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# *Chapter*

# 7

## **IMPACT OF PROTEIN ENERGY MALNUTRITION ON THYROID SIZE IN IODINE DEFICIENT POPULATION OF GUJARAT: IS IT AN AETIOLOGICAL FACTOR FOR GOITRE?**

### **7.1. SUMMARY**

The aim of the study was to assess the severity of protein energy malnutrition (PEM) in iodine deficient subjects and to assess the impact of PEM on thyroid size.

Iodine status of 1002 (530 school-aged children and 472 adults) subjects was assessed by estimations of urine iodine (UI), blood TSH levels and thyroid-volume (TV) by ultrasonography. The results showed that Gujarat State a very high prevalence of goitre (>90%) as assessed by ultrasound. Urinary iodine levels were not congruent with the observed goitre rate suggesting a role for other aetiological factors, such as malnutrition and or goitrogenic factors. Hence these iodine deficient subjects were assessed for the severity of protein energy malnutrition (PEM).

Nutritional status was assessed 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), and Z-scores for weight-for-age (WAZ), height-for-age (HAZ), and weight-for-height (WHZ). Severity of PEM was based on the World Health Organization (WHO) criteria and the threshold on the Waterlow classification.

Linear regression analysis was performed between TV and anthropometric parameters to assess the impact of PEM on thyroid size.

90% of *Children* had severe malnutrition as evident from BMI < 16 kg/ m<sup>2</sup> (WHO, 1999). The WHO percentage prevalence of stunting (low height-for-age means HAZ is < -2 SD) in 64%, wasting (WHZ < -2 SD) in 43%; underweight (WAZ < -2 SD) in 82% pointed to severe PEM.

Waterlow classification showed that *children* were either stunted or wasted, or stunted and wasted, or stunted and obese. Nearly 100% (529/530) of the children had goitre as evidenced from enlarged TV-for-BSA when compared with the 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 a negative correlation between TV and WHZ, BMI and TSF (r = 0.1 - 0.2).

*Adults* had PEM as evident from BMI < 18.5 kg/ m<sup>2</sup> in 54% subjects. Median MUAC of 22.7 cm reveals prolonged severe PEM. Eighty-two percent had enlarged TV (> 20 ml). There was a significant (P = 0.01) negative correlation between TV and MUAC.

This study concluded that higher prevalence of goitre may be due to macro-nutrient malnutrition (PEM) in the face of micro-nutrient malnutrition (iodine deficiency disorders).

## 7.2. INTRODUCTION

The possibility that factors other than iodine deficiency contributes to the production of endemic goitre were perceived as early as 1924 and the role of malnutrition was postulated then (Geraldo AM, 1980). The term "malnutrition" encompasses the *severe* form of wasting characterized by the clinical conditions of marasmus and kwashiorkor as well as *milder* forms of under-nutrition, characterized by a significant deficit in one or more of the anthropometric indices. Malnutrition is synonymous with protein-energy malnutrition (PEM) and in children also with growth failure - malnourished children are shorter and lighter than they should be for their age. It is now recognized that poor growth in children results not only from a deficiency of protein and energy but also from an inadequate intake of vital minerals (such as iron, zinc and iodine) and vitamins (such as vitamin A), and often essential fatty acids as well. These minerals are needed in tiny quantities, and are consequently called micronutrients, and are needed for the production of enzymes, hormones and other substances that are required to regulate biological processes leading to growth, activity, development and the functioning of the immune and reproductive systems. Thus commonly encountered nutritional disorders are protein energy malnutrition (PEM), and vitamin A, iron and iodine deficiencies (IDD). Although IDD is a specific nutritional disorder due to deficiency of the micronutrient iodine, the effects of generalized PEM on the expression and severity of IDD, in particular goitre, remains to be elucidated

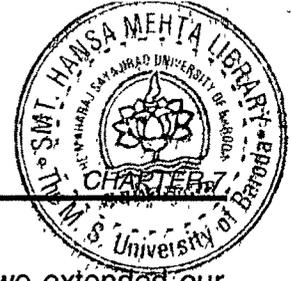
PEM occurs primarily in developing nations in endemic forms. The prevalence may approach 25%. Of the World's undernourished people more than half live in India whereas IDD is no more confined to sub-Himalayan belt despite the National IDD Control Program since 1962. The National Nutrition Policy (1993) had drawn an Action Plan to achieve a goal of improvement for IDD and PEM by year 2000 (Indira Nath, 1999).

Although IDD is a specific nutritional disorder due to deficiency of the micronutrient iodine, the effects of generalized protein energy malnutrition (PEM) on the expression and severity of IDD remains to be elucidated. The probability that factors other than iodine deficiency contribute to the production of endemic goitre was perceived as early as 1924 but the changes in thyroid homeostasis in PEM were not given much attention. It was suggested that research be required to define the role of generalized PEM in the pathogenesis of iodine deficiency goitre (Koutras, 1973).

