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Potential health risk assessment through the consumption of arsenic-contaminated groundwater in parts of the middle Gangetic plain

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Abstract

Background Arsenic toxicity in humans is well recognized. It has been classified as a class I human carcinogen by the International Agency of Research on Cancer. Arsenic enters the human body mainly through drinking water, dermal contact, food chain, and inhalation. The Gangetic belt of India is considered as one of the most arsenic-affected sites in India. Health risk assessment of the human population exposed to arsenic in drinking water is important. The present study was conducted to assess the groundwater quality and associated health risks on the people of Samastipur district in the middle Gangetic belt of Bihar. Groundwater samples from 40 different study sites were collected and analyzed for various physico-chemical properties of water.

Results Arsenic (> 0.01 mg/L) was present in 33% of the water samples analyzed. Subsequently, an assessment for carcinogenic risk and non-carcinogenic health risk (HQ) for children, females, and males in the study area was performed. Risk assessment showed that 100% of the population may be at carcinogenic health risk and 35% may be at non-carcinogenic health risk, and among these, children were at maximum risk. Furthermore, the computational assessment of the arsenic–protein interactome revealed the enrichment of cancer-related pathways.

Conclusions It is recommended to provide arsenic-free alternate sources of water in the study area.

Keywords Gangetic plain, Groundwater, Arsenic, Health risk assessment, Toxicity

Background

Arsenic is called "silent toxin" (Bhattacharya et al. 2007; Roy et al. 2014). It has been classified as a class I human carcinogen by the International Agency of Research on Cancer (Martinez et al. 2011) and others (Tapio and Grosche 2006; Baastrup et al. 2008; Benbrahim-Tallaa and Waalkes 2008; Kuo et al. 2017; Kesh Kumar and Bharti 2021; Chen et al. 2022). It is found that even a minimum concentration of arsenic becomes lethal to human beings (Xu et al. 2021). Arsenic enters the human body mainly through drinking water, dermal contact, food chain, and inhalation (McCarty et al. 2011; Chung et al. 2014; Mandal 2017; Shahab et al. 2019) and causes arsenicosis (Saha 2003; Brinkel et al. 2009; Guha Mazumder and Dasgupta 2011; Singh et al. 2011, 2014). It may adversely affect human health resulting in genetic disorders, neurotoxicological disorders and carcinogenicity (Ratnaike 2003; Guha Mazumder 2008; Jomova et al. 2011; Hong et al. 2014). Arsenic affects various enzyme systems of the body by binding itself with biological ligands (Kazi et al. 2009; Shen et al. 2013; Veas 2021). Several acute

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and chronic symptoms of arsenicosis have been reported, such as, in acute cases, it causes stomach disorders, gastric problems, and vomiting; however, in chronic cases, it leads to keratosis, melanosis, and cancer (Guha Mazumder 2008; Guha Mazumder and Dasgupta 2011).

According to the World Health Organization (WHO) and Bureau of Indian Standards (BIS), the permissible limit of arsenic in drinking water is 0.01 mg/L (Edition 2011; Bureau of Indian Standards 2012). Globally, 108 countries have been identified with arsenic (>0.01 mg/L)-contaminated groundwater. Africa, North America, Bangladesh, India, Pakistan, China, Nepal, Vietnam, Burma, Thailand, and Cambodia are the worst affected by arsenic in groundwater (Shaji et al. 2021). About 220 million people worldwide are at potential risk due to the consumption of arsenic-contaminated drinking water (Podgorski and Berg 2020). Ganges–Brahmaputra–Meghna belt (20 states and four union territories) is considered as one of the most arsenic-affected sites in India (Rahman et al. 2006). According to Chakraborti et al. (2018), entire basin of the River Ganges has very high arsenic concentrations, including 16 districts of Bihar with arsenic-contaminated groundwater (Kumar et al. 2016).

In various parts of the world, researchers (Ricolfi et al. 2020; Wu et al. 2020) have evaluated human health risks upon exposure to arsenic in drinking water by classifying populations into different age groups (males, females, and children). This health risk assessment includes carcinogenic and non-carcinogenic health risks (Singh et al. 2021). No such health risk assessment has been done for the Samastipur human population of Bihar; therefore, this work was carried out to understand the occurrence of arsenic and the extent of its contamination in the aquifers of Samastipur district. An attempt has also been made to assess the health risk posed by arsenic in drinking water in terms of carcinogenicity.

Methods

Study area

The study area lies in the Samastipur district of the state of Bihar, India (Fig. 1). It falls in the Gangetic alluvial plain (Survey of India Toposheet nos. 72 G, 72 F, and 72 K) within the coordinates 25° 30′ 0″ N to 25° 42′

