Chapter 5

ASSESSMENT OF IODINE DEFICIENCY DISORDERS BY CLINICAL AND BIOCHEMICAL PREVALENCE INDICATORS IN RURAL AND TRIBAL CHILDREN FROM GUJARAT

5.1. SUMMARY

Iodine deficiency may either act alone or in concert with other environmental factors to produce a spectrum of clinical conditions, iodine deficiency disorders (IDD). These environmental factors include dietary substances that interfere with normal thyroid function and promote thyroid growth (termed goitrogens). The majority of the studied tribal and rural population group of Gujarat (India) is mainly vegetarian hence the role of confounding factors such as high goitrogen intake and malnutrition may be significant. There is no study reported from this part of the World where each of the two commonest monitoring methods like urinary iodine estimation (UIE) and childhood goitre rate (assessed by palpation and ultrasonography) is applied for assessment of IDD. UIE is used as an indicator of present iodine intake, and childhood goitre rate indicates past history of iodine deficiency. 530 schoolchildren (6 - 15 years) were studied from two districts (Baroda and Dang) and data was

collected on dietary habits and parameters such as height, weight, thyroid size by palpation and ultrasonography, urinary iodine (UI), blood Thyroid-stimulating-hormone (TSH). Drinking water was analyzed for iodine content and food articles for goitrogens.

The present study found that in Gujarat children median UI was 56 µg/l and the interquartile range was 30-96 µg/l thereby showing that IDD is a severe public health problem in Gujarat. The mean TSH was quiet high (1.71 ± 2.10 mU/L).

The goitre by palpation was seen in 30% and the median TV was 27.8 (IQR was 23 - 35) ml. Applying the WHO ultrasonography reference to Gujarat children resulted in an enlarged TV-for-BSA in almost 100% of subjects. Three-to-eight times larger TV were seen in all subjects as compared to European children. Dang children were severely malnourished. Flavonoids like vitexin, glycosyl-vitexin and apigenin were detected in pearl- millet. Apigenin was never identified in pearl millet. Dang district water lacked in iodine content.

The data from this study, therefore, suggest that Gujarat may be labeled as having a severe IDD problem based on clinical measurement of thyroid size and mild IDD based on biochemical indicators. Thus the study highlights the complexity of assessing the severity of iodine deficiency in the presence of multiple confounding but interacting variables of not only a lack of iodine but also the presence of malnutrition and high goitrogen intake. The consistent enlargement of thyroid by ultrasonography suggests that TV measurement is the best prevalence indicator of IDD.

5.2. INTRODUCTION

Iodine deficiency is one of the oldest and most insidious of human health disorders and the fight against iodine deficiency remains one of the major public health challenges at the beginning of the 21st century. Iodine deficiency may either act alone or in concert with other environmental factors to produce a spectrum of clinical conditions - iodine deficiency disorders (IDD). These environmental factors include dietary substances that interfere with normal thyroid function and promote thyroid growth (termed goitrogens).

The most apparent manifestation of iodine deficiency is goitre, an enlargement of the thyroid gland; and the region is considered endemic when more than 5% (previously 10%) of the residing population has thyroid enlargement (WHO, 1994). Endemic goitre reflects the adaptive response of the thyroid to a lack of iodine. Although the thyroid gland may become very enlarged it is not usually associated with morbidity. By contrast, the most damaging and pernicious effect of iodine deficiency is on the developing brain, an effect mediated by perturbations to maternal and fetal thyroid hormone homeostasis (Boyages SC, 1993). All iodine deficiency disorders are preventable. Although iodine supplementation programs have been implemented in various countries since 1924, IDD remains a significant world health problem. According to 1999 ICCIDD report on the global status of IDD, two billion people are at risk of IDD. The major health organizations have determined agreed criteria for a population to be considered iodine replete (WHO/ICCIDD/UNICEF, 1994). Although the technology and methods of implementation of iodine supplementation programs are relatively simple, the monitoring and timely assessments of such programs are more difficult.

This is, in part, related to the low sensitivity and low specificity of monitoring methods. The two commonest methods of monitoring are urinary iodine estimation (UIE) and childhood goitre rate (assessed by palpation). UIE is

used as an indicator of present iodine intake, whereas goitre rate indicates past history of iodine deficiency. Surveys for assessing the prevalence of goitre relied on thyroid palpation (WHO, 1994) and thyroid size was usually scored according to WHO classification (WHO, 1994). Although in areas of severe or moderate iodine deficiency, thyroid palpation provides a reliable method for goitre assessment, serious problems are encountered in areas with mild iodine deficiency, where most goitrous subjects have small goitres (Delange, 1986). Moreover, thyroid palpation is less reliable in children than in adults (Gutekunst, 1986). The more refined method for determining the magnitúde of iodine deficiency in a population is by estimating the proportion of children with enlarged thyroid volumes based on ultrasonography (Bürgi H, 1999). Correct interpretation of ultrasonography results depends upon the availability of valid reference values. Recently the World Health Organization (WHO) has adopted a new thyroid volume international reference for assessing IDD (WHO, 1997). Palpation is most useful, as an initial signal that IDD may be present and as an indicator that more refined assessment is needed. If palpation suggests that IDD is a problem, then ultrasonography of the thyroid gland should be performed. Thyroid ultrasonography is a cheap and reliable method for the evaluation of thyroid volume and has proven to be a useful and practical method for the assessment of thyroid size (Ueda, 1990). The availability of portable ultrasound equipment has facilitated its application to epidemiological field studies (WHO, 1994). Ultrasonography is a safe, noninvasive technique that provides a more precise and objective method of determining thyroid volume than inspection and palpation, particularly in areas where rates of goitre are low. It gives a quantitative measure of thyroid volume that is largely free of observer bias. The procedure can be used to measure thyroid volumes in several hundred subjects in a day. Ultrasonography is rapidly replacing palpation, and has thrown doubt on the validity of many older surveys. In the epidemiological surveys, the use of this technique is at present strongly recommended to define the goitre endemia in areas of mild iodine deficiency (WHO, 1997).

