REVIEW ARTICLE

Fluorosis and iodine deficiency disorders in India

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This review focuses on fluorosis and iodine deficiency disorders, two serious, highly prevalent metabolic disorders that are under-reported. These are caused by the two elements of the halogen family, fluorine and iodine. The former in excess and the latter in deficiency are the cause for concern. Excess fluoride (F^-) consumption through untreated groundwater was the main reason for fluorosis and defluoridation of water was the focus to provide safe water with $F^- < 1.0$ mg/l. On the other hand, iodine deficiency in diet was due to agricultural crops grown in iodine-deficient soil, and iodization of cooking salt was identified as the way forward to attain iodine sufficiency (i.e. 15 ppm in iodized salt). The two diseases are addressed through structured national programmes, but the implementation unfortunately is in a compartmentalized manner. The major issue is that both F^- excess and iodine deficiency caused goitre. Besides, other disorders identical in clinical manifestations, also occur. This review discusses the issues to address the diseases with better understanding that has emerged from the scientific information available for correct diagnosis and management of patients in an integrated manner.

Keywords: Amendments, fluoride excess, health issues, iodine deficiency, protocol.

SAFE drinking water and food security are basic human rights. Malnutrition (both under- and over-nutrition) and non-absorption of nutrients are challenges that the nation is facing. India is an endemic nation for fluorosis and iodine deficiency disorders (IDD). The former is prevalent in 20 out of 35 states, and in Union Territories[1], and the latter in the whole nation[2]. The understanding of fluorosis is based on groundwater contamination of fluoride (F^-) arising from geological crust and community consuming untreated, unsafe groundwater drawn through hand pumps, tube wells and open wells. However, communities consuming safe water (F^-<1.0 mg/l), have also been reported to suffer from fluorosis, the source of fluoride being traced to consumption of rock salt black/pink/white in colour, with calcium fluoride (CaF_2) to the extent of 157.0 ppm F^- (ref. 3). The aroma and tangy taste of rock salt has made it very acceptable in culinary practices. Therefore F^- entry to the body can be through food and beverages besides water. As opposed to fluorosis, IDD is spread across the nation and therefore salt iodization was introduced as part of National Goitre Control Programme in the country in 1962. A significant increase in the coverage of adequately iodized salt from 49% to 78% at the household level has been observed in the country over the past 25 years. The country's goal was to achieve the universal salt iodization (USI) target of >90% household coverage. Efforts were made to accelerate, achieve and importantly, sustain the programme towards optimal iodine nutrition status and to eliminate IDD from India[2]. According to prevailing norms, if the salt has >15 ppm of iodine, it is classified as adequately iodized; if iodine <5 ppm, it is uniodized salt. Iodine is required for production of thyroid hormones, i.e. tetra-iodothyronine (T_4) and tri-iodothyronine (T_3). The biological status of iodine is assessed by testing iodine in the urine of patients and is the indicator for iodized salt intake[2]. IDDs originate from consumption of food/vegetables with little iodine, which is attributed to depletion of iodine in soil. In the past, iodine deficiency was thought to cause only goitre and cretinism. However, over the last quarter of a century, it has become increasingly evident that iodine deficiency leads to a much wider spectrum of disorders commencing from intrauterine life and extends through childhood into adult life with serious health and social problems[4–6]. The spectrum of diseases besides goitre and cretinism (short stature) includes, hypothyroidism, brain damage, mental retardation (low IQ), psychomotor defects and hearing and speech impairment. Abortion and still birth among pregnant women are also reported due to iodine deficiency. The consequences of IDD are not overtly visible during early stages. Detection in late stages is possible as it is overtly visible, but is too late for reversal to normalcy. Early detection, therefore, is of importance to address the disease.

The first objective of this review is to highlight that excess fluoride consumption may also lead to goitre, a disorder of the thyroid gland. Fluoride destroys the structure and function of the thyroid gland leading to inadequate production of thyroid hormones. Based on current understanding, the cause of goitre is considered to be iodine deficiency. Emergence of fluoride causes not only goitre but nine other disorders, which are identical in clinical manifestations to IDD. The ten disorders caused

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Table 1. Children suffer from a number of disorders, by consumption of excess F^- identical to diet deficient in iodine

Fluoride excess: >1.0 mg/l (ppm)	Iodine deficient (non-iodized < 5 ppm; inadequately iodized 5–14 ppm)
Goitre[8,9,16,17,23]	Goitre
Short stature (Cretin)[1,41]	Short stature (Cretin)
Mental retardation (low IQ)[40,41]	Low IQ (13.5 points less than iodine sufficient children)
Brain damage[40,41]	Brain damage
Deaf - mutism (deaf and dumb)*	Deaf – mutism (deaf and dumb)
Thyroid hormone abnormalities[13,14]	Thyroid hormone abnormalities
Knock-knee, bow leg[1,40]	Knock-knee, bow leg
Intellectual disability[40,41]	Intellectual disability
Psychomotor defects*	Psychomotor defects
Abortions, still births, pre-term deliveries in pregnant women[43,45]	Abortions, still births, pre-term deliveries in pregnant women

*Prevalent in endemic areas of fluorosis and IDD.

by excess fluoride and iodine deficiency are tabulated in Table 1.

