REVIEW OF LITERATURE
1. GEOCHEMISTRY, DISTRIBUTION & EXPOSURE OF FLUORIDE

Fluorine is the ninth element of the periodic table with atomic weight 18.99. Elemental fluorine is never found in the free form in nature, as it is the most electronegative and reactive of all elements\(^\text{10}\). Fluorine in the environment is therefore found as fluorides which represent about 0.06–0.09 per cent of the earth's crust. It is the 13th most abundant element, commonly occurring in the minerals fluor spar (fluorite;\text{CaF}_2), cryolite (\text{Na}_3 \text{AlF}_6) and fluorapatite (3\text{Ca}_3 (\text{PO}_4)_2 \text{Ca FC}_1_2)\(^\text{10}\). The sources of fluoride include soil, water, air, food, beverages, dental products and industrial products.

1.1. SOIL

The chief natural source of fluoride in soil is fluorite, which occurs mostly as an accessory mineral in granite rocks. The fluoride content in soil normally ranges from 200 to 300 ppm. Since fluorides are retained by soil through strong association with soil components, fluoride is not readily leached from soil\(^\text{11}\). Nommik observed that fluoride content in soil increases with depth, and only 5 to 10\% of the total fluoride in soil is water-soluble\(^\text{12}\). The rate of fluoride release into soil also depends on the chemical form, rate of deposition, soil chemistry and climate. Greater fluoride content is observed in ground water of irrigated lands, mainly due to alkalinisation\(^\text{2}\).
1.2. WATER

Drinking water is typically the largest single contributor to daily fluoride intake in human beings\textsuperscript{13}. Fluoride is found in all natural waters at some concentration. The highest natural water level of fluoride reported is 2800 ppm from the Kenyan lake Nakuru\textsuperscript{1}. In India, concentrations of 0.1 to 0.3 ppm of fluoride are reported in rain water\textsuperscript{14}. Surface water concentration generally ranges from 0.01-0.3 ppm. Seawater typically contains fluoride in the concentration range of 1.2 - 1.5 ppm\textsuperscript{11} while rivers and lakes generally exhibit concentrations of less than 0.5 ppm. In groundwater, however, low or high concentrations of fluoride can occur, depending on the nature of the rocks and the occurrence of fluoride-bearing minerals. Concentrations in water are limited by fluorite solubility\textsuperscript{15}. For a given individual, fluoride exposure via drinking-water is determined by the fluoride level in the water and the daily water consumption (liters per day). Water consumption increases with temperature, humidity, exercise and state of health, and is modified by other factors including diet\textsuperscript{16}.

1.3. AIR

Due to dust, industrial production of phosphate fertilizers, coal ash from the burning of coal and volcanic activity, fluorides are widely distributed in the atmosphere. However, air is typically responsible for only a small fraction of total fluoride exposure\textsuperscript{1}. In non-industrial areas, the fluoride concentration in air is
typically quite low (0.05–1.90 μg m⁻³ fluoride). In areas where fluoride-containing coal is burned or phosphate fertilizers are produced and used, the fluoride concentration in air is elevated leading to increased exposure by the inhalation route. High levels of atmospheric fluoride occur in some areas of Morocco and China. In some provinces of China, fluoride concentrations in indoor air ranged from 16 to 46 μg m⁻³ owing to the indoor combustion of high-fluoride coal for cooking, drying and curing food. 16.5 million cases of dental fluorosis are reported here as a result of coal smoke pollution alone.

1.4. FOOD AND BEVERAGES

Virtually all foodstuffs contain at least trace amounts of fluoride as it is ubiquitous in the environment. Fluoride is entering human food-and-beverage chain in increasing amounts through the consumption of tea, wheat, spinach, cabbage and carrots. The fluoride in these items presumably results from the use of soil or fertilizer-borne fluoridated water for food and beverage processing. Tea plants are found having high fluoride uptake and 97% of it gets accumulated in leaves. The fluoride content of tea leaves is about 1,000 times the soluble fluoride content of soil. Regular-strength preparation of instant tea in distilled water showed a fluoride concentration of 3.3 ppm. Excessive consumption of black tea has been identified as a causative factor of dental fluorosis.
1.5. DENTAL PRODUCTS

A number of products administered to, or used by, children to reduce dental decay contain fluoride. This includes toothpaste, fluoride solutions, gels for topical treatment and fluoride tablets. These products contribute to total fluoride exposure, albeit to different degrees. It is estimated that the swallowing of toothpaste by some children may contribute about 0.50 or 0.75 mg fluoride per child per day\textsuperscript{20}.

1.6. OTHER SOURCES

Industrial sources of fluoride include textile dyeing plants, plastic factories, thermal power plants, plants manufacturing hydrofluoric acid, phosphate fertilizers, enamel, glass, tiles, semiconductors and integrated circuits\textsuperscript{1}. Cigarettes, with an average 236 ppm fluoride, contribute significantly in fluoride intake by human\textsuperscript{21}. Teflon-lined cookware may also contribute to fluoride uptake by humans. The concentration of fluoride was found to be nearly 3 ppm in teflon-coated cookware. In stainless steel and Pyrex ware also fluoride concentration was found to be high, but to a lesser degree\textsuperscript{22}. Fluoride (primarily as sodium fluoride) has also been used in the treatment of osteoporosis\textsuperscript{23}. A large number of pharmaceutical products contain fluoride in varying concentrations.
2. EFFECTS OF FLUORIDE IN THE HUMAN BODY

2.1. ABSORPTION, DISTRIBUTION AND EXCRETION

Ingested sodium fluoride is rapidly absorbed from the gastrointestinal tract. Peak plasma levels were reached 30–60 minutes after the ingestion of 0.5 to 10 mg fluoride. The extent of dietary fluoride absorption was greater than 90% in studies with human volunteers. The absorption of fluoride from stomach is by a passive diffusion process inversely proportional to pH, but is a rapid diffusion from small intestine after gastric emptying. The presence of a diet rich in calcium reduces the fluoride absorption.

Once absorbed into the blood, fluoride readily distributes throughout the body. Up to 75% of absorbed fluoride may be deposited in calcified tissues, with the highest deposition found in children with active bone growth or individuals consuming fluoridated drinking water. Approximately 99% of total body fluoride is localized in calcified tissues (i.e., bones and teeth), where it is substituted for hydroxyl ions (OH–) in hydroxy-apatite, forming fluorapatite.

