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Hydrogeochemical forecasting in a tribal stretch infected with chronic kidney disease of unknown etiology

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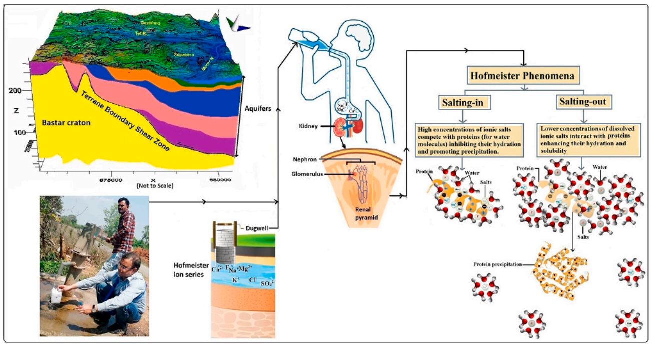
HIGHLIGHTS

- CKDu is more severe at Supebeda (India) than in most Sri Lankan cases.
- Key undersaturated minerals forecast severe fluorosis and CKDu infections.
- Hofmeister ion series is hypothesized as playing a role in CKDu's induction.
- The 95th percentile ADD values of Hofmeister ions exceed their thresholds by 5–15 %.
- Increased water hardness, Na^+/Ca^{2+} ratio, and F- ions may induce CKDu infection.

GRAPHICAL ABSTRACT



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ABSTRACT

A tribal stretch in central India has been silently suffering from the enigmatic chronic kidney disease of unknown etiology (CKDu) for the past many years. It drew national attention in 2018 when over a quarter of the population from a single village of 1200 people got hospitalized with at least 100 deaths in a few years' span. This contribution tries to understand the geochemical genesis of the problem and its evolution process through a study of major rock-water interactions. The future hydrogeochemical environment of the area has been forecasted based on saturation indices of several key minerals. Finally, a probabilistic estimation of the population's exposure to the Hofmeister ion series has been made to understand the role of the specific ion effect on the onset of CKDu. Three distinct chemical facies have been identified based on the analytical results of 27 groundwater samples: Ca^{2+}-Mg^{2+}-HCO_3^- (55.56 %), Ca^{2+}-Mg^{2+}-Cl^--SO_4^{2-} (29.63 %), and Na^+-K^+-HCO_3^- (14.81 %). The positive loadings (*r*) of EC and TDS with Ca^{2+} (0.89; 0.98), Mg^{2+} (0.79; 0.89), Na^+ (0.78; 0.48), Cl^- (0.99; 0.93), and NO_3^- (0.72; 0.85) have led to groundwater hardness and salinity. Ion exchange processes and saturation indices of the geogenic minerals, such as anhydrite, gypsum, fluorite, halite, and sylvite, play crucial roles in the mineralization process. As these minerals progress toward full saturation, their dissolution with the host aquifers releases more of Ca^{2+}, Na^+, K^+, SO_4^{2-}, Cl^- and F^- ions continually. This exacerbates the fluorosis problem besides

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increasing salinity and water hardness in the study area. The combined effects of Ca^{2+}+Mg^{2+} ions with a control on the total hardness, increased Na^+/Ca^{2+} ratio, and excess F^- ions in groundwater are suspected to be the inducing factors for CKDu. This hypothesis is strongly supported by the occurrence of Hofmeister phenomena in the tubular areas of human kidneys through ingested groundwater.

1. Introduction

A tribal stretch in Chhattisgarh State in central India has been suffering from renal diseases for the past many years. It drew national attention in 2018 with the death of over 100 patients and >300 cases of emergency hospitalizations in a span of just few years from a single village, Supebeda, of only 1200 population. As a reply to the national media attention and public outcry, many government agencies rushed to the area to find an immediate solution. After a thorough examination, the medical teams coined the malady as "chronic kidney disease of unknown etiology (CKDu)", a term never heard in this region before (Chowdhary et al., 2020). But the inhabitants were not happy with this acronym and blamed the health hazard on groundwater contamination, since they have been consuming this precious resource historically for ages. Two of our authors conducted a reconnaissance study and collected 27 groundwater samples from strategic locations from around the village for appraisal of pollution sources (Dewangan and Verma, 2022). Although this initial examination did not reveal any significant quality deterioration, further study by Herojeet et al. (2023) did identify groundwater contamination due to excess fluoride and nitrate ions. Further study by this team characterized the area geochemically through a thorough examination of rock-water interactions and source apportionment of the prevailing contaminants (Rajkumar et al., 2025a). Groundwater too was classified based on usage perspective (Rajkumar et al., 2025b). The present investigation aims at the future forecasting of the region's geochemical environment based on the saturation indices of several key minerals. A probabilistic estimation of the population's exposure to the Hofmeister ion series too has been made to understand the role of the specific ion effect on the onset of CKDu - an analysis not attempted by any worker before.

Ions present in a solution usually define their physicochemical properties. However, within the solution itself, only a few of the ions decide its chemical properties as the activity coefficient of one ion significantly affects the coexistence of another ion (Zhang et al., 2023). The phenomenon controlling this ion-ion effect is called the specific ion effect (SIE) (Gregory et al., 2022). The solubility or precipitation of compounds and formation of complexes depend on the SIE. It has very wide implications in biogeochemistry and was observed for the first time by Hofmeister (1888) and his student Lewith (1887). While studying the effect of cations and anions on the solubility of proteins, they arranged specific ions in a series, known today as Hofmeister ion series, based on their lyotropic properties (Hyde et al., 2017). The salting in and salting out processes that occur in the tubular areas of kidneys is often termed as 'Hofmeister phenomena' in scientific literature. Since chronic kidney diseases are intimately related to protein intake by humans (Fouque and Aparicio, 2007; Zha and Qian, 2017; Shirai et al., 2024), an attempt has been made in this contribution to make a probabilistic estimation of the population's exposure to the Hofmeister ion series from groundwater, a unique analysis still unexplored by scientists.

The disease, CKDu, is a condition characterized by a slow decline in kidney function not associated with diabetic nephropathy or hypertensive nephropathy (Jayasumana et al., 2017; Jolly and Thomas, 2022; Shi et al., 2023). Mostly marginalized agricultural communities in specific regions of the world are its victims (Paidi et al., 2021). It has been reported in Sri Lanka (Abeysekera et al., 1996), Central American countries (Trabanino et al., 2002), Egypt (Minshawy, 2011), Tunisia (Abid et al., 2003) and India (Rajapurkar et al., 2012) in scattered pockets. There are at least 700 million people around the globe infected with chronic kidney diseases (CKD) with a global prevalence of 9.1 % (GBD-CKDC, 2020), making it the third-fastest growing cause of death worldwide (Foreman et al., 2018). Although no clear distinction between the global figures of CKDk (chronic kidney disease of known etiology) and CKDu patients has yet been made, the rapid rise of CKDu cases around the globe is a matter of great concern. In fact, as per a World Bank analysis, any form of chronic kidney disease (CKD) is the highest economic burden of any disease group on the affected population, particularly in low- and lower-middle-income countries (Essue et al., 2018; Levin et al., 2023). The fact that about one quarter of the population in the present study area is infected with this disease, the magnitude of social and economic turmoil due to CKDu in this part of the world can very well be imagined.

Many pockets in India have been identified as suffering from CKDu (Rajkumar et al., 2025a, b). Studies in these areas have been conducted mostly from medical perspectives with little focus on hydrochemistry (Herojeet et al., 2023; Rajkumar et al., 2025a). The present contribution is a predictive hydrogeochemical work with a focus on saturation indices of the suspect minerals and a probabilistic estimation of the exposure of the affected population to the Hofmeister ion series through ingestion of drinking water (groundwater), suspected to be one of the leading causes of CKDu in the affected region.

2. Materials and methods

2.1. Study area

Supebeda is a small village in the administrative district of Gariabandh in Chhattisgarh State, India (Fig. 1). It occupies a geographical area of 3 km^2 beside the river Tel that separates Chhattisgarh State with that of Odisha in the east. With a population of only about 1200 people, the male-female ratio is about 50 % (983 females to 1000 males). There are 313 households in the village and an average of 4 persons live in a family. People depend mostly on agricultural activities for their livelihood. Rathore et al. (2022) describe the living style of the local inhabitants. Herojeet et al. (2023) give a detailed account of the area including the groundwater sampling locations and analytical procedures of the 27 groundwater samples collected from strategic locations.

2.2. Local geology & hydrogeology

Topographically, Supebeda represents a plain region with surface elevations varying between 230 and 320 m above the mean sea level (AMSL). The ground has a general slope of about 4 m/km toward the east. The Tel River is perennial in nature while all other tributaries flow intermittently. Geomorphologically, the region is broadly divided into three categories: pediplain (shallow), pediplain (moderate) and valley fill deposits. The shallow pediplain is generally weathered upto a depth of about 10 m and that of moderate pediplain up to about 20 m. The thickness of the valley fill deposits varies up to a depth of 10 m along the major drainage lines. Most of the area is covered by reddish soil and cultivated land (Fig. S1a, b).

The early workers, Gupta et al. (2000) and Neogi and Das (2000), have identified three lithological units in the Supebeda region, viz., (i) migmatitic quartzofeldspathic gneiss, (ii) banded augen gneiss, and (iii) hornblende granite. The migmatitic quartzofeldspathic gneisses are grey-colored and medium-grained consisting typically of finely laminated alternations of felsic (quartz + plagioclase + K-feldspar) and mafic (biotite+ hornblende) bands. The augen gneisses are pink-colored and medium- to coarse-grained rocks, and the bandings within them are defined by the mafic and felsic layers of K-feldspar augen and quartz lenticels. The hornblende granite intrude into the banded gneiss. It is pink colored and coarse grained, typically consisting of microcline, quartz, hornblende, and biotite.

Groundwater occurs in both unconfined and confined conditions in the aquifers (Fig. 1). Unconfined conditions occur in the weathered portions at shallower level up to about 20 m depth. Semi-confined to confined conditions prevail in fractured zones at depth (CGWB, 2001).

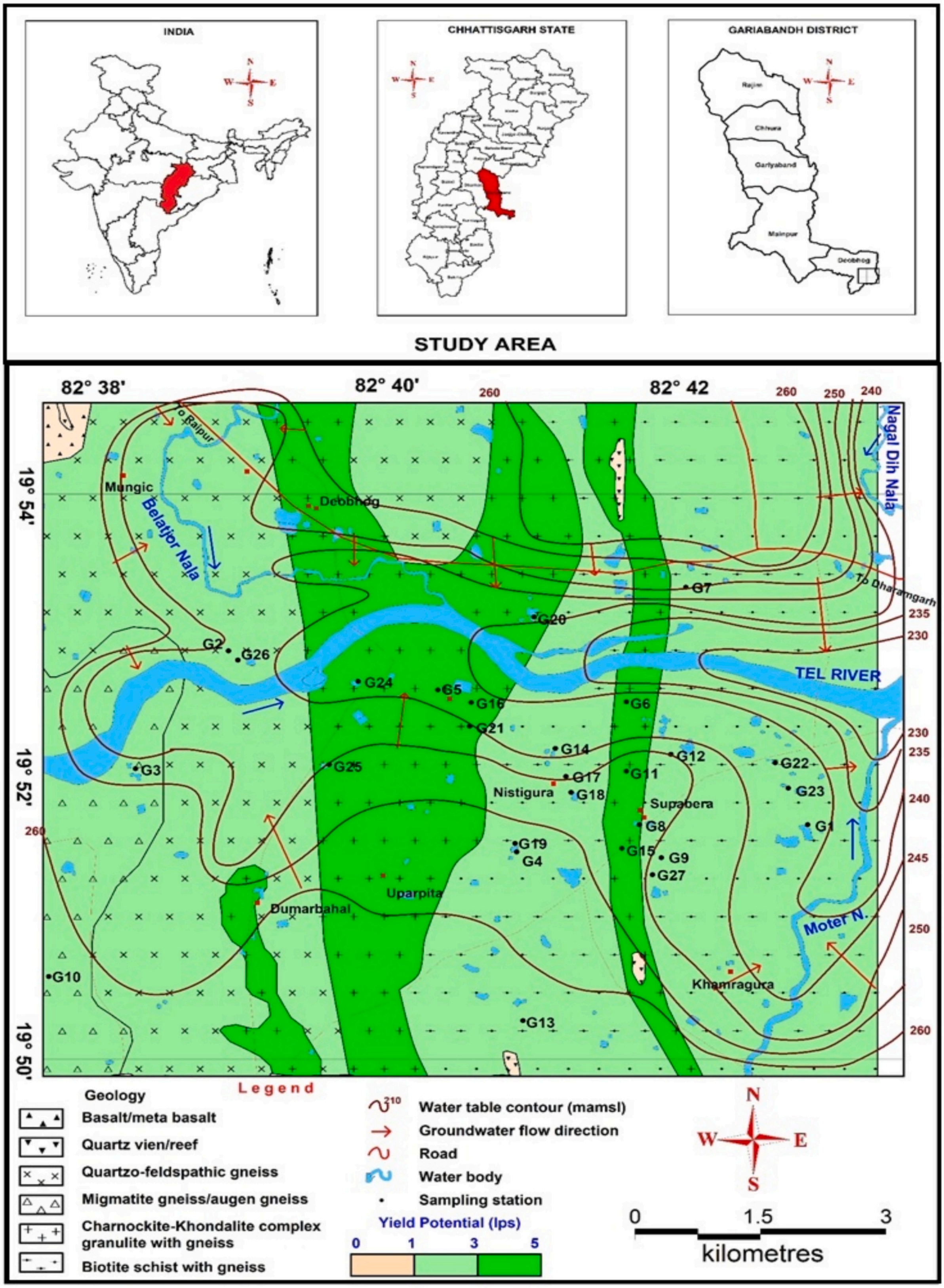

Fig. 1. Sampling locations and hydrogeology in the village Supebeda, district Gariabandh, Chhattisgarh State, India.