Chapter 5 and 6 indicated that *Gujarat has* a very high prevalence of goitre in children (> 90%) by ultrasound in comparison to WHO reference; not congruent with urinary iodine (UI) levels (median urinary iodine 56 µg/l) thereby suggesting a role of malnutrition. If PEM was a significant factor then apart from its effects on increasing thyroid size, it would further compromise thyroid hormone homeostasis.

The adult population also had a high prevalence of goitre (> 20 ml in 82%) for their iodine deficiency (median urinary iodine 72 µg/l). We speculated significant contribution of PEM as evidenced from BMI that was used with age-independent cut-off values to define thinness.

Anthropometry is the single most portable, universally applicable, inexpensive, and non-invasive technique for assessing nutritional status of the population. Using various calculated derived indices from these methods, a population, in particular children can be classified according to the Waterlow and WHO categories. In a given population, a high prevalence of anthropometric deficit will be indicative of significant health and nutritional problems, however, it is not only those individuals below the cut-off point who are at risk; the entire population is at risk.



As wasting is a preferred indicator for thinness in children, we extended our study in this iodine deficient population aged >5 years to find out the extent of PEM by direct and derived anthropometric indices. Z- score deficits (<-2 SD) giving rise to anthropometric indicators were calculated for height-for-age (HAZ), weight-for-age (WAZ) and weight-for-height (WHZ) based on World Health Organization (WHO) growth reference that classify severity of PEM for children by the percentage prevalence ranges (1995). Threshold of PEM was established by Waterlow classification (Gross R, 1997). Thus we have tried to elucidate the relative contribution of PEM on thyroid size as determined by ultrasound as this confounding factor would further compromise thyroid hormone homeostasis.

The principle aim of the present study was to determine the relative contribution of PEM as determined by direct and derived anthropometric indices on the thyroid size in the mild to moderate iodine deficient schoolchildren and adults of Gujarat, India. This contribution may help to decide its aetiological role in the process of goitrogenesis.

### **7.3. SUBJECTS AND METHODS**

A total of 1002 subjects having mild to moderate iodine deficiency were included in the study. The detailed results of their IDD status as indicated by outcome indicators, age, sex, geographical distribution and data on their diet have been reported in chapter 5 and 6. Serum thyroxine was not measured in these subjects due to their poor sensitivity but the blood spot TSH was measured in all 1002 subjects. There were 530 children aged 6 – 15 years and 472 adults aged 16 - 83 years from Baroda and Dang districts of Gujarat State. A thorough clinical examination was carried out to find out stigmata of malnutrition like xerophthalmia, Bitot's spots, skin changes and a detailed diet history was recorded. PEM was assessed by direct anthropometric

measurements like height, weight, mid upper arm circumference (MUAC), thigh circumference (TC) and triceps skinfold (TSF) thickness and derived indices like body surface area (BSA), body mass index (BMI), arm muscle area (AMA) and arm fat area (AFA). AMA measures lean body mass whereas AFA reflects the subcutaneous adipose tissue.

### **7.3.1. WORLD HEALTH ORGANIZATION CLASSIFICATION FOR PEM**

Criteria to establish severity of PEM are not available for children > 5 years hence the WHO data for < 5 years as shown in chapter 3 was used.

### **7.3.2. WATERLOW CLASSIFICATION (COMBINATION OF HEIGHT-FOR-AGE & WEIGHT FOR HEIGHT)**

This scheme uses plots to combine variables where index weight-for-height is the abscissa and height-for-age index is plotted on the ordinate as shown in chapter 3. Waterlow classification presents an overview of the thresholds of malnutrition in a population in to one of the six groups from A to F. The subjects falling in B are stunted and wasted together whereas those falling in A, F, D and E are either wasted or stunted alone.

### **7.3.3. THYROID VOLUMES (TV):**

In schoolchildren the thyroid glands were classified as “normal” or “enlarged” using the 97<sup>th</sup> percentile of the WHO reference values as cut off (WHO, 1997). In adults, TV > 20 ml was considered as enlarged (Larsen PR, 1998).

## 7.4. RESULTS

Subjects (adults and children) had no clinical signs of vitamin A deficiency. However as reported in chapters 5 and 6 they were mild to moderately iodine deficient.

