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The Relationship between Blood Arsenic Level and Cognitive Function of Adolescents in Nyaungdone Township, Ayeyawaddy Region

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This study was aimed to find out the relationship between blood arsenic levels and its effect on cognitive function in 120 adolescents of mean age (16±1.9 years) who drank arsenic contaminated groundwater (10 to 200 µg/l) for more than 5 years in Mazali Village, Nyaungdone Township, Ayeyawaddy Region, Myanmar. The blood arsenic concentration was measured by graphite furnace atomic absorption spectrophotometer (GF-AAS) and cognitive function was assessed by General Memory Scale (GMS). This is the first study that used GMS to relate with blood arsenic level in Myanmar. The blood arsenic level of study population ranged from 0 to 0.09 µg/ml and mean value was 0.03±0.02 µg/ml. Among study population, blood arsenic levels of 69 subjects (57.5%) were within normal range: 0-0.025 µg/ml and they were regarded as low arsenic group. Those of remaining 51 subjects (42.5%) were higher than normal blood arsenic level and they were regarded as high arsenic group. The duration of arsenic exposure in subjects of high arsenic group is significantly longer than that of low arsenic group (16±1.83 *vs.* 12±4.78, years, $p<0.05$). There were weakly inverse correlations between blood arsenic level (µg/ml) and Mental Control and Paired Associate Learning ($n=120$, $r=-0.19$, $p<0.05$), respectively. The mean score of Mental Control in low arsenic group was also significantly higher than that of high arsenic group (3.70±1.42 *vs.* 2.92±1.61, $p<0.05$). Moreover, total scores of cognitive function test in high arsenic group is significantly lower than that of low arsenic subjects (50.93±14.48 *vs.* 56.85±14.88, $p<0.05$). Therefore, this study suggested that prolonged drinking of arsenic contaminated water might effect on cognitive function.

Keywords: Blood arsenic, Cognitive function, Adolescents

INTRODUCTION

Arsenic is a naturally occurring element present in the environment. It is found in organic as well as inorganic forms. Inorganic arsenic of geological origin is more toxic to environment and settles to the groundwater used as drinking water in several parts of world. Of all the sources of human exposure to arsenic, the main source is ingestion of food and water and many outbreaks of arsenic poisoning are related to drinking of water from arsenic contaminated wells. The minimal permissible level for arsenic in drinking water is 0.01 mg/l or 10 µg/l.[1] The arsenic concentration in ground-water reportedly has a very large range from <0.5 to 5000 µg/l.[2] Chronic effects of arsenic poisoning include skin lesions, neurological effects, hypertension, peripheral vascular disease, cardiovascular disease, respiratory disease, diabetes mellitus, and malignancies.[3]

Neurotoxicological impairments include poor cognitive performance and disturbances in attention, psychomotor speed, visual perception, speech and memory.[4] In Myanmar, arsenic contamination of ground-water first came to attention in the year 2000.[5] A cross-sectional survey was

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conducted to assess the arsenic content in groundwater in three regions: Ayeyawaddy, Bago and Mandalay and three states: Kachin, Shan and Rakhine.[6]

Rural Health Centre of Mazali village, Nyaungdone Township reported that 36% of tube well samples have arsenic concentration less than 50 µg/l, 34% of tube wells have arsenic concentration 50-100 µg/l and 30% of tube well samples are between 101-200 µg/l. So, the arsenic content of this area was higher than the maximum permissible limit of arsenic recommended by WHO. Most of people in this area use groundwater for the primary source of drinking. Although amounts of arsenic in groundwater are too small to cause immediate health impact, consuming over a long time may cause adverse health effects. Of all the reason, this study was aimed to find out the health impact of arsenic on cognitive function of adolescents in this area. This is the first study that used GMS to relate with blood arsenic level in Myanmar.

MATERIALS AND METHODS

Study population

Apparently healthy 120 subjects aged between 13-19 years of continuous drinking arsenic contaminated water for more than 5 years were selected by history taking and clinical examination according to proforma at Rural Health Centerin Mazali Village, Nyaungdone Township, Ayeyawady Region. Exclusion criteria included current acute illness, neurological deficit; abnormalities detected in general physical examination, history of epilepsy, history of lead contact and history of head injury with loss of consciousness.