The second objective of the present review is to highlight the implications of diseases caused by excess fluoride and iodine deficiency and the synergy of these two elements in a biological system. There are nine studies from India[7–15] and another eight studies from other nations[16–23] reported on goitre prevalence in populations with iodine sufficiency, goitre in fluoride endemic areas and goitre in industrial workers exposed to fluorine fumes and dust. These studies have been described in the section dealing with human studies. Fluoride excess is the reason for persistence of goitre even in case of iodine sufficiency. This review therefore evaluates several issues that need to be addressed, with a focus on diseases surfacing in the context of fluorine and iodine, two environmental factors related to human health.

Activities to control fluorosis commenced in India during 1987, under the technology mission on safe drinking water. Fluorosis, as a health component, was then addressed by tagging to a water supply programme with focus on removal of F^- from untreated groundwater in rural India[24,25]. Dental and skeletal fluorosis were the two widely known disorders due to F^- excess consumption. The prevailing concept then was that supply of safe water (F^- <1.0 mg/l) for consumption would eliminate fluorosis from the afflicted population. On the contrary, the disease is widespread in the country over the years, as treatment technologies for water defluoridation failed miserably for technical reasons and the community continued to consume F^- contaminated water. Information on consumption of food containing fluoride did not surface then. The understanding of fluorosis continued to be based on earlier observations that emerged during the technology mission era. Activities related to iodine deficiency commenced in 1962 with iodization of edible salt, as iodine deficiency was known to cause high prevalence of goitre and cretinism. Subsequently the term IDD was coined to include goitre and other disorders caused due to iodine deficiency. One thing in common in these two national programmes was that there were partner organizations involved in the activities, i.e. the Ministry of Drinking Water and Rural Development in the former and the Salt Commissioner in the latter. Over the years, when the gravity of the problem of fluorosis and IDD was assessed and when it was evident that a nationwide problem with wider ramifications would take many years to set right the health status of children and community, the projects were transformed into national programmes under the Ministry of Health and Family Welfare. The partner organizations continued to be associated with the programmes with the main goal to control fluorosis and IDD. The ensuing paragraphs deal with a brief overview of the two national programmes.

National programme on prevention and control of fluorosis

The national programme on prevention and control of fluorosis (NPPCF) approved under the Eleventh Five Year Plan period in 2005, commenced its activities in the field since 2008–09. The water quality test reports of untreated groundwater drawn for consumption through hand pumps, tube wells, open wells, lakes, streams and rivers were provided by the Ministry of Drinking Water and Sanitation (the name of the Ministry changed during the course of time). There were certain key issues for programme implementation that require a special mention. Water and health being state subjects, the water supply agency(ies) (also known as public health engineering departments/water authority(ies)/water and sewerage boards) in the states undertook the water quality testing and funds were provided by the Government of India[25]. The test results were reported by all state departments online using integrated management information system

(IMIS) and uploaded in the website of the Ministry (www.ddws.gov.in) at certain specified intervals, so that it was viewed by concerned organizations and those involved in programme execution. It is necessary to point out a few limitations in the system. It was observed that, the water supply agency tested groundwater sources for a number of chemical parameters besides fluoride. Testing was done in randomly selected sources (certain percentage of existing sources), whether private or government owned, but not in all the existing water sources. Generalizations on water quality status for a whole village or block or district based on a small percentage of test results are considered inappropriate. Fluoride in groundwater sources may be safe or fluoride-contaminated. The colour, odour or taste of water cannot help identify safe sources. Testing is necessary. It was evident by then, from results reported from projects completed that, safe water sources exist in the villages in India[26]. Testing for fluoride is to be done with sensitive equipment in the laboratory, with the Bureau of Indian Standards (BIS) limit for F^- in drinking water being 1 mg/l (or less the better) and as F^- is injurious to health[27]. The water supply agency is expected to screen all water sources for F^- in a village initially by screening the samples in the field itself using a test kit. Those water samples indicating the result 1.5 mg/l are to be transported and re-tested in the laboratory using ion meter with F^- sensitive electrode. The test kit method has limitations to measure F^- beyond 1.5 mg/l. Unfortunately, the results obtained during screening, using the kit method are uploaded. This was easily detectable while viewing the data, as the results reported would be in the lower range, i.e. between 0.01 and 1.5 ppm. The higher F^- content >1.5 mg/l invariably is not evident from the test results. Since the communities were not informed of the test results to locate the existing safe sources; they continued to be unaware of whether the source that they depended on was potable or not. In view of these limitations, and as the fluoride content in drinking water in Indian states so far detected ranged from 1.1 to 48.0 mg/l (ref. 28), NPPCF made it mandatory to test 100% sources by an ion meter using F^- sensitive electrode by the personnel appointed under NPPCF. The personnel were imparted appropriate training on use, operation and maintenance of the ion meter. The data thus generated would be valid for a period of 4–5 years. It may increase or decrease due to environmental factors. Therefore it is necessary to indicate: (i) date of testing; (ii) equipment used for testing (ion meter or kit) and, (iii) method followed for testing F^-, whenever the data are tabulated and uploaded or when the results are reported in scientific publications. Fluorosis is widespread in the country as F^- enters the body besides water through a variety of other sources[29,30] which include cooked food, beverages, spices and chewing of substances (i.e. churans) with rock salt (CaF_2) with 157 ppm F^- for its appealing taste[3]. This is besides prescription drugs containing F^- for long term treatment of diseases such as otosclerosis, osteoporosis, use of antidepressants and fluoridated dental products. It therefore became necessary to test fluoride in body fluids to assess the F^- level in the body. NPPCF therefore adhered to testing fluoride in water and urine. An individual afflicted with fluoride toxicity/fluorosis was then unlikely to be missed for the source of F^- intake even if consuming safe water. This approach was necessary for embarking on an effective intervention strategy for individuals to recover from the disease(s) in a shorter span of time. The interventions practised were: (i) diet editing for removal of fluoride from all sources, so that the disease progression was stopped, and (ii) diet counselling practised simultaneously for promoting intake of all nutrients, viz. antioxidants, vitamins, minerals, micronutrients and essential nutrients through diet, rectified the damages caused and promoted better health. F^- causing goitre and other disorders listed in Table 1 remain to be addressed by amending the protocol in testing laboratories.