### **7.4.1. PREVALENCE OF PEM AND GOITRE**

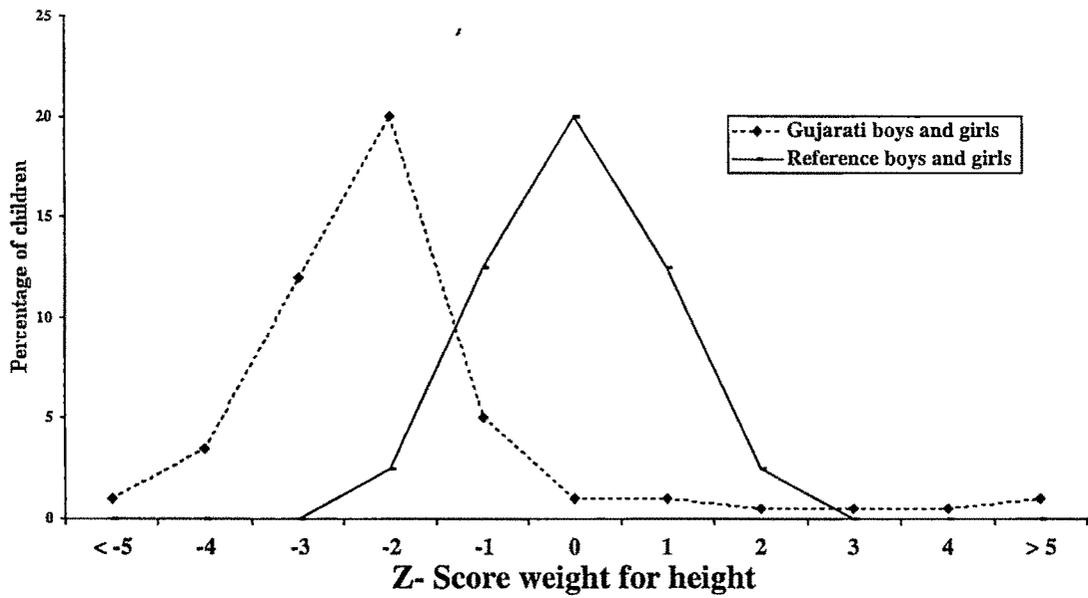
#### **7.4.1.1. CHILDREN AGED 6-15 YEARS (n=530)**

PEM as assessed by the WHO percentage prevalence of three indicators of stunting, wasting and underweight was highly prevalent in both the Baroda and Dang districts children. Sixty four percent (339/ 530) of children had stunted growth, 57% (273/ 481) had wasting and 82% (434/ 530) were underweight.

As Z- score deficits ( $< -2$  SD) are preferred in children aged 6 - 10 years (n = 179) we analyzed them thus stunting was seen in 45%, wasting in 55% and 81% were underweight.

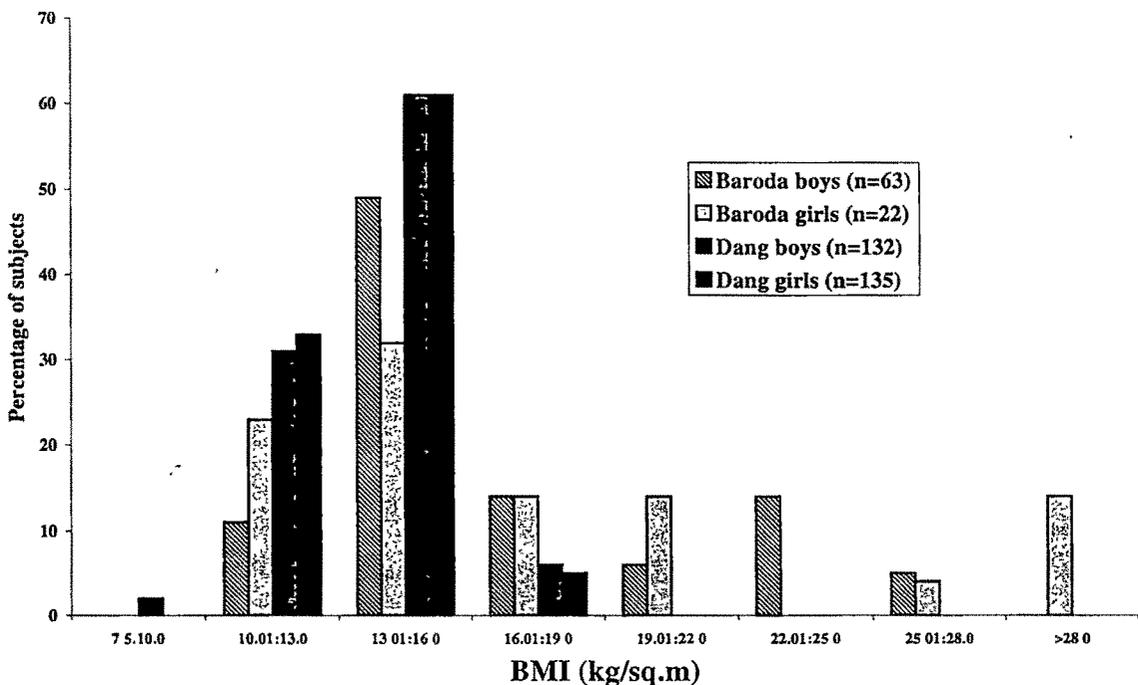
The curve comparing z- score for weight-for-height of Gujarati rural and tribal children with WHO in Figure 7.1. has shown that the curve for Gujarati children has shifted to left with so many of these children to be below the cut-off score of  $-2$  SD.

