

Research Participants' Attitudes towards Receiving Information on Genetic Susceptibility to Arsenic Toxicity in Rural Bangladesh

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Keywords

Arsenic · Environmental risk factors · Ethics of genetic research · Return of genetic results

Abstract

Background: In human genetics research, it has become common practice for researchers to consider returning genetic information to participants who wish to receive it. Research participants in lower-resource settings may have barriers or competing interests that reduce the benefit or relevance of such information. Thus, the decision to return genetic information in these settings may involve special considerations of participants' interests and preferences. In this project, our goal was to assess Bangladeshi research participants' attitudes towards receiving information regarding genetic susceptibility to the effects of consuming arsenic-contaminated drinking water, a serious environmental health concern in Bangladesh and other countries. **Methods:** We administered a short questionnaire to 200 individuals participating in the Health Effects of Arsenic Longitudinal Study. Associations between survey responses and participant characteristics were estimated using logistic regression. **Results:** Overall, 100% of our participants were inter-

ested in receiving information regarding their genetic susceptibility to arsenic toxicities, and 91% indicated that being at increased genetic risk would motivate them to make efforts to reduce their exposure. Lower levels of education showed evidence of association with less concern regarding the health effects of arsenic and lower levels of motivation to reduce exposure in response to genetic information. **Conclusions:** Research participants in this low-resource setting appeared interested in receiving information on their genetic susceptibility to arsenic toxicity and motivated to reduce exposure in response to such information. Additional research is needed to understand how best to communicate genetic information in this population and to assess the impact of such information on individuals' behaviors and health.

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Introduction

Returning genetic results to research participants has become a topic of debate in recent years [1–3] due in part to increasing availability of whole-genome genotyping and sequencing data and an improved understanding of

genetic causes of disease. Whole-genome sequencing data can contain information relevant to the health care of a research participant, although not necessarily relevant to the research questions; this has been termed “incidental findings.” There is a growing consensus that researchers should offer to return such incidental findings to research participants [4]. Groups such as the American College of Medical Genetics (ACMG) have provided recommendations regarding which genes and variants should be considered “medically relevant” and offered to participants as part of the incidental findings [5].

In addition, there is a trend among researchers and funders to make research participants’ genetic data freely available to them should they want access to it [1–5]. These types of data could be specific research results (i.e., the specific genetic variant[s] under study in meeting a research project’s aims) [6] or genome-wide measures of genetic variation (potentially communicated as polygenic estimates of risk for specific diseases or as an interpretation of participants’ genetic ancestry). It has been suggested that providing participants their genetic results is one way by which researchers can demonstrate respect for participants and enhance participants’ engagement in research [3]. However, returning results could be harmful if participants misinterpret the significance of the information received. Returning results may also overburden researchers with limited resources [3, 7–9].

The debate surrounding returning genetic information has primarily occurred among research communities in North America, Europe, and high-income countries, as the majority of human genetic research occurs in these settings. However, there are emerging initiatives to facilitate genomic research in lower-resource settings, including the NIH-funded H3Africa (Human Heredity and Health in Africa) program [10]. Research participants in lower-resource settings may have additional threats, barriers, and/or competing interests that may reduce the benefit or relevance of returning genomic results [11] (e.g., less formal education, poverty, malnourishment, contaminated water, violence). Thus, the decision to return (or not return) genetic information to participants in these settings may involve special considerations not relevant in high-resource settings. Additional research is needed in lower-resource settings to better understand participants’ attitudes towards receiving genetic results and how best to communicate them in order to best serve participants’ interests and avert potential harm.

In this study, we surveyed participants’ attitudes towards receiving genetic results in Bangladesh. More specifically, we collected data on attitudes towards receiving

Table 1. Descriptive characteristics of the survey participants ($n = 200$; Araihaazar, Bangladesh)

Sex	
Male	43 (21.5)
Female	157 (78.5)
Mean age at interview, years	44.3
Age categories	
20–29 years	20 (10)
30–39 years	54 (27)
40–49 years	53 (26.5)
50–59 years	54 (27)
60–69 years	17 (8.5)
70–79 years	2 (1)
Education	
0 years	103 (51.5)
>0 years	97 (48.5)
Urine arsenic, µg/g creatinine	
Mean	100.3
25th percentile	41.5
Median	70.5
75th percentile	139.0

Values are n (%) unless otherwise indicated.

information regarding genetic susceptibility to arsenic toxicity, as these participants reside in a rural area where a substantial percentage of drinking wells are naturally contaminated with arsenic, a known human carcinogen and toxicant [12]. Thus, these participants are unique both in terms of the research setting *and* their environmental exposures [13]. Collecting these data is timely, as we now know of inherited genetic variation that impacts arsenic metabolism efficiency, as well as the risk of arsenic toxicity [13] and arsenic-associated diseases [14–20]. Thus, researchers studying arsenic-exposed populations (several of which would be considered “low resource”) have the opportunity to consider returning genetic results to participants that are highly relevant to their susceptibility to the effects of arsenic exposure.

