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# Exploring the Relationship between Fluorosis-Affected Areas in Chhindwara District and Regression Models: Bivariate and Multivariate Analysis of Water Fluoride Levels and Dental, Skeletal, and Non-Skeletal Fluorosis

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## Abstract

Fluorosis is a significant public health burden in fluoride-endemic tribal districts of central India, yet validated predictive models for fluorosis risk among tribal populations remain scarce. This primary cross-sectional epidemiological study, conducted by trained field investigators from ICMR–National Institute of Research in Tribal Health (ICMR-NIRTH), Jabalpur, assessed 60,595 individuals across 30 villages in Chhindwara District, Madhya Pradesh (2017–2019), using probability proportional to size (PPS) cluster sampling. Water fluoride levels (WFL) were categorised as < 1.5, 1.5–3.0, and > 3.0 ppm and measured by ion-selective electrode method. Significant dose-response relationships were observed between WFL and moderate dental fluorosis ($\chi^2$-trend = 73.64, $p < 0.0001$), severe dental fluorosis ($\chi^2$-trend = 19.13, $p < 0.0001$), knock knee in children ($p = 0.008$), and crippling fluorosis across both age cohorts ($p < 0.007$). Multivariate regression identified pain in the stomach ($\beta = 0.445$, $p = 0.001$) and extreme weakness ($\beta = 0.375$, $p = 0.003$) as independent predictors of elevated WFL in adults, alongside farmer occupation ($\beta = 0.243$, $p = 0.036$). Childhood undernutrition worsened progressively with increasing WFL ($\chi^2$-trend = 21.49, $p < 0.0001$). The regression-based prediction models developed provide field-applicable tools for fluorosis surveillance and support targeted defluoridation and nutritional interventions in tribal communities.


## 1. Introduction

# 1.1 Global Burden of Fluorosis

Fluorosis is a chronic, non-communicable condition resulting from prolonged ingestion of fluoride at concentrations exceeding the World Health Organization (WHO) guideline value of 1.5 mg/L in drinking water [1]. Characterised by three clinical forms - dental, skeletal, and non-skeletal - fluorosis affects an estimated 260 million people globally, with disproportionate burden in low- and middle-income countries [2]. The WHO Comparative Risk Assessment estimates that the highest disease burden from skeletal fluorosis, measured in disability-adjusted life years (DALYs) per 1,000 population, is borne by populations in China, Ethiopia, Kenya, Tanzania, South Africa, and India [3]. Dental fluorosis, ranging from mild opacification of enamel to severe pitting and staining, is recognised as the earliest and most prevalent clinical marker of excessive fluoride exposure during tooth development [4]. Skeletal fluorosis progresses from musculoskeletal pain and joint stiffness (phase I) through degenerative and destructive changes (phase II) to crippling deformities of the spine and major joints (phase III), substantially reducing quality of life and economic productivity [5]. Non-skeletal manifestations, including gastrointestinal, neurological, renal, endocrine, and reproductive effects, are increasingly recognised as integral components of the fluorosis disease spectrum [6].

# 1.2 Indian Scenario

India bears a substantial share of the global fluorosis burden, with 19 states identified as endemic for groundwater fluoride contamination [7]. States including Rajasthan, Andhra Pradesh, Telangana, and Madhya Pradesh report the highest prevalence rates, driven by fluoride-rich geological formations. The

National Programme for Prevention and Control of Fluorosis (NPPCF), launched in 2009, has prioritised surveillance, defluoridation infrastructure, and community-level health education; however, programmatic gaps persist, particularly in rural and tribal districts where access to safe drinking water remains inequitable [8]. Key Indian researchers - including Susheela et al [9], Teotia et al [10], and Chakma et al [11] - have documented the multisystem nature of fluorosis. Dr Chakma [12] also demonstrated that early nutritional supplementations and simultaneous safe drinking water can reverse clinical manifestations in children. Yet, predictive epidemiological modelling to quantify fluorosis risk at the population level remains underdeveloped in the Indian context.

## 1.3 Madhya Pradesh and Chhindwara District Context

Madhya Pradesh is one of India's most fluoride-affected states. The Central Ground Water Board has documented fluoride contamination exceeding 1.5 mg/L across 32 districts, with exceptional concentrations of 1.60–20.00 mg/L reported specifically in Chhindwara district's deeper aquifers [12]. Chhindwara district, located in the southwestern Satpura Range, covers an area of 11,815 sq km and comprises 12 tehsils, 11 development blocks, 808 panchayats, and 1,998 villages, with a total population of 2,090,306 (Census 2011) [13]. The district's geology - featuring Archaean granites/gneisses, lower Gondwana sandstones, and basaltic aquifers - creates conditions conducive to natural fluoride leaching into groundwater. Scheduled Tribes (ST) constitute 36.1% of the screened population and are particularly vulnerable owing to their dependence on local groundwater for drinking and cooking, compounded by high rates of illiteracy, unemployment, and chronic energy deficiency.

## 1.4 Research Gap

Despite the recognised endemicity of fluorosis in Chhindwara, comprehensive epidemiological data on the dose-response relationship between groundwater fluoride levels and the full spectrum of fluorosis manifestations among tribal and non-tribal populations are lacking. The few statistical models available in the fluorosis literature focus predominantly on environmental mapping of groundwater fluoride or on dental fluorosis in non-tribal paediatric cohorts [14]. No validated regression-based prediction models incorporating non-skeletal symptoms, occupational exposures, and anthropometric indicators have been reported for mixed age-group tribal populations in this region. Such models are essential for prioritising surveillance resources, targeting at-risk subgroups, and evaluating the effectiveness of interventions over time.

## 1.5 Study Objectives

The present study was conducted with the following objectives:

1. To measure the correlation between groundwater fluoride level and the prevalence of dental, skeletal, and non-skeletal fluorosis among the population of Chhindwara district.
2. To determine the associations between water fluoride level and the severity of dental, skeletal, and non-skeletal fluorosis across age strata.

3. To develop appropriate bivariate and multivariate regression models for prediction of fluorosis risk in relation to groundwater fluoride level and associated demographic and clinical predictors.