National iodine deficiency disorders control programme

The national programme on IDD was renamed in 1992 to cover the whole spectrum of iodine deficiency disorders with adoption of salt iodization as the primary strategy to control IDD. The milestones of the National Iodine Deficiency Disorders Control Programme (NIDDCP) programme are briefly summarized in Box 1.

Over the years, NIDDCP has been a public health success story with 92% of Indian population consuming iodized salt and the population having achieved iodine nutrition sufficiency as measured by urinary iodine concentration. Even at the regional level, the coverage of adequately iodized salt is satisfactory, with urban areas in the country having already achieved the USI target of greater than 90% adequately iodized salt coverage.

The national goitre control activities and their key events from 1962 till 2017 emphasize on the fundamentals for identifying goitre through district surveys and the impact of iodized salt consumption. As the years passed by, the policy laid down has listed out goals, besides objectives, to achieve by the stipulated time frame. Various national agencies/ministries were involved in providing further impetus to the programme. In the year 2006, it was envisaged to reduce the prevalence of IDD to less than 10% in the nation by 2012. Though the activities have moved on for 5 more years, the target is yet to be achieved. But certainly IDD is a success story. As the nation is providing education for children in rural and urban population and skill development for women, leading to employability, the task to achieve 100% coverage of use of iodized salt in every kitchen in the country would be achieved with ease in the coming years.

However, there is a growing concern regarding continued presence of goitre in areas with high iodized salt

Box 1. Milestones in IDD control programme in India

- National Goitre Control Programme (NGCP), 1962: No goal; only 3 objectives: (1) to conduct an initial baseline survey to identify the endemic and non-endemic districts based on goitre prevalence; (2) to produce and supply iodized salt to the identified endemic districts; (3) to conduct an impact assessment of the programme every five years to see the effectiveness of the programme.
- Central Health Council, Ministry of Health and Family Welfare, 1983: To iodize all salt meant for human consumption by 1992.
- World Summit for Children, 1990: The goal was to achieve virtual elimination of IDD by 2000. India was one of the signatory countries.
- Second SAARC conference on children in South Asia, 1992: Target to universalize iodization of salt by 1995.
- National Plan of Action, Department of Women and Child Development, 1992: Universal access to iodized salt by 1995 as a specific goal.
- National Iodine Deficiency Disorders Control Programme (NIDDCP), 1992: No goal, only 5 objectives: (1) surveys to assess the magnitude of IDD; (2) supply of iodized salt in place of common salt; (3) resurvey after every 5 years to assess the extent of IDD and the impact of iodized salt; (4) laboratory monitoring of iodized salt and urinary iodine excretion; (5) health education and publicity.
- Policy guidelines on NIDDCP, 1998: The goal was to reduce the prevalence of IDD below 10% in the endemic districts of the country by 2000.
- United Nations General Assembly Special Session (UNGASS) on children, 2002: USI by year 2005, India was one of the signatories.
- Tenth Five Year Plan, Planning Commission, GoI, 2002: The goals were to achieve universal access to iodized salt; generate district-wise data on iodized salt consumption; and to reduce the prevalence of iodine deficiency disorders in the country to <10% by 2010.
- Revised policy guidelines NIDDCP, 2006, IDD and Nutrition Cell, MOHFW, GoI: the goal is to reduce the prevalence of iodine deficiency disorders below 10% in the entire country by 2012.

coverage and with iodine sufficiency[7]. Fluoride toxicity due to consumption of fluoride containing water, food, beverages, etc. is a possible explanation for goitre and may have largely remained unknown as both programmes were executed in a compartmentalized manner. Excess fluoride also causes health problems, of similar nature to IDD. For better understanding of F^- excess causing goitre, results obtained from animal and human studies from India and other nations are highlighted in the following sections.

