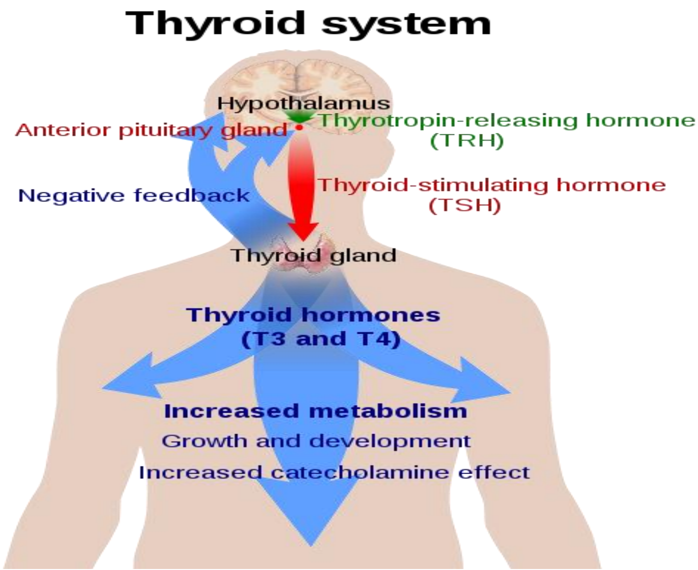
INTRODUCTION

1.1 Iodine and Thyroid hormone

Iodine is an essential micronutrient required for normal thyroid function, growth and development (WHO/FAO, 2004). Iodine is present in the superficial layers of the soil and absorbed by crops grown on it. Glaciations, heavy snow and rain leach away iodine from the soil leading to iodine deficiency in the crops grown on it. Thus consumption of crops grown on iodine deficient soils leads to iodine deficiency in populations which is solely dependent on this vegetation for their iodine requirements (WHO, 2007). When iodine intake falls below the recommended levels, the thyroid may no longer be able to synthesize sufficient amounts of thyroid hormone. The resulting low level of thyroid hormones in the blood (hypothyroidism) is the principal factor responsible for damage to the developing brain and other harmful effects known collectively as "iodine deficiency disorders" (WHO, 2007).

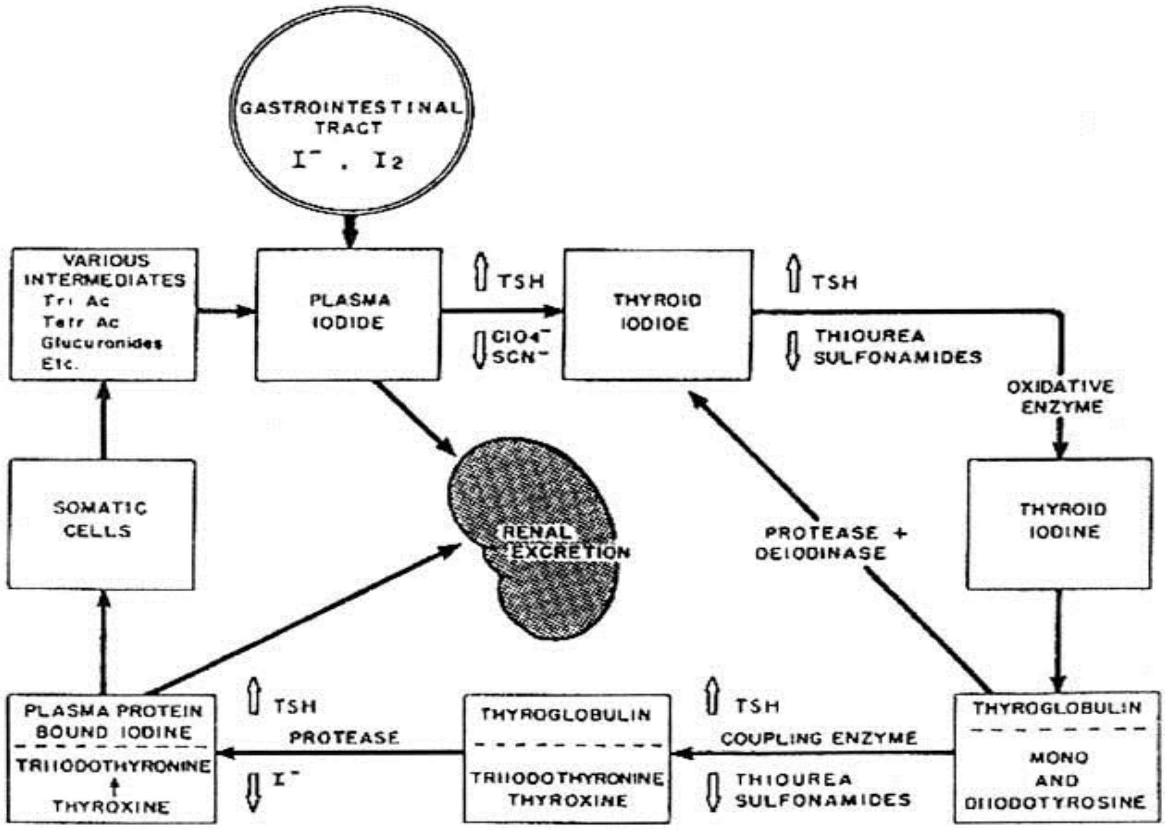
Iodine enters the body in the form of iodate or iodide in the water we drink or in the food we consumed; the iodate is converted to iodide (I-) in the stomachand distributed to extracellular fluids.But the concentration of I- in the extracellular fluid is usually low because of the rapid uptake by the thyroid gland and the renal clearance.The thyroid gland traps and concentrates iodide and uses it in the synthesis and storage of thyroid hormones **(Figure 1)**. About two-thirds of the iodide is used in hormone synthesis, and the remaining amount is being released back into the extra cellular fluid. The thyroid produces thyroxine (T4) and triiodothyronine (T3). The production of thyroxine and triiodothyronine is regulated by thyroid stimulating hormone (TSH), released by the anterior pituitary. TSH production is suppressed when the T4 levels are high, and vice versa. The TSH production itself is modulated by thyrotropin-releasing hormone (TRH), which is produced by the hypothalamus. These hormones regulate the rate of metabolism and affect the physical and mental growth and rate of function of many other systems in the body. The thyroid is controlled by the hypothalamus and pituitary iodine (Kapil, 2007)**(Figure 2)**.