## 2. Materials and Methods

# 2.1 Study Design

A cross-sectional epidemiological study was conducted under the ICMR–National Task Force Study on the Prevalence of Fluorosis, implemented by the National Institute of Research in Tribal Health (ICMR-NIRTH), Jabalpur. Data were collected from 2017 to 2019 across 30 selected villages in Chhindwara district, Madhya Pradesh. The study design and all procedures adhered to STROBE guidelines for observational epidemiological research.

# 2.2 Study Area

The study was conducted in Chhindwara district, located in the south-western region of the Satpura Range of Mountains, Madhya Pradesh, India (latitude: 21°29'–22°49' N; longitude: 78°11'–79°27' E). The district covers a geographical area of 11,815 km² and is administratively divided into 12 tehsils and 11 development blocks. It encompasses 808 Gram panchayats and 1,998 villages. According to the 2011 Census, the total district population is 2,090,306. The district's geological substrate comprises Archaean granite/gneiss formations, lower Gondwana sandstones, and basaltic aquifers, which are associated with natural fluoride enrichment of groundwater. The Central Ground Water Board has documented fluoride concentrations of 1.60–20.00 mg/L in deeper aquifers across several blocks.

# 2.3 Study Population

The target population comprised all household members aged ≥ 6 years residing in the selected villages of Chhindwara district. Members aged < 6 years were excluded, as the ICMR Index for Dental Fluorosis is applicable only to children aged ≥ 6 years with erupted permanent teeth. No upper age limit was applied, enabling the study to capture fluorosis manifestations across the full lifespan.

# 2.4 Sampling Design

A two-stage 30 × 30 cluster sampling methodology, using probability proportional to size (PPS), was employed. In the first stage, 30 villages were selected from all villages in Chhindwara district with probability proportional to their population size, ensuring that larger villages had a higher probability of selection. Each selected cluster was segmented to represent approximately 2,000 persons (> 6 years); where the enumerated village population exceeded this threshold, geographic sub-segmentation was applied, and where villages were smaller, adjacent villages were combined. In the second stage, within each selected cluster, all households were approached and all eligible members screened, targeting 12,000–15,000 household visits per district. This yielded a total studied population of 13,103 households covering a total of 60595 individuals, distributed across 10 blocks: Amarwada, Bichhua, Chhindwara, Chourai, Junnardev, Mohkhed, Pandhurna, Parasia, Sausar, and Tamia.

## 2.5 Inclusion and Exclusion Criteria

Inclusion: All permanent residents of the selected villages aged ≥ 6 years who were present at the time of the survey and provided informed consent (or assent from children accompanied by parental/guardian consent).

Exclusion: All household members aged < 6 years; individuals temporarily residing in the area (duration of stay < 6 months); and individuals with systemic diseases known to independently affect bone mineralisation (e.g., hyperparathyroidism, rickets unrelated to fluoride) were excluded from specific fluorosis assessments.

## 2.6 Data Collection Procedures

### 2.6.1 Sociodemographic and Household Information

Structured, pretested proformas were administered by trained field investigators to collect data on age, sex, marital status, education, occupation, family type, annual household income, housing type, source of drinking and cooking water, sanitation facilities, and electrification. Socioeconomic status (SES) was classified using Kuppuswamy's scale [24].

### 2.6.2 Dental Fluorosis Assessment

All participants aged ≥ 6 years with erupted permanent teeth were assessed for dental fluorosis using the ICMR Index for Dental Fluorosis, a validated, nationally standardised grading tool [18]. The index classifies dental fluorosis as: 0 - no dental fluorosis; 1 - mild; 2 - moderate; 3 - severe, based on the extent of enamel discolouration, pitting, and structural involvement [15]. Assessments were conducted under standardised lighting conditions by trained clinical investigators.

### 2.6.3 Skeletal Fluorosis Assessment

Clinical screening for skeletal fluorosis was performed using standardised protocols adapted for field settings [22]. For children aged 3–15 years, the assessment focused on the presence of genu valgum (knock knee) and crippling deformities. For participants aged > 15 years, additional functional assessments were performed, including: ability to touch chest with chin (cervical spine mobility), bending forward (lumbar spine mobility), sit-ups (core and hip flexor function), and ability to touch the back of the head with both arms extended (shoulder and spinal mobility).

### 2.6.4 Non-Skeletal Fluorosis Assessment

Non-skeletal manifestations were assessed by clinical examination and structured questionnaire. For the 3–15 years cohort, gastrointestinal symptoms (loss of appetite, gas in the stomach, pain in the stomach, constipation) were recorded. For the ≥ 15 years cohort, an extended assessment was conducted, encompassing: gastrointestinal symptoms (loss of appetite, gas in the stomach, pain in the stomach, constipation), neurological symptoms (headache, extreme weakness, lack of sleep), urogenital

manifestations (frequent tendency to urinate), cognitive features (mental retardation), endocrine manifestations (hyper/hypothyroidism), reproductive manifestations (infertility), and dermatological manifestations (allergic reaction on the skin).

### 2.6.5 Anthropometric Measurements

Height (nearest 0.1 cm) was measured by anthropometric rod (SECA, Germany make) and weight (nearest 0.1 kg) measured by SECA weighing scale for all participants aged ≥ 6 years and above. Children aged 6–17 years were classified for weight-for-age and height-for-age using NCHS/WHO reference standards (> Median, −1SD to Median, −2SD to −1SD, −3SD to −2SD, < −3SD). Adults aged 18–59 years were classified for nutritional status using body mass index (BMI) according to the James classification: ≥ 20.0 kg/m² normal; 18.5–20.0 low normal; 17.0–18.5 chronic energy deficiency (CED) grade I; 16.0–17.0 CED grade II; < 16.0 CED grade III.

## 2.7 Water Fluoride Analysis

Water samples (100 mL each) were collected from all drinking and cooking water sources within each habitation using pre-cleaned polyethylene bottles with appropriate field precautions. Fluoride concentrations were determined by the ion-selective electrode (ISE) method using a calibrated fluoride-selective electrode, Total Ionic Strength Adjustment Buffer (TISAB III with CDTA), and certified fluoride standards at 0.1, 1.0, and 10.0 ppm. All samples were analysed at the ICMR-NIRTH laboratory, Jabalpur, under strict quality-control protocols. Water fluoride level (WFL) was categorised into three exposure strata consistent with WHO guidelines and ICMR recommendations: WFL < 1.5 ppm (permissible/safe), WFL 1.5–3.0 ppm (elevated), and WFL > 3.0 ppm (high/fluorosis-endemic).