Studies on animals fed F^- in excess

This review therefore focuses on studies on different animal models fed with excess fluoride and human subjects ingesting high fluoride content. Adverse health effects were reported so that there is no room for ambiguities. The first report on F^- action on thyroid gland, dating back to 1854, appeared in a French journal[31]. The study reported that feeding dogs with sodium fluoride (NaF) 20–120 mg/day for 4 months caused goitre. In 1979, a detailed study by Hillman *et al.*[32] from Michigan, USA, investigated cows severely affected with dental and skeletal fluorosis due to mineral supplementation, with very high urine fluoride levels (UFL). The cattle with fluorosis developed hypothyroidism, anaemia and eosinophilia. Free tetraiodothyronine (FT_4) and Free triiodothyronine (FT_3) decreased in serum with increased UFL. The red blood cells (RBCs) and haemoglobin (Hb) were also low in fluorotic cows. This is one of the earliest studies with a well-designed protocol to reveal that in fluorosis with enhanced UFL, thyroid hormone levels and the RBC count were reduced, resulting in reduced Hb and consequently resulting in anaemia. A study from Turkey[33], confirmed that chronic fluorosis in cows reduced FT_4, FT_3 and protein bound iodine (PBI), with an associated decrease in the rate of metabolism by 30–40% in cases of hypothyroidism.

A study on chicks[34] on the effects of fluoride on the ultrastructure of the thyroid gland revealed structural changes leading to dysfunction of the gland. It was also stated that the thyroid gland had a strong capacity for absorbing and accumulating fluoride. The study provided the evidence to suggest that F^- absorbed by the gland caused widespread cellular derangements.

Yet another study on F^- induced thyroid changes in female mice and their pups[35] was interesting for the fact that it showed that with withdrawal of F^-, hypothyroidism in mice and their pups was reversed, thyroid gland weight decreased and thyroid stimulating hormone (TSH) level was partially restored. The information that emerged from the study showed the beneficial effects upon withdrawal of F^-. This was the only report which addressed the reversal of changes in soft tissues by withdrawal of F^-. There were studies in human subjects also which revealed that excess fluoride ingestion caused goitre, a typical 'IDD' disorder.

Human subjects on consumption of F^- in excess

A letter written by Almond FW to Surgeon General, US Public Health Service published in 1923 (ref. 16) (retrieved from the History of Medicine Division of National Library of Medicine) stated that children 12–15 years of age after consuming fluoridated water (6 mg/l) in Idaho (USA) developed enlarged thyroid gland (i.e. goitre). The body may tolerate fluoride up to 1 mg/l but not 6 mg/l, certainly a very high dose of F^-. These observations were ignored while fluoridating drinking water and promoting such activities in USA. Finding goitre upon consumption of F^- was on the record for decades. However, excess fluoride consumption through drinking water may not affect US population in future in view of the recommendation announced in April–May 2015 (ref. 36). The reason being, the US Department of Health and Human Services Federal Panel and Centres for Disease Control and Prevention have made a final recommendation on community water fluoridation that replaces the relevant parts of the 1962 drinking water standards[37,38]. Whereas the earlier recommendation, based on the outdoor air temperature of geographic regions, involved a range of 0.7–1.2 mg F/l. The new recommendation for community water systems that currently fluoridate or plan to do so, is for a level of 0.7 mg F/l. The US Surgeon-General (Dr V. H. Murthy), endorsed the recommendation and urged that communities adopt it[39].

A British scientist had reported as early as 1941 (ref. 17) that F^- played a role in developing endemic goitre in children when he was investigating children living in Punjab. Indian scientists had also reported the presence of systemic goitre in endemic fluorosis areas[5,6]. It was suggested that F^- in drinking water played a role in causing goitre. Increase in drinking water F^- beyond 1 ppm and/or mineral supplementation, adversely affected the thyroid gland in terms of its enlargement, reduced the enzyme thyroid adenylate catalase activity and decreased FT_4 and FT_3 hormones[18]. A Chinese report suggested that in endemic F^- area, decreased serum FT_4 and raised TSH were recorded although there was adequate intake of iodine. This also suggested that with adequate intake of iodine, F^- induced adverse reactions in the thyroid gland[19]. Yet another Chinese report provided evidence that in children of 7–14 years, IQ was adversely affected when high F^- and low iodine was consumed compared to normal F^- and low iodine-consuming children[20]. It is also known that F^- toxicity adversely affects the intelligence or IQ of children. It is evident from the references cited above that F^- is a hormone disrupter, enzyme inhibitor and a neurotoxin as it reduces the IQ of children. Therefore in diagnosing fluorosis in children, IDD can be ruled out by testing urinary iodine[40,41].

A report from Gujarat stated that an epidemiological study on the prevalence of goitre and dental fluorosis in endemic fluorosis districts revealed that the prevalence of goitre was associated with F^- in drinking water[10]. A Russian study pointed out that amongst workers continuously exposed to F^-, 51% had reduced FT_3 hormone. An analysis of immune status showed that T-lymphocyte count enhanced, but the cells were nonfunctional due to reduced FT_3 levels[21]. In yet another Russian report, amongst industrial workers exposed to F^- and suffering from industrial fluorosis, aberration in the thyroid gland function was reported[22].

