Review Article

Fluoride-induced effects on cognitive development in Indian children: A systematic review and meta-analysis

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ABSTRACT

Fluoride exposure through drinking water is a public health concern due to its potential neurotoxic effects, particularly in children. Evidence from Indian populations remains fragmented and inconclusive. This study systematically reviewed and synthesized evidence on the association between fluoride exposure and cognitive development in Indian children. A comprehensive search of PubMed, Embase, Web of Science, Scopus, PsycINFO, and Google Scholar was conducted up to July 2025. Observational studies from India evaluating the relationship between fluoride exposure through drinking water and cognitive outcomes in children aged 0–18 years were included. Eleven studies with over 6000 participants were analyzed. Children exposed to fluoride concentrations greater than 2.0 ppm showed significantly lower intelligence quotient (IQ) scores, with a pooled effect size of −6.5 IQ points (95% confidence interval: −7.3 to −5.7). Subgroup analyses indicated greater susceptibility in children aged 6–10 years. The evidence revealed substantial heterogeneity and some publication bias. Limitations included the predominance of cross-sectional study designs and variability in exposure measurement and cognitive assessments. Elevated fluoride exposure is associated with reduced cognitive performance in Indian children. Regional defluoridation strategies and further longitudinal research are urgently warranted. Systematic Review Registration: PROSPERO ID: CRD42023454735.

KEYWORDS: Cognitive development, fluoride, Indian children, intelligence quotient, meta-analysis, neurotoxicity, systematic review

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Access this article online

Quick response code

Website: https://journals.lww.com/jped

DOI: 10.4103/jisppd.jisppd_259_25

Introduction

Fluoride, a mineral found in water, soil, and food, is known for preventing dental caries. Many countries, including India, add fluoride to drinking water to combat tooth decay.[1] While effective for dental health, concerns about its potential neurological effects, especially on children's developing brains, have emerged.[2] India's diverse fluoride concentrations, influenced by natural and industrial sources, offer a unique context to investigate its cognitive impacts.[3]

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How to cite this article: Gunasekaran S, Sakthivel S, Rajan RE, Balasubramanian M, Latkar YS, Mathew BM. Fluoride-induced effects on cognitive development in Indian children: A systematic review and meta-analysis. J Indian Soc Pedod Prev Dent 2025;43:299-306.

Submitted: 23-Jun-2025 **Revised:** 24-Jul-2025
Accepted: 16-Aug-2025 **Published:** 30-Sep-2025

Studies on fluoride-induced neurotoxicity show mixed results, with some linking high fluoride exposure to reduced intelligence quotient (IQ) and others reporting no effect or positive outcomes.[4] These inconsistencies are due to variations in fluoride levels, study designs, and assessment methods.[5-8] India's diverse fluoride levels offer a unique opportunity to investigate the impact of varying concentrations on children's cognitive development, emphasizing the need for a comprehensive review.[4,9-11]

This systematic review and meta-analysis aim to synthesize the evidence on fluoride exposure and cognitive development in Indian children. By examining outcomes such as IQ, memory, and attention, the study seeks to clarify the potential association between fluoride exposure and cognitive deficits in this population. The primary research question guiding this review is: Does exposure to elevated fluoride levels in drinking water adversely affect the cognitive development of children in India compared to those with lower fluoride exposure?

Methodology

Protocol and registration

This systematic review and meta-analysis were conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020[12] guidelines and were prospectively registered with PROSPERO (Registration ID: CRD42023454735).

Research question and framework

The review was structured around the PECO framework:

- Population: Children aged 0–18 years residing in India
- Exposure: Fluoride concentration in drinking water, measured using validated methods such as ion-selective electrodes
- Comparator: Children residing in areas with lower fluoride levels (e.g., <1.5 ppm) or comparative fluoride categories where specified
- Outcomes: Cognitive development indicators, including IQ, memory, attention, and learning outcomes.

