CD Alert

National Centre for Disease Control,
Directorate General of Health Services, Government of India

March, 2022

Fluorosis

1. Introduction

This piece of information is specially designed for the benefit of Professionals and Scientists from different disciplines addressing communicable and non-communicable diseases in India and elsewhere. Fluorosis is a disease caused by ingestion / inhalation of Fluoride in excess, which the human body is unable to tolerate [1].

While Fluoride, in recommended doses, has been proved to have beneficial effects on skeletal and dental health, its toxicity at greater than the recommended dosage, has been widely reported. Fluoride interferes with enzyme activities, induces oxidative stress and causes hormonal disturbances. The health impacts of increased Fluoride exposition in millions of people in the world are of global public health concern [2].

2. Fluorosis: Global Scenario

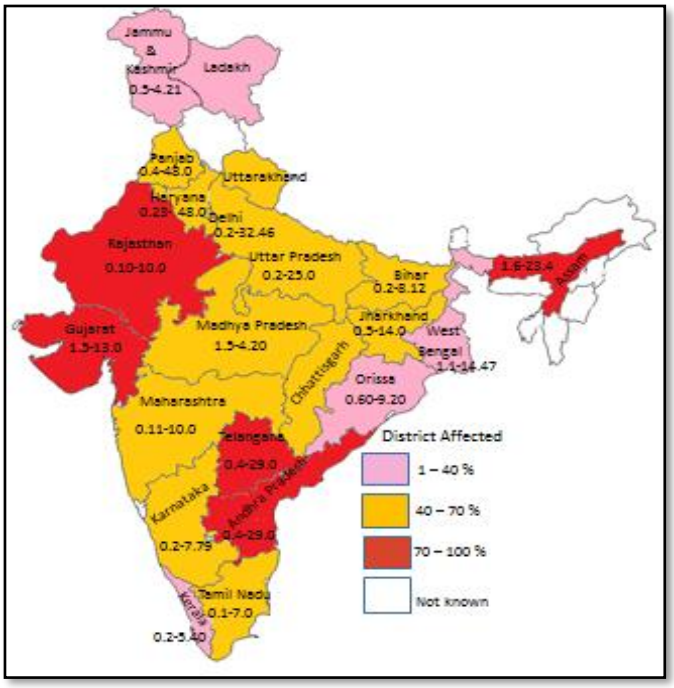
The problem of excessive Fluoride in drinking and cooking water is prevalent in many parts of the world. Water sources found at foot of high mountains and in areas having geological deposits of sea origin are rich in Fluoride content. WHO has estimated that around 260 million people inhabit locations having excessive Fluoride levels in drinking water (>1.5 mg/L) globally [2].

Fluorosis has been reported from several areas throughout the world that lie within the Fluoride belt. Major Fluoride belts on earth span from (i) Syria through Jordan, Egypt, Libya, Algeria, Sudan and Kenya, from (ii) Turkey through Iraq, Iran, Afghanistan, India, northern Thailand and China and there are (iii) similar belts in the America and Japan [1].

High Fluoride concentrations in ground water are found in the Africa, America, Europe and Asia. The ground water Fluoride concentration is high in countries within East African Rift Valley like Tanzania, Kenya and Ethiopia. The highest Fluoride concentration is reported in Lake Nakuru in Kenya (2800 mg/L) [3].

3. Fluorosis in India

Fluorosis has a history of about 85 years in India. Excess Fluoride in ground water and prevalence of Fluorosis was detected in British India in Nellore district of Andhra Pradesh [4] and in Madras Presidency [5]. High levels of Fluoride have been reported in several States (18 States and 1 UT) of our country indicating that endemic Fluorosis has emerged as one of the public health problems of the country [6]. Millions of people living in high Fluoride habitations are at risk for developing Fluorosis. In parts of Gujarat and Uttar Pradesh, industrial Fluorosis is also seen. The desirable limit of Fluoride in water, as per Bureau of Indian Standards (BIS), is 1ppm (parts per million) or 1 mg/L, the lesser the better [7]. In India, Fluorosis has been reported to occur even at 1.5 mg /L Fluoride, therefore the BIS standard 1.0 mg /L is the upper limit. So far 48 mg/L of Fluoride has been reported in water sources in India; however, there may be odd sources with much higher Fluoride concentration existing in India but may not be in regular water use.



