Biological and Clinical Sciences Research Journal
eISSN: 2708-2261; pISSN: 2958-4728
www.bcsrj.com
DOI: https://doi.org/10.54112/bcsrj.v2024i1.1071
*Biol. Clin. Sci. Res. J., Volume, **2024**: 1071*
Original Research Article

NATURAL EXPOSURE TO ARSENIC-INDUCED GENOTOXIC EFFECTS IN DIABETIC AND NON-DIABETIC INDIVIDUALS

MAHMOOD S[*1], HUSSAIN Y[2], LATIF I[2], MAHMOOD R[3], IRSHAD F[2], ISLAM EU[4], MAQSOOD H[5]

[1]*Institute of Microbiology, GC University Faisalabad, Pakistan*
[2]*Department of Zoology, University of Sialkot, Pakistan*
[3]*Institute of Microbiology, Agriculture University Faisalabad, Pakistan*
[4] *Pakistan Institute of Engineering and Applied Sciences (PIEAS), Islamabad, Pakistan*
[5]*Department of Zoology, University of Education Lahore, Pakistan*
**Corresponding author`s email address:* saramahmood@gcuf.edu.pk

(Received, 28th May 2024, Revised 29th August 2024, Published 3rd September 2024)

Abstract: *Arsenic contamination in drinking water is a global health issue linked to various adverse health outcomes, including genotoxic effects. Understanding these effects in different populations, including diabetic and non-diabetic individuals, is critical for developing targeted public health interventions.* ***Objective:*** *This study aimed to investigate the genotoxic effects of arsenic exposure in diabetic and non-diabetic individuals residing in arsenic-contaminated and control areas.* ***Methods:*** *In this cross-sectional study conducted from January to June 2024, 100 participants were recruited from areas with known differences in arsenic water contamination levels. Participants were divided equally between arsenic-contaminated and non-contaminated regions, with 15 diabetic and 20 non-diabetic individuals selected from each group. A standard questionnaire was administered to collect demographic data and medical history. Additionally, 12 water samples from the contaminated area were analyzed for arsenic concentration. Genotoxic effects were assessed using the comet assay, and DNA damage was quantified using an empirical numerical rating system.* ***Results:*** *Significant DNA damage was observed in the blood cells of individuals from the arsenic-contaminated area compared to those from the non-contaminated area. Diabetic individuals showed similar patterns of DNA damage to non-diabetics within the same exposure group. Even in the non-contaminated group, slight DNA damage was detected, suggesting potential contributions from other environmental factors.* ***Conclusion:*** *The findings demonstrate that arsenic exposure is associated with significant genotoxic effects in both diabetic and non-diabetic populations. DNA damage in non-contaminated areas also indicates a possible impact of other environmental factors. These results highlight the need for ongoing monitoring and mitigation strategies to address arsenic contamination and its health impacts.*

Keywords: Arsenic, Drinking Water, Genotoxicity, Comet Assay, Diabetes

Introduction

Arsenic (As) is a naturally occurring element in the Earth's crust and is widely distributed in rocks, soil, water, and air. In its inorganic form, arsenic exists mainly as arsenate (As^{5+}) and arsenite (As^{3+}), with arsenate typically present as a negatively charged ion at a pH range of 6.5–8.5 (1). In contrast, arsenite remains neutral under similar conditions. While arsenic contamination is generally present in small amounts globally, elevated levels can be found in certain regions due to natural conditions or anthropogenic activities such as coal combustion and fertilizers (2). Human exposure to arsenic can occur through air, food, and water, with drinking water posing the most significant health risks (3, 4). Long-term exposure to arsenic, primarily from contaminated drinking water, has been linked to a variety of health issues, including dermatological manifestations such as hyperpigmentation and keratosis, as well as more severe outcomes like cancer, cardiovascular diseases, and diabetes (5-7).

Inorganic arsenic compounds, particularly those containing trivalent arsenic (As^{3+}), are highly toxic and readily absorbed through the gastrointestinal tract, distributing them throughout body tissues (Lai, 2004). Arsenic toxicity is dose-dependent and influenced by the rate of ingestion and excretion, with accumulation typically occurring in hair and nails (8). Unfortunately, there is no definitive treatment for arsenic-related diseases, and prevention relies on avoiding exposure, either by switching to uncontaminated water sources or by removing arsenic from water before consumption (9). Despite this, arsenic-contaminated aquifers remain a significant public health concern in many regions, including Pakistan, where groundwater contamination in Punjab has been reported, with arsenic levels reaching up to 2.4 mg/L (10).

Emerging evidence suggests that environmental toxicants, including arsenic, may play a role in the development of diabetes mellitus (11). Several studies have demonstrated an association between chronic arsenic exposure and an increased risk of type II diabetes, particularly in regions with high arsenic levels in drinking water, such as Taiwan and Bangladesh (12). In vitro studies have further suggested that arsenic interferes with insulin-related gene expression, impairing glucose uptake (13). Chronic exposure, known as arsenicosis, has been documented in various parts of the world, including China, where consuming contaminated water has had significant health impacts (14).