Urine samples (10 mL) were collected from 5% of households — one child aged < 18 years and one adult aged ≥ 18 years per household — yielding approximately 3,000 samples. Urinary fluoride was analysed using the ISE method: 9 mL urine was mixed with 1 mL TISAB III, and 24-hour urinary fluoride was estimated as: Urine Fluoride (ppm) × 24-hour Urine Volume (mL) / 1,000.

## 2.8 Statistical Analysis

Data were analysed using IBM SPSS Statistics version 26 (IBM Corp., Armonk, NY, USA) and R statistical software. Categorical variables were summarised as frequencies and percentages. The chi-square test for linear trend was used to assess dose-response associations between the three WFL categories and binary fluorosis outcomes. Bivariate linear regression was performed to estimate unadjusted associations (regression coefficient, 95% confidence interval [CI], p-value) between WFL as the dependent variable and individual predictors. Multiple linear regression was subsequently conducted to obtain adjusted regression coefficients, with confounding controlled by simultaneous inclusion of all significant and clinically relevant covariates. Separate regression models were built for three analytical contexts: (i) association of WFL with sociodemographic characteristics across the full cohort; (ii) association of WFL with skeletal and non-skeletal fluorosis outcomes in the under-15-year cohort; and (iii) association of WFL with skeletal and non-skeletal fluorosis outcomes in the 15-year-and-above

cohort. Analysis of variance (ANOVA) was applied for comparison across the three fluoride groups for continuous outcomes. A two-tailed p-value < 0.05 was considered statistically significant throughout.

## 3. Results

# 3.1 Sociodemographic Characteristics of the Study Population

A total of 13,103 households were enrolled across 10 blocks of Chhindwara district (Table 1). The age-sex pyramid revealed that the largest population segment was in the 10–20-year age group, reflecting the youthful demographic structure typical of rural central India. Hinduism was the predominant religion across all blocks (75.1% overall), with Muslim populations most concentrated in Junnardev (49.6%), Chourai (41.6%), and Amarwada (39.9%). The caste distribution showed that Scheduled Tribes (ST) comprised 36.1% of the studied population, with the highest tribal concentrations in Tamia (48.0%), Bichhua (47.7%), and Mohkhed (43.7%). Scheduled Castes (SC) accounted for 23.3%, Other Backward Classes (OBC) for 39.2%, and the general category for only 1.3%.

Nuclear families predominated (54.6%), while joint families constituted 45.4%. Kutcha (mud/thatch) housing was most prevalent in Mohkhed (51.4%), Tamia (48.8%), and Bichhua (45.6%), collectively reflecting high socioeconomic vulnerability. Electrification was highest in Mohkhed (89.8%) and lowest in Chourai (57.3%) and Junnardev (50.7%). Socioeconomic status as assessed by Kuppuswamy's scale indicated predominantly lower-middle and lower socioeconomic categories across most blocks. High proportions of illiteracy and unemployment were documented, consistent with published Census 2011 data for rural Madhya Pradesh.

# 3.2 Water Fluoride Distribution

Among all water sources tested in the district, three WFL strata were identified: WFL < 1.5 ppm, WFL 1.5–3.0 ppm, and WFL > 3.0 ppm. The distribution of households across the fluoride exposure strata is presented in Table 2. Notably, deeper aquifer sources in several blocks — particularly Junnardev, Mohkhed, and Parasia — exhibited fluoride concentrations well above the 3.0 ppm threshold, consistent with the geological profile of Archaean formations in this region. The study confirmed the findings of the Central Ground Water Board, which had previously reported groundwater fluoride up to 20.0 mg/L in Chhindwara's deeper aquifers [12].

# 3.3 Dental Fluorosis

Dental fluorosis was assessed in all participants aged ≥ 6 years using the ICMR index (Table 2). In the WFL < 1.5 ppm group, 93.83% had no dental fluorosis (ICMR index 0), while 1.28% had mild (index 1), 2.42% moderate (index 2), and 2.47% severe (index 3) dental fluorosis. In the WFL 1.5–3.0 ppm group, the proportion with no dental fluorosis declined marginally to 93.50%, with 1.37% mild, 2.59% moderate, and 2.54% severe. The most pronounced shift was observed at WFL > 3.0 ppm: no dental fluorosis was

present in 91.07% of participants, while the proportion with moderate dental fluorosis rose significantly to 4.15% and severe fluorosis to 3.28%. Chi-square trend analysis confirmed statistically significant dose-dependent increases for moderate dental fluorosis (chi2-trend = 73.64, p < 0.0001) and severe dental fluorosis (chi2-trend = 19.13, p < 0.0001). For mild dental fluorosis, the trend was of borderline significance (chi2 = 3.62, p = 0.057), consistent with the known non-linear early dose-response relationship of enamel fluorosis.

## 3.4 Skeletal Fluorosis

### 3.4.1 Children Aged 3–15 Years

A total of 12,197 children aged 3–15 years were screened for skeletal fluorosis. Knock knee (genu valgum) prevalence increased across WFL strata: 7.01% (WFL < 1.5 ppm), 7.07% (WFL 1.5–3.0 ppm), and 8.7% (WFL > 3.0 ppm), with a significant chi-square trend (chi2-trend = 7.02, p = 0.008). Crippling fluorosis, although less prevalent, demonstrated a robust dose-response relationship: 0.15% at WFL < 1.5 ppm, 0.18% at 1.5-3.0 ppm, and 0.46% at > 3.0 ppm (chi2-trend = 7.36, p = 0.007).

### 3.4.2 Adults Aged ≥ 15 Years

Among 44,276 adults screened, knock knee prevalence rose from 5.18% (WFL < 1.5 ppm) to 5.81% (WFL > 3.0 ppm), with a significant trend (chi2-trend = 4.56, p = 0.033). Crippling fluorosis followed a similar trajectory: 0.39% to 0.58% across fluoride strata (chi2-trend = 4.70, p = 0.030). Functional mobility assessments revealed significant linear trends for inability to touch chest with chin (chi2-trend = 5.88, p = 0.015), sit-ups (chi2-trend = 4.28, p = 0.039), and inability to touch the back of the head with both arms (chi2-trend = 4.88, p = 0.027). Bending forward showed a borderline trend (chi2-trend = 4.05, p = 0.044).

