2. IODINE DEFICIENCY DISORDERS

Iodine is an essential micronutrient required for the normal mental and physical growth and development of human. Iodine deficiency has now been recognized by WHO as the most preventable cause of brain damage in the world today. Iodine deficiency is a naturally occuring ecological phenomenon that is manifested as Goitre and Cretinism in different parts of the world and was known as endemic iodine deficiency.

Since a wide variety of physical and mental disorders are associated with iodine deficiency, the term "Iodine Deficiency Disorders" (IDDs) in place of endemic goitre, was introduced by Hetzel in 1983.

The term **Iodine Deficiency Disorders** (IDDs) refers to a spectrum of disabling conditions affecting the health of human being starting from foetal life through adulthood resulting from inadequate dietary intake of iodine.

Prevalence

The existence of iodine deficiency goitre was mentioned in Ancient chinese, Greek, Roman, Indian Writings. Now IDD is a major public health problem round the globe.

In mid 1990s, it was estimated that more than 2 billion people from 130 countries were 'at-risk' of IDD.

According to the estimates of WHO in 1999, about 741 millions people were affected by goitre about, 13% of the world's total population. In 2020, more than 1.9 million individuals have inadequate iodine nutrition, of which 285 million are school aged children.

In 2006, it was estimated that there only 47 countries where IDD countries to be a public-health problem compared to 54 in 2004 and 126 in 1993.

In the developed countries, the problem of IDD has been virtually eliminated through implementation of effective control measures, such as fortification of bread, salt etc., implemented since early 20th century.

IDDs contribute to the major health problems in Latin America, Africa and Asia.

In India, about 200 million people are exposed to the risk of IDD in India. Out of this, about 70 millions suffer from goitre and other IDDs. In India, 54 million people are suffering from goitre, 2.2 million from cretinism and contributes 90,000 still births and neonatal deaths.

In India, the IDDs belts extends from Jammu and Kashmir in the west, through Northen parts of states of Himachal Pradesh, Punjab, Uttar Pradesh and Eastern zones like West Bengal, Assam, Sikkim, Bihar, Tripura and Arunachal Pradesh. In addition, the other pockets of endemic goitre include Aravalli Hills in Rajasthan, sub–vindhya hills of Madhya Pradesh, Narmada valley of Gujrat, Estern Ghat of Orissa, Andhra Pradesh, Western Ghats of Karnataka and Kerala and the districts of Aurangabad, Pune in Maharastra.

The overall prevalence of total goitre among 6 to 11 years old children was about 4 percent which is below the cut–off point to indicate endemicity of IDD. The prevalence is higher in Maharastra (11·9%) and West Bengal (9%) according to prevalence study conducted by NIN (2003 to 2004).

Aetiology of IDD

The factors that are involved in occurrence of IDD are the followings :

Low iodine intake : Iodine deficiency disorders are the results of low iodine intake. It has been found that goitre is usually seen when the iodine intake is < 50 µg / day and critinism is usually seen when the iodine is < 30 µg / day.

Environmental factors : Iodine deficiency is an ecological problem due to low iodine in soil. The iodine deficiency are commonly found in all elevated regions subjected to heavy rainfall with run–off into rivers. High rainfall, snow and flooding increase the loss of iodine through leaching into water and loss of soil iodine which previously denuded by past glaciation.

The sea water contains iodine in excess at the level of 50–60 µg / litre. Sea water evaporates iodine to form cloud and then condensed in the form of rain and enriches the hilly area with iodine. It is believed that environmental factor such as Trypanosome parasitic infestation can cause goitre.

Goitrogens : Goitrogens are certain chemical substances which interfere with iodine metabolism in the body. They can interfere at various stages of thyroid hormone homeostasis such as; uptake of iodine, oxidation of iodine and conversion of thyroxine (T_4) to triiodothyronine (T_3) by the enzymes. NADPH + H^+ oxidase, thyroid peroxidase and 5' – deiodinase respectively.

Some of the known goitrogens found in environment are thiocyanate, isothiocyanate, thiooxazolidone, flavonoids, disulphides, phenols, pthalates, biphenyl and lithium (used in neurological drug). These substances are known to be found in tapioca, sorghum, finger millet, okra, sweet potatoes, almonds, peaches, soyabeans, bamboo shoots, lima bean, cassava, ground nuts, cabbage, mustard, caulliflower, strawberries etc.

On the basis of their level of interference, goitrogens are classified into 3 classes :

Class I : Thiocyanate, isothiocyanate and cyanogenic glycosides, which inhibit iodine uptake by the thyroid gland, are grouped in this class, found in brassica family plants mainly; such as rape seeds, mustard, cabbage, turnips, ground nut etc.