Dugwells are prevalent with a depth range of 7–16 m and a yield of 25–40 m^3/day. Borewells are 50–80 m deep and yield about 85–430 m^3/day (Dewangan and Verma, 2020). Groundwater level in the unconfined aquifer follows the surface topography. Water table elevation contours range between 240 and 260 m AMSL and the groundwater flows are directed toward the Tel River from both North and South directions. Fracture zones are encountered at 40–45, 60–65, and 75–80 m depth (CGWB, 2022). Transmissivity ranges between 15 and 45 m^2/day and occasionally goes up to 100 m^2/day (CGWB, 2023).

2.3. Calculation of saturation indices (SI) of minerals in groundwater

A saturation index (*SI*) (Table 1) is used to understand the degree of a specific mineral dissolution and precipitation in the water system. This index enables prediction of the state of thermodynamic equilibrium of minerals (dissolution and precipitation) vis-à-vis the types of water–rock (sediment) interaction (Khan et al., 2021; Liu et al., 2021). It is defined by the logarithm (base 10) of the ratio of ionic activity product (*IAP*) to mineral solubility product constant (K_{sp}) in an aquifer system (Rajkumar et al., 2023) and is evaluated by using Eq. 1.

$$SI = log_{10}IAP/K_{sp} \tag{1}$$

The *SI* values of (i) less than zero ($SI < 0$), (ii) equal to zero ($SI = 0$), and (iii) more than zero ($SI > 0$) imply the thermodynamic state of a particular mineral (solute) in the solution phase, i.e., whether it is in an undersaturated, saturated, and supersaturated condition, respectively (Zhang et al., 2020; Singh et al., 2020b). In the present study, the geochemical modeling software PHREEQC 3.1.2 has been employed to extract the various minerals present in the host rocks.

2.4. Probabilistic estimation of people's exposure to Hofmeister phenomena

Hofmeister phenomena refer to the specific effects of different ions on the stability and solubility of proteins. These specific effects largely depend on their ionic strengths and concentrations. When the effect of ion–ion, and therefore, the solute–solute interaction is greater than that of solute–solvent, there occurs decrease in solubility and consequent precipitation of proteins by salting-out processes (Baldwin, 1996). Conversely, the salting-in process enhances the solubility of a solute and maintains the stability of proteins in the solution. Hofmeister ions play a vital role in the biological and physicochemical functions, such as in enzyme activities, solubility of hydrophobic ions and their interactions, and ionic osmosis along ion-channels (Kang et al., 2020).

Dharma-Wardana et al. (2015) opine that prolonged use of excessively ionic water causes CKDu by a Hofmeister-type of protein denaturing mechanism in the kidney. To examine the latent linkage between CKDu and water quality, Dharma-Wardana (2018) applied a quantitative electrochemical model to estimate Gibb's free energy required for the formation of Hofmeister-type of ion-pairs in water. Our study, quite different from his work, makes a probabilistic estimation of the people's exposure to Hofmeister ions from the groundwater they regularly drink so that the effect of the Hofmeister series of ions on human kidneys could be assessed.

There is a probability that the prolonged exposure to certain ions (Ca^{2+}, Mg^{2+}, Na^+, K^+, Cl^-, SO_4^{2-}, F^-) from drinking water may cause Hofmeister effect in the tubular areas of the kidneys, thereby restricting their adsorption. The interaction of these ions may form metal complexes, thereby binding to the active sites of metallo-proteins, causing organelle disruption and electrolyte imbalance (Adamek et al., 2005;

Table 1
Saturation indices (*SI*) of groundwater samples from the village Supebeda, Chhattisgarh State, India.

Samples nos.	Anhydrite	Gypsum	Fluorite	Halite	Sylvite	Gibbsite	Aluminum hydroxide	Alunite
	$CaSO_4$	$CaSO_4$: H_2O	CaF_2	NaCl	KCl	$Al(OH)_3$	$Al(OH)_3$	$KAl_3(SO_4)_2(OH)_6$
G1	−3.57	−3.27	−0.89	−7.29	−9.11	4.56	1.87	1.26
G2	−3.28	−2.98	−1.74	−7.53	−8.59	4.52	1.83	2.27
G3	−3.40	−3.10	−1.84	−7.34	−8.15	4.57	1.88	2.99
G4	−3.54	−3.23	−0.95	−7.82	−9.50	4.32	1.63	0.19
G5	−3.26	−2.95	−1.59	−7.85	−8.51	4.64	1.95	3.06
G6	−3.29	−2.99	−1.70	−8.02	−8.23	4.42	1.73	2.68
G7	−3.24	−2.93	−2.42	−8.03	−8.63	4.23	1.54	1.94
G8	−3.35	−3.04	−0.82	−7.70	−9.25	4.12	1.43	−0.37
G9	−3.11	−2.80	−0.86	−7.83	−8.99	4.29	1.60	0.88
G10	−3.18	−2.87	−1.48	−7.94	−8.92	4.39	1.70	1.53
G11	−3.31	−3.01	−2.66	−8.09	−9.06	4.31	1.62	1.27
G12	−3.00	−2.70	−1.00	−7.67	−8.97	4.22	1.53	0.84
G13	−2.91	−2.61	−1.50	−7.63	−8.69	4.39	1.70	2.19
G14	−2.26	−1.96	−0.83	−7.42	−8.63	4.52	1.83	4.63
G15	−3.32	−3.02	−0.68	−6.73	−7.32	4.56	1.87	2.49
G16	−2.22	−1.92	−1.52	−7.71	−8.52	4.21	1.52	4.04
G17	−1.71	−1.41	−1.86	−5.75	−7.09	5.36	2.67	9.29
G18	−3.02	−2.72	−1.02	−5.79	−7.31	5.27	2.58	5.70
G19	−2.88	−2.57	−2.01	−7.04	−7.71	4.88	2.19	5.00
G20	−2.69	−2.38	−0.97	−7.46	−8.90	4.09	1.40	1.59
G21	−2.59	−2.28	−0.92	−7.77	−9.02	4.76	2.07	4.92
G22	−2.44	−2.14	−1.03	−6.84	−7.85	4.72	2.03	4.76
G23	−1.96	−1.66	−2.04	−7.32	−8.10	4.21	1.52	4.10
G24	−2.12	−1.82	−1.33	−7.03	−7.87	4.76	2.07	5.22
G25	−1.87	−1.57	−2.28	−6.44	−7.31	5.17	2.48	7.91
G26	−2.48	−2.18	−1.31	−6.50	−7.47	4.90	2.21	5.59
G27	−2.12	−1.81	−1.81	−6.85	−7.84	4.80	2.11	5.73
Mean	−2.82	−2.52	−1.45	−7.31	−8.35	4.56	1.87	3.40
Minimum	−3.57	−3.27	−2.66	−8.09	−9.50	4.09	1.40	−0.37
Maximum	−1.71	−1.41	−0.68	−5.75	−7.09	5.36	2.67	9.29

Note: (i) *SI* values less than zero ($SI < 0$) depict undersaturated condition, (ii) *SI* values equal to zero ($SI = 0$) divulge saturated state, and (iii) *SI* values more than zero ($SI > 0$) imply supersaturated condition.

Table 2a
Probabilistic values of the ions through oral pathway with respect to drinking water standards in the village Supebeda, Chhattisgarh State, India.

Ions/ parameters	Distribution	Min.	Max.	Likeliest	References
Ca^{2+}	Triangular	11	300	75	Wood et al., 2022; WHO, 2022; BIS, 2020
Mg^{2+}	Triangular	11	100	30	Wood et al., 2022; WHO, 2022; BIS, 2020; SLS, 2013
Na^+	Uniform	43	200		Wood et al., 2022; WHO, 2022; Health Canada, 2020; SLS, 2013; European Union 2023
K^+	Uniform	1.5	12		Wood et al., 2022; WHO, 2022
Cl^-	Triangular	128	1000	250	Wood et al., 2022; WHO, 2022; BIS, 2020; USEPA, 2023; NHMRC, 2011; Health Canada, 2020; SLS, 2013; European Union 2023
SO_4^{2-}	Triangular	46	500	200	Wood et al., 2022; BIS, 2020; NHMRC, 2011; Health Canada, 2020
F^-	Triangular	0.1	4	1	Wood et al., 2022; BIS, 2020; NHMRC, 2011; Health Canada, 2020; SLS, 2013

Table 2b
Statistical description of the probabilistically calculated exposure to Hofmeister ions from drinking water in the village Supebeda, Chhattisgarh State, India, and their threshold values.

Parameters	Probabilistically estimated adult daily intake doses (mg/day/kg)				Threshold values (THV) (mg/day/kg)	% above the THV
	Mean	Stdev	5th percentile	95th percentile		
Ca^{2+}	1.18	−0.11	0.06	3.63	2.24	9.92
Mg^{2+}	0.37	0.00	0.02	1.10	0.81	5.47
Na^+	1.13	−0.15	0.07	3.43	2.12	8.88
K^+	0.04	0.00	0.00	0.12	0.12	NIL
Cl^-	1.46	−2.80	0.04	5.76	7.20	NIL
SO_4^{2-}	0.86	−4.09	0.02	2.64	4.30	NIL
F^-	0.02	0.00	0.00	0.05	0.03	14.49

Schenk et al., 2008; Agalakova and Gusev, 2012). The exposure to these ions through ingestion pathway primarily from the water environment can be assessed by the average daily dose (ADD) estimation formulated by the USEPA (2011) (Eq. 2).

$$ADD_{ingestion} = \frac{C_M \times IR_w \times EF_r \times ED}{BW \times AT_r} \tag{2}$$

We have used a probabilistic approach, namely the Monte Carlo Simulation (MCS), for this assessment using a computer program in Oracle Crystal Ball (version: 11.1.2.4.850). This software configures a statistical distribution array in the form of probabilistic approximation of a mathematical equation to generate more corroborated reproducible results that minimize analytical bias (Herojeet et al., 2023). Here, the threshold value of each Hofmeister ion, as an essential acceptable daily intake element, has been determined from drinking water. The typical input variables are ingestion rate (IR_w), exposure frequency (EF), exposure duration (ED), and body weight (BW) (Table S1). All these parameters use 5000 permutations to reach numerical stability for the computation of ADD oral ingestion and threshold value of each ion. The water quality standards of various countries available in the literature have been used to extract the most suitable probability distribution function and define the threshold value of each Hofmeister ion (Ca^{2+}, Mg^{2+}, Na^+, K^+, Cl^-, SO_4^{2-}, F^-) (Table 2a). These threshold values are considered as acceptable standard limits for the assessment of $ADD_{ingestion}$ from groundwater in the study area (Table 2b).

3. Results and discussions

Table S2 lists all analytical data of the physicochemical parameters and Table S3 their descriptive statistics along with the percentage/number of samples exceeding their prescribed limits for drinking water (BIS, 2020; WHO, 2022). All these tables are self-explanatory. Some of the parameters, such as EC, TDS, TH, Ca^{2+}, Mg^{2+}, Cl^-, NO_3^- and F^-, are the violating parameters that exceed their acceptable limits by 11, 34, 45, 33, 11, 11, 37 and 41 %, respectively. In the case of F^-, more than a quarter of the samples (26 %) exceed their permissible limit of 1.5 mg/L. Health hazards caused by excess NO_3^- and F^- ions are explained by Herojeet et al. (2023) and Rajkumar et al. (2025a,b).

3.1. Correlation analysis

A correlation matrix of the analyzed datasets is prepared to examine the various interionic relationships among the physicochemical parameters and extract valuable information about the probable sources affecting the groundwater quality (Table S4). The absolute correlation value (r) >0.75 reveals a strong relationship between the parameters (Hossain et al., 2020; Rajkumar et al., 2023). A strong negative relationship (r) of pH with EC (−0.74), TH (−0.86), Ca^{2+} (−0.85), Mg^{2+} (−0.77), Cl^- (−0.80), and NO_3^- (−0.83) is indicative of the impact of these parameters on pH. Both EC and TH are strongly correlated with each other and have strong positive loadings (r) with Ca^{2+} (0.89; 0.98), Mg^{2+} (0.79; 0.89), Na^+ (0.78; 0.48), Cl^- (0.99; 0.93), and NO_3^- (0.72; 0.85). This indicates that these ionic species cause mineralization leading to hardness and salinity in groundwater (Herojeet et al., 2017; Subba Rao et al., 2021; Rajkumar et al., 2023; Taoufiq et al., 2023).

Moreover, Ca^{2+} shows a significant positive correlation with Mg^{2+} (0.78), Cl^- (0.92), and NO_3^- (0.84) and a weak relationship with Na^+ (0.47). Similarly, Mg^{2+} is significantly correlated with Cl^- (0.82), and NO_3^- (0.75). This depicts dissolution of carbonate minerals, reverse exchange processes, permanent hardness and anthropogenic inputs in the aquifer system (Manikandan et al., 2020; Dinka et al., 2015). Finally, the positive relationships of Na^+ with HCO_3^- (0.80) and Cl^- (0.68), and Cl^- with NO_3^- (0.77), reflect the weathering of silicate minerals and the effect of human-induced contamination (agrochemicals, septic tanks, and domestic sewage, etc.) (Nematollahi et al., 2018; Zhang et al., 2018; Sangwan et al., 2021; Su et al., 2023; Taoufiq et al., 2024a). Moreover, the application of chemical fertilizers, such as anhydrous ammonium chloride, ammonium nitrate, and urea in agricultural land, tends to release high amount of inorganic chlorine and nitrogen as contaminants in the groundwater system (Herojeet et al., 2016; Taoufiq et al., 2024b).

