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REGULAR ARTICLE

A consecutive study on arsenic exposure and intelligence quotient (IQ) of children in Bangladesh

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Abstract
Objective In a recent cross-sectional investigation, we reported the intellectual function of adolescents (aged 14 and 15 years) in Bangladesh who had been exposed to arsenic (As). Here, we report a consecutive investigation on the intelligence quotient (IQ) of 408 children who are living in the Sonargoan Thana of Bangladesh (two age groups: 9 and 10 years; 4 and 5 years) were exposed to high levels of As in the groundwater.
Methods Urine and water samples were collected to assess As exposure. The IQ of the children was estimated using the Raven's Standard Progressive Matrices and the Kaufman Brief Intelligence Test. Information on parents' socioeconomic status (SES) was collected as confounding factors.
Results The results indicate that As exposure was responsible for a lower IQ. The concentration of urinary As ($[As]_u$) was associated with reduced intellectual function in a dose–response manner. A stronger association was found between reduced intellectual function (IQ) and $[As]_u$ than the level of As in the drinking water $[As]_w$. There was no association between verbal IQ scores and $[As]_u$ of children in early childhood (aged 4 and 5 years).
Conclusion Based on these results, we conclude that current levels of As in the urine ($[As]_u$), which we considered to reflect recent exposure to As from all possible sources, including groundwater, food, among others, were negatively associated to the IQ of the children tested, and that this adverse effect of As may also gradually accumulate over time among the poor.

Keywords Arsenic · Children · Groundwater · Intelligence quotient

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Introduction

A prime factor that has been implicated in cognitive and neurological deficits is environmental or occupational exposure to toxic metals. Environmental exposure to neurotoxic metals can occur via contaminated air, food, and water, or in hazardous occupations. Arsenic (As) is a naturally occurring trace element found in rocks, soils, and the waters in contact with these. It occurs within organic compounds (combined with hydrogen and carbon) and within inorganic compounds (combined within sulphur, chlorine or oxygen). It has long been recognized as a toxic element and as well as a neurotoxicant. The rural population of Bangladesh relies mostly on tubewells for their supply of drinking and cooking water. Among the 160 million inhabitants of Bangladesh, approximately 80 million people are affected by As via the groundwater, supplied by approximately ten million tubewells [1]. Children are particularly at risk for high exposure in the As-affected areas because they are highly vulnerable. During the development of the nervous system, vulnerable periods are sensitive to environmental insults because the developments then taking place are dependent on the temporal and regional emergence of critical processes (i.e., proliferation, migration, differentiation, synaptogenesis, myelination, and apoptosis). Evidence from numerous sources demonstrates that neural development extends from the embryonic period through adolescence [2]. Children may, therefore, be particularly susceptible to neurotoxic substances. Research on the possible impairment of children's intellectual function in relation to As exposure in utero and during childhood is limited, and the effect of As on children's intellectual function, as measured by the intelligence quotient (IQ), especially during their childhood development, is not well elucidated. For example, Wasserman et al. [3] found that water As was negatively associated with the IQ of children, especially with the nonverbal and performance test score—but not with verbal score. On the contrary, Calderón et al. [4] found an association between water As concentrations and verbal IQ in Mexican children. Wright et al. [5] reported adverse associations between hair As and hair Mn concentrations and general intelligence scores, particularly verbal scores. Thus, As effects on intellectual function are still under debate, especially in young children, and the age at which As starts to act on the intellectual function has not yet been clarified. In a related investigation [6], we recently observed poorer intellectual function (IQ) in adolescents (14- and 15-year-olds) from a region in Bangladesh where household well water As concentrations were high. We sought to expand these findings on children's intellectual function to younger age groups. Moreover, there has been no consecutive study in Bangladesh that has reported on children's intellectual function in relation to As exposure in the same population at different developmental stages. The aim of our study was, therefore, to investigate the intellectual function (IQ) of children in the early childhood to late childhood age groups. To this end, we studied 408 children from two age groups (4 and 5 years, and 9 and 10 years, respectively) who lived in a highly As-exposed area, Sonargong thana, Bangladesh, for a 3-year period between 2010 and 2012.

