ABSTRACT

Arsenic, universally recognized as a widespread environmental contaminant, is associated with several adverse health effects, including an increased risk for type 2 diabetes mellitus (T2DM). This investigation explored the diabetogenic effects of arsenic and its molecular basis in the districts of Kasur and Lahore, Punjab, Pakistan. Through the assessment of arsenic concentrations in drinking water, 40 sites were identified for study, equally divided between Kasur and Lahore. The study encompassed 4,000 individuals, methodically divided into four groups: G1 –Control (As <10 µg/L); G2 –T2DM with low arsenic exposure (As <10 µg/L); G3 – Control with high arsenic exposure (As >10 µg/L); and G4 – T2DM with high arsenic exposure (As >10 µg/L). This study analyzed a wide array of factors including demographic (age, BMI, gender, education, occupation, residence, physical activity), physiological (duration of diabetes, family history, blood pressure), and environmental (water source, smoking habits, proximity to industrial sites, industry type, residency duration, stomach issues, numbness, skin allergies) through a detailed questionnaire. It identified significant links between demographic, physiological, and environmental variables with arsenic exposure and the incidence of type 2 diabetes. Mean arsenic concentrations in Kasur were recorded at 36.84 µg/L in water, 2.57 µg/L in blood, and 23.69 µg/L in urine. Lahore showed slightly lower averages: 31.12 µg/L (water), 2.16 µg/L (blood), and 16.6 µg/L (urine), measured using atomic absorption spectrometry. Diabetics (Group 4) in Kasur and Lahore exhibited significant higher fasting, random glucose and HbA1c levels. Higher arsenic exposure in Kasur and Lahore was linked to an increased incidence of prediabetes and diabetes, along with adverse effects like lipid imbalance, renal impairment, and liver dysfunction in diabetics, with statistically significant correlations ($p < 0.01$). The study identified Mustafa Abad in Kasur and Nishtar in Lahore as arsenic hotspots, with water arsenic levels reaching 113.8 µg/L and 95.72 µg/L, respectively. Residents showed not only elevated arsenic levels in blood and urine but also increased glucose and other biochemical parameters, indicating a high risk of T2DM. Genetic analysis in Kasur and Lahore revealed that mutations in the AS3MT gene and specific SNPs (rs11191439 and rs10748835) were significantly associated with T2DM in individuals with high arsenic exposure. Genetic predisposition and biochemical changes in populations exposed to arsenic play a critical role in elevating diabetes risk, emphasizing the importance of genetic factors. In Kasur and Lahore, patients with T2DM from areas with high arsenic exposure demonstrated significantly elevated serum proteinlevels, particularly highlighting the AS3MT protein as a pivotal biomarker. This was established through advanced proteomic techniques, including SDS polyacrylamide gel electrophoresis for protein isolation, and further confirmed by HPLC and identified by MALDI TOF mass spectrometry. ELISA analysis revealed 260-fold increase in AS3MT protein levels in diabetics versus controls, linking arsenic exposure to a higher risk of T2DM through the significant role of AS3MT gene mutations and protein expression alterations.

Keywords: Arsenic Exposure, Type 2 Diabetes Mellitus (T2DM), Drinking Water Quality, Demographic Factors, Biochemical Markers, Genetic Variants, Proteomic Techniques