3.2. *Geochemical genesis and its evolution processes*

Geochemical processes play a vital role in the chemical composition of different water sources that exhibit spatial and temporal variations in water quality. The composition of groundwater depends on the type of aquifer material, its lithology, geochemical processes, and diverse regional dynamics (Herojeet et al., 2013; Brindha and Kavitha, 2015; Okiongbo and Douglas, 2015). The Piper diagram (Piper, 1944) (Fig. S2) depicts that the groundwater of the area is predominantly dominated by alkaline earths over alkalies and weak acids over strong acids. These are represented by three hydrochemical facies: Ca^{2+}-Mg^{2+}-HCO_3^- (55.56 %), Ca^{2+}-Mg^{2+}-Cl^--SO_4^{2-} (29.63 %), and Na^+-K^+-HCO_3^- (14.81 %) (Table S5). Also, the groundwater samples are further classified into four distinct water types: Ca^{2+}-HCO_3^- (55.56 %), Ca^{2+}-Cl^- (7.40 %), Ca^{2+}-Mg^{2+}-Cl^- (22.22 %), and Ca^{2+}-Na^+-HCO_3^- (14.81 %). The difference between “hydrochemical facies” and “hydrochemical types” in Piper diagram is that “hydrochemical facies” are classifications that group water samples with similar ionic compositions, reflecting the dominant chemical characteristics of groundwater, while “hydrochemical types” are specific categories within these facies, further differentiating the water samples based on the relative concentrations of the major ions. Accordingly, the Ca^{2+}-HCO_3^- water type in the Piper diagram indicates dissolution of carbonate minerals with percolating water in the aquifers through irrigation runoff/return flow and precipitation (Singh et al., 2020a; Herojeet et al., 2016). The cation triangle shows that the majority (70.37 %) of the samples do not belong to any dominant zone, and the remaining 11.11 %, 14.82 %, and 3.70 % of the samples can be termed as Ca^{2+}, Na^+, and Mg^{2+} water types. In the anion triangle, around 70.37 % of the samples fall under HCO_3^- water type, indicating weathering of carbonates and silicates minerals and ion exchange processes (Nematollahi et al., 2018). The 22.22 % of the samples belonging to Cl^- water type depict the role of anthropogenic factors, evaporite, and halite dissolution (Marghade et al., 2021).

Gibbs diagram (Fig. S3a) reveals that most groundwater samples (88.89 %) are grouped under the rock dominance zone due to interaction of the percolating water with aquifers, chemical solute exchange processes, and salt precipitation of aquifer minerals (Gibbs, 1970). The remaining samples (11.11 %) fall in the evaporation zone, indicating secondary evaporation. Anthropogenic factors enhance the groundwater salinity by the affecting the TDS and elevating the Na^+ and Cl^- concentrations (Gupta et al., 2008; Aravinthasamy et al., 2020; Krishan et al., 2023). Further, the semi-arid conditions of the study area plays a pivotal role in regulating the secondary evaporation and enhancing groundwater salinity. The diagram results are further elucidated by the end-member plots, i.e., Ca/Na vs. HCO_3^-/Na, and Ca/Na vs. Mg/Na (Brindha et al., 2017; Singh et al., 2020a).

Fig. S3 (b,c) is indicative of the groundwater samples being influenced by the weathering and dissolution of silicate minerals. Few scattered samples in the silicate-evaporation mixing zone indicate dominance of Na^+ over Mg^{2+} ions (reflecting anthropogenic inputs) and climatic conditions affecting the Na^+ ions (causing groundwater salinity) (Fig. S3c). The general silicate weathering reaction with carbonic acid is expressed as (Rajkumar et al., 2023):

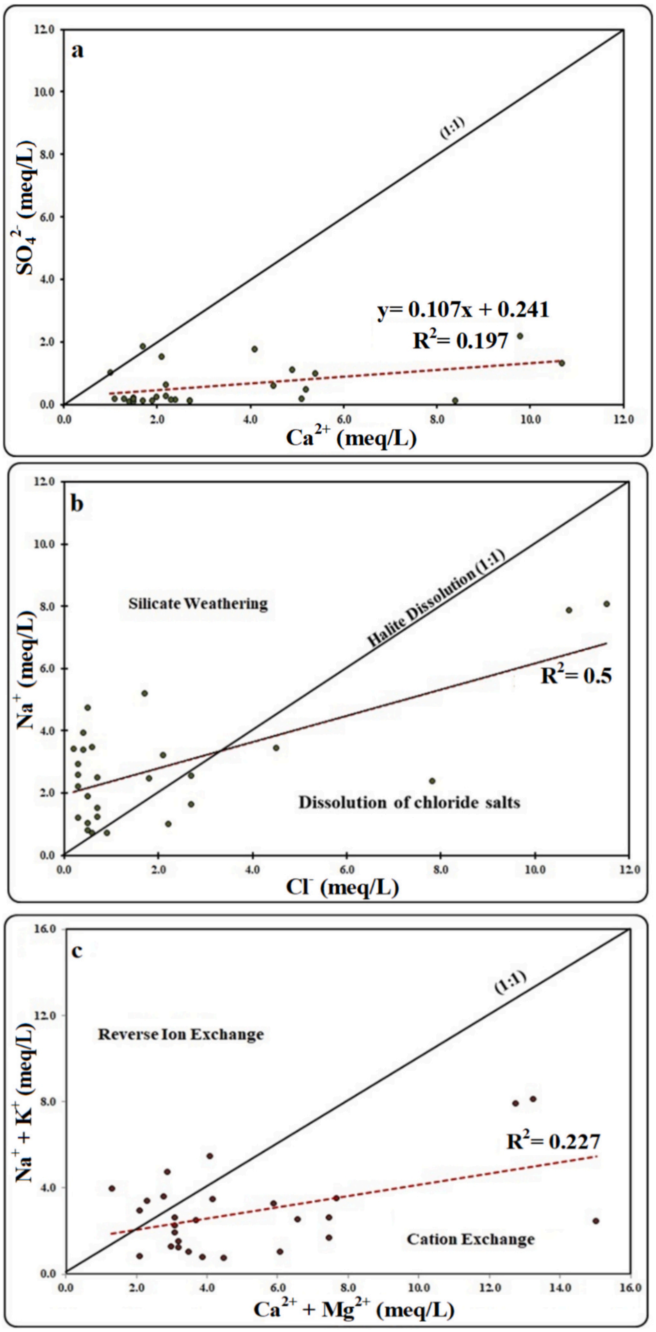

Fig. 2. Interionic relationship between the major ions in groundwater around the village Supebeda, Gariabandh District, Chhattisgarh State, India. (a) Ca^{2+} vs SO_4^{2-}, (b) Na^+ vs Cl^-, and (c) (Na^++K^+) vs (Ca^{2+}+Mg^{2+}).

$$(Na, K, Ca, Mg)silicate + H_2CO_3 \rightarrow H_4SiO_4 + HCO_3^- + Na^+ + K^+ + Ca^{2+} + Mg^{2+} + Clay \quad (3)$$

The Revelle index ($RI = Cl^-/(HCO_3^- + CO_3^-)$) (Eq. 4) (Revelle, 1941) defines the salinization in semi-arid and arid regions (Singh et al., 2020b). As per *RI*, ~ 77.78 % of samples fall under the “unaffected by salinity” and ~ 22.22 % under “slightly affected by salinity” categories indicating lack of acute Cl^- contamination in groundwater (Table S6, Fig. S4).

3.3. *Dissolution of minerals and their saturation indices (SI) in groundwater*

The *SI* values, estimated based on Eq. 1, range from −3.57 to −1.71 for anhydrite ($CaSO_4$), −3.27 to −1.41 for gypsum ($CaSO_4.H_2O$), −2.66 to −0.68 for fluorite (CaF_2), −8.09 to −5.75 for halite (NaCl), and −

9.50 to −7.09 for sylvite (KCl) (Table 1). The undersaturated conditions of these minerals enhance their dissolution in the groundwater to release Ca^{2+}, Na^+, K^+, SO_4^{2-}, Cl^-, and F^- ions through rock-water interactions. The dissolution rates of few undersaturated minerals with respect to their *SI* mean values are: CaF_2 (−1.45) > $CaSO_4.H_2O$ (−2.52) > $CaSO_4$ (−2.82) > NaCl (−7.31) > KCl (−8.35).

The dissolution of gypsum mineral can be predicted by scattering relationship between Ca^{2+} vs. SO_4^{2-} (Fig. 2a). About 92.6 % of the samples plotting below the equiline (1:1) indicate the role of gypsum ($CaSO_4.2H_2O$) dissolution as insignificant (Eq. 5), while the remaining samples (7.4 %) falling along the equiline depict the dissolution of anhydrite ($CaSO_4$) mineral in groundwater (Purushothaman et al., 2014; Kumari et al., 2018). Again, the 7.40 % of the samples falling on the equiline (1:1) in the Na^+ vs. Cl^- plot indicate that halite dissolution does

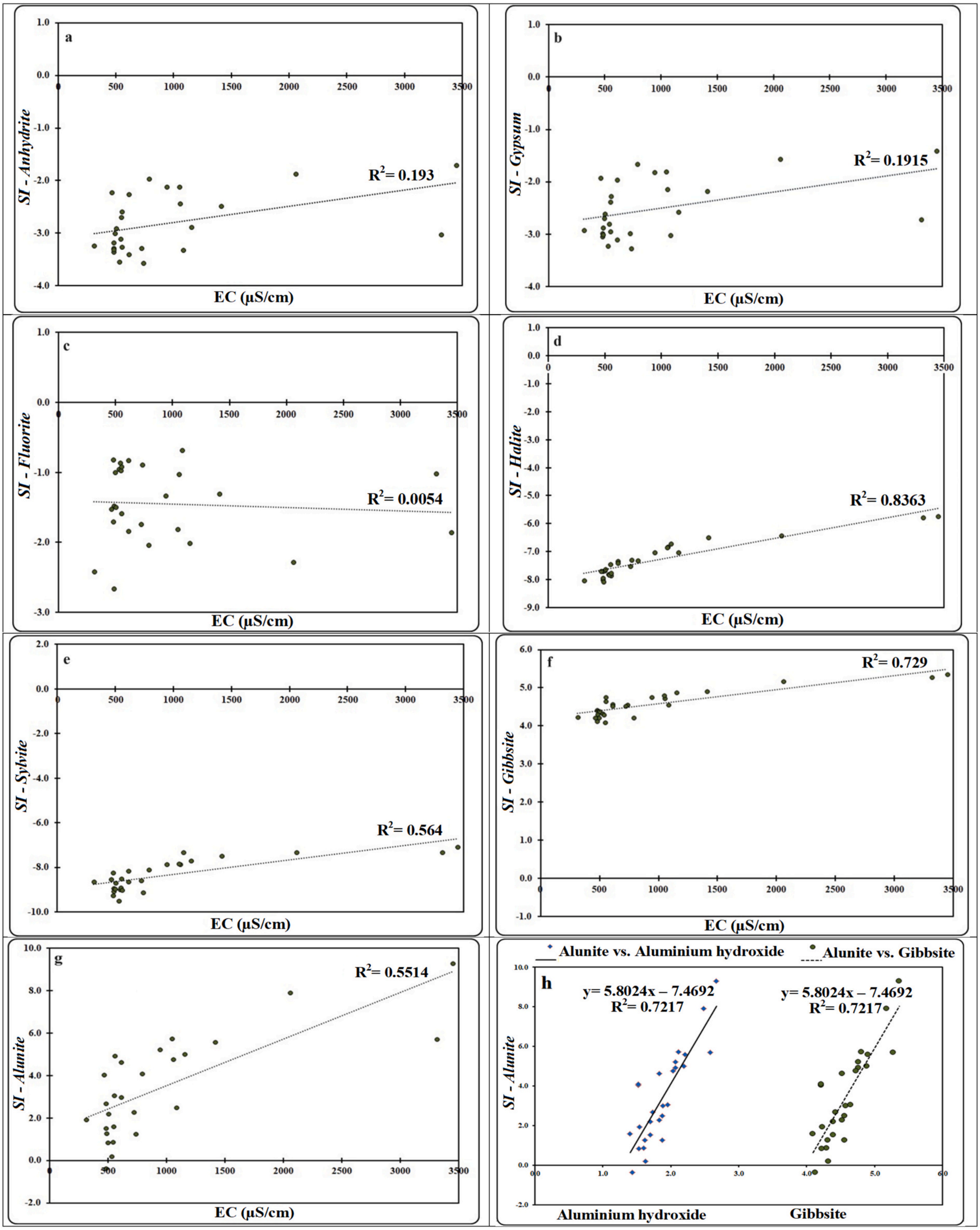

Fig. 3. Plots of saturation index (SI) values of (a) Anhydrite, (b) Gypsum, (c) Fluorite, (d) Halite, (e) Sylvite, (f) Gibbsite, and (g) Alunite vs. EC and (h) plot of SI of Alunite vs. Aluminum Hydroxide, and Gibbsite in the village Supebeda, Chhattisgarh State, India.

not significantly affect the concentrations of Na^+ and Cl^- ions in the aquifer system (Eq. 6) (Wang et al., 2009; Rajkumar et al., 2023; Singh et al., 2020b; Laghrib et al., 2024) (Fig. 2b). The correlation between the scatter plots of Ca^{2+} vs. SO_4^{2-} (Fig. 2a) and Na^+ vs. Cl^-, and the *SI* values of anhydrite, gypsum, and halite, illustrate the limited roles of these minerals on the groundwater chemistry of the study area.

$$\underset{\text{(Gypsum)}}{CaSO_4.2H_2O} \rightarrow Ca^{2+} + SO_4^{2-} + 2H_2O \tag{5}$$

$$\underset{\text{(Halite)}}{NaCl} \rightarrow Na^+ + Cl^- \tag{6}$$

The plots of *SI* values of anhydrite, gypsum, and fluorite vs. EC with their R^2 at 0.1913, 0.1915, and 0.0054 [Fig. 3(a,b,c)], respectively, indicate that further dissolution of these minerals may not have direct adverse impact on the groundwater salinity. However, the regression lines of the plots of halite and sylvite vs. EC with their R^2 at 0.8363 and 0.564 [Fig. 3(d, e)], respectively, depict that groundwater salinity in the study area may be linked directly to the further dissolution of these minerals in the future (Rajkumar et al., 2023; Taoufiq et al., 2024b).

