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A REVIEW OF IODINE STATUS AMONG LACTATING WOMEN AND ITS ASSOCIATION WITH NUTRITIONAL STATUS OF INFANTS

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Abstract

Lactating period is considered as the most critical period with the increased demand of iodine because of the increased thyroid hormone production and enrichment of iodine in breast milk. The recommended intake of iodide during breast feeding is 250 µg/day. Infants are very sensitive to iodine deficiency because of their high demands and low storages of iodine. The first 2 years of age is a crucial time for neurological development and growth. Even mild iodine deficiency may lead to irreversible damage during this period. Impaired production of thyroid hormones during breastfeeding and low iodine intake results in the development of hypothyroidism and goitre which could affects brain and growth development in the progeny. Iodine deficiency could impair somatic growth, cognitive performance and motor function. Severe iodine deficiency in the new-borne leads to cretinism. Nevertheless, the efforts of USI programme have led to an improvement in iodine status nationwide and iodized salt being cost effective but there is still *much work to be done. Studies have shown the effects of maternal iodine deficiency and hypothyroidism on pregnancy outcomes, such as intrauterine growth restriction, fetal death, preterm, and low birth weight. Although data to conduct a scoping review of iodine status among women of in the India was scarce, majority of the articles reviewed demonstrate emergent iodine deficiency in this population of women of reproductive age, indicating alarm for a public health concern needing immediate attention.*

Keywords: Iodine, Iodine deficiency, Iodine status, Urinary iodine

1. Introduction

Iodine, one of the essential trace elements of thyroid hormones, which synthesis thyroid hormone i.e. triiodothyronine (T_3) and thyroxine (T_4), (Delange 2000; Zimmermann 2011) and plays an important role in physical growth and mental development (Delange 2001; Zimmermann 2007; Zimmermann 2012; Bath et al., 2013). The first 1000 days of life considered as most crucial as consequences of iodine deficiency can occur at this stage. In India, estimated 350 million people are at risk of iodine deficiency disorder and none of the state is free from iodine deficiency (Vir 2002). Almost two billion people worldwide are estimated to be at risk of developing regions such as South Asia and Sub-Saharan Africa (Rodgers et al., 2002). According to United Nations Children's Fund, 2008 (UNICEF), over thirty five million newborns currently remain unprotected against the iodine deficiency range from mild intellectual blunting to cretinism, which is associated with brain damage. Brain damage increases along with deaf-mutism, stunting, impaired gait and motor function (Delange 1994). Researcher showed that regardless of subsequent supplementation inadequate supply of iodine in intrautero reduces IQ level of the infants (Andersson 2012; Cao et al., 1994).

Physiological function of iodine:

Iodine is vital micronutrient, of which 5 gram is sufficient to sustain with a lifespan of 70 years (Dhaar et al., 2008). T_3 and T_4, are the iodinated molecules of the essential amino acid tyrosine which is necessary for protein synthesis (Hetzel 1997) and regulates protein production, fat metabolism, and glucose utilization (Rivkees et al., 1988; Tarım 2011).

A healthy adult body contains 15-20 mg of iodine, 70-80% of which is stored in the thyroid gland. Daily intake of iodine by an individual amounts to 500 micrograms, in which 120 micrograms of iodide are taken up by the thyroid gland for the synthesis of thyroid hormones (Khurana 2006; Pal 2007; Pearce 2014). The secretion of Iodine from the gland increases which trigger hypothalamus for the increased production of Thyroid Stimulating Hormone (TSH) from the pituitary gland, causes remarkable enlargement of thyroid gland (Stanbury 1987). The resulting inadequate hormone in the blood is the principal factor responsible for the series of functional and developmental abnormalities, commonly termed as *iodine deficiency disorders, or IDD*.