[Citation: Mahmood, S., Hussain, Y., Latif, I., Mahmood, R., Irshad, F., Islam, E.U., Maqsood, H. (2024). Natural exposure to arsenic-induced genotoxic effects in diabetic and non-diabetic individuals. *Biol. Clin. Sci. Res. J.*, **2024***: 1071*. doi: https://doi.org/10.54112/bcsrj.v2024i1.1071]

In Pakistan, arsenic contamination has become a pressing public health issue, particularly in southern Punjab and central Sindh, where millions of people are at risk of arsenic exposure from groundwater (15, 16). Notably, cases of bone deformities in children have been reported in villages such as Chahklalanwala near Lahore, highlighting the potential for severe health consequences. Globally, arsenic contamination has affected populations in regions such as Bangladesh, West Bengal (India), Chile, Argentina, China, and parts of the United States (17).

This study was designed to investigate the genotoxic and hematological parameters of diabetic and non-diabetic individuals residing in arsenic-contaminated areas of Pakistan. Specifically, we aimed to evaluate the potential relationship between chronic arsenic exposure and adverse health effects in both diabetic and non-diabetic populations, with a focus on Manga Mandi, an arsenic-contaminated area, and non-contaminated control areas in Sialkot. By assessing the genotoxic and hematological changes in these populations, we aim to provide further insight into the long-term health effects of arsenic exposure, particularly its potential role in the development and progression of diabetes.

Methodology

A total of 6 mL of venous blood was collected from each individual using sterile, disposable syringes. The collected blood was immediately transferred into sterile heparinized vacutainers to prevent clotting. For further analysis, 3 mL of the blood sample was allocated for arsenic determination, hematological assessments, and DNA analysis. The remaining 3 mL was centrifuged at 3000 rpm for 10 minutes to obtain serum, which was stored at -20°C until further use for enzymatic assays. Drinking water samples from contaminated and control areas were collected in pre-sterilized bottles and transported to the laboratory under excellent, sterile conditions for analysis. Additionally, surface soil samples (0–20 cm depth) were collected from arsenic-contaminated and non-contaminated areas in sterilized plastic bags and stored at room temperature for subsequent analysis.

Hematological parameters were measured using freshly collected blood samples analyzed with an automatic electronic blood cell counter (Sysmex KX-21, Japan). The evaluated hematological parameters included:

Hemoglobin (Hb): The blood's total hemoglobin concentration (g/dL).

Hematocrit (HCT): The percentage of red blood cells (RBCs) in whole blood.

Total RBC count: The number of red blood cells per milliliter.

Serum biochemical parameters, including blood glucose, alanine aminotransferase (ALT), aspartate aminotransferase (AST), and alkaline phosphatase (ALP), were analyzed using an automatic biochemical analyzer (Microlab 300, Merck, Germany). The analysis was performed with commercially available biochemical kits from DiaSys, Germany, following the manufacturer's protocols. These parameters were selected for their relevance in assessing liver function and systemic responses to arsenic exposure.

The alkaline comet assay (single-cell gel electrophoresis) was performed to assess DNA damage, following the modified protocol of Singh et al. (1988). Blood samples were processed to isolate lymphocytes embedded in low-melting agarose on glass slides. Electrophoresis was performed under alkaline conditions after lysis and unwinding of the DNA (pH > 13). Cells were then stained with ethidium bromide, and the DNA damage was visualized using a fluorescence microscope. The degree of DNA damage was quantified by measuring the comet tail length (μm), as defined by:

Comet tail length (μm) = (maximum total length) – (head diameter)

Comets were analyzed using an ocular micrometer, previously calibrated with a stage micrometer. Apoptotic cells were excluded from the analysis, identified by the absence of a head or a highly dispersed head. The mean tail length was calculated for each group as a quantitative measure of DNA damage.

The arsenic concentration in blood, water, and soil samples was determined using an acid digestion method followed by a highly sensitive detection kit (Merck, Germany). For soil and water samples, arsenic was measured following established protocols for environmental sample analysis. Blood samples were acid-digested to release arsenic, and the concentration was quantified using a commercial arsenic detection kit, with sensitivity sufficient to detect low levels of arsenic contamination.

All statistical analyses were performed using the SPSS software (version 25) package. Data were tested for normality, and differences between control and exposed groups were analyzed using one-way analysis of variance (ANOVA). Where applicable, post hoc comparisons were conducted using Tukey's HSD test to identify significant differences between individual groups. Continuous variables were expressed as mean ± standard deviation (SD) or mean ± standard error (SE), as appropriate. A p-value < 0.05 was considered statistically significant for all analyses.

Results

The Kit method determined the arsenic concentration in water samples from the arsenic-contaminated area. The standard chart for determining arsenic concentration in samples is shown (Fig. 1) as given in Kit (MERCK, Germany). The values of two different samples were obtained: 100ppb and 5ppb in samples from the arsenic-contaminated area (Fig. 2). The concentration of arsenic is significantly high in soil samples from the arsenic-contaminated area (Fig. 3).