Figure 1: Thyroid System



Source:https://en.wikipedia.org/wiki/Thyroid

Figure 2: Iodine Metabolism



Source: FAO, 2001

1.2 Consequences of Iodine deficiency

The term iodine refers to all the ill-effects of iodine deficiency in a population that can be prevented by ensuring that the population has an adequate intake of iodine. These effects are listed in **Table 1**. Brain damage and irreversible mental retardation are the most important disorders by iodine deficiency (WHO, 2007).

Iodine deficiency affects all the stages of human development starting from the fetal life to the adulthood. If the diet of a pregnant woman lacks iodine, then the fetus is also deprived of adequate iodine and hence cannot produce enough thyroxin resulting in fetal growth damage (WHO, 2007). Hypothyroid fetuses often perish in the womb, and many infants die within few weeks of birth whereas those born with hypothyroidism have global developmental delay and limits intellectual growthresulting in low IQ of the child (Liu et al, 1994; Momotani et al, 2012). They are also often incapable of completing school. Studies have reported that areas with prevalence of mild to moderate iodine deficiency, the school children are on an average have 13.5 points of IQ below those living in iodine sufficient areas (Bleichrodt and Born, 1994).

Severe iodine deficiency during pregnancy increases the risk of stillbirth, congenital abnormalities, perinatal and infant mortality and impairs physical, motor and cognitive development of the fetus (Zimmermann et al, 2011). Fetal and early childhood brain damage is often irreversible, causing mental retardation and reduced school performance (Zimmermann, 2008; Zimmermann, 2009). In adults, iodine deficiency also reduces work productivity (Zimmermann et al, 2008). As a result, the mental ability of ostensibly normal children and adults living in areas of iodine deficiency is reduced compared to what it would be otherwise.

Thus, the potential of a whole community is reduced by iodine deficiency. Where the deficiency is severe, there is little chance of achievement and underdevelopment is perpetuated (WHO, 2001).In an iodine-deficient population, everybody may seem to be slow and rather sleepy. The quality of life is poor, ambition is blunted, and the community becomes trapped in a self-perpetuating cycle. Even the domestic animals, such as village dogs, are affected and livestock productivity also dramaticallyreduced (Hetzel and Pandav, 1996).

Therefore, widespread iodine deficiency in the population poses a significant threat to national economic growth and development and slows down progress towards health for all, education for all, particularly in developing countries (Engle et al, 2007).

The consequences of iodine deficiency in humans in different human cycle are depicted in **Table 1**.

Table 1: Consequences of Iodine Deficiency in Humans

Age Group	**Effects**	
	Mortality	**Morbidity**
Fetus	• Spontaneousabortions • Stillbirths • Perinatal mortality	• Birth defects • Defects of speech & hearing • Psychomotor defects • Cretinism
Neonate	• ↑Neonatal mortality	• Neonatal Goitre • Neonatal Hypothyroidism
Children & adolescents		• Goitre • Hypothyroidism • Retarded physical development • Impaired mental function (↓13 IQ points)
Adults		• Goitre & its complications • Hypothyroidism • Impaired mental function • Iodine induced hyperthyroidism

Source: WHO, 2007

1.3 Sources of Iodine

The rich sources of iodine are sea fish, green vegetables and leaves like spinach grown on iodine rich soil. The common sources are milk, meat, and cereals. Certain vegetables: cabbage, cauliflower and radish contain glucosinolates. If soil is deficient in Iodine then the food sources are likely to be deficient in iodine. High amount of iodine is also found in seaweeds & sea fish (Kapil, 2007).

In India, only a small proportion of population consumes iodine rich sea foods and that too in very small quantity. Sea salt is a poor source of iodine (< 0.5 ppm of Iodine is present in Sea Salt) (Pandav, 2016).

Common salt fortified with small quantities of sodium or potassium iodate is now compulsorily made available in the market as iodized salt to control iodine deficiency disorder (Kapil, 2007).

1.4 Daily Iodine Requirement

WHO/UNICEF/ICCIDD (2007) recommended that the daily intake of iodine should be as depicted in **Table 2**.

Table 2: Daily iodine requirement at different age group

Age Group	Iodine Requirement
0 – 59 months	90 µg/day
6 – 12 years	120 µg/day
≥ 12 years	150 µg/day
Pregnant and Lactating women	250 µg/day

Source: WHO/UNICEF/ICCIDD (2007)