Although there have been several reports highlighting the pitfalls of both methods, there are few studies that have applied each method to a population group, and specifically in areas where confounding factors such as high goitrogen intake and malnutrition may be significant.

The aims of the present study were:

1) to assess the severity of IDD in Gujarat (Western India) by testing various prevalence indicators of IDD in this population;
2) to determine the relative contribution of nutritional iodine deficiency and goitrogens as causative factors in the aetiology of goitre in this region;
3) to identify the best prevalence indicator of IDD and
4) to describe thyroid volumes measured by ultrasonography in Gujarat schoolchildren and compare these with European schoolchildren (WHO has recently adopted thyroid volume ultrasonography results from European schoolchildren (WHO, 1997) as the international reference).

5.3. SUBJECTS AND METHODS

5.3.1. DIET

The majority of the population of Gujarat is mainly vegetarian and the diet consists of cereals like pearl millet, jowar, wheat and rice, pulses (tuver dal and udad) and vegetables like onion, chili, ginger, garlic, cabbage and beans. In addition to cereals, pulses and vegetables consumed by the rural population, the tribal population from Dang consumed nagli (a cereal), kharsani (type of oil used for cooking) and bamboo shoots as vegetables. The main evening meal for both the tribal and rural populations consists of pearl millet pancakes.

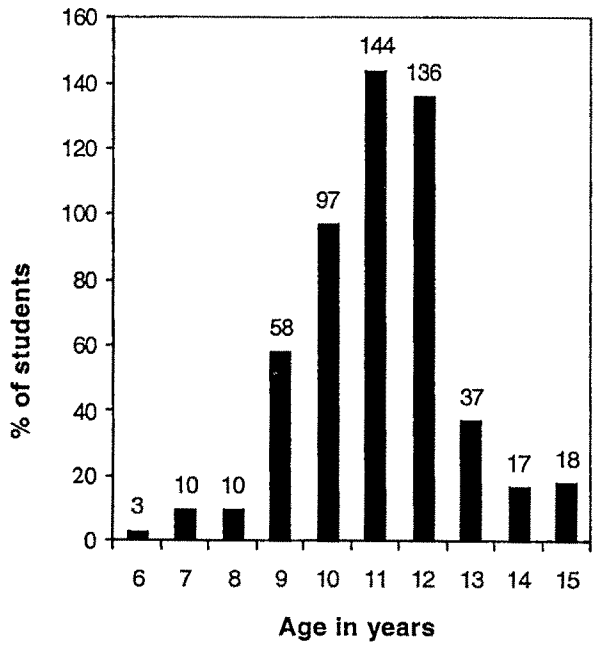
5.3.2. POPULATION STUDIED

Five hundred and thirty schoolchildren aged 6-15 years were selected randomly by home surveys (118 rural schoolchildren from Muval and Tentalav - two villages in the Baroda district) and school visits (412 tribal children from Dang). The study group comprised 283 boys and 247 girls (M: F ratio = 1.15: 1). Figure 5.1. shows their age distribution.

5.3.3. THE IDD STATUS

This was measured by clinical (thyroid size) and biochemical indicators.

FIGURE 5.1. AGE DISTRIBUTION



5.3.3.1. THYROID SIZE

Palpation and ultrasonography that measured thyroid volume (TV) scored thyroid size. Random urine samples for urinary iodine (UI) and blood spots for thyroid stimulating hormone (TSH) determination were collected from all subjects.

Ultrasound scanning for TV determinations was carried out as detailed in chapter 3. Thyroid glands were classified as `normal' or `enlarged' using the WHO reference (thyroid volume-for-age and thyroid volume-for-body surface area (Delange, 1997). Thyroid volumes greater than the 97th percentile values were considered abnormally large and those less than or equal to the 97th percentile values as normal. Determination of TV by ultrasonography can show an inter-observer error of up to 30% and intraobserver variation of 2 ± 15%.

Statistical evaluation was performed by linear regression analysis.

5.3.3.2. URINARY IODINE

Casual urine samples were collected, packed and personally transported to Sydney (Australia) according to the standard protocol. Collection and transport containers were provided by endocrinology laboratory of ICPMR, Westmead Hospital. All the UI tests were performed in Iodine laboratory. Urinary iodine analysis used a modified acid- digestion method (method E), based on the reaction between cerium IV and arsenic III (Sandell-Kolthoff Reaction) using a Technicon Autoanalyzer II. The results were expressed as micrograms of iodine per litre of urine (µg/l). The method does not separate out the interfering substances. The interfering substances were removed from the urine samples to arrive at true urine iodine value determinations.