Class II : Thiourea, thioamides and flavonoids which affect the stages of organification and coupling in the process of thyroxine synthesis.

Class III : Excess iodine and Lithium, which interfere at the stage of proteolysis–a step necessary for utilization of thyroxine.

The goitrogen thioxazolidone is present in raw cabbage, turnip and brussel sprouts, but destroyed after cooking.

Sulphur containing goitrogens, such as thioglycosides, thiocyanate are present in plants in inactive forms but when taken by animals, are converted to active goitrogens.

Cabbage has a thioglycoside–progoitrin which is converted to 5–vinyl 2–thio oxazolidone, which an active goitrin. The ability of the plant and animals to convert these inactive forms of goitrogens to active goitrin may vary. Cattle may consume large amount of this vegetables and may pass on goitrogens into the milk.

There is a seasonal and regional variation in goitrogen thiocyanate content in foods.

The antibiotics sulphonamide and vitamin like substance para aminobenzoic acid (PABA) reduce iodine oxidation to iodide necessary in thyroid hormone synthesis.

People who live in goitrous zones should avoid goitrogenous foods. People who live in non–goitrous areas can include goitrogenous foods in their diet in moderation. Goitrogenous foods should not taken as staple foods.

Deficiency of selenium : Selenium also plays a role is preventing goitre. Selenium is a part of enzyme thyroxine 5' – de–iodinase which is essential for conversion of thyroxine (T_4) to triiodothyronine (T_3), which is the active form of the hormone. Therefore, in selenium deficiency goitre may occur.

Intrinsic factors : Some of the intrinsic factors such as failure to synthesize the thyroid hormone due to inherited and congenital defects in the hormone synthesis and secretion and peripheral resistance to thyroid hormones can also result in goitre. However, the incidence of goitre due to such intrinsic factors is sporadic in nature.

The spectrum of IDD

IDD includes a sequence of clinical features at all stages of human growth and development–from foetus, infant, children, adolescents to adult human.

Deficiency of iodine may lead to different types of disorders :

Still birth : In human, thyroid and pituitary endocrinal glands are developed by the first 12 weeks of gestation and the hypothalamus develops between 10th to 30th weeks. During intrauterine life, due to failure to convert T_4 to T_3, failure to prepare the organism for the metamorphosis from intrauterine to extrauterine life can be seen. Therefore, still birth may occur as a part of spectrum of IDD.

Goitre : Goitre is defined as non–neoplastic, non–inflammatory and non-toxic enlargement of thyroid gland.

The term **'Goitre'** is used to denote the enlargement of thyroid gland associated with either normal, hypo or hyperfunction of thyroid gland (Fig. 5.19 and 5.20).

The normal thyroid gland has some of iodine. In simple goitre, this amount may be reduced to 1 mg, even though the gland is larger. The gland is unable to produce thyroxine which contains 64% iodine.

CLASSIFICATION OF GOITRE BY WHO (2001)

Grade	Signs and symptoms
Grade 0	Not palpable or visible goitre
Grade 1	A mass in the neck that is consistent with an enlarged thyroid that is palpable but not visible when the neck is in normal position. It moves upward in the neck as the subject swallows. Nodular alterations can occur even when thyroid is not enlarged
Grade 2	A swelling in the neck that is clearly visible when the neck is in a normal position and is consistent with an enlarged thyroid when the neck is palpated

[Source : WHO / UNICEF / ICCIDD, 2001]

Thyroid gland enlarges due to deficient output of thyroid, hormone which produces hyper secretion of TSH from the pituitary and consequent enlargement of thyroid gland.

Therefore the enlargement is apparently a compensatory adaptation to lack of iodine required for the synthesis of thyroid hormones.

Normal thyroid gland is not palpable or is barely palpable. According to definition by Perez and co–workers (1980), a thyroid gland whose lobes have a volume greater than the terminal phalanx of thumb of the subject examined, will be considered goitrous. The normal weight of thyroid gland is about 20 to 25g, but in goitre, the enlarged gland weighs about 0.45 to 0.67 kg or more.