(Fig. 1): Map of India showing in endemicity of Fluorosis

The map of India shown here is the compilation of information by UNICEF, India to enable record of the endemicity of Fluorosis disease (Fig. 1) [8]. In each state there are two numbers recorded - the minimum and the maximum Fluoride - detected so far. It is evident that safe and unsafe water sources co-exist and the community is unaware of the safe and unsafe sources. The consumption of unsafe sources continues, may be to a lesser extent.

4. Fluorine and Fluoride

The elemental Fluorine exists as a diatomic molecule with remarkably low dissociation energy (38 Kcal/ molecule). It is highly reactive and has a strong affinity to combine with other elements to produce Fluoride(s) [9].

Fluorine is the most electronegative of all elements and the strongest oxidizing agent known. When Fluorine combines with Hydrogen, the reaction produces a temperature of 4700°C, which is even hotter than that obtained by burning atomic hydrogen in oxygen which generates heat at 4200°C.

Ground water in earth's crust is surrounded by Fluoride bearing minerals, which leach out in water. When such ground water is drawn for drinking & cooking purpose, Fluoride gains easy access to the body [2,10]. The mineral Calcium Fluorite is the major source of Fluoride, having a concentration of 157 ppm Fluoride [6]. Fluoride is also consumed unknowingly through food and beverages containing spices with rock salt, which are used for enhancing aroma.

5. Conventional Forms of Fluorosis and their Diagnoses

Dental and Skeletal Fluorosis are the two conventional forms of Fluorosis. Another form of Fluorosis manifests as the 'Linked Disorders'. The 'Fluorosis and Linked Disorders' refer to the "soft tissue manifestations" [11].

1) Dental Fluorosis

Dental Fluorosis is usually one of the first indicators of Fluorosis. It occurs mostly in the permanent teeth because of hypomineralization of the enamel due to excessive exposure to Fluoride during enamel mineralization. Although Dental Fluorosis occurs only in children, adults may present signs of Dental Fluorosis due to childhood exposure to Fluoride. Discoloration due to excess Fluoride intake will be visible to the naked eye in children who are 8 years and above. The discoloration shall be seen on the enamel surface away from the gums.

(Fig. 2): Dental Fluorosis in school-going children of Madhya Pradesh and Uttar Pradesh

However, the discoloration near the gums is due to dirty teeth and should never be mistaken for Dental Fluorosis. Furthermore, the discoloration is observed in teeth in pairs based on developmental pattern and never in a single isolated tooth. Both the inner and outer surface of the teeth are affected [12].

Dental Fluorosis manifests in the form of Yellowish, Brownish or Black discoloration of the teeth. The discoloration may be observed as spots or streaks, which are always horizontal in orientation. The enamel may be pitted, rough and hard to clean and it becomes a permanent feature (Fig. 2).

The commonly affected teeth are:

- Central incisors,
- Lateral incisors and
- Molars of the permanent dentition [13]

Dental Fluorosis in Children:

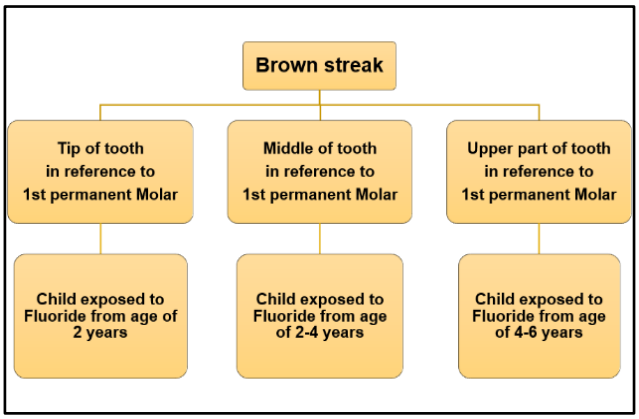
Children aged 8 years and younger are highly susceptible to Dental Fluorosis because this is the age when permanent teeth develop. Some sources of Fluoride include Fluoride contaminated water, certain food items, tinned food containing higher levels of fluoride, fluoridated toothpastes - if swallowed by young children [13,14].