Materials and methods

In the Sonargong thana most of the inhabitants drink and use groundwater for their daily activities that they have obtained through tubewells. The groundwater is known to be heavily polluted with As. The children enrolled in our study were randomly selected from different villages at Sonargong thana where 89 % of the tubewells are contaminated with As. The study groups were comprised of individuals who had been exposed to As.

The study protocol was approved by the ethics committees of the Faculty of Agriculture, Saga University, the Graduate School of Medicine, University of Tokyo, Japan, and the Bangladesh Medical Research Council. Moreover, written consent was obtained from the parents and teachers of the school before conducting this study. Data were collected in two ways. First, some of the data were collected from the village and some from the school. Information on socioeconomic status (SES) and drinking habits were collected through a structured questionnaire that was completed during a visit to each respondent's home. Data on family demographics (e.g. parental education, occupation, income, housing type, etc.) were obtained from interviews with the parents during enrollment of their children in the study. Raven's Standard Progressive Matrices (SPM) [7] test was used to assess the IQ of children in the 9- and 10-year-old group, and the Kaufman Brief Intelligence Test (KBIT) [8] was used for the children in the 4- and 5-year-old group. In the SPM test, IQ is expressed on a seven-grade scale (grades V, IV−, IV, III, II, II+, I).The IQ tests of the 9- and 10-year-old children were conducted in the school; during the test all children were given the same series of SPM problems irrespective of age differences. They were asked to work at their own pace and were left uninterrupted from the beginning until the end of the test. The IQ tests of individual children in the 4- and 5-year-old group were conducted in the village. During the survey period, all children were persuaded to provide spot urine and water samples for the measurement of As concentration in urine ($[As]_u$) and water ($[As]_w$), respectively. Collected samples were frozen and transported to Japan where they were kept at −30 °C until analysis. The $[As]_u$ and $[As]_w$ were determined at the Graduate School of Medicine, The University of Tokyo. As concentration was determined by inductively coupled plasma mass spectrometry (Agilent 7500ce; Agilent Technologies, Santa Clara, CA) with an octopole collision/reaction cell. The details of this procedure are described in full in our previous study [6]. The subjects were divided into three groups based on published reference levels of $[As]_u$. The $[As]_u$ values of the low, medium, and high groups range from $1 < [As]_u \leq 137$ μg/L, $137 < [As]_u \leq 400$ μg/L, and $[As]_u > 400$ μg/L, respectively. Accordingly, the lowest reference level of $[As]_u$ (137 μg/L) is the so-called 'non-effective level' [9] and that of 400 μg/L refers to the 'dermatological level'. There are more reference values, especially in the 'non-effective level', however, these do not change the findings observed in this study.

Data were entered into SPSS for Windows, ver. 20. One-way analysis of variance (ANOVA) was employed for analyzing the differences between the groups of transformed data, whereas analysis of covariance (ANCOVA) was used to measure the effect of $[As]_w$ and $[As]_u$ on the measured IQ by controlling for the socioeconomic indicators.

Results

The socio-demographic factors and $[As]_u$ of the respondents are summarized in Table 1. The walls and roof of most of the houses in the survey area are made of corrugated tin. Most of the households are engaged in a business of some kind, but these are primarily very small businesses, such as vegetable selling and shopkeeping. In many cases the families grow and sell their own vegetables. Bangladesh is a developing country, and the majority of households fall into the low income stratum. Thus, the majority of participating households in this study belonged to the low to low–medium income strata. More than 50 % of household heads were illiterate or had just attended the primary education.