Many of the factors affecting the uptake and retention of fluoride in bone also affect fluoride concentrations in teeth, with the exception that tooth enamel and dentin do not undergo continuous remodelling. Enamel fluoride concentrations decrease with distance from the tooth surface and also vary with location, surface wear, age and degree.
Fluoride does not accumulate in most soft tissue but may enter the intracellular fluid of soft tissues as hydrogen fluoride\textsuperscript{28}. The concentration of fluoride in soft tissues is reflected by that in blood. Fluoride is concentrated in high levels within kidney tubules and has a higher concentration than plasma\textsuperscript{11}. So, kidney could be a potential target of chronic fluoride toxicity.

The plasma half-life of fluoride in humans ranges from 2 to 11 hours following single or multiple oral doses of Sodium fluoride (3.0–40 mg fluoride)\textsuperscript{25}. Fluoride is excreted primarily via the urine, with perspiration, saliva, breast milk and faeces making smaller contributions to daily body clearance. In adult humans, approximately 50–75\% of an oral dose of fluoride appears in the urine within 24 hours after ingestion. Under conditions of relatively constant exposure, urinary excretion correlates well with drinking water fluoride levels and is often used as an indicator of exposure\textsuperscript{11}. Urinary fluoride clearance increases with urine pH due to a decrease in the concentration of Hydrogen Fluoride. Numerous factors (e.g. diet and drugs) can affect urine pH and thus affect fluoride clearance and retention\textsuperscript{25}.

Fluoride is readily transferred from mother to foetus across the placenta but poorly transported from plasma to milk\textsuperscript{30}. Fluoride levels of 5-10 \( \mu \) g/L have been measured in human milk. Saliva excretes approximately 1\% or less of ingested fluoride and concentration of fluoride in saliva appears to mirror plasma fluoride.
Levels of fluoride in sweat are approximately 20% of plasma levels. Renal excretion of fluoride typically equals 35 to 70% of intake in adults. So, urine, plasma, or saliva can be used as biomarkers of acute exposure to fluoride.

2.2. ACUTE TOXICITY

In humans, acute ingestion of fluoride can result in nausea, vomiting, abdominal pain, diarrhoea, fatigue, drowsiness, coma, convulsions, cardiac arrest and death. Effects are most severe following ingestion of the more soluble fluoride salts. The lethal dose of fluoride in the average adult has been estimated to be 32–64 mg/kg body weight, and deaths in children have been reported after ingestion of as little as <5–30 mg/kg body weight.

2.3. EFFECTS ON TEETH

2.3.1. FLUORIDE AND DENTAL CARIES

Dental caries is an infectious and multifactorial disease, which is characterized by demineralization of inorganic components of teeth and dissolution of organic substance of microbial aetiology. Caries is the result of bacterial growth in unhygienic oral cavity, leading to acid production by fermentation, which etches away the enamel leaving black spots or cavity on the tooth. These microorganisms may penetrate the underlying dentin and progress into the soft pulp tissue. The untreated caries can lead to incapacitating pain,
bacterial infection leading to pulpal necrosis, tooth extraction, loss of dental function, and may even lead to an acute systemic infection. The specific bacteria streptococcus mutans and lactobacilli in dental plaque are the major etiologic factors responsible for this disease. The prevalence of these cavities can be effectively quantified by using the DMFT (number of decayed, missing, or filled teeth) or DMFS (number of decayed, missing, or filled tooth surfaces) indices developed by oral epidemiologists.

2.3.1.1. MECHANISM OF CARIES PREVENTION BY FLUORIDE

Most of the epidemiologic research suggests that the actions of fluoride in preventing dental caries are primarily topical which includes the inhibition of bacterial activity in dental plaque preventing demineralization and enhancing remineralization of dental enamel. Enamel and dentin are composed primarily of mineral crystals of calcium and phosphate, which are embedded in an organic protein/lipid matrix. Fluoride is taken up by cariogenic bacteria during the fermentation process, which produce acids. Once fluoride finds its way inside the bacterial cells, it can interfere and alter the enzyme activity of the bacteria. This inhibits acid production, thereby reducing the demineralization of dental mineral. The calcium ions in saliva are attracted to tooth surface by the already adsorbed fluoride. Fluoride aids the calcium and phosphate ions to involve in the chemical reaction that takes place, producing a crystal surface that is much less
soluble in acid than the original tooth mineral thereby enhancing remineralization\textsuperscript{36}. Of late, there is a growing consensus in this view that it is through interaction with the surface of enamel (topical action) that fluoride in saliva and dental plaque inhibits the demineralization and promotes the remineralization of dental enamel\textsuperscript{11}.

2.3.1.2. EFFICACY OF FLUORIDE ON PREVENTION OF DENTAL CARIES

Fluoride is often called a double-edged sword because deficiency of fluoride intake leads to dental caries while an excess consumption leads to dental fluorosis. This dose-response curve is represented in figure 1.

\textbf{Fig 1.} Relation between DMF teeth (dotted line). Severity of dental fluorosis & fluoride concentration of the water (Adopted from Hodge and Smith) 1950

\begin{center}
\begin{tikzpicture}
\begin{axis}[
axis y line=left,
axis x line=bottom,
width=\textwidth,
height=0.5\textwidth
]
\addplot [mark=none, dashed] table[x=Fluorosis rate,y=Decayed Missing & Filled permanent teeth] {data.csv};
\addplot [mark=none] table[x=Fluorosis rate,y=Severe] {data.csv};
\addplot [mark=none] table[x=Fluorosis rate,y=moderate] {data.csv};
\addplot [mark=none] table[x=Fluorosis rate,y=mild] {data.csv};
\addplot [mark=none] table[x=Fluorosis rate,y=very mild] {data.csv};
\end{axis}
\end{tikzpicture}
\end{center}

\begin{center}
\begin{tabular}{c}
\textbf{Fluorosis rate} \\
\text{Decayed Missing & Filled permanent teeth} \\
\text{Severe} \\
\text{moderate} \\
\text{mild} \\
\text{very mild} \\
\end{tabular}
\end{center}

\begin{center}
\begin{tabular}{c}
\text{Index of Fluorosis} \\
\text{Parts per million Fluoride} \\
\end{tabular}
\end{center}
The difference between the desirable dose (to prevent dental caries) and the toxic dose leading to fluorosis is narrow. The benefits and effects of fluoride in drinking water has been a matter of scientific debate as many research findings are contradicting or inconclusive. The debate still continues over how much fluoride is too much and whether presence of fluoride in drinking water is necessary or essential in preventing tooth decay.