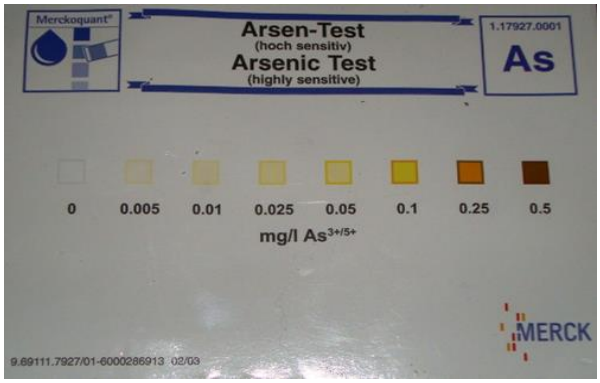

Figure 1: Standard Chart for Arsenic Test by MERCK Kit

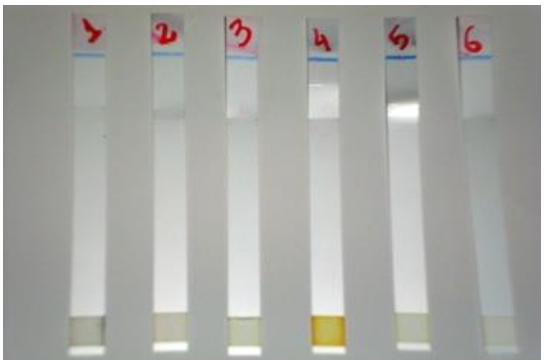

Figure 2: Arsenic determination in water samples of contaminated area

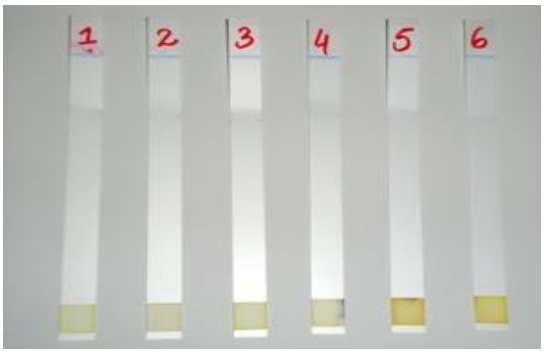

Figure 3: Arsenic determination in soil samples of contaminated area

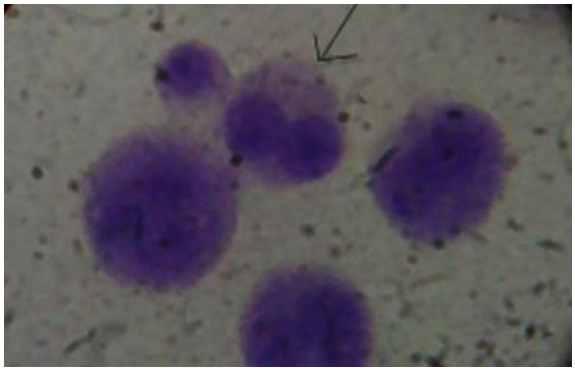

Figure 4: A bi-nucleated lymphocyte of a Non-contaminated individual stained with Giemsa

Figure 5: Comet Assay on Lymphocytes of Arsenic contaminated area individual

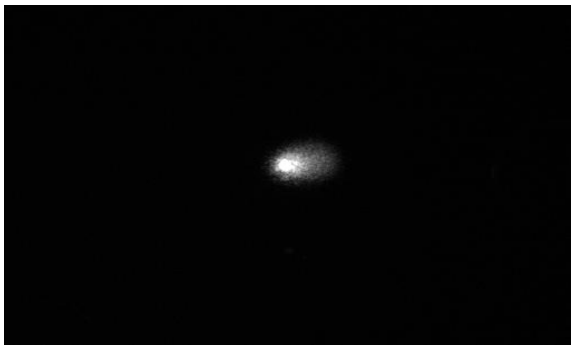

Figure 6: Comet Assay on lymphocytes of arsenic-contaminated area individual

Liver enzymes are important health biomarkers in biomonitoring disease status. The value of ALT was not significantly different in contaminated individuals (Diabetic and non-diabetic) and non-contaminated individuals (diabetic and non-diabetic) ($p > 0.05$). The normal reference range of ALT is 40 IU/l. The AST and ALP values were found to be nonsignificant in contaminated individuals (Diabetic and non-diabetic) and non-contaminated individuals (diabetic and non-diabetic) ($p > 0.05$) (Table 1). These results suggest that exposure did not change the liver enzymes in diabetic patients as compared to the control group.