All groundwater samples are supersaturated with gibbsite [$Al(OH)_3$] and aluminum hydroxide, with their *SI* values ranging between 4.09-5.36 and 1.40–2.67, respectively (Table 1). The intense weathering and dissolution of granite rocks by the hydrolysis reaction has converted gibbsite into a secondary clay mineral (precipitated in the aquifer) (Dolui et al., 2016; Gupta et al., 2000). Chemical reactions of K-feldspar (with CO_2), microcline (with H^+ formed by the CO_2 dissolution), and kaolinite minerals in the study area are shown below (Eqs. 7–9).

$$\underset{\text{(K – feldspar)}}{KAlSi_3O_8} + CO_2 + 2H_2O \rightarrow AI(OH)_3 + K^+ + 3SiO_2 + HCO_3^- \tag{7}$$

$$\underset{\text{(Microcline)}}{KAlSi_3O_8} + H^+ + 7H_2O \rightarrow Al(OH)_3 + K^+ + 3H_4SiO_4 \tag{8}$$

$$\underset{\text{(Kaolinite)}}{Al_2Si_2O_5(OH)_4} + H_2O \rightarrow 2SiO_2 + Al(OH)_3 \tag{9}$$

The *SI* values (−0.37 to 9.29) of alunite [$KAl_3(SO_4)_2(OH)_6$] depict that 93.6 % of the samples are saturated/supersaturated with it (Table 1). The weathering of K feldspar, biotite, and microcline are the main sources of K^+ ions. The presence of SO_4^{2-} content may be attributed to the leaching of inorganic sulfides present in the sediments through percolating water, weathering of pyrite-sulfide bearing minerals, and biological oxidation of sulfur-containing compounds in soil (Gupta et al., 2000; Amadi et al., 1987; Herojeet et al., 2023). The dissociation of aluminum hydroxide [$Al(OH)_3$] by reaction with H^+ ions forms Al^{3+} ions and H_2O (Eq. 10). Further, the hydrolysis chemical reaction of K^+, Al^{3+}, and SO_4^{2-} ions in the aquifer system precipitates into alunite minerals as given in Eq. 11 (Wang et al., 2021). Thus, K^+ and SO_4^{2-} ions are the least concentrated among cations (Ca^{2+}, Mg^{2+}, Na^+) and weak–strong acids (HCO_3^-, Cl^-) in the groundwater system (Table S3, Fig. S5).

$$Al(OH)_3 + H^+ = Al^{3+} + 3H_2O \tag{10}$$

$$K^+ + 3Al^{3+} + 2SO_4^{2-} + 6H_2O = \underset{\text{(Alunite)}}{KAl_3(SO_4)_2(OH)_6} + 6H^+ \tag{11}$$

The mutual independence EC vs. *SI* values of gibbsite ($R^2 = 0.729$) and alunite ($R^2 = 0.5514$) is indicated by the trendline values that display faster dissolution of granite rocks enhancing mineralization and precipitation of these minerals in groundwater [Fig. 3(f, g)]. The same score loading ($R^2 = 0.72$) and slope ($y = 5.8024x - 7.4692$) between alunite vs. aluminum hydroxide, and alunite vs. gibbsite indicate that both aluminum hydroxide and gibbsite have the same mineral composition originating from the analogous sources. Thus, their dissolution contributes to the formation of alunite minerals in the aquifer (Fig. 3h).

3.4. Influence of fluoride and total hardness on CKDu

The excess concentrations of fluoride and total hardness in groundwater (as a drinking water source) has been accepted as the causative risk factors for CDKu by many workers (Wasana et al., 2016; Dissanayake and Chandrajith, 2019; Nanayakkara et al., 2020; Rajkumar et al., 2025a). In the study area, 40.7 % of the water samples have F^- content above the acceptable limit of 1.0 mg/L including 25.9 % of the samples exceeding the permissible limit of 1.5 mg/L (BIS, 2020). Literature reveals that the excessive F^- intake may develop fluorapatite, hydroxyapatite, and aluminum fluoride complexes in humans forming intra-renal nanoparticles leading to the impairment of kidney (Ileperuma et al., 2009; Wimalawansa and Dissanayake, 2019). The direct ingestion of F^- contents above 2.0 mg/L causes kidney dysfunction in children (Xiong et al., 2007).

Fig. 4a indicates F^- showing positive trendline with pH, Na, and HCO_3^-. This infers that the alkaline pH (mean: 7.9; Table S3) with higher concentrations of Na^+ and HCO_3^- ions in groundwater favors dissolution of F^- ions from the fluoride-bearing minerals through rock-water interactions (Su et al., 2013; Subba Rao et al., 2020; Herojeet et al., 2023). The weathering processes of fluoride-bearing rocks replacing F^- ions with OH^- ions in the lattices of different minerals, namely muscovite, biotite, amphibole and hornblende, have enriched the F^- concentrations in Supebeda's groundwater (Herojeet et al., 2023).

The Gibbs diagram divulges that 88.89 % of the samples point toward rock-water interactions resulting in the elevated concentration of F^- in groundwater (Subba Rao, 2017; Adimalla and Wu, 2019). Further, the possibility of F^- enrichment in groundwater can be examined by HCO_3^-/Ca^{2+}ratio. Majority of the groundwater samples (~85 %) have HCO_3^-/Ca^{2+}ratio > 1 (Table S7), signifying that hydrogeochemical conditions are still favorable for further accumulation of fluoride ions in the study area. This is confirmed by the negative saturation indices (−2.66 to −0.68) signaling undersaturated condition of the fluoride-enriching minerals, such as fluorite (Table 1). Chowdhary et al. (2020) report that Supebeda's CDKu patients have elevated urinary fluoride levels and some of them have even radiological features of skeletal fluorosis. Fernando et al. (2020) report that the oral intake of high F^- water is the latent reason for elevated fluoride levels in urinary excretion and higher serum fluoride levels in patients suffering from CKDu in Sri Lanka. Herojeet et al. (2023) reveal that in Supebeda area, oral ingestion is the primary mode of F^- intake in all categories of population, and 80 % of the oral F^- intakes in infants and children and 50 % of such intakes in teens and adults are absorbed and retained in the body. Therefore, the susceptibility to fluorosis is, indeed, formidable in Supebeda area.

Dharma-Wardana (2018) and Balasooriya et al. (2020) consider total hardness (TH) of groundwater as one of the potential latent factors for CDKu. The classification of groundwater based on TH values (Sawyer and McCarthy, 1967) divulges that 3.70 % of the samples in Supebeda area are soft (<75 mg/L), 22.22 % are moderately hard (75–150 mg/L), 44.44 % are hard (150–300 mg/L) and 29.63 % are very hard (>300 mg/L). Wasana et al. (2016) report average water hardness of 230 mg/L in the high-CKDu-prevalent zone in North Central Province of Sri Lanka. In Supebeda study area, the mean total hardness is 257 mg/L with 44.44 % and 11.11 % of the samples above the acceptable (200 mg/L) and permissible limits (600 mg/L) of BIS (2020), respectively. The bivariate plot $Na^+ + K^+$ vs $Ca^{2+} + Mg^{2+}$ confirms that majority of the samples (77.78 %) fall below the 1:1 equiline indicating the dominance of the alkaline earths (Ca^{2+} and Mg^{2+}) over alkalis ($Na^+ + K^+$) (Fig. 2c). Thus, the dissolution of carbonate, calc-silicate, and ferromagnesian minerals in the metamorphic rocks are possibly the main sources of TH in groundwater.

The Na^+/Ca^{2+} ratio helps to understand the role of Na^+ and Ca^{2+} ions in enriching F^- concentration and enhancing hardness in

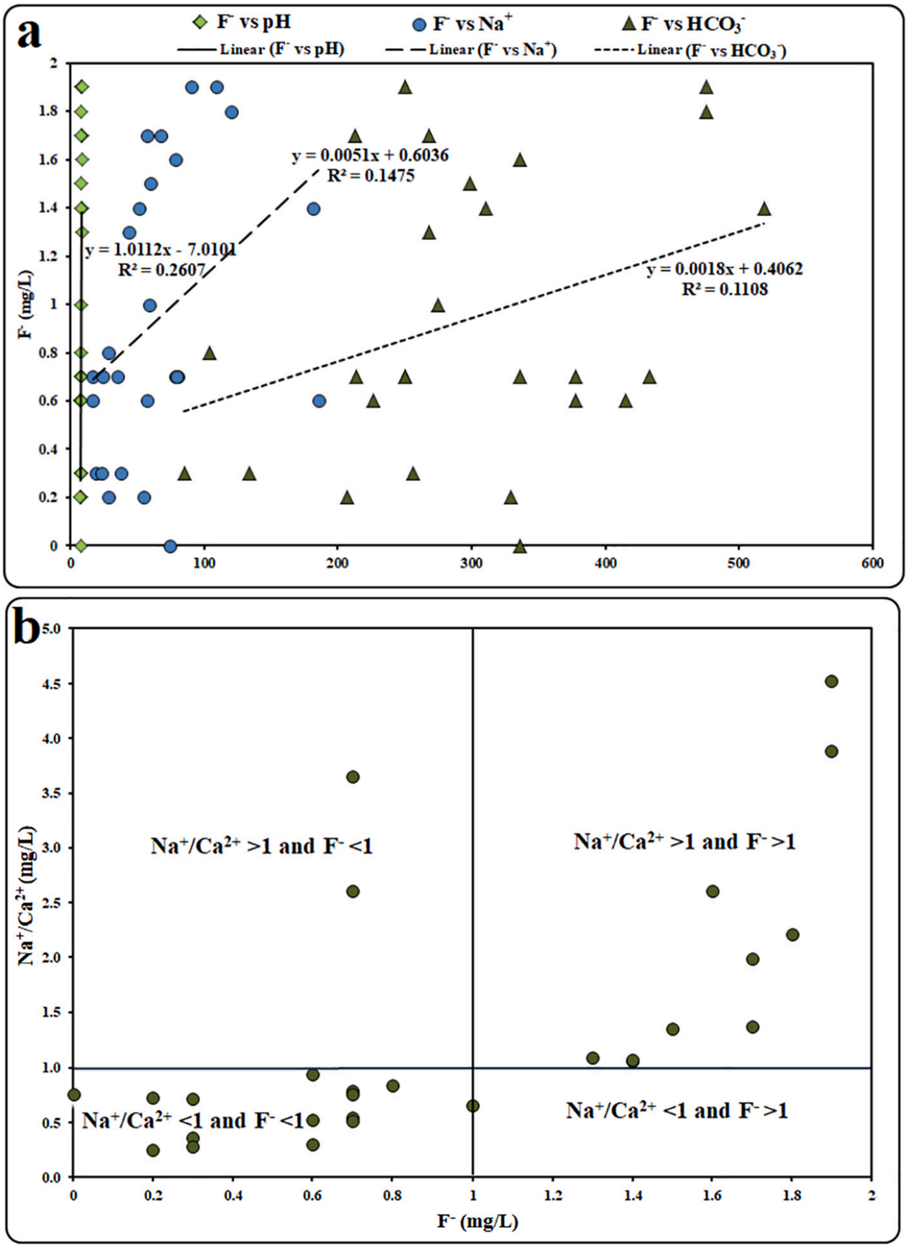

Fig. 4. Multiple binary plots of (a) F^- vs pH, Na^+, and HCO_3^-, (b) Na^+/Ca^{2+} vs F^-, (c) TH vs Ca^{2+} and Mg^{2+}, and (d) TH vs F^-.

groundwater. In a CKDu affected area in Medawachchiya, Sri Lanka, the kidney patients drink groundwater in which the Na^+/Ca^{2+} ratio range between 0.22 and 2.89 with a mean of 1.6 (Chandrajith et al., 2011). In Supebeda study area, the Na^+/Ca^{2+} ratio varies from 0.26 to 4.53 with a mean of 1.35 (Table S7). About 44 % of samples have Na^+/Ca^{2+} ratio $>$ 1, reflecting lower Ca^{2+} activity by precipitating it and increasing the Na^+ concentrations, thus favoring the enrichment of F^- ions in groundwater (Fig. 4b). The remaining 56 % of groundwater samples show Na^+/Ca^{2+} ratio $<$ 1 depicting rock-water interactions enhancing the activities of Ca^{2+} ions due to the dissolution of carbonate and silicate minerals, but F^- concentration level remaining below 1 mg/L (Fig. 4b). In fact, the saturation indices of Ca-minerals, such as anhydrite, gypsum, and fluorite, are under undersaturated condition (Table 1), and further dissolution of these minerals shall enrich the activities of Ca^{2+}, F^-, and SO_4^{2-} ions in groundwater. As per Yong and Hue (1991), endemic fluorosis is very common in areas with high F^- concentration along with high Ca^{2+} activity in groundwater. Chandrajith et al. (2011) report that F^- shows an enhanced affinity with Ca^{2+}. Therefore, as the Ca-rich unsaturated minerals get gradually saturated in-situ, there will be further enrichment of F^- ions in Supebeda's groundwater.

Liyanage et al. (2022) report that in Monaragala CKDu area in Sri Lanka, the Mg^{2+} concentration range from 4.23 to 44.2 mg/L (mean: 24.8 mg/L) with 37 % samples above the Sri Lankan drinking water standard (30 mg/L). In Supebeda study area, Mg^{2+} content varies from 3.6 to 52.8 mg/L (mean: 21 mg/L) with 11.11 % groundwater samples exceeding the acceptable limit of 30 mg/L (BIS, 2020) (Table S3). The positive loadings with strong correlation between TH vs Ca^{2+} (R^2 = 0.963) and TH vs Mg^{2+} (R^2 = 0.788) indicate alkaline earths directly contributing to the total hardness in groundwater (Fig. 4c). This possibly has a synergistic effect on the onset of CKDu in the study area (Balasooriya et al., 2020; Wasana et al., 2016).