It has been considered that oral fluoride is an effective means of reducing dental caries even from 1930s and historically, populations consuming fluoridated drinking water were found having much lower prevalence of caries than those consuming non-fluoridated drinking water. Of late, credible evidence from most of the systematic scientific research substantiates the role of fluoride in preventing dental caries. It was reported that there is clinically important reduction in the incidence of dental caries at a natural fluoride concentration of around 1 ppm\(^{37}\) and that too, in a wide range of 3 to 75 years of age\(^{38-40}\). WHO Expert Committee in 1994, after examining the effects of fluoride on dental health suggested an optimum fluoride level of 1ppm for maximum dental caries protection\(^{41}\). In 1996, WHO categorized fluoride among 'potentially toxic elements, some of which may nevertheless have some essential functions at low levels' and recommended it as a desirable or essential element for humans in preventing dental caries\(^{42}\). Depending upon the annual average maximum daily air temperature, WHO, framed permissible limits ranging from 0.5 to 1.2 ppm\(^{11}\).
It is reported that due to water fluoridation, the mean DMFT among persons aged 12 years in the United States declined 68%, from 4.0 in 1966-70 to 1.3 in 1988-94\(^4\). Centre for Disease Control and Prevention (CDC) hails water fluoridation as one of the ten most important public health measures currently available\(^4\),\(^3\). Globally, the population consuming fluoridated drinking water was estimated as about 210 million in 1994\(^4\), 350 million in 2004\(^4\) and around 355 million in 2005\(^4\). In addition, around 50 million people receive water naturally fluoridated at a concentration of around 1 ppm\(^4\).

McDonagh et al. presented a summary of the best available and most reliable evidence on the safety and efficacy of water fluoridation through a systematic review\(^4\). This review thoroughly analyzed the researches investigating the association between fluoride and dental caries between 1969 and 1999. The 'best available evidence' suggests that fluoridation of drinking water supplies does reduce caries prevalence, both as measured by the proportion of children who are caries free (an increase of 14.8%) and by the mean change in DMFT (a decrease of 2.25 teeth). The analysis of cross-sectional random samples published recently in countries that have introduced fluoridation to monitor the dental effects of fluoride among children aged 5 to 15 years also support this observation\(^4\). Since fluoride is most effective when continually present at low levels in saliva and plaque fluid, WHO\(^1\) recommended the use of fluoridated mouth rinses for individuals with an elevated risk of dental
caries. Also, fluoridated toothpastes (96% of it contains 1000 to 1500 ppm fluoride) are found responsible for the gradual decline in the prevalence of dental caries in most industrialized countries\textsuperscript{11}.

It is equally important and worth mentioning that many scientific researches fail to support the effectiveness of fluoride in preventing tooth decay\textsuperscript{49-51}. It is suggested that dental caries in children is a bacterial disorder the intensity of which varies with several factors viz. nutrition, oral bacteria, oral hygiene, educational and economic status of parents. Also, large temporal reductions in tooth decay can mainly be attributed to the dietary patterns and immune status of populations and that dietary control of caries, without the use of fluoride is possible as even chewing cheese reduces tooth decay\textsuperscript{52}. It is also observed that tooth decay is increasing together with increases in sugar and other fermentable carbohydrates in the diet in several developing countries\textsuperscript{53}. There is more to diet than sugar, as certain foods which do not contain fluorides like wholegrain cereals, nuts and diary products may protect against tooth decay\textsuperscript{54}. Since no disease can be shown to be caused by its deficiency, it is argued that fluoride cannot be an essential nutrient to humans. Moreover, none of the animal experiments addressing whether fluorine is an essential element provide strong evidence that it really is\textsuperscript{2}. It is stated that for humans, the essentiality has not been demonstrated unequivocally, and no data indicating the minimum nutritional requirement are available\textsuperscript{14}. 

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Since more than 85% of tooth decay occurs on pits and fissures of the tooth, where fluoride has always been recognized to be ineffective, it is pointed out that fluoride acts topically (at the surface of the teeth) and that there is negligible benefit in actually ingesting it\textsuperscript{55}. Many scientific studies also showed that there is little or no significant difference in tooth decay in permanent teeth between many comparable fluoridated and non-fluoridated regions of the world\textsuperscript{56-59}.

2.3.2. DENTAL FLUOROSIS

Dental fluorosis, an irreversible toxic effect on teeth, is the earliest sign of fluoride attack visible to the naked eye. Histologically, it presents as a hypocalcification, while clinically it ranges from barely visible white striations on the teeth through to gross defects and staining of the enamel\textsuperscript{60}. The exact mechanisms of dental fluorosis development have not been fully elucidated.

2.3.2.1. HISTORY OF DENTAL FLUOROSIS

Dr. Frederick S. McKay is the first to report the development of an unusual permanent stain or “mottled enamel” on teeth surface and to initiate research on its relation with fluoride in drinking water\textsuperscript{61}. Dental fluorosis was first related to drinking water in 1925, though several more years before it was shown to be specifically caused by fluoride in drinking water\textsuperscript{62}. Fluorosis as an occupational disease was identified in 1930 and subsequently, occurrence of skeletal fluorosis in cryolite miners in Denmark was reported in 1932\textsuperscript{63}.
2.3.2.2. FLUORIDE AND DENTAL FLUOROSIS

Most of the recent research has focused on the theory that dental fluorosis results from a fluoride-induced delay in the hydrolysis and removal of amelogenin matrix proteins during enamel maturation and subsequent effects on crystal growth. Amelogenins, the proteins secreted by ameloblasts, inhibit the growth of enamel crystallites. In the early maturation phase of tooth development, amelogenins are removed from the enamel matrix by amelogeninases, dramatically increasing the crystallite growth. This phase of enamel maturation appears to be most sensitive to elevated fluoride levels\textsuperscript{64}.

The calcium rich constituents of teeth, viz. enamel and dentin, have strong affinity for fluoride during the formation of teeth. It is also suggested that fluoride combines with calcium forming calcium fluoroapatite crystals during mineralization. So, as fluoride accumulates, calcium is lost from the teeth. A gradual reduction in the calcium content occurs in the fluorosed teeth from the 'mild to severe' state. Thus, due to fluorides, the teeth become weaker by loosing calcium ions\textsuperscript{65}. The severely fluorosed enamel is more porous, pitted, discolored and is prone to wear and fracture because the well mineralized zone is very fragile to mechanical stress. Due to gross structural alterations, reduction in mineral content, impairment of enamel mineralization and morphological aberrations on the teeth surface, the fluorosed teeth readily gets fractured\textsuperscript{66}. 