The mean $[As]_u$ of the children aged 9 and 10 years (181.9 μg/L) was above the non-effective level (137 μg/L) and that of the children aged 4 and 5 years was 126 μg/L which is below the non-effective level. In comparison, in a previous study the mean $[As]_u$ of children aged 14 and 15 years was found to be 205.3 μg/L [6]. The mean $[As]_u$ gradually increased with age; with a long duration of exposure resulting in increased As concentration. In general, the results presented in Table 1 indicate that most of the respondents came from families with poor SES, and thus they are consuming tubewell water that is highly contaminated with As. The results of the ANOVA revealed that $[As]_u$ significantly differed by parental income (SES) for both the 9- and 10-year-olds ($p < 0.05$) and the 4- and 5-year-olds ($p < 0.05$). More specifically, in both age groups, the $[As]_u$ of the children in the low-income group was significantly higher ($p < 0.05$) than that of children in the medium-income group. This finding suggests that socio-demographic conditions have an influence on As exposure; individuals with higher income can take preventive measures. However, no significant relationship was found between As contamination, as indicated by the $[As]_u$ and other socio-economic indicators, such as education, sanitation, and house type.

The predicted means and standard deviations of the IQ percentile according to the three $[As]_u$ and the two age groups are presented in Table 2. The IQ in the high $[As]_u$ group of the children aged 9 and 10 years did not differ from that in the medium $[As]_u$ group. There were differences in the IQ in the $[As]_u$ groups for the children aged 4 and 5 years. The percentage distributions of IQ grades for the three $[As]_u$ groups (low, medium and high) for children aged 9 and 10 years are shown in Fig. 1. These indicate that only a very small percentage of the respondents from the high $[As]_u$ groups possessed above-average intellectual capacity (>grade III)—rather most had average and below-average IQ grades. In contrast, a comparatively higher percentage of the respondents from the low $[As]_u$ groups possessed above-average intellectual capacity. One-way ANOVA was applied to assess the differences in IQ means and variances, and the results indicated that IQ percentile

Table 1 Sample characteristics

Variable	Study age groups	
	9- and 10-year-old group	4- and 5-year-old group
Subjects	232	176
House type		
Soil wall/tin roof	33 (14.2)	29 (16.5)
Corrugated tin wall and roof	162 (69.8)	34 (19.3)
Brick wall/tin roof	37 (15.9)	113 (64.2)
Occupation of household head		
Wage labor	64 (27.6)	23 (13.1)
Farmer	17 (7.3)	6 (3.4)
Business	83 (35.8)	69 (39.2)
Paid jobs	28 (12.1)	36 (20.5)
Others	40 (17.2)	42 (23.9)
Income of household head		
Low	109 (47.0)	40 (22.7)
Low–medium	89 (38.4)	70 (39.8)
Medium	34 (14.7)	66 (37.5)
Education of household head		
Illiterate	69 (29.7)	32 (18.2)
Primary	87 (37.5)	70 (39.8)
Secondary	59 (25.4)	55 (31.3)
Higher secondary and above	17 (7.3)	19 (10.8)
$[As]_u$ (μg/L) (range)	0.6–2,336	5.0–1,021

Unless indicated otherwise, data are presented as the number with the percentage given in parenthesis

Table 2 Intelligence quotient in the different age groups and according to urinary arsenic levels

Age groups	$[As]_u$ (μg/L) groups[a]	IQ percentile[b]
9 and 10 years	Low ($n = 143$)	45.8 ± 22.9 b
	Medium ($n = 61$)	32.4 ± 23.0 a
	High ($n = 28$)	33.9 ± 19.8 a
4 and 5 years[c]	Low ($n = 112$)	57.6 ± 34.7 b
	Medium ($n = 51$)	45.9 ± 35.3 b
	High ($n = 13$)	19.0 ± 18.4 a

[a] $[As]_u$, Urinary arsenic (As) concentration: Low ($1 < [As]_u \leq 137$ μg/L); medium ($137 < [As]_u \leq 400$ μg/L); high ($[As]_u > 400$ μg/L)

[b] Data are presented as the mean ± standard deviation. Values followed by different lowercase letters within the same row are statistically different