1.5 Prevalence of Iodine Deficiency

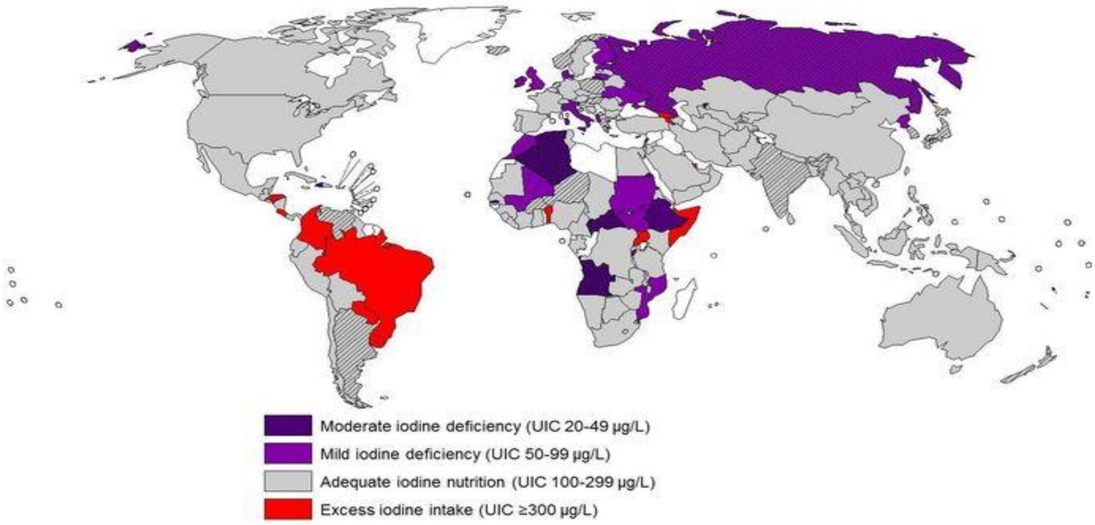
1.5.1 Global Scenario

Iodine deficiency is a major global public health challenge. Recent data on iodine status globally has reported that using median UIC in school-age children as proxy for iodine status in the general population, 19 countries have changed their iodine status. Eight countries that was previously classified as mildly or moderately deficient have now reached sufficient iodine nutritional status at the national level (these include Afghanistan, Australia, Ghana, Guatemala, Hungary, Mongolia, New Zealand, and Papua New Guinea) (Global Iodine Score card, 2015; IDD Newsletter, 2015; UNICEF, 2008; Andersson et al, 2012; Zimmermann and Andersson, 2012). According to the recent reports, in 2015, only 25 countries remained iodine deficient, compared to 32 in 2011 (Global Iodine Score Card, 2015) (**Figure 3 and 4**). This remarkable progress reflects a growing global awareness of iodine deficiency disorder and the tremendous success of iodization programs worldwide. Overall, global iodine status continues to improve. According to the recent data, Haiti is the only country which changed status from mildly to moderately deficient. Remarkably, there have been no countries in the "severely deficient" category (i.e., with a median urinary iodine concentrationlevel of <20µg/l for more than a decade, which is a testament to the countries' commitment to sustaining their IDD achievements(Global Iodine Score card, 2015; IDD Newsletter, 2015; UNICEF; Andersson et al, 2012; Zimmermann and Andersson, 2012)

.

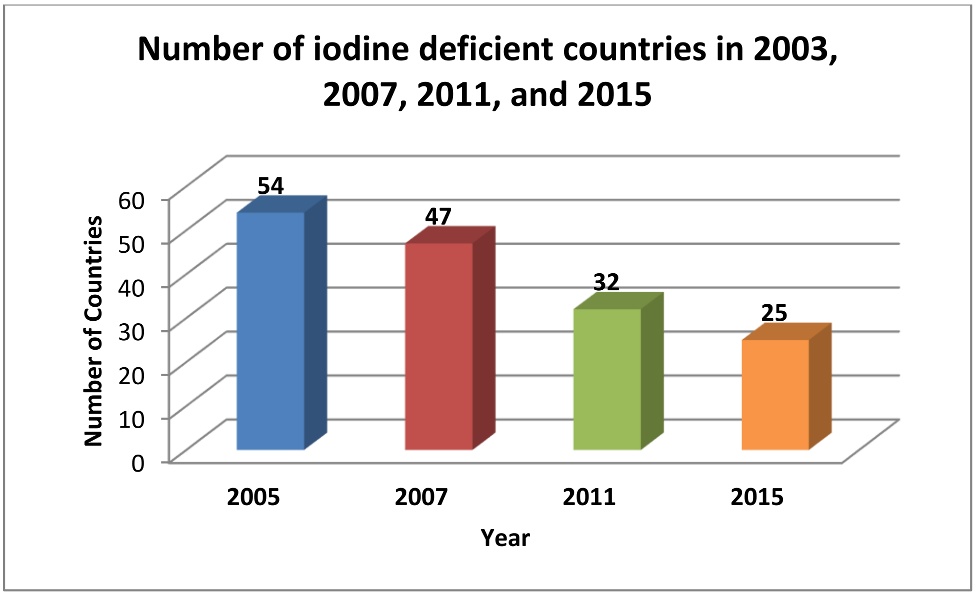
In 2014, the urinary iodine concentration data cover approximately 97.8% of the world's population of school-age children, compared to 96% in 2012. Countries that previously had no data that have new urinary iodine concentration estimates include South Sudan, Sierra Leone, North Korea, South Korea, and Thailand. The proportion of the global population covered by national-level surveys has also increased, now at 71% compared to 60% in 2012. National-level data were previously not available for Australia, Austria, Brazil, Ghana, Guatemala, Papua New Guinea, Qatar, and Venezuela. Yet, data is still missing for 41 countries. And although these include only 2% of the world's population of children, they also include countries with relatively large populations, such as Israel, Iraq, Syria and Congo (Global Iodine Score Card, 2015; UNICEF, 2008; Andersson et al, 2012; Zimmermann and Andersson, 2012).

Figure 3: Global status of iodine deficiency in 2015



Source: Global Iodine Score Card, 2015

Figure 4: Number of iodine deficient countries



Source: Global Iodine Score card, 2015; IDD Newsletter, 2015; UNICEF, 2008; Andersson et al, 2012; Zimmermann and Andersson, 2012)

1.5.2 Indian Scenario

There has been a gradual improvement in iodine deficiency status amongst population of India. Still there are many states which are endemic to iodine deficiency, especially the hilly terrains. Many research studies have been conducted on this aspects by different researchers (Kapil et al, 2007; Kapil et al, 2014; Mittal et al, 2000; Misra et al, 2007; Joshi et al, 2014).

Surveys conducted by the Central and State Health Directorates, Indian Council of Medical Research (ICMR) and medical institutes since 1950s have clearly demonstrated that iodine deficiency disorder is a public health problem in all States and union territories in India. Of the 325 districts surveyed in India so far, 263 districts are IDD-endemic, *i.e.* the prevalence of IDD is above 10 per cent in the population (Department of Health and Family Welfare, 2011). As per the survey conducted by the National Nutrition Monitoring Bureau (NNMB) in 2000-2001 in rural areas of Kerala, Tamil Nadu, Karnataka, Andhra Pradesh, Maharashtra, Madhya Pradesh, Orissa and West Bengal, the overall prevalence of Total Goitre Rate (TGR) among six to twelve year old children was about 4 percent. The prevalence of goitre was highest in Maharashtra (11.9%) and West Bengal (9.0%) (NNMB, 2003).