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2.3.2.3. PHYSICAL SYMPTOMS OF DENTAL FLUOROSIS

Dental fluorosis occurs in children during the developmental stages when the teeth are exposed to fluoride. Depending upon the severity of exposure, colour of teeth may progress from white, yellow, brown to black. Teeth become rough resulting in a mottled appearance characterized by chalky white patches and bands of brown pigmentation. Small pits may also be present on the surface of teeth. In severe cases, teeth may even appear corroded. Such teeth may show a tendency for wear and even fracture of the enamel.

The discolouration appears away from the gums on the enamel surface and becomes an integral part of the tooth matrix and as a result, the enamel will lose its lustre and shine. If the discolouration is along the gums and on the periphery of the teeth, it is due to other reasons viz. dirty teeth, smoking, tobacco chewing and coffee or tea stains. Since the enamel lines are laid down in incremental lines during prenatal and postnatal periods, dental fluorosis is invariably seen as horizontal lines or bands on the surface of the teeth and never as vertical bands. For the same reason, it will be seen in pairs based on developmental pattern and never alone in a single isolated tooth. While all the teeth may be affected, mottling is usually best seen on the incisors of the upper jaw. Teeth commonly affected are the incisors and molars of the permanent dentition.
2.3.2.4. PSYCHO SOCIAL EFFECTS OF DENTAL FLUOROSIS

Teeth are important components of the facial skeleton. Apart from the function of mastication of food, teeth add to the aesthetics, phonation and speech. Dental fluorosis deserves special attention because of its unfavourable effects on teeth and ultimately on individual's personality. It is hard to smile for a person with dental fluorosis, though an attractive smile is an important personal and social asset. An individual with discoloured teeth develops an inferiority complex, due to distress and anxiety presenting as psycho social problems to self and family. They will be under the shadow of 'impaired self-image' or 'loss of self-esteem'. Even from an early age, they are more likely to experience embarrassment, isolation and discrimination. Such conditions can precipitate feelings of frustration and anger, which could in turn lead to deep psychological depression^70-72.

In 1994, a Kenyan survey noted that between 60 and 84% of respondents viewed dental fluorosis as an important problem because of its unfavorable effects on an individual's personality^67. A Canadian study examined the influence of fluoride exposure on the wide-spread "aesthetic problems" caused by dental fluorosis. It acknowledged that forty six percent (nearly half) of the participants had dental fluorosis. The effect on personal appearance, as defined by the participants themselves, was more prevalent in the over-11 age group^68. The
trauma experienced by young people with dental fluorosis is depressingly apparent in a South African study conducted by the North West Province Department of Health:69: "The psychological effect in terms of the unsightly, brown-stained teeth has induced the adolescents with fluorosed teeth to demand that these teeth be extracted and replaced with dentures." American and English researchers noted that the prevalence of dental fluorosis appears to be on the increase. "Although in its mild form the condition is not considered to be of cosmetic significance, the more severe forms can cause great psychological distress to the affected individual."70 An Australian Health Department study analyzed society's perceptions of dental fluorosis, based on over 3,000 responses. Lay and professional observers recognized that higher degrees of fluorosis increasingly embarrass the child. All observers, except the dentists, felt that the more severe fluorosis indicated neglect on the part of the child.71 Egyptian researchers observed that friends and relatives ridicule the patient by inferring that these stains are associated with smoking and/or poor oral hygiene. They noted that such personal remarks lead to severe depression.72

2.3.2.5. EPIDEMIOLOGY OF DENTAL FLUOROSIS

There is a growing body of evidence, which indicates that, the prevalence and severity of dental fluorosis is increasing in all regions of the world as a consequence of increased fluoride intake through multiple sources. The
relationship between prevalence of dental fluorosis and concentration of fluoride in water is well established and documented\textsuperscript{11,47}. It has been observed that children and adolescents aged 8-16 years are more susceptible to dental caries as approximately 80\% of absorbed fluoride is retained in young children compared to 50\% in adults\textsuperscript{73}. According to the Indian health survey data of fluorosis from nine states, the percentage of children between 6-14 years of age affected by dental fluorosis was in the range of 5-20\%. Also, the affected adults, without any gender difference was 2-30\%. Some studies in India showed 100\% prevalence of dental fluorosis at a fluoride level of 3.4 to 3.8 ppm\textsuperscript{74}. The observations by Wang et al are unique as it reported that the development of dental fluorosis was not affected by the level of arsenic in water. Also, fluoride was observed exerting dental fluorosis (14\%) at 0.2 ppm in drinking water. At a fluoride concentration of 3.5 ppm, over 90\% of children of the age group 8-15 years, developed dental fluorosis, irrespective of arsenic level in the water\textsuperscript{75}.

A significant dose-response relationship between fluoride in water and prevalence of dental fluorosis was identified by univariate regression analysis through a systematic review by McDonagh et al. after analyzing 88 studies (mainly cross-sectional) from 30 countries\textsuperscript{47}. The prevalence of dental fluorosis at a water fluoride level of 1 ppm was estimated to be 48\% in fluoridated areas and 15\% in non-fluoridated areas. Limiting consideration to aesthetically important levels of severity, the prevalence of fluorosis is 12.5\% in fluoridated areas and
6.3% in non-fluoridated areas. Also, results show that there are relatively large differences in the prevalence of dental fluorosis at the level of water fluoridation 0.7-1.2 ppm when compared with an area with theoretical low water fluoride content (0.4 ppm). Increasing the level of water fluoride concentration from 0.4 ppm to a slightly higher figure of 1.0 ppm, would lead to one extra person with dental fluorosis for every 6 people receiving the new higher level of water fluoride. The difference between the proportions of population affected with fluorosis of aesthetic concern at 0.4 ppm compared with 0.7 ppm is considerably lower than the difference in the proportion comparing 0.4 to 1.0 ppm and 1.2 ppm. Increasing the water fluoride level from 0.4 to 1.0 ppm, would mean that one additional person for every 22 people would have fluorosis of aesthetic concern, but with no risk. The level of evidence clearly demonstrated that benefit of reduction in caries due to fluoride should be, and can only be, considered together with the increased prevalence of dental fluorosis. Another finding by Mcdonagh et al. is that there is no statistically significant difference between artificially fluoridated and naturally fluoridated water though there is inadequacy of data to make a detailed comparison.

2.3.2.6. MEASUREMENT OF DENTAL FLUOROSIS

Several indices have been used to describe the clinical appearance of dental fluorosis. The three principal indices in use today are those developed by Dean.
A recent index developed by Pendrys [1990] is Fluorosis Risk Index. Dental mottling due to fluoride toxicity can be classified as:

- Grade 1- white opacities, faint yellow line;
- Grade 2- changes of grade 1+ brown stain;
- Grade 3- brown line, pitting and chipped off edges;
- Grade 4- brown black and fall of teeth.