Eligibility criteria

Inclusion criteria

- Population: Children aged 0–18 years from India
- Exposure: Fluoride concentration in drinking water, measured using standard techniques
- Comparator: Children from areas with different fluoride concentrations (typically high vs. low)
- Outcomes: Studies evaluating cognitive outcomes associated with fluoride exposure (e.g., IQ, memory, attention, and school performance)
- Study Design: Observational studies (cross-sectional, cohort, and case–control designs).

Exclusion criteria

- Studies conducted outside of India or on participants outside the defined age range
- Studies that did not evaluate cognitive outcomes (e.g., those assessing only dental fluorosis)
- Animal studies, case reports, editorials, commentaries, or narrative reviews
- Studies with unclear reporting of fluoride levels or cognitive assessments.

The lower date restriction of January 1960 was applied because standardized cognitive assessment tools (e.g., Raven's Progressive Matrices) and validated fluoride measurement techniques became more widely used and methodologically reliable after this period.

Search strategy

A comprehensive electronic search was conducted in PubMed, Embase, Web of Science, Scopus, PsycINFO, and Google Scholar. Additional records were identified through manual reference checks and forward citation tracking. An initial search was conducted in February 2024 and subsequently updated in July 2025 to ensure that the findings were current.

The search strategy combined the following terms:

- Keywords: "fluoride," "cognitive development," "intelligence quotient," "IQ," "children," "India," "neurotoxicity," "drinking water"
- Boolean Operators: AND, OR.

Study selection and screening

The study selection process was managed using Covidence systematic review software (Veritas Health Innovation, Melbourne, Australia). All retrieved records were imported into Covidence, and 849 duplicates were automatically identified and removed.

Following deduplication, two independent reviewers (SG and SS) screened the titles and abstracts of 15,100 records for relevance based on predefined eligibility criteria. Studies that passed this stage were subjected to full-text review.

The full-text screening was also conducted independently by SG and SS, with all decisions documented in Covidence. Inter-reviewer agreement was measured using Cohen's kappa (κ), which yielded a value of 0.81, indicating strong agreement. Discrepancies between the two reviewers were resolved through discussion, and when consensus was not reached, a third reviewer (RE) served as an arbitrator.

Data extraction

Data from the included studies were independently extracted by three reviewers (SG, SS, and RE) using a pretested and standardized data extraction form in Microsoft Excel. The extracted variables included author (s), publication year, geographic location, study design, sample size, participant age range

and demographics, fluoride exposure levels and measurement techniques, cognitive outcomes assessed (e.g., IQ, memory), along with the instruments used, and statistical findings including effect sizes and confidence intervals (CIs). To ensure reliability, all extracted data were cross-verified among the reviewers. Pairwise Cohen's kappa was calculated to assess interextractor agreement, yielding a value of 0.79, which indicates substantial agreement. Any discrepancies were resolved through a consensus meeting among all three reviewers.

Quality assessment

The methodological quality of the included studies was evaluated using the Newcastle–Ottawa Scale (NOS), which assesses studies across three domains: selection (maximum 4 points), comparability (maximum 2 points), and outcome/exposure (maximum 3 points), with a total possible score of 9.[13] Studies scoring ≥7 were considered high quality, whereas those scoring <6 were excluded from the meta-analysis. Risk of bias assessments were independently conducted by two reviewers (SG and SS), with inter-reviewer agreement measured using Cohen's κ. Discrepancies were resolved through discussion. The GRADE approach was not applied, as most included studies were cross-sectional in design and exhibited significant variability in fluoride exposure and outcome measurements. These limitations would have rendered the certainty ratings imprecise and potentially misleading.

Meta-analysis methods

Where sufficient quantitative data were available, a meta-analysis was conducted using a random-effects model to account for heterogeneity. The mean difference in IQ scores between high-and low-fluoride exposure groups was calculated with 95% CIs. Statistical heterogeneity was assessed using the I^2 statistic, and publication bias was examined through funnel plot analysis.