Methods

We administered a questionnaire to 200 individuals participating in The *Health Effects of Arsenic Longitudinal Study* (HEALS) [21] in Araihaazar, Bangladesh, a rural area with high exposure to arsenic through naturally contaminated groundwater [13]. HEALS was initiated in 2000–2002 with the recruitment of ~12,000 healthy individuals (aged 18–75 years), with additional recruitment in 2006–2014 resulting in a cohort of >20,000 individuals. At recruitment, participants were residents of Araihaazar for >5 years and primarily consumed water from a local well. A multifaceted arsenic

Table 2. Survey question responses (*n* = 200; Araihaazar, Bangladesh)

Survey questions	Yes	No	Don't know
Q4. Are you concerned about the health effects of arsenic-contaminated drinking water?	173 (86.5)	27 (13.5)	NA
Q5. If your genes could provide you information on your susceptibility to arsenic toxicities, would you be interested to receive this information?	200 (100)	0 (0)	NA
Q6. Is your primary water source believed to be “arsenic free”?	117 (58.5)	66 (33)	17 (8.5)
Q7. At this point in time, is it possible for you to take steps to further reduce your and/or your family's exposure to arsenic in water used for drinking and cooking?	98 (49)	102 (51)	NA
Q8. If your genes indicated you (or your family members) were at elevated risk for arsenic toxicities, would this information motivate you to alter your family's water sources to reduce your family's arsenic exposure?	182 (91)	18 (9)	NA
Q9. If your genes indicated that you were at elevated risk for arsenic toxicity, would you be comfortable disclosing this information to others in your family?	199 (99.5)	1 (0.5)	NA
Q10. If your genes indicated that you were at elevated risk for arsenic toxicity, would you want to keep this information confidential from non-family members?	59 (29.5)	141 (70.5)	NA
Values are <i>n</i> (%).			

mitigation program was implemented after baseline (2000–2002) [22]. Interventions included person-to-person reporting of well arsenic levels and health education, labeling of wells to indicate arsenic concentration, village-level health education, and installation of deep, low-arsenic wells in villages with high exposure. Currently, the participants' communities label wells to reflect arsenic concentration, enabling avoidance of high-arsenic wells – the most effective method of reducing exposure in this community [23].

A questionnaire to assess attitudes towards receiving information on genetic susceptibility to arsenic toxicity was developed by Drs. Pierce, Ahsan, and Eunos (online suppl. File 1; for all online suppl. material, see www.karger.com/doi/10.1159/000505632), consisting of seven questions designed to gauge concern about arsenic exposure, interest in receiving information on genetic susceptibility to arsenic toxicity, and expected behavioral responses to receiving such information. All questions were translated into Bengali by Dr. Eunos (online suppl. File 2). The questionnaire included text intended to orient the respondents to the idea that inherited genetic variation can impact susceptibility to the effects of arsenic exposure. This was done to attempt to increase participants' understanding of genetic susceptibility, as this community has low levels of formal education (Table 1). The questionnaire was administered by Dr. Eunos and his staff to 200 participants visiting the HEALS health clinic in Araihaazar (July–October 2014); 67 of the 200 joined HEALS at the original baseline visit (2000–2002), while 133 were recruited during expansion efforts (2006–2014).

Urine samples were collected at recruitment and follow-up visits. Arsenic concentrations were measured using graphite furnace atomic absorption (Perkin-Elmer Analyst 600 graphite furnace system) (limit of detection = 5 µg/L) at the Columbia University Trace Metal Core Laboratory [24, 25]. For some newly recruited participants, follow-up arsenic measurements are not yet available. For this work, we used individuals' most recent urine arsenic measurement as a measure of exposure (*n* = 196).

Associations between survey responses and participant characteristics were estimated using logistic regression, adjusting for sex, age, and education status (categorized as 0 vs. >0 years of formal education). Analyses were conducted using R (version 3.5.2).