In the same Monaragala CKDu area, the mean content of Ca^{2+} (57.7 mg/L) is 2.33 times more than that of the Mg^{2+} (24.8 mg/L) in groundwater (Liyanage et al., 2022). In another Sri Lankan CKDu area of

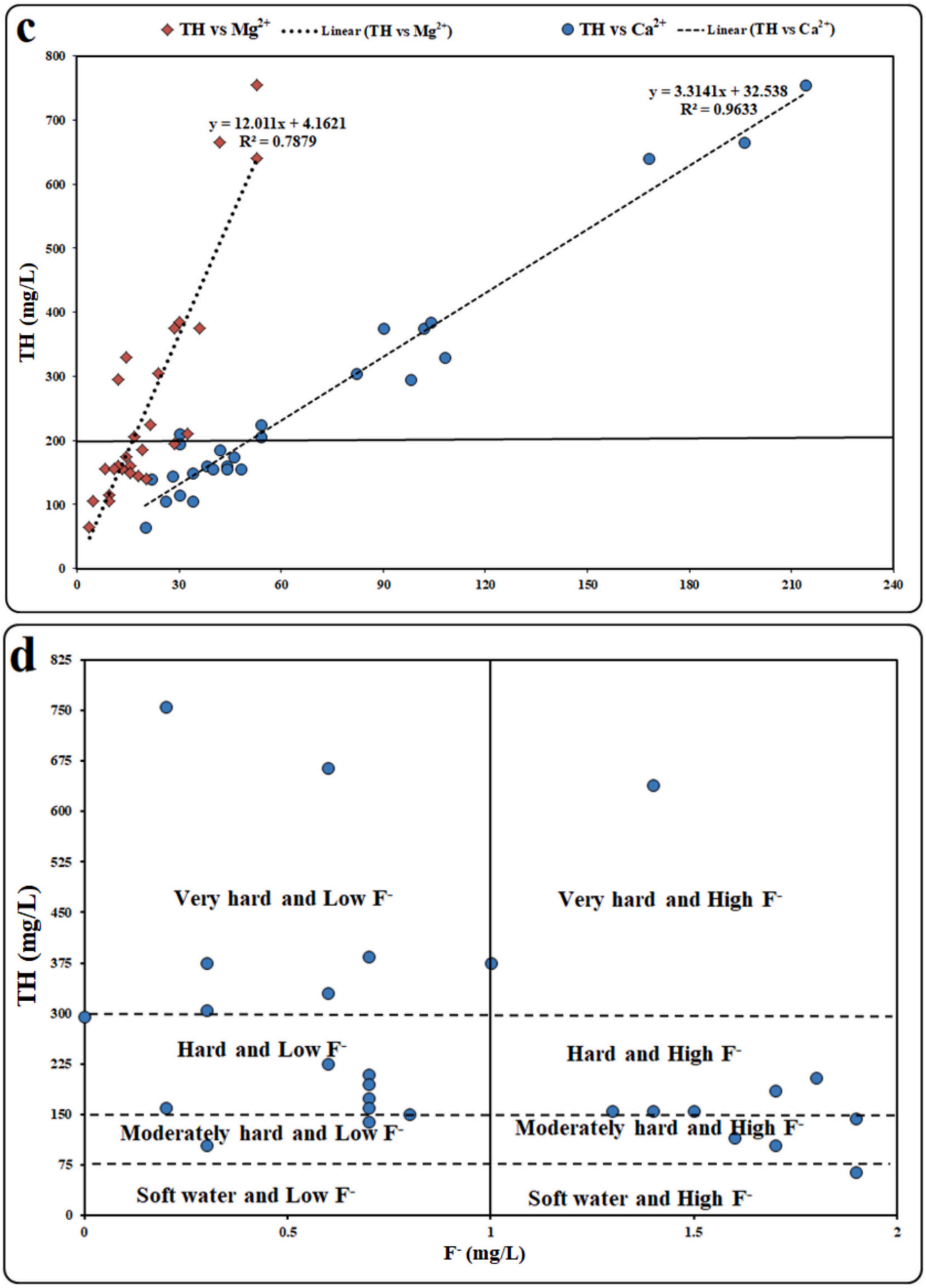

Fig. 4. (*continued*).

Ginnoruwa, Ca^{2+} mean concentration (30.7 mg/L) is 2.03 times more than that of the Mg^{2+} (15.1 mg/L) (Balasooriya et al., 2020). In Supebeda area, the mean concentration of Ca^{2+} (67 mg/L) is 3.19 times more than that of Mg^{2+} (21 mg/L) in groundwater (Table S3). Fig. 4c depicts that 44.44 % of Ca^{2+} and Mg^{2+} samples are above the TH's acceptable limit of 200 mg/L (BIS, 2020). This indicates that although the concentration of Mg^{2+} is less than Ca^{2+}, it possibly has equivalent influence in water hardness in Supebeda's hydrochemical facies, i.e., Ca^{2+}-Mg^{2+}-HCO_3^- (55.56 %), and Ca^{2+}-Mg^{2+}-Cl^--SO_4^{2-} (29.63 %) (Fig. S2).

There are studies that elucidate the presence of excess fluoride and water hardness, with higher content of Mg, causing CKDu in Sri Lanka (Liyanage et al., 2022; Chandrajith et al., 2024). Dharma-Wardan (2018) states that the influence of F^- in Mg^{2+}-hard water may cause nephrotoxicity due to the formation of paired $(Mg—F)^+$ ions. The breaking down of the $(Mg—F)^+$ ion complexes can disturb the protein structure and its functionality, enhancing the toxic nature of fluoride. All above arguments surmise that both calcium and magnesium hardness in the groundwater may induce CKDu in an area, and possibly in Supebeda too.

The binary plot of TH vs F^- (Fig. 4d) infers that about 41 % of the groundwater samples fall in moderately hard to very hard water type with higher F^- contents (≥1 mg/L), which may possibly be playing a major role in CKDu infection in Supebeda compared to the remaining 59 % samples belonging to moderately hard to very hard water category with low F^- level (<1 mg/L). To confirm this finding, as stated before, Chowdhary et al. (2020) affirm higher levels of urinary fluoride and suggestive features of skeletal fluorosis in CKDu patients from Supebeda area. Workers elsewhere find that the long-term consumption of hard water threatens urinary health with elevated risks of kidney stones (Zhao et al., 2024; Zhang et al., 2024) and kidney dysfunctions (Sengupta, 2013; Wasana et al., 2017).

Normally, high concentrations of fluoride and higher level of water hardness do not occur simultaneously (Handa, 1975; Subba Rao, 2011; Gevera and Mouri, 2018). But there are two independent processes working synchronously in Supebeda region with regard to co-occurrence of excess fluoride level as well as higher hardness in groundwater. While elevated F^- concentrations are due to the weathering of fluoride-bearing minerals (fluorite, amphiboles, biotite, hornblende, granite gneiss, etc.) through rock water interactions (Fig. S3) (Herojeet et al., 2023), an inference also reached by many other workers elsewhere before (Arveti et al., 2011; Adimalla and Venkatayogi, 2017; Su et al., 2023), the excess Ca^{2+} and Mg^{2+} ions, giving rise to water hardness, are attributed to 63 % of the samples exhibiting cation exchange processes ($Ca^{2+}, Mg^{2+}, Cl^- < Na^+ + K^+$) and weathering of carbonate (calcite, dolomite), anhydrite, gypsum, calc-silicate (anorthite, plagioclase, amphiboles) and ferro-magnesian (hornblende, biotite) minerals in the metamorphic rocks (Rajkumar et al., 2025a). Supebeda lies in a metamorphic terrain and experiences a dry sub-tropical climate where the maximum temperature reaches upto 46 °C with a prolonged dry span with limited rainfall and excessive evaporation throughout the year, except for the monsoon season. Rainfall is the primary source for groundwater recharge and as per the meteoric genesis index (*r2*) (Soltan, 1998), most groundwater samples (~63 %; Table S7) in this area fall under 'shallow meteoric water percolating' category with HCO_3^- type of chemical composition (anion) at the shallower depth (Rajkumar et al., 2025a). In such dry semi-arid conditions, the dissolved constituents, especially Ca^{2+} and Mg^{2+} ions through cation exchange processes, are readily concentrated and precipitated by evaporation in the soils, thereby releasing hardness-causing ions through the natural recharge from meteoric water as well as from irrigation infiltration. Thus, the water-sediment interactions affect the prevailing redox conditions leading to excessive water hardness in groundwater. Therefore, excess F^- ions and higher water hardness can coexist together under certain circumstances, which depend mostly on lithology and climate. This, in fact, is a unique finding coming out of this research.

In support, Wickramarathna et al. (2017) generalize that CKDu hotspot areas have high fluoride levels and high water hardness in the metamorphic terrains in the drier regions. At Supebeda, the mean concentration of TH with F^- levels ≥1 mg/L and < 1 mg/L are 209.1 mg/L (TH): 1.6 mg/L (F^-), and 289.4 mg/L (TH): 0.5 mg/L (F^-), respectively. This indicates that the TH values are above the BIS (2020) acceptable limit of 200 mg/L at both low and high F^- levels in groundwater. Such hydrochemical relationships between F^- and TH are unique features encountered in the CKDu affected regions of Sri Lanka as well (Wasana et al., 2016; Dissanayake and Chandrajith, 2019; Nanayakkara et al., 2020; Balasooriya et al., 2020; Liyanage et al., 2022). In fact, two comparative studies in Sri Lanka reveal increased water hardness and F^- concentrations in CKDu infected areas than in non-CKDu areas (Balasooriya et al., 2020; Liyanage et al., 2022).

While analyzing all these quality data, it can be inferred that the combined effects of Ca^{2+} and Mg^{2+} ions controlling the total hardness, higher Na^+/Ca^{2+} ratio, and increased F^- concentration are possibly the inducing factors for CKDu in Supebeda area. Similar results are obtained in many other CKDu infected areas in Sri Lanka too (Wasana et al., 2017; Balasooriya et al., 2020; Sandanayake et al., 2023). The synergetic impact of these parameters needs further systematic studies, ideally combined with animal models, to unravel the CKDu's etiological mechanisms.

An experimental study shows abnormal behavior of zebrafish due to the exposure to high F^+ and TH that disturb their expression gene markers linked to kidney, thus systematically impairing its functionality (Yang et al., 2022). Similarly, the oral ingestion of excess F^- and TH by experimental rats shows elevated serum creatinine levels and acute tubular injury as compared to distilled water fed control group rats (Perera et al., 2020). Further studies are needed to unravel CKDu's causative risk factors in the Supebeda region in terms of heavy metals, agrochemicals, family history, general lifestyles including frequency, type and magnitude of alcohol consumption, tobacco use, and tea consumption, etc.

3.5. *Risk complexity of exposure to Hofmeister ions*

The descriptive statistics, such as mean, standard deviation, 5th percentile (minimum), and 95th percentile (maximum) of the probabilistically estimated $ADD_{ingestion}$ values of Hofmeister ions (Ca^{2+}, Mg^{2+}, Na^+, K^+, Cl^-, SO_4^{2-}, F^-) are presented in Table 2b. The mean values of the exposure from $ADD_{ingestion}$ of these ions are less than their respective threshold values in the Hofmeister series. However, the 95th percentile ADD values of Ca^{2+} (3.63), Mg^{2+} (1.10), Na^+ (3.43), and F^- (0.05) ions are noticeably above their respective threshold values (Ca^{2+}: 2.24, Mg^{2+}: 0.81, Na^+: 2.12, and F^-: 0.03 in the Hofmeister ion series) by 9.92, 5.47, 8.88, and 14.49 %, respectively, signaling effect of possible exposure from these ions for the onset and progression of CKDu in Supebeda region (Table 2b). The higher bioavailability of these ions through their combined/cumulative interactions poses a threat to organ dysfunction, such as that of the kidney.

However, the ADD values of other ions such as K^+ (0.12), Cl^- (5.76), and SO_4^{2-} (2.64) at their 95th percentile levels are below or equal to their respective threshold limits of K^+ (0.12), Cl^- (7.20), and SO_4^{2-} (4.30) in the Hofmeister ion series. This finding depicts that the maximum exposure and the bioavailability of these ions (K^+, Cl^-, and SO_4^{2-}) through oral ingestion may not contribute to the development of CKDu in the study area.

There are credible findings that link chronic kidney problems to excess fluoride exposure, indicating different degrees of tubular epithelia injuries, namely necrosis, apoptosis, cytoplasmic vacuolation, nuclear condensation, cell swelling, and lysis (Quadri et al., 2018; Zuo et al., 2018). Further, the biochemical effects of F^- exposure inhibit collagen synthesis, eventually breaking down the collagen in kidneys as well as other body organs, such as lungs, trachea, bone, muscles, and skin (Veron et al., 1993; Yiamouyiannis, 1983). The collagen breakdown by the nephrotoxic effects of F^- exposure is a major cause of kidney dysfunction and associated problems. Studies show that about 33 % of the ingested fluoride is excreted in the urine from kidney by glomerular filtration within 24 h of intake (Jankauskas, 1974). But the content of F^- in urine discharge decreases when the kidneys are severely damaged. Instead, its concentration is significantly enhanced as serum fluoride (Exner, 2001). Chowdhary et al. (2020) confirm elevated urinary as well as serum fluoride levels in CDKu patients from Supebeda village.

Fluoride is a highly electronegative element that gets readily formed and becomes stable. Therefore, in nature, metal-fluoride complexes are poorly soluble (Dharmaratne, 2019). Ca^{2+}, Mg^{2+} and Al^{3+} are the most favorable ions to react with F^- to form stronger complexes that do not readily associate with other elements (Johnston and Strobel, 2020). Zager and Iwata (1997) report that F^- induces dose-dependent cytotoxicity that occurs through phospholipase-A_2 (PLA_2) and Ca^{2+} dependent mechanisms in cultured human proximal tubular cells. A significant clinical cytotoxicity is observed in PLA_2 enzymes at a certain F^- level, which inhibits the homeostatic and stronger cell signaling process. Borke and Whiteford (1999) suggest that both acute and chronic F^-

exposure producing high plasma F^- levels may occur in humans. This may decrease the rate of Ca^{2+} transport across endoplasmic reticulum (ER) and plasma membrane (PM) of renal tubule, thereby reducing the amount of PM and ER Ca^{2+} pump protein in the kidney membranes.