5.3.3.3. BLOOD SPOT TSH

Commercially available Bioclone neonatal TSH Elisa kits (Bioclone Australia Private Limited, Marrickville, NSW, Australia) for the quantitative determination of thyroid stimulating hormone (TSH) in Human neonatal blood spots were used for the estimation of TSH in children of our survey.

5.3.4. DIETARY GOITROGENS ANALYSIS

Cereal grains and pulses were examined for the presence few goitrogens and their quantity was determined.

5.3.5. ANTHROPOMETRY

Weights and standing heights were collected. The BSA and BMI was calculated

5.4. RESULTS

Male and female children of Gujarat, from the Dang and Baroda districts had similar distributions for variables of age, height, weight, and BSA. Although BSA did not show a significant difference between the two districts ($P < 0.6$), body mass index (BMI) was significantly lower for the children from the Dang district compared with children from the Baroda district ($P < 0.0001$) (Table 5.1.). These effects are probably explained by a greater degree of malnutrition in the Dang children. Iodine content of drinking water was adequate (32 μg/l) in the Baroda district while it was lacking (0 μg/l) in the Dang district (Table 5.2.).

The median UI (and interquartile range) for all children from Gujarat was 56 (30 - 96) µg/l. Children from Dang had lower median UI concentrations [50 (27 - 90) µg/l] as compared to Baroda children having median UI as 79 (48 - 117) µg/l. Based on these values Dang district would be categorized as having moderate iodine deficiency and Baroda as having mild iodine deficiency. Statistically highly significant gender differences were noted in median urinary iodine values, with females being more severely affected from both districts ($p = 0.01$) (Table 5.1.).

The frequency distribution of the severity of iodine deficiency for male and female children from Dang and Baroda districts is shown in figures 5.2. A and B respectively. Fifty four percent of females and 45% of males from Dang had UI levels below 50 µg/l [ideally < 20% of samples should be below 50 µg/l (WHO/UNICEF/ICCIDD)]. By contrast in Baroda, 35% of females and 25% of males were below 50 µg/l.

The Gujarat children had a relatively high mean blood TSH level of 1.71 ± 2.10 mU/L The blood TSH levels were significantly different in boys and girls ($p = 0.01$) from Dang but not in Baroda ($p = 0.59$). Females were more likely to have elevated TSH values (Table 5.1.). Blood spot TSH values > 5 mU/L were seen in 5% of girls and 3% of boys from Dang and 4% of both sexes in Baroda. TSH values > 3 mU/L were noted in 30% of girls and 27% of boys from Dang and 21% of girls and 11% of boys from Baroda. Figure 5.3. A (Dang) and B (Baroda) show the frequency distribution of TSH values by sex for the described ranges. TSH distribution curves were shifted to the right in children from the Dang district as compared with those from the Baroda district [Figure 5.3. A, B and Table 5.1.]. There have been no population normative values for TSH published for this population nor for schoolchildren from an iodine replete environment.

TABLE 5.1. DISTRIBUTION OF CLINICAL, BIOCHEMICAL AND ANTHROPOMETRIC PARAMETERS BY DISTRICT AND GENDER

BARODA(n = 118)	*GIRLS (n = 28)*			*BOYS (n = 90)*			*P*
	Range	Mean ± SD	Median (IQ)	Range	Mean ±SD	Median (IQ)	
Age	6 - 15	11.7 ± 2.3	12 (11-13)	6 - 15	11.6 ± 2.5	12 (10-13)	NS
Height	80 - 154	124 ± 19.6	129(109-138)	76 - 164	127 ± 18.3	130(119-140)	NS
Weight	13 - 46	27 ± 7	27 (22-31)	15 - 45	26 ± 7	25 (20-30)	NS
BSA	0.6 - 1.36	0.95 ± 0.2	0.93 (0.8-1.1)	0.5 -1.4	0.96 ± 0.2	0.93.(0.8-1.4)	NS
BMI	9.3 - 38	18.5 ± 8	16 (13-20)	9.6 - 32	16.5 ± 5	14 (13– 18.6)	NS
UI	0 - 190	69 ± 49	63.5 (30-92)	0 - 400	98 ± 65	84 (54-120)	0.01
TSH	0 - 25	2.35 ± 5.15	1.13 (0.3-2.5)	0 - 8	1.2 ± 1.4	0.8 (0.2-1.5)	0.59
TV 1	8 - 40.5	25.0 ± 9.6	28.2 (17-31)	6.5 - 56	23 ± 12	20 (13-32)	0.2
TV 2	8.7 - 44	27.1 ± 10	30.7 (19-34)	7 - 61	25 ± 13	22(14-35)	0.2
DANG (n=412)	***GIRLS (n = 219)***			***BOYS (n = 193)***			
Age	6 - 15	11 ± 1	11 (10-12)	8.0 - 15	11 ± 1	11 (10-12)	NS
Height	112 - 149	131 ± 7	131(126-136)	112 - 164	131± 9	130(126-136)	NS
Weight	9 - 40	23 ± 4.5	23 (20-25)	11 - 47	23 ± 4.7	23 (20-25)	NS
BSA	0.7 - 1.3	0.93 ± 0.11	0.9 (0.9 -1.0)	0.7 - 1.46	0.9 ± 0.1	0.9 (0.9-1.0)	NS
BMI	10.5 - 18	13.2 ± 1.4	13.2 (12-14)	7.0 - 18	13.3 ± 1.4	13 (12.6-14)	NS
TSH	0 –12	1.96 ± 2.05	1.58 (0.3-3.1)	0.0 – 6	1.5 ± 1.6	1.0 (0 – 3)	0.01
TV 1	11 - 112	27.4 ± 11.5	25 (21–31.6)	11.6 - 84	29 ± 9	27 (23 – 33)	.003
TV 2	12 - 121	29.7 ± 12.5	27 (23 – 34)	13 - 91.6	31.6 ± 9.8	30 (25 – 36)	.003
UI	0 - 288	58 ± 46	48 (27 – 80)	0 - 336	72 ± 56	57 (30 – 108)	0.01