State level IDD surveys were carried out in seven States (Kerala, Tamil Nadu, Orissa, Rajasthan, Bihar, Goa and Jharkhand) from 2000 to 2006 by International Council for Control of Iodine Deficiency Disorders (ICCIDD) in collaboration with State medical colleges, Micronutrient Initiative (MI) and UNICEF. It was found that the household level consumption of adequately iodized salt (≥15 ppm) ranged from 18.2 per cent in Tamil Nadu to 91.9 per cent in Goa. The median urinary iodine excretion ranged from 76µg/l in Goa to 173.2µg/l in Jharkhand, whereas TGR ranged from 0.9 per cent in Jharkhand to 17.5 per cent in Goa. These State level IDD surveys are the only sub-national level IDD surveys in India where all three indicators were used(ICCIDD, 2006). In India, the entire population is prone to IDD due to deficiency of iodine in the soil of the subcontinent and consequently the food derived from it. Of these, an estimated 350 million people are at risk of IDD as they consume salt with inadequate iodine content. Every year nine million pregnant women and eight million newborns are at risk of IDD in India(UNICEF, 2009). A recent (2014-2015) survey on National Iodine and Salt Intake Survey (NISI) by ICCIDD/UNICEF/MI reported that the median urinary iodine concentration level at the national level was found to be 158µg/L among women of reproductive age (non pregnant), reflecting optimal iodine nutrition in India. But the median urinary iodine concentration level varied significantly between the rural (148.5 µg/L) and urban (167.9 µg/L) areas. The central zone of India reported the lowest median UIC level (128.6 µg/L) and the North zone reported the highest (204.0 µg/L), but both were adequate in iodine. Moreover, the iodine intake was found to be adequate across all zones and in both urban and rural areas of India (ICCIDD, 2015).

1.5.3 Iodine deficiency in Uttarakhand state

Iodine deficiency is a major public health problem in Uttarakhand state, India. In 1962, the National Goiter Control Programme was launched in eight hilly districts namely: (Uttarkashi, Chamoli, Pithoragarh, Tehri Garhwal, Pauri Garhwal, Dehradun, Nainital, and Almora and in Bijnor district in Uttarakhand) which were identified as endemic to iodine deficiency (Kapil, 1991). Various studies conducted in different district of Uttarakhand reported high prevalence of iodine deficiency amongst school age children. In district Nainital, the prevalence rate of goiter according to a survey conducted amongst school age children in 2003 was found to be 6.9% and median urinary iodine concentration level as 110µg/l (NRHM, 2013). According to WHO, global database on iodine deficiency amongst school age children in Nainital, Median UIC level was found to be 110µg/l (WHO database, 2013).Earlier studies conducted in the year 1999 and 2003 from adjoining districts reported the median UIE level of 175µg/l and 110µg/l, respectively (Kapil et al, 1999; NIN, 2003).

In state of Uttarakhand, an increase in supply of iodized salt was observed in the year 2008-2009 with 13.50 to 19.49 thousands of tonnes (2009-2010). According to NFHS-3 survey, less than half of households in Uttarakhand (46%) were using sufficiently iodized salt which is less than the percentage observed during NFHS-2 (60%) survey. The consumption of iodized salt has been reported to be low by the population in the state (NFHS-3). The low consumption of adequately iodized salt in Uttarakhand state could be due to number of factors, including the scale of salt production, transportation requirements, enforcement efforts, differences in state regulations, the pricing structure, and storage patterns.

1.6 Public health strategies to combat iodine deficiency disorder

1.6.1 Salt iodization strategy

Salt is the preferred vehicle for iodization, since it is consumed by everyone, has stable consumption rates throughout the year, addition of iodine does not affect the taste or colour of salt, importation/production is often limited to a few producers, iodization technology is easy to implement and readily available at a reasonable cost and the quality of iodized salt can be easily monitored (WHO, 2014).

Iodization is the process of fortifying salt for human consumption with iodine and is an effective strategy to increase iodine intake at the population level. The public health goals of reducing salt and increasing iodine intake through salt iodization are compatible as the concentration of iodine in salt can be adjusted as needed. Monitoring the levels of iodine in salt and the iodine status of the population are critical for ensuring that the population's needs are met and not exceeded (WHO, 2007).

A meta analysis of two RCTs, 6 non-RCTs, 20 quasi-experimental studies, 16 cohort studies, 42 multiple cross- sectional studies, and 3 studies with mixed designs reported that iodized salt has a large effect on reducing the risk of goitre, cretinism, low cognitive function and iodine deficiency. Robust monitoring of salt iodization programmes is important, to ensure safe and effective levels of iodine consumption, especially as countries implement programmes to reduce population salt intake (Aburto et al, 2014).

Some of the barriers to salt iodization include:

- Production-level constraints
- Supply problems, including the procurement of potassium iodate (KI03)
- Weak enforcement of regulations and policy
- Inadequate demand on the part of consumers

1.6.1.1 Universal salt iodization

In nearly all countries where iodine deficiency occurs, it is now well recognized that the most effective way to eliminate IDD is through USI (WHO, 2001). Salt is an ideal vehicle for fortification because it is consumed by everyone throughout the year, its production is usually limited to a few centers which facilitates its quality control, salt iodization is easy to implement and is cost-effective and the addition of iodine to the salt does not change color and flavor.

Salt is iodized by the addition of fixed amounts of potassium iodate (KIO3) or potassium iodide (KI), as either a dry solid in a powder form or an aqueous solution, at the point of production. The amount of iodine added to salt should be in accordance with the regulation of the specific country where it will be used. Iodate is recommended as fortificant in preference to iodide because it is much more stable (WHO, 1991; Mannar, 1995).

In order to achieve an optimal iodine intake through salt iodization the following factors have to be considered: 1) the consumption of salt per person, 2) the degree of iodine deficiency, 3) the iodine losses during storage and transport. Consequently, the optimal level of salt iodization varies from country to country (Delange et al, 2001). However, WHO/UNICEF/ICCIDD recommend that iodine concentration should be 20-40 mg/kg salt in typical circumstances, where the average daily salt intake is 10 g per person, 20% of iodine from salt is estimated to be lost during transport from production to household and 20% during cooking (WHO, 1996).