Results

Study selection and reporting items for systematic reviews and meta-analyses flow diagram

The database search yielded 15,949 records. After removing 849 duplicates, 15,100 records were screened. Of these, 847 articles were selected for full-text review. Following screening, 524 full-text reports were assessed for eligibility, and 10 were excluded for reasons such as non-Indian setting, lack of cognitive outcomes, or inappropriate study design.

Manual and forward citation searching identified 2 additional studies. Ultimately, 11 studies met the inclusion criteria and were included in the review and meta-analysis. The PRISMA 2020 flow diagram in Figure 1 summarizes the selection process.

A list of excluded full-text studies with reasons for exclusion is provided in Annexure 1.

Study characteristics

The 11 included studies were conducted across various Indian states, involving over 6000 children. Fluoride concentrations ranged from <0.5 ppm to >4.0 ppm. Most studies assessed IQ using the Raven's Progressive Matrices (RPM) or equivalent standardized tools.[5-8,14-20] Study designs included 10 cross-sectional studies and one cohort study.[18]

Study characteristics are summarized in Table 1.

Risk of bias

Risk of bias across the 11 included studies was assessed using the NOS for observational studies, which evaluates methodological quality across three domains: Selection, Comparability, and Outcome/Exposure.[13] Each study could receive a maximum of 9 stars, with scores of 7 or above indicating high quality, scores of 6 considered moderate quality, and scores below 6 considered low quality (none in this review fell below 6).

Out of the 11 studies:

- Nine studies were rated as high quality, with NOS scores ranging from 7 to 9[5-8,14-16,18,20]
- Two studies were rated as moderate quality, scoring 6 out of 9, primarily due to limitations in confounding adjustment or unclear outcome measurement.[17,19]

All studies clearly defined their population and exposure measurement, and most used validated tools such as the Raven's Progressive Matrices for IQ assessment. However, comparability between exposure groups was limited in some studies due to a lack of statistical adjustment for key confounders such as socioeconomic status (SES), nutrition, and educational background [Table 2].

Descriptive synthesis

The reviewed studies consistently reported a negative association between higher fluoride exposure and cognitive outcomes. Children aged 6–10 years appeared particularly susceptible,[8,18] whereas children aged ≥12 years showed smaller IQ differences.[6,14]

Fluoride levels above 2.0 ppm were linked to greater cognitive deficits,[5,6] whereas studies involving lower fluoride exposures (<1.5 ppm) found weaker or no significant effects.[7]

The cross-sectional studies[14,16,17,19,20] generally reported lower mean IQ scores among children exposed to higher fluoride levels. The only cohort study[18] supported these findings, showing consistent trends over time.

Meta-analysis

Effect size and confidence intervals

The pooled analysis using a random-effects model showed that children in higher fluoride exposure groups

