

ABSTRACT

Iodine Deficiency Disorders (IDD) is a Global problem affecting more than two billion people (Hetzel B S, 2002) in 130 countries worldwide based on total goitre rate (TGR). IDD is one of the oldest and most insidious of human health disorders and the fight against it remains one of the major public health challenges even at the beginning of the 21st century.

The adoption of the term IDD reflects a new dimension of understanding of the full spectrum of the effects of iodine deficiency on the fetus, the neonate, the child, the adolescent, and the adult in the whole population as shown below:

Fetus: Abortion, Still births, Brain damage– cretinism	Neonate: Neonatal goitre, Brain damage
Child: Goitre, Thyroid deficiency (lethargy) Impaired school performance Retarded physical development	Adult: Goitre with its complications Thyroid deficiency (lethargy) Impaired mental function

Goitre, an enlargement of the thyroid gland, is the most apparent manifestation of iodine deficiency; and the region is considered endemic when more than 10% of the residing population or 5% of the school-aged children population has goitre. Goitre reflects the adaptive response of the thyroid to iodine deficiency.

Epidemiological studies of IDD encounters problems like any other thyroid disorders and various limitations of such a study must be recognised. Their manifestations vary considerably from area to area and are determined principally by the availability of iodine in the diet.

One teaspoon of iodine, consumed over a lifetime in tiny amounts each day, is all that is needed to prevent IDD. The cumulative consequences in iodine-deficient populations spell diminished performance for the entire economy due to decreased individual and national productivity and these in turn put brakes on socio-economic development of affected nation.

Iodine deficiency may either act alone or in concert with other environmental factors to produce the spectrum of clinical conditions now classed as IDD. These environmental factors include dietary substances (termed goitrogens) that interfere with normal thyroid function and promote thyroid growth. IDD are caused by decreased production of thyroid hormones vital to both the physical and mental growth and development. Large populations at risk of IDD are in developing countries, particularly in Asia, including India, Africa and Latin America. India was declared IDD prone country, based on goitre estimates in 1989. The consumption of goitrogens in India is far greater than the developed Western countries due to differences in the ethnic background, culture, dietary habits, religious bindings, standard of living, and caste system. Another fact that Protein energy malnutrition (PEM) is highly prevalent in India encouraged this study. We selected the State of Gujarat that has cultural diversity of all.

Between 1972-1992 Goitre surveys were conducted in the State of Gujarat based on inspection and palpation of the neck. TGR is an indicator of iodine deficiency in the past. The highest TGR prevalence of 44.4% was seen in the Dang district; there was no data available for Baroda district (Desai VK, 1994).

The first task for this study was to assess the severity of IDD in Gujarat State using biochemical prevalence indicators. Biochemical parameters (urinary iodine and thyroid related hormones) are short time markers indicating current status of iodine deficiency. The districts of Baroda and Dang were

selected for the assessment of IDD because Dang had highest prevalence of goitre and IDD status for Baroda was not known (Desai VK, 1994). Data were collected on dietary habits and anthropometric parameters such as height, weight, and biochemical parameters like urinary iodine (UI) and blood thyroid stimulating hormone (TSH) of the population (adult (n=959) and children (n=1363). Body Surface Area (BSA) and Body Mass Index (BMI) was calculated. Drinking water and cooking salts were analyzed for iodine content. The results showed that there was a definite mild to moderate iodine deficiency in Baroda district and severe IDD in Dang District. Baroda district (rural) is a new pocket of IDD. We detected interfering substances in urine samples that were postulated to be goitrogens. Drinking water in Dang district lacked in iodine. Iodine content of cooking salt varied with the levels around 7 to 10 parts per million (PPM) from most places with one exception having 2000 PPM. Thus, based on these biochemical prevalence indicators, IDD was found to be a major public health problem in both districts Gujarat. The excessive use of dietary goitrogens appeared to be the main cause of IDD in Baroda.

