or animal fecal contamination. Animals harbor many pathogens capable of infecting humans and producing acute or long-term adverse health outcomes,[36] thus attention should be given to separating both human and animal feces from stored drinking water.

Storing drinking water in containers in the household was associated with substantially higher odds of both *E. coli* and pesticide detection. More than half of households using piped drinking water reported that their water was cut off at least once in the week prior to the first study visit, and household drinking water storage was common. Results are consistent with previous research showing post-collection contamination of stored water, with considerable change in quality for water that was relatively uncontaminated at the source.[37,38] However, few other studies also highlight the chemical risks of drinking water storage. Uncovered storage containers and containers on the ground had substantially higher odds of *E. coli* contamination, suggesting that safe drinking water storage–in which water containers have small, covered openings, and a small valve or spigot for pouring–could be beneficial.[39] Safe storage messaging may be particularly beneficial in agricultural communities, as odds of detecting a pesticide in drinking water tended to be higher when the mother or father of the study infant worked in agriculture.

We did not evaluate factors associated with pesticide contamination in stored samples only, as there were few stored drinking water samples (N = 4) that did not have pesticide contamination.

Limitations

Our study had a small sample size and limited power to detect associations between water quality and health outcomes. Our assessment of microbial water quality as a risk of subsequent infant enteropathogen infection was limited by the fact that not all infants were consistently given drinking water from the household's primary drinking water source, thus contamination of drinking water may not have aligned with a risk of exposure. Misclassification of enteropathogen infection is possible due to laboratory methods: for example, the Luminex gastrointestinal pathogen panel has low specificity for *Salmonella* spp.,[40] which may have been over-diagnosed in this population. We did not have consistent definitions of urban, peri-urban, or rural neighborhoods in our study, making hypotheses about common exposures in these geographically distinct settings challenging. We also did not have information on the specific providers of piped drinking water.

Conclusions

Our study took a holistic approach to examine a range of drinking water exposures in Peruvian households with infants. We found widespread microbiological and chemical contamination of drinking water in these households, despite most having access to piped drinking water. Drinking water storage was associated with higher odds of microbiological and pesticide contamination, and water was often stored in uncovered containers or on the ground, which was positively associated with detection of *E. coli* in water samples. Infants in this study are at high risk of exposure to drinking water contaminants that have previously been linked with impaired cognitive growth; furthermore, the majority (68%) of study infants had evidence of an enteropathogen infection at a young age, which is also of concern for cognitive development and other health outcomes.[2–4] The range of drinking water contaminants and enteropathogen

exposures suggests that infants may be subject to persistent immune system disruption or gut inflammation during a critical period of development.

Caretakers of young children should be made aware of the risks of concurrent microbiological, heavy metal, and chemical contamination of drinking water in households in low-income settings and potential acute and long-term impacts on child health. Pregnant women should also be made aware of the potential risks of *in utero* exposure to arsenic via drinking water. Mitigation efforts that address drinking water quality should consider microbiological, HMM, and chemical quality in tandem. Further research into the sources of these contaminants should be conducted in this setting. Following exclusive breastfeeding recommendations for infants ≤ 6 months of age[41] and safe drinking water storage can be protective against multiple types of drinking water contaminants and should be promoted.

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DISCLOSURES

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Table 1. Demographic, household, and clinical characteristics among 96 households and study infants — Piura, Peru, 2016

	Study infants/households (N = 96)
Demographic characteristics (study infant)	
Female	41 (42.7%)
Age (months): median (range)	7.0 (5.7–8.0)
Demographic characteristics (study mother)	
Completed secondary school or above	67 (69.8%)
Enrolled at Santa Rosa hospital	45 (46.9%)
Enrolled at José Cayetano Heredia hospital	51 (53.1%)
Household	
Household has a refrigerator	65 (67.7%)
Animals reside in or around the house	69 (71.9%)
Dog	38 (39.6%)
Cat	24 (25.0%)
Other mammal*	8 (8.3%)
Chickens or other birds	34 (35.4%)
Has toilet connected to piped sewerage	62 (64.6%)
Other child(ren) < 5 years old reside in the household†	39 (40.6%)
Primary drinking water source	
Piped drinking water	76 (79.2%)
Indoor piped water connection	70 (72.9%)
Outdoor piped water connection	2 (2.1%)
Neighbor's piped water connection	4 (4.2%)
Non-piped drinking water	20 (20.8%)
Improved sources:	
Protected well	7 (7.3%)
Public water basin	5 (5.2%)
Tanker truck or other bought/bottled water	7 (7.3%)
Unimproved sources:	
Unprotected well	1 (1.0%)
Drinking water was stored in the household prior to collection‡	36 (37.5%)
Drinking water service was cut off in the last week (N = 75)§	39 (52.0%)
Infant feeding (Visit 1)	
Ever breastfed	96 (100.0%)
Still breastfed	90 (93.8%)
Eats solid food	93 (96.9%)
Infant drank water in the previous week**	85 (88.5%)
Diarrhea and enteropathogen infection	
Caretaker reported diarrhea at Visit 1 (N = 96)††	19 (19.8%)
Caretaker reported diarrhea at Visit 2 (N = 94) ††	13 (13.8%)
Enteropathogen detected in stool at Visit 2 (N = 94)	64 (68.1%)
Enteropathogens detected in stool at Visit 2: median (range)	1 (0–5)

* Other mammals included were pigs, sheep, goats, and rabbits.