While there is much data on the effects of the health benefits of iodized oil, there is a lack of such data on iodized salt. However, long-term effects of USI are well known. Bürgi et al, (1990) has reviewed the effects of iodized salt in Switzerland, which has first started the introduction of iodized salt in 1922. After 1930 no new born endemic cretins have been identified, and goiter disappeared rapidly in newborns and school children, more slowly in army recruits, and incompletely in elderly adults. A study by Lamberg et al, 1981 in Finland found the goiter prevalence among school children decreased generally to 1-4%, having been 15-30% in most parts in the early 1950's.

However, results on the elimination of endemic cretinism, the prevention of blunting of intellectual and socio economic potential and reduction in perinatal morbidity and mortality through salt iodization are needed (Delange et al, 2001).

The stability of iodine in salt and levels of iodization and packaging are related to issues of quality assurance. Conditions of high humidity result in rapid loss of iodine from iodized salt, with iodine loss ranging anywhere from 30 to 98% of the original iodine content (Diosady et al, 1998). By refining and packaging salt in a good moisture barrier, such as low density polyethylene bags, iodine losses can be significantly reduced, during storage periods of over six months.

1.6.1.2 Universal salt iodization in India

The salt iodization program was introduced in India in 1962 as the National Goitre Control program. At that time, a very limited quantity of iodized salt was being produced in the public sector (about 0.14 lakh MTs). In 1983, the Government of India opened up iodized salt production to the private sector by making iodization of salt for edible purposes mandatory. In 1992 the program was renamed as the National Iodine Deficiency Disorders Control Program (NIDDCP) to reflect the spectrum of disorders, including goiter, that occur due to iodine deficiency (UNICEF, 2010).

Iodine deficiency was recognized as a national public health concern in India immediately after it earned its independence and began supplying iodised salt to its endemic population as early as the 1960's (Pandav et al, 2003).

1956: A seminal study conducted in 1956 in the Kangra Valley, Himachal Pradesh in North India established iodine deficiency as a major cause of endemic goitre and demonstrated a significant decline in goitre prevalence in the areas receiving iodised salt (Sooch & Ramalingaswami, 1965; Sooch et al, 1973).

1962: This led the Government of India to launch the National Goitre Control Programme (NGCP) in 1962, in an attempt to provide iodised salt to identified goitre endemic districts (Pandav et al, 2003).

1983: A turning point came in 1983 when, as a result of high-level advocacy, the Prime Minister accepted the importance of IDD elimination, and the eradication of goitre was included as 'Point Eight' in the Prime Minister's 20-point National Development Programme (Pandav et al, 2003). The Central Council of Health, the highest health policymaking body in India, also made a recommendation in 1983 that as all states were IDD prone, iodised salt should be made available to the entire population (The Government of India, 1994; Pandav et al, 2003).

1986: Efforts were made in a phased manner starting in April 1986, to increase the production, demand and supply of iodised salt (The Government of India, 1994; Pandav et al, 2003). In 1986, the USI policy was announced and the 'smiling sun' logo, a voluntary certification of iodised salt, was developed (The Salt Department, 1994). The subsidisation of potassium iodate continued until 1992 (Pandav et al, 2003).

1992: In 1992, the NGCP was renamed the National Iodine Deficiency Disorders Control Programme (NIDDCP), reflecting the government's commitment to eliminating the whole spectrum of IDD (Tiwari et al, 1995; Pandav et al, 2003; Ministry of Health and Family Welfare, 2006).

1996: In 1996, the salt industry was de-licensed, making it difficult for the Salt Department to regulate (Pandav et al, 2003).

1997: In 1997, the Central Government enacted a national ban on the sale of non-iodised salt for edible purposes, under the Prevention of Food Adulteration (PFA) Act, 1954 (The Salt Department, 2007). The PFA Act stipulates the minimum iodine content of salt at the production and consumption levels at 30 and 15 ppm, respectively (The Salt Department, 2007).

Prior to the issue of this notification, all states except Kerala, Andhra Pradesh and Maharashtra imposed a state-level ban on the sale of non-iodised salt for human consumption. However, due to the dissenting voices raised against USI, the central ban was lifted in 2000 (Ministry of Health and Family Welfare, 2000).While the majority of the states maintained the ban, Gujarat and Orissa revoked it (Kotwal, 2010). It took 5 years of intensive advocacy with the central government to reinstate a nationwide ban on the sale of non-iodised salt in 2005 (Ministry of Health and Family Welfare 2005). At present, all states have also imposed a complete ban (Sundaresan et al, 2009).

In 1998-1999: A countrywide evaluation survey conducted under NFHS-2, in 1998–1999 measured the iodine content of cooking salt. Less than half of the households use cooking salt that is iodized at the recommended level of 15 parts per million, suggesting that iodine deficiency disorders are likely to be a serious problem. Rural households and households with a low standard of living are much less likely than other households to be using adequately iodized cooking salt. While 88–91 percent of households in Himachal Pradesh, Mizoram, Delhi, and Manipur consume adequately iodized salt, only 21 percent of households in Tamil Nadu and 27 percent in Andhra Pradesh do so (NFHS-2).

In 2005-2006:A countrywide evaluation survey conducted under NFHS-3, in 2005–2006 measured the iodine content of cooking salt. Overall, 49% of the households used salt that was iodized at the recommended level of 15 ppm or more. It was found that the use of IS varied dramatically from one state to another. The use of IS was high (90% and more) in the north- eastern region where salt is transported by railways. However, all the states in the southern region had low levels of use of adequately IS, ranging from only 21% in Tamil Nadu to 43% in Karnataka (NFHS-3).