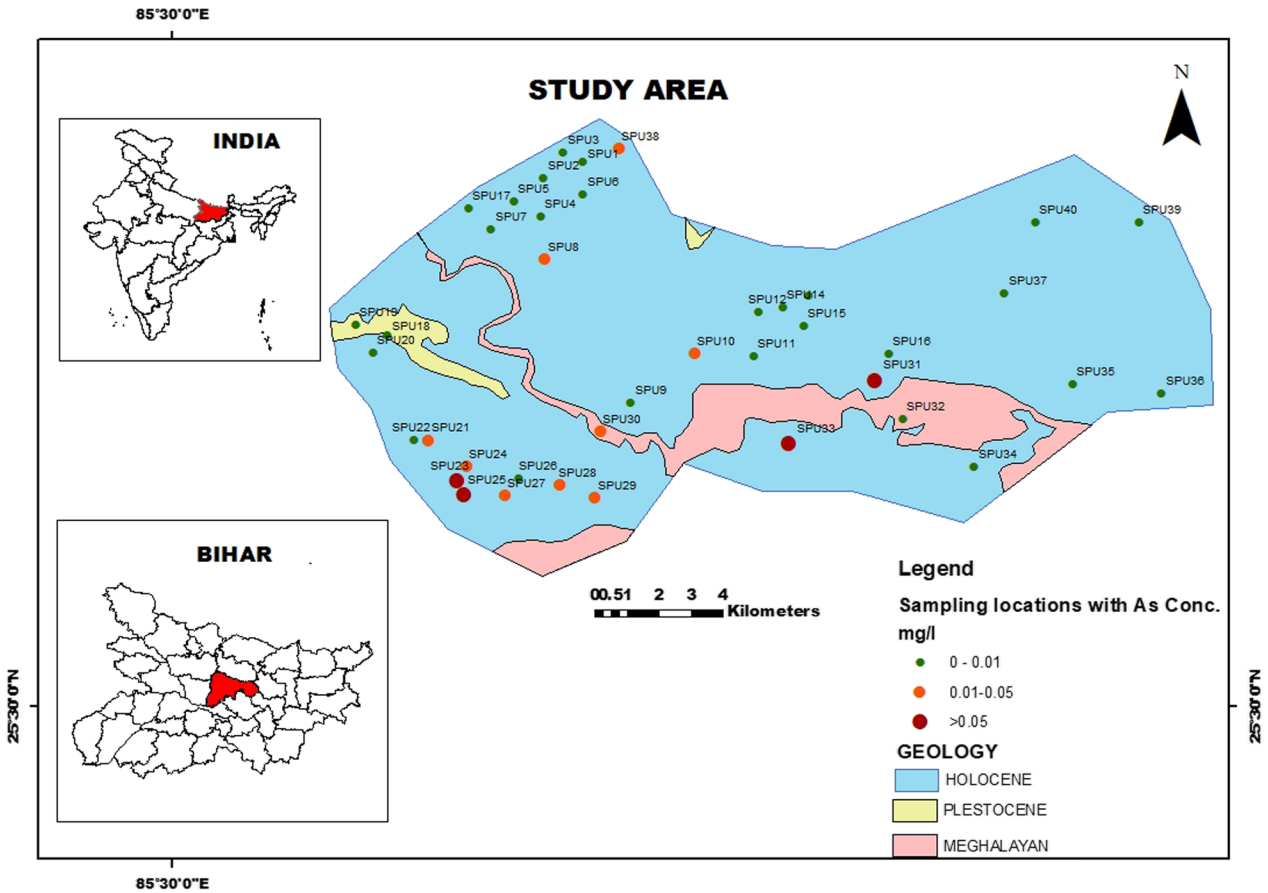

Fig. 1 Study area map showing sampling locations

0″ N and 85° 27′ 0″ E to 85° 48′ 0″ E. The River Ganges flows toward the southern part of the study area. Parts of four administrative blocks, namely Patori, Mohanpur, Mohiuddinagar, and Vidyapatinagar, with a total area of 216.041 Km^2 were covered in this study. Geologically, the lower Gangetic basin has unconsolidated quaternary alluvial sediment. The alluvial deposit comprises clay, silt, and layers of coarse sand and gravel. Topographically, highlands of older alluvium belong to Pleistocene age in large parts of the district and are protected from flooding during the monsoon season. Younger alluvium constitutes floodplains and terraces, which belong to the Holocene period (Sahu and Saha 2015). Rainfall during the monsoon season (July to September) recharges groundwater, and it receives an average annual rainfall of about 1142 mm. The study area has hot and humid summer months (March to June) and a cold winter season (November to February).

Ground water sample collection

The sampling sites were selected according to human habitation and accessibility. The minimum distance between two sites was 500 m. Forty water samples were collected from hand pumps in November 2021. Purging of the tubewell was done for 5–10 min depending upon the depth of the aquifer (more purging for deeper aquifers in order to empty the volume of standing water from the underground pipes of the tubewell and to collect flowing water from aquifers directly). Water samples were collected in one-liter high-density polyethylene (HDPE) bottles, for major cation and anion analysis. Bottles were fully filled with no air space or air bubbles. Similarly, for heavy metal analysis, water samples were collected in 250-ml HDPE bottles. For this, first of all water was collected in a glass beaker, then water from this beaker was filtered using syringe filters of 0.45-µm pore size, and few drops of HNO_3 were added as preservative. All the collected samples were taken to the laboratory for further analysis. The analyses were performed within one week of sample collection. Global positioning system (Garmin GPS) was used to find out coordinates of the sampling locations. The sampling locations were named as SPU1 to SPU40 (Table 3).

The analysis of physico-chemical characteristics of water samples

The physico-chemical characteristics of these water samples were analyzed following the APHA (American Public Health Association et al. 2014) standard methods. Electrical conductivity (EC) and pH values were estimated on the spot at the sampling location using a Eutech portable pH meter and EC meter, respectively. The volumetric method was used to measure Ca^{2+}, Mg^{2+}, Cl^-, HCO_3^-, and total hardness (TH) concentrations. Na^+ and K^+ were analyzed by flame emission photometry (Systronics 128). Anions such as SO_4^{2-} and NO_3^- were estimated using a UV–visible spectrophotometer (Systronics 2202). Arsenic and iron were determined using inductively coupled plasma mass spectroscopy. To ensure quality control, duplicate samples and spike samples were analyzed. GraphPad Prism 8, Aquachem, and Arc-GIS 10.4 were used to prepare different graphs, figures, and maps.