**FIGURE 7.1. COMPARISON OF Z-SCORE FOR WEIGHT-FOR-HEIGHT BETWEEN GUJARATI AND WHO REFERENCE CHILDREN**



Median BMI for all children was  $13.4 \text{ kg/ m}^2$  (IQR =  $12.6 - 14.4 \text{ kg/ m}^2$ ) with 80% of children having BMI  $< 15 \text{ kg/ m}^2$  thereby suggesting that the total body fat content is less than 5% of body-weight. As BMI is an important index for thinness in children after 10 years of age its frequency distribution is shown for 11 - 15 year children in Fig 7.2. that shows few children have BMI  $> 19 \text{ kg/ m}^2$ . These children belonged to Baroda district and were severely stunted (HAZ  $< -2 \text{ SD}$ ) thus BMI  $> 25$  may be misleading.

**FIGURE 7.2. BMI FREQUENCY DISTRIBUTION FOR GUJARAT CHILDREN  $>10$  TO 15 YEARS**

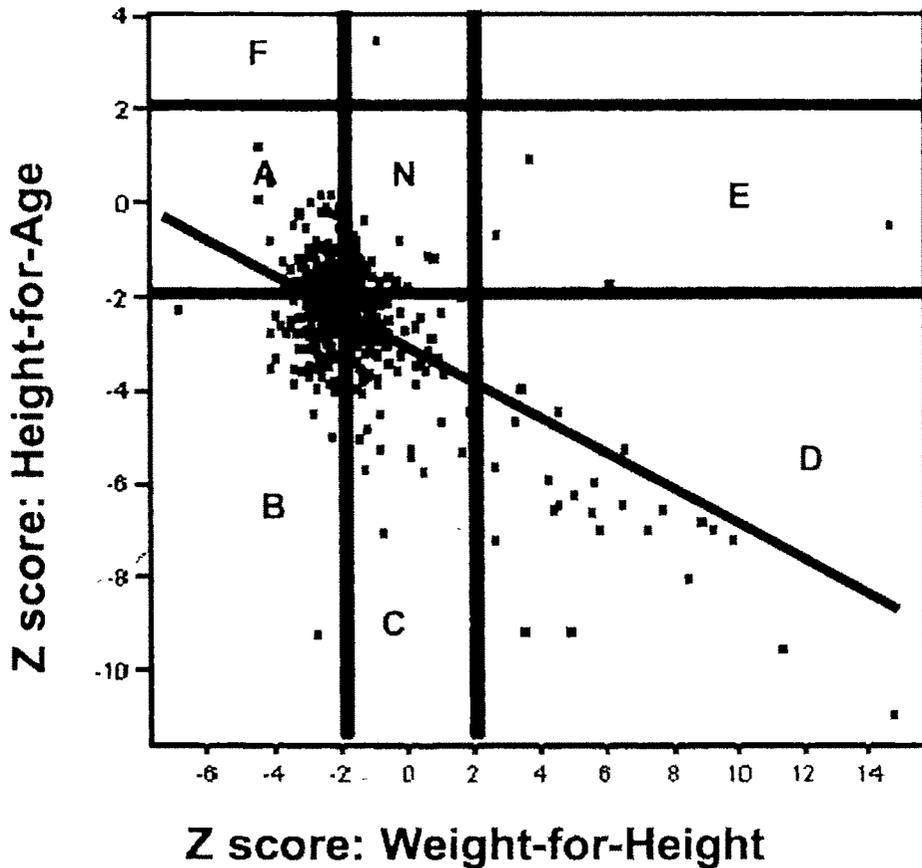


The Waterlow classification (figure 7.3.) showed that only few children were normal and the rest were either stunted or wasted or both wasted and stunted or obese and stunted. There was a very strong correlation ( $r = 0.6$ ) between wasting (low WHZ) and stunting (low HAZ).

The percentage of children in each category was as follows:

- A (wasted) = 15.8%
- B (wasted and stunted together) = 26.5%
- C (stunted) = 34.3%
- D (stunted and obese) = 5.5%
- N (normal) = 17.7%.