† Does not include the study infant.

‡ Refers to households where the sample collected from the primary drinking water source had been stored in a container in the household prior to collection.

§ Among 75 households with piped water as the primary drinking water source with non-missing information on drinking water service cuts during the week before Visit 1. One household had missing data on water service cuts.

** Infant drank water alone or mixed with formula in the week prior to Visit 1, as reported by their caretaker.

†† Caretakers reported whether infants had diarrhea in the week prior to Visit 1 and between Visit 1 and Visit 2. Visit 2 occurred a median of 6 days after Visit 1, with 94% of second visits occurring within 4–10 days after the first visit (range 4–27 days). Information on Visit 2 diarrhea and enteropathogen detection was available for 94 of the 96 infants.

Table 2. Association between demographic, household, and water sample characteristics and *Escherichia coli* detection in 319 drinking water samples collected from households with infants — Piura, Peru, 2016

	E. coli detected in drinking water samples* (N = 319)	OR (95% CI)	aOR (95% CI)
Demographic & household characteristics			
Enrollment hospital			
Santa Rosa	56/143 (39.2%)	1.18 (0.59–2.38)	--
José Cayetano Heredia	62/176 (35.2%)	ref.	
Household has a refrigerator			
Yes	73/223 (32.7%)	0.55 (0.26–1.16)	--
No	45/96 (46.9%)	ref.	
Mother's highest level of education:			
Less than secondary school	49/98 (50.0%)	2.20 (1.06–4.56)†	--
Completed secondary school	69/221 (31.2%)	ref.	
Animals reside in or around the household			
Yes	98/225 (43.6%)	2.86 (1.35–6.06)†	2.37 (1.09–5.13)
No	20/94 (21.3%)	ref.	ref.
Has a toilet connected to piped sewerage			
Yes	55/201 (27.4%)	0.33 (0.16–0.67)†	0.45 (0.21–0.95)
No	63/118 (53.4%)	ref.	ref.
Additional children (aged < 5 years) besides the study infant reside in the household			
Yes	55/126 (43.7%)	1.60 (0.78–3.27)	--
No	63/193 (32.6%)	ref.	
Water Sample Characteristics			
Piped drinking water‡	70/230 (30.4%)	0.37 (0.18–0.76)†	--
Indoor piped water connection	55/209 (26.3%)	--	--
Outdoor piped water connection	3/4 (75.0%)	--	--
Neighbor's piped water connection	12/17 (70.6%)	--	--
Non-piped drinking water	48/89 (53.9%)	ref.	
Improved sources:			
Protected well	24/32 (75.0%)	--	--
Public water basin	12/22 (54.5%)	--	--
Tanker truck or other bought/bottled water	10/32 (31.3%)	--	--
Unimproved sources:			
Surface water	1/1 (100.0%)	--	--
Unprotected well	1/2 (50.0%)	--	--
Drinking water was stored in the household prior to collection§			
Yes	105/221 (47.5%)	5.92 (2.79–12.6)†	4.50 (2.04–9.95)
No	13/98 (13.3%)	ref.	ref.

E. coli: indicator *Escherichia coli*; (a)OR: (adjusted) odds ratio; aORs are adjusted for other variables in the model, i.e., those with aORs listed; CI: confidence interval; ref.: referent group.

* The numerator is the number of samples positive for *E. coli*; the denominator is the total number of samples in the category with available *E. coli* results. Primary, secondary, and tertiary samples are included.

† Met the screening criterion for inclusion in a multivariable model ($p < 0.10$ in univariate analysis); adjusted odds ratio is reported only if the variable met the criterion for the final multivariable model ($p < 0.05$ in multivariable analysis).

‡ Piped water compared to non-piped water in models; sub-categories of these sources were not individually considered in models.

§ Refers to water samples that enumerators collected from containers of stored drinking water in the household.