Determination of cognitive function

The cognitive function of the subjects was assessed by using 5 subtests from the General Memory Scale (GMS). It was originated from the Weschler Memory Scale (1956) and adopted to Myanmar version by Ohn Kyaw and Ohn Hlaing (1980).

It has been widely used in Myanmar since then. It was a 20-minutes interview by researcher in the room which was not been disturbed especially noise. The included subtests in this study were Mental Control for attention and concentration, Logical Memory for short-term memory on information registration, coding and retrieval process, Digit Span for ability to remember the sequence of the numbers (backward and forward), Paired Associate Learning for new concepts formation and Visual Memory for recall and recognition. These tests measured 3 cognitive domains-attention, learning and memory.[7]

Determination of blood arsenic level

Two milliliters of venous blood were taken using disposable syringe. Samples were collected in plastic test tube with cap and carried in cold chains (4°C). For analysis, serum samples were obtained by centrifuging and stored at -20°C for arsenic determination at the laboratory of Common Research Laboratory, University of Medicine 2. Then, the arsenic levels of the samples were determined by atomic absorption spectrophotometer (model GBC 932) equipped with GF 3000 graphite furnace system plus PAL 3000 auto sampler.[8]

Statistical analysis

Data were analyzed by using the statistical package for Social Sciences (SPSS) software version 15. For descriptive purpose, the continuous data (such as age, arsenic levels) were expressed by mean and standard deviation. For statistical analysis, Student's 't' test (unpaired) was applied to calculate difference between the means of the parameters (serum arsenic and GMS scores).

Statistical significance of results were set at $p=0.05$. Pearson's correlation coefficient was calculated to assess the relationship between blood arsenic level and cognitive function of the study group.

RESULTS

Out of total 120 populations, 28 (23.33%) subjects had duration of drinking arsenic contaminated water for 5 to less than 10 years. 37 (30.33%) subjects had 10 to 15 years duration and 55 (45.83%) subjects had more than 15 years duration. Blood arsenic level of the subjects in this study was 0.03 µg/ml and there was a significant positive correlation (r=0.249, n=120, p<0.05) between blood arsenic level and duration of arsenic exposure in all subjects.

Among the five subtests of cognitive function tests, the Mental Control test was weakly correlated (Pearson's r=-0.19, n=120, p<0.05) with blood arsenic level (Fig. 1) and the Paired Associate Learning test was also weakly correlated (Pearson's r=-0.19, n=120, p<0.05) with blood arsenic level in study population (Fig. 2).

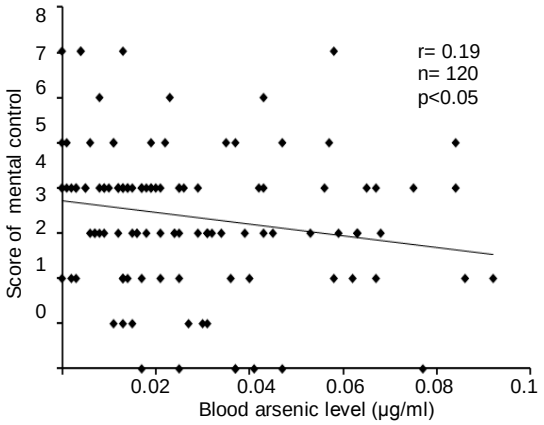

Fig. 1. Correlation between blood arsenic level and mental control of cognitive function

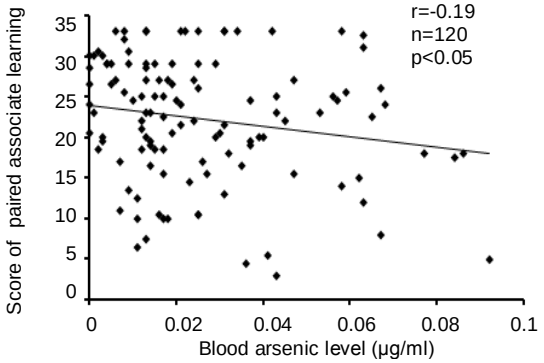

Fig. 2. Correlation between blood arsenic level and Paired Associate Learning of cognitive function test

The other three subtests, Logical Memory, Digit Span and Visual Memory tests were not significantly correlated (n=120, Pearson's r=-0.14; r=-0.035 and r=-0.16, respectively) with blood arsenic level in study population. The reference range of blood arsenic level is 0.001-0.025 µg/ml. In this study, sixty-nine subjects (57.5%) had the blood arsenic level <0.025 µg/ml and was regarded as low blood arsenic group. Fifty-one subjects (42.5%) was ≥0.025 µg/ml and was regarded as high blood arsenic group.