Health consequences of IDD at different life stages:

- *All ages:* Goiter including toxic nodular goitre; increased occurrence of hypothyroidism in moderate-to-severe iodine deficiency; reduced occurrence of hypothyroidism in mild-to-moderate iodine deficiency; enhanced susceptibility of the thyroid gland to nuclear radiation
- *Fetus:* abortion, stillbirth, congenital anomalies, perinatal mortality, neonatal cretinism, diplegia squint, psychomotor defects, hypothyroidism
- *Neonate:* Infant mortality; endemic cretinism
- *Child and adolescent:* Impaired mental function; delayed physical development, neurological cretinism
- *Adults:* Impaired mental function; overall, moderate-to-severe iodine deficiency causes subtle but widespread adverse effects in a population secondary to hypothyroidism, including decreased educability, apathy, and reduced work productivity, resulting in impaired social and economic development, decreased fertility rate.

Potential risk factors that may leads to Iodine Deficiency Disorder:

- Low dietary iodine
- Iron and selenium deficiency (iron, selenium are contained in proteins that are important for the synthesis of thyroid hormones, for example peroxidases)
- Pregnancy
- Exposure radiation
- Increased intake of goitrogens (calcium), such as some drugs and

antibiotics which interfere with iodine uptake in thyroid gland
- Gender: more prevalent among women
- Oral contraceptives
- High consumption of conserved, pickled foods
- Smoking tobacco (thyocynate)
- Age (*different type of deficiency at different stages*)

Diet and Iodine Deficiency Disorder

Diet is the sole source of iodine for the population, which includes dairy products or seafood and large amounts of goitrogen-containing foods (Haldimann et al., 2005). Unlike other micronutrients deficiency, Iodine deficiency disorders (IDD) is associate to iodine present in the soil and is ingested through foods grown on that soil. However, iodine present in the top soil got leached due to glaciations, frequent flooding, rivers changing course and deforestation. Therefore, it successively leads to mineral depletion in food crops grown on iodine-deficient soil which in lieu provide inadequate iodine to the population and livestock (Kapil 2007; Chandrakant et al., 2013).

Dietary iodine deficiency stimulates TSH secretion, which results in thyroid hypertrophy. The enlargement of the thyroid gland due to dietary iodine deficiency leads to goitre, if it is present in more than 5% of the general population or more than 10% of the children in school of a defined geographic area is defined as *endemic goitre*. Iodine intakes consistently lower than 50 µg/day usually result in goitre. Severe and prolonged iodine deficiency, may lead to a deficient supply of thyroid hormones. This condition is referred to as *hypothyroidism* (Hetzel 1997).

Government Policies on IDD in our country

Universal Salt Iodization program was started in 1983 by GoI, to iodize all salt meant for human consumption. Despite of the implementation of public health policies in India via the National Iodine Deficiency Disorders Control Programme, 1992 (NIDDCP) (Kumar 1995; Kochupillai et al., 2008), prevalence of IDD remains an issue in some regions (Ayturk et al., 2009; Rendina et al., 2012). Policies for salt is the effective cheap vehicle for providing iodine to the public. The standards for iodized salt have been laid down under PFA Act, 1954. The iodine content of salt at production and consumption level should be at least 30 and 15 ppm respectively. WHO recommended less than 5 gram of salt to achieve maximum health benefits (WHO, 2007). According to Zimmermann 2011, salt intake should be 5 g a day or less, but all salt consumed should be iodized. Indeed, the worldwide National Family Health Survey (NFHS-4) 2015–2016, revealed that salt was tested among all households in which 98.4 percent using iodized salt in Delhi. Recent study showed that iodized salt i.e. ≥ 15 parts per million (ppm) was consumed by 17% of the household when measured by a titration method (Bulliyya et al., 2008). Another study conducted by Rana et al., 2013 revealed that loss of iodine during boiling, roasting, deep frying and microwave cooking were found to be 40.23%, 10.57%, 10.40% and 27.13% respectively. Since, the general population is not consuming the iodized salt and most of them are vegan by choice or due to economic reason, therefore, it is concern to eradicate IDD in our country.