Table 1: Serum Biochemical Parameters of Arsenic contaminated and Non-contaminated groups

Parameters	Contaminated Diabetic	Contaminated, Non-diabetic	Non-contaminated Diabetic	Non-contaminated, Non-diabetic	F-value	p-value
ALT (IU/l)	30.27 ±19.058	29.60 ±30.741	29.00 ±12.967	24.05 ±9.411	0.37	0.775
ALP (IU/l)	254±134.369	252.55±118.891	215.87±92.948	257.20±87.074	0.50	0.682
AST (IU/l)	43.60±20.928	40.95±22.956	35.20±18.323	35.35±9.005	0.86	0.469

RBC count in individuals in contaminated areas was found to be significantly lower than that of individuals in non-contaminated ($p< 0.05$). The standard reference range for total RBC count is 4.2 to 6.9 million/ul. Levels of Haemoglobin (Hb) and Haematocrit (HCT) were also found to be significantly different in both contaminated and non-contaminated groups ($p< 0.05$). For adults, the reference value for Hb ranges from 13.5 to 17.5 g/dl, and the HCT value ranges from 40-54%. Levels of Hb and HCT were found to be lower in individuals of contaminated area groups (diabetic and non-diabetic) than those of noncontaminated area groups (diabetic and non-diabetic). Values of MCV were also significantly higher in arsenic non-contaminated area groups (diabetic & non-diabetic) than in contaminated area groups (diabetic and non-diabetic) ($p<0.05$) (Table 2). The normal range of MCV is 81-101 fl.

[Citation: Mahmood, S., Hussain, Y., Latif, I., Mahmood, R., Irshad, F., Islam, E.U., Maqsood, H. (2024). Natural exposure to arsenic-induced genotoxic effects in diabetic and non-diabetic individuals. *Biol. Clin. Sci. Res. J.*, **2024***: 1071*. doi: https://doi.org/10.54112/bcsrj.v2024i1.1071]

Table 2: Haematological Parameters of Arsenic contaminated and non-contaminated groups

Parameters	Contaminated Diabetic	Contaminated, Non-diabetic	Non-contaminated Diabetic	Non-contaminated, Non-diabetic	F-value	p-value
RBCs (/ul)	(2.11± 1.563) *10^6	(2.04± 0.483) *10^6	(5.37 ± 0.813) *10^6	(4.95 ± 1.064) *10^6	52.29	0.00
HCT (%)	15.29 ± 2.59	17.12 ± 4.89	33.51 ± 6.81	37.125 + 12.95	33.24	0.00
MCV(fl)	82.51 ± 8.07	81.51 ± 6.79	62.32 ± 8.19	79.48 + 7.01	25.26	0.00
Hb (g/dl)	7.34 ± 0.35	7.82 ± 0.91	13.13 ± 1.83	13.71 ± 3.49	44.92	0.00

The total WBC count is significantly higher in individuals from arsenic-non-contaminated areas than in contaminated areas. However, the groups' values were within the normal reference range (Table 3). The standard reference range for WBC count is 4,500 to 10,000 /ul.

Table 3: Leukocytic Parameters of arsenic-contaminated and non-contaminated groups

Parameters	Contaminated Diabetic	Contaminated , Non-diabetic	Non-contaminated Diabetic	Non-contaminated, Non-diabetic	F-value	p-value
WBCs(/ul)	1753.85 ± 714.86	176 ± 531.5	4436.36 ± 2318.738	4610.00 ± 1503.65	23.047	.000
Lymphocytes (%)	90.22 ± 4.35	89.52 ± 3.71	49.95 ± 13.98	47.34 ± 12.57	96.740	.000

The values in the table are represented as Mean ± SD.

The frequency of MN in contaminated area individuals is higher than the frequency of MN in non-contaminated area individuals ($p<0.05$), as shown in (Table 4) micronuclei in the bi-nucleated cells of an individual of the contaminated area. Bi-nucleated lymphocytes in an individual of the non-contaminated area were also evident (Fig 4)

Table 4: Frequency of Micronuclei in Lymphocytes of contaminated and non-contaminated groups studied

Cell Type	Contaminated Diabetic	Contaminated, Non-diabetic	Non-contaminated Diabetic	Non-contaminated, Non-diabetic	F-value	p-value
Lymphocytes	21.33 ± 9.612	18.55 ± 7.466	1.20 ± .941	1.10 ± .788	56.662	0.00

The values in the table are given as Mean per 500 cells (± SD). DNA damage is observed in most of the samples in the contaminated area. The scores of comets in each of the four classes of lymphocytes of arsenic-contaminated and non-contaminated groups were observed (Tables 5 & 6). The comets produced in lymphocytes of individuals in arsenic-contaminated areas indicate DNA damage in these cells (Fig. 5 & 6). There was slight DNA damage in the non-contaminated population, possibly due to some environmental effects.