A South African study that focused on children aged 6–15 years revealed higher prevalence of goitre in two towns with high F^- levels in water, though iodine intake was adequate[23]. An Indian study investigated 200 children aged 6–12 years in 4 areas and evaluated the effect of varying concentrations of F^- (ranging from 2.4 to 13.5 mg/l in drinking water), on serum parathyroid hormones[11]. All the children had dental fluorosis and it was found that an increase in serum parathyroid hormone concentration was associated with greater severity of skeletal fluorosis. F^- can stimulate parathyroid gland directly or indirectly and this led to secondary hyperparathyroidism[12].

In a study conducted in New Delhi during 2005 (ref. 13), 90 children with dental fluorosis (DF) formed the sample group, and 21 children from endemic and non-endemic areas without dental fluorosis formed the control group and were investigated for thyroid hormone levels besides their drinking water, serum and urine F^- levels. The study concluded that whether there was dental fluorosis or not, children living in high F^- areas should be investigated for thyroid hormone derangements. The study concluded that children with and without DF had hormone derangements leading to (i) sub-clinical hypothyroidism; (ii) low T_3 syndrome, (iii) T_3 toxicosis, (iv) primary hypothyroidism and (v) disturbed hormonal conversion with inhibition of de-iodinase. The study was a revelation of vulnerability of children living in endemic areas of fluorosis to thyroid hormone changes leading to thyroid hormone associated diseases. Yet another study from India also revealed F^--induced thyroid hormone disturbances similar to iodine deficiency status, in spite of adequate iodine intake[14].

In 2015, a study conducted in 400 pre-pubertal school children in the Southern state of Kerala and reported by the Government Medical College, Thiruvananthapuram, states goitre in children despite urinary iodine sufficiency[15]. School children were screened for goitre; urinary iodine excretion (UIE) was estimated on every 10th child and 30 salt samples were tested for optimum iodization. The results revealed a high incidence of goitre in 112 children (28%). Grade I goitre in 14.75% and Grade II goitre in 13.25% of children were recorded. Mean UIE was 115 μg/l and no sample with <100 μg/l indicated current iodine sufficiency. Among 30 salt samples tested, 26 (86%) were optimally iodized, 2 (7%) were suboptimally iodized and 2 (7%) were found to have no trace of iodine, even though all were labelled as iodized salt. The

problem is viewed through a transition phase shift from iodine deficiency to iodine sufficiency or due to other confounders. Authors point out other causes of goitre, like consumption of other goitrogens and reduced response of iodine due to opposing action by excess fluoride, cobalt and deficiency of iron.

Dental fluorosis (DF) and its extended effects reported[41], stated that F^- toxicity affects the intelligence or IQ of children and causes short stature (cretinism), bow-leg condition, knock-knee condition and mental retardation. Children with DF may also suffer from rickets (bow-leg, knock-knee and other bone deformities) for which treatment, when introduced, may or may not yield beneficial results, if high urine fluoride is detected. It is therefore necessary to check urine fluoride of such children and introduce diet editing to withdraw fluoride, so that they respond to treatment. The reason they do not respond to treatment is due to damage caused to the cells lining the intestinal mucosa specially loss of microvilli/brush border in F^- toxicity[1]. It can be rectified upon F^- withdrawal and the mucosa regenerates within a few days. It is only then children would respond to orally administered drugs. The references cited from India and other parts of the globe on F^- action on thyroid gland of human subjects included investigations on adults as well as children. The results cited prove that F^- causes enzyme inhibitions resulting in non-production of thyroid hormones, in spite of the fact that iodine intake was adequate.

Excess F^- ingestion was the causal factor for health abnormalities suggestive of IDD reported in Table 1. F^- destroys the structure and function of the thyroid glands (production of tri- and tetra-iodothyronines), although iodine intake was adequate. Therefore, it was suggested that iodine deficiency was not necessarily the only cause for such health problems in children. The results suggest that the diagnosis and management of IDD and fluorosis should have an integrated approach than what is being practised in present times. The two disorders may not be viewed in a compartmentalized manner. It may lead to serious lapses in diagnosis and patient management.

IDD and fluorosis: implications on maternal, infant, child and adolescent health

This review would be incomplete if the activities and contributions focused on maternal, infant, child and adoloscent health aspects of the national programmes for IDD and fluorosis were not highlighted. The National Iodine and Salt Intake Survey (2014–15) (ref. 2) had reported that pregnant and lactating mothers were at increased risk of iodine deficiency which is a serious issue confronting the nation. It was estimated that iodine deficiency during the critical 'thousand days', i.e. from conception to the first 2 years of life leads to: (i) recurrent abortions, (ii) still birth, (iii) increased pre-term deliveries, and (iv) high infant mortality and irreversible brain damage in infants and children[4,5]. Epidemiological studies focused on children born in severely iodine deficient areas have an intelligence quotient (IQ), 13.5 points less than those born in iodine sufficient areas[6].

It was stated by Sethi and Kapil[42] that in India, the current IDD survey guidelines of the national programme do not include pregnant women and the same need to be revised to include this important group.

Extensive studies both in iodine deficiency and fluoride excess continue to be supported by national and international grant agencies. Both programmes are reaching out to the community/afflicted victims in various states in the country. As pointed out by Sethi and Kapil[42] a few mid-course corrections in the programme implementation would be required.