WHO recommends that for prevention of dental caries, toothpaste should contain at least 1000 ppm of fluoride but no more than 1500 ppm of Fluoride to prevent Fluoride related toxicity. Children less than 3 years of age should use rice grain size amount while children aged 3 - 6 years should use pea size amount of the regular Fluoridated toothpaste under strict supervision of parents/caregivers to ensure that toothpaste slurry is not swallowed but spat out [15].

Dental Fluorosis is not just a cosmetic problem, as generally perceived, but also a window to what might happen to some of the vital organs in the body. Not only the pitted enamel seen in Dental Fluorosis aggravates dental damage but also a long- term intake of Fluoride may lead to a crippling disorder i.e., Skeletal Fluorosis.

Once Dental Fluorosis has set in, it is irreversible. However, the dentist can help in changing the appearance of the Fluorosis affected teeth by a variety of treatments in aesthetic dentistry. The dating of Fluoride exposure can be traced back depending on the level of tooth discoloration [14], as displayed in the diagram below.

Correlation between teeth discoloration and age of exposure of Fluoride:



2) Skeletal Fluorosis

Skeletal Fluorosis is not easily recognizable until the disease has developed to an advanced stage. Manifestations of Skeletal Fluorosis are seen in the young as well as the adults. Fluoride, after entering the body, rapidly moves to the bones and other hard tissues. Here, most of it is retained while a fraction is excreted

daily. Maximum ill-effects of Fluoride are detected in the neck, vertebral column, pelvic girdle, knee and shoulder joints. It also affects small joints of the hand and feet (Fig. 3) [14].

The effects of Fluoride are cumulative, and no known drug can cause Fluoride mobilization from the bones. The skeletal changes caused by chronic poisoning of Fluoride thus progress through a number of stages.

Endemic, crippling Skeletal Fluorosis occurs in individuals exposed continuously for years to very high levels of 5 to 10 ppm of Fluoride in drinking water. Malnutrition and/or renal dysfunction may aggravate Skeletal Fluorosis. The severity of Fluorosis may vary in a given population residing in the same area because no two individuals are the same [14].

Clinical Manifestations of Skeletal Fluorosis	
Preclinical Phase	Largely asymptomatic with slight radiographically detectable increase in bone mass.
Phase-I Musculoskeletal Fluorosis:	Sporadic pain; stiffness of joints; osteosclerosis of pelvis and spine.
Phase-II Degenerative and Destructive Fluorosis:	Chronic joint pain; arthritic symptoms; slight calcification of ligaments; increased osteoporosis of long bones.
Phase-III Crippling Fluorosis:	Limitation of joint movement; calcification of ligaments/neck, spinal column; crippling deformities/spine and major joints; muscle wasting; neurological defects /compression of spinal cord.

(Fig. 3): Skeletal Fluorosis cases in Haryana and Karnataka

Studies on Skeletal Fluorosis in humans and in Fluoride toxicity-induced animal models have elucidated that one of the earliest manifestations of Fluoride toxicity is in and around the osteoblast or an osteocyte and can be detected from the accumulation of glycosaminoglycans (GAG) [16].

As GAG formation is in and around osteoblasts and osteocytes, it is unlikely that a needle biopsy from patients may be helpful. Therefore, blood samples have been investigated for GAGs and the glycoprotein (sialic acid). The blood samples obtained from Fluorosed humans or from Fluoride toxicity-induced animal models have revealed that GAGs are significantly enhanced; however, sialic acid content is reduced [16].