Table 1. Cognitive function scores (mean±SD) of low blood arsenic and high blood arsenic groups

	Arsenic group		P value
	Low blood (n=69) (<0.025 µg/ml)	High blood (n=51) (≥0.025 µg/ml)	
Mental control	3.70±1.42	2.92±1.61	0.006*
Logical memory	13.72±7.54	11.39±6.36	0.076
Digit span	10.70±2.32	10.39±2.38	0.485
Visual memory	5.56±0.61	5.42±0.72	0.263
Paired associate learning	23.17±6.95	20.80±8.09	0.088
Total score	56.85±14.88	50.93±14.48	0.031*

*indicates significant difference between two groups

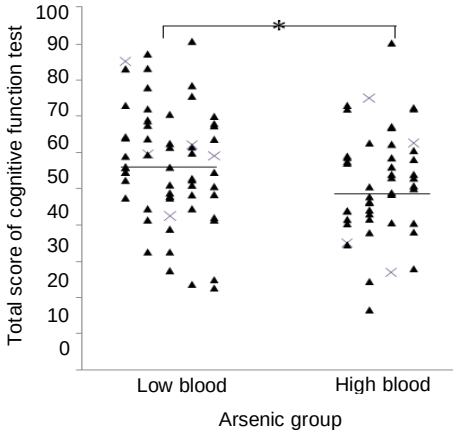

Fig. 3. Total score of cognitive function in low and high blood arsenic groups

Table 1 shows comparison of cognitive function scores in low and high blood arsenic groups. Out of five subtests of GMS, mean score of Mental Control test

was significantly lower in the high blood arsenic group than that of in the low blood arsenic group ($p<0.05$) and total cognitive function score was also significantly lower in the high blood arsenic group than that of in the low blood arsenic group ($p<0.05$) (Fig. 3).

DISCUSSION

The mean age of adolescents in this study was 16 years. The majority were road venders, manual workers and farmers. They used tube well water for drinking purpose in this area. The minimal permissible level for arsenic in drinking water is 0.01 mg/l or 10 µg/l. Most of the subjects (55%) in this study drank the water containing arsenic concentration 10-50 µg/l and 30% drank 50-100 µg/l of arsenic contaminated water and only about 15% drank between 101-200 µg/l of arsenic contaminated water.

The blood arsenic levels of study population ranged from 0 to 0.09 µg/ml and mean value is 0.03 µg/ml. Low blood arsenic group of 69 subjects (57.5%) were within normal range (0-0.025 µg/ml) and their mean value was 0.01±0.01 µg/ml. The high blood arsenic group of 51 subjects (42.5%) were higher than normal blood arsenic level (i.e., >0.025 µg/ml) and mean blood arsenic level was 0.05±0.02 µg/ml. Variation in blood arsenic level of subjects may be affected by arsenic concentration of drinking water, amount of water intake, individual body defense, nutritional status and antioxidant level. Even within a small geographic area, the arsenic level may be varied from one tube well to the next and blood arsenic level may be varied from person to person.

In this study, blood arsenic level of the subjects who drank arsenic contaminated water for 5 to less than 10 years duration was significantly lower than that of the subjects who drank for 10 to 15 years duration and more than 15 years duration.

A study reported a significantly positive correlation between blood arsenic level and duration of arsenic exposure in drinking water in total subjects.[9] Moreover, duration of arsenic exposure to the subjects of high blood arsenic group (16±1.83 years) in this study is significantly longer than that of low blood arsenic group (12±4.78 years). Therefore, the longer the duration of drinking arsenic contaminated water, the higher the blood arsenic level and might be effect on the health of the person.

One study reported the effect of arsenic on many organs or systems and the development of arsenicosis may take 5-15 years.[10] In this study, the total scores of cognitive function in high blood arsenic group subjects (50.93±14.48) are significantly lower than that of low blood arsenic subjects (56.85±14.88).