Table 5: Frequency of Micronuclei in Lymphocytes of contaminated groups studied

Parameters	Contaminated Non-diabetic		Contaminated Diabetic		F-value	p-value
Comet Class	Number of cells	Mean ± SD	Number of cells	Mean ± SD		
Comet-0	241	12.05 ± 13.15	302	20.13 ± 17.16	2.695	.053
Comet-1	411	22.20 ± 19.31	444	27.40 ± 19.20	1.105	.353
Comet-2	593	28.70 ± 13.16	438	29.53 ± 13.979	43.874	.000
Comet-3	462	23.10 ± 17.912	330	22.00 ± 15.942	18.133	.000
Comet-4	145	7.25 ± 8.045	122	6.80 ± 8.930	5.748	.001

Table 6: Frequency of Micronuclei in Lymphocytes of Non-contaminated groups studied

Parameters	Non-contaminated, Non-diabetic		Non-contaminated Diabetic		F-value	p-value
Comet Class	Number of cells	Mean ± SD	Number of cells	Mean ± SD		
Comet-0	339	17.45 ± 14.71	400	26.67 ± 16.82	2.695	.053
Comet-1	374	18.70 ± 13.37	263	17.53 ± 13.99	1.105	.353
Comet-2	40	2.00 ± 1.686	49	3.27 ± 2.685	43.874	.000
Comet-3	21	1.05 ± 1.050	25	1.53 ± 1.642	18.133	.000
Comet-4	15	.75 ± .786	25	1.67 ± 1.175	5.748	.001

Discussion

Previous studies established a link between high levels of exposure to arsenic (As) and diabetes, but low-level exposure effects remained unknown. Insulin is a vital hormone in the body, converting sugars, starches, and other foods into energy for essential metabolic functions. Insulin-sensitive cells that are exposed to insulin and sodium arsenic take in less glucose than cells exposed only to insulin. Arsenic could affect genetic factors interfering with insulin sensitivity and other processes (18). Arsenic also may contribute to oxygen-related cell damage, inflammation, and cell death, all of which are linked to diabetes. According to a study, exposure to arsenic, typically through drinking water, is a source of diabetes (19). A study supports the effects of air pollution on diabetes mortality and agrees

[Citation: Mahmood, S., Hussain, Y., Latif, I., Mahmood, R., Irshad, F., Islam, E.U., Maqsood, H. (2024). Natural exposure to arsenic-induced genotoxic effects in diabetic and non-diabetic individuals. *Biol. Clin. Sci. Res. J.*, **2024***: 1071*. doi: https://doi.org/10.54112/bcsrj.v2024i1.1071]

with other studies correlating arsenic, beryllium, cadmium, and nickel with diabetes prevalence (20). Numerous factors have been associated with diabetes, including genetics, age, and obesity. As obesity rates have increased in America, type 2 diabetes has also increased. The odds of developing diabetes have doubled over the last three decades. Risk factors underlying the development and progression of some of the less well-recognized complications of type 2 diabetes, including cognitive impairment and non-alcoholic fatty liver disease, are poorly understood (21). Cardiovascular disease is not specific to diabetes; it is more prevalent among patients with type 1 or type 2 diabetes than among those without diabetes (22). Cardiovascular disease (CVD) is the major cause of morbidity and mortality in the diabetic population, causing up to 80% of deaths in these patients (23).

The main objective of the present study was to detect the effects of arsenic in diabetic patients. An attempt was made to evaluate it by possible hematological and hemodynamic analysis of diabetic and non-diabetic individuals living in arsenic-contaminated and non-contaminated areas. In this study, micronuclei and comet assay were used as molecular biomarkers to evaluate cytogenetic damage in cells of diabetic individuals.

Arsenic is an element that raises much concern from both environmental and human health standpoints (24). Humans may encounter arsenic in water from wells drilled into arsenic-rich groundwater contaminated by industrial or agrochemical waste because arsenic is in the bedrock and quickly dissolves into the surrounding water. Inorganic arsenic is frequently present at elevated concentrations in groundwater. World Health Organization (WHO) guideline for concentration in drinking water was reduced from 50 µg/L to 10 µg/L in 1993 (25).According to the WHO recommendation, many developed countries changed the maximum admissible concentrations to 10 µg/L. However, the developing countries where arsenicosis is more widespread are still using the previous guideline value (50 µg/L) due to the lack of facilities to analyze smaller concentrations precisely.

The Asian region is much more affected by arsenic than other regions. Many underground waters worldwide are intoxicated with high concentrations of arsenic, which is considered a significant health hazard (26). The arsenic problem in Pakistan has recently surfaced as a result of field testing, firstly from an investigation on arsenic in groundwater of Attock and Rawalpindi districts (2000) conducted through a joint study by the Pakistan Council of Research in Water Resources (PCRWR) and the United Nations Children Fund (UNICEF) and secondly from National Water Quality Monitoring Program (NWQMP) of PCRWR. In some districts of Sindh, the arsenic contamination exceeded 200 ppb. In 2005, with the collaboration of UNICEF, 19,307 water sources were tested in Rahim Yar Khan District, Pakistan. It was observed that of these samples, 9644 samples were within the safer limits of <10 µg/L (49.95%), and the remaining 9663 samples (50.05%) were found to have arsenic concentrations ranging from 20 to 500 µg/L (27).