6. Why Tooth and Bone are Afflicted Preferentially in Fluorosis

The disease nomenclature denotes that Fluoride preferentially afflicts tooth and bone. To understand the primary reason for the affliction, the chemical configuration of the matrices of the two mineralized tissues (tooth and bone) were examined. The tooth and bone matrices are predominantly constituted of collagen protein; however, the two other constituents of the matrix, which play a role in the pathogenesis of Fluorosis are:

- glycosaminoglycans and
- sialic acid (glycoprotein)

Glycosaminoglycans occur in the matrices of tooth and bone as sulphated and non-sulphated isomers. Sulphated isomers of GAGs, such as dermatan sulphate play a prominent role in mineralization as well as hypomineralization. Dermatan sulphate, which is absent in normal mineralized tissues, develops after exposure to Fluoride and leads to demineralization. Similarly, Dermatan sulphate content is significantly enhanced in Fluorosed teeth as compared with control samples from Fluorosis-endemic and non-endemic areas. Overtly visible dental discolouration suggestive of Fluorosis has been evident only in subjects with high dermatan sulphate content. This primarily may be the impetus for Fluorosis development, preferentially compared to other soft tissues, viz. ligament, skin, muscles and the aorta.

On the contrary, the soft tissues which are not destined to be mineralized have high concentrations of dermatan sulphate. Upon exposure to Fluoride, dermatan sulphate begins to disappear and the soft tissues get mineralized (ectopic calcification). The calcification of ligaments in Fluorosis, as seen in radiographs is a classic example of mineralization of the soft tissues. Dermatan sulphate, therefore appears to be the crux of the problem of Fluorosis/ Fluoride toxicity leading to demineralization in bone and tooth and mineralization in the soft tissues [14,16].

7. Fluorosis and Linked Disorders - Earliest Manifestations

The earliest manifestations of Fluorosis, involving soft tissue, are appropriately designated as “Fluorosis and Linked Disorders”. It is unfortunate for nearly half a century “Linked disorders” were not paid adequate attention because of soft tissue involvement. The earliest manifestations are essentially required to

suspect Fluorosis. They are listed in a chronological order [17]:

- Gastro-intestinal discomfort (40-50% individuals may complain of IBS)
- Weakness / fatigue - these complaints are due to muscle damage (30-40% individuals may suffer from this)
- Polyuria and polydipsia - excessive tendency to urinate and excessive thirst (2-20% individuals may suffer from these two complaints)
- Low hemoglobin and anemia (a high percentage suffer from this)
- Pain in the major joints (10-30% individuals may have this complaint)

The above complaints, early manifestations, should not be dismissed as "Non-specific" because that would lead to Fluorosis of a severe form, which may be irreparable [11,17].

8. New Born, Infants and Children Afflicted with Fluoride Poisoning

Ingestion of Fluoride in high concentrations (>1.0 mg/L), during pregnancy, affects the mother and the fetus in utero. The baby may be born premature (prior to 34 weeks of gestation) or term babies may have body weight less than 2.5 kg, including the possibility of intrauterine death (IUD). Physical and mental disabilities begin to surface in children as they grow up. For example, children may appear with knock-knee, bow-leg, short stature (cretinism) and may also present low IQ. Children with Dental Fluorosis, may also have several other health problems, including thyroid function (FT_3 & FT_4) abnormalities.

The above-mentioned abnormalities due to Fluoride poisoning may also be seen in children with Iodine deficiency, as has been proven in recent years. Therefore, it emerges that to confirm whether it is Fluoride poisoning effect or Iodine deficiency, the body fluids of the child should be tested both for Fluoride and Iodine. It is also necessary to test Fluoride in drinking/ cooking water of the family.

Until recent years, Fluoride was tested in blood and urine of children to diagnose Fluorosis. Similarly, Iodine was tested in urine of children and if found less than normal, suspected of Iodine Deficiency Disorders (IDD). These tests conducted in isolation are considered inadequate to confirm the true reason for the health abnormalities in children. The testing laboratories may report the disease due to (i) Fluoride poisoning, or (ii) Iodine deficiency and /or (iii) Fluoride excess and Iodine deficiency. It is noteworthy that the two tests are absolutely necessary to be done in the body fluids of the same child [18].

9. Fluoride Testing

Fluoride, being a hormone disruptor, neurotoxin and enzyme inhibitor, leads to severe health issues. Testing for Fluoride in body fluids is mandatory to understand the underlying reasons for health problems. Fluoride testing should become a common routine test in all testing laboratories, which presently is not happening to the desirable extent. Methods for testing Fluoride in water, include:

- Colorimetric (SPADNS) method
- Photometric method and
- Ion- Selective Electrode (ISE) method

The most accurate and reliable method for testing Fluoride in the water and body fluids (blood serum and urine) is the Ion- Selective Electrode (ISE) method using Fluoride Ion-meter. Fluoride testing by ISE method requires trained manpower [6].