Since the brain is the one of the target organ for arsenic toxicity, chronic arsenic exposure is associated with wide range of neurological complication especially in learning and memory. In this study, GMS test was used to evaluate the attention, concentration, learning and short term memory. Out of the 5 subtests of GMS, Mental Control which is tested for attention and concentration and Paired Associate Learning which is tested for new concepts formation and learning were weakly inverse correlated with blood arsenic level in study population with ($n=120$, $r=-0.19$, $p<0.05$*) and ($n=120$, $r=-0.19$, $p<0.05$*), respectively. Thus, there were weak inverse correlation between blood arsenic level and 2 out of 5 subtests of GMS in total subjects of arsenic exposed population.

The model of memory has a strong serial structure which includes sensory memory, short-term memory and long-term memory. Information coming into the sensory register can pass to short term storage via intentional processes and only then onto long-term memory. In short-term memory, disability in remembering items may be correlated with damage to subcomponents of working

memory system.[11] Thus, GMS used in this study measured 3 cognitive domains-attention, learning and memory in arsenic contaminated subjects.

In the present study, the total score of high blood arsenic group (50.93±14.48) was significantly lower than that of low blood arsenic group (56.85±14.88) and the scores of mental control were significantly decreased in the high blood arsenic group (2.92±1.61) compared with the low blood arsenic group (3.70±1.42). Moreover, the other subtests of General Memory Scale (GMS) such as Logical Memory (13.72 ±7.54 *vs*. 11.39±6.36), Digit Span (10.70 ±2.32 *vs.* 10.39±2.38), Visual Memory (5.56 ±0.61 *vs.* 5.42±0.72) and Paired Associate Learning (23.17±6.95 *vs.* 20.80±8.09) were decreased in the high blood arsenic group than the low blood arsenic group.

Therefore, chronic arsenic toxicity may have high risk to impair the cognitive function. It may be due to alter metabolism of various neurotransmitters in brain. Arsenic can cross the blood-brain barrier and it inhibits the synthesis, liberation and alters metabolism of various neurotransmitters such as monoamines, acetylcholine, gamma amino butyric acid, and glutamate.[12]

In addition, arsenic-induced oxidative stress in brain causes oxidative DNA damage and subsequent cells death and induce the degeneration of dopaminergic neurons.[13] Arsenic and its metabolites suppress the NMDA receptors in hippocampus, which play a pivotal role in synaptic plasticity, learning and memory, leading to neurobehavioral disorders and cognitive dysfunction.[14] Whatever the mechanism, the present study revealed that chronic arsenic exposure was inversely associated with some cognitive domains of adolescents.

One study in Mexican also showed a significant inverse association between urinary arsenic level (58.1±33.2 µg/l) and five out of eleven cognitive function tests ie., Visual-Spatial Abilities with Figure Design, the Peabody Picture Vocabulary Test, the WISC-RM Digit Span subscale, Visual Search and Letter Sequencing Tests in 602 children (6-8 years of age).[15]

In 2003, the study in Taiwan reported a significant difference between the participants who had high cumulative arsenic level and those of low cumulative arsenic level in three neurobehavial tests ie., continuous performance test, pattern memory and switching attention in 109 adolescents (14 years mean age).[16]

Another two studies in Bangladesh pointed out the association between arsenic toxicity and cognitive functions. They assessed the children's intellectual function of 201 children (10 years of mean age) by using Wechsler Intelligence Scale for Children, version 3 and found that significantly lower ($p<0.05$) in Performance and Full-Scale scores in children with water arsenic levels >50 µg/l than <5.5 µg/l.

After that, they continued the study on 301 children (6 years of mean age) for association between drinking arsenic contaminated water and cognitive function in 2007 and reported that subjects who drank arsenic contaminated water were significantly associated with reduced intellectual function such as performance and processing speed in children. The above-mentioned studies pointed that drinking arsenic contaminated water was associated with impaired intellectual function in dose response manner in children.[17]

There were some limitations in this study as the other cross-sectional studies. The present study excluded individuals with known history of neurological impairments and diseases and those with overt clinical symptoms of neurobehavioral abnormalities by history taking and clinical examination. But, cognitive function may be impaired in anaemia and other poisonings like lead, mercury and manganese. In addition, intelligence levels of the subjects could not be measured.

Our study suggested that the subjects who used the arsenic contaminated well water for long duration had high blood arsenic level and low in total cognitive function scores. Thus, arsenic exposure by drinking and using arsenic contaminated well water may affect the cognitive function in adolescents. Therefore, the people living in arsenic-exposed area should be advised to drink safe water such as rain water and to use surface water by storing for several days before use. Moreover, they should be provided safe water supply and knowledge about arsenic-induced health problems.

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