Table 1 Statistical summary of the physico-chemical parameters of water samples analyzed in this study from 40 different sites

Parameters	Min	Max	Mean	SD	AL	PL	No. of samples > AL	No. of samples with > PL
pH	6.15	7.5	6.97	0.24	6.5	8.5	Nil	Nil
EC*	161.9	2230	939.41	424.24	–	1500	–	4
TH	76	640	344.91	115.04	200	600	36	1
Ca^{+2}	10	126	50.36	20.14	75	200	4	Nil
Mg^{+2}	2.74	109.35	51.22	26.18	30	100	31	2
Na^{+}*	1.53	164.33	54.02	45.89	200	NR	Nil	Nil
K^{+}*	0.6	121.62	11.71	20.01	12	300	4	Nil
HCO_3^-	73.8	633.45	431.91	120.62	200	600	38	4
Cl^-	7.09	453.76	68.81	84.54	250	1000	1	Nil
SO_4^{-2}	0	121.7	22.71	24.28	200	400	Nil	Nil
NO_3^-	0	24.73	7.66	9.87	45	NR	Nil	Nil
Fe	0	5.117	0.99	1.4	1	NR	10	10
As	0.00004	0.912	0.01	0.02	0.01	NR	13	13

*Compared with WHO standards (2011) and remaining parameters with BIS (2012). All parameters are expressed in mg/l except EC in µS/cm and pH

AL acceptable limit, *PL* permissible limit, *SD* standard deviation

Table 2 Correlation matrix for different water quality parameters in the study area

Parameters	pH	EC	TH	Ca^{+2}	Mg^{+2}	Na^{+}	K^{+}	HCO_3^{-}	Cl^{-}	So_4^{-2}	NO_3^{-1}	Fe	As
pH	**1**												
EC	*−0.16*	**1**											
TH	*−0.29*	**0.65**	**1**										
Ca^{+2}	0.15	0.42	0.30	**1**									
Mg^{+2}	*−0.46*	0.56	**0.83**	*−0.13*	**1**								
Na^{+}	*−0.03*	**0.88**	0.34	0.35	0.24	**1**							
K^{+}	0.12	**0.61**	0.19	0.32	0.07	**0.61**	**1**						
HCO_3^{-}	*−0.41*	**0.76**	**0.68**	0.36	0.59	**0.60**	0.37	**1**					
Cl^{-}	0.02	**0.87**	0.49	0.32	0.42	**0.82**	0.56	0.42	**1**				
So_4^{-2}	0.05	**0.60**	0.40	0.33	0.28	0.53	**0.6**	0.37	0.41	**1**			
NO_3^{-}	*−0.11*	**0.66**	0.26	0.18	0.33	**0.60**	0.45	0.42	**0.64**	0.27	**1**		
Fe	0.00	*−0.14*	0.14	*−0.16*	0.19	*−0.22*	*−0.16*	0.06	*−0.18*	*−0.31*	*−0.12*	**1**	
As	0.00	*−0.14*	0.14	*−0.16*	0.19	*−0.22*	*−0.16*	0.06	*−0.18*	*−0.31*	*−0.12*	**0.92**	**1**

*Bold good correlation ($r \geq 0.6$) Italic poor correlation ($r \leq 0$)

Human health risk assessment

The following references and formulae were used to calculate the hazard quotient (HQ)/non-carcinogenic risk and carcinogenic risk (CR) for humans.

Step I Average daily intake (ADI) was calculated as the product of concentration of the arsenic (As) in mg/L, ingestion rate (L/day), exposure frequency (EF in days/year), exposure duration (ED is age in years) divided by the product of average body weight (ABW in Kg), and average time of life (ATL in days).

$$\mathrm{ADI} = (C * \mathrm{IR} * \mathrm{EF} * \mathrm{ED})/(\mathrm{ABW} * \mathrm{ATL})$$

Step II Hazard quotient (HQ) was calculated by dividing ADI by reference dose (RfD which is 0.0003 mg/kg*day for arsenic) (IRIS 2017).

HQ > 1 indicates health risks other than cancer.

Step III Carcinogenic risk was calculated by the product of ADI and slope factor for carcinogenic contaminants (SF was 1.5 mg/kg*day) (IRIS 2017).

CR > 0.000001 indicated carcinogenic risk (Alidadi et al. 2019).

In silico arsenic–protein interactome analysis

To study the targets of arsenic, STITCH online tool (search tool for interactions of chemicals) was used (Kuhn et al. 2014). This tool integrates information about the interactions of a chemical molecule with proteins and demonstrates the chemical–target relationships. For creating the arsenic–protein network, the STITCH tool was adjusted for a few parameters including the interaction score set at the confidence of 0.7 with 100 interactors in the first shell. Subsequently, the KEGG pathway was analyzed for arsenic–protein interactome.

