Prevalence and incidence of dental fluorosis in India: protocol for a systematic review and Meta-analysis

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Protocol

**Keywords:** Epidemiology, Prevalence, Incidence, Dental Fluorosis, Mottled Enamel, Risk factors, India, Humans

**DOI:** https://doi.org/10.21203/rs.3.rs-332595/v1

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Abstract

**Background** Dental fluorosis has lifelong health impacts which can range from risk of dental caries to loss of teeth as well as aesthetic issues having psychological effects. The dental fluorosis burden in terms of its overall prevalence in India is lacking. Knowledge about the prevalence of dental fluorosis is important for healthcare planning and resource allocation. Therefore, this study aimed to estimate the pooled prevalence of dental fluorosis in India and its associated factors.

**Methods** A systematic search of electronic databases viz. MEDLINE (via PubMed), IndMed, Web of Science, and the Cochrane Central Register of Controlled Trials (CENTRAL), and WHOLIS (WHO library database) will be undertaken from inception to 15th February 2021. Two investigators will independently screen the search results followed by full-text screening for inclusion in the review as per predefined criteria. The data will be extracted for included studies using a pre-designed data extraction form and results will be presented in tabulated form. The meta-analysis will be performed for a homogeneous group of studies if found any. Sensitivity analysis will be performed to address the heterogeneity across studies.

**Discussion** This review will describe and summarize the available epidemiological evidence in India in terms of overall prevalence, geographical distribution, and associated factors of dental fluorosis. Further, the finding of this systematic review will be the result of the methodological assessment of the published literature. Understanding the epidemiology of dental fluorosis terms would help in identifying focus areas for intervention as well as better planning and utilization of scarce resources.

**Systematic review registration:** PROSPERO, CRD42021235670

**Introduction**

India lies within the geographical fluoride belt which extends from Turkey to China and the effect of fluoride on the dentition is dose-dependent. The reference dose suggested by USEPA is 0.06 mg fluoride/kg/ day, which is the estimate of daily exposure that is likely to be without any appreciable risk of deleterious effects (any degrees of dental fluorosis) during a lifetime. Fluoride has been used for many years in carries prevention whereas its excess concentration above certain levels results in dental fluorosis.

Dental fluorosis is hypoplasia or hypo-mineralization of tooth enamel or dentin, produced by the chronic ingestion of excessive amounts of fluoride during a period when teeth are developing in a range of intensity from barely noticeable whitish striations to confluent pitting and staining. Dental fluorosis decreases the mineral content of tooth enamel by creating porosity resulting in a brittle enamel surface. The literature suggests severe dental fluorosis with pitting to be a risk factor for dental caries. Also, dental fluorosis in all degrees leads to aesthetic issues such as discoloration of anterior teeth which
affects the psychological well-being of affected persons.\textsuperscript{7,8} Thus, dental fluorosis has lifelong health impacts which can range from loss of teeth to debilitating pain.

The primary sources identified as being potentially responsible for the prevalence of dental fluorosis are related to the basic necessity of life such as drinking water and food along with fluoride-containing dental products.\textsuperscript{9} Drinking water is typically the largest single contributor to daily fluoride intake.\textsuperscript{10,11} For a given individual, fluoride exposure (mg/kg of body weight per day) via drinking water is influence by age, climate, and temperature. Other sources include certain foods, certain beverages especially tea, flavored beverages and soft drinks (sugar cane, green tea) also contain a high level of fluorides.\textsuperscript{12,13,14}

Many researchers tried to investigate the pooled prevalence of dental fluorosis in various countries through systematic review and meta-analysis viz. Iran\textsuperscript{15} (52.6%), Brazil\textsuperscript{16} (8.92 % in non-fluoridated areas and of 51.96 artesian wells water supply regions), Ethiopian rift valley\textsuperscript{17} (28%), and Saudi Arabia\textsuperscript{18} (46.52%). The prevalence studies on dental fluorosis in India are highly scattered with varied prevalence at various times and in several regions. Dental fluorosis is considered to be a major public health problem with almost 230 districts of 19 states in India which are endemic for fluorosis. However, data on the overall burden of dental fluorosis in India is lacking. Also, the scientific evidence regarding the pattern of fluorosis in the Indian population is scarce. Dental fluorosis is an irreversible condition but can be limited or prevented by following the ‘recommended limits for fluoride exposure’, suggested by US Environmental Protection Agency (USEPA).\textsuperscript{3} Therefore, this study aimed to estimate the pooled prevalence of dental fluorosis in India which will help to systematically analyze and summarize the literature for better utilization. Also, the associated factors for dental fluorosis will be evaluated as part of this review.