10. Fluorosis Management and Recovery

Fluorosis disease does not require drugs/ medicines for treatment. Prevention is the way forward. Recovery from the disease is possible upon early detection. Prevention is best achieved through safe drinking water and nutritional interventions. Interventions involve ●Diet editing for withdrawal of Fluoride consumption, ●Diet counselling for promotion of all nutrients, vitamins, antioxidants and minerals [19, 20].

➢ Safe Drinking Water Intervention

It must be ensured that the Fluoride level of drinking water does not exceed the permissible limit of 1ppm. In most areas, safe and unsafe sources of drinking water co-exist. Water from safe sources should only be used for cooking and drinking purposes. A family of four requires 20 L of safe drinking water. For washing, bathing, etc., one can use the water from unsafe sources also. Wells or Handpumps with safe and unsafe water should be marked as:

This water is safe for drinking and cooking purpose.

This water is unfit for drinking. You can use it for other household purposes.

If the water from all sources in a particular area is unsafe, then following measures can be taken:

- Low-Fluoride water from a distant source may be pumped.
- Treatment of surface water to remove turbidity and bacteria making it safe for drinking and cooking.
- Lowering of the Fluoride concentration in water by mixing high-Fluoride water with low-Fluoride water in appropriate proportion, if a source with acceptable water exists within reasonable distance.
- In area with heavy rainfall, rainwater harvesting can be carried out.

In case, all the above-mentioned techniques cannot be used, then defluoridation should be carried out by one of the following methods:

- Nalgonda technology developed by NEERI, Nagpur
- Activated alumina technology by IIT, Kanpur
- Reverse Osmosis filters

Since all defluoridation methods produce a sludge with very high concentration of Fluoride that must be disposed of, it needs to be emphasized that only water for drinking and cooking purposes should be treated.

➢ **Nutritional Interventions**

Intake of vitamin C, vitamin E, Calcium and antioxidants helps in the prevention and control of Fluorosis [19, 20, 21].

Sources:

- **Vitamin C** - Amla, lemon, oranges, tomato, green leafy vegetables, sprouted cereals and pulses, etc.
- **Vitamin E** - Vegetable oil, nuts, whole grain, cereals, green vegetables, dried beans, etc.
- **Calcium** - Milk, yogurt, green vegetables, jaggery, sesame, cheese, lotus stem, green leafy vegetables, colocasia, drumsticks and its leaves, cumin seeds, etc.
- **Antioxidants** - garlic, ginger, carrot, white onion, green leafy vegetables, papaya, pumpkin, etc.

11. Combating Fluorosis : Initiative by Ministry of Health & Family Welfare, Government of India

To address the country's Fluorosis problem, the Ministry of Health & Family Welfare, Government of India launched the "National Program for Prevention and Control of Fluorosis (NPPCF)" as a new health initiative during the 11th Five Year Plan (2007-12) and the same is now being expanded in a phased manner. Program was implemented in 100 districts of 17 States during the 11th Five Year Plan and additional new districts were taken up in a phased manner during the 12th Five Year Plan (2012-17). Moreover, during the 12th Five Year Plan, the program has been brought under the NCD Flexi-pool of National Health Mission (NHM). Currently, the Program is being implemented in 157 districts of 18 States and 1 UT [6].

Goal of NPPCF

The NPPCF aims to reduce Fluorosis problem in the country by preventing and controlling the disease [6].