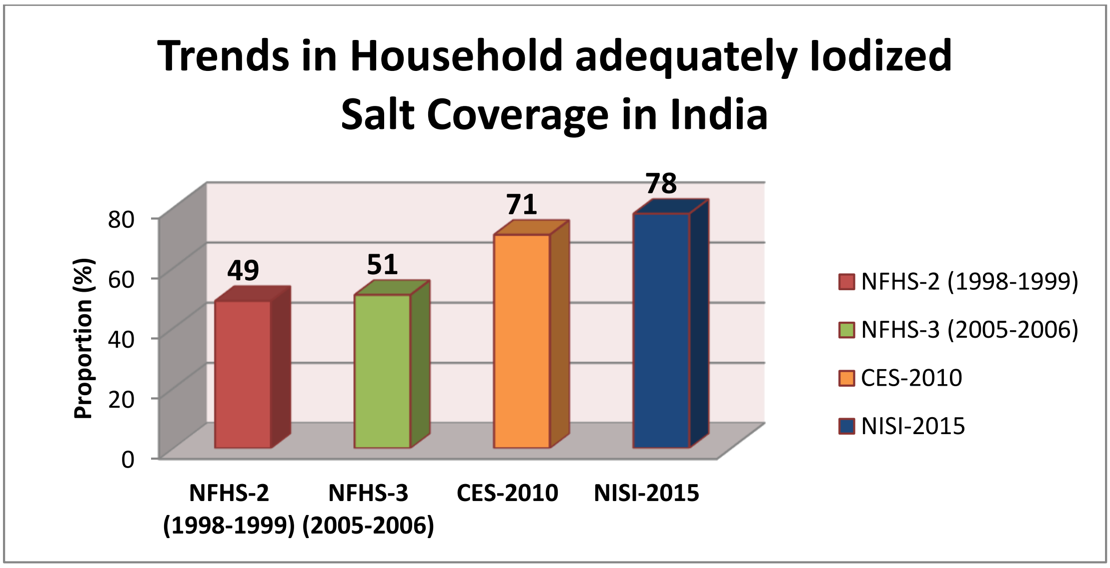
Just over half of households in India (51 percent) were using sufficiently iodized salt at the time of the survey, virtually the same as the percentage observed at the time of NFHS-2 (50 percent). Use of iodized salt varies greatly by region; it is highest in the Northeast Region, in some states in the North Region, and in Kerala, and is over 90 percent in Manipur (NFHS-3).

In 2010: A Coverage Evaluation Survey was conducted in 2009, reported that 91.0% of households had access to iodized salt, of whom 71.0% consumed adequately iodized salt. Another 9.0% consumed salt with no iodine. There were wide rural and urban variations in household coverage of adequately iodized salt (83.2% in urban areas vs. 66.1% in rural areas). Wide variation was also seen across different States/UTs; with Chhattisgarh (31.6%), Karnataka (35.5%) and Jharkhand (41.4%) being the low coverage States and Manipur (98.3%), Meghalaya (98%) and Nagaland (97.1%) being high coverage States (UNICEF, 2010).

In 2015: According to National Iodine and Salt Intake Survey (NISI-2015), nationally, household coverage with iodized salt was 92%, and 78% with adequately iodized salt (≥15 ppm). Only 14% of households were still consuming inadequately iodized salt (iodized at 5–14.9 ppm), and 8% were using salt with no detectable amounts of iodine (90% household access to adequately iodized salt). However, nationally, India has yet to achieve universal coverage. It was reported that 67% of households were consuming refined salt, and 33% non-refined salt (including 23% consuming washed salt, 7% crystal salt, and 3% large crystal or 'phoda' salt). While the households consuming refined salt have already achieved USI, there is a need to ensure that all types of salt being consumed are adequately iodized. The salt industry, including salt production and iodization, should be consolidated, modernized, and mechanized (ICCIDD, 2015).Nevertheless, efforts to intensify USI activities, especially in the past few years, have led to a remarkable improvement in the consumption of adequately iodised salt, with the national coverage reaching 51% in 2005–2006 and 78% in 2015 (NFHS-2; NISI-2015). Still, in 2015, nearly 14% of households were found to be consuming inadequately iodised salt and 8% using salt that was not iodised (ICCIDD-2015).

A trend of adequately iodized salt coverage in India at the household level is depicted in **Figure 5**.

Figure 5: Trends in Household adequately iodized salt coverage in India



Source: NFHS-2, NFHS-3, UNICEF;CES-2010, NISI-2015

1.6.2 Other methods to Control Iodine Deficiency

1.6.2.1 Iodized Water

Water has some of the advantages as salt as a vehicle for iodine fortification. Both are daily necessities and thus their iodization will reach the most vulnerable groups – the poor and the isolated. Water fortified at a regular rate with iodine provides the thyroid with a steady daily ration, which is physiologically desirable (Fisch et al, 1993).

The two main strategies to correct iodine deficiency are supplementation and fortification. Iodization of salt, irrigation water, drinking water or bread is possibilities to fortify with iodine. DeLong et al, 1997 showed that iodine supplementation of irrigation water of wheat in areas of severe iodine deficiency decreases neonatal and infant mortality. However, besides salt fortification neither of the other strategies has been used in large scale.

A review of water iodization programs (Clements et al, 1970) concluded that when properly monitored, the procedure is efficient in controlling iodine deficiency in smaller communities. But it is generally more expensive than iodized salt in large-scale national programs and that it is unlikely to be self-sustaining in poor rural countries and thus requires permanent external funding.

The first iodised bottled water has been introduced in Ghana. Sky Water, as it is called, contains bio natural active iodine which fights a number of diseases that are associated with lack of iodine in the human system (ICCIDD Newsletter, Feb 2016).

1.6.2.2 Iodized Oil

Although salt fortification has been the ultimate goal, the use of iodized oil is recommended when immediate iodine supplementation is needed during the implementation of USI. The most frequently used iodized oil is Lipidol, a seed-oil from the opium poppy, in which iodine atoms are bound to the polyunsaturated fatty acids (Ingenbleek et al, 1997). A portion of the iodized fatty acids is stored in adipose tissue (Wei & Li, 1985), permitting a slow release of iodine and thus providing long-lasting supplies. One year of iodine needs can be achieved with 200 to 480 mg in the form of oral Lipidol (Benmiloud et al, 1994; Elnagar et al, 1995). The advantage of oral iodized oil is that it can be selectively applied to circumscribed regions or geographical pockets of severe iodine deficiency, and within such a region, it can be restricted to certain target populations to reduce costs (Bürgi & Helbling, 1996).