Dean's index is popularly accepted as a standard for the assessment of dental fluorosis. Grading of dental fluorosis by Dean's index is as below:

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Description of enamel</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>Smooth, glossy, pale creamy-white translucent surface</td>
</tr>
<tr>
<td>Questionable</td>
<td>A few white flecks or white spots</td>
</tr>
<tr>
<td>Very Mild</td>
<td>Small opaque, paper white areas covering less than 25% of the tooth surface</td>
</tr>
<tr>
<td>Mild</td>
<td>Opaque white areas covering less than 50% of the tooth surface</td>
</tr>
<tr>
<td>Moderate</td>
<td>All tooth surfaces affected, marked wear as biting surfaces, brown stain may be present</td>
</tr>
<tr>
<td>Severe</td>
<td>All tooth surfaces affected, discrete or confluent pitting, wide-spread brown stains, teeth often appear corroded</td>
</tr>
</tbody>
</table>
In order to compare the severity and distribution of dental fluorosis in various communities, Dean developed an epidemiological index, according to which each tooth is allotted a score which is given a corresponding weighting:

0- normal 0 1- questionable 0.5
2- very mild 1.0 3- mild 2.0
4- moderate 3.0 5- severe 4.0

On the basis of the number and distribution of the individual scores a Community Index of Dental Fluorosis (F_c) could be calculated:\[ F_c = \frac{\text{Number of individuals} \times \text{statistical weight}}{\text{Total number of individuals examined}} \]

Example:

<table>
<thead>
<tr>
<th>Number of persons</th>
<th>Score</th>
<th>Sum of statistical weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>50</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>25</td>
<td>0.5</td>
<td>12.5</td>
</tr>
<tr>
<td>15</td>
<td>1</td>
<td>15</td>
</tr>
<tr>
<td>10</td>
<td>2</td>
<td>20</td>
</tr>
<tr>
<td>5</td>
<td>3</td>
<td>15</td>
</tr>
<tr>
<td>5</td>
<td>4</td>
<td>20</td>
</tr>
<tr>
<td><strong>Total- 110</strong></td>
<td></td>
<td><strong>82.5</strong></td>
</tr>
</tbody>
</table>

\[ F_c = \frac{82.5}{110} = 0.75 \]
Dean stated that "For public health administrative guidance a community index of dental fluorosis of 0.4 or less is of no concern from the standpoint of mottled enamel per se; when however, the index rises above 0.6 it begins to constitute a public health problem warranting increasing consideration" 82.

2.4. SKELETAL EFFECTS OF FLUORIDE

Skeletal fluorosis is an excessive accumulation of fluoride in bone associated with increased bone density and outgrowths (exostoses)11. Fluoride incorporated into bone (i.e., as fluorapatite) produces a crystal lattice that undergoes less resorption (i.e., less soluble; more stable) and has an increased compression strength, but is more brittle and has a decreased tensile strength83. Characteristic signs and symptoms of skeletal fluorosis range from asymptomatic radiographic enlargement of spinal trabeculae in the preclinical form to the severe calcification of ligaments, spine and joint deformities, muscle wasting and neurological defects observed in crippling skeletal fluorosis. The more severe symptoms tend to be associated with the vertebral column in the lower, weight-bearing parts of the body84.

Endemic skeletal fluorosis is known to occur with a range of severity in several parts of the world, including India, China and northern, eastern, central and southern Africa. It is primarily associated with the consumption of drinking water containing elevated levels of fluoride but exposure to additional sources of
fluoride such as burning coal containing high fluoride is also potentially important. This is compounded by a number of factors which include climate, related to water consumption, nutritional status and diet, including additional sources of fluoride and exposure to other substances that modify the absorption of fluoride into the body. Evidence from occupational exposure also indicates that exposure to elevated concentrations of fluoride in the air may also be a cause of skeletal fluorosis.

Other than dental fluorosis, skeletal effects were the most studied potential adverse effect of fluoride. Although there are a large number of epidemiological studies available, the data are such that it is difficult to determine a clear exposure–response relationship. One possible feature of fluorosis is bone fracture, although some studies have reported a protective effect of fluoride on fracture. In an epidemiological study in China the relationship between fluoride intake via drinking water and all other sources, and all fractures, followed a U shaped dose response with higher rates of fracture at very low intakes below 0.34 mg l−1 and high intakes above 4.32 mg l−1 (total intake 14 mg per day). It was concluded by the International Programme on Chemical Safety that for a total intake of 14 mg per day there is a clear excess risk of skeletal adverse effects and there is suggestive evidence of an increased risk of effects on the skeleton at total fluoride intakes above about 6 mg per day.
2.5. OTHER FLUORIDE INDUCED ADVERSE EFFECTS

Apart from teeth and bones, the interaction and involvement of soft tissues, organs and other systems of the body with fluoride leads to non-skeletal fluorosis. The skeletal muscles, erythrocytes, gastro-intestinal mucosa, ligaments, spermatozoa and thyroid glands will be affected or damaged. Destruction of actin and myosin filaments in the muscle tissues due to fluoride ultimately leads to depletion of muscle energy. So, it is evident that the skeletal muscle is directly involved in fluorosis. This is the main reason for muscle weakness and corresponding loss of muscle energy in fluorosed patients, which renders them unfit for normal routine activities\(^4\).

Of late, numerous epidemiological and experimental studies in many countries have attempted to address the growing concern related to the relationship between consumption of drinking water with fluoride and morbidity or mortality due to cancer. A positive correlation between water fluoridation and increased cancer risk was first suggested by Yiamouyiannis and Burk\(^8\), but many subsequent reviews have not accepted these findings\(^88\). Positive correlations were also reported by different studies citing statistically significant associations between fluoridation index and cancer\(^90-91\). From among these studies the observation of a dose-response trend in the occurrence of osteosarcomas in male rats\(^91\) deserves special significance as the occurrence of
a rare tumor in the tissue in which fluoride is known to accumulate cannot be casually dismissed.11

In contrast, ecological studies by Hoover et al92 (including 1,250,000 incident cancers and 2.3 million cancer deaths, with follow-up for up to 35 years of fluoridation) and Freni et al93 suggested no correlation between cancer and fluoridation. The reports from Centre for Disease Control in 1999 concluded that studies to date have produced no credible evidence of an association between fluoridated drinking water and an increased risk for cancer43,44. In their exhaustive systematic review, McDonagh et al.47 analyzed 26 studies looking at the association of a broad number of cancer incidence with water fluoride exposure, including 12 studies comparing artificially fluoridated areas with areas having low natural fluoride level. Using 'the best available evidence,' no statistically significant association between water fluoridation and cancer incidence (irrespective of whether is artificially or naturally fluoridated) could be found out. Also, it was pointed that the reported studies were inadequate on cancer incidence and mortality reporting using natural source of fluoride. It is cautioned that studies in this area should be of higher quality which should address and use appropriate methods to control for confounding factors. The general conclusion by different reputed organizations including WHO is that 'the weight of evidence' does not support the hypothesis that fluoride causes cancer in humans and many of the findings suggesting a correlation suffers from
methodological flaws\textsuperscript{11,68}. Although most of the ecological studies performed in many countries do not support the hypothesis of an association, their considerable limitations preclude firm conclusions from being drawn regarding the carcinogenicity of fluoride in humans\textsuperscript{11}.