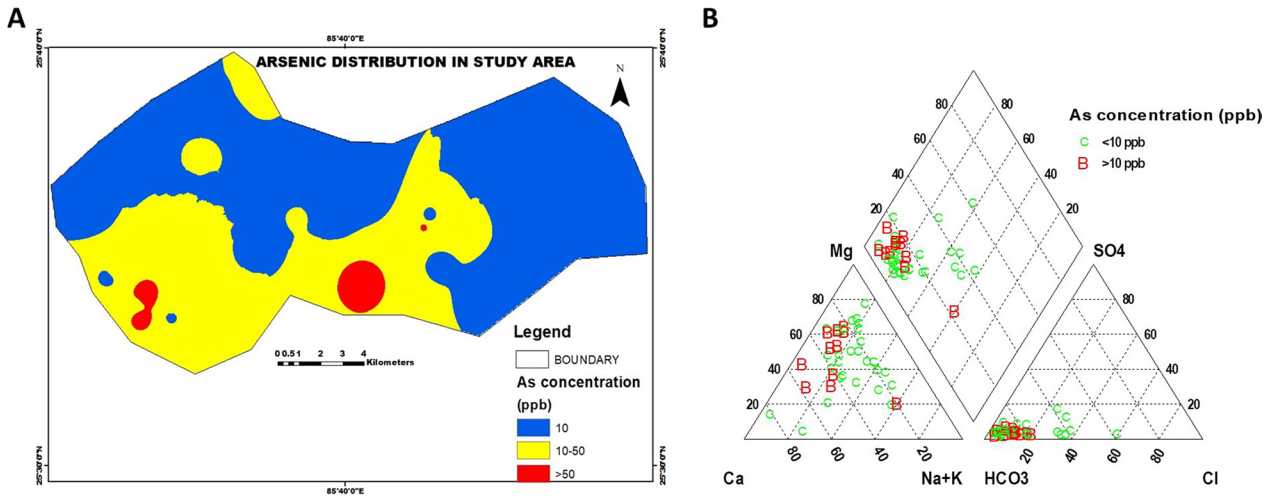

Fig. 2 **A** Spatial distribution of arsenic in groundwater. **B** Piper plot elucidating hydrochemical facies

Table 3 Hazard quotient (HQ)/non-carcinogenic risk and carcinogenic risk (CR) in males, females, and children

S. no.	Latitude	Longitude	HQ Children	HQ Females	HQ Males	CR Children	CR Females	CR Males
SPU1	25.6582	85.6105	0.466159	0.407482	0.344792	0.00021	0.000183	0.000155
SPU2	25.65957	85.60757	0.462312	0.404119	0.341947	0.000208	0.000182	0.000154
SPU3	25.65864	85.60749	0.018305	0.016001	0.013539	8.24E−06	7.2E−06	6.09E−06
SPU4	25.642	85.59857	0.256445	0.224166	0.189679	0.000115	0.000101	8.54E−05
SPU5	25.64166	85.59607	0.373838	0.326781	0.276507	0.000168	0.000147	0.000124
SPU6	25.64372	85.6155	1.414372	1.236339	1.046133	0.000636	0.000556	0.000471
SPU7	25.63373	85.58974	0.014613	0.012774	0.010809	6.58E−06	5.75E−06	4.86E−06
SPU8	25.62533	85.60505	3.023864	2.643238	2.236586	0.001361	0.001189	0.001006
SPU9	25.58533	85.62896	0.019536	0.017077	0.014449	8.79E−06	7.68E−06	6.5E−06
SPU10	25.59881	85.64713	1.896602	1.657869	1.402812	0.000853	0.000746	0.000631
SPU11	25.59834	85.66358	0.105372	0.092109	0.077938	4.74E−05	4.14E−05	3.51E−05
SPU12	25.61136	85.67376	0.090758	0.079334	0.067129	4.08E−05	3.57E−05	3.02E−05
SPU13	25.61229	85.67231	0.063915	0.05587	0.047274	2.88E−05	2.51E−05	2.13E−05
SPU14	25.61202	85.67163	0.174676	0.152689	0.129198	7.86E−05	6.87E−05	5.81E−05
SPU15	25.60676	85.67754	0.00746	0.006521	0.005518	3.36E−06	2.93E−06	2.48E−06
SPU16	25.59907	85.70122	0.110689	0.096756	0.081871	4.98E−05	4.35E−05	3.68E−05
SPU17	25.63976	85.58333	0.025407	0.022209	0.018792	1.14E−05	9.99E−06	8.46E−06
SPU18	25.60266	85.55633	0.249891	0.218436	0.184831	0.000112	9.83E−05	8.32E−05
SPU19	25.60229	85.5527	0.117833	0.103001	0.087155	5.3E−05	4.64E−05	3.92E−05
SPU20	25.6023	85.55416	0.732937	0.640679	0.542113	0.00033	0.000288	0.000244
SPU21	25.57447	85.56771	2.543595	2.223422	1.881357	0.001145	0.001001	0.000847
SPU22	25.5747	85.56806	0.440084	0.384689	0.325506	0.000198	0.000173	0.000146
SPU23	25.56428	85.58041	15.8242	13.83234	11.70429	0.007121	0.006225	0.005267
SPU24	25.56398	85.58026	4.461319	3.899755	3.299792	0.002008	0.001755	0.001485
SPU25	25.55934	85.58227	11.81667	10.32926	8.74014	0.005318	0.004648	0.003933
SPU26	25.55936	85.59411	0.165337	0.144525	0.122291	7.44E−05	6.5E−05	5.5E−05
SPU27	25.55891	85.59382	5.00009	4.370708	3.698291	0.00225	0.001967	0.001664
SPU28	25.56183	85.60916	2.082041	1.819966	1.539971	0.000937	0.000819	0.000693
SPU29	25.55839	85.61918	4.463605	3.901752	3.301483	0.002009	0.001756	0.001486
SPU30	25.57694	85.62067	1.751669	1.531179	1.295613	0.000788	0.000689	0.000583
SPU31	25.59505	85.69933	9.5486	8.346678	7.062574	0.004297	0.003756	0.003178
SPU32	25.58063	85.70515	0.627944	0.548903	0.464456	0.000283	0.000247	0.000209
SPU33	25.57368	85.67339	14.67051	12.82387	10.85097	0.006602	0.005771	0.004883
SPU34	25.56723	85.72538	0.11938	0.104353	0.088298	5.37E−05	4.7E−05	3.97E−05
SPU35	25.5903	85.75289	0.054644	0.047766	0.040417	2.46E−05	2.15E−05	1.82E−05
SPU36	25.58778	85.77789	0.056338	0.049246	0.04167	2.54E−05	2.22E−05	1.88E−05
SPU37	25.61579	85.73378	0.515225	0.450371	0.381084	0.000232	0.000203	0.000171
SPU38	25.67356	85.61946	6.978943	6.100475	5.16194	0.003141	0.002745	0.002323
SPU39	25.63578	85.77152	0.802346	0.701352	0.593451	0.000361	0.000316	0.000267
SPU40	25.63593	85.74256	0.739494	0.646411	0.546963	0.000333	0.000291	0.000246