Objectives

- To assess and use the baseline survey data of Fluorosis provided by the Department of Drinking Water and Sanitation, Ministry of Jal Shakti [6]
- To comprehensively manage Fluorosis in the selected areas [6]
- To undertake capacity building for prevention, diagnosis and management of Fluorosis cases [6]

Intervention Strategies

Surveillance in the community to identify cases

Capacity building and training of human resources to provide manpower support where needed

Establishing diagnostic facilities in the district

Providing health education for prevention and control of Fluorosis cases

Managing Fluorosis cases including supplementation, surgery and rehabilitation

12. Program Activities

Program activities

- **Fluorosis community diagnosis by village/ block/ cluster**
- **Facility mapping- village/ block/ district level**
- **Gap analysis in facilities, as well as the organisation of physical and financial support**
- **Behavioural changes as a result of an effective IEC stragtegy**
- **All persons with Fluorosis should be educated and monitored to improve their health**
- **Referrals for serious cases, as well as follow up**

13. Achievements of NPPCF so Far

- The Program is being implemented in 157 districts of 18 States and 1 UT [6, 22]
- To improve linkages and coordination with Ministry of Jal Shakti (nodal Ministry for drinking water), meetings have been organized by MoHFW [22]
- As part of the IEC strategy, posters, audio & video spots on prevention and control of Fluorosis have been circulated to the States [22]

- Control of Fluorosis has been included as a component of “Anemia Mukt Bharat” Guidelines issued by MoHFW in April, 2018 [22]
- Modules for Training of Trainers (TOTs), training of Medical Officers, Laboratory Technicians and ASHAs on Fluorosis under NPPCF have been finalized [22]

14. Tips for Health Surveyors to Detect Fluorosis Cases

➢ **Check list**

A. Food Habits

- Chewing of tobacco, paan, beetle nut (supari) and gutkha
- Consumption of black tea
- Consumption of red rock salt
- Consumption of black rock salt
- Use of Fluoridated toothpaste

B. Sources of Drinking Water

Ground water, bore well water, river water, hand-pump, municipal supply, open well, etc.

C. Early Warning Symptoms

Gastrointestinal complaints (nausea, loss of appetite, pain in stomach, gas formation, constipation followed by intermittent diarrhea), anemia, headache, depression, polydipsia, muscle fatigue and pain in major joints [23, 24].

Important: Fluoride may always not be the only cause for the above-mentioned complaints. It should be kept as a part of differential diagnosis.

D. Diagnosis of Dental Fluorosis

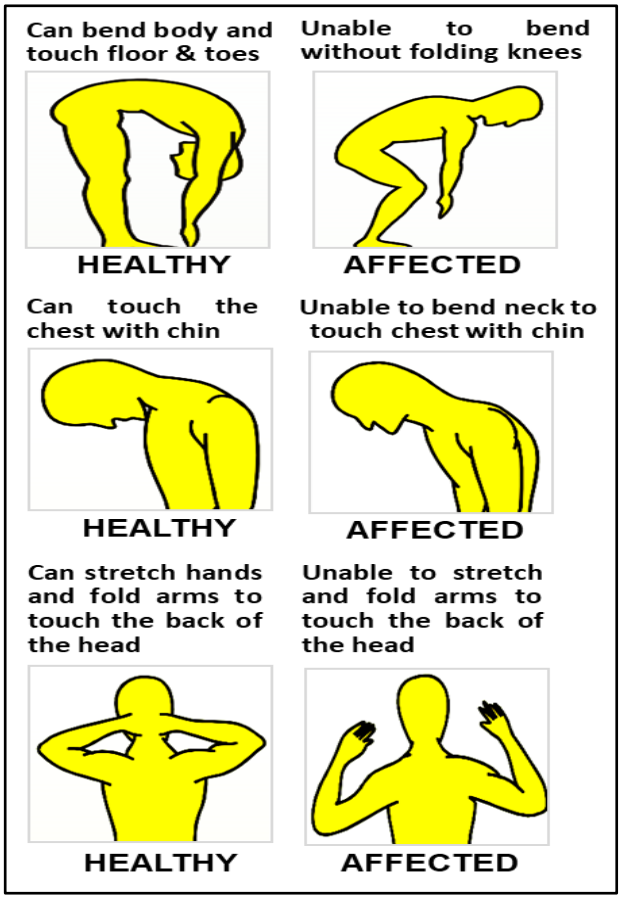
In Dental Fluorosis (Fig. 2), the disease may occur as discoloration in:

- The teeth in pairs based on development, have white opacities and faint yellow horizontally aligned lines
- The teeth in pairs have brown stains, spot or lines
- The teeth may get pitted, perforated and chipped off at edges, which are the signs of hypomineralization or demineralization (Fig. 2)

E. Diagnosis of Skeletal Fluorosis

In Skeletal Fluorosis (Fig. 3), the disease may occur as:

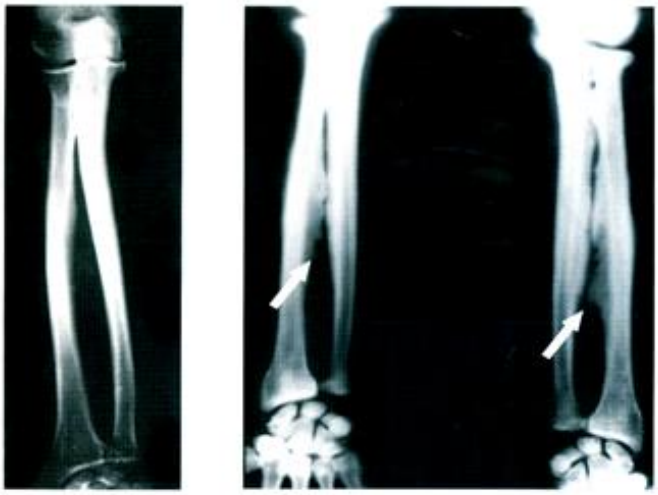
- The patients are symptomatic with aches and pain in major joints, vertebral column and difficulty in walking (Fig. 4) [6, 20]
- The patients are symptomatic with involvement of restricted movements of spine, neck and joints with rigidity, crippling deformity and fracture of bones (Fig. 4) [6, 20]
- The patient may appear asymptomatic but radiographs reveal increase in bone density and bone mass (Fig. 5)



(Fig. 4): How to Test Pain in Major Joints (Possibly Skeletal Fluorosis)

F. High Risk Groups

- Children
- Elderly people
- Pregnant women & lactating mothers
- Patients with cardiovascular diseases
- Patients with kidney disease



Normal: (Smooth outline of radius and ulna)
Fluorosed: (Increase in bone mass and bone density
Calcified interosseous membrane (arrow)

(Fig. 5): X-ray radiograph of forearm

G. Laboratory Investigations

Dental Fluorosis is diagnosed without any laboratory tests but through overtly visible discoloration present on teeth with specific characteristics (Fig. 2).

Skeletal Fluorosis is diagnosed with four different laboratory tests. (1) Drinking water is tested for Fluoride (>1.0 mg/L), (2) Urine sample is tested for Fluoride (>1.0 mg/L), (3) Serum sample is tested for Fluoride (0.02 - 0.05 mg/L), (4) X-ray radiograph of forearm (Fig. 5) (either right or left arm) is checked for calcified interosseous membrane with enhanced bone mass and bone density [6, 20].

Way Forward:

- Post-intervention through diet editing to retrieve health complaints with focus on early manifestations of Fluorosis
- Diet editing & diet counselling would become a way of life
- Safe water, safe food and nutritive diet is the message for prevention of Fluorosis
- Mothers in affected areas should be encouraged to breastfeed since breast milk is usually low in fluoride

Adverse Effects of Fluoride

Excessive exposure to Fluoride causes:

1. Dental Fluorosis
2. Skeletal Fluorosis
3. Thyroid malfunctions
4. Abnormalities in babies born to women with Fluorosis
5. Gastrointestinal disturbances
6. Anemia
7. Allergic manifestation
8. Calcification of ligaments & blood vessels
9. Abnormalities in sperms

Excessive exposure to Fluoride increases the risk of:

- Osteoporosis
- Hip fractures
- Teeth damage

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References:

1. *World Health Organization. Water Sanitation. Water Related Diseases. Fluorosis. Available online: https://www.who.int/water_sanitation_health/diseases-risks/diseases/fluorosis/en.*
2. *Jha PK, Tripathi P. 2021. Arsenic and fluoride contamination in groundwater: A review of global scenarios with special reference to India. Groundwater for Sustainable Development. 13, 100576.*
3. *Demelash H, Beyene A, Abebe Z, Melese A. 2019. Fluoride concentration in ground water and prevalence of Dental Fluorosis in Ethiopian Rift Valley: systematic review and meta-analysis. BMC Public Health. 19, 1-9.*
4. *Shortt HE, Pandit CG, Raghavachari TNS. 1937. Endemic Fluorosis in the Nellore District of South India. Indian Med. Gaz. 72, 396-398.*
5. *Shortt HE, Mcrobert GR, Barnard TW, Nayar ASM.1937. Endemic Fluorosis in the Madras Presidency. Indian Journal of Medical Research. 25, 553-68.*
6. *National Program for Prevention and Control of Fluorosis (NPPCF), Revised Guidelines. 2014. Directorate General of Health Services, Ministry of Health & Family Welfare, Government of India.*
7. *BIS - 2012. IS 10500 - Standard of drinking water - Central Ground Water Board / Central Pollution Control Board.*
8. *UNICEF- State of art report on the extent of Fluoride in drinking water and resulting endemicity in India. 1999. Printed by FRnRDF, New Delhi.*
9. *World Health Organization. 1984. Fluorine and Fluorides-Environmental Health Criteria. 36.*
10. *Francisca MM, Patrick CK, Peter GN. 2017. Assessment of the Impact of Groundwater Fluoride on Human Health: A Case Study of Makindu District in Kenya. J Earth Sci Clim Change. 8,4.*
11. *Susheela A K. 2020. Treatise on Fluorosis and Linked Disorders Revised 4th Edition.*
12. *Molina-Frechero N, Nevarez-Rascon M, Nevarez-Rascon A, Gonzalez-Gonzalez R, Irigoyen-Camacho M E, Sanchez-Perez L, Lopez-Verdin S, Bologna-Molina R. 2017. Impact of Dental Fluorosis, Socioeconomic Status and Self-Perception in Adolescents Exposed to a High Level of Fluoride in Water. Int. J. Environ. Res. Public Health. 14, 73.*
13. *Beltran-Aguilar ED, Griffin SO, Lockwood SA.2002. Prevalence and Trends in Enamel Fluorosis in the United States from the 1930s to the 1980s. J. Am. Dent. Assoc. 133, 157-165.*
14. *Susheela AK. 2007. Treatise on Fluorosis: Revised 3rd Edition.*
15. *World Health Organization (WHO). 2019. Preventing disease through healthy environments. Inadequate or excess fluoride: A major public health concern. (WHO/CED/PHE/EPE/19.4.5). Geneva.*
16. *Susheela AK and Sharma K. 1988. Bio-chemical characterization of GAGs in Fluoride exposure leads to Dermatan Sulphate formation. Arch Toxicology, 62, 328 - 330.*
17. *Susheela A K and Toteja GS. 2018. Prevention & control of Fluorosis & linked disorders: Developments in the 21st Century - Reaching out to patients in the community & hospital settings for recovery. Ind J Med. Res. 148: 539 - 547.*
18. *Susheela AK. 2018. Fluorosis and Iodine Deficiency Disorders in India. Current Science.115, 860 - 867.*
19. *Susheela AK. 1994. Studies on some aspects of Fluorosis in Recent Trends in Nutrition. Edited by C. Gopalan. Oxford Univeristy Press, 143 - 157.*
20. *Susheela AK. 2015. Fluorosis mitigation: guidelines for program execution for policy makers, health administrators and doctors.*
21. *Susheela AK. 2016. Healthy life in an era with diseases: First Edition.*
22. *Annual Report 2020 - 2021, Department of Health and Family Welfare, Ministry of Health and Family Welfare, Government of India. Available online: https://main.mohfw.gov.in.*
23. *Susheela AK, Gupta R, Mondal NK. 2016. Anemia in adolescent girls: An intervention of diet editing and counselling. Nat. Med. J.India. 29 (4), 200 - 204.*
24. *Susheela AK, Mondal NK, Gupta R, Sethi M, Pandey RM. 2018. Fluorosis is linked to Anaemia - Current Science, 115(4), 692 - 700.*

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