**FIGURE 7.3. WATERLOW CLASSIFICATION**



Goitre by ultrasonography was seen in almost 100% (529/ 530) of children compared with WHO TV-for-BSA reference and in 97% (515/ 530) of children compared with the WHO TV-for-age.

Table 7.1. shows the detailed results of anthropometric and clinical parameters used to assess nutritional status and thyroid size for children. Dang children were more malnourished than Baroda children as evidenced by BMI, weight, height, MUAC, TC and TSF thickness ( $p < 0.001$ ).

There was a lack of relation between thyroid volume and the extent of iodine intake as seen from UI on one hand and different ranges of z-scores for weight for height on the other hand due to the inter-play of multiple factors and goitre in all the children (Table 7.2. A). A bimodal relation between thyroid volume and WHZ is evident.

**TABLE 7.1. ANTHROPOMETRICAL PARAMETERS AND THYROID VOLUME IN CHILDREN FROM BOTH DISTRICTS BY GENDER**

	Dang (n = 412)			Girls (n=219)			Boys (n = 193)			P value
	Range	Mean ± SD	Median (IQR)	Range	Mean±SD	Median (IQR)	Range	Mean±SD	Median (IQR)	
WAZ	3.8 : 2.0	-2.4 ± 0.6	-2.5(-2.8 : -2.1)	-4.4: 0.7	-2.4 ± 0.6	-2.5 (-2.8 : -2)				NS
HAZ	5.2 : 3.5	-2.3± 1	-2.4 (-2.8 : -1.6)	-4.2: 2.5	-2.1 ± 1	-2.3 (-2.7 : -1.5)				NS
WHZ	3.7 : -10	-1.9 ± 0.8	-2.0 (-2.4 : -1.4)	-6.9 : 0.7	-2 ± 0.9	-2 (-2.5 : -1.5)				NS
TSF	4 : 14	8 ± 2	7.5 (6.5 : 9)	3 : 12	6 ± 1.7	6 (5 : 7)				0.01
MUAC	12 : 21.5	16.3 ± 1.7	16 (15 : 17)	13 : 23	16.2 ± 1.5	16 (15 : 17)				NS
TC	25 : 40	30.6 ± 2.8	30.5 (29 : 32)	22 : 47	31.5 ± 3	31.5 (30 : 33.5)				0.01
BMI	10.5 : 18	13.9 ± 5.4	13.2 (12 : 14)	7 : 18	13.5 ± 2.4	13.2 (12.6 : 14)				NS
TV	12 : 121	29.7 ± 12.5	27 (23 : 34)	13 : 92	32 ± 10	30 (25 : 36)				0.01
<b>Baroda (n=118)</b>										
<b>Girls (n = 28)</b>										
WAZ	-4 : -0.3	-2.3 ± 0.7	-2.3 (-2.8 : -2.3)	-4 : -0.4	-2.5 ± 0.7	-2.5 (-2.9 : -2)				NS
HAZ	-11 : 0.1	-3.9 ± 3	-3.4 (-5.4 : -2.0)	-9 : 1.2	-3.3 ± 2.2	-2.5 (-5 : -2)				NS
WHZ	-4.4 : 14	-1.4 ± 4.4	0 (-1.2 : 2.1)	-4.5 : 10	0.29 ± 3.4	-9 (-2.0 : 1.7)				NS
TSF	5 : 20	9.6 ± 3.7	9 (7 : 11)	4 : 19	8.1 ± 2.9	7 (6 : 9)				0.02
MUAC	14 : 26	18.1 ± 2.9	17 (16 : 20)	7.5 : 23	17.1 ± 2.3	17 (16 : 18)				0.07
TC	18 : 54	33.3 ± 6.7	32 (30 : 36.6)	22 : 47	32.6 ± 4.5	32 (29 : 35.5)				NS
BMI	9.3 : 38	18.5 ± 8	16 (13 : 20)	9.6 : 32	16.5 ± 5	14 (13 : 18.6)				NS
TV	8.7 : 44	27.1 ± 10	30.7 (19 : 34)	7 : 61	25 ± 13	22 (14 : 35)				NS
<b>Boys (n = 90)</b>										

NS = Not significant

**TABLE 7.2. A THYROID VOLUME (ML) IN CHILDREN ACCORDING TO THEIR URINARY IODINE EXCRETION AND Z-SCORES WEIGHT-FOR-HEIGHT (WHZ) INDEX**