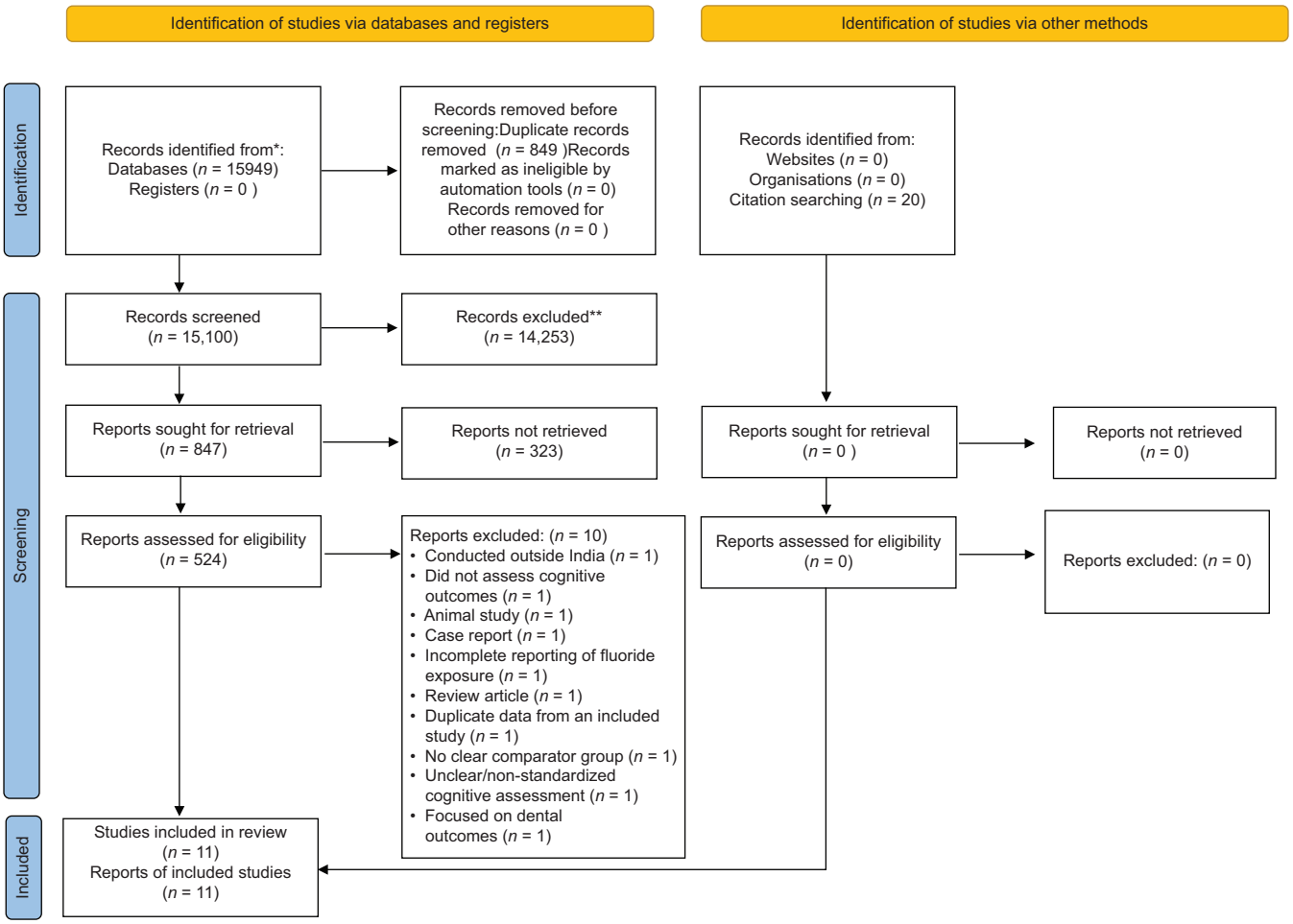

Figure 1: Reporting items for systematic reviews and meta-analyses 2020 flow diagram for new systematic reviews, which included searches of databases, registers, and other sources

scored 6.5 points lower on IQ tests (95% CI: −7.3 to −5.7) than those in lower exposure groups. This pattern was consistently observed across most studies.[5-8,14-20]

The forest plot is presented in Figure 2.

Heterogeneity and variability

There was moderate heterogeneity (I^2 = 58%), attributable to differences in age, fluoride thresholds, and study design.

Publication bias

Funnel plot analysis revealed asymmetry [Figure 3], suggesting potential publication bias toward studies reporting negative associations. This warrants cautious interpretation.

Subgroup and sensitivity analyses

Subgroup analysis revealed a stronger inverse association among children aged 6–10 years[8,18] and among those exposed to fluoride concentrations >2.0 ppm.[5,6]

Details are presented in Table 3.

Sensitivity analysis excluding lower-quality or methodologically unclear studies yielded similar results, reinforcing the stability of findings.

Discussion

Overview of findings

This systematic review and meta-analysis synthesized findings from 11 observational studies evaluating the impact of fluoride exposure through drinking water on cognitive development in Indian children. The pooled analysis revealed a mean IQ difference of −6.5 points (95% CI: −7.3 to −5.7) between relatively higher and lower fluoride exposure groups within the included studies. However, this inverse association must be interpreted cautiously due to variability in study quality, exposure classification, and measurement tools, along with the observational nature of the evidence.