Table 3. Association between demographic, household, and water sample characteristics and arsenic detection (exceeding standard of 10 µg/L) in 96 drinking water samples collected from households with infants — Piura, Peru, 2016

	Arsenic concentration ≥10 µg/L in drinking water samples* (N = 96)	OR (95% CI)
Demographic & household characteristics		
Enrollment hospital		
Santa Rosa	24/45 (53.3%)	n/a
José Cayetano Heredia	0/51 (0.0%)	
Household has a refrigerator		
Yes	15/65 (23.1%)	0.73 (0.28–1.93)
No	9/31 (29.0%)	ref.
Mother's highest level of education:		
Less than secondary school	7/29 (24.1%)	0.94 (0.34–2.58)
Completed secondary school	17/67 (25.4%)	ref.
Mother or father works in agriculture		
Yes	4/16 (25.0%)	1.00 (0.29–3.45)
No	20/80 (25.0%)	ref.
Insecticides are used in the home		
Yes	15/38 (39.5%)	3.55 (1.35–9.31)†
No	9/58 (15.5%)	ref.
Water Sample Characteristics		
Piped drinking water‡	22/76 (28.9%)	3.67 (0.78–17.1)
Indoor piped water connection	19/70 (27.1%)	--
Outdoor piped water connection	1/2 (50.0%)	--
Neighbor's piped water connection	2/4 (50.0%)	--
Non-piped drinking water	2/20 (10.0%)	ref.
Improved sources:		
Protected well	1/7 (14.3%)	--
Public water basin	0/5 (0.0%)	--
Tanker truck or other bought/bottled water	0/7 (0.0%)	--
Unimproved sources:		
Unprotected well	1/1 (100%)	--
Drinking water was stored in the household prior to collection§		
Yes	9/36 (25.0%)	1.00 (0.39–2.60)
No	15/60 (25.0%)	ref.

OR: odds ratio; CI: confidence interval; ref.: referent group.
* The numerator is the number of samples with arsenic concentration ≥10 µg/L; the denominator is the total number of samples in the category with available arsenic concentrations.
† Met the screening criterion for inclusion in a multivariable model ($p < 0.10$ in univariate analysis); because only one variable met the screening criterion, no multivariable model is presented.
‡ Piped water compared to non-piped water in models; sub-categories of these sources not considered in models.
§ Refers to water samples that enumerators collected from containers of stored drinking water in the household.

Table 4. Association between demographic, household, and water sample characteristics and pesticide detection in drinking water samples from 92 households with infants — Piura, Peru, 2016

	≥ 1 pesticide* detected in drinking water samples (N = 92)	OR (95% CI)
Demographic & household characteristics		
Enrollment hospital		
Santa Rosa	24/43 (55.8%)	0.46 (0.19–1.09)†
José Cayetano Heredia	36/49 (73.5%)	ref.
Household has a refrigerator		
Yes	40/64 (62.5%)	0.67 (0.25–1.75)
No	20/28 (71.4%)	ref.
Mother's highest level of education:		
Less than secondary school	20/27 (74.1%)	1.79 (0.66–4.83)
Completed secondary school	40/65 (61.5%)	ref.
Mother or father works in agriculture		
Yes	13/16 (81.3%)	2.67 (0.70–10.2)
No	47/76 (61.84%)	ref.
Insecticides are used in the home		
Yes	25/38 (65.8%)	1.04 (0.44–2.50)
No	35/54 (64.8%)	ref.
Water sample characteristics		
Piped drinking water‡	45/73 (61.6%)	0.43 (0.13–1.42)
Indoor piped water connection	40/68 (58.8%)	--
Outdoor piped water connection	2/2 (100.0%)	--
Neighbor's piped water connection	3/3 (100.0%)	--
Non-piped drinking water	15/19 (78.9%)	ref.
Improved sources:		
Protected well	7/7 (100.0%)	--
Public water basin	2/5 (40.0%)	--
Tanker truck or other bought/bottled water	5/6 (83.3%)	--
Unimproved sources:		
Unprotected well	1/1 (100.0%)	--
Water sample was stored in the household prior to collection§		
Yes	29/33 (87.9%)	6.55 (2.05–21.0)†
No	31/59 (52.5%)	ref.

OR: odds ratio; CI: confidence interval; ref.: referent group.

* The numerator is the number of samples with at least one pesticide detected; the denominator is the total number of samples in the category with available pesticide results. Target pesticides were atrazine, diazinon, chlorpyrifos, p,p'-dichlorodiphenyldichloroethylene, permethrin, and cypermethrin.

† Met the screening criterion for inclusion in a multivariable model ($p < 0.10$ in univariate analysis); because only one variable met the criterion for inclusion in the final multivariable model ($p < 0.05$ in multivariable model), no adjusted model is presented.

‡ Piped water compared to non-piped water in models; sub-categories of these sources not considered in models.

§ Refers to water samples that enumerators collected from containers of stored drinking water in the household.