The gastrointestinal system is one of the most sensitive systems in the body to react adversely to fluoride toxicity. Symptoms of gastric irritation, such as nausea, vomiting, and gastric pain, have been observed shortly after exposure to fluoride in drinking water\textsuperscript{94}. The early warning signs of fluoride toxicity also include loss of appetite, gas formation and nagging pain in stomach, chronic diarrhea, chronic constipation and persistent headache. Unusual fatigue, loss of muscle power and weakness, excessive thirst and frequent urination, depression, tingling sensation in fingers and toes, allergic manifestations are also reported. The irritation of the gastric mucosa is attributed to fluoride forming hydrofluoric acid in the acidic environment of the stomach\textsuperscript{95}.

Susheela and Jethanandani observed significant reduction in serum testosterone levels in persons diagnosed with skeletal fluorosis\textsuperscript{96}. Fluoride can cause pathological changes like lipid peroxidation and DNA damage in human\textsuperscript{97} and is also reported to suppress the immune system\textsuperscript{98}. Though some genotoxic effect cannot be excluded, the overall evidence has not established that fluoride
is genotoxic nor allergic in humans. The review by McDonaugh et al. also found no evidence of reproductive toxicity in humans due to fluoride.

2.6. EFFECT OF NUTRITIONAL FACTORS ON FLUOROSIS

The research in India provides ample evidence on the critical role of malnutrition and poverty on the incidence and severity of fluorosis. Comparison of dietary adequacy, water fluoride levels, and incidence of skeletal fluorosis in several villages in India suggest that vitamin C deficiency and poor nutrition play a major role in fluorosis. ‘Genu valgum’ is more predominant in children poorly nourished with low calcium intake in endemic areas of fluorosis.

Chen et al. studied the fluoride intake, diet, and health status of children in two dental fluorosis-afflicted areas in the Province of Jiangxi, China. Average body weight of the children approximated that of the national standard. Protein intake was above the national standard of 0.75 g/kg body weight/day, but the protein was derived mainly from plant sources. Calcium intake was found to be insufficient. Based on the diet and fluoride intake of the studied groups, the areas with a better nutritional status were found to have a lower incidence of dental fluorosis. The incidence among milk-consuming children was lower than that of non-milk consuming children.

The enamel and dentin of teeth from individuals in Delhi and Bombay had a much higher fluoride content than would be expected in view of the low fluoride
content of water supplies in these communities. The fluoride value of the enamel and dentin of Boston teeth were in the same low range as has been reported for the teeth of individuals in other low-fluoride communities in the temperate zone. Only part of the difference in fluoride content between teeth of Boston individuals and those of Delhi and Bombay can be explained by the probable higher water consumption among the Indian citizens. The remainder of the difference would appear to be due to an additional source of fluoride in diet with sea salt as a logical possibility or to a higher rate of absorption and utilization of the ingested fluoride or combination of these two factors.\textsuperscript{103}

Chan JT et al have demonstrated that the incidence of dental fluorosis has increased during the past decade. Greater availability and use of fluoride-containing gels, mouth rinses, dentifrices, etc., improper prescribing of fluoride supplements and ingestion of fluoride dentifrice by some children are some of the suggested determinants of dental fluorosis. However, based on the increase in consumption of tea, coffee, and other caffeine-containing beverages by the children, and the augmentative effect of caffeine on fluoride bioavailability, they theorized that the rise in incidence of dental fluorosis in North America is mainly due to the replacement of water intake by caffeine-containing beverages among the young population.\textsuperscript{104}
2.7. GENETIC DETERMINANTS OF FLUOROSIS

Everett et al. hypothesized that genetic determinants influence an individual's susceptibility or resistance to develop dental fluorosis. They tested this hypothesis using a mouse model system (continuous eruption of incisors) where genotype, age, gender, food, housing and drinking water fluoride can be rigorously controlled. Examination of 12 inbred strains of mice showed differences in dental fluorosis susceptibility/resistance. The A/J strain mice is highly susceptible, with a rapid onset and severe development of dental fluorosis compared with that in the other strains tested, whereas the 129P3/J mouse strain is least affected, with minimal dental fluorosis. These observations support the contribution of a genetic component in the pathogenesis of dental fluorosis.

In a recent study from Russia, the phenotype frequency distributions of several classical blood genetic markers were analyzed in workers of Siberian aluminum plants who had occupational fluorosis. Comparison with healthy workers revealed significant differences in frequencies of several markers in fluorosis victims. The researchers concluded that Phenotypes B (AB0), D (Rh), MN (MN), P1 (P), Le a (Lewis), Gc 2-1, Cx (on both hands), Th/I+ (on the left hand), C3, and C4 (HLA) were associated with higher risk of occupational fluorosis.
3. FLUOROSIS AND ALTITUDE

Asoku et al. in their study "Risk factors associated with dental fluorosis in Central Plateau State, Nigeria" explains that the fluorosis prevalence was significantly associated with altitude. The occurrence of dental fluorosis in Central Plateau could be because of the high altitude of the area and the fluoride concentration of the water consumed in the district\textsuperscript{107}.

Pantio et al determined the prevalence and severity of dental fluorosis in Mexican adolescents. A cross sectional epidemiological study was carried out in 1024 adolescents residing in three naturally fluoridated areas at high altitudes above sea level. A relationship between fluoride concentration in water in each community and fluorosis was observed. The high fluorosis prevalence and severity might possibly be associated with the high altitude of the communities\textsuperscript{108}.