Thyroid volume 1 derived by WHO formula (1997)
Thyroid volume 2 by rotation ellipsoid model formula as used by A–Lombardi 1997
NS = Not significant

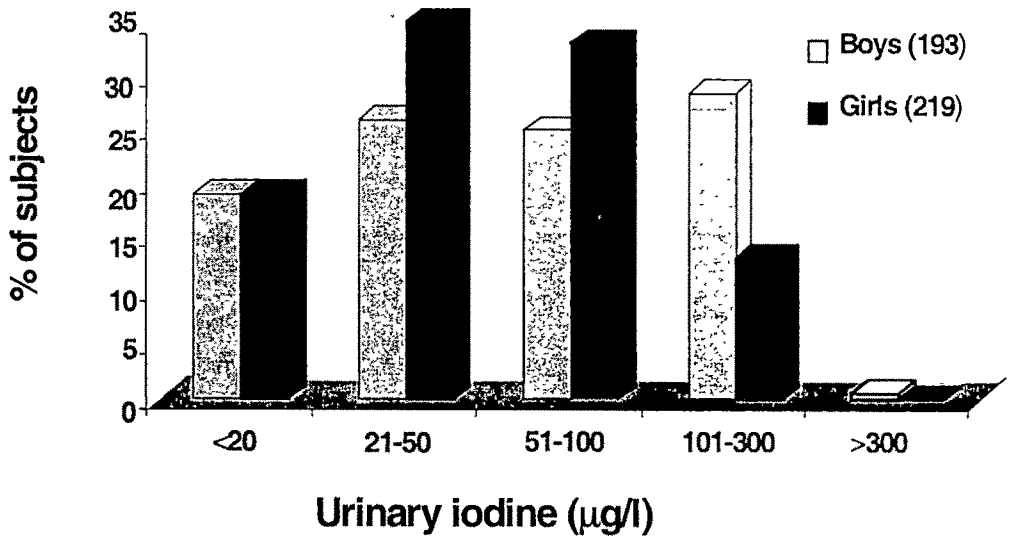
TABLE 5.2. THYROID SIZE AS DETERMINED BY PALPATION V/S ULTRASOUND (WHO)

Goitre	Male n (%)	Female n (%)	Baroda n (%)	Dang n (%)
Thyroid Palpation				
Grade 0	196 (69)	177 (72)	111 (94)	262(63.6)
Grade 1	85 (30)	70 (28)	07 (6)	148 (35.7)
Grade 2	2 (01)	0 (0)	0 (0)	2 (0 .7)
Total n = 530	283 (100)	247 (100)	118 (100)	412 (100)
Thyroid Ultrasound				
Enlarged TV for age	269 (95)	245 (99)	107 (91)	407 (99)
Enlarged TV for BSA	282 (~100)	247 (100)	117 (~100)	412 (100)
Iodine content in water in µg/ l	-	-	32	0

TV = thyroid volume

FIGURE 5.2. FREQUENCY DISTRIBUTION OF URINARY IODINE IN μg/l A (DANG) AND B (BARODA)