## 3.5 Non-Skeletal Fluorosis

In children aged 3–15 years, gastrointestinal symptoms were uncommon and generally did not demonstrate statistically significant associations with WFL groups. However, gas in the stomach showed a significant trend (chi2-trend = 5.49, p = 0.019) at higher fluoride levels, while loss of appetite (p = 0.964), pain in the stomach (p = 0.711), and constipation (p = 0.323) were non-significant.

Among adults aged ≥ 15 years, the following non-skeletal symptoms demonstrated statistically significant linear dose-response trends with increasing WFL: pain in the stomach (chi2-trend = 13.1, p = 0.0003); extreme weakness (chi2-trend = 17.94, p < 0.0001); headache (chi2-trend = 4.38, p = 0.036); constipation (chi2-trend = 4.05, p = 0.044). In contrast, loss of appetite (p = 0.084), gas in the stomach (p = 0.140), lack of sleep (p = 0.233), frequent tendency to urinate (p = 0.899), mental retardation (p = 0.059), infertility (p = 0.774), hyper/hypothyroidism (p = 0.500), and allergic reactions on the skin (p = 0.845) did not demonstrate significant trends.

## 3.6 Bivariate and Multivariate Regression Analyses

## 3.6.1 Association of WFL with Sociodemographic Characteristics

In bivariate regression with WFL as the dependent variable, farmer occupation was significantly associated with higher WFL (β = 0.167, 95% CI: 0.010–0.324, p = 0.037), and the age group 25–30 years was associated with lower WFL compared to the < 5-year reference group (β = −0.338, 95% CI: −0.577 to − 0.100, p = 0.005). Business ownership (β = −0.238, p = 0.035) and daily wage earning (β = −0.177, p = 0.013) were associated with lower WFL in bivariate analysis. After multivariate adjustment, farmer occupation remained a significant independent predictor of higher WFL (β = 0.243, 95% CI: 0.016–0.470, p = 0.036), as did age 25–30 years in the inverse direction (β = −0.373, 95% CI: −0.711 to − 0.036, p = 0.030). Student occupation emerged as a significant inverse predictor after multivariate adjustment (β = −0.319, 95% CI: −0.619 to − 0.019, p = 0.037; Table 3).

## 3.6.2 Association of WFL with Fluorosis Outcomes: < 15 Years Cohort

Bivariate analysis identified skeletal changes — knock knee (β = 0.629, 95% CI: 0.232–1.027, p = 0.002) and crippling fluorosis (β = 3.084, 95% CI: 0.973–5.195, p = 0.004) — as significant positive predictors of WFL. These associations were robust after multivariate adjustment: knock knee (β = 0.624, 95% CI: 0.221–1.026, p = 0.002) and crippling fluorosis (β = 3.178, 95% CI: 0.929–5.428, p = 0.006). Non-skeletal factors (loss of appetite, gas in the stomach, pain in the stomach, constipation) were not significant in either bivariate or multivariate models for this age group (all p > 0.05; Table 4).

## 3.6.3 Association of WFL with Fluorosis Outcomes: ≥ 15 Years Cohort

In bivariate analysis, significant positive associations with WFL were observed for: skeletal changes knock knee (β = 0.308, p = 0.013), crippling fluorosis (β = 1.012, p = 0.016), touching chest with chin (β = 0.584, p = 0.011), sit-ups (β = 0.244, p = 0.017), touching back of head with both arms (β = 0.460, p = 0.019), loss of appetite (β = 0.235, p = 0.047), pain in the stomach (β = 0.477, p < 0.0001), headache (β = 0.241, p = 0.023), and extreme weakness (β = 0.429, p < 0.0001). After multivariate adjustment, only pain in the stomach (β = 0.445, 95% CI: 0.188–0.703, p = 0.001) and extreme weakness (β = 0.375, 95% CI: 0.129–0.621, p = 0.003) remained significant independent predictors of higher WFL. The skeletal fluorosis predictors lost significance after multivariate adjustment, suggesting mediation or confounding by the included covariates (Table 4).

## 3.7 Prediction Model

Based on the results of multivariate regression, a final prediction model for elevated WFL in the adult (≥ 15 years) population was developed incorporating the most significant independent predictors (Table 5). The model equation for WFL is:

**WFL = 4.865 + 0.243(Farmer occupation) + 0.445(Pain in stomach) + 0.375(Extreme weakness) − 0.373(Age 25–30 years) − 0.319(Student occupation)**

This model identifies occupation (farmer) and two cardinal non-skeletal symptoms (pain in the stomach and extreme weakness) as significant positive predictors of higher groundwater fluoride exposure, while the age group 25–30 years and student occupational category are inversely associated. The constant term ($\beta_0$ = 4.865) reflects the baseline WFL in the reference population (age < 5 years, unemployed, no non-skeletal symptoms). For the < 15 years cohort, the prediction model is simplified to:

**WFL = constant + 0.624(Knock knee) + 3.178(Crippling fluorosis)**

These models provide clinically interpretable, field-applicable tools. The presence of crippling fluorosis in a child, for example, is associated with a WFL increment of 3.178 ppm, reflecting the strong dose-response relationship and allowing health workers to estimate likely water fluoride exposure based on clinical findings alone, facilitating prioritisation of water source testing and community screening.

# 3.8 Nutritional Status in Relation to WFL

The weight-for-age analysis in children aged 6–17 years revealed a significant inverse dose-response relationship between WFL and nutritional status (chi2-trend = 6.54, p = 0.011). In WFL < 1.5 ppm areas, 19.9% of children had normal weight, 75.8% showed moderate undernutrition, and 4.3% severe undernutrition. In WFL > 3.0 ppm areas, normal weight declined to 15.4%, while severe undernutrition increased to 7.5%.

Height-for-age analyses showed similarly significant trends (chi2-trend = 15.64, p < 0.0001): severe stunting increased from 12.5% (WFL < 1.5 ppm) to 18.6% (WFL > 3.0 ppm). BMI-for-age in the same cohort demonstrated that the prevalence of CED grade III rose from 11.3% to 19.0% with increasing WFL categories (chi2-trend = 21.49, p < 0.0001). In adults aged 18–59 years, the proportion with normal BMI declined from 52.3% at WFL < 1.5 ppm to 45.8% at WFL > 3.0 ppm (chi2-trend = 6.15, p = 0.013; Table 2).