**Objectives:**

**Primary objective**

to determine the prevalence and incidence of dental fluorosis in India.

**Secondary objectives**

to study the impact of factors such as age, gender, water fluoride concentration, dietary factors climate, and altitude, etc on the prevalence of dental fluorosis.

**Methods**

This systematic review protocol has been developed according to the recommendations from the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA-P) 2015 statement\textsuperscript{19} (supplementary file 1). The protocol of this systematic review has been registered in the International Prospective Register of Systematic Reviews (PROSPERO) no CRD42021235670.

**Eligibility criteria**
The eligibility criteria for the selection of studies to be included in the systematic review are based on PECOS (Table 1.)

**Population**

The population of interest will include Indian individuals of all ages and gender with dental fluorosis.

**Exposure**

People exposed to different fluoride concentrations through drinking water or other sources in different geographical areas of India

**Comparator**

People without dental fluorosis if reported to explore associated factors.

**Outcome**

The primary outcome will be the point prevalence; cumulative incidence and incidence rate of dental fluorosis recorded with any validated index. We will also explore factors associated with dental fluorosis.

**Study design**

All observational study designs such as cross-sectional studies, cohort studies, and case-control studies will be included. The studies will be limited geographically to India. Studies with no restrictions on publication year and publication status will be included. Non-research letters and editorials, narrative reviews, systematic reviews, case series, and animal studies will be excluded. Randomized controlled trials or intervention studies will also be excluded based on methodological inappropriateness of research design for the epidemiological type of questions to be answered.

**Information sources/ Search strategy:** A systematic search of many databases viz. MEDLINE (via PubMed), IndMed (via http://indmed.nic.in/), Web of Science, and the Cochrane Central Register of Controlled Trials (CENTRAL) and WHOLIS (WHO library database) via WHO website will be undertaken from inception to 15-02-2021. Gray literature will also be searched through Google scholar rand, research gate, and the website for Rajiv Gandhi University of health sciences, etc. The reference lists of published systematic reviews, narrative reviews on dental fluorosis will also be checked for eligible papers addressing the prevalence, incidence, and risk factors of dental fluorosis. The reference lists of all included articles published will also be searched for any additional sources of information.

Detailed search strategies were developed combining controlled vocabulary and free text terms for each database searched. To construct a comprehensive set of possible search terms, we list indexing terms (for example, subject headings and subheadings, publication types) and text words used to describe concept clusters (single words or phrases that may appear in titles or abstracts, both in full and in various truncations). The detail of each search strategy and the keywords used are adapted from various
systematic reviews of dental fluorosis conducted in other countries. The search strategy was developed by the research team using MeSH terms and entry terms for key concepts for MEDLINE search is presented in additional file 2. After MEDLINE strategy is finalized, it will be adapted to the syntax and subject headings of other databases. The rules of each database will be respected, and the Booleans ‘OR’ and ‘AND’ will be used to combine the MeSH, synonyms, and free terms according to the syntax rules of each database. No language or year restrictions will be imposed in the searches. The searches will be conducted independently by two authors.

Table 1
Detailed inclusion and exclusion criteria

<table>
<thead>
<tr>
<th>Inclusion</th>
<th>Exclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Population</td>
<td>animal studies</td>
</tr>
<tr>
<td>Population of interest is individuals of all ages and gender in India</td>
<td></td>
</tr>
<tr>
<td>Study design</td>
<td>Randomized controlled trial, narrative reviews, systematic reviews, case series, case report</td>
</tr>
<tr>
<td>All observational study design such as cross-sectional studies, cohort studies, and case-control studies</td>
<td></td>
</tr>
<tr>
<td>Outcome</td>
<td></td>
</tr>
<tr>
<td>Prevalence, point prevalence; cumulative incidence, and incidence rate of dental fluorosis recorded with any validated index</td>
<td></td>
</tr>
<tr>
<td>Type of publication</td>
<td></td>
</tr>
<tr>
<td>Studies published in the English language</td>
<td>Other language studies, non-research letters, and editorials</td>
</tr>
</tbody>
</table>

Data Management

We will implement the search strategies and import all references identified to Zotero. The search results from the different electronic databases will be combined in a single Zotero's library and we will remove duplicate records of the same reports.

Selection Process

Two reviewers (RKS and HCM) will independently screen titles and abstracts following inclusion and exclusion criteria specified in Table 1 will be included for full-text screening. Studies with no abstract will also be included for full-text screening. Population bases studies/hospital-based studies. Contact with authors for further information will be made when necessary. The full-text will be retrieved for included titles as per screening and will be evaluated by two reviewers independently for eligibility for inclusion in the systematic review. In case of disagreement between two reviewers will be resolved by discussion or by the involvement of a third reviewer. Studies included during screening titles and abstract but excluded after full-text review will be listed in the table with the reason for exclusion. A PRISMA flow diagram of the study selection procedure will be prepared to show the data collection process.