Table 5. Association between demographic, household, infant, and water sample characteristics and enteropathogen infection at follow-up Visit 2 among 94 infants — Piura, Peru, 2016

	≥1 enteropathogen detected in stool (N = 94 samples)	OR (95% CI)	aOR (95% CI)
Demographic & household characteristics			
Enrollment hospital			
Santa Rosa	29/45 (64.4%)	0.73 (0.30–1.73)	--
José Cayetano Heredia	35/49 (71.4%)	ref.	
Household has a refrigerator			
Yes	43/64 (67.2%)	0.88 (0.34–2.25)	--
No	21/30 (70.0%)	ref.	
Mother's highest level of education:			
Less than secondary school	19/28 (67.9%)	0.99 (0.38–2.54)	--
Completed secondary school	45/66 (68.2%)	ref.	
Animals reside in or around the household			
Yes	48/68 (70.6%)	1.50 (0.58–3.87)	--
No	16/26 (61.5%)	ref.	
Has a toilet connected to piped sewerage			
Yes	44/61 (72.1%)	1.68 (0.69–4.12)	--
No	20/33 (60.6%)	ref.	
Additional children (aged < 5 years) besides the study infant reside in the household			
Yes	26/39 (66.7%)	0.90 (0.37–2.15)	--
No	38/55 (69.1%)	ref.	
Infant characteristics			
Caretaker reported giving the study infant water in the week before enrollment			
Yes	60/83 (72.3%)	4.57 (1.22–17.1)*	4.36 (1.11–17.1)
No	4/11 (36.4%)	ref.	ref.
Water sample characteristics (primary drinking water source)			
Any *E. coli* detected			
Yes	19/26 (73.1%)	1.36 (0.49–3.74)	--
No	42/63 (66.7%)	ref.	
Arsenic concentration ≥10 µg/L			
Yes	13/24 (54.2%)	0.44 (0.17–1.15)	--
No	51/70 (72.9%)	ref.	
Any pesticide detected			
Yes	45/59 (76.3%)	3.01 (1.20–7.60)*	2.93 (1.13–7.61)
No	16/31 (51.6%)	ref.	ref.

(a)OR: (adjusted) odds ratio; aORs are adjusted for other variables in the model, i.e., those with aORs listed; CI: confidence interval; ref.: referent group.

* Met screening criterion for inclusion in a multivariable model ($p < 0.10$ in univariate analysis); adjusted odds ratio reported only if variable met the criterion for final multivariable model ($p < 0.05$ in multivariable analysis).

Figure 1. Household visits for water quality study in 96 households with infants — Piura, Peru, 2016

Figure 2. Detection of *Escherichia coli*, arsenic, and pesticides in samples collected from primary drinking water sources from 96 household with infants — Piura, Peru, 2016

CO-AUTHOR CONTACT INFORMATION

Miranda J. Delahoy

Gangarosa Department of Environmental Health, Rollins School of Public Health, Emory University, Atlanta, Georgia, United States

mirandadelahoy@gmail.com

Sydney Hubbard

Gangarosa Department of Environmental Health, Rollins School of Public Health, Emory University, Atlanta, Georgia, United States

sydney.corinne.hubbard@emory.edu

Mia Mattioli

Gangarosa Department of Environmental Health, Rollins School of Public Health, Emory University, Atlanta, Georgia, United States

kuk9@cdc.gov

Carlos Culquichicón

Gangarosa Department of Environmental Health, Rollins School of Public Health, Emory University, Atlanta, Georgia, United States

Emerge, Emerging Diseases and Climate Change Research Unit, School of Public Health and Administration, Universidad Peruana Cayetano Heredia, Lima, Peru

School of Health Sciences, Universidad Nacional de Piura, Piura, Peru

carlos.culquichicon@gmail.com

Jackie Knee

Disease Control Department, London School of Hygiene & Tropical Medicine, London, United Kingdom

jacqueline.knee@lshtm.ac.uk

Joe Brown

Department of Environmental Sciences and Engineering, Gillings School of Global Public Health, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina, United States

joebrown@unc.edu

Lilia Cabrera

Asociación Benéfica PRISMA, Lima, Peru

lcabrera@prisma.org.pe

Dana Boyd Barr

Gangarosa Department of Environmental Health, Rollins School of Public Health, Emory University, Atlanta, Georgia, United States

dbbarr@emory.edu

P. Barry Ryan

Gangarosa Department of Environmental Health, Rollins School of Public Health, Emory University, Atlanta, Georgia, United States

bryan@emory.edu

Andres G. Lescano

Emerge, Emerging Diseases and Climate Change Research Unit, School of Public Health and Administration, Universidad Peruana Cayetano Heredia, Lima, Peru

willy.lescano@upch.pe

Robert H. Gilman

Johns Hopkins Bloomberg School of Public Health, Baltimore, Maryland, United States

rgilman1@jhmi.edu

Karen Levy

Department of Environmental and Occupational Health Sciences, School of Public Health, University of Washington, Seattle, Washington, United States

klevyx@uw.edu

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