A



B

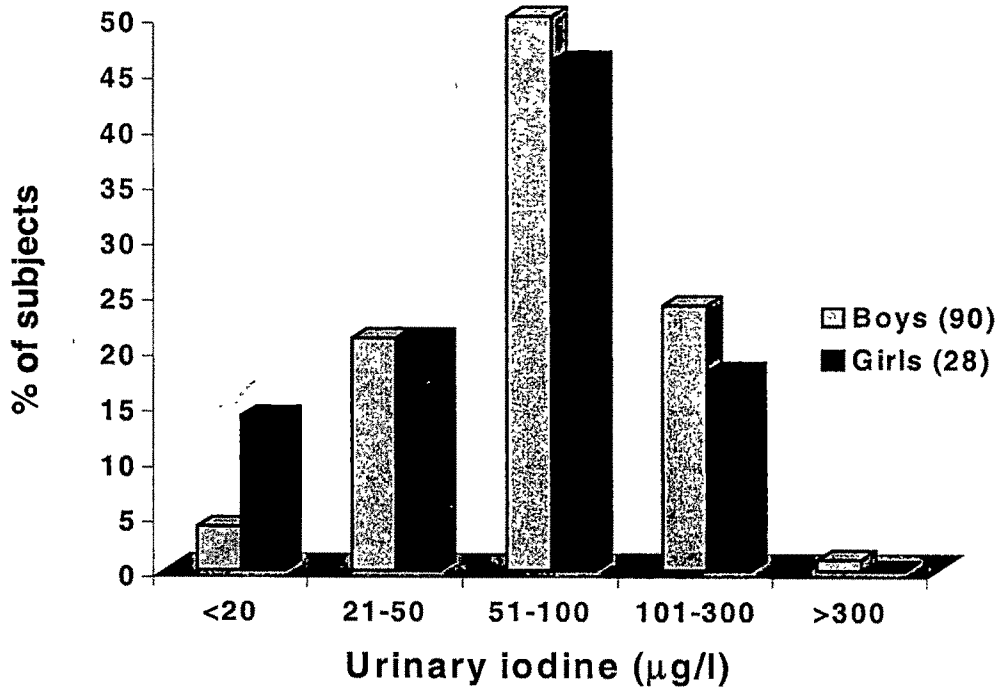
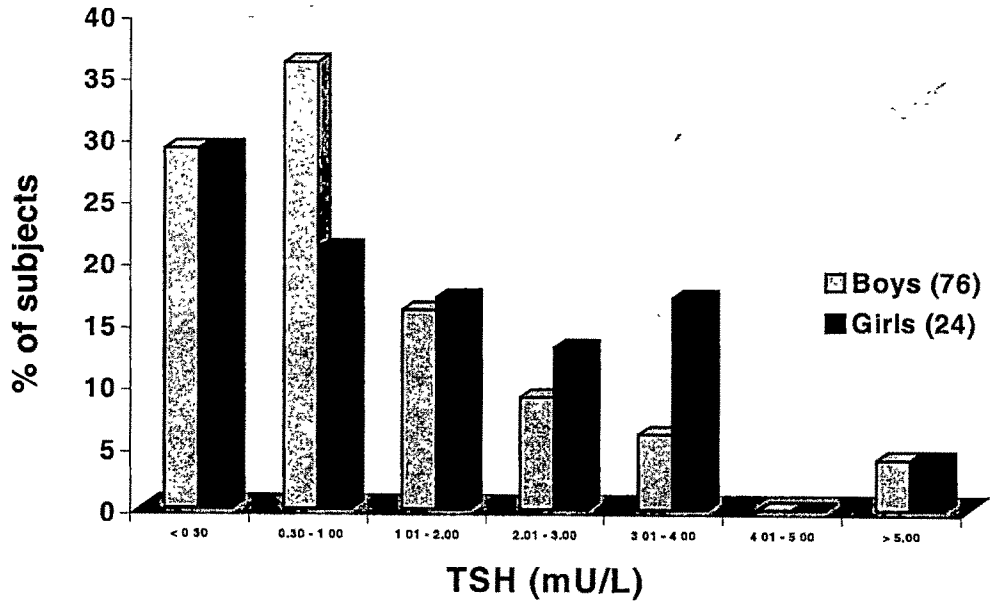
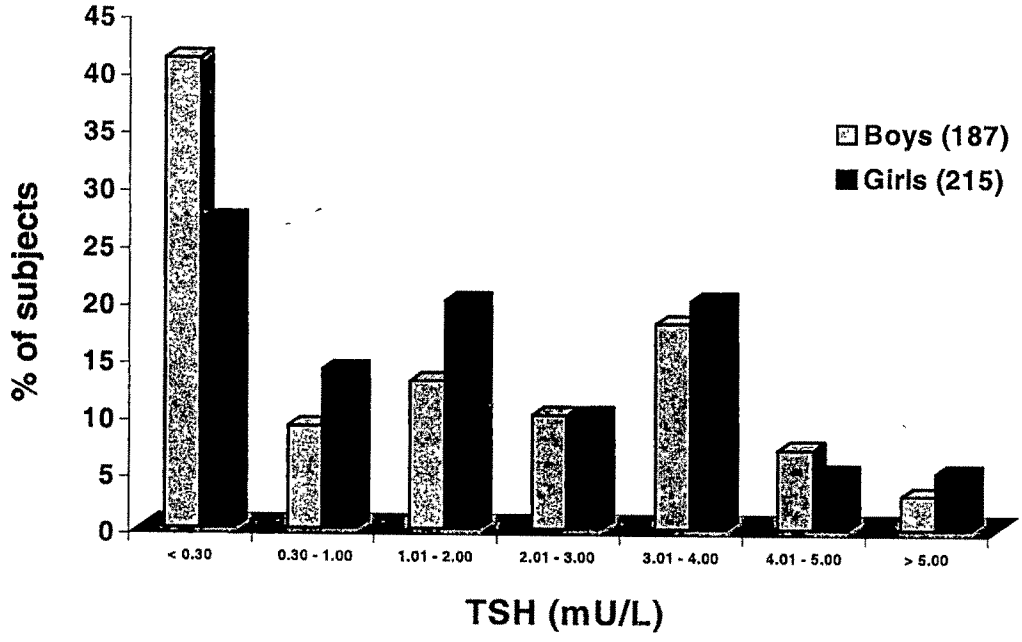


FIGURE 5.3. THE FREQUENCY DISTRIBUTION OF TSH VALUES BY SEX FOR THE DESCRIBED RANGES. A (DANG) AND B (BARODA):

A





Goitre by palpation was found in 157 out of 530 (30%) children with most of them having grade 1 goitre according to the WHO classification. Grade 2 goitre was seen in two boys. In Dang district, goitre was palpable in 36% of children whereas in Baroda district, goitre was palpable in 6% of children. (Table 5.2.)