Extensive additional studies on the use of iodized oil in the correction and prevention of IDD have been conducted in Latin America, Africa, Asia and Eastern Europe. The physiology and pharmacology of iodized oil in goiter prophylaxis has been extensively reviewed (Dunn et al, 1996). More than 20 million injections of iodized oil have been given since 1974 with very little side effects apart from a rare abscess at the site of injection. Refrigeration is not required, which is a great advantage. However the necessity for an injection has been questioned, in view of the costs of the syringe and needles and the necessity to have specially trained staff to give the injections. If the oil is given orally, it is often possible to use village health volunteers to supervise administration. Another advantage of the oral preparation is the freedom from the risk of hepatitis infection from contaminated syringes, although this can be eliminated by proper sterilization of needles or by using disposable syringes. Recent experience has confirmed the convenience of the oral administration of iodized oil at yearly intervals through the primary health care system at the village level. In general, the effect of oral administration lasts half the time of the same dose given by injection (Wolff et al, 2001; Leverge et al, 2003; Tonglet et al, 1992; Zimmermann et al, 2000).

Recommendations from WHO-UNICEF-ICCIDD for oral iodized oil supplementation of women and children are shown in **Table 3.**

Iodized oil was first used for the correction of iodine deficiency in Papua New Guinea (Dunn, 1996). In a controlled trial conducted by McCullagh et al. in the Boana area of the Huon Peninsula of New Guinea, with follow-up for 3 years, the sharp reduction in goiter by treatment with iodized oil (McCullagh et al, 1963) was reported. In subsequent studies on the same population, Buttfield and Hetzel demonstrated the effectiveness of a single iodized oil injection (4 ml) in correcting iodine deficiency for a period of up to 4 1/2 years (Buttfield and Hetzel, 1967). Another trial conducted in the Western Highlands of New Guinea demonstrated prevention of endemic cretinism and a reduction in fetal and neonatal deaths in the iodine treated group, if the iodized oil injection was given before pregnancy (Dunn, 1996). Goiter in the treated population often resolved one to three months after the injection.

Table 3: Recommendations for iodine supplementation in pregnancy and infancy in areas where <90% of households are using iodized salt and the median UI is <100 µg/L in schoolchildren

Women of child bearing age	A single annual oral dose of 400 mg of iodine as iodized oil OR A daily oral dose of iodine as potassium iodide should be given so that the total iodine intake meets the RNI of 150 µg/d of iodine.
Women who are pregnant or lactating	A single annual oral dose of 400 mg of iodine as iodized oil OR A daily oral dose of iodine as potassium iodide should be given so that the total iodine intake meets the new RNI of 250 µg/d iodine. Iodine supplements should not be given to a woman who has already been given iodized oil during her current pregnancy or up to 3 months before her current pregnancy started
Children aged 0-6 months	A single oral dose of 100 mg of iodine as iodized oil OR A daily oral dose of iodine as potassium iodide should be given so that the total iodine intake meets the of 90 µg/d of iodine Should be given iodine supplements only if the mother was not supplemented during pregnancy or if the child is not being breast-fed.
Children aged 7-24 months old	A single annual oral dose of 200 mg of iodine as iodized oil as soon as possible after reaching 7 months of age OR A daily oral dose of iodine as potassium iodide should be given so that the total iodine intake meets the RNI of 90 µg/d of iodine

An iodized oil supplementation program is necessary when other methods have been found ineffective or are inapplicable (Eastman et al, 2008). Iodized oil can be regarded as an emergency measure for the control of severe IDD until an effective iodized salt program can be introduced. The spectacular and rapid effects of iodized oil in reducing goiter can be important in demonstrating the benefits of iodization, which can lead to community demand for iodized salt. In general, iodized oil administration should be avoided over the age of 45 because of the possibility of precipitating hyperthyroidism in subjects with longstanding goiter.

1.6.2.3 Iodized Bread

Iodized bread has been used effectively in the State of Tasmania in Australia (Li et al, 2014). Successful use of iodized bread was also reported in Russia (Gerasimov et al, 1997).

1.6.3 Iodised salt Versus Iodized oil in Prevention of IDD

The inexpensive technology, a time honored and time tested one, for the control of goitre is the iodization of common salt. Programmes for IDD control should rest squarely and socially on this technology. Periodic parenteral administration of iodated oil (not presently manufactured in India) has been suggested as an alternative approach especially in areas inaccessible to common salt. It is difficult to imagine any areas in India, which are now inaccessible to common salt but readily accessible to disposable syringes and to an army of 'injectors'. There has been a steep rise in the HIV seropositivity rate among drug addicts in India during the last few years. Those familiar with real life situations in the field will realize that disposable syringes will not be dutifully disposed off. Under the circumstances, the consequences of resorting to a technology which is dependent on repeated injections (using disposable syringes) could be disastrous and is not recommended (Kapil, 2010).

1.7 Assessment and monitoring of iodine deficiency

1.7.1 Thyroid size

The traditional method for determining thyroid size is inspection and palpation. Ultrasonography provides a more precise and objective method. Assessment of thyroid size by palpation is the time-honoured method of assessing IDD prevalence. However, because of the lack of sensitivity to acute changes in iodine intake, this method is of limited usefulness in assessing the impact of programmes once salt iodization has commenced. In this case, urinary iodine is the most useful indicator because it is reflective of the current intake of iodine in the diet (WHO, 2007). Since most countries have now started to implement IDD control programmes, urinary iodine rather than thyroid size. Thyroid size is more useful in baseline assessments of the severity of IDD, and also has a role in the assessment of the long-term impact of control programmes. The introduction of ultrasonography for the assessment of thyroid size has been a significant development. In areas of mild to moderate IDD, measurement of thyroid volume using ultrasound is preferable to palpation for grading goitre. New international reference values for thyroid volume by ultrasound have recently become available and can be used for goitre screening in the context of IDD monitoring (Zimmermann et al, 2004).