Results

Characteristics of our 200 respondents are shown in Table 1. The majority of participants were female (79%) and over half (52%) had no formal education. Responses to our survey are described in Table 2. Most notably, 100% of our participants reported being interested in receiving genetic information regarding their susceptibility to arsenic toxicities (question 5 [Q5]). Furthermore, 91% of respondents

Fig. 1. Attitudes towards arsenic-related risks and genetic susceptibility by education status. **a** The percent of participants with formal education (vs. without), stratified by concern regarding the health effects of arsenic exposure (Yes/No, Q4). **b** The percent of individuals with formal education (vs. without), stratified by motivation to reduce exposure to arsenic in response to learning they are at elevated risk (Yes/No, Q8).

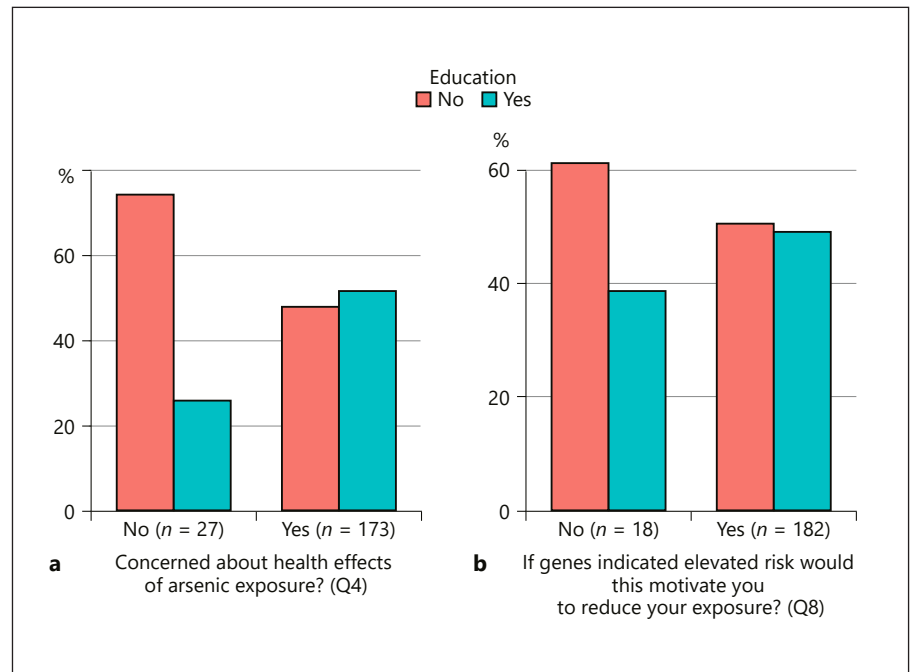


Table 3. Response to survey question 6 stratified by median creatinine-adjusted urine arsenic concentration ($n = 196$; Araihaazar, Bangladesh)

Survey question	Creatinine-adjusted urine arsenic		<i>p</i> value
	≤143 µg/g	>143 µg/g	
Q6. Is your primary water source believed to be “arsenic free”?			
Yes	75 (75.8)	41 (42.3)	<0.001
No	18 (18.2)	45 (46.4)	
Don’t know	6 (6.1)	11 (11.3)	
Values are <i>n</i> (%).			

indicated that they would be motivated to change their family’s water source in order to reduce their family’s exposure if their genes indicated they (or family members) were at elevated risk for arsenic toxicities (Q8). All but one respondent indicated that they would be comfortable disclosing to family members that they were at elevated risk (Q9), while 30% indicated they would keep this information confidential from non-family members (Q10).

To validate our respondent’s knowledge regarding levels of arsenic in their drinking water, we stratified participants by median urine arsenic concentration. Using

logistic regression, we observed that individuals who reported an “arsenic-free” primary water source were more likely to have lower arsenic concentrations in urine ($p < 0.001$; Table 3), as expected.

We then sought to determine whether concern regarding arsenic (Q4) was related to the perceived impact of genetic information on motivation to reduce exposure (Q8). Concern regarding arsenic toxicities did not show a clear association with individuals’ motivation to act on genetic information (OR = 1.14; CI: 0.24–3.98; $p = 0.84$); however, our power to estimate this association was limited due to the small number of individuals answering “no” to Q4 and Q8. Nonetheless, it remains possible that participants’ self-reported concern regarding arsenic may be unrelated to their reported intention to act on genetic information.