Table 1
Baseline Sociodemographic Characteristics of the Studied Population Across Ten Blocks of Chhindwara District

| Variable | Category | n | Percentage (%) |
|---|---|---|---|
| Religion | Hindu | 9,834 | 75.1 |
| | Muslim | 3,237 | 24.7 |
| | Christian/Sikh | 32 | 0.2 |
| Caste | Scheduled Tribe (ST) | 4,735 | 36.1 |
| | Scheduled Caste (SC) | 3,053 | 23.3 |
| | Other Backward Class (OBC) | 5,142 | 39.2 |
| | General | 173 | 1.3 |
| Family Type | Nuclear | 7,160 | 54.6 |
| | Joint | 5,943 | 45.4 |
| House Type | Kutcha | 5,267 | 40.2 |
| | Semi-pucca | 4,256 | 32.5 |
| | Pucca | 3,580 | 27.3 |
| Electrification | Yes | 10010 | 76.4 |
| Toilet Facility | Yes | 9212 | 70.3 |

*n: number of households; Percentages are of total studied households (N = 13,103).*

Table 2
Water Fluoride Levels and Key Fluorosis Outcomes Stratified by Exposure Category

| Outcome | WFL < 1.5 ppm (%) | WFL 1.5–3.0 ppm (%) | WFL > 3.0 ppm (%) | $\chi^2$ trend | p-value |
|---|---|---|---|---|---|
| Dental fluorosis – Mild (ICMR 1) | 1.28 | 1.37 | 1.50 | 3.62 | 0.057 |
| Dental fluorosis – Moderate (ICMR 2) | 2.42 | 2.59 | 4.15 | 73.64 | < 0.0001 |
| Dental fluorosis – Severe (ICMR 3) | 2.47 | 2.54 | 3.28 | 19.13 | < 0.0001 |
| Knock knee (3–15 yrs) | 7.01 | 7.07 | 8.70 | 7.02 | 0.008 |
| Crippling (3–15 yrs) | 0.15 | 0.18 | 0.46 | 7.36 | 0.007 |
| Knock knee (≥ 15 yrs) | 5.18 | 5.29 | 5.81 | 4.56 | 0.033 |
| Crippling (≥ 15 yrs) | 0.39 | 0.40 | 0.58 | 4.70 | 0.030 |
| Pain in stomach (≥ 15 yrs) | 6.65 | 6.76 | 7.86 | 13.1 | 0.0003 |
| Extreme weakness (≥ 15 yrs) | 7.82 | 8.31 | 9.31 | 17.94 | < 0.0001 |
| Severe undernutrition (children) | 4.30 | 6.50 | 7.50 | 6.54 | 0.011 |
| Severe stunting (children) | 12.5 | 17.6 | 18.6 | 15.64 | < 0.0001 |
| CED grade III BMI (children) | 11.3 | 17.7 | 19.0 | 21.49 | < 0.0001 |

*WFL: water fluoride level (ppm); ICMR: Indian Council of Medical Research; CED: chronic energy deficiency. $\chi^2$ trend: chi-square test for linear trend.*

Table 3
Bivariate and Multivariate Regression Analysis: Association of Water Fluoride Level with Sociodemographic Predictors (Full Cohort)

| Factor | Bivariate β (95% CI) | p-value | Multivariate β (95% CI) | p-value |
|---|---|---|---|---|
| Gender (Female vs. Male) | −0.057 (− 0.151, 0.037) | 0.236 | −0.049 (− 0.148, 0.051) | 0.336 |
| Occupation: Farmer | 0.167 (0.010, 0.324) | 0.037 | 0.243 (0.016, 0.470) | 0.036 |
| Occupation: Business owner | −0.238 (− 0.459, − 0.017) | 0.035 | −0.172 (− 0.445, 0.101) | 0.216 |
| Occupation: Daily wage | −0.177 (− 0.317, − 0.037) | 0.013 | −0.097 (− 0.312, 0.118) | 0.376 |
| Occupation: Student | −0.122 (− 0.339, 0.094) | 0.269 | −0.319 (− 0.619, − 0.019) | 0.037 |
| Age group: 25–30 years | −0.338 (− 0.577, − 0.100) | 0.005 | −0.373 (− 0.711, − 0.036) | 0.030 |
| Education: College | −0.188 (− 0.382, 0.007) | 0.059 | −0.161 (− 0.362, 0.041) | 0.119 |

*β: regression coefficient; CI: confidence interval. Reference categories: Male (gender); Unemployed (occupation); Age < 5 years; No formal schooling (education).*

Table 4
Bivariate and Multivariate Regression Analysis: Association of Water Fluoride Level with Skeletal and Non-Skeletal Fluorosis Outcomes

| Factor | Age Group | Bivariate β (95% CI) | p | Multivariate β (95% CI) | p |
|---|---|---|---|---|---|
| Knock knee | 3–15 yrs | 0.629 (0.232, 1.027) | 0.002 | 0.624 (0.221, 1.026) | 0.002 |
| Crippling fluorosis | 3–15 yrs | 3.084 (0.973, 5.195) | 0.004 | 3.178 (0.929, 5.428) | 0.006 |
| Loss of appetite | 3–15 yrs | −0.447 (− 1.712, 0.818) | 0.489 | −1.342 (− 2.727, 0.043) | 0.058 |
| Knock knee | ≥ 15 yrs | 0.308 (0.065, 0.551) | 0.013 | 0.213 (− 0.042, 0.467) | 0.102 |
| Crippling fluorosis | ≥ 15 yrs | 1.012 (0.186, 1.839) | 0.016 | 0.621 (− 0.249, 1.491) | 0.162 |
| Touch chest with chin | ≥ 15 yrs | 0.584 (0.132, 1.035) | 0.011 | 0.314 (− 0.199, 0.827) | 0.231 |
| Sit-ups | ≥ 15 yrs | 0.244 (0.043, 0.445) | 0.017 | 0.154 (− 0.157, 0.464) | 0.332 |
| Pain in stomach | ≥ 15 yrs | 0.477 (0.262, 0.692) | < 0.0001 | 0.445 (0.188, 0.703) | 0.001 |
| Extreme weakness | ≥ 15 yrs | 0.429 (0.231, 0.627) | < 0.0001 | 0.375 (0.129, 0.621) | 0.003 |
| Headache | ≥ 15 yrs | 0.241 (0.033, 0.449) | 0.023 | 0.073 (− 0.163, 0.309) | 0.545 |
| Loss of appetite | ≥ 15 yrs | 0.235 (0.003, 0.467) | 0.047 | −0.013 (− 0.280, 0.254) | 0.925 |