Calcium enhances the sodium-fluoride (NAF) toxicity by inducing morphological degenerative changes and impairment of tissues that fail to restore the renal cortex damages in rats (Al-tai, 2023). Even at the limited concentration of NAF, acute exposure to Ca^{2+} induces detrimental renal implications in rats. Tubular dysfunction directly results in the diluted urine, impaired protein reabsorption, and increased Ca^{2+} and phosphate urinary excretion (Santoyo-Sanchez et al., 2013).

The chronic exposure to F^-, Mg^{2+}, and Al^{3+} ions at elevated concentrations may contribute to protein denature of glomerular basement membrane which could cause synergic effects leading to chronic renal failure (Dharma-Wardana et al., 2015; Dharma-Wardana, 2018). Work by Ng et al. (2004) on the influence of F^-, Mg^{2+}, and Al^{3+} ions on the development of renal osteodystrophy (ROD) in patients reveals that the chronic exposure of F^- interferes with bone mineralization by decreasing bone microhardness and increasing osteoid content, resulting in bone disorder and osteomalacia injury. Their work also reveals that the association of Al^{3+} with F^- enhances the osteomalacic lesion, and Mg^{2+} suppresses the parathyroid hormone secretion affecting the bone turnover in aplastic bone disorder, thus leading to an increase in microhardness and bone mineralization. Further, the interaction of Mg^{2+} with Al^{3+} may exacerbate bone pain and proximal myopathy as the common ROD clinical symptoms. Thus, the effects of F^- and Mg^{2+} with Al^{3+} may be a deadly combination worsening the problem of bone quality in kidney patients.

Based on the above analyses, the excess intake of F^-, Ca^{2+}, Mg^{2+}, and Na^+ through drinking water may cause Hofmeister phenomena leading to kidney dysfunction besides having other implications, such as inhibition of tubular reabsorption, alteration in urinary ion excretion, dysfunctional pathways for kidney enzymes, interruptions in the biosynthesis of collagen, and finally the fatal renal failure. The hydrogeochemical relationships between these ions and their combined/cumulative effects are possibly the inducing factors for CKDu in Supebeda region. This argument is well-supported by the chronic exposure of the population to the Hofmeister ions at elevated levels, much above their threshold limits. Further, the *SI* values of minerals, namely fluorite, anhydrite, gypsum, and halite, are still in undersaturated state (Table 1). The dissolution of these minerals shall further enrich the concentrations of F^-, Ca^{2+}, and Na^+ ions in groundwater. Exposure to their increased ionicity through ingestion route may further aggravate the Hofmeister phenomena disrupting the most vulnerable tubular areas of the human kidney.

4. Conclusions

Various scatter plots identify the geochemical signatures and genesis of chemical parameters, such as for Ca^{2+} and Mg^{2+} (dissolution of carbonate, calcsilicate, ferromagnesian, and reverse ion exchange processes), Na^+ and K^+ (silicates, K-feldspar, cation exchange, and anthropogenic inputs), HCO_3^- (carbonate, calcsilicate, silicate, and ion exchange processes), Cl^- (halite, silicate, and anthropogenic sources), and for SO_4^{2-} (gypsum, anhydrite, and other factors). The *SI* values support the findings of the scatter plots that anhydrite, gypsum, halite, and sylvite minerals are in undersaturated states, and that further dissolution of these minerals would increase the ionic concentrations of Ca^{2+}, Na^+, K^+, SO_4^{2-}, and Cl^- in groundwater. The dissolution of K-feldspar, microcline, and kaolinite minerals has supersaturated the gibbsite and aluminum hydroxides. Further, alunite precipitation occurs due to the hydrolysis chemical reaction of K^+, Al^{3+}, and SO_4^{2-} ions in the aquifer system.

A probabilistic estimate of human health risk assessment due to exposure to Hofmeister ions by the Supebeda's population through drinking water reveals that the 95th percentile ADD values of Ca^{2+} (3.63), Mg^{2+} (1.10), Na^+ (3.43), and F^- (0.05) ions are noticeably above their respective threshold values generally found in the Hofmeister ion series, i.e., Ca^{2+} (2.24), Mg^{2+} (0.81), Na^+ (2.12), and F^- (0.03), signaling Hofmeister phenomena occurring in human kidneys due to ingestion of groundwater. These ions play a key role in 'salting-in' and 'salting-out' processes of protein complexes that cause kidney diseases due to their excess bioavailability. The percentage of water samples having these ions above their threshold values are Ca^{2+} (9.92 %), Mg^{2+} (5.47 %) Na^+ (8.88 %) and F^- (14.49 %) in Supebeda's groundwater, showing their excess bioavailability through combined/cumulative hydrogeochemical interactions.

Besides, there are credible evidences linking chronic kidney diseases to excess fluoride exposure. The combined effects of F^- and Mg^{2+} with Al^{3+} is a deadly combination worsening bone problems in kidney patients. Again, since the *SI* values of minerals, namely fluorite, anhydrite, gypsum, and halite, are still in undersaturated state, the dissolution of these minerals shall further enrich the concentrations of F^-, Ca^{2+}, and Na^- ions in groundwater. The relative increase in ionicity content of these ions through ingestion route may further aggravate the Hofmeister phenomena disrupting the most vulnerable tubular areas of the kidney.

Finally, while analyzing all quality and hydrogeochemical data, it can be inferred that the combined effects of Ca^{2+} and Mg^{2+} ions controlling the total hardness, higher Na^+/Ca^{2+} ratio, and increased F^- concentration are possibly the inducing factors for CKDu in Supebeda region. Further studies are needed to decipher CKDu's causative risk factors in terms of heavy metals, agrochemicals, family history, general lifestyles including frequency, type and magnitude of alcohol consumption, tobacco use, etc. The synergetic impact of these parameters needs closer appraisal, ideally combined with animal models, to further unravel the CKDu's etiological mechanisms.

CRediT authorship contribution statement

Rajkumar Herojeet: Writing – original draft, Visualization, Validation, Software, Methodology, Formal analysis, Conceptualization. **Pradeep K. Naik:** Writing – review & editing, Visualization, Validation, Supervision, Resources, Project administration, Formal analysis, Conceptualization. **Rakesh K. Dewangan:** Project administration, Investigation, Formal analysis, Data curation. **Janak R. Verma:** Software, Project administration, Investigation, Data curation. **Prabir K. Naik:** Resources, Investigation.

Ethics approval

The present study did not involve any human or animal experimentation.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.scitotenv.2025.178906.

Data availability

The datasets generated during and/or analyzed during the current study are already presented in the form of tables and figures in the manuscript. In case of any specific requirement, the corresponding author may please be contacted for the needful.

References

Abeysekera, D.T.D.J., Kaiyoom, S.A.A., Dissanayake, S.U., 1996. Place of peritoneal dialysis in the management of renal failure patients admitted to General Hospital Kandy. In: Kandy Society of Medicine, 18th Annual Academic Conference, Vol. 19.

Abid, S., Hassen, W., Achour, A., Skhiri, H., Maaroufi, K., Ellouz, F., Creppy, E., Bacha, H., 2003. Ochratoxin A and human chronic nephropathy in Tunisia: is the situation endemic? Hum. Exp. Toxicol. 22 (2), 77–84.

Adamek, E., Pawłowska-Go`ral, K., Bober, K., 2005. In vitro and in vivo effects of fluoride ions on enzyme activity. Ann. Acad. Med. Stetin. 51, 69–85.

Adimalla, N., Venkatayogi, S., 2017. Mechanism of fluoride enrichment in groundwater of hard rock aquifers in Medak, Telangana State, South India. Environ. Earth Sci. 76, 45. https://doi.org/10.1007/s12665-016-6362-2.

Adimalla, N., Wu, J., 2019. Groundwater quality and associated health risks in a semi-arid region of south India: implication to sustainable groundwater management. Hum. Ecol. Risk. Assess. 25 (1–2), 191–216. https://doi.org/10.1080/10807039.2018.1546550.

Agalakova, N.I., Gusev, G.P., 2012. Molecular mechanisms of cytotoxicity and apoptosis induced by inorganic fluoride. Int Sch Res Not 2012 (1), 403835.

Al-tai, F.T., 2023. Histological study of the effects of sodium fluoride and the protective role of vitamin E on the testis of albino rats. Eastern Journal of Medicine 28 (4), 585. https://doi.org/10.5505/ejm.2023.26429.

Amadi, P.A., Ofoegbu, C.O., Morrison, T., 1987. Hydrogeochemical assessment of groundwater quality in parts of the Niger Delta, Nigeria. Environ. Geol. Water Sci. 14, 195–202. https://doi.org/10.1007/BF01705131.

Aravinthasamy, P., Karunanidhi, D., Subramani, T., Srinivasamoorthy, K., Anand, B., 2020. Geochemical evaluation of fluoride contamination in groundwater from Shanmuganadhi River basin, South India: implication on human health. Environ. Geochem. Health 42, 1937–1963. https://doi.org/10.1007/s10653-019-00452-x.

Arveti, N., Sarma, M.R.S., Aitkenhead-Peterson, J.A., Sunil, K., 2011. Fluoride incidence in groundwater: a case study from Talupula, Andhra Pradesh, India. Environ. Monit. Assess. 172, 427–443. https://doi.org/10.1007/s10661-010-1345-3.

Balasooriya, S., Munasinghe, H., Herath, A.T., Diyabalanage, S., Ileperuma, O.A., Manthrithilake, H., Daniel, C., Amann, K., Zwiener, C., Barth, J.A.C., Chandrajith, R., 2020. Possible links between groundwater geochemistry and chronic kidney disease of unknown etiology (CKDu): an investigation from the Ginnoruwa region in Sri Lanka. Expo. Health 12, 823–834. https://doi.org/10.1007/s12403-019-00340-w.

Baldwin, R.L., 1996. How Hofmeister ion interactions affect protein stability. Biophys. J. 71 (4), 2056–2063.

BIS (Bureau of Indian Standards), 2020. Product Manual for Drinking Water According to IS 10500: 2012, New Delhi. https://www.bis.gov.in/wp-content/uploads/2020/10/PM-IS-10500.pdf.

Borke, J.L., Whiteford, G.M., 1999. Chronic fluoride ingestion decreases 45Ca uptake by rat kidney membranes. J. Nutr. 129, 1209–1213. https://doi.org/10.1093/jn/129.6.1209.

Brindha, K., Kavitha, R., 2015. Hydrochemical assessment of surface water and groundwater quality along Uyyakondan channel, south India. Environ. Earth Sci. 73, 5383–5393. https://doi.org/10.1007/s12665-014-3793-5.

Brindha, K., Pavelic, P., Sotoukee, T., Douangsavanh, S., Elango, L., 2017. Geochemical characteristics and groundwater quality in the Vientiane Plain, Laos. Expo. Health 9, 89–104. https://doi.org/10.1007/s12403-016-0224-8.

CGWB (Central Ground Water Board), 2001. Basic Data Report of Exploratory Drilling at Deobhog in Raipur District, Madhya Pradesh. North Central Chhattisgarh Region, Raipur, CGWB, Govt. of India.

CGWB (Central Ground Water Board), 2022. Hydrogeology of Chhattisgarh. North Central Chhattisgarh Region, Raipur, CGWB, Govt. of India.

CGWB (Central Ground Water Board), 2023. Aquifer Mapping and Groundwater Management Plan of Gariyaband District, Chhattisgarh, North Central Chhattisgarh Region, Raipur, CGWB, Govt. of India.

Chandrajith, R., Dissanayake, C.B., Ariyarathna, T., Herath, H.M.J.M.K., Padmasiri, J.P., 2011. Dose-dependent Na and Ca in fluoride-rich drinking water—another major cause of chronic renal failure in tropical arid regions. Sci. Total Environ. 409 (4), 671–675. https://doi.org/10.1016/j.scitotenv.2010.10.046.

Chandrajith, R., Nanayakkara, N., Zwiener, C., Daniel, C., Amann, K., Barth, J.A., 2024. Geochemical characteristics of groundwater consumed by patients with chronic kidney disease with unknown aetiology in the crystalline dry zone terrain of Sri Lanka. Expo. Health 16 (1), 183–195. https://doi.org/10.1007/s12403-023-00547-y.

Chowdhary, P., Rathore, V., Jain, K., Galhotra, A., Verma, N., Kale, S.A., Nagarkar, N.M., Jha, V., 2020. CKD of unknown origin in Supebeda, Chhattisgarh, India. Kidney Int Rep. 6 (1), 210–214. https://doi.org/10.1016/j.ekir.2020.10.007.

Dewangan, R., Verma, J.R., 2022. Groundwater Quality in Supebeda Area of Gariabandh District Chhattisgarh. Central Groundwater Board, North Central Chhattisgarh Region Raipur, Department of Water resources, River Development and Ganga Rejuvenation, Ministry of Jal Shakti, Government of India, pp. 1–21.

Dharmaratne, R.W., 2019. Exploring the role of excess fluoride in chronic kidney disease: a review. Hum. Exp. Toxicol. 38 (3), 269–279.

Dharma-Wardana, M.W.C., 2018. Chronic kidney disease of unknown etiology and the effect of multiple-ion interactions. Environ. Geochem. Health 40, 705–719. https://doi.org/10.1007/s10653-017-0017-4.

Dharma-Wardana, M.W.C., Amarasiri, S.L., Dharmawardene, N., Panabokke, C.R., 2015. Chronic kidney disease of unknown aetiology and groundwater ionicity: study based on Sri Lanka. Environ. Geochem. Health 37 (2), 221–231. https://doi.org/10.1007/s10653-014-9641-4.

Dinka, M.O., Loiskandlb, W., Ndambukic, J.M., 2015. Hydrochemical characterization of various surface water and groundwater resources available in Matahara areas, Fantalle Woreda of Oromiya region. J. of Hydrol. Reg. Stud. 3, 444–456. https://doi.org/10.1016/j.ejrh.2015.02.007.

Dissanayake, C., Chandrajith, R., 2019. Fluoride and hardness in groundwater of tropical regions-review of recent evidence indicating tissue calcification and calcium phosphate nanoparticle formation in kidney tubules. Ceylon J Sci. 48, 197–207. https://doi.org/10.4038/cjs.v48i3.7643.