Data Extraction Process
Two independent researchers (RKS and HCM) will perform the data extraction in duplicate from the included studies as per the protocol. In case of any discrepancy, the third contributor will be consulted to address the concern. Data extraction will include the following data items:

1. Publication details: author, year, study area
2. Study design i.e. type of study
3. Sampling type population or hospital-based study
4. Sample size and study population
5. Sample characteristics Age, gender, geography
6. Prevalence and incidence of dental fluorosis & index used for assessment
7. Severity of dental fluorosis
8. Risk factors viz. water fluoride levels, dietary factors, altitude, temperature, and rainfall

**Risk Of Bias In Individual Studies**

The quality of included studies will be assessed by the National Institute of Health (NIH) quality assessment tools. The tools include items for evaluating potential flaws in study methods or implementation, including sources of bias (e.g., patient selection, performance, attrition, and detection), confounding, study power, the strength of causality in the association between interventions and outcomes, and other factors (Available at https://www.nhlbi.nih.gov/health-topics/study-quality-assessment-tools). The tool addresses issues of internal and external validity of prevalence data as well as can be used across different study designs. Quality assessment will be carried out by two reviewers independently. Discrepancies in quality appraisal scores will be resolved through discussion or referred to a third reviewer. The outcome of the assessment will be presented in tabulated form.

**Data synthesis**

Data extraction from eligible studies will be done following pre-piloted proforma created for extraction items and will be presented in evidence tables. All the eligible studies meeting the inclusion criterion will be included for the meta-analysis of outcome variables. The meta-analysis will be conducted if there is uniformity in reporting the outcome estimates among the studies. A narrative synthesis will provide a summary of the prevalence of dental fluorosis in India.

Further, the individual prevalence and incidence rate estimates from observational studies will be pooled using the fixed effect and random effect models as appropriate. The choice of random-effects model will be based on clinical and methodological diversity across the included studies. Where available, the prevalence-adjusted or incidence-adjusted odds ratios relating to the stratification of risk of dental fluorosis among the patients as discussed in the respective observational studies will also be pooled using random-effect models. We will investigate the potential source of heterogeneity related to both methodological and clinical characteristics of the studies which will be assessed by the Cochran's Q test.
(P-value < 0.1 considered significant) and $I^2$ (> 50 % representing moderate heterogeneity) statistics. A prediction interval will also be calculated to understand the possible range of prevalence/incidence of dental fluorosis if a new study is conducted in India as suggested by Higgins and Thompson. The publication bias will also be assessed (if we identify at least 10 studies). Publication bias will be assessed by funnel plot and its asymmetry will be tested by Egger's linear regression method ($P < .10$ will be considered as significant). A P-value of < .05 will be considered statistically significant for the effect of study-level covariates. The advice from GRADE guidance will be used to evaluate the quality of evidence.

A predefined subgroup analysis will be conducted to explore subgroup effects. Statistical analysis will be performed using Stata v16.2 (StataCorp, College Station, Texas, USA) and Review Manager v5.4 (the Nordic Cochrane Centre, Rigshospitalet, Denmark). If the number of studies allows, we will analyze by subgroup according to age, sex, year of reporting, geographic location.

**Summary**

This systematic review and meta-analysis will be performed to evaluate the relevant literature on the epidemiology of dental fluorosis in India. This review aims to identify and report the estimated prevalence and incidence of dental fluorosis in India and reported associated factors with subgroup analysis for age, gender, and geographical location. Understanding the epidemiology of dental fluorosis terms would help in identifying focus areas for intervention as well as better planning and utilization of scarce resources. Further, the finding of this systematic review will be the result of the methodological assessment of the published literature. The findings of this review will also be compared with other similar published reviews. Finally, conclusions will be drawn from this systematic review highlighting the prevalence and incidence of dental fluorosis and its associated factors. Limitations of the studies will be discussed in detail. In addition, suggestions for future research will also be provided through this review.

**Abbreviations**


**Declarations**

**Acknowledgements:** None

**Authors’ contributions:** HCM, RB and RKS initiated the protocol, conceptualized the research plan for the proposed systematic review. HCM, RB, RKS, and UM critically reviewed the methodology, wrote the
manuscript, and reviewed it for important intellectual content. All authors read and approved the final manuscript.

**Funding:** None

**Availability of data and materials:** Not applicable, no data was generated or analyzed during the current study

**Ethics approval and consent to participate:** Not applicable.

**Consent for publication:** Not applicable.

**Competing interests:** None

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**References**


Supplementary Files

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