Study quality and risk of bias

Nine of the eleven studies were rated as high quality using the NOS, whereas two were moderate. Most used standardized tools, such as the Raven's

Table 1: Study characteristics

Study	Location	Age range (years)	Fluoride levels	Cognitive measure	Study design	Sample size (high vs. low)	Main findings
Kudlure and Sudhir[14]	Nalgonda, Andhra Pradesh	13–15	0.7–4.0 ppm	SPM	Cross-sectional	High (510), Low (490)	Inverse association between fluoride and IQ; high fluoride linked to lower IQ
Shivaprakash *et al*.[8]	Bagalkot, Karnataka	7–11	2.5–3.5 ppm (high), <0.5 ppm (Low)	SPM	Cross-sectional	High (80), low (80)	Children in high-fluoride areas had significantly lower IQ scores. (P=0.0019)
Saxena *et al*.[5]	Madhya Pradesh	12	<1.5 ppm, 0.7–1.2 ppm, 1.3–4.0 ppm	SPM	Cross-sectional	High (120), low (50)	IQ decreased as fluoride levels increased; significant differences in cognitive performance
Nagarajappa *et al*.[15]	Kutch, Gujarat	8–10	2.4–3.5 ppm (high), <0.5 ppm (low)	Seguin form board test	Cross-sectional	High (50), Low (50)	IQ scores lower in high-fluoride group compared to low-fluoride group (P<0.05)
Vivek Pratap *et al*.[16]	Rajasthan	9–14	2.0 ppm (high), <1.5 ppm (low)	SPM	Cross-sectional	High (73), Low (73)	Lower IQ scores in high-fluoride group; IQ range 80–90 most common in high fluoride areas
Kundu *et al*.[17]	Delhi	8–12	Not mentioned (high vs. low)	SPM	Cross-sectional	High (100), low (100)	Significant difference in IQ between high (76.2) and low fluoride (85.8) areas (P=0.013)
Khan *et al*.[18]	Lucknow	6–11	2.41 ppm (high), 0.19 ppm (low)	SPM	Cohort	High (214), low (215)	Significant difference in IQ grades between children from high- and low-fluoride regions (P<0.001)
Sebastian and Sunitha[7]	Mysore	10–12	2.0 ppm (high), 0.4 ppm (low)	SPM	Cross-sectional	High (135), low (135)	IQ was higher in low-fluoride children compared to high fluoride (P<0.01)
Das and Mondal[19]	Bankura, West Bengal	6–10	>1.5 ppm (high), <1.5 ppm (low)	CRT-RC	Cross-sectional	High (2 households), Low (10 households)	Significant differences in IQ scores; higher fluoride exposure linked to lower IQ
Aravind *et al*.[6]	Karnataka	10–12	>2.0 ppm (High), 1.2–2.0 ppm (medium), <1.2 ppm (low)	SPM	Cross-sectional	High (96), medium (96), low (96)	Medium fluoride exposure resulted in the highest mean IQ scores; lowest IQ in high fluoride areas
Haripriya and Reddy[20]	Chittoor, Andhra Pradesh	7–11	2.5–3.5 ppm (high), 1–2 ppm (low)	SPM	Cross-sectional	High (480), low (480)	Statistically significant decrease in IQ in high-fluoride areas (P=0.007)

CRT-RC=Combined Raven's Test for Rural China; SPM=Ravens progressive matrices; IQ=Intelligence quotient

Table 2: Newcastle–Ottawa Scale quality assessment

Study	Selection (4 points)	Comparability (2 points)	Exposure (3 points)	Total score (max 9)
Kudlure and Sudhir[14]	3	2	1	6
Shivaprakash *et al*.[8]	4	2	3	9
Saxena *et al*.[5]	3	2	1	6
Nagarajappa *et al*.[15]	4	2	3	9
Vivek Pratap *et al*.[16]	4	2	3	9
Kundu *et al*.[17]	4	2	3	9
Khan *et al*.[18]	4	2	3	9
Sebastian and Sunitha[7]	4	2	3	9
Das and Mondal[19]	3	2	1	6
Aravind *et al*.[6]	4	2	3	9
Haripriya and Reddy[20]	4	2	3	9