Previous studies have reported higher dental fluorosis prevalence in high altitude communities than in low altitude communities. This investigation determined and compared dental fluorosis prevalence in populations of children living at high and low altitudes in Mexico. The results led to the conclusion that the difference in fluorosis prevalence in Mexico City and Veracruz could not be explained by differences in fluoride content of the salt or water samples, self-reported exposure to fluorosis risk factors or estimated fluoride intake\textsuperscript{108}.
4. TEMPERATURE AND FLUORIDE INGESTION

According to Galagan et al. the single most important factor determining the amount of water consumed is the maximum daily temperature in the area concerned. Roughly, there seems to be an inverse relationship between the amount of water consumed and the distance from the equator. Failure to make adjustment in water fluoride level for this factor may result in a higher prevalence of fluorosis. The relationship between fluoride levels, fluorosis and temperature is depicted in figure 2.

![Figure 2](image)

Relationship between fluoride levels, fluorosis and temperature (USPHS)
5. WATER HARDNESS AND FLUOROSIS

Water hardness is the traditional measure of the capacity of water to react with soap, hard water requiring a considerable amount of soap to produce lather. Scaling of hot water pipes, boilers, and other household appliances is due to hard water. Water hardness is caused by dissolved polyvalent metallic ions. In fresh water, the principal hardness-causing ions are calcium and magnesium; the ions strontium, iron barium and manganese also contribute.

Hardness is usually measured by the reaction of the polyvalent metallic ions present in a water sample with a chelating agent such as EDTA and is expressed as an equivalent concentration of calcium carbonate. Hardness may also be estimated by determination of individual concentrations of the components of hardness, their sum being expressed in terms of an equivalent quantity of calcium carbonate. The degree of hardness of drinking water has been classified in terms of its equivalent CaCO$_3$ concentration as follows:

- **Soft**: 0-60 mg/litre
- **Medium hard**: 60-120 mg/litre
- **Hard**: 120-180 mg/litre
- **Very hard**: 180 mg/litre and above

It is generally observed that fluoride containing water is usually soft with lesser calcium content and with high alkalinity. Fluoride concentration of even
less than 1 ppm along with high alkalinity of more than 300 mg/l was found to be associated with 10 per cent dental fluorosis in Punjab\textsuperscript{112}.

7. GLOBAL SCENARIO OF FLUOROSIS

![Global Fluoride Map](image)

**Figure 3. Global Fluoride Map**

(WHO Fluoride and arsenic in drinking water 2005)

Fluorosis is endemic in many parts of the world and its severe form, skeletal fluorosis have been reported world wide\textsuperscript{2}. Belyakova and Zhavoronkov suggested that fluorosis might be one of the most widespread of endemic health...
problems associated with natural geochemistry\textsuperscript{113}. As per the latest statistics, fluorosis relics as an endemic public health problem in at least 25 nations around globe. Ground water with high fluoride occurs in large parts of Africa, China, the Middle East and southern Asia (India and Sri Lanka). One of the best known high fluoride belts on land extends along the East African Rift from Eritrea to Malawi. There is another belt from Turkey through Iraq, Iran, Afghanistan, India, northern Thailand and China. The Americas and Japan have similar belts\textsuperscript{114}.

The intensity of fluorosis problem is very badly felt in the two heavily populated countries of the world, India and China\textsuperscript{2}. In 1995, one tenth of the population of China has been exposed to endemic fluorosis. It has been estimated that over 26 million people in China suffer from dental fluorosis due to elevated fluoride in their drinking water, with a further 16.5 million cases of dental fluorosis resulting from coal smoke pollution\textsuperscript{115}. Wang et al. reported the highest level of fluoride in well water as 21.5 ppm in the low-lying land of Zhuiger Basin in the Kuitun area of China in 1997\textsuperscript{116}. High fluoride concentrations in groundwater are reported from United States of America in the hot springs and geysers in Yellowstone National Park having 25-50 ppm, deep aquifers of Western US with 5-15 ppm and Southern California Lakeland having 3.6-5.3 ppm\textsuperscript{117}. In Mexico, 5 million people (about 6% of the population) are affected by fluoride in groundwater\textsuperscript{107}. Throughout Canada, there are a number of communities whose sources of drinking water contain elevated levels of fluoride (as high as 4.3 ppm)
from natural sources. Poland, Finland and the Czech Republic have levels of fluoride in drinking water as high as 3 ppm. In Ethiopian Rift Valley, fluoride concentrations in the range of 1.5 to 177 ppm are reported. The other worst affected areas include the arid parts of northern China (Inner Mongolia), African countries like Ivory Coast, Senegal, North Algeria, Uganda, Ethiopia, Northern Mexico and Argentina\textsuperscript{118}.

Nearly 25% of the population in the developing world still does not have access to safe source of water. The excess fluoride in groundwater adds much to this tragedy. Tanzania, covering some of the highly fluorotic rift valley areas, is one of the most severely fluoride affected countries in the world. The water is found having fluoride concentration in the range of 8.0-12.7 ppm in various seasons, inducing fluorosis in acute proportions. In many fluorotic areas, people, children in particular, are facing mobility difficulties due to crippling skeletal fluorosis\textsuperscript{119}.

**INDIAN SCENARIO**

Endemic fluorosis remains a challenging and extensively studied national health problem in India. In 1991, 13 of India’s 32 states and territories were reported to have naturally high concentrations of fluoride in water, but this had risen to 20 by 2004\textsuperscript{4}. The most seriously affected areas are Andhra Pradesh, Punjab, Haryana, Rajasthan, Gujarat, Tamil Nadu and Uttar Pradesh. The
The highest concentration observed to date in India is 48 ppm in Rewari District of Haryana. The high concentrations in groundwater are a result of dissolution of fluorite, apatite and topaz from the local bedrock. Handa (1975) noted the general negative correlation between fluoride and calcium concentrations in Indian groundwater. 

Fluoride Map of India
(Susheela AK: A Treatise on Fluorosis 2nd ed. 2003.)
The problem of fluorosis has been known in India for a long time. The disease, earlier called "mottled enamel" was first reported by Viswanadhan to be prevalent in human beings in Madras Presidency in 1933\textsuperscript{121}. However Shortt (1937) was the first to identify the disease as fluorosis in human beings in Nellore district of Andhra Pradesh\textsuperscript{122}.

According to a study conducted in various places in India, a statistically significant increase in the prevalence of dental fluorosis was found: (a) with higher levels of fluoride in drinking water, (b) with rise in age, peak being found at 15 to 19 years of age group, and (c) amongst the bonafide residents of the area. A significant positive correlation was found between fluoride in drinking water and community fluorosis index \textsuperscript{123}.

A study conducted in Delhi reveals the prevalence of skeletal and non-skeletal manifestations of fluorosis in 36 patients investigated at the All India Institute of Medical Sciences. In the study area covering 1485 sq. km with a population of 9 million, people consumed water naturally contaminated with fluoride up to 32.46 ppm \textsuperscript{124}.