[c] Nonverbal IQ scores

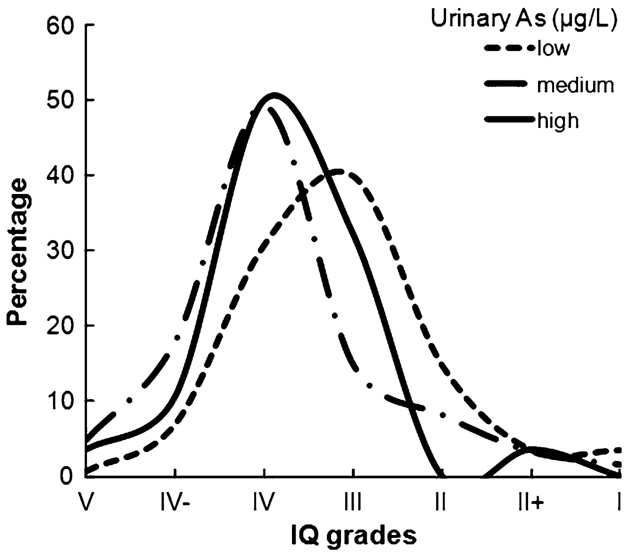

Fig. 1 Percentage distribution of intelligence quotient (*IQ*) grades according to urine arsenic (*As*) concentration ($[As]_u$) in children of the 9- and 10-year-old age group

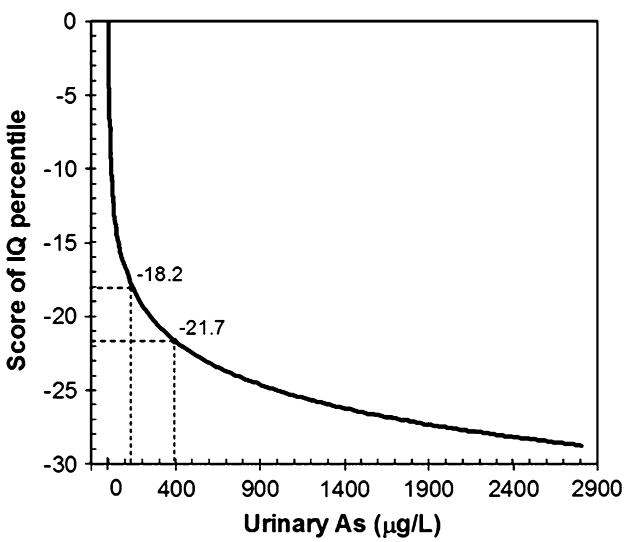

Fig. 2 Relation between IQ and $[As]_u$ of children aged 9 and 10 years

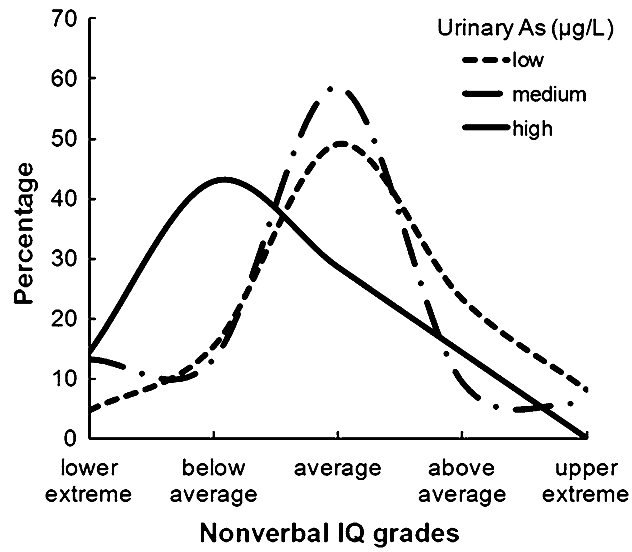

Fig. 3 Percentage distribution of nonverbal IQ grades according to $[As]_u$ in children of the 4- and 5-year-old age group