<i>WHZ index</i>	Thyroid volume (ml)			
	<i>Urinary iodine (µg/l)</i>			
	< 50 (n = 217)	51-100 (n = 158)	101-300 (n = 108)	Total (483)
< - 3 (n = 40)	29.75	23.99	26.98	27.44
- 2 to - 3 (n = 165)	28.35	29.37	29.33	28.92
- 1 to - 2 (n = 173)	29.19	30.68	35.97	30.96
> - 1 (n = 105)	26.65	26.15	27.8	26.85

**TABLE 7.2.B THYROID VOLUME (ML) IN CHILDREN ACCORDING TO THEIR TSH AND Z- SCORES WEIGHT-FOR-HEIGHT (WHZ) INDEX.**

<i>WHZ index</i>	Mean thyroid volume (ml)			
	<i>Blood TSH levels</i>			
	0-0.15 (n = 111)	0.16-1.0 (n = 106)	1.01-3.00 (n = 121)	> 3.0 (n = 111)
< - 3 (n = 37)	27.62	25.22	20.26	31.24
- 2 to - 3 (n = 157)	27.32	27.84	28.46	32.11
- 1 to - 2 (n = 166)	28.96	32.87	31.45	30.34
> - 1 (n = 88)	28.32	23.40	30.79	31.20

#### **7.4.1.2. ADULTS**

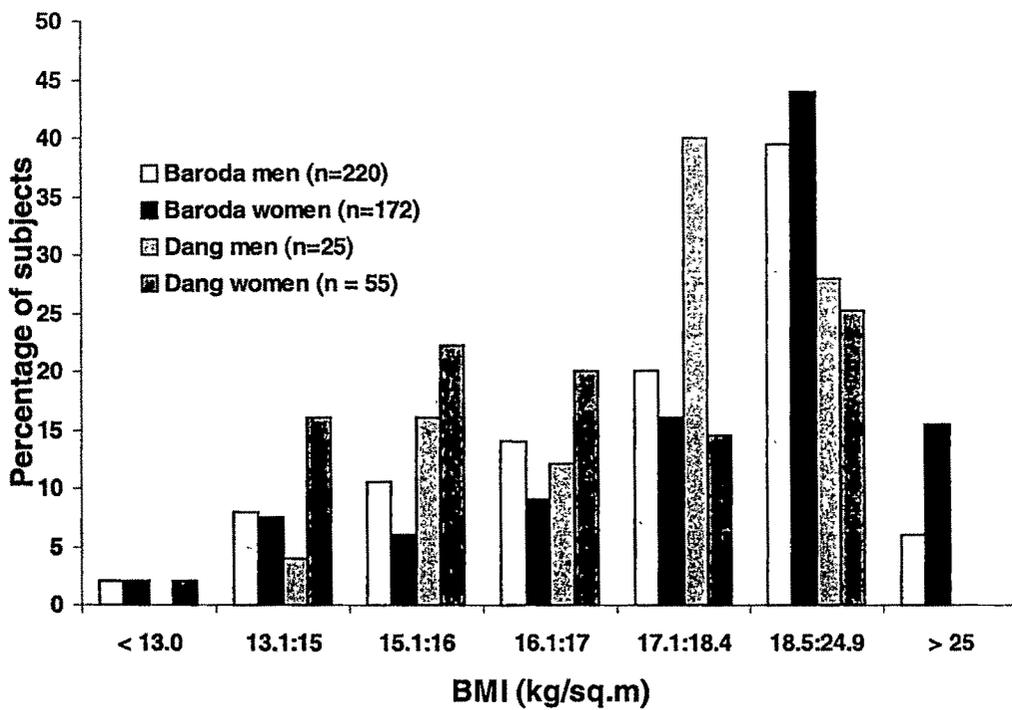
Table 7.3. shows detailed results of anthropometric and clinical parameters used to assess nutritional status and thyroid size of adult population. Fifty four percent of total adult subjects had PEM (mild to severe) as evident from BMI < 18.5 kg/m<sup>2</sup>.