Results

Physico-chemical assessment of groundwater quality revealed the arsenic contamination

To understand the quality of groundwater, the samples from the SPU1–SPU40 sites were collected and their physico-chemical properties were analyzed. The results obtained from the analysis of groundwater obtained from different blocks of Samastipur district, Bihar, are summarized in Table 1. The pH of all samples ranged from 6.15 to 7.5. The electrical conductivity of water samples varied between 161.9 and 2230 µS/cm. Higher EC indicates more amounts of dissolved salts, and in 10% of samples, it exceeded the standard limit prescribed by WHO. In 90% of water samples, the calculated value of total

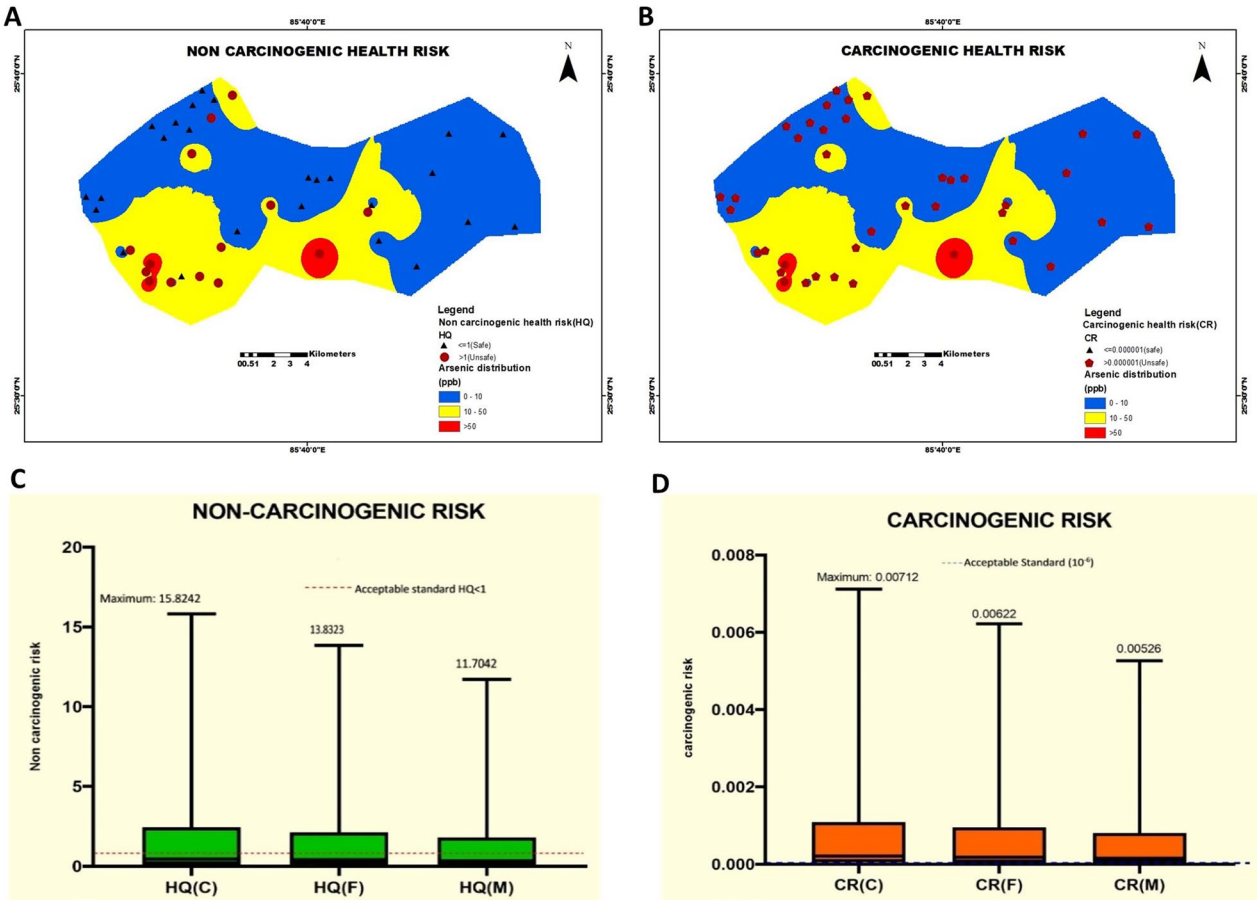

Fig. 3 **A** Non-carcinogenic health risk in human population of study area. **B** Carcinogenic health risk in human population of study area. **C** Box plot representing non-carcinogenic risk for population of different types (male, female, and child).*HQ(C) is non-carcinogenic risk for child, HQ(F) is non-carcinogenic risk for female, and HQ(M) is non-carcinogenic risk for male population. **D** Box plot representing carcinogenic risk for population of different age groups. *CR(C) represents carcinogenic risk for child, CR(F) is carcinogenic risk for female, and CR(M) is carcinogenic risk for male population