Dolui, G., Chatterjee, S., Das Chatterjee, N., 2016. Geophysical and geochemical alteration of rocks in granitic profiles during intense weathering in southern Purulia district, West Bengal, India. Model. Earth Syst. Environ. 2, 132. https://doi.org/10.1007/s40808-016-0188-5.

Essue, B., Laba, T.L., Knaul, F., Chu, A., Minh, H., Nguyen, T.K.P., Jan, S., 2018. Economic Burden of Chronic Ill-health and Injuries for Households in Low-and Middle-income Countries. Disease Control Priorities: Improving Health and Reducing Poverty. https://opus.lib.uts.edu.au/bitstream/10453/135163/1/TL_DCP3%20Volume%209_Ch%206.pdf.

European Union (EU), 2023. European Union (Drinking Water) Regulations 2023 S.I. No. 99 of 2023, pp. 1–79.

Exner, F.B., 2001. A response to the American dental association’s booklet fluoridation facts (compiled by Anita Shattuck). In: Bennett, E. (Ed.), The Fluoride Debate. Health Way House, San Marcos, pp. 62–63 (Question 31).

Federal-Provincial Subcommittee on Drinking Water (Health Canada), 2020. Guidelines for Canadian Drinking Water Quality. Canadian Government Publishing.

Fernando, W.B.N.T., Nanayakkara, N., Gunarathne, L., et al., 2020. Serum and urine fluoride levels in populations of high environmental fluoride exposure with endemic CKDu: a case–control study from Sri Lanka. Environ. Geochem. Health 42, 1497–1504. https://doi.org/10.1007/s10653-019-00444-x.

Foreman, K.J., Marquez, N., Dolgert, A., Fukutaki, K., Fullman, N., McGaughey, M., Pletcher, M.A., Smith, A.E., Tang, K., Yuan, C.W., Brown, J.C., 2018. Forecasting life expectancy, years of life lost, and all-cause and cause-specific mortality for 250 causes of death: reference and alternative scenarios for 2016–40 for 195 countries and territories. Lancet 392 (10159), 2052–2090.

Fouque, D., Aparicio, M., 2007. Eleven reasons to control the protein intake of patients with chronic kidney disease. Nat. Clin. Pract. Nephrol. 3 (7), 383–392. https://doi.org/10.1038/ncpneph0524.

GBD-CKDC (GBD Chronic Kidney Disease Collaboration), 2020. Global, regional, and national burden of chronic kidney disease, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017. Lancet 395, 709–733. https://doi.org/10.1016/S0140-6736(20)30045-3.

Gevera, P., Mouri, H., 2018. Natural occurrence of potentially harmful fluoride contamination in groundwater: an example from Nakuru County, the Kenyan Rift Valley. Environ. Earth Sci. 77, 1–19. https://doi.org/10.1007/s12665-018-7466-7.

Gibbs, R.J., 1970. Mechanism controlling world water chemistry. Sciences 170, 795–840.

Gregory, K.P., Elliott, G.R., Robertson, H., Kumar, A., Wanless, E.J., Webber, G.B., Craig, V.S., Andersson, G.G., Page, A.J., 2022. Understanding specific ion effects and the Hofmeister series. Phys. Chem. Chem. Phys. 24 (21), 12682–12718. https://doi.org/10.1039/D2CP00847E.

Gupta, S., Bhattacharya, A., Raith, M., Nanda, J.K., 2000. Contrasting pressure–temperature–deformation history across a vestigial craton–mobile belt boundary: the western margin of the Eastern Ghats Belt at Deobhog, India. J. Metamorph. Geol. 18 (6), 683–697.

Gupta, S., Maheto, A., Roy, P., Datta, J.K., Saha, R.N., 2008. Geochemistry of groundwater, Burdwan district, West Bengal, India. Environ. Geol. 53, 1271–1282.

Handa, B.K., 1975. Geochemistry and genesis of fluoride containing groundwaters in India. Groundwater 13, 275–281. https://doi.org/10.1111/j.1745-6584.1975.tb03086.x.

Herojeet, R.K., Rishi, S.M., Sidhu, N., 2013. Hydrochemical characterization, classification, and evaluation of groundwater regime in Sirsa watershed, Nalagarh Valley, Himachal Pradesh, India. Civ. Environ. Res. 3 (7), 47–57.

Herojeet, R.K., Madhuri, S.R., Renu, L., Ranjna, G., 2016. Application of environmetrics statistical models and water quality index for groundwater quality characterization of alluvial aquifer of Nalagarh Valley, Himachal Pradesh, India. Sustain. Water Resour. Manag. 2, 39–53. https://doi.org/10.1007/s40899-015-0039-y.

Herojeet, R., Rishi, M.S., Lata, R., et al., 2017. Quality characterization and pollution source identification of surface water using multivariate statistical techniques, Nalagarh Valley, Himachal Pradesh, India. Appl Water Sci 7, 2137–2156. https://doi.org/10.1007/s13201-017-0600-y.

Herojeet, R., Dewangan, R.K., Naik, P.K., Verma, J.R., 2023. Probabilistic modelling is superior to deterministic approaches in the human health risk assessment: an example from a tribal stretch in central India. Sci. Rep. 13, 19351. https://doi.org/10.1038/s41598-023-45622-1.

Rajkumar, K., Naik, P.K., Dewangan, R.K., Verma, J.R., Naik, P.K., 2025a. Geochemical characterization of groundwater and source apportionment of potential pollutants in a tribal stretch infected with chronic kidney disease of unknown etiology (CKDu). Chemosphere.

Rajkumar, H., Dewangan, R.K., Naik, P.K., Verma, J.R., Naik, P.K., 2025b. Groundwater usage characterization in a tribal stretch infected with chronic kidney disease of unknown etiology (CKDu). J. Environ. Sci.

Hofmeister, F., 1888. On the understanding of the effects of salts. Naunyn Schmiedeberg’s Arch. Pharmacol. 24, 247–260.

Hossain, S.M.S., Haque, Md.E., Pramanik, Md.A.H., Uddin, Md.J., Al Harun, Md.A.Y., 2020. Assessing the groundwater quality and health risk: a case study on Setabganj sugar mills limited, Dinajpur, Bangladesh. Water Science 34 (1), 110–123. https://doi.org/10.1080/11104929.2020.1790184.

Hyde, A.M., Zultanski, S.L., Waldman, J.H., Zhong, Y.L., Shevlin, M., Peng, F., 2017. General principles and strategies for salting-out informed by the Hofmeister series. Org. Process. Res. Dev. 21 (9), 1355–1370.

Ileperuma, O.A., Dharmagunawardhane, H.A., Herath, K.P.R., 2009. Dissolution of aluminum from sub-standard utensils under high fluoride stress: a possible risk factor for chronic renal failure in the North-Central Province. J. Natl. Sci. Found. 37 (3), 219. https://doi.org/10.4038/jnsfsr.v37i3.1217.

Jankauskas, J., 1974. Effect of fluoride on kidney (a review). Fluoride 7, 93–105.

Jayasumana, C., Orantes, C., Herrera, R., Almaguer, M., Lopez, L., Silva, L.C., Ordunez, P., Siribaddana, S., Gunatilake, S., De Broe, M.E., 2017. Chronic interstitial nephritis in agricultural communities: a worldwide epidemic with social, occupational and environmental determinants. Nephrol. Dial. Transplant. 32 (2), 234–241.

Johnston, N.R., Strobel, S.A., 2020. Principles of fluoride toxicity and the cellular response: a review. Arch. Toxicol. 94 (4), 1051–1069.

Jolly, A.M., Thomas, J., 2022. Chronic kidney disease of unknown etiology in India: a comparative study with Mesoamerican and Sri Lankan nephropathy. Environ. Sci. Pollut. Res. 29 (11), 15303–15317. https://doi.org/10.1007/s11356-021-16548-w.

Kang, B., Tang, H., Zhao, Z., Song, S., 2020. Hofmeister series: insights of ion specificity from amphiphilic assembly and interface property. ACS Omega 5 (12), 6229–6239. https://doi.org/10.1021/acsomega.0c00237.

Khan, F., Krishnaraj, S., Raja, P., Selvaraj, G., Cheelil, R., 2021. Impact of hydrogeochemical processes and its evolution in controlling groundwater chemistry along the east coast of Tamil Nadu and Puducherry, India. Environ. Sci. Pollut. Res. 28, 18567–18588. https://doi.org/10.1007/s11356-020-10912-y.

Krishan, G., Lapworth, D.J., MacDonald, A.M., Rao, M.S., 2023. Groundwater recharge sources and processes in northwest India: evidence from high frequency water isotope observations. Journal of Hydrology: Regional Studies 50, 101570.

Kumari, R., Datta, P.S., Rao, M.S., Azad, C., 2018. Anthropogenic perturbations induced groundwater vulnerability to pollution in the industrial Faridabad District, Haryana India. Environ. Earth Sci. 77, 187. https://doi.org/10.1007/s12665-018-7368-8.

Laghrib, F., Bahaj, T., El Kasmi, S., Hilali, M., Kacimi, I., Nouayti, N., Dakak, H., Bouzekraoui, M., El Fatni, O., Hammani, O., 2024. Hydrogeochemical study of groundwater in arid and semi-arid regions of the Infracenomanian aquifers (Cretaceous Errachidia basin, Southeastern Morocco). Using hydrochemical modeling and multivariate statistical analysis. J. Afr. Earth Sci. 209, 105132. https://doi.org/10.1016/j.jafrearsci.2023.105132.

Levin, A., Okpechi, I.G., Caskey, F.J., Yang, C.W., Tonelli, M., Jha, V., 2023. Perspectives on early detection of chronic kidney disease: the facts, the questions, and a proposed framework for 2023 and beyond. Kidney Int. 103 (6), 1004–1008.

Lewith, S., 1887. Zur Lehre der Wirkung der Salze. Erste Mittheilung. Arcli. Exp. Pathol. Pharmakol. 24, 1–16.

Liu, J., Peng, Y., Li, C., Gao, Z., Chen, S., 2021. An investigation into the hydrochemistry, quality and risk to human health of groundwater in the central region of Shandong Province, North China. J. Clean. Prod. 282, 125416. https://doi.org/10.1016/j.jclepro.2020.125416.

Liyanage, D.N.D., Diyabalanage, S., Dunuweera, S.P., Rajapakse, S., Rajapakse, R.M.G., Chandrajith, R., 2022. Significance of Mg-hardness and fluoride in drinking water on chronic kidney disease of unknown etiology in Monaragala, Sri Lanka. Environ. Res. 203, 111779. https://doi.org/10.1016/j.envres.2021.111779.

Manikandan, E., Rajmohan, N., Anbazhagan, S., 2020. Monsoon impact on groundwater chemistry and geochemical processes in the shallow hard rock aquifer. Catena 195, 104766. https://doi.org/10.1016/j.catena.2020.104766.

Marghade, D., Malpe, D.B., Duraisamy, K., Patil, P.D., Li, P., 2021. Hydrogeochemical evaluation, suitability, and health risk assessment of groundwater in the watershed of Godavari basin, Maharashtra, Central India. Environ. Sci. Pollut. Res. 28, 18471–18494. https://doi.org/10.1007/s11356-020-10032-7.

Minshawy, O., 2011. End stage renal disease in El-Minia Governorate, Egypt: data of the year 2007. Nephro-Urology Monthly 3 (2), 118–121.

Nanayakkara, S., Senevirathna, S.T.M.L.D., Harada, K.H., Chandrajith, R., Nanayakkara, N., Koizumi, A., 2020. The influence of fluoride on chronic kidney disease of uncertain aetiology (CKDu) in Sri Lanka. Chemosphere 257, 127186. https://doi.org/10.1016/j.chemosphere.2020.127186.

National Health and Medical Research Council (NHMRC), 2011. Australian Drinking Water Guidelines Paper 6 National Water Quality Management Strategy. National Health and Medical Research Council, National Resource Management Ministerial Council, Commonwealth of Australia, Canberra, pp. 5–7.

Nematollahi, M.J., Clark, M.J.R., Ebrahimi, P., Ebrahimi, M., et al., 2018. Preliminary assessment of groundwater hydrogeochemistry within Gilan, a northern province of Iran. Environ. Monit. Assess. 190 (4), 242. https://doi.org/10.1007/s10661-018-6543-4.

Neogi, S., Das, N., 2000. Lithotectonic domains and metamorphic history of the boundary zone of the Eastern Ghats mobile belt and the Bastar craton, Deobhog area, Central India. Geol. Surv. India Spec. Publ. 57, 180–204.

Ng, A.H.M., Hercz, G., Kandel, R.E., Grynpas, M.D., 2004. Association between fluoride, magnesium, aluminum and bone quality in renal osteodystrophy. Bone 34 (1), 216–224.

Okiongbo, K.S., Douglas, R.K., 2015. Evaluation of major factors influencing the geochemistry of groundwater using graphical and multivariate statistical methods in Yengoa city, Southern Nigeria. Appl Water Sci 5, 27–37.

Paidi, G., Jayarathna, A.I.I., Salibindla, D.B.A.M.R., Amirthalingam, J., Karpinska-Leydier, K., Alshowaikh, K., Ergin, H.E., 2021. Chronic kidney disease of unknown origin: a mysterious epidemic. Cureus 13 (8), e17132. https://doi.org/10.7759/cureus.17132.

Perera, T., Ranasinghe, S., Alles, N., Waduge, R., 2020. Experimental rat model for acute tubular injury induced by high water hardness and high water fluoride: efficacy of primary preventive intervention by distilled water administration. BMC Nephrol. 21, 103. https://doi.org/10.1186/s12882-020-01763-3.

Piper, A.M., 1944. A graphical procedure in the geochemical interpretation of water analysis. Am Geophys Union Trans 25, 914–928. https://doi.org/10.1029/TR025i006p00914.

Purushothaman, P., Someshwar Rao, M., Rawat, Y.S., et al., 2014. Evaluation of hydrogeochemistry and water quality in Bist-Doab region, Punjab, India. Environ. Earth Sci. 72, 693–706. https://doi.org/10.1007/s12665-013-2992-9.