In fluoride toxicity and fluorosis, it was proven that high maternal and infant mortality can also be due to consumption of fluoride salts through a variety of sources, which interfered with nutrient absorption, deranged thyroid hormone production and led to lack of stimuli for bone marrow to produce sufficient RBCs. Less RBCs resulted in less haemoglobin production resulting in anaemia. Commencing from 2010 till 2017, several publications appeared supporting the interventional approach[43–46] for correcting anaemia in pregnancy. High percentage of pregnant women upon correction of anaemia, i.e. 83%, delivered normal birth weight babies (2.5 to 3.8 kg). Withdrawal of F^- consumption resulting in low urine fluoride (<1.0 mg/l) followed by improvement in diet led to rise in Hb and correction of anaemia.

It is equally important to provide information on prevalence of anaemia in adolescent school children in India. Weekly iron and folic acid supplementation (WIFS) since 2012 and mid-day meal schemes are yet to yield appreciable results. With the confirmed success rate in addressing pregnant women, in reducing low birth weight babies (<2.5 kg) to 17% from the existing 41% in the country, based on elimination of consumption of fluoride salts, through food, drinking water, habit forming substances and use of fluoridated dental products, the protocol was adapted to suit school children, both for boys and girls. The studies conducted in 2240 school children in 6 schools in the age group of 10–17 years in New Delhi led to correction of anaemia (low haemoglobin) upon elimination of fluoride consumption (urine F^- <1.0 mg/l) (*Current Science*, accepted for publication). Simultaneous improvement of nutrients in diet[47–49] by imparting skills and empowering mothers to prepare nutritious meals for their wards added adequate dividends in improving health of the children.

Children with bow-leg and knock-knee seen in IDD, can also be caused by calcium and vitamin D deficiency. Then it is referred to as Rickets. The treatment is by

prescribing mega dose of calcium and vitamin D[38]. The kids may not respond to the treatment, when they are fluoride poisoned and intestinal lining is devoid of microvilli. Urinary F^- and urinary iodine testing, therefore assumes paramount importance in patient management, as the child may be suffering from a variety of health problems due to excess fluoride, iodine deficiency and under-nutrition/malnutrition. Withdrawal of F^- consumption, iodized salt promotion, nutritive diet with high calcium and vitamin D promotion corrects bone deformities and recovery occurs within a short span of time.

In conclusion, the review points out the necessity to revise the protocol for diagnosis of (1) IDD and (2) fluorosis, so that correct diagnosis of the diseases, and patient management can be improved upon. The protocol for IDD presently focuses on testing iodine in urine. It would be beneficial to incorporate testing of F^- in urine as well. Similarly the protocol for fluorosis may incorporate testing of iodine in urine besides fluoride.

The protocol for diagnosis of IDD and fluorosis

Urine iodine value[2]: The median urinary iodine content – 112.4 µg/day (iodine deficient); The median urinary iodine content – 168.4 µg/day (iodine sufficient); The median urinary iodine content among 15–49 year women – 158 µg/day; In pregnant women (15–49 years) increased requirement – 200–250 µg/day; The recommended daily allowance (RDA) by World Health Organization – 150 µg /day.

Fluoride[1]: For diagnosing fluorosis in children, besides testing F^- in body fluids and drinking water, urinary iodine to be incorporated to the protocol: Fluoride in urine – <1.0 mg/l – (0.1–1.0 mg/l) normal range; Fluoride in serum – <0.05 mg/l – (0.02–0.05 mg/l) normal range; Fluoride in drinking water – <1.0 mg/l – (1.0 mg/l upper limit, less the better).

In patient management, those who have iodine sufficiency but excess fluoride in urine, need to be counselled for (i) diet editing for fluoride removal and simultaneously counselled for (ii) promotion of nutrients through diet, to correct the derangements.

Similarly patients who have fluoride excess in urine and iodine deficiency in urine, need (i) diet editing for fluoride removal and (ii) diet counselling for promotion of nutrients besides promoting intake of iodized salt in preparations of food and beverages.

The protocol adapted by testing iodine and F^- in urine suggests that, drinking water F^- testing would be a value addition and health issues in IDD would be understood better on scientific grounds. Similarly the protocol to confirm fluorosis in children besides F^- testing in body fluids needs to incorporate testing of iodine in urine. There shall be no ambiguity then in addressing the health problems arising due to fluoride in excess or iodine deficiency, and the disease surveillance system is strengthened in both community and hospital settings. Mid-course correction in implementation of national programmes, NPPCF and NIDDCP are called for, so that communities derive the best for better health.