hardness exceeded the acceptable limit of BIS (Bureau of Indian Standards 2012). The value of Mg^{2+} ion concentration ranged between 2.74 and 109.35 mg/L and was also found to be high in 77.5% of the samples which may be the contributory factors for the hardness of the water. Ca^{2+} ion concentration varied between 10 and 126 mg/L, and in 10% of water samples, its value exceeded the acceptable limit of BIS (Bureau of Indian Standards 2012). Na^{+} and K^{+} were found low in groundwater samples with minimum and maximum values ranging from 1.53 to 164.33 mg/L and 0.6 to 121.62 mg/L, respectively. However, the concentration of K^{+} ions in 10% of water samples exceeded the standard limit of WHO. The value of HCO_3^{-} ion concentration was in the range of 73.8–633.45 mg/L. In 95% samples, bicarbonate (HCO_3^{-}) exceeded the permissible limit of BIS (Bureau of Indian Standards 2012). Cl^{-} ion concentration ranged between 7.09 and 453.76 mg/L. Concentrations of SO_4^{2-} and NO_3^{-} were within the permissible limit of BIS (Bureau of Indian Standards 2012), with values ranging between 0 and 121.7 and 0 and 24.73 mg/L, respectively. The iron concentration varied from 0 to 5.117 mg/L and exceeded the permissible limit of BIS (Bureau of Indian Standards 2012) in 25% of water samples. Arsenic concentration ranged from 0.0004 to 0.0912 mg/L and exceeded the permissible limit in 33% of water samples (Table 1).

The correlation matrix for different physico-chemical parameters of groundwater of the study area is shown in Table 2. The strongest correlation ($r=0.92$) was observed between iron and arsenic, indicating that the presence of iron complements the presence of arsenic and vice versa. Electrical conductivity showed a significant positive correlation ($r \geq 0.6$) with cations Na^{+} and K^{+} and anions HCO_3^{-}, Cl^{-}, SO_4^{-2}, and NO_3^{-}. The strongest correlation of electrical conductivity was observed with Na^{+} and Cl^{-}. These two ions may be responsible for the salinity of water. A strong positive correlation was also observed between Na^{+} and Cl^{-}, K^{+} and SO_4^{-2}, and Cl^{-} and NO_3^{-}.

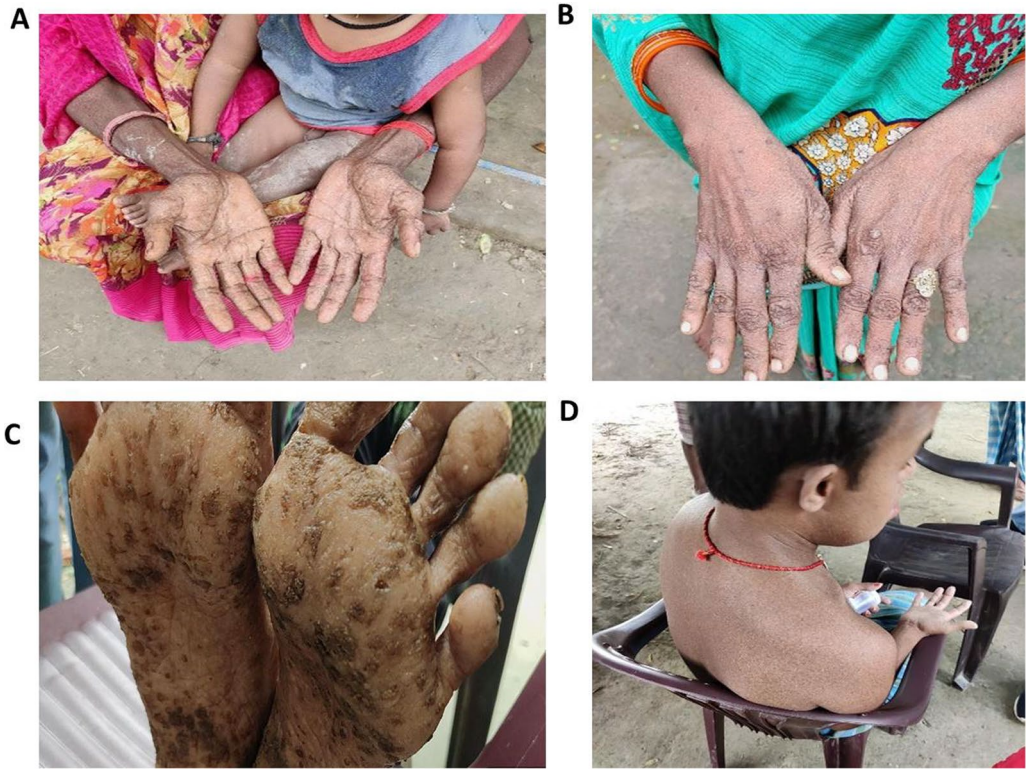

Fig. 4 Arsenicosis symptoms seen in the villagers exposed to arsenic in the Samastipur region, Bihar. **A** Keratosis on palms. **B** Keratosis on hands. **C** Hyperkeratosis on sole. **D** Rain-drop pigmentation on neck and back

Altogether, correlations between different physico-chemical parameters were observed in the study area.

The spatial distribution of arsenic and hydrochemical facies of groundwater in the study area

The study area falls in the Ganga–Brahmaputra–Meghna (GBM) basin belt (Fig. 1). The present study revealed that the Holocene aquifers had arsenic concentrations up to 0.912 mg/L, which is beyond the permissible limit of BIS (2012). 92% (12 out of 13 arsenic-rich samples) of the arsenic-contaminated area were found in Holocene aquifer (Fig. 1). The remaining one arsenic-rich sample was found in the Meghalayan aquifer. Groundwater from Dumduma handpump (SPU12), Rajajan handpump (SPU16), Sarari handpump (SPU27), Mohanpur Dih handpump (SPU29), Mohanpur handpump (SPU30), Banghra handpump (SPU31), Dumri North handpump (SPU33), Jalalpur handpump (SPU34), Dasahra (SPU35), Kurshaha (SPU36), Tetarpur handpump (SPU37), Dubha Paschim Tola handpump (SPU39), and Kancha handpump (SPU40) had arsenic in the range of > 0.01 to 0.912 mg/L. These areas were toward the southern side, closer to the River Ganges, and lying in the Mohanpur and Mohiuddinagar blocks belonging to the Holocene aquifer (Figs. 1, 2A).