Quadri, J.A., Sarwar, S., Sinha, A., Kalaivani, M., Dinda, A.K., Bagga, A., Roy, T.S., Das, T.K., Shariff, A., 2018. Fluoride-associated ultrastructural changes and apoptosis in human renal tubule: a pilot study. Hum. Exp. Toxicol. 37 (11), 1199–1206.

Rajapurkar, M.M., John, G.T., Kirpalani, A.L., Abraham, G., Agarwal, S.K., Almeida, A.F., Gang, S., Gupta, A., Modi, G., Pahari, D., Pisharody, R., 2012. What do we know about chronic kidney disease in India: first report of the Indian CKD registry. BMC Nephrol. 13, 1–8.

Rajkumar, H., Naik, P.K., Singh, G., Rishi, M., 2023. Hydrogeochemical characterization, multi-exposure deterministic and probabilistic health hazard evaluation in groundwater in parts of Northern India. Toxin Rev. 42 (1), 204–227. https://doi.org/10.1080/15569543.2022.2080222.

Rathore, V., Pal, R., Galhotra, A., Nayak, S., Snehalata, Jha, V., Nagarkar, N. M., 2022. Community perception of chronic kidney disease in Supebeda, Chhattisgarh. IJCRR 14 (2), 23–28. https://doi.org/10.31782/IJCRR.2022.14210.

Revelle, R., 1941. Criteria for recognition of the sea water in ground-waters. Eos. Trans. AGU 22, 593–597. https://doi.org/10.1029/TR022i003p00593.

Sandanayake, S., Diyabalanage, S., Edirisinghe, E.A.N.V., Guo, H., Vithanage, M., 2023. Hydrogeochemical characterization of groundwater with a focus on Hofmeister ions and water quality status in CKDu endemic and CKDu non–endemic areas, Sri Lanka. Environ. Pollut. 328, 121596. https://doi.org/10.1016/j.envpol.2023.121596.

Sangwan, P., Rishi, M.S., Singh, G., 2021. Assessment of drinking water quality and non-carcinogenic health risk associated with the feed and treated water of water treatment devices (WTDs) in southwest Punjab, India. Toxin Rev. 41 (2), 536–550. https://doi.org/10.1080/15569543.2021.1906707.

Santoyo-Sanchez, M.P., del Carmen Silva-Lucero, M., Arreola-Mendoza, L., Barbier, O.C., 2013. Effects of acute sodium fluoride exposure on kidney function, water homeostasis, and renal handling of calcium and inorganic phosphate. Biol. Trace Elem. Res. 152, 367–372.

Sawyer, G.N., McCarthy, D.L., 1967. Chemistry of Sanitary Engineers, 2nd edn. McGraw Hill, New York, p. 518.

Schenk, G., Elliott, T.W., Leung, E., Mitić, N., Gahan, L.R., Guddat, L.W., 2008. Crystal structures of a purple acid phosphatase, representing different steps of this enzyme's catalytic cycle. BMC Struct. Biol. 8, 1–13.

Sengupta, P., 2013. Potential health impacts of hard water. Int. J. Prev. Med. 4 (8), 866–875.

Shi, Q., Gao, Z., Guo, H., Zeng, X., Sandanayake, S., Vithanage, M., 2023. Hydrogeochemical factors controlling the occurrence of chronic kidney disease of unknown etiology (CKDu). Environ. Geochem. Health 45 (5), 2611–2627. https://doi.org/10.1007/s10653-022-01379-6.

Shirai, Y., Miura, K., Ishizuka, K., Ando, T., Kanda, S., Hashimoto, J., Hamasaki, Y., Hotta, K., Ito, N., Honda, K., Tanabe, K., 2024. A multi-institutional study found a possible role of anti-nephrin antibodies in post-transplant focal segmental glomerulosclerosis recurrence. Kidney Int. 105 (3), 608–617. https://doi.org/10.1186/s40562-024-00343-9.

Singh, G., Rishi, M.S., Herojeet, R., Kaur, L., Sharma, K., 2020a. Multivariate analysis and geochemical signatures of groundwater in the agricultural dominated taluks of Jalandhar district, Punjab, India. J. Geochem. Explor. 208, 106395. https://doi.org/10.1016/j.gexplo.2019.106395.

Singh, G., Rishi, M.S., Herojeet, R., Kaur, L., Sharma, K., 2020b. Evaluation of groundwater quality and human health risks from fluoride and nitrate in semi-arid region of northern India. Environ. Geochem. Health 42, 1833–1862. https://doi.org/10.1007/s10653-019-00449-6.

Soltan, M.E., 1998. Characterisation, classification, and evaluation of some ground water samples in upper Egypt. Chemosphere 37 (4), 735–745. https://doi.org/10.1016/S0045-6535(98)00079-4.

Sri Lanka Standards Institution (SLS), 2013. Sri Lanka standards institution specification for potable water, first revision. In: Speciation for Portable Water, 1st edn. Sri Lanka Standards Institution.

Su, C., Wang, Y., Xie, X., Li, J., 2013. Aqueous geochemistry of high-fluoride groundwater in Datong Basin, Northern China. J. Geochem. Explor. 135, 79–92. https://doi.org/10.1016/j.gexplo.2012.09.003.

Su, C., Wang, M., Xie, X., Han, Z., Jiang, J., Wang, Z., Xiao, D., 2023. Natural and anthropogenic factors regulating fluoride enrichment in groundwater of the Nansi Lake Basin, Northern China. Sci. Total Environ. 904, 166699. https://doi.org/10.1016/j.scitotenv.2023.166699.

Subba Rao, N., 2011. High-fluoride groundwater. Environ. Monit. Assess. 176, 637–645. https://doi.org/10.1007/s10661-010-1609-y.

Subba Rao, N., 2017. Controlling factors of fluoride in groundwater in a part of South India. Arab. J. Geosci. 10, 524. https://doi.org/10.1007/s12517-017-3291-7.

Subba Rao, N., Ravindra, B., Jianhua, Wu., 2020. Geochemical and health risk evaluation of fluoride rich groundwater in Sattenapalle region, Guntur District, Andhra Pradesh, India. Hum. Ecol. Risk. Assess. 26 (9), 2316–2348. https://doi.org/10.1080/10807039.2020.1741338.

Subba Rao, N., Dinakar, A., Sravanthi, M., Kumari, B.K., 2021. Geochemical characteristics and quality of groundwater evaluation for drinking, irrigation, and industrial purposes from a part of hard rock aquifer of South India. Environ. Sci. Pollut. Res. 28, 31941–31961. https://doi.org/10.1007/s11356-021-12404-z.

Taoufiq, L., Kacimi, I., Saadi, M., Nouayti, N., Kassou, N., Bouramtane, T., El-Mouhdi, K., 2023. Assessment of physicochemical and bacteriological parameters in the Angads Aquifer (Northeast Morocco): application of principal component analysis and piper and schoeller–berkaloff diagrams. Appl. Environ. Soil Sci. 2023 (1), 2806854. https://doi.org/10.1155/2023/2806854.

Taoufiq, L., Kacimi, I., Saadi, M., Nouayti, N., Kassou, N., El-Mouhdi, K., 2024a. Monitoring the overall quality of groundwater using a geographic information system in the Angads plain (Oujda, Morocco). Sci. World J. 2024 (1), 7511804. https://doi.org/10.1155/tswj/7511804.

Taoufiq, L., Kacimi, I., Saadi, M., Mabrouki, J., Nouayti, N., Kassou, N., Bouramtane, T., El-Mouhdi, K., 2024b. Determination of the Physico-chemical and bacteriological characteristics of the groundwater of Angads (Oujda, Morocco) by principal component analysis (PCA). In: Mabrouki, J., Mourade, A. (Eds.), Technical and Technological Solutions Towards a Sustainable Society and Circular Economy. World Sustainability Series. Springer Nature Switzerland, Cham, pp. 509–518. https://doi.org/10.1007/978-3-031-56292-1_41.

Trabanino, R.G., Aguilar, R., Silva, C.R., Mercado, M.O., Merino, R.L., 2002. End-stage renal disease among patients in a referral hospital in El Salvador. Revista panamericana de salud publica=. Pan Am. J. Public Health 12 (3), 202–206.

USEPA (U.S. Environmental Protection Agency), . Exposure Factors Handbook ed (Final). http://cfpub.epa.gov/ncea/risk/recordisplay.cfm?deidD236252. US Environmental Protection Agency, Washington DC.

USEPA (US Environmental Protection Agency), 2023. National primary drinking water regulations. Available at https://www.epa.gov/ground-water-and-drinking-water/national-primary-drinking-water-regulations (Accessed June 08, 2024).

Veron, M.H., Couble, M.L., Magloire, H., 1993. Selective inhibition of collagen synthesis by fluoride in human pulp fibroblasts in vitro. Calcif. Tissue Int. 53, 38–44.

Wang, Y., Shvartsev, S.L., Su, C., 2009. Genesis of arsenic/fluoride-enriched soda water: a case study at Datong, northern China. Appl. Geochem. 24 (4), 641–649. https://doi.org/10.1016/j.apgeochem.2008.12.015.

Wang, L., Xue, N., Zhang, Y., Hu, P., 2021. Controlled hydrothermal precipitation of alunite and natroalunite in high-aluminum vanadium-bearing aqueous system. Minerals 11, 892. https://doi.org/10.3390/min11080892.

Wasana, H.M., Aluthpatabendi, D., Kularatne, W.M., Wijekoon, P., Weerasooriya, R., Bandara, J., 2016. Drinking water quality and chronic kidney disease of unknown etiology (CKDu): synergic effects of fluoride, cadmium and hardness of water. Environ. Geochem. Health 38 (1), 157–168. https://doi.org/10.1007/s10653-015-9699-7.

Wasana, H.M., Perera, G.D., Gunawardena, P.S., Fernando, P.S., Bandara, J., 2017. WHO water quality standards vs synergic effect(s) of fluoride, heavy metals and hardness in drinking water on kidney tissues. Sci. Rep. 7, 42516. https://doi.org/10.1038/srep42516.

WHO (World Health Organization), 2022. WHO guidelines for drinking water quality. In: Incorporating the First and Second Addenda, fourth ed. World Health Organization, Geneva.

Wickramarathna, S., Balasooriya, S., Diyabalanage, S., Chandrajith, R., 2017. Tracing environmental aetiological factors of chronic kidney diseases in the dry zone of Sri Lanka—a hydrogeochemical and isotope approach. J. Trace Elem. Med. Biol. 44, 298–306. https://doi.org/10.1016/j.jtemb.2017.08.013.

Wimalawansa, S.J., Dissanayake, C.B., 2019. Factors affecting the environmentally induced, chronic kidney disease of unknown aetiology in dry zonal regions in tropical countries—novel findings. Environments 7 (1), 2. https://doi.org/10.3390/environments7010002.

Wood, W.W., Smedley, P.L., Lindsey, B.D., Wood, W.T., Kirchheim, R.E., Cherry, J.A., 2022. Global groundwater solute composition and concentrations. Groundwater 60 (6), 714–720.

Xiong, X.Z., Liu, J.L., He, W.H., Xia, T., He, P., Chen, X.M., Yang, K.D., Wang, A.G., 2007. Dose–effect relationship between drinking water fluoride levels and damage to liver and kidney functions in children. Environ. Res. 103, 112–116. https://doi.org/10.1016/j.envres.2006.05.008.

Yang, Y.-F., Li, W.-G., Wen, P.-P., Jia, P.-P., Li, Y.-Z., Li, T.-Y., Pei, D.-S., 2022. Exposure to Sri Lanka's local groundwater in a CKDu prevalent area causes kidney damage in zebrafish. Aquat. Toxicol. 251, 106276. https://doi.org/10.1016/j.aquatox.2022.106276.

Yiamouyiannis, J., 1983. Fluoride, the Aging Factor, vol. 6439. Health Action Press, Delaware.

Yong, L., Hue, Z.W., 1991. Environmental characteristics of regional groundwater in relation to fluoride poisoning in North China. Environ. Geol. Water Sci. 18, 3–10.

Zager, R.A., Iwata, M., 1997. Inorganic fluoride. Divergent effects on human proximal tubular cell viability. Am. J. Pathol. 150 (2), 735–743.

Zha, Y., Qian, Q., 2017. Protein nutrition and malnutrition in CKD and ESRD. Nutrients 9 (3), 208. https://doi.org/10.3390/nu9030208.

Zhang, Y., Wu, J., Xu, B., 2018. Human health risk assessment of groundwater nitrogen pollution in Jinghui canal irrigation area of the loess region, northwest China. Environ. Earth Sci. 77 (7), 273. https://doi.org/10.1007/s12665-018-7456-9.

Zhang, Q., Xu, P., Qian, H., 2020. Groundwater quality assessment using improved water quality index (WQI) and human health risk (HHR) evaluation in a semi-arid region of Northwest China. Expo. Health 12, 487–500. https://doi.org/10.1007/s12403-020-00345-w.

Zhang, A., Yang, X., Yang, F., Zhang, C., Zhang, Q., Duan, G., Jiang, S., 2023. Research progress of the ion activity coefficient of polyelectrolytes: a review. Molecules 28 (5), 2042. https://doi.org/10.3390/molecules28052042.

Zhang, J., Luo, H., Wu, H., Qian, Y., Tang, Z., Wang, J., Li, Z., Zheng, H., Tang, F., He, Z., 2024. The association between domestic water hardness and kidney stone disease: a prospective cohort study from the UK Biobank. Int. J. Surg. https://doi.org/10.1097/JS9.0000000000002198.

Zhao, J., Wang, M., Jiang, T., Wang, F., Shi, X., Zhang, Y., Xu, K., 2024. Soft tap water urgently needed for reducing risks of kidney stones at the rural villages in Yangxin, a poverty-alleviated county in central China. Front. Water 6, 1464783. https://doi.org/10.3389/frwa.2024.1464783.

Zuo, H., Chen, L., Kong, M., Qiu, L., Lü, P., Wu, P., Yang, Y., Chen, K., 2018. Toxic effects of fluoride on organisms. Life Sci. 198, 18–24.