To determine whether motivation to change behavior based on genetic information was related to education, we tested the association of education status with (1) concern regarding the health effects of arsenic (Q4) and (2) the perceived impact of genetic information on motivation to reduce exposure (Q8). Individuals with lower education were less likely to be concerned about the effects of arsenic (Q4) (OR = 1.12; CI: 1.02–1.23; $p = 0.025$; Fig. 1). Similarly, there was a lower percentage of individuals with formal education among those reporting that genetic information would motivate them to reduce exposure (Q8), but statistical power was limited due to the few people who answered “no” to Q8 (OR = 1.29; CI: 0.46–3.82; $p = 0.62$; Fig. 1)

Discussion

In this survey of Bangladeshi research participants, we assessed attitudes towards receiving information regarding individuals' genetic susceptibility to the effects of arsenic, an exposure of concern in the participants' community. Our most striking observation is that 100% of respondents were interested in receiving genetic information, demonstrating a clear interest in access to personal genetic information in this community.

A substantial percentage of participants (13.5%) were not concerned about the health effects of arsenic (Q4). However, all of these "unconcerned" participants reported being interested in receiving information on genetic susceptibility to arsenic toxicities (Q5). This finding suggests that concern regarding arsenic and interest in receiving information regarding their genetic susceptibility are perceived somewhat differently. This finding also speaks to the possibility that returning genetic information could modify individuals' concern regarding arsenic exposure, with a "return of results" intervention among highly susceptible individuals potentially increasing their motivation to reduce exposure.

Participants with higher levels of formal education were more likely to be concerned about arsenic (Q4) and appeared more motivated to reduce exposure based on increased genetic risk (Q8). This suggests that education may impact the effectiveness of interventions aimed at reducing exposure (including those involving returning genetic results) and should be considered when designing such intervention studies.

Within HEALS, we have the opportunity to study the impact of returning information on genetic susceptibility to arsenic toxicity. Using genetic variation in the AS3MT (arsenic methyltransferase) and FTCD (formiminotransferase cyclodeaminase) regions known to impact arsenic metabolism efficiency and arsenic-induced skin lesion risk [13, 26, 27], we can identify participants at high risk for arsenic toxicities. In the context of an exposure reduction intervention (i.e., Chen et al. [22] and Huhmann et al. [28]), informing high-risk individuals of their increased genetic risk may provide additional motivation to change behavior and reduce exposure, potentially increasing the effectiveness of an intervention among those most susceptible to the effects of exposure.

There are potential risks when returning genetic results to participants (such as misinterpretation of results, stigmatization, or psychosocial stress), and additional research is needed to understand how best to communicate genetic information in this population, in order to minimize the risk

of potential harm. Despite these concerns, the practice of returning results is becoming more widely accepted, including plans within the National Institutes of Health (NIH) All of Us cohort to have genetic results responsibly returned to participants who are interested in receiving them.

There are two primary arguments motivating the return of genetic results to research participants, both of which are potentially relevant to our participants. The first is that participants have a right to genetic data (should they want it), and the second is that researchers have an obligation to return results that are important to participants' health and potentially actionable. In the context of genetic susceptibility to the effects of environmental exposures, returning genetic information could be viewed as a component of precision public health, a term defined as "providing the right intervention at the right time to the right population" [29]. In this way, we could target high-risk individuals using genetic information, and provide this information to participants as a piece of a larger public health effort in this population.

The HEALS participants surveyed in this study are individuals who visited the HEALS clinic, a sample which may not be representative of the larger cohort. Regarding participants' understanding of genetic concepts, research staff attempted to convey these concepts with the help of the explanatory text on the survey, but we did not assess their understanding.

Conclusion

In conclusion, our results indicate that research participants in this rural, low-resource setting are interested in receiving information on their genetic susceptibility to the effects of arsenic exposure. The vast majority of participants report being motivated to reduce their exposure if they learned they were at elevated genetic risk for arsenic toxicities. Similarly, past studies conducted in higher-resource settings have demonstrated that the public's attitude toward receiving genetic information is generally positive, across a range of different diseases [30–33]. Additional research is needed to understand how best to communicate genetic information in this population and to assess the impact of such information on individuals' behaviors, arsenic exposure status, and psychosocial health. The questions of whether and how genetic information should be returned in low-resource settings are likely to require research to understand population-specific needs, preferences, and barriers related to receiving, understanding, and using such information.

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Statement of Ethics

This research was approved by the Institutional Review Board of the University of Chicago (IRB16-1236). Verbal informed consent was obtained from all participants.

Disclosure Statement

The authors declare that no conflict of interest, financial or other, exists.

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Author Contributions

This paper was the original concept of L.I.T., B.L.P., and H.A., with contributions related to data collection and interpretation from A.A., H.S., R.H., G.S., H.M.E., and H.L. All authors were involved in the writing of the manuscript.

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