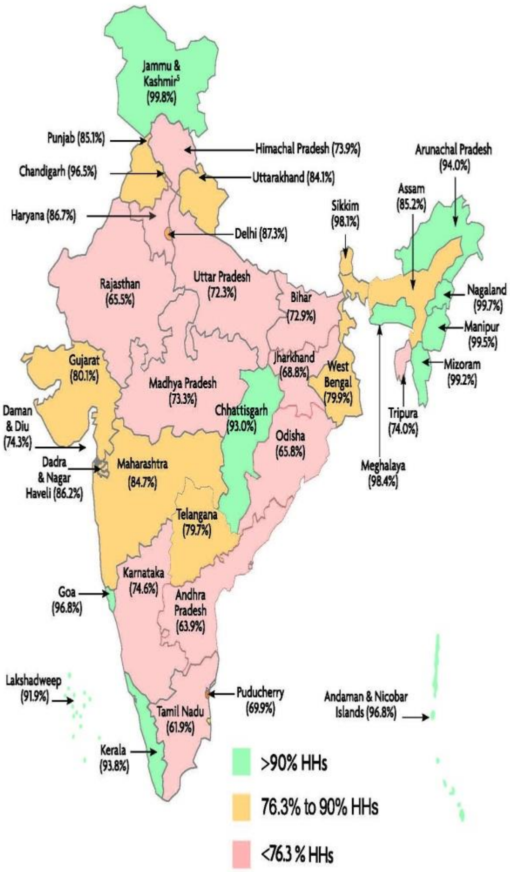
According to India Iodine survey (2018-19) conducted by AIIMS, New Delhi and ICCIDD (Indian Coalition for the Control of Iodine Deficiency Disorder) across all 29 states and 7 Union Territories in India to estimate the household coverage of iodised salt and among women of age 15-49 years. The following key points of the finding are:

- State with the highest iodine consumption through salt (≥ 15ppm) was Jammu & Kashmir (99.8%) followed by Nagaland (99.7%), Manipur (99.5%), Mizoram (99.2%) and Meghalaya (98.4%).

- The median urinary iodine concentration (UIC) for lactating women was 172.8 µg/L as per WHO guidelines.

Awareness about the iodised salt among urban respondent (62.2%) was higher than the rural respondent (50.5%).

Figure 1
Household coverage of Iodized



Salt

From the above demographic map, the following key points be interpreted:

- The household coverage of iodised salt (≥15 ppm) at national level is 76.3 per cent.
- The percentage of households consuming the refined salt is 82.1 percent.

Lactating women and infant:

Lactating women are more perceptible to low iodine intake because of the high demand of iodine for the iodine. In the lactating woman, iodine deficiency is related to disorders that affect mothers and infants: intellectual disability, endemic cretinism, neonatal hypothyroidism, neonatal hyperthyrotropenemia and growth retardation (WHO 2007; Remer et al, 2010). During the period of brain development, even mild iodine deficiency can cause damage. Following delivery, there is decrease in maternal and infant hormone requirements and transfer of T4 and iodine from mother to fetus is no longer required (Smyth 2007). However, loss of iodide in breast milk occurs during lactation, causing an increase in dietary iodine requirement in the lactating mother. The infant also needs a supply of iodine for normal thyroid activity, vital for brain development in the first two years of life (Zimmermann 2011). The neonatal full-term thyroid gland contains about 100 µg of iodine under conditions of iodine sufficiency (Etling 1986).

The activities of sodium/iodine symporter (NIS) and 5'- deiodinase in mammary breast cells increases the concentration gradient by 20-50% higher than in plasma which in turn increases the activity of iodine in breast milk (Tazebay 2000). Hence, the iodine status of breastfed infants is better than that of formula fed infants. However, the iodine concentration in human milk varies widely due to environmental, pharmacological and maternal physical factors, and this change poses an important effect on infant's growth and development.

Factors affecting breast milk iodine:

In iodine sufficiency, iodine content of breast milk is 150-180µg/L. Daily loss of iodine in the lactating woman is measured to be approximately 75-200 µg per day in which milk production ranges from 0.5 to 1.1 litre per day up to six months postpartum. Therefore, the iodine requirement during lactation is 225-350 µg/day. The requirement of iodine in neonates was estimated to be at least 15 µg/kg in full term and 30µg/kg in preterm infants per day, corresponding to 90 µg/day (WHO, 2007).

According to WHO, 2007 the median urinary iodine excretion is the recommended biomarker to monitor daily iodine intake in a given population, and approximately 90% of the ingested iodine is excreted through urine. According to Laurberg 2014, lactating women who consume the recommended 250 µg iodine per day, around 40%–45% of the iodine intake is transported into breastmilk by the sodium iodide transporter (NIS) and urinary iodine excretion is consequently lower. Study conducted by Majumder, 2014 in Kolkata shows that out of 73 lactating mothers, 24 (33%) exhibited insufficient iodine nutrition (UIE < 100 µg/l).

Recommendation proposed by WHO/ICCIDD/UNICEF states that the median urinary level of more than 100 µg/L among lactating women is considered sufficient (Table 1 and 2).

Table 1
The median urinary iodine concentration of lactating women.

Population Group	Median urinary iodine concentration (µg/L)	Category of iodine Intake
Lactating women	<100	Insufficient
	≥100	Adequate
Note: Adopted from WHO, 2007		

Table 2
Recommended iodine intake (µg/day) for lactating women and infants in the first year of life.

Subjects	Institute of Medicine	World Health Organization	
		2001	2005
Lactating women	209 (EAR)	200	250
	290 (RDA)		
Infants 0-6 months	110 (AI)	90	90
Infants 7-12 months	130 (AI)	90	90
Note: Revised and completed from Semba & Delange 2001. EAR, Estimated average requirement; RDA, Recommended dietary allowance;AI, Average intake			

Though WHO define India as an iodine sufficient country, pockets of iodine deficiency still exist. Previous studies conducted by Majumder et al, 2016 on lactating women had shown a prevalence of iodine deficiency by 87.5%. Another study administered by Shaw A et al, 2014 showed 22% of iodine deficiency and also urine iodine content of lactating women was less than 86 mcg/l along with 38 % of subjects consumed salt with <15ppm iodine content.

Study conducted by Yang et al, 2017 suggested that the maternal iodine status during lactation may be related to their infant anthropometric index. A positive correlation was found between maternal and infant urinary iodine concentration (r=0.203,P< 0.01). The mean HAZ and WAZ values were lowest in the infants whose mothers had UIC below 50 µg/L (n= 41). Infant WAZ with maternal UIC below 50 µg/L was significantly lower than those with maternal UIC of 50 µg/L or above (P= 0.043).

Another study by Maheswari et al, 2019 showed that out of 40 salt samples, 19 samples (Fine – 5 and Coarse – 14) found to have <15ppm of iodine. According to Kapil et al, 1998 out of the total coarse salt samples, 95.3% had less than 15 ppm of iodine and out of powdered salt, 61.4% had less than 15 ppm of iodine.

But in spite of evidence of a high prevalence of iodine deficiency among lactating women, there is limited information available on it. Moreover, there is a need to assess the iodine deficiency among lactating subjects and its association with infant weight and height (<6 months).

Table 1
Details of some of the studies conducted for assessing the prevalence of Iodine deficiency in India among lactating women

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Reference	Study Design	Results
Menon et al, 2011 (Nagpur)	*The effect of maternal iodine status on infant outcomes in an iodine-deficient Indian population* - Pregnant women (n=220) were recruited at 13-22 weeks gestation, and again visited at 2-4 weeks postpartum with their infants.	-The MUIC at recruitment was 106 μg/L, which declined to 71 μg/L at 34.5 weeks similar to the postpartum MUIC of 69 μg/L, indicating that these women were iodine deficient. -Infant (mean age=2.5 weeks) MUIC was 168 μg/L. Median maternal TSH and free thyroxine concentrations at first and second visits were 1.71 and 1.79 mIU/L and 14.4 and 15.4 pmol/L, respectively.
Lean et al, 2013 (Pune)	*Iodine status during pregnancy in India and related neonatal and infant outcomes.* -Longitudinal study following mothers through pregnancy and offsprings up to 24 months. Pregnant mothers at 17 (n=132) and 34 weeks (n=151) gestation and their infants from birth to the age of 24 months.	-Median urinary iodine concentration (UIC) was 203 and 211 μg/l at 17 and 34 weeks of pregnancy, respectively (range 26-800 μg/l). -Offspring developmental outcomes differed between the lowest and highest UIC quartiles (abdominal circumference at 24 months, subscapular and triceps skinfolds at 12 and 24 months).
Shaw, 2014	*A Study on the Effect of Iodine Content of Salt Samples on the Iodine Nutrition Status of Pregnant, Lactating and Healthy*	-22% of lactating subjects had Insufficient Iodine intake and their median UIC was 86μg/l

Reference	Study Design	Results
	NPNL Women. -Pregnant (n=511), lactating (n=208) and NPNL (n=120) women belonging to age group 20-45 years	- 38% of Insufficient iodine intake lactating women was found to consume inadequately iodized salt which had <15ppm iodine content.
Majumder et al, 2014 (Kolkata)	*Prevalence of iodine deficiency among pregnant and lactating women.* -UIC was assessed among 237 pregnant women, 73 lactating mothers and 59 healthy non-pregnant female controls.	-Out of 73 lactating mothers, 24 (33%) exhibited insufficient iodine nutrition (UIE < 100 µg/l) and only 3% female control subjects exhibited insufficient iodine nutrition (UIE < 100µg/l).
Majumder et al, 2016 (Kolkata)	*Iodine Nutrition among the Pregnant and Lactating Women.* -237 pregnant women, 73 lactating mothers and 59 healthy non-pregnant female controls	88% pregnant women was found to be Iodine insufficient, 87.5% lactating woman were iodine Insufficient. -almost (100%) of insufficient female control were adding salt in the initial stages of cooking.
Karmakar et al, 2019 (Tripura)	*Knowledge, attitude, and practice regarding household consumption of iodized salt among rural women.* -Community-based study was conducted among 270 rural women residing at Madhupur village, Tripura.	-Knowledge and attitude regarding iodized salt consumption were significantly associated with age groups ≤36 years, literacy, and general caste ($P< 0.05$), but practice was not significant ($P> 0.05$). -Attitude regarding use of iodized packed salt were less than half (46.7% and 41.1%, respectively), but higher level (83.3%) of correct practice was found ($P> 0.05$)
Majumder et al, 2019	*A cross-sectional study on iodine status among pregnant and non-pregnant women of Tripura: a*	-Median value of UIE in pregnant and non-pregnant women of Tripura was 155.0µg/L and 130.0µg/L.

Reference	Study Design	Results
(Tripura)	*North-Eastern state of India* -urine samples collected from pregnant and non-pregnant women was 538 and 533 respectively.	-In pregnant women percentage prevalence of severe (<20µg/L), moderate (20-49µg/L) and mild iodine deficiency (50-149µg/L) was found in 4.1%, 15.1% and 29.6% subjects.

Conclusion: IDD being a success story of public health, it is still prevalent among Indian population irrespective of age, physiological status and geographical location. Urgent, targeted and comprehensive intervention is required with effective and efficient coordination among all stakeholders in lieu to eliminate IDD. In addition, to sustain IDD control goal, on-going actions will be necessary to achieve it.

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