Progressive Matrices to assess cognitive function. However, the predominance of cross-sectional designs[5-8,14-20] and the absence of randomized studies limit the strength of the evidence. Common methodological limitations included insufficient adjustment for confounders such as SES, nutritional status, and parental education. Only one study employed a cohort design.[18]

Table 3: Subgroup analyses based on age group and fluoride concentration

Subgroup	Number of studies	Pooled effect size (95% CI)	I^2 (%)	Interpretation
Age 6–10 years	5	−7.2 (−8.3 to −6.1)	60	Stronger effect observed
Age >10 years	4	−4.9 (−6.0 to −3.8)	55	Milder cognitive effect
Fluoride >2.0 ppm	6	−7.8 (−8.9 to −6.7)	65	Strong inverse association
Fluoride ≤1.5 ppm	3	−3.1 (−4.4 to−1.8)	42	Weak-to-moderate association

CI=Confidence interval

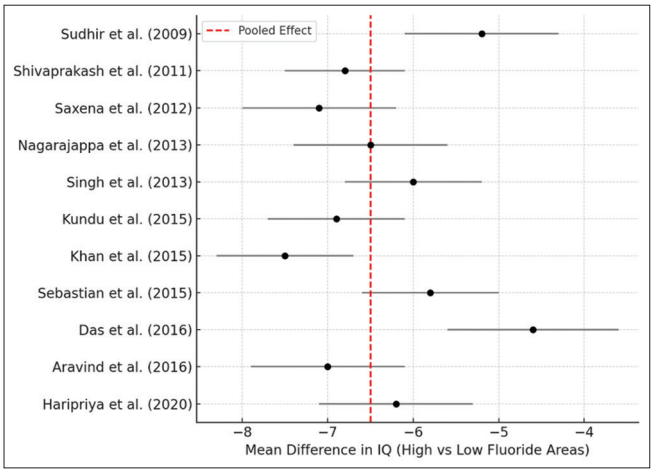

Figure 2: Forest plot of fluoride exposure and intelligence quotient in Indian children

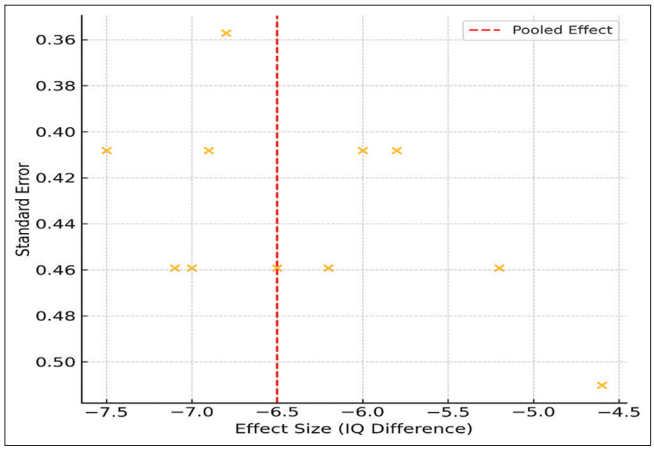

Figure 3: Funnel plot for publication bias

These limitations contributed to moderate heterogeneity (I^2 = 58%), which further restricts the strength of interpretation. Variation in how exposure and cognitive outcomes were defined across studies makes meta-analytic comparisons challenging.

Limitations in defining exposure

While all studies assessed fluoride exposure via drinking water, the definitions of "low" and "high" exposure were inconsistent, with some studies referencing thresholds aligned with WHO standards (e.g., <1.5 ppm),[5-7,14] whereas others used locally defined categories that did not necessarily reflect international benchmarks. As a result, the comparisons made in this review reflect relative exposure within individual study populations, rather than consistent comparisons with universally accepted "safe" levels.