A piper trilinear diagram (Fig. 2B) was used to analyze the hydrochemical facies of the region. The major cations were Ca^{+2} and Mg^{+2}, and the major dominant anion present was HCO_3–. Thirty-six (92%) water samples comprised Ca_2^{+}–Mg_2^{+}–HCO_3^{-} water type, three samples were of Na^{+}–K^{+}–HCO_3^{-}, and one sample was of Ca_2^{+}–Mg_2^{+}–Cl^{-}–SO_4^{-2} water type (Fig. 2B).

Risk assessment in inhabitants due to arsenic toxicity

The non-carcinogenic and carcinogenic risks for children, males, and females were calculated, and it was found that children were most vulnerable to arsenic toxicity followed by females and males (Table 3). 35% of the population was prone to non-carcinogenic risk where the value of HQ was greater than 1 (Fig. 3A). Furthermore, it was observed that 100% population of children, females, and males were at carcinogenic risk, where the CR value was > 0.000001 (Fig. 3B). Box plots (Fig. 3C, D) represent non-carcinogenic and carcinogenic risks for populations of different age/sex groups together. In this study, it was observed that several individuals had symptoms related to arsenic toxicity including arsenicosis (Fig. 4).

To understand the mechanism of non-carcinogenic and carcinogenic risk exhibited by the arsenic in the affected

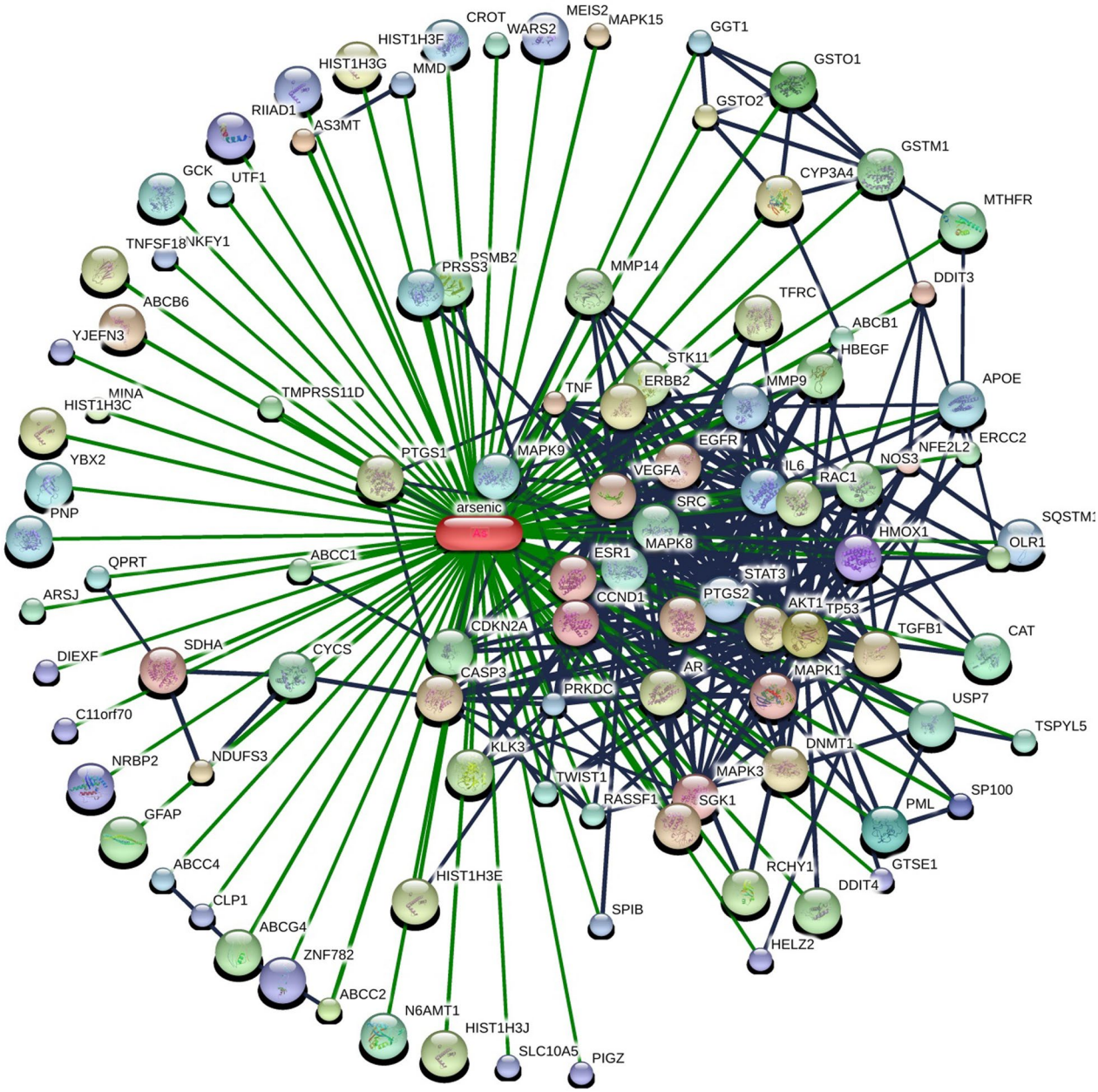

Fig. 5 Arsenic–protein interactome showing the interaction of arsenic with different proteins. Stronger associations are represented by thicker lines. Protein–protein interactions are shown in gray and chemical–protein interactions in green

population, the protein targets of arsenic were studied using computational tools. STITCH webtool was used to analyze the arsenic–protein interactions. The arsenic–protein interactome data show its interactions with several MAP kinases, such as TNF, Myc, p53, and TGF (Fig. 5). The KEGG analysis of arsenic–protein interactome showed the enrichment of various types of cancers including pancreatic, bladder, colorectal, prostate, endometrial, glioma, melanoma, and acute and chronic myeloid leukemia (Table 4).