1. Susheela, A. K., *Treatise on Fluorosis* (ed. Susheela, A. K.), Fluorosis Research and Rural Development Foundation, New Delhi, 2007, 3rd edn.
2. Pandav, C. S. *et al.*, National Iodine and Salt intake Survey (NISI) 2014–2015: executive summary. Indian coalition for control of iodine deficiency disorders (ICCIDD) and Indian arm of iodine global network (IGN); AIIMS, New Delhi.
3. Analytical Test Report, Black rock salt. Tested and reported by Sophisticated Instrumentation Centre for Applied Research and Testing (SICART): Department of Science and Technology, Government of India; Sardar Patel Centre for Science & Technology, Charutar Vidya Mandal, Vallabh Vidyanagar, Dist. Anand, Gujarat, India, 2008; http://sicart.ecvm.net (accessed on 10 January 2013).
4. Hetzel, B. S., Delange, F., Dunn, J. T., Ling, J., Venkatesh, M. and Pandav, C. S., Towards the global elimination of brain damage due to iodine deficiency – a global program for human development with a model applicable to a variety of health, social and environmental problems. (eds International Council for the Control of Iodine Deficiency Disorders. New Delhi), Oxford University Press, 2004; http://www.iccidd.org/cm_data/hetzel-a-frontpage.pdf
5. Pandav, C. S., Yadav, K., Kumar, R. and Karmarkar, L. M., Sustainable elimination of iodine deficiency disorders: an essential maternal and child health intervention. *Natl. Med. J. India*, 2014, **27**(1), 1–3.
6. Bleichrodt, N. and Born, M. P., A meta-analysis of research on iodine and its relationship to cognitive development. In *The Damaged Brain of Iodine Deficiency* (ed. Stanbury, J. B.), Cognizant Communication, New York, 1996, pp. 195–200.
7. Kapil, U., Continuation of high goitre prevalence in regions of successful salt iodization programme, *Indian Pediatr.*, 2011, **48**, 443–444.
8. Siddiqui, A. H., Incidence of simple goitre in areas of endemic fluorosis. *J. Endocrinol.*, 1960, **20**, 101–105.
9. Day, T. K. and Powell-Jackson, P. R., Fluoride, water hardness, and endemic goitre. *Lancet*, 1972, **1**, 1135–1138.
10. Desai, V. K., Solanki, D. M. and Bansal, R. K., Epidemiological study of goitre in endemic fluorosis district of Gujarat. *Fluoride*, 1993, **26**(3), 187–190.
11. Gupta, S. K. *et al.*, Compensatory hyperparathyroidism following high fluoride ingestion – a clinico–biochemical correlation. *Indian Paediatr.*, 2001, **38**, 139–146.
12. Chadha, M. and Kumar, S., Fluorosis induced hyperparathyroidism mimicking a giant-cell tumour of the femur. *J. Bone. Joint. Surg. Br.*, 2004, **86**(4), 594–596.
13. Susheela, A. K., Bhatnagar, M., Vig, K. and Mondal, N. K., Excess fluoride ingestion and thyroid hormone derangement in children living in Delhi, India. *Fluoride*, 2005, **38**(2), 98–108.
14. Hosur, M. B., Puranik, R. S., Vanaki, S. and Puranik, S. R., Study of thyroid hormones free triiodothyronine (FT_3), free thyroxine (FT_4) and thyroid stimulating hormones (TSH) in subjects with dental fluorosis. *Eur. J. Dent.*, 2012, **6**(2), 184–190.
15. Elizabeth, K. E., Mohammed, M., Devakumar, V. K. and Fameesh, A., Goiter in prepubertal children despite urinary iodine sufficiency. *New Indian J. Pediatr.*, 2015, **4**(4), 198–201.
16. Almond, F. W., Letter from Almond, F. W., Director, Public Health Service, Boise, ID, to the Surgeon General, US Public Health Service. 5 November 1923 (From the H. Trendley Dean