An epidemiological survey carried out by Chakma et al. in a village of Mandla district of Madhya Pradesh revealed high prevalence of dental fluorosis (74.4\%) and genu valgum (51.1\%) among the subjects below 20 years (Genu valgum is the skeletal deformity leading to nock knee). The fluoride content of the water
used from the deep bore wells was ranged from 9.22 to 10.83ppm. The depth of the bore wells ranged from 37meters to 43meters as per the records of the Public Health Engineering Department, Mandla\textsuperscript{125}.

Rajasthan is one of the worst affected states in India. More than 50% of districts are with high fluoride in drinking water. According to a study conducted by Choubisa et al, out of 978 children and 1305 adults, 312 (31.9\%) and 436 (33.4\%) were affected with dental fluorosis with varying grades. Most of the adults suffered from diffused type of dental fluorosis. There was not remarkable difference in the prevalence of fluorosis in both sexes and between children and adults. The prevalence of dental fluorosis increased proportionately with increase in fluoride concentration in water. A heterogeneous fluoride distribution in the range of 0.2 to 5.5 mg/L has been observed in the villages surveyed\textsuperscript{126}.

A study conducted in school children in Rajura Taluk of Chandrapur district in Maharashtra showed that the people in that area appear at risk for fluorosis. The water fluoride level of 20 ppm from the village of Dhoptala is the highest reported fluoride concentration in drinking water in Maharashtra\textsuperscript{127}.

Gopalakrishnan et al. estimated that the overall prevalence of dental fluorosis among children in the age group of 10-15 years in Ambalappuzha Taluk of Alappuzha District in Kerala was 35.64\%. The prevalence was higher in urban area (55.28\%) compared to that in rural area (16.84\%) and in girls (39.21\%)
compared to boys (31.25%). The main risk factor associated with prevalence of dental fluorosis was high fluoride content in drinking water.\(^9\)

Karthikeyan et al had conducted water analysis from 255 villages in the Krishnagiri revenue block of Tamil Nadu in South India for fluoride and other water quality parameters. The results of chemical analysis showed that 39 villages of only 3 Panchayaths, namely Mallinayanapalli, Periyamuthur and Kallukuruki contained water sources having fluoride within the tolerable limits. The remaining 84.7% had their drinking water sources contaminated with excessive fluoride. Eleven Panchayats had fluoride in the range between 1-2ppm, seven Panchayats had 2-3ppm, three Panchayats had 3-4ppm and five had 4-5.1ppm.\(^{128}\)

Choubisa in his study "Endemic fluorosis in southern Rajasthan, India" shows that the chronic fluoride intoxication in the form of osteo-dental fluorosis was investigated in 21 villages of Banswara, Dungarpur and Udaipur districts of southern Rajasthan, where fluoride concentrations in drinking water range from 1.5 to 4.0ppm. Interestingly, a variable prevalence of fluorosis was observed in villages having almost the same fluoride concentrations. At 1.5ppm, 21.3, 25.6 and 38.9% of children and 33.3, 36.9 and 44.8% of adults in different villages of these districts were found to be affected with dental fluorosis. The maximum prevalence of dental fluorosis is (77.1%) was found in the 17-22 year age group.
No significant correlation was found between prevalence figures and gender. At the 1.5ppm fluoride concentration, 6.1, 6.8, and 9.5% of adults in villages of Banswara, Udaipur and Dungarpur districts, respectively showed evidence of skeletal fluorosis\textsuperscript{129}.

Khandare et al. studied the effect of tamarind ingestion on fluoride excretion. 20 healthy boys were included in the study and 18 completed the study. Each subject consumed 10gm of tamarind daily with lunch for 18 days at a Social Welfare Boys Hostel in Nalgonda and R R Districts of Andhra Pradesh. Tamarind intake led to significant increase (p = < 0.001) in the excretion of fluoride in 24 hours urine (4.8±0.22mg/day) as compared to excretion on control diet (3.5±0.22mg/day). Tamarind intake is likely to help in delaying progression of fluorosis by enhancing urinary excretion of fluoride\textsuperscript{130}.

Sharma S K had studied the water fluoride content of 9 States in India viz: Jammu and Kashmir, Himachal Pradesh, Rajasthan, haryana, Bihar, West Bengal, Chattisgarh, Orissa and Maharashtra. The surface, subsurface and thermal water sample analysis indicate that fluoride concentration ranging from <0.2 to 18ppm in the States of Jemmu and Kashmir, <0.2 to 6.5 in Himachal Pradesh, <1.5ppm in Rajasthan,0.2 to 0.6 in Haryana, 0.35 to 6.0 in Maharashtra, indicating that except in Haryana, the concentration of fluoride is very high up to 20ppm.\textsuperscript{131}
Chandrasekhar et al. have assessed the prevalence of dental fluorosis and its relationship with fluoride levels in drinking water in 12 villages of Davangare district of Karnataka state in India. The study group consisted of 1131 school children in the age group of 12 - 15 years. The prevalence of dental fluorosis ranged from 13.2% to 100% at a water fluoride level of 0.22ppm to 3.41ppm\textsuperscript{132}.

An investigation was undertaken in six endemic villages of Mundargi Taluk of Gadag district and two of Hungund Taluk of Bagalkot district to assess the clinical symptoms of both dental and skeletal fluorosis and in turn to find out the severity of the disease. Among the 832 subjects (532 and 300 from Mundargi and Hungund Taluk respectively) surveyed, 328 (61.65%) and 194 (64.67%) patients exhibited the symptoms of either dental or skeletal or both types of fluorosis. The fluoride content in drinking water of Mundargi Taluk ranged from 4 to 10.5ppm, while that of Hungund Taluk ranged from 2.04 to 3.2ppm\textsuperscript{133}.

Tamil Nadu is one of the seven southern states of India having 10 out of the 29 districts affected with fluorosis. A cross-sectional study was conducted by the authors in 13 selected villages of five contiguous north western districts of Tamil Nadu viz: Vellore, Dharmapuri, Krishanagiri, Salem and Erode to assess the prevalence of fluorosis adopting stratified random sampling procedure. A total of 8700 individuals including 1745 children in the age group of 5-14 years were examined. Community bore well formed the major source of drinking water and
the mean fluoride content of water was found to be more than the WHO cut of level of 1.5ppm in seven of the 13 villages. The prevalence of dental fluorosis was high among the total population in the district of Dharmapuri (36%), Krishnagiri (24%) and Salem (33%), where the mean fluoride levels were 2.7, 2.2 and 1.2ppm respectively. The prevalence of dental fluorosis was still high among children in the above three districts (53%, 43%, and 42% respectively).