This study studied different hematological parameters, including RBC count, Hb, HCT, and cell indices, namely MCV, in all groups belonging to contaminated (diabetic and non-diabetic) and non-contaminated (diabetic and non-diabetic) areas. Results in this study showed a significant decrease in RBC count in individuals living in contaminated areas as compared to the control group ($p<0.05$) living in non-contaminated areas. Levels of Haemoglobin (Hb) and Haematocrit (HCT) were found to be significantly decreased in contaminated area (diabetic and non-diabetic) individuals as compared to non-contaminated area (diabetic and non-diabetic) individuals. These values also reached statistical significance. The cell indices, i.e., MCV in individuals, were found to be slightly increased in individuals living in contaminated areas (diabetic and non-diabetic) as compared to those living in non-contaminated areas (diabetic and non-diabetic). Previous studies showed that in arsenic-contaminated areas, RBC, Hb, and HCT were found to be lower and were declared as one of the causes of anemia. Decreased production of red blood cells is a common complication of some kidney diseases, including diabetic nephropathy. (28).

As a result, in subjects living in contaminated areas (both diabetic and non-diabetic), the total White Blood Cell count was found to be significantly lower as compared to those living in non-contaminated areas (diabetic and non-diabetic) ($p<0.05$). The lymphocytic % values in individuals in contaminated areas (diabetic and non-diabetic) were found to be slightly higher than those in the individuals (diabetic and non-diabetic) from non-contaminated areas. The lower WBC count in individuals in arsenic-contaminated areas may be attributed to some blood diseases.

Liver function enzymes, namely AST, ALT, and ALP, were used as important biomarkers for the detection of the hepatotoxic effects of arsenic on diabetes. The values of AST, ALT, and ALP were found to be not significantly different in both groups, which shows that there was no difference in the values of these enzymes in the individuals living in contaminated areas (diabetic and non-diabetic) and non-contaminated area groups (diabetic and non-diabetic). All LFT values were found to be within the normal reference range.

The hemodynamic parameters revealed that the combination of arsenic and diabetes increases blood pressure in subjects. A significant increase was observed in the systolic blood pressure of diabetic individuals in both the contaminated and non-contaminated areas (data not shown).

Cytogenetic damage seems to be an essential biomarker in determining the effects of exposure to chromosomal damaging agents, like arsenic, present in contaminated areas. An increase in the frequency of chromosome breaks has been recently demonstrated to be an initial event in carcinogenesis. It is generally considered to play an important role in assessing oncogenic risk. The underlying mechanism is associated with arsenic-induced DNA methylation. In addition, both hypo- and hyper-methylation of DNA could cause aberrant expression of genes (such as oncogenes or tumor-suppressor genes), which in turn cause abnormality in cell proliferation, leading to carcinogenesis (29). Micronuclei assay was used as a biomonitoring tool to detect chromosomal damage in individuals living in arsenic-contaminated areas. Results obtained from this study indicate a highly significant ($p<0.05$) increase in MN frequency in the blood lymphocytes of individuals living in arsenic-contaminated areas. The present study indicates a lower frequency of micronuclei in the control population. Such variations may arise due to differences in the living

style, environmental exposures, or variations resulting from the experimental procedures used (i.e., protocol or scoring criteria). In addition, the use of the MN assay in peripheral blood lymphocytes has been declared to be a good tool in determining the potential cytogenetic damage induced by different environmental pollutants due to its sensitivity and reliability and its potential applicability to different kinds of cells (30). In addition, a recent study has confirmed its usefulness as a surrogate biomarker of cancer risk (31). Thus, results obtained with this biomarker are good indicators of the genotoxic risk associated with a defined compound or exposure to a toxic compound.

This study measured the apparent induction of DNA damage with comet assay. At this point, the comet assay measures primary DNA damage, while the micronucleus assay measures fixed damage. According to previous studies, the Johns Hopkins Bloomberg School of Health (under the National Health and Nutrition Examination Survey, USA) studied 788 adults with urine tested for arsenic exposure toxicity in 2003-2004. Participants with type II diabetes had a 26% higher level of total arsenic in their urine than those without diabetes. Low levels of exposure to inorganic arsenic in drinking water, a widespread exposure worldwide, may play an essential role in diabetes prevalence and progression (32). A study provides limited support for the possibility that occupational arsenic exposure could play a role in the development of diabetes mellitus. Arsenic exposure could sometimes play a part in the development of diabetes mellitus (Rahman & Axelson, 1995). A study found greater mortality for males and females who had vascular disease, ischemic heart disease, diabetes mellitus, and bronchitis caused by high levels of arsenic in drinking water. An increased level of toxic metals is associated with diabetes mellitus. Thus, this element may play a role in the development and pathogenesis of diabetes mellitus. This study suggests that arsenic exposure is a risk factor for diabetes mellitus (33). Study results suggest that post-challenge hyperglycemia is associated with increased risk of all-cause and CVD mortality independently of other CVD risk factors (34). A study suggests that aberrant expression of human epithelial cells caused by endogenous or exogenous factors may lead to the abnormal function of mitochondria that may ultimately result in genotoxicity and carcinogenesis determined by different analyses such as cell proliferation assay and comet assay (35, 36).