Median TV measured by US was 27.8 (23 - 35) ml. Enlarged TV-for-BSA was seen in almost 100% of schoolchildren. TV-for-age above 97th percentile (WHO) was seen in 99% of children from Dang and 91% of children from Baroda. Ninety nine percent of girls and 95% of boys had enlarged TV-for-age. (Table 5.2.). Although both the districts revealed high prevalence of goitre by ultrasound (TV calculated by both the formulae), thyroid volumes were significantly higher ($p < 0.001$) in Dang compared to rural subjects from Baroda (Table 5.1.). Gender wise TV was significantly different in Dang with boys having larger thyroid but not in Baroda district children ($p = 0.003$ and $p = 0.2$ respectively). Clinically this gender difference was not significant in Dang. Median values for thyroid volumes were significantly higher ($p < 0.02$) in Tentalav than Muval village of Baroda district.

Cereals like wheat, rice, 'pearl millet', 'jowar', 'nagli' and pulses like 'tuver dal' and 'udad" were examined for the presence of dietary goitrogens. We identified various flavonoids like apigenin, vitexin and glycosyl vitexin in pearl millet. The quantity of vitexin and apigenin was highest in pearl millet from Tentalav (Table 5.3.).

TABLE 5.3. IDENTIFICATION AND QUANTIFICATION OF DIFFERENT FLAVONOIDS IN PEARL MILLET FROM VILLAGES IN BARODA DISTRICT

Baroda	Apigenin	Vitexin	Glycosyl Vitexin
Muval	1.4 mg/ kg	38.9 mg/ kg	Present
Tentalav	2.8 mg/ kg	166.5mg/ kg	Present

In other cereals (wheat, rice, jowar and nagli) and pulses (tuver, and udad dal) flavonoids were not identified. Other goitrogens were detected but remain unidentified from Dang district kharsani oil.

There was a weak but statistically significant positive correlation ($p < 0.01$) between thyroid volume and BSA, weight and height ($r = 0.17$, 0.10 and 0.2 respectively) whilst BMI, and UI showed no significant correlation ($r = 0.06$) with the thyroid volume ($p = 0.17$). However a logarithmic regression of thyroid volume against BMI, showed a weak correlation ($r = - 0.11$ and $p = 0.009$). The best fitting multivariate linear regression model for thyroid volume selected using backward elimination accounted for only 15% (R^2) of the variability in thyroid volume as shown in Table 5.4.

TABLE 5.4. LINEAR REGRESSION ANALYSIS RESPONSE: THYROID VOLUME (CALCULATED BY WHO FORMULA)

Parameter	Coefficient	Standard error	P – value
Constant	- 47.257	14.223	0.001
Weight (kg)	- 2.519	0.789	0.002
BMI (kg/m^2)	1.531	0.474	0.001
District	8.440	1.484	0.000
Urinary iodine (μg/l)	0.018	0.008	0.029
Nagli*	- 8.538	1.407	0.000
Kharsani oil#	6.483	1.247	0.000
BSA (m^2)	105.15	27.763	0.000

f : 520 RSq : 0.151

* Nagli is a type of cereal consumed by Dang District Tribals.

Kharsani oil – consumed by Dang District Tribals.

The BSA of children from Gujarat is much lower in comparison to European children. The TV-for-age and TV-for-BSA of Gujarat schoolchildren (both males and females) were from 3 to 8 times higher compared to the 50th and 97th percentile values for iodine-replete European schoolchildren including the WHO reference norms. (Table 5.5. and 5.6.). However, the comparisons could be made only for children with BSA = 0.8 to 1.2 m^2 (Note: 9% our study population had BSA < 0.8 m^2 and only 1% had BSA > 1.2 m^2).

The detailed results of urinary iodine and thyroid volume of Gujarat schoolchildren by district villages and their comparisons with available European countries etc are shown in Tables 5.7. to 5.8.

TABLE 5.5. COMPARISON OF THYROID VOLUME MEASURED BY ULTRASOUND IN CHILDREN FROM GUJARAT† AS A FUNCTION OF AGE AND SEX WITH WHO‡, GUTEKUNST** AND SWITZERLAND¶ REFERENCE VALUES

	50th percentile				97th percentile		
Age	WHO	*Gujarat*	Gutek	Switzer-	WHO	*Gujarat*	Gutek
Male	‡	*†*	unst**	land¶	‡	*†*	unst**
6	3.2	*21.3*	1.5	2.5	5.4		3.5
7	3.4	*25.5*	1.8	2.9	5.7		4.0
8	3.7	*20.8*	2.0	3.5	6.1		4.5
9	4.1	*24.1*	2.4	4.2	6.8		5.0
10	4.5	*28.8*	2.8	4.7	7.8	*53.8*	6.0
11	5.1	*27.3*	3.1	6.1	9.0	*55.8*	7.0
12	5.7	*24.6*	3.7	5.3	10.4	*45.0*	8.0
13	6.5	*26.0*	4.2	7.3	12.0		9.0
14	7.3	*25.2*	5.0	9.6	13.9		10.5
15	8.2	*23.0*	5.8	10.3	16.0		12.0
Female							
6	2.9	*20.8*	2.2	2.5	5.0		3.8
7	3.4	*27.6*	3.0	3.6	5.9		4.3
8	3.9	*22.7*	3.4	3.8	6.9		5.0
9	4.4	*25.6*	5.0	3.9	8.0	*40.0*	5.3
10	5.0	*26.0*	4.0	5.3	9.2	*46.8*	6.7
11	5.7	*25.0*	4.2	5.7	10.4	*58.3*	7.8
12	6.3	*26.0*	6.5	7.7	11.7	*69.8*	8.6
13	7.0	*28.9*	9.9	9.6	13.1		9.1
14	7.7	*31.1*	8.8	7.7	14.6		11.0
15	8.4	*20.3*	9.0	9.0	16.1		12.2