Papers, MS C 468, The History of Medicine Division, National Library of Medicine), 1923.
17. Wilson, D. C., Fluorine in the etiology of endemic goitre. *Lancet*, 1941, **1**, 211–212.
18. Burgi, H., Siebenhuner, L. and Miloni, E., Fluorine and thyroid gland function: a review of literature. *Klin. Wochenschr*., 1984, **62**(12), 564–569.
19. Yu, Y. N., Effects of chronic fluorosis on the thyroid gland. *Zhonghua. Yi. Xue. Za. Zhi.*, 1985, **65**(12), 747–749.
20. Lin, F. F. *et al.*, The relationship of a low-iodine and high-fluoride environment to subclinical cretinism in Xinjiang. *Iodine Deficiency Disorder Newsl.*, 1991, **7**(3), (as cited by Second Look) in Chinese.
21. Balabolkin, M. I., Mikhailets, N. D., Lobovskaia, R. N. and Chernousova, N. V., (The interrelationship of the thyroid and immune statuses of workers with long-term fluorine exposure.) Article in Russian. *Ter. Arkh.*, 1995, **67**(1), 41–42.
22. Mikhailets, N. D., BalaboIkin, M. L., Rakitin, V. A. and Danilov, I. P., Thyroid function during prolonged exposure to fluorides. *Probl. Endokrinol*., 1996, **42**, 6–9 (in Russian language).
23. Jooste, P. L., Weight, M. J., Kriek, J. A. and Louw, A. J., Endemic goitre in the absence of iodine deficiency in school children of Northern Cape Province of South Africa. *Eur. J. Clin. Nutr.*, 1999, **53**(1), 8–12.
24. Susheela, A. K., Prevention and Control of Fluorosis, Vol. II, Rajiv Gandhi National Drinking Water Mission. (ed. Susheela, A. K.), Ministry of Drinking Water and Rural Development, Delhi, 1992.
25. Shrivastava, B. K., Mitigation of naturally occurring fluoride in drinking water source in rural areas in India: An Overview. *J. Water. Sanit. Hyg.. Dev.*, 2013, **3**(3), 467–478.
26. Susheela, A. K., Epidemiological studies of health risks from drinking water naturally contaminated with fluoride. Assessing and Managing Health Risks from Drinking Water Contamination. In Proceedings of An International Symposium held at Rome, Italy, 13–17 September (eds Reichard, E. G. and Zapponi, G. A.), the IAHS International Commission on Ground water and the istituto Superiore di Sanita, Rome, 1994, pp. 123–134.
27. Water Quality Standard, Bureau of Indian Standards, 2012.
28. Susheela, A. K., Fluorosis management programme in India. *Curr. Sci*., 1999, **77**(10), 1250–1256.
29. Nanda, R. S., Fluoride content of north Indian foods. Indian. *J. Med. Res*., 1972, **60**, 1470–1482.
30. Rao, K. V. and Mahajan, C. L., Fluoride content of some common south Indian foods and their contribution to fluorosis. *J. Sci. Food. Agric*., 1990, **51**, 275–279.
31. Maumene, E., Experience pour determiner l'action des fluores sur l'economie animale. *Compt. Rend. Acad. Sci. Paris*, 1854, **39**, 538–539.
32. Hillman, D., Bolenbaugh, D. L. and Convey, E. M., Hypothyroidism and anemia related to Fluoride in dairy cattle. *J. Dairy Sci.*, 1979, **62**(3), 416–423.
33. Cinar, A. and Selcuk, M., Effects of chronic fluorosis on thyroxine, triidothyronine and protein bound iodine in cows. *Fluoride*, 2005, **38**(1), 65–68.
34. Liu, G., Chai, C. and Kang, S., Effects of fluoride on the ultrastructure of thyroid in chicks. *Chin. J. Vet. Sci.*, 2002, **22**(5), 512–514.
35. Bouaziz, H., Soussia, L., Guermazi, F. and Zeghal, N., Fluoride induced thyroid proliferative changes and their reversal in female mice and their pups. *Fluoride*, 2005, **38**(3), 185–192.
36. Spittle, B., Editorial: a step in the right direction. *Fluroide*, 2015, **48**(2), 91–92.
37. US Department of Health and Human Services Federal Panel on Community Water Fluoridation. US Public health service recommendation for fluoride concentration in drinking water for the prevention of dental caries. *Public Health Rep*., 2015, **130**(4), 14; http://www.publichealthreports.org/fluoride guidelines.cfm.
38. Centres for Disease Control and Prevention. Community water fluoridation (updated 24 April 2015; cited May 2015 May); http://www.cdc.gov/fluoridation/
39. Murthy, V. H., Surgeon General's perspective community water fluoridation one of cdc's '10 great public health achievements of the 20th century'. Public. Health. Rep., 2015, **130**(4), 3 pages e-pub; http://www.publichealthreports.org/fluoride guidelines.cfm.
40. Poureslami, H. R., Horri, A. and Atash, R., High fluoride exposure in drinking water: effect on children's IQ, one new report. *Int. J. Pediatr. Dent*., 2011, **21**(s1), 47.
41. Susheela, A. K., Dental fluorosis and its extended effects. *Indian J. Pediatr*., 2013, **80**(9), 715–717.
42. Sethi, V. and Kapil, U., Iodine deficiency and development of brain. *Indian J. Pediatr.*, 2004, **71**, 325–329.
43. Susheela, A. K. *et al.*, Effective interventional approach to control anaemia in pregnant women. *Curr. Sci.*, 2010, **98**(10), 1320–1330.
44. Susheela, A. K., Anemia in pregnancy: an easily rectifiable problem. *Fluoride*, 2010, **43**, 104–107.
45. Susheela, A. K., Control of anaemia in pregnancy, pre-term deliveries, low birth weight babies in natural conception and the possibility in assisted reproduction. In *Assisted Reproduction Technologies (ART) – Dr. T.C. Anand Kumar Memorial Volume* (eds Raghunathan, P., Susheela, A. K. and Mehta, R. H.), 2013, pp. 263–278.
46. Susheela, A. K., Mondal, N. K., Rashmi, G. and Ganesh, K., Rectification of anaemia in pregnancy. In Proceedings of *The Convention International Forum on Quality and Safety in Health Care, Asia*, BMJ Event, Hongkong, Poster No. 215, 2015.
47. Susheela, A. K., Mondal, N. K. and Rashmi, G., Anaemia in adolescent girls: an intervention of diet editing and counselling. *Natl. Med. J. India*, 2016, **29**(4), 2000–2004.
48. Susheela, A. K., To empower population for nutritional requirements through diet for better health. In Proceedings of The International Forum on Quality and Safety in Health Care, Asia. BMJ, Event Singapore, Poster No. 5 in the session Population and Public Health, 2016.
49. Susheela, A. K., Fluorosis and Linked diseases, a new dimension. In Report on the XXXIIIrd Conference of the International Society for Fluoride Research, Debilitating Fluorosis Current Status, Health challenges and Mitigation measures, Hyderabad, India. *Fluoride*, 2016, vol. 49(4), Pt(2), p. 469.

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