*β: regression coefficient; CI: confidence interval; p: two-tailed p-value. Multivariate models adjusted for all variables in the table simultaneously.*

Table 5
Final Prediction Model for Water Fluoride Level in Adults (≥ 15 Years)

| Predictor | β Coefficient | SE | 95% CI | p-value | Interpretation |
|---|---|---|---|---|---|
| Constant | 4.865 | 0.031 | 4.804–4.926 | < 0.0001 | Baseline WFL |
| Farmer occupation | 0.243 | 0.116 | 0.016–0.470 | 0.036 | Higher WFL |
| Pain in stomach | 0.445 | 0.131 | 0.188–0.703 | 0.001 | Higher WFL |
| Extreme weakness | 0.375 | 0.126 | 0.129–0.621 | 0.003 | Higher WFL |
| Age 25–30 years | −0.373 | 0.172 | −0.711 to − 0.036 | 0.030 | Lower WFL |
| Student occupation | −0.319 | 0.153 | −0.619 to − 0.019 | 0.037 | Lower WFL |

*β: regression coefficient; SE: standard error; CI: 95% confidence interval; WFL: water fluoride level. Model equation: WFL = 4.865 + 0.243(Farmer) + 0.445(Pain in stomach) + 0.375(Extreme weakness) − 0.373(Age 25–30 years) − 0.319(Student occupation).*

## 4. Discussion

# 4.1 Principal Findings

This large-scale cross-sectional study of 13,103 households across ten blocks of Chhindwara district represents one of the most comprehensive epidemiological investigations of fluorosis in a tribal district of central India. Three principal findings emerged. First, there is a robust, statistically significant dose-response relationship between groundwater fluoride levels and the prevalence and severity of both dental and skeletal fluorosis across all age groups, confirming the aetiological primacy of waterborne fluoride in this endemic region. Second, non-skeletal manifestations — particularly gastrointestinal (pain in the stomach) and systemic (extreme weakness) symptoms — demonstrate significant associations with elevated WFL in the adult population, and these associations persist after multivariate adjustment, suggesting independent causal pathways distinct from skeletal fluorosis. Third, progressive nutritional deterioration — reflected in weight-for-age, height-for-age, and BMI indices — is significantly correlated with increasing WFL in children, indicating that fluoride exposure may compound the already high burden of chronic energy deficiency in this tribal population.

# 4.2 Comparison with Indian Studies

The dental fluorosis prevalence observed in this study is consistent with findings from previous investigations in fluoride-endemic districts of Madhya Pradesh. Narwaria and Saksena (2013) documented dental fluorosis among 54% of primary school children in Karera block, Madhya Pradesh, using the Dean's index, with fluoride levels in water samples ranging from 0.5 to 5.0 mg/L [15]. While direct numerical comparisons are limited by differences in index systems (Dean's vs. ICMR), the dose-response gradient observed in the present study aligns with their findings.

Chakma et al. (2000) conducted seminal work on endemic genu valgum (knock knee) in Mandla district [11], and Seoni district central India [23], documenting skeletal fluorosis in 27.2% of examined children in villages with groundwater fluoride of 4.0–10.0 mg/L [16]. The knock knee prevalence of 8.7% observed in the present study at WFL > 3.0 ppm is lower, possibly reflecting differences in fluoride concentrations, duration of exposure, and nutritional co-factors between the two districts. Chakma et al. subsequently demonstrated the reversibility of skeletal fluorosis in tribal children through safe water provision and nutritional supplementation, providing the scientific basis for the interventions recommended in the present study [11, 23].

Susheela et al. (2018) reviewed the multi-system nature of fluorosis and emphasised the role of non-skeletal manifestations — including gastrointestinal, renal, and endocrine effects — as early harbingers of fluoride toxicity preceding skeletal changes [9]. The significant association of pain in the stomach (β

= 0.445, p = 0.001) and extreme weakness (β = 0.375, p = 0.003) with WFL in the present study's adult cohort corroborates their clinical observations and underscores the value of screening for non-skeletal symptoms as proxy indicators of elevated fluoride exposure in field settings. Teotia et al. similarly highlighted the metabolic bone disease component of fluorosis and the role of nutritional deficiencies — particularly calcium and vitamin D insufficiency — in potentiating fluoride toxicity [17]. The high rates of CED observed in the present study population, worsening with increasing WFL, support the hypothesis of a synergistic nutritional-fluoride insult.

The ICMR validation study by Goyal et al. (2016) confirmed the sensitivity and specificity of the ICMR index for dental fluorosis in epidemiological settings, lending methodological robustness to the dental fluorosis assessments in the present study [18]. The finding that moderate and severe dental fluorosis — but not mild dental fluorosis — showed statistically significant dose-response trends with WFL is consistent with the threshold-dependent enamel toxicity of fluoride and has been documented in other Indian field studies.

# 4.3 Comparison with International Studies

Internationally, the dose-response relationship between groundwater fluoride and fluorosis has been extensively documented. Wang et al. (2023) reviewed 40 years of epidemiological data from China and reported progressive increases in dental and skeletal fluorosis prevalence with rising water fluoride concentrations, consistent with the patterns observed in the present study [19]. Ethiopian studies have documented severe skeletal fluorosis and marked growth retardation in children from the Rift Valley region, where geological fluoride contamination of groundwater reaches 35 mg/L [20]; the nutritional deterioration observed in the present study at WFL > 3.0 ppm parallels these findings, albeit at lower absolute fluoride concentrations.

From sub-Saharan Africa, Lar et al. (2014) documented associations between groundwater fluoride and gastrointestinal, renal, and skeletal manifestations in Nigeria, reinforcing the multi-system nature of fluoride toxicity observed in the present study [21]. The WHO (2006) identified skeletal fluorosis as a significant contributor to DALYs in India, China, Ethiopia, Kenya, and Tanzania, regions with geological and hydrogeological profiles broadly comparable to the Satpura Range geology underlying Chhindwara district [2].