Conclusion

Our results conclude that, although a potential genotoxic effect can be associated with exposure to arsenic, this potential risk is low in terms of damage to human beings and may have a lower role in causing diabetes.

Declarations

Data Availability statement
All data generated or analyzed during the study are included in the manuscript.

Ethics approval and consent to participate
Approved by the department concerned. (IRB-SHZH-9232/22)

Consent for publication
Approved

Funding
Not applicable

Conflict of interest

The authors declared the absence of a conflict of interest.

Author Contribution

SARA MAHMOOD
Conception of Study, Development of Research Methodology Design, Study Design,, Review of manuscript, final approval of manuscript.
YASIR HUSSAIN
Coordination of collaborative efforts.
IRAM LATIF
Study Design, Review of Literature.
RAFIDA MAHMOOD
Conception of Study, Final approval of manuscript.
FAIQA IRSHAD
Manuscript revisions, critical input.
EJAZ UL ISLAM
Data entry and Data analysis, drafting article.
HINA MAQSOOD
Manuscript drafting.

References

1. Sanna Angotzi M, Mameli V, Fantasia A, Cara C, Secci F, Enzo S, et al. As (III, V) uptake from nanostructured Iron Oxides and Oxyhydroxides: the complex interplay between sorbent surface chemistry and Arsenic equilibria. Nanomaterials. 2022;12(3):326.
2. Herath I, Vithanage M, Bundschuh J, Maity JP, Bhattacharya P. Natural arsenic in global groundwaters: distribution and geochemical triggers for mobilization. Current Pollution Reports. 2016;2:68-89.
3. Arslan B, Djamgoz MB, Akün E. Arsenic: a review on exposure pathways, accumulation, mobility and transmission into the human food chain. Reviews of Environmental Contamination and Toxicology Volume 243. 2017:27-51.
4. Singh S, Yadav R, Sharma S, Singh AN. Arsenic contamination in the food chain: a threat to food security and human health. J Appl Biol Biotechnol. 2023;11:24-33.
5. Mian M, Silfvast-Kaiser A, Paek S, Kivelevitch D, Menter A. A review of the most common dermatologic conditions and their debilitating psychosocial impacts. Int Arch Int Med. 2019;3:018.
6. Mazumder DG. Health effects chronic arsenic toxicity. Handbook of arsenic toxicology: Elsevier; 2015. p. 137-77.
7. Mazumder DG. Chronic arsenic toxicity & human health. Indian Journal of Medical Research. 2008;128(4):436-47.
8. Flora S. Preventive and therapeutic strategies for acute and chronic human arsenic exposure. Arsenic in drinking water and food. 2020:341-70.
9. Bhowmick S, Pramanik S, Singh P, Mondal P, Chatterjee D, Nriagu J. Arsenic in groundwater of West Bengal, India: a review of human health risks and assessment of possible intervention options. Science of the Total Environment. 2018;612:148-69.
10. Riaz RMY, Murtaza G, Farooqi ZUR, Ali S, Aziz H, Mahboob S, et al. Assessment of arsenic contamination in