‡ Source: WHO/ICCIDD, 1997. ** Source: Gutekunst, 1988,1993. ¶ Source: Hans Bürgi, 1999. † 97th percentile data available for age groups 9 -12 years only; due to small sample size in other groups

TABLE 5.6. COMPARISON OF THE THYROID VOLUMES (MEASURED BY ULTRASOUND AS A FUNCTION OF BODY SURFACE AREA) BETWEEN GUJARAT AND WHO REFERENCE CHILDREN

BSA (m^2)	*50th percentile*		*97th percentile*	
	WHO	*Gujarat*	WHO	*Gujarat*
Males				
0.8	3.0	*23.1*	4.7	*44.5*
0.9	3.2	*27.9*	5.3	*54.7*
1.0	3.8	*25.8*	6.0	*47.2*
1.1	4.2	*28.2*	7.0	*56.2*
1.2	4.9	*23.2*	8.0	
Females				
0.8	3.1	*25.0*	4.8	*40.5*
0.9	3.4	*24.2*	5.9	*45.5*
1.0	4.0	*27.2*	7.1	*79.4*
1.1	4.6	*27.4*	8.3	
1.2	5.2	*31.3*	9.5	

WHO Source: WHO/ICCIDD, 1997.

Highlighted data pertain to the present study

*97th percentile could not be calculated for the group of males with BSA = 1.2 m^2 and females with BSA >1.0 m^2 due to small sample size.

Note: 9 % children in the present study group had BSA < 0.8m^2

The results of our male and female children for thyroid volume (mean with SD, median and range) were also compared to those of Gutekunst study in children from iodine deficient (Germany) and sufficient (Sweden) as shown in Table 5.7. and 5.8.

TABLE 5.7. COMPARISON OF THYROID VOLUMES OF MALE CHILDREN FROM INDIA (GUJARAT) WITH OTHER COUNTRIES: GERMANY (IODINE DEPLETE) & SWEDEN (IODINE REPLETE)

Thyroid volume.(ml)	Sweden	Northern Germany	Southern Germany	*India (Gujarat)*
Mean	4.1	6.0	12.0	*29.46*
SD	1.65	3.19	5.71	*11.36*
Range	1.9 – 9.4	2.6 – 15.4	5.0 – 27.1	*7.0 – 91.62*
Median	3.9	4.4	11.3	*27.95*

TABLE 5.8. COMPARISON OF THYROID VOLUMES OF FEMALE CHILDREN FROM INDIA (GUJARAT) WITH OTHER COUNTRIES: GERMANY (IODINE DEPLETE) & SWEDEN (IODINE REPLETE)

Thyroid volume (ml)	Sweden	Northern Germany	Southern Germany	*India (Gujarat)*
Mean	4.3	8.0	14.4	*29.43*
SD	1.72	4.62	7.5	*12.286*
Range	1.4 – 11.5	2.9 – 26.2	5.5 – 31.4	*8.68 – 121.4*
Median	4.0	6.7	12.5	*27.64*

TABLE 5.9. DETAILED RESULTS OF IDD SURVEY IN SCHOOLCHILDREN (N = 530) FROM GUJARAT

Parameter	Range	Mean ± SD	Median (IQR)	97th percentile
Age (years)	6 - 15	11.1 ± 1.6	11.0 (10.0-12.0)	15.0
Height (cm)	76 - 164	130.3 ± 11.4	130 (125-138)	149
Weight (kg)	11 - 47	23.8 ± 5.2	23 (20-26)	35
BMI (Kg/m$^{2)}$	6.9– 46.9	14.1 ± 3.4	13.4 (12.6-14.4)	24.0
True UI (μg/l)	0 – 400	70.5 ± 55.5	56 (30-96)	204
TSH (mU/L)	0.0 – 25.8	1.71 ± 2.10	1.O9 (0.16-3.01)	5.26
TV 1	6.45-111.8	27.1 ± 10.9	25.6 (21.0-32.1)	52.5
TV 2	7.0- 121.4	29.4 ± 11.7	27.8 (22.8-34.8)	57.0
BSA (m)^2	0.53- 1.46	0.94 ± 0.13	0.93 (0.85-1.00)	1.24

TV 1 = Thyroid volume calculated by WHO formula

TV 2 = Thyroid volume calculated by rotation ellipsoid model formula

TABLE 5.10. IODINE (μg/l) IN WATER AND URINE FROM GOITRE AREAS OF GUJARAT

District	Village	Water	UI	%Goitre		
		Iodine	Median (IQR)	palpation	T V/Age	TV/BSA
Baroda	Muval	32	82 (48 – 120)	5	82.5	99
	Tentalav	7	78 (48 – 108)	5	99	100
Dang	Vaghai	0	48 (27 – 90)	43	99	100
	Rambhas	0	54 (28 – 96)	15	99	100
	Baripada	0	49 (21 – 96)	38	99	100