If in an area, the **total goitre rate** among the children aged six to twelve years is equal to or more that 5%, the area is said to be endemic for goitre. [WHO / UNICEF / ICCIDD, 2001]

$$\text{Total Goitre Rate [TGR]} = \frac{\text{Number of goitre cases of Grade 1 and Grade 2}}{\text{Total number of examined}} \times 100$$

Types of goitre : Simple goitre may be of the following types :

- **Colloid goitre :** This is also known as endemic or benign goitre. This is mainly due to inadequate supply of iodine in diet. The alveoli are distended with colloid lined by cubical and flattened epithelial cells. Usually hypertrophy or hyperplasia is not common. Use of iodised salt reduces this type of goitre.
- **Diffused parenchymatus goitre :** The alveoli are not distended with colloid as in the case of colloidal goitre. The cells lining the aveoli are of columnar type. Hypertrophy and multiplication of alveolar epithelial cells are common. Lumens of some alveoli are almost obliterated.
- **Nodular or adenomatous goitre :** In nodular goitre, there is development of nodules which are localized areas of cellular proliferation within the gland. Hyperthyroidism and malignant changes occur very rarely in nodular goitre.
- **Toxic goitre :** Enlargement of thyroid gland along with excessive excessive secretion of thyroid hormone are the common characteristics of this type of goitre. Epithelial cells are hypertrophied and hyperplastic. Toxicosis may occur due to hyperthyroidism. Grave's disease is always associated with toxic goitre.

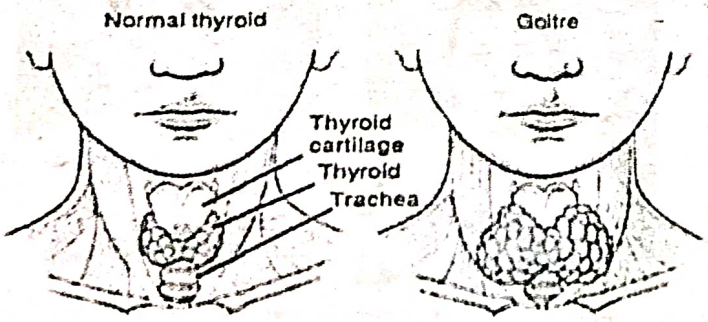

Fig. 5.19 : Thyroid gland enlargement in goitre.

- **Hokkaido goitre :** While low iodine intake causes endemic goitre or cretinism, a very high concentration may also causes hypothyroidism by inhibiting iodine organification–which is called **Wolf–Chaikoff effect.** In Hokkaido, the Japanese people consume large amount of sea weed providing 8 to 25 mg of iodine per day or more. Iodine in large doses can interfere with the release of T_3 and T_4. Parenchymal hyperplasia is marked and majority of patient become hyper thyroidic.

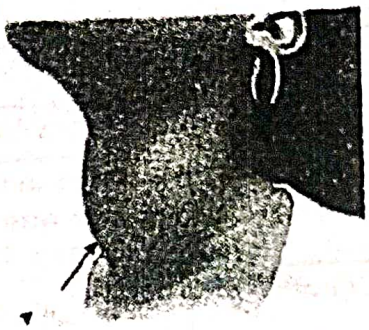

Fig. 5.20 : Thyroid gland enlargement in goitre

Biochemical changes in goitre : From the biochemical aspect, goitre can also be clearly stated. About half of the total iodine from the food is taken up by the gland and the remaining half is excreted in urine. If dietary iodine is inadequate then plasma iodine level also falls and urinary excretion of iodine decreases.

Pituitary responses by increasing secretion of TSH and so a very common biochemical feature is high level of TSH in the plasma. In mild cases the normal plasma concentrations for both T_3 and T_4 are maintained.

Cretinism

Endemic cretinism is often associated with severe iodine deficiency during intrauterine life. It is prevalent in those areas where the prevalence of goitre is very high. A wide range of defects such as mental refardation, deaf–mutism and spastic paralysis of lower limbs of varying degrees are associated with this condition. Clinically cretinism can be manifested as :

Fig. 5.21 : A child suffering from cretinism.

Neurological cretinism : Severe mental retardation, deaf–mutism, squint and spastic diplegia–spastic rigidity affecting the lower limbs leading to characteristic gait and brisk reflexes are the features of neurological cretinism. Stunting is not a regular feature. Iodine deficiency during pregnancy retards brain and cochlear development leading to neurological dysfunctions in new born (Fig. 5.21).

Myxoedematous cretinism : These cretins exhibit signs of hypothyroidism, such as coarse and dry skin, swollen tongue, deep hoarse voice, apathy and mental deficiency, memory loss, skeletal growth retardation, weak abdominal muscle, sluggish bowel function, and delayed tendon reflexes. ECG shows small voltage QRS complexes and flattening of T–wave.

Neurological cretinism is predominantly in areas with environmental iodine deficiency, where as myxoedematous cretinism is seen in areas where consumption of goitrogenous foods is common *e.g.*, taploca eating population in Zaire are commonly affected by Myxoedematous cretinism.

Hypothyroidism : Hypothyroidism is characterise by coarse and dry skin, husky voice, delayed tendon reflexes, epiphysial dysgenesis as evidenced by X-rays and ECG showing small voltage QRS and flattened

Fig. 5.22 : Myxoedema patient (before and after treatment with thyroid hormone therapy).