groundwater and associated human health risk. Sustainability. 2022;14(19):12460.
11. Bonini MG, Sargis RM. Environmental toxicant exposures and type 2 diabetes mellitus: two interrelated public health problems on the rise. Current opinion in toxicology. 2018;7:52-9.
12. Wang S-L, Chang F-H, Liou S-H, Wang H-J, Li W-F, Hsieh DP. Inorganic arsenic exposure and its relation to metabolic syndrome in an industrial area of Taiwan. Environment International. 2007;33(6):805-11.
13. Khan F, Hodjat M, Rahimifard M, Nigjeh MN, Azizi M, Baeeri M, et al. Assessment of arsenic-induced modifications in the DNA methylation of insulin-related genes in rat pancreatic islets. Ecotoxicology and environmental safety. 2020;201:110802.
14. Palma-Lara I, Martínez-Castillo M, Quintana-Pérez J, Arellano-Mendoza M, Tamay-Cach F, Valenzuela-Limón O, et al. Arsenic exposure: A public health problem leading to several cancers. Regulatory Toxicology and Pharmacology. 2020;110:104539.
15. Mushtaq N, Masood N, Khattak JA, Hussain I, Khan Q, Farooqi A. Health risk assessment and source identification of groundwater arsenic contamination using agglomerative hierarchical cluster analysis in selected sites from upper Eastern parts of Punjab province, Pakistan. Human and Ecological Risk Assessment: An International Journal. 2021;27(4):999-1018.
16. Ahmed J, Wong LP, Channa N, Ahmed W, Chua YP, Shaikh MZ. Arsenic contamination and potential health risk to primary school children through drinking water sources. Human and Ecological Risk Assessment: An International Journal. 2023;29(2):369-89.
17. Bundschuh J, Schneider J, Alam MA, Niazi NK, Herath I, Parvez F, et al. Seven potential sources of arsenic pollution in Latin America and their environmental and health impacts. Science of the Total Environment. 2021;780:146274.
18. Tseng C-H. The potential biological mechanisms of arsenic-induced diabetes mellitus. Toxicology and applied pharmacology. 2004;197(2):67-83.
19. Sánchez-Rodríguez B, Castillo-Maldonado I, Pedroza-Escobar D, Delgadillo-Guzmán D, Soto-Jiménez M. Association of obesity, diabetes, and hypertension with arsenic in drinking water in the Comarca Lagunera province (north-central Mexico). Scientific Reports. 2023;13(1):9244.
20. Asgary S, Movahedian A, Keshvari M, Taleghani M, Sahebkar A, Sarrafzadegan N. Serum levels of lead, mercury and cadmium in relation to coronary artery disease in the elderly: a cross-sectional study. Chemosphere. 2017;180:540-4.
21. Eslam M, El-Serag HB, Francque S, Sarin SK, Wei L, Bugianesi E, et al. Metabolic (dysfunction)-associated fatty liver disease in individuals of normal weight. Nature reviews Gastroenterology & hepatology. 2022;19(10):638-51.
22. Rawshani A, Rawshani A, Franzén S, Eliasson B, Svensson A-M, Miftaraj M, et al. Mortality and cardiovascular disease in type 1 and type 2 diabetes. New England journal of medicine. 2017;376(15):1407-18.
23. Fan W. Epidemiology in diabetes mellitus and cardiovascular disease. Cardiovascular Endocrinology & Metabolism. 2017;6(1):8-16.
24. Balali-Mood M, Naseri K, Tahergorabi Z, Khazdair MR, Sadeghi M. Toxic mechanisms of five heavy metals: mercury, lead, chromium, cadmium, and arsenic. Frontiers in pharmacology. 2021;12:643972.
25. Organization WH. Nickel in drinking water: background document for development of WHO Guidelines for drinking-water quality. World Health Organization; 2021.
26. Prakash S, Verma AK. Arsenic: it's toxicity and impact on human health. International Journal of Biological Innovations, IJBI. 2021;3(1):38-47.
27. Uqaili A, Mughal A, Maheshwari B. Arsenic contamination in ground water sources of district Matiari, Sindh. International Journal of Chemical and Environmental Engineering. 2012;3(4-2012).
28. Samsu N. Diabetic nephropathy: challenges in pathogenesis, diagnosis, and treatment. BioMed research international. 2021;2021(1):1497449.
29. Merrick BA, Phadke DP, Shah RR, Mav D, Tokar EJ. Cause or Consequence: Epigenomic DNA Methylation Changes in Arsenic-Mediated in Vitro Transformation of Human Prostate Cells. Genomic and Epigenomic Biomarkers of Toxicology and Disease: Clinical and Therapeutic Actions. 2022:395-413.
30. Park SY, Choi J. Cytotoxicity, genotoxicity and ecotoxicity assay using human cell and environmental species for the screening of the risk from pollutant exposure. Environment International. 2007;33(6):817-22.
31. Gion M, Pérez-García JM, Llombart-Cussac A, Sampayo-Cordero M, Cortés J, Malfettone A. Surrogate endpoints for early-stage breast cancer: a review of the state of the art, controversies, and future prospects. Therapeutic advances in medical oncology. 2021;13:17588359211059587.
32. Rahaman MS, Rahman MM, Mise N, Sikder MT, Ichihara G, Uddin MK, et al. Environmental arsenic exposure and its contribution to human diseases, toxicity mechanism and management. Environmental Pollution. 2021;289:117940.
33. Farkhondeh T, Samarghandian S, Azimi-Nezhad M. The role of arsenic in obesity and diabetes. Journal of cellular physiology. 2019;234(8):12516-29.
34. Liu Q, Hu F, Zeng J, Ma L, Yan S, Li C, et al. Islet function changes of post-glucose-challenge relate closely to 15 years mortality of elderly men with a history of hyperglycemia. Heliyon. 2023;9(3).
35. Choudhuri S, Kaur T, Jain S, Sharma C, Asthana S. A review on genotoxicity in connection to infertility and cancer. Chemico-Biological Interactions. 2021;345:109531.
36. Cordelli E, Bignami M, Pacchierotti F. Comet assay: a versatile but complex tool in genotoxicity testing. Toxicology Research. 2021;10(1):68-78.

[Citation: Mahmood, S., Hussain, Y., Latif, I., Mahmood, R., Irshad, F., Islam, E.U., Maqsood, H. (2024). Natural exposure to arsenic-induced genotoxic effects in diabetic and non-diabetic individuals. *Biol. Clin. Sci. Res. J.*, **2024***: 1071*. doi: https://doi.org/10.54112/bcsrj.v2024i1.1071]