**TABLE 7.3. ANTHROPOMETRIC PARAMETERS AND TV IN ADULTS**

	Dang (n = 80)				Baroda (n = 392)				P	
	Women (n = 55)		Men (n = 25)		Women (n = 172)		Men (n = 220)			
	Range	Mean±SD	Median (IQR)	Range	Mean ±SD	Median (IQR)	Range	Mean ±SD	Median (IQR)	
BMI	11 - 26	17.2 ± 2.7	16 (15.6 - 18.3)	14 - 23	18 ± 2	17.9 (17 - 19)	11 - 31	18.8 ± 3.4	18 (16 - 21)	0.0001
BSA	1.11 - 1.6	1.3 ± 0.1	1.3 (1.2 - 1.36)	1.3 - 1.7	1.46 ± 0.1	1.45 (1.4 - 1.5)	1.07 - 1.9	1.5 ± 0.14	1.5 (1.4 - 1.6)	0.0001
TSF	3 - 15	8.3 ± 3.0	8.5 (6 - 10.5)	4 - 13	8.1 ± 2.9	8 (5 - 10)	3 - 19	7.8 ± 2.9	7 (6 - 10)	0.0001
MUAC	18 - 28	21 ± 1.9	21 (20 - 22)	17.5 - 30	23 ± 2.4	22.5 (22 - 24)	12 - 33	23.2 ± 2.9	23 (21.5 - 24.5)	NS
T C	23 - 53.5	38.7 ± 4.4	39 (36 - 41)	34 - 45	39.5 ± 2.9	39.5 (37.5 - 42)	24 - 58.5	40 ± 5.5	40 (36 - 43)	NS
TV	30 - 179	50 ± 25	46 (39 - 59)	24.5 - 86	51 ± 15	47 (39 - 60)	7 - 89	35.5 ± 16	36.4 (21 - 46)	NS
Baroda (n = 392)										
BMI	11.5 - 34	20.3 ± 4.6	19 (17 - 22.6)	11 - 31	18.8 ± 3.4	18 (16 - 21)	11 - 31	18.8 ± 3.4	18 (16 - 21)	0.0001
BSA	1.02 - 1.8	1.4 ± 0.14	1.4 (1.3 - 1.5)	1.07 - 1.9	1.5 ± 0.14	1.5 (1.4 - 1.6)	1.07 - 1.9	1.5 ± 0.14	1.5 (1.4 - 1.6)	0.0001
TSF	3 - 33	11.7 ± 4.5	11 (9 - 14.5)	3 - 19	7.8 ± 2.9	7 (6 - 10)	3 - 19	7.8 ± 2.9	7 (6 - 10)	0.0001
MUAC	14 - 36.5	23 ± 3.5	23 (20.5 - 25)	12 - 33	23.2 ± 2.9	23 (21.5 - 24.5)	12 - 33	23.2 ± 2.9	23 (21.5 - 24.5)	NS
T C	27 - 61	40.7 ± 6.8	40 (36 - 45)	24 - 58.5	40 ± 5.5	40 (36 - 43)	24 - 58.5	40 ± 5.5	40 (36 - 43)	NS
TV	10 - 111	33.5 ± 16	30 (21 - 42)	7 - 89	35.5 ± 16	36.4 (21 - 46)	7 - 89	35.5 ± 16	36.4 (21 - 46)	NS

Figure 7.4. shows frequency distribution of BMI with some obese subjects only in Baroda (BMI > 25 kg/ m<sup>2</sup>)

**FIGURE 7.4. BMI FREQUENCY DISTRIBUTION IN ADULTS >15 YEARS FROM DANG AND BARODA**



**BMI RANGE**

< 15.0 = Very severe malnutrition; total body fat is < 5% of body

15.1to 16.0 = Severe malnutrition

16.1 to 17.0 = Moderate malnutrition

17.1 to 18.4 = Mild malnutrition

18.5 to 24.9 = Normal

Enlarged thyroid volume (> 20ml) was found in 388/ 472 adult subjects (82.2%). Females were more affected in number as well as by goitre size. Thyroid ultrasound revealed 100% goitre prevalence in Dang and 77% in Baroda. Median thyroid volume was 46.8ml in Dang and 32.7ml in Baroda ( $p < 0.001$ ).

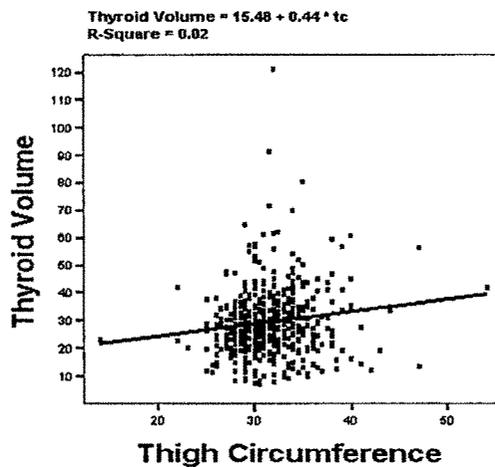
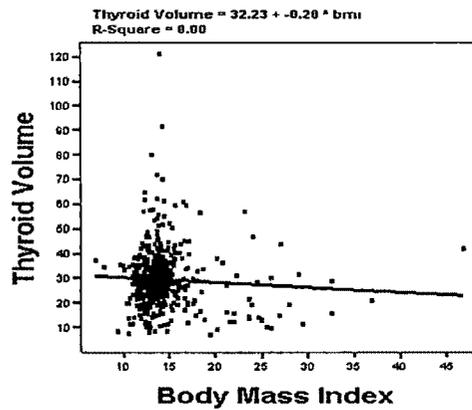
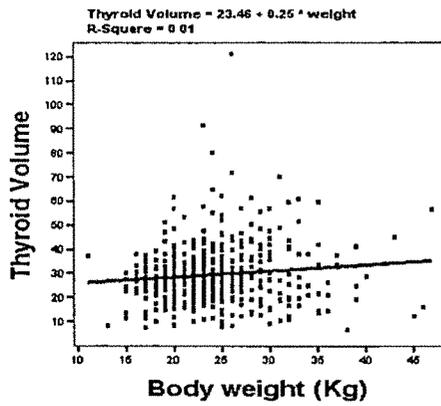
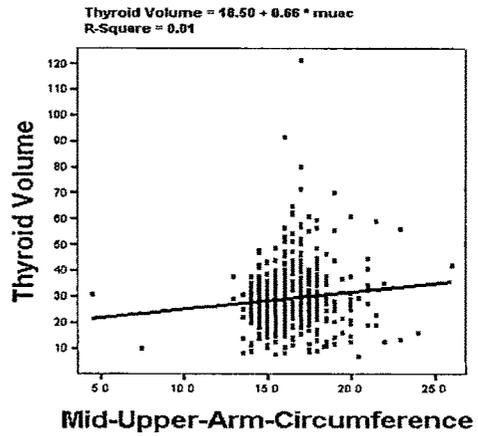
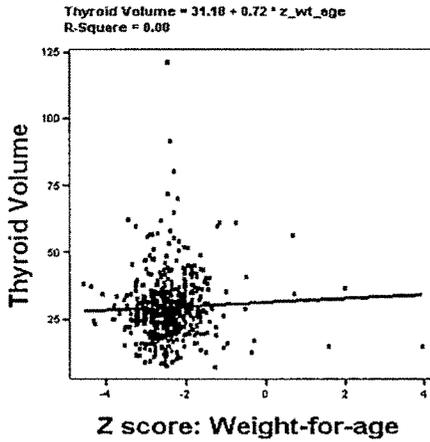
## **7.4.2. REGRESSION ANALYSIS**

Regression analysis was conducted to determine the relation of PEM with thyroid volume. The results indicate a strong relation of nutritional factors with thyroid size independent of the effects of iodine (Table 7.1.).

### **7.4.2.1. CHILDREN**

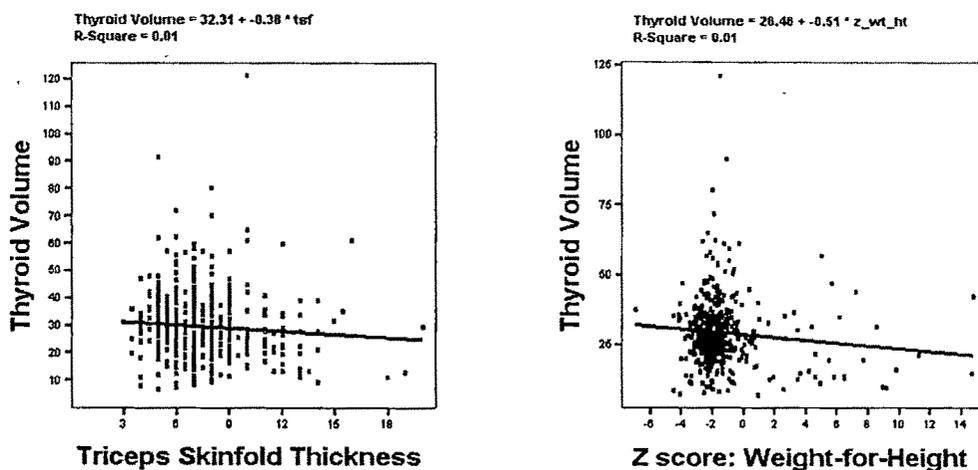
In children there was a weak but statistically significant ( $p < 0.05$ ) positive correlation between TV and the variables BSA, weight, height, MUAC, TC, and HAZ (stunting) ( $r = 0.17, 0.11, 0.2, 0.11, 0.14, 0.15$  respectively) (figure 7.4.). All these indices are directly or indirectly related to growth in children hence the expected positive correlation.

FIGURE 7.5. REGRESSION ANALYSIS



A weak but statistically significant ( $p < 0.05$ ) negative correlation ( $r = 0.1$ ) between TV and the variables TSF and WHZ (wasting which is the preferred index for thinness in children) was seen (Figure 7.6.).

**FIGURE 7.6. REGRESSION ANALYSIS SHOWING  
NEGATIVE CORRELATION**