It was necessary to determine the aetiology of IDD in Gujarat and to identify the best prevalence indicator of IDD. IDD status was assessed by both clinical (thyroid size) and biochemical parameters. Thyroid size was determined initially by traditional method of palpation of the neck and was scored according to 1994 World Health Organization (WHO) classification. Then the safe and noninvasive technique of thyroid ultrasonography provided a more precise and objective method of determining the thyroid volume. It gives a quantitative measure of thyroid volume that is largely free of observer bias. Although in areas of severe or moderate iodine deficiency, thyroid palpation provides a reliable method for assessment of goitre prevalence rate (TGR), serious problems are encountered in areas with mild iodine deficiency, where most goitrous subjects have small goitres. At the same time thyroid palpation is less reliable in children than in adults. The more refined method for determining the magnitude of iodine deficiency in a population is by estimating the proportion of children with enlarged thyroid volumes based

on ultrasonography. Correct interpretation of ultrasonography results depends upon the availability of valid reference values. WHO had adopted a thyroid volume international reference for assessing IDD (WHO 1997). Palpation, an initial signal of IDD, pointed to the grave endemic goitre problem in Gujarat hence more refined assessment was needed. As WHO has strongly recommended the use of ultrasonography technique to define the goitre endemia in areas of mild iodine deficiency epidemiological surveys, this reliable method for the evaluation of thyroid volume proved a useful and practical method for Gujarat especially Baroda that showed mild iodine deficiency in first preliminary study. The availability of portable ultrasound equipment facilitated its application to our epidemiological field studies. The procedure was used to measure thyroid volumes in several hundred subjects in a day. Applying the WHO ultrasonography reference to Gujarat children resulted in an enlarged TV-for-body surface area in almost 100% of subjects. Food articles were analyzed for goitrogens. Flavonoids like vitexin, glucosyl-vitexin and apigenin were detected in pearl millet. Apigenin was never identified in pearl millet. This study in schoolchildren showed that measuring the thyroid size by ultrasound is the best prevalence indicator of IDD and iodine deficiency is the principal but not the only cause of endemic goitre in Gujarat. The additional role of naturally occurring goitrogens mainly the flavonoids like apigenin, vitexin and glycosyl-vitexin in pearl millet was postulated along with primary protein energy malnutrition.

The next step was to assess the severity of protein-energy-malnutrition (PEM) in iodine deficient subjects and to assess the impact of PEM on thyroid-size. 1002 confirmed iodine deficiency subjects (530 school-aged children and 472 adults) were assessed for PEM by direct anthropometric measurements of height, weight, triceps-skin-fold (TSF) thickness, mid-upper-arm-circumference (MUAC) and thigh-circumference (TC) and derived indices of body-surface-area (BSA), body-mass-index (BMI); Z-scores for weight-for-age (WAZ), height-for-age (HAZ), weight-for-height (WHZ). Severity of PEM was based on World Health Organization (WHO) criteria and threshold on

Waterlow-classification. Thyroid-size was measured by ultrasonography to determine the thyroid volume (TV). Linear regression analysis was performed between TV and anthropometric parameters. Children had severe PEM as evident from WHO percentage-prevalence of stunting (64%), wasting (43%) and underweight (82). Waterlow-classification showed that children were either stunted or wasted or stunted and wasted or stunted and obese. Nearly 100% (529/530) children had goitre as evidenced from enlarged TV-for-BSA when compared to WHO reference. There was a weak but statistically significant ($p<0.05$) positive correlation between TV and BSA, weight, height, MUAC, TC and HAZ but negative correlation between TV and WHZ, BMI and TSF ($r=-0.1-0.2$). Adults had PEM as evident from $BMI<18.5$ kg/m² in 54% subjects. Median MUAC of 22.7cm revealed prolonged severe PEM. Eighty-two percent had enlarged TV >20 ml. There was a significant ($p=0.01$) negative-correlation between TV and MUAC. Thus the severity of acute (wasting) and chronic (stunting) PEM was very high in Gujarati children. They were stunted or wasted or stunted and wasted or stunted and obese. Gujarati adults were thin with low protein and fat reserves. Anthropometric parameters showed a significant ($p<0.001$) correlation ($r=0.1-0.2$) with thyroid size. Higher prevalence of goitre may be due to *macronutrient-malnutrition* (PEM) on the face of *micronutrient-malnutrition* (IDD).