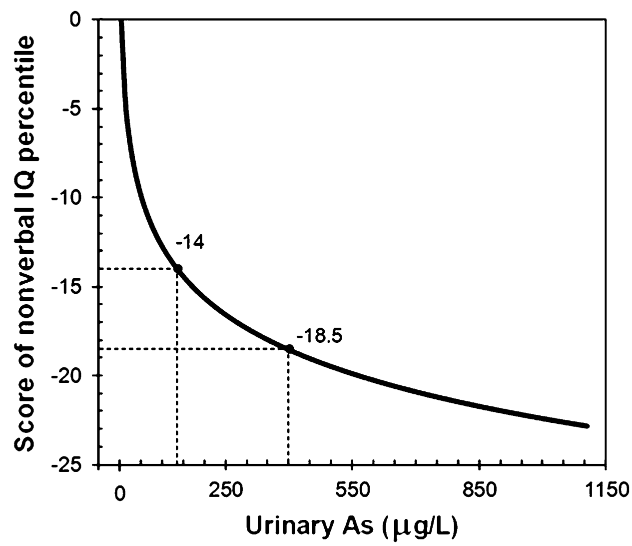

Fig. 4 Relation between IQ and $[As]_u$ of children aged 4 and 5 years

significantly differed among the $[As]_u$ groups and among children aged 9 and 10 years [$F(2, 229) = 9.1$, $p < 0.001$]. Finally, after controlling for income, IQ was significantly related with $[As]_u$ in the 9- and 10-year-old age group. The relationship between $[As]_u$ and IQ percentile score is shown in Fig. 2. $[As]_u$ was negatively associated with IQ, with 137 and 400 µg/L of $[As]_u$ associated with a decrease in IQ percentile scores of 18.2 and 21.7 points, respectively.

Percentage distributions of nonverbal IQ grades according to the three $[As]_u$ groups in children aged 4 and 5 years are presented in Fig. 3. In this group, the IQ, as determined with the KBIT test, is represented as one of five possible IQ grades (lower extreme, below average, average, above average, upper extreme). Figure 3 shows that a comparatively higher percentage of the respondents from the low $[As]_u$ group possessed an above-average intellectual capacity. The nonverbal IQ percentile significantly differed among the $[As]_u$ groups [$F(2, 169) = 5.3$, $p < 0.01$]. After controlling for income, we found that the IQ was significantly related to $[As]_u$ ($p < 0.05$). The relationship between $[As]_u$ and percentile score of nonverbal IQ is presented in Fig. 4. The dotted perpendicular lines illustrate the loss in nonverbal IQ percentile score associated with $[As]_u$.

Discussion

We report here the results of a consecutive study on the effect of As on the intellectual function (IQ) of young children. The focus of our research was children in early childhood and adolescence. We have accepted the definitions of early childhood spanning ages 2 to 6 years, late childhood as spanning ages 6 to 10 years, and adolescence as spanning ages 10 to 14 years. Thus, we selected children aged 4 and 5 years (early childhood) and those aged 9 and 10 years (late childhood) as subjects for our study. Villages of the Sonargong thana in the Narayanganj district of Bangladesh are isolated, low-income areas with a relatively low economic development and poor communication with the outside world, resulting in poor living conditions for the majority of the residents. In our survey, we observed that the confounding factor SES, especially income, had an influence on exposure to As contamination in groundwater. The rural people participating in the survey were unable to take any measures to use As-free water due to their poor socioeconomic conditions (SEC). Thus, it is very possible that poor SEC propagates As contamination. Among the subjects, the mean $[As]_u$, which was high in the 9- and 10-year-old group, was above the non-effective level; in comparison, the mean $[As]_u$ for those children aged 4 and 5 years was lower. One explanation is that children aged 9 and 10 years consume a relatively higher amount of water daily compared to those in the younger age group (4 and 5 years). We estimated the daily intake of drinking water in this context and observed that the children from the older age group (9 and 10 years) consumed an average of 3.0 l drinking water per day. This is similar to the daily water consumption of adults, based on the results of Watanabe et al. [10], and is higher than that of younger age group (4 and 5 years). Another possibility for the relatively higher mean $[As]_u$ in the children aged 9 and 10 years is their longer exposure to As-contaminated water.