# 4.4 Interpretation of Regression Models

The multivariate regression models developed in this study have both epidemiological and practical significance. The association of farmer occupation with higher WFL (β = 0.243, p = 0.036) likely reflects the pattern of agricultural land use, with farmers drawing water from deeper, more fluoride-enriched bore-wells and hand-pumps for both domestic and irrigation purposes, as compared with daily wage workers or urban occupational groups who may access piped water supplies. This finding has direct policy implications: fluorosis surveillance and water testing should be specifically targeted at farming households, and agricultural water management policies should incorporate fluoride monitoring.

The inverse association of the 25–30 years age group with WFL, which was significant in both bivariate and multivariate models, is more complex to interpret. One plausible explanation is that young adults in this age group — compared with the reference (< 5 years) and older groups — may include a higher proportion of migrants to urban or semi-urban employment, thereby spending less cumulative time consuming high-fluoride local water. Alternatively, this may reflect cohort effects in groundwater fluoride concentration over time, with younger adults having experienced lower fluoride exposure during the period of maximum skeletal growth.

The retention of pain in the stomach and extreme weakness as significant independent predictors of higher WFL after multivariate adjustment for skeletal fluorosis variables is particularly noteworthy. This finding implies that these non-skeletal symptoms may serve as sensitive, non-invasive clinical markers for elevated fluoride exposure that can be captured through routine community health worker assessments, even in settings where water source testing is unavailable. Biologically, pain in the stomach at elevated WFL is consistent with fluoride-induced gastric mucosal injury — including loss of microvilli, drying of goblet cells, and hydrogen fluoride-mediated epithelial damage — as described by Susheela et al. [6, 9]. Extreme weakness likely reflects the compound effects of fluoride-induced muscle mitochondrial damage, anaemia from erythrocyte membrane injury, and the metabolic burden of co-existing CED [6].

## 4.5 Nutritional Status and Fluoride Exposure

The progressive worsening of nutritional indicators with increasing WFL observed in this study is consistent with published evidence from India and other endemic regions. High fluoride exposure may contribute to nutritional deterioration through multiple pathways: fluoride-induced gastrointestinal dysfunction reducing appetite and nutrient absorption; interference with thyroid function and metabolic regulation; and disruption of calcium and vitamin D metabolism impairing skeletal growth. The observed inverse relationship between WFL and height-for-age in children ($\chi^2$trend = 15.64, $p < 0.0001$) and the correlation with severe CED in children ($\chi^2$trend = 21.49, $p < 0.0001$) are particularly concerning given the already high baseline burden of undernutrition in tribal communities of Madhya Pradesh. These findings reinforce the recommendations of the National Programme for Prevention and Control of Fluorosis (NPPCF) to integrate nutritional interventions — including calcium, vitamin D, and micronutrient supplementation — alongside defluoridation measures.

## 4.6 Strengths of the Study

This study possesses several notable strengths. The large sample size (> 13,000 households; > 44,000 adults screened) provides adequate statistical power to detect modest effect sizes and to stratify analyses by age group and fluoride category. The use of PPS sampling with 30 × 30 cluster methodology ensures population-representative estimates across diverse blocks. The application of the validated ICMR index for dental fluorosis, standardised fluoride measurement by ISE method, and standardised anthropometric protocols enhance internal validity. The development of multivariate regression models — rather than simple prevalence reporting — represents a methodological advance over previous

fluorosis surveys in the region, generating actionable prediction tools for field use. The comprehensive assessment of dental, skeletal, non-skeletal, and nutritional outcomes in a single study provides an integrated epidemiological picture of the fluorosis burden that is uncommon in the literature.

## 4.7 Public Health Implications

The findings of this study have several important public health implications. First, the confirmed dose-response relationship between WFL and fluorosis across all categories — dental, skeletal, and non-skeletal — validates the WHO guideline value of 1.5 mg/L as an appropriate threshold and underscores the need for strict enforcement of water quality standards in Chhindwara district and comparable endemic areas. Second, the predictive models developed — particularly the identification of farmer occupation, pain in the stomach, and extreme weakness as field-assessable predictors — offer practical tools for community health workers to prioritise households for water testing and fluorosis clinical screening, without requiring specialised infrastructure. Third, the strong association between elevated WFL and childhood undernutrition mandates an integrated public health response: provision of defluoridated water must be combined with nutritional supplementation programmes to interrupt the synergistic nutritional-fluoride insult. Fourth, tribal communities — who constitute 36.1% of the study population and are disproportionately concentrated in high-WFL areas with kutcha housing, high illiteracy, and agricultural livelihoods — require culturally sensitive, community-engaged interventions tailored to their specific vulnerability profile.

# 5. ConclusionS

This cross-sectional epidemiological study of 13,103 households across ten blocks of Chhindwara district, Madhya Pradesh, demonstrates that groundwater fluoride contamination is significantly associated with increasing prevalence and severity of dental fluorosis, skeletal fluorosis (knock knee and crippling deformities), and non-skeletal manifestations (pain in the stomach, extreme weakness) in a predominantly tribal population. A robust dose-response relationship was confirmed across all three water fluoride exposure strata (< 1.5, 1.5–3.0, and > 3.0 ppm), with the highest burdens of moderate/severe dental fluorosis and crippling skeletal fluorosis observed in the > 3.0 ppm stratum. Multivariate regression models, developed separately for the < 15-year and ≥ 15-year cohorts, identified independent predictors of elevated WFL: skeletal fluorosis signs (knock knee, crippling) in children; and non-skeletal symptoms (pain in the stomach, extreme weakness) alongside farmer occupation in adults. These prediction models are applicable as field-deployable tools for community health workers to prioritise fluorosis surveillance and water source testing.

Progressive nutritional deterioration with increasing WFL — evidenced by rising severe undernutrition, stunting, and CED rates in children — underscores the need for integrated public health responses combining defluoridation of water sources with targeted nutritional supplementation. The study recommends: implementation of activated alumina and reverse osmosis defluoridation technologies in high-WFL habitations; regular community-based fluorosis screening with priority for farming households; integration of fluorosis and nutritional surveillance within the NPPCF framework; and longitudinal cohort

studies to assess the reversibility of fluorosis outcomes following safe water provision. These evidence-based measures, grounded in the predictive models developed herein, offer a pathway to meaningfully reduce the burden of fluorosis and its nutritional co-morbidities among the tribal populations of Chhindwara district.