TABLE 5.11. THYROID VOLUME DATA IN DISTRICTS CALCULATED BY ROTATION ELLIPSOID FORMULA

Districts	Villages	Range	Mean ± SD	Median IQR
Baroda	Muval	7.0 – 61.08	24.12 ± 13.6	19.97 (12.8-33.8)
	Tentalav	12.07 – 55.0	28.19 ± 9.05	26.18 (22.3-34.8)
Dang	Vaghai	12.63 – 121.4	30.90 ± 12.5	27.99 (23.2-35.1)
	Baripada	24.11 – 51.46	34.72 ± 7.51	33.42 (29.0-42.6)
	Rambhas	11.54 – 56.53	28.39 ± 7.17	27.73 (24.4-33.1)

5.5. DISCUSSION

We used all prevalence indicators and epidemiological criteria to assess the severity of IDD in the state of Gujarat, aiming at a large target population of schoolchildren. Using criteria recommended by WHO (1994) for defining the severity and prevalence of IDD as a public health problem, Gujarat may be labeled as having a severe IDD problem based on clinical measurement of thyroid size, and mild IDD based on biochemical indicators. Thus, the study highlights the complexity of assessing the severity of iodine deficiency in the presence of multiple confounding but interacting variables of not only a lack of iodine but also the presence of malnutrition and high goitrogen intake.

The Dang district was more severely affected by iodine deficiency than the Baroda district. The median values for thyroid volume were higher in children from the Dang district as compared with those from the Baroda district. Lack of iodine in drinking water, along with known (flavonoids in pearl millet) and unknown goitrogens is probably the explanation for these differences. Nutritional factors may also be responsible, as protein calorie malnutrition

(PCM) has been reported to contribute to goitre development. By comparison, despite having adequate iodine in drinking water, Baroda schoolchildren showed a high prevalence of goitre possibly due to the concomitant effects of high intake of dietary goitrogens in their staple diet (various flavonoids identified by us in pearl millet).

In both districts, girls were more severely affected than boys as determined by biochemical indicators of UI and TSH. However, this was not reflected in thyroid size, either determined by palpation or by ultrasonography but a greater number of girls had enlarged TV-for-age. Previous authors had suggested that sex might influence the development of thyroid size. A number of studies based on ultrasonography in iodine-sufficient areas have found that girls have larger thyroids compared with boys during puberty (WHO, 1997 and Delange F, 1997) whereas others report no difference in thyroid size by sex (Gutekunst R, Ueda D, Ivarsson SA and Xu F). Our study showed statistically significant thyroid volume gender differences in children from the Dang district, with boys having greater TV, but clinically this difference was not important. There have been no population normative values for TSH published for this population nor for schoolchildren from an iodine-replete environment. This is an area of further research that is required. Furthermore, the data high-light the at-risk nature of the female population, given that a larger number of women in the child-bearing age group will still be iodine deficient. This is particularly important because iodine deficiency in fetuses and infants can lead to irreversible intellectual deficits with great impact on the population (Boyages SC, 1993). A similar finding of females having lower median UI values than males has also been reported in iodine-replete populations, in the National Health and Nutrition Examination Surveys I and III (Hollowell, 1998).

We have identified apigenin in pearl millet from the Baroda district and its quantity was almost double in one of the villages (Tentalav). The relatively greater intake of flavonoids in children from Tentalav than those from Muval is

reflected in higher median values for thyroid volume. Apigenin, an aglycone of flavonoid glycoside, has been identified from 6-propyl-thiouracil (PTU), an antithyroid drug, but had not previously been reported from pearl millet (Gaitan E, 1989). These previous studies have attributed the potent antithyroid effects of millet to the flavonoid vitexin, glycosyl vitexin and glucosylorientin, accounting for 67% of these effects in vitro. Apigenin is 3 to 5 times more active than vitexin, glycosyl vitexin and glycosyl orientin. In our study, flavonoids in the form of apigenin, vitexin and glycosyl vitexin were identified in pearl millet, a staple diet of Baroda schoolchildren. Interestingly, levels of apigenin and vitexin were higher in pearl millet from Tentalav compared with that from Muval (Table 5.3.).

Flavonoids interfere with the synthesis of thyroid hormones not only by inhibiting the thyroid peroxidase enzyme (catalyzing iodide oxidation) and thereby the organification processes, but also by inhibiting the peripheral metabolism of thyroid hormones by acting on the iodothyronine deiodinase enzyme. The additive effects exerted by flavonoid metabolites further enhance this greater inhibitory effect and these are formed after ingestion of flavonoid glycoside mixtures present in many plant foodstuffs. As a result, the antithyroid effects of flavonoid glycoside present in pearl millet may make a major contribution to, and be primarily responsible for, its antithyroid effects including causation of large goitre in the affected population.

The dissonance of thyroid size and biochemical indicators of iodine deficiency is explained by several factors. First, it may be explained by the difference in the temporal nature of these indicators, where biochemical indicators are short-term markers of iodine deficiency, whereas measures of thyroid size are longer-term indicators. Secondly, thyroid size as determined by palpation underestimates the extent of the problem and is inaccurate in the assessment of grade 1 goitre, and has low specificity and sensitivity in goitres of grades 0 and 1.

From our study it is apparent that thyroid palpation is of limited value for epidemiological surveys of IDD and is insensitive in the assessment of schoolchildren. The best clinical indicator for the assessment of the severity and extent of IDD is estimation of thyroid volume by ultrasound. The present study highlights that the BSA reference should be preferred to the age-based reference range. The additional utility of thyroid ultrasonography is that it provides an integrated assessment tool for the multiple factors that influence the development of goitre and thus the risk of other IDD.