Our results confirm the impact of $[As]_u$ on the IQ of the children. Exposure to high As concentrations significantly lowered the mean IQ percentile. The IQ fell with increasing $[As]_u$, and the scores of below average IQ increased in the late childhood age group. Conversely, $[As]_u$ was significantly negatively associated with the nonverbal scores of the early childhood age group (4 and 5 years), while the verbal and composite IQ scores remained unaffected. This negative association is due to the effects of As as a neurotoxin affecting brain functions. However, the brain function of children could also be affected via maternal exposure to As. The study area is a region that is highly contaminated, and the respondents are consuming drinking water that is highly contaminated with As; despite their knowledge of this, they have no other option due to their poor SEC. The children from older age groups (9 and 10 years, and 14 and 15 years) consume water not only from their own tubewells but also from other tubewells (such as from their school's tubewells) because they are school-age children. To the contrary, children aged 4 and 5 years most drink water from their own tubewells and also drink relatively less water than the older children. Our proposed explanation for the differences observed across the age groups implies that younger children have been exposed to As for a relatively shorter period and that their reduced exposure may have attenuated, to a degree, the adverse consequences of As on intellectual function; also there might have been a lower stability of estimates of children's intelligence at a younger age (see Bartels et al. [11]; Petrill et al. [12]). We therefore suggest that our findings indicate that younger children, with their shorter exposure, might manifest less adverse consequences than those seen in older children who have been exposed to As for longer periods.

The results of our study are consistent with the findings recorded by Wasserman et al. [3, 13] of an inverse correlation between intelligence and water As content. These researchers conducted their study on As exposure in 10-year-old children and found a stronger association of IQ with As in tubewell water ($[As]_w$) than with $[As]_u$. Wasserman et al. [3] also studied As exposure in 6-year-old children and reported that with covariate adjustment, $[As]_w$ remained significantly negatively associated with both performance and processing speed raw scores; however, the associations were less strong than those in their previously studied group of 10-year-olds. However, in our study we found a stronger association between IQ and $[As]_u$ than between IQ and As content in tubewell water. We suggest that our finding is more reasonable because $[As]_u$ reflects the total ingestion of As from all possible sources. Wasserman et al. [3, 13] did not find an association between As exposure and aspects of verbal intelligence in their studies on both age groups. In comparison, we did not find any association between As exposure and aspects of verbal intelligence in children aged 4 and 5 years. However, a significant relationship between As and the verbal intelligence of children have been reported in a number of studies conducted in other parts of the world. For example, in their study Calderón et al. [4] controlled demographic covariates and found a negative association between $[As]_u$ and verbal intelligence among 80 children aged 6 years who lived near a lead smelter in Mexico. In another small pilot study of 31 children aged 11–13 years who resided in a former lead and zinc mining site containing tons of mining waste or chat, Wright et al. [5] found adverse associations between both hair As content and hair Mn content and general intelligence scores, particularly verbal scores. One possible explanation for our not finding any association between As exposure and aspects of verbal intelligence in the early childhood age groups in this study might be the lack in development of higher cognitive function, especially language and hearing. C.A. Nelson of Harvard University carried out a study in 2000 in which he reported that human brain development, especially higher cognitive function, starts from birth and continues to around 15 years of age and that the language and sensory pathways (vision, hearing) are developed up to 6 years of age. It would appear that the younger children (4 and 5 years group) in our survey were ashamed to answer because it was an individual test. We could not use the same SPM test among all the children from different representative groups because there is an age limitation of using SPM. Since there was no Bangladeshi standardized norm for SPM and since Bangladesh and India have almost the same cultural condition we used the Indian norm, although SPM is a culture-free test. However, we feel that this limitation did not change the findings observed in this study.

Future research should include the estimation of As intake from all possible sources, including drinking water at the time of the study, drinking water before the study, water used for cooking, and food stuffs. Overall, our findings are consistent with those reported earlier in that they document the adverse impact of As exposure on child developmental outcomes, especially children's intelligence. They also confirm concerns on the effects of As neurotoxicity on younger children. We conclude that As affects the cognitive functions (IQ) which develops with age. Effects could also be detected in preschool-aged children. More research is needed on the effects of As on very young children (age <4 and 5 years) to fully define the dose–response relationships and vulnerable periods.

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Conflict of interest None.

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