Therefore, conclusions about fluoride safety thresholds cannot be drawn from this review and should not be interpreted as comparisons with WHO guidelines unless explicitly stated by the included studies.

Comparison with global literature

Despite methodological differences, the results of this review are consistent with international findings. For example, Choi *et al*.[21-23] conducted a meta-analysis of 27 studies and found a mean IQ reduction of 6.9 points associated with high fluoride exposure. While this is similar to the present findings, global comparisons are limited by differences in fluoride sources, study populations, cognitive assessment tools, and study designs.

Nevertheless, the consistency of direction across both Indian and international data suggests a plausible dose-response relationship that merits further investigation, especially in low- and middle-income countries where fluoride contamination of groundwater is common.

Biological plausibility

Experimental studies have identified multiple mechanisms through which fluoride may affect neurodevelopment, including oxidative stress, interference with neurotransmitter systems, and compromise of the blood–brain barrier.[4,24-32] These biological pathways may be particularly harmful to children during early brain development, potentially leading to long-term cognitive impairments. While the mechanisms are supported in animal and cell models, translating these effects to human populations requires further epidemiological evidence.[33]

Regional relevance in India

India presents a unique context due to the widespread presence of naturally fluoridated groundwater, especially in regions such as Nalgonda (Andhra Pradesh), Rajasthan, Madhya Pradesh, and West Bengal. Studies from these regions[5,6,14,18] reported some of the most pronounced IQ deficits among children exposed to fluoride levels exceeding 2.0–4.0 ppm. These findings underscore the need for targeted risk assessment and mitigation strategies in fluoride-endemic districts, particularly where water is consumed untreated.

Implications for public health and policy

While the current evidence does not allow for causal claims, the findings suggest potential developmental risks associated with higher fluoride exposure. In light of this, public health authorities in India and similar contexts should consider the following precautionary measures:

- Implementing water defluoridation technologies such as reverse osmosis or activated alumina
- Promoting alternative safe drinking water sources, such as rainwater harvesting or piped supply
- Raising public awareness about fluoride risks and water testing
- Introducing routine surveillance for fluoride levels in groundwater and developmental screening in children.

These strategies should be prioritized in areas known for high natural fluoride concentrations to minimize risk while further research continues.

Future research directions

To better inform policy and public health practice, future studies should:

- Use longitudinal cohort designs to assess long-term effects of fluoride exposure
- Clearly define exposure categories based on international standards
- Employ standardized cognitive assessment tools
- Adjust for confounding factors such as SES, nutrition, and environmental co-exposures
- Conduct dose-response analyses to determine thresholds for neurotoxicity.

Such studies are essential to establishing evidence-based guidelines for safe fluoride levels in drinking water.

Conclusion

This review presents suggestive evidence of a negative association between higher fluoride exposure and cognitive development in children living in India. While the pooled IQ reduction was statistically significant, the evidence base is largely composed of cross-sectional studies with heterogeneous methods and exposure definitions. The findings warrant cautious interpretation and call for more rigorous longitudinal research. In the interim, precautionary public health actions in fluoride-endemic areas are justified to reduce potential harm.

Ethical consideration

This article is a systematic review of previously published studies and does not involve any new human participants or animal experiments. Therefore, ethical approval and informed consent were not required.The authors declare that they have no conflicts of interest. This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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Annexure 1: List of excluded studies at full-text screening stage

Study	Reason for exclusion
Agarwal *et al*. (2012)	Conducted outside India
Raghavan *et al*. (2014)	Did not assess cognitive outcomes
Iyer *et al*. (2016)	Animal study
Sen *et al*. (2010)	Case report
Patel *et al*. (2015)	Incomplete reporting of fluoride exposure
Mehta *et al*. (2013)	Review article
Verma *et al*. (2017)	Duplicate data from an included study
Dey *et al*. (2011)	No clear comparator group
Mishra *et al*. (2018)	Unclear or nonstandardized cognitive assessment
Saxena *et al*. (2011)	Focused on dental outcomes