T-waves. Serum T_4 levels will be low with normal T_3 and elevated TSH level. The BMR is reduced. This condition is generally found among adults.

Psychomotor defects : Studies have shown that the children from iodine deficient areas show poor scores on IQ tests and impaired school performance. They also exhibit poor motor co-ordination.

Impaired mental function : Population residing in iodine deficient areas usually exhibit reduced mental function, low intelligence levels and high degree of apathy, reflected in lack of initiative and decision making capacities of the people.

SPECTRUM OF IODINE DEFICIENCY DISORDERS IN DIFFERENT AGE GROUPS

Stage of life cycle	Signs and symptoms
Foetus	Abortions Still birth Congenital anomalies Increased perinatal mortality Increased infant mortality Neurological cretinism Myxoedematous cretinism Psychomotor defects
Neonate	Neonatal goitre Neonatal chemical hyothyroidism
Children and adolesents	Goitre Juvenile hypothyroidism Impaired mental function Retarded physical development
Adults	Goitre with its complications Hypothyroidism Impaired mental functions

Grading of IDD

Depending upon median urinary iodine exeretion levels, prevalence of total goitre rate (TGR) in the community and the severity of endemicity of IDD is graded as following :

Sl. No.	Parameter	Mild IDD	Moderate IDD	Severe IDD
1.	Urinary iodine (µg / dl)	5.0 – 9.99	2.0 – 4.99	< 2.0
2.	Goitre prevalence rate (%)	10 – 13	20 – 25	30 – 100
3.	Thyroid hormones activity	Adequate	Impaired	Risk of marked hypothyroidism
4.	Mental and physical development	Normal	No overt case of cretinism	Mental retardation, overt cretinism

Prevention and control of IDD

The only way to combat IDD is to provide iodine to the community. In India, the National Goitre Control Programme (NGCP) was started in 1960. Later on, in 1962, this programme is replaced

by the name **National Iodine Deficiency Control Programme (NIDDCP)** as goitre is not only the symptom of iodine deficiency. In the year 1992, this programme was included in the Prime Minister's 20–point Development Programme during the 7th five–year plan. Not only this programme was carried out in goitre belts but was also carried out in Gujarat, Punjab, MadhyaPradesh, Maharastra, Arunachal Pradesh and Kerala. This programme comprises of following components :

Iodine fortification of salt and other foods : The only way to combat the problem of IDD is to fortify common foods with iodine to ensure adequate iodine intake.

Fortification of common food items such as bread, wheat flour, milk, sugar, drinking water and specifically common salt are in practice in different parts of the world.

But in India the most common vehicle for iodine fortification is through common salt.

Potassium Iodate (KIO_3) was used for the process of iodinisation, because it is comparatively more stable than potassium iodide (KI). KIO_3 was more suited for the process of iodinisation of crude moist salts.

The aim is to increase the daily intake of iodine to about 100 – 300µg.

The amount added to the salt is related to the usual consumption of salt in the community. About 10kg of salt mixed with 1g Potassium Iodide which provides 1mg of KI in 10g daily salt intake [1mg of KI = 765µg Iodine].

The iodine content of salt should be 30 ppm at the production level and 15 ppm at the consumer level as per specification laid by Prevention of Food Adulteration Act (PFA, 1954).

Iodised oil supplementation : Oil fortified with iodine is available for oral or intramuscular infection.

In places, where iodised salt is not available or in case of severe cretinism iodized oil injections are suggested.

In France, iodized oil from poppy seeds oil for injection (Lipiodol) and oral (Oriodol) administration are in use commercially.

An intramuscular injection of 1ml of iodized oil containing 480mg of iodine can maintain satisfactory level of iodine for 2 to 3 years, while the oral dose lasts for 1 year.

Iodination of water supply : An iodinator consisting of canisters containing iodine crystals are connected to main pipes and fraction of water diverted through them. Iodine added directly to drinking water can correct IDD. The drinking water should contain at least 150µg of iodine/litre.

Iodine monitoring : For implementing the NIDDCP, requires a network of laboratories for iodine monitoring and surveillance. The laboratories are essential for ;

- Iodine excretion assessment.
- Determination of iodine in salt, soil, water and food as a part of epidemiological studies.
- Determination of iodine in salt for quality control.

Man power training : The health workers and others engaged in the NIDDCP should be full motivated and trained in all aspects of IDD control along with legal enforcement and public education.

Mass communication : Mass communication is also essential for increasing awareness of people about IDD and its management through nutrition education.

Supplementation of iodine can also be given in bread and other commonly used foods. Sea-foods, eggs, can be suggested for people who are at risk.

Presently, UNICEF has joined hands with our central Government to carry out NIDDCP and non–iodised salt is now–banned from many states.