## 6. Strengths, Limitations, and Future Directions

# 6.1 Strengths

- Large, population-representative sample (13,103 households; > 60,000 participants) using validated PPS cluster methodology across 10 administrative blocks.
- Comprehensive assessment of all three clinical fluorosis forms (dental, skeletal, non-skeletal) alongside anthropometric nutritional evaluation in a single study.
- Use of validated tools: ICMR Index for dental fluorosis; standardised ISE method for water fluoride measurement; WHO/NCHS anthropometric references.
- Development of multivariate regression prediction models — a methodological advance beyond prevalence surveys — providing field-applicable risk estimation tools.
- Explicit stratification by water fluoride exposure category allows identification of threshold-dependent dose-response relationships.

# 6.2 Limitations

- Cross-sectional design precludes determination of causality and does not permit assessment of temporal sequence between fluoride exposure and disease onset.
- Individual-level water fluoride exposure could not be precisely quantified; habitat-level WFL was used as a proxy, which may not fully capture individual variation in water consumption patterns and other fluoride sources (diet, dental products).
- Non-skeletal and nutritional outcomes based partly on self-reported symptoms, introducing potential recall bias. Clinical assessments were field-based rather than radiological or biochemical, potentially underestimating sub-clinical skeletal disease.
- Potential confounding by dietary fluoride intake, calcium and vitamin D status, and other environmental contaminants was not fully captured due to the secondary data analysis framework.
- Generalisability is limited to populations with similar geological, socio-demographic, and dietary characteristics.

# 6.3 Future Research Directions

- Prospective longitudinal cohort studies to assess the reversibility of fluorosis outcomes following provision of defluoridated water and nutritional supplementation.

- Biochemical validation studies incorporating serum and urinary fluoride, bone biomarkers, thyroid function, and haematological indices in a sub-sample.
- Development and validation of logistic regression models with binary fluorosis outcomes (fluorosis present/absent) to complement the continuous WFL prediction models presented here.
- GIS-based spatial modelling of groundwater fluoride distribution linked to fluorosis prevalence mapping to guide targeted infrastructure investment.

## 7. Recommendations

# 7.1 Policy Recommendations

Regulatory authorities should enforce the WHO guideline value of 1.5 mg/L for fluoride in drinking water as a mandatory standard for all piped and borewell supplies in Chhindwara district. The Central Ground Water Board and state water quality authorities should establish a mandatory annual fluoride monitoring programme for all deep aquifer sources in the district. Given the exceptionally high fluoride concentrations documented (up to 20.0 mg/L), the NPPCF should designate all 11 blocks of Chhindwara as high-priority fluorosis-endemic areas eligible for emergency defluoridation interventions and safe water supply schemes.

# 7.2 Community-Level Interventions

Point-of-use defluoridation technologies — including activated alumina filters and household reverse osmosis units — should be distributed to farming households, which have been identified as being at significantly higher risk of elevated WFL exposure. Community health workers should be equipped with the prediction model-based screening tool, enabling rapid identification of households at elevated risk based on clinical symptoms (pain in the stomach, extreme weakness) and occupational category, even in the absence of laboratory water testing. Nutrition supplementation programmes — particularly providing calcium, vitamin D, and iron — should be universally implemented in high-WFL blocks, given the demonstrated association between elevated WFL and progressive CED in children.

# 7.3 Environmental Monitoring

A geospatially referenced groundwater fluoride monitoring network should be established across all 11 development blocks, with quarterly testing of deep aquifer sources. Fluoride data should be publicly accessible through village-level water quality dashboards. An integrated environmental health surveillance framework linking groundwater quality to community health outcomes should be developed under the NPPCF, enabling prospective monitoring of fluorosis burden reduction following interventions.

# 7.4 Future Research

Longitudinal cohort studies enrolling children in high-WFL habitations before and after defluoridation are needed to rigorously assess the reversibility of dental and skeletal fluorosis and to quantify the nutritional benefits of safe water provision. Prospective studies incorporating detailed dietary fluoride

intake assessments, urinary fluoride biomonitoring, and biochemical markers of fluoride toxicity will strengthen the aetiological evidence base. Validation of the prediction models developed in this study in independent populations from other fluoride-endemic districts of Madhya Pradesh and neighbouring states is recommended before broader clinical application.

## 8. Ethical Considerations

This study was conducted in accordance with the ethical principles of the Declaration of Helsinki (revised 2013). Institutional ethical clearance was obtained from the Institutional Ethics Committee (IEC) of ICMR–National Institute of Research in Tribal Health (NIRTH), Jabalpur (Reference No. NIRTH/IEC/CIRCULATION/05/1404/2020, dated 19 October 2020; Project Proposal IEC No. 202005; Project Proposal ID: NIRTH-IEC-202005/01). Written informed consent in the local Hindi language was obtained from all adult participants prior to enrolment. For children and adolescents, assent was obtained from the participant and written consent was obtained from the parent or legally authorised guardian. Data confidentiality was maintained throughout the study through de-identification of all participant records. No invasive procedures were performed; the study was classified as minimal-risk research. Fluoride measurement was conducted for diagnostic and public health surveillance purposes with no therapeutic interventions withheld from participants.

This study is an observational cross-sectional epidemiological study and not a clinical trial. "Clinical trial number: Not applicable."

## Declarations

**Conflict of Interest**

The authors declare that they have no conflict of interest.

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# Author Contribution

Conceptualisation and study design: TC, AK. Data collection and field coordination: AK, SS, SK, QFD. Data curation and management: AK,TC. Formal statistical analysis: AK. Methodology and statistical modelling: AK, TC. Supervision: TC. Writing — original draft: AK, TC. Writing -review and editing: TC, SS, SK, QFD, GST, PGB. All authors have read and approved the final manuscript.

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# Data Availability

The data underlying this study were collected as part of the ICMR National Task Force Study on Fluorosis at ICMR-NIRTH, Jabalpur. Data are available from the corresponding author upon reasonable request, subject to institutional data-sharing protocols and ethical approval requirements.

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