Discussion

Arsenic (maximum value = 0.0912 mg/L) was found in the aquifers of the study area. The study area falls in the Ganga–Brahmaputra–Meghna basin (GBM). GBM, covering a large area of South Asia, is the world's most severely arsenic-affected region (Khashogji and

Table 4 The GO annotation showing the terms related to KEGG pathways that were enriched in arsenic–protein interactome dataset

Pathway ID	KEGG pathway description	False discovery rate
5200	Pathways in cancer	5.97E−17
5206	MicroRNAs in cancer	5.97E−17
5212	Pancreatic cancer	2.41E−16
5205	Proteoglycans in cancer	1.90E−15
5219	Bladder cancer	9.76E−14
5161	Hepatitis B	3.40E−13
4068	FoxO signaling pathway	1.09E−12
5210	Colorectal cancer	6.97E−12
4066	HIF-1 signaling pathway	1.06E−10
5223	Non-small cell lung cancer	1.54E−10
4917	Prolactin signaling pathway	1.40E−09
4668	TNF signaling pathway	2.81E−09
4932	Non-alcoholic fatty liver disease (NAFLD)	3.65E−09
5215	Prostate cancer	7.50E−09
4370	VEGF signaling pathway	9.18E−09
4915	Estrogen signaling pathway	1.48E−08
5203	Viral carcinogenesis	2.58E−08
5145	Toxoplasmosis	6.98E−08
5213	Endometrial cancer	7.34E−08
4012	ErbB signaling pathway	1.11E−07
4151	PI3K–Akt signaling pathway	1.53E−07
5152	Tuberculosis	1.57E−07
4150	mTOR signaling pathway	2.00E−07
5214	Glioma	2.43E−07
4115	p53 signaling pathway	4.08E−07
2010	ABC transporters	4.61E−07
4010	MAPK signaling pathway	4.81E−07
5218	Melanoma	4.81E−07
5220	Chronic myeloid leukemia	4.81E−07
4510	Focal adhesion	5.94E−07

El Maghraby 2013; Chakraborti et al. 2018; Shaji et al. 2021). Flood plains closer to the River Ganges comprise Holocene aquifers, and the arsenic-rich spots discovered during this study belong to this aquifer. The presence of calcite and dolomite minerals in the aquifer may be the contributory factor for the HCO_3^- ion, as weathering results in an enhancement of Ca^{2+}, Mg^{2+}, and HCO_3^- ion concentrations in the groundwater (Khashogji and El Maghraby 2013).

The risk assessment data revealed that children were most vulnerable to arsenic toxicity, followed by females and males. According to Kumar et al. (2019), less body weight of children compared to females and males may be responsible for greater non-carcinogenic and carcinogenic risks. Chronic arsenic exposure activates different molecular mechanisms such as oxidative stress, inflammation, and cytotoxicity that affects structures and functions of different organs and systems resulting in severe skin damage, cardiovascular diseases, immunosuppression, hematologic disorders, neurological disorders, hepatic, renal, and pancreatic damage (Yoshida et al. 2004; Kapaj et al. 2006; Guha Mazumder 2008; Mitra et al. 2020; Martínez-Castillo et al. 2021). Furthermore, the data presented here support the previously reported studies on humans that have demonstrated that arsenic has cancer-causing ability. Arsenic may cause cancer by inducing oxidative stress, suppression of p53, altered DNA repair, altered DNA methylation, altered growth factors, histone modification, and miRNA expression (Pershagen 1981; Stýblo et al. 2002; Qian et al. 2003; Martinez et al. 2011; Bustaffa et al. 2014; Hong et al. 2014). The KEGG analysis of arsenic–protein interactome also showed the enrichment of various types of cancers that confirms the carcinogenic potential of arsenic. Interaction with the affected residents showed the lack of awareness toward arsenic poisoning; hence, some awareness program at the village/panchayat level is urgently required. This study recommends provision of arsenic-free water in the affected areas.

Conclusions

In the present study, high arsenic concentration (> 0.01 mg/L) was found in 33% of the total numbers of water samples analyzed in Samastipur district of Bihar, India. These samples were unsafe and not suitable for drinking. Younger alluvial deposits (Holocene) were found to be the arsenic hotspots. Children were found to be the most affected group of the population, followed by females and males. 35% of the population had HQ value > 1, indicating non-carcinogenic health risk, and 100% population were at carcinogenic risk with CR value > 0.000001. Urgent intervention by the local governing body is recommended in the affected arsenic-contaminated areas.

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Author contributions

SY and SK contributed to the study conception and design. Material preparation, data collection, and analysis were performed by MJ, SK, TBNS and SKS. GKA worked on the STITCH tool. The first draft of the manuscript was written by MJ, and all the authors commented on previous versions of the manuscript. All the authors read and approved the final version of the manuscript.

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Availability of data and materials
The datasets generated during and/or analyzed during the current study are not publicly available but are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
Not applicable.

Consent for publication
Not applicable.

Competing interests
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