1.7.2 Urinary iodine

Most iodine absorbed in the body eventually appears in the urine. There- fore, urinary iodine excretion is a good marker of very recent dietary iodine intake. In individuals, urinary iodine excretion can vary some- what from day to day and even within a given day. However, this variation tends to even out among populations (WHO, 2001). Studies have convincingly demonstrated that a profile of iodine concentrations in morning or other casual urine specimens (child or adult) provides an adequate assessment of a population's iodine nutrition, provided a sufficient number of specimens are collected (WHO, 2007). Round the clock urine samples are difficult to obtain and are not necessary. Relating urinary iodine to creatinine, as has been done in the past, is cumbersome, expensive, and unnecessary. Indeed, urinary iodine/ creatinine ratios are unreliable, particularly when protein intake – and consequently creatinine excretion – is low (WHO, 2007).

1.7.3 Blood constituents

Two blood constituents, TSH and Tg, can serve as surveillance indicators. In a population survey, blood spots on filter paper or serum samples can be used to measure TSH and/or Tg.

Determining serum concentrations of the thyroid hormones, thyroxin (T4) and triiodothyronine (T3), is usually not recommended for monitoring iodine nutrition, because these tests are more cumbersome, more expensive, and less sensitive indicators. In iodine deficiency, the serum T4 is typically lower and the serum T3 higher than in normal populations. However, the overlap is large enough to make these tests impractical for ordinary epidemiological purposes (WHO, 2007).

Thyroid stimulating hormone (TSH): TSH levels in neonates are particularly sensitive to iodine deficiency, and although difficulties in interpretation remain, there is a potential future for the use of neonatal TSH in the identification of IDD and their control; although the cost of implementing a TSH screening programme is too high for most developing countries. Measurement of Tg in children is a sensitive indicator of iodine status and improving thyroid function after iodine repletion. A standardized dried blood spot Tg assay has been developed and can be used for assessing and monitoring iodine nutrition in the field (WHO, 2007).

The pituitary secretes TSH in response to circulating levels of T4. Serum TSH rises when serum T4 concentrations are low, and falls when they are high. Iodine deficiency lowers circulating T4 and raises the serum TSH, so iodine-deficient populations generally have higher serum TSH concentrations than do iodine-sufficient groups. However, the difference is not great and much overlap occurs between individual TSH values. Therefore, the blood TSH concentration in school-age children and adults is not a practical marker for iodine deficiency, and its routine use in school-based surveys is not recommended. In contrast, TSH in neonates is a valuable indicator for iodine deficiency. The neonatal thyroid has a low iodine content compared to that of the adult, and hence iodine turnover is much higher. This high turnover, which is exaggerated in iodine deficiency, requires increased stimulation by TSH. Hence, TSH levels are increased in iodine-deficient populations for the first few weeks of life – this phenomenon is called transient hyperthyrotopinemia (Delange et al, 1985).

The prevalence of neonates with elevated TSH levels is a valuable indicator to assess the severity of iodine deficiency. It has the additional advantage of highlighting the fact that iodine deficiency directly affects the developing brain.

1.7.4 Determining salt iodine levels

The iodine content of salt can be determined quantitatively with the titration method, and qualitatively using rapid test kits. In addition to the titration method the iodine content of salt can be assessed quantitatively using potentiometry or spectrophotometry. A simple and portable single wavelength spectrophotometer has recently been developed. All of these methods have certain advantages and disadvantages which generally influence the choice of method in specific circumstances. Titration method is by far the most commonly used quantitative method, but still remains the reference method for determining the iodine concentration in salt. When other methods are used, it should be standardized against the titration method. Facilities for titration are usually available in public health or food standards laboratories. In addition, ideally it should be standard practice for salt producers to use the titration method to routinely check the accuracy of their salt iodization at the site where salt is iodized. Titration should preferably be carried out on-site (WHO, 2007).

1.8 Rationale of the study

The entire state of Uttarakhand in India is a known iodine endemic state for more than 6 decades. In 1962, the National Goiter Control Programme was launched in eight hilly districts namely: (Uttarkashi, Chamoli, Pithoragarh, Tehri Garhwal, Pauri Garhwal, Dehradun, Nainital, and Almora and in Bijnor district in Uttarakhand) which were identified as endemic to ID.A significant progress has been made in the control of iodine deficiency disorder through supply of iodised salt. The pregnant mothers, neonates, school age children (6-12 years) and adolescent girls are the most vulnerable groups as they are especially sensitive to even marginal iodine deficiency. There are some reports covering small populations from different districts of Uttarakhand which have reported high prevalence of iodine deficiency amongst school age children (Kapil et al, 2007; Kapil et al, 2003).

In state of Uttarakhand according to NFHS-3 survey, less than half of households in Uttarakhand (46%) were using sufficiently iodized salt which is less than the percentage observed during NFHS-2 (60%) survey (NFHS-3). The consumption of iodized salt has been reported to be low by the population in the state (NFHS-3). NFHS -3 data documented only the consumption of iodized salt at the household level.

However, data on pregnant mothers, neonates and adolescent girls of this region is not available. Thusthere is a lack of large scale data on effects of iodine deficiency on these 4 vulnerable groups from Uttarakhand state. Environmental influences like food and water also play a major role in iodine status of the population. As consumption of crops and plants grown on iodine deficient soils leads to iodine deficiency in populations solely dependent on this vegetation for their iodine requirements. We do not have data on the environmental influences (iodine content in water and food samples) on iodine deficiency from Uttarakhand state.Hence, the study was conducted to assess the environmental influences (iodine content in water and food samples) and iodine nutritional status amongst pregnant mothers, neonates, school age children (6-12 years) and adolescent girls in three districts of Uttarakhand state, utilizing indicators recommended by WHO (2007).

Thus to fill the gap in the existing knowledge the present study was conducted with the following objectives:

Objectives of the Study:

i. Assessment of iodine nutritional status amongst pregnant mothers, neonates, school age children (6-12 years) and adolescent girls in the selected 3 districts namely Nainital, Udham Singh Nagar and Pauri Garhwal, from three regions of Uttarakhand namely: i) Kumaon, ii) Terain (Plain) and iii) Garhwal.

ii. Assessment of Iodine content of salt consumed by the population in the selected 3 districts namely Nainital, Udham Singh Nagar and Pauri Garhwal, from three regions of Uttarakhand namely: i) Kumaon, ii) Terain (Plain) and iii) Garhwal.

iii. To assess Environmental influences; iodine content in water and food samples of Uttarakhand state.