For the assessment of TGR in our children by ultrasonography we compared our results of thyroid volume to World Health Organization and International Council for the Control of iodine deficiency disorders (IDD) (WHO/ICCIDD) reference (1997). We used this WHO/ICCIDD reference due to the lack of local thyroid volume reference in India, a developing country. We wanted to develop a local normative ultrasonography standard reference for thyroid size for the use in the country. We selected Baroda, as it is an industrial and educational Centre with a remarkably cosmopolitan cultural life. To avoid the discrimination of child growth retardation in a developing country, the affluent class children of Private Schools were selected for the study of thyroid volume reference. Good income is necessary to afford iodized salt and good nutrition for their kids. The median and 97th percentiles for TV for

schoolchildren were estimated for age and BSA by gender. These are compared with the WHO/ICCIDD-recommended normative reference for the assessment of IDD. A national sample of 1541 Indian schoolchildren aged 6-15 years was studied for nutritional status, urinary iodine and thyroid size. 479 children were in the range of 6-10 years. The children showed a low prevalence of stunting, wasting and undernutrition. Goitre prevalence by palpation was below 1%. Eighty five percent and 81% of schoolchildren had enlarged thyroid volume for BSA and age, respectively. The median and upper limits (97th percentiles) of thyroid volume based on BSA and age for these children were 2-3 times greater than European schoolchildren in WHO reference. When these present study data were compared to iodine deficient children of our previous study, their thyroid size for BSA and age was much smaller. This study thus proved the important role played by goitrogens.

As there is a regional dietary variation in all the States of India, a state other than Gujarat from North India was selected to study the aetiological role played by dietary flavonoids. Himachal Pradesh (HP) is a mountainous hilly State and coloured vegetables and fruits (except apples) are costly due to expenses incurred to transport them. This would limit their excessive use unlike Gujarat. At the same time this State is declared as iodine sufficient recently. Goitre endemia was a common occurrence for last 40 years but the Government introduced mandatory salt iodization in 1970 that really helped IDD control. The vegetables and cooking-oils consumed in this mountainous area are different to those used in Gujarat hence to establish normative thyroid volume reference data study was conducted in the Shimla; Capital City of HP. 6-19 year old iodine sufficient and well-nourished affluent schoolchildren from Private schools were palpated first for goitre and the thyroid volume (TV) was then measured ultrasonographically using a 7.5MHz probe. Urine samples were collected for iodine (UI) measurement (Method L). Anthropometric measurements were performed. BSA and Z score for weight-for-age, height-for-age, and weight-for-height and BMI were derived. Medians and 97th percentiles thyroid volumes of 6-15 year children were compared to

both WHO references of 1997 and 2001. We found that the nutritional status of children was comparable to Indian normative reference developed from metro cities affluent schoolchildren. WHO based classification showed 4% of boys were either stunted or undernourished. Girls were affected more than the boys were by malnutrition. Their thyroid size was not enlarged. Goitre prevalence by palpation was 1% and by ultrasound 0%. The median and 97th percentiles for TV were estimated for age and BSA by gender and were much smaller (almost one third to one half) than European schoolchildren of WHO 1997 or the corrected 2001 reference. This may be due to the mandatory salt iodization policy imposed by the State Government or due to hypoxia prevailing in hilly regions. By comparison thyroid size for BSA and age was greater in iodine sufficient children from Gujarat. The median UI for 6-15 year schoolchildren and >15 year subjects was 201.5 $\mu\text{g/l}$ and 209 $\mu\text{g/l}$ respectively

The last part of the study comprised of work in Tamil Nadu State that is the southern state of India. The Aryans never brought their meat-eating influence to this extreme south, so most of the Tamil Nadu is more or less totally vegetarian. Dosas and idlis have become enormously popular all over the country. Mounds of rice accompany every meal, sweets are a favourite, and coffee is more popular than tea. Chennai, the capital of Tamil Nadu, is India's fourth largest booming cosmopolitan city and was known as Madras formerly. This city had different castes people from all over south including Christians and Muslims. Due to city life most of the children gave the history of consumption of a mixed diet including non-vegetarian dishes at least once a week. The schoolchildren studied belonged to lower socioeconomic status. The ground nut oil was used for cooking by 1-2% of children whereas most of the schoolchildren consumed sunflower oil. Pearl millet was not consumed in this state. The main vegetables consumed were potatoes, tomatoes, ladies fingers and carrots. The children had median urinary iodine > 200 $\mu\text{g/l}$ in all segments of population and were thus iodine replete. 65% of children were pale due to iron deficiency and none had vitamin A deficiency. The children

were definitely malnourished as evidenced from wasting, stunting and undernutrition indices deficits. The goitre (by palpation as well as by ultrasonography) was seen in 10% of schoolchildren. Thus mild iodine deficiency disorders were evident despite no dietary iodine deficiency. The problem site may be the manufacture process of thyroid hormone in the acinar cell where pumped iodide is converted in to elemental iodine with the help of peroxidase enzyme or the following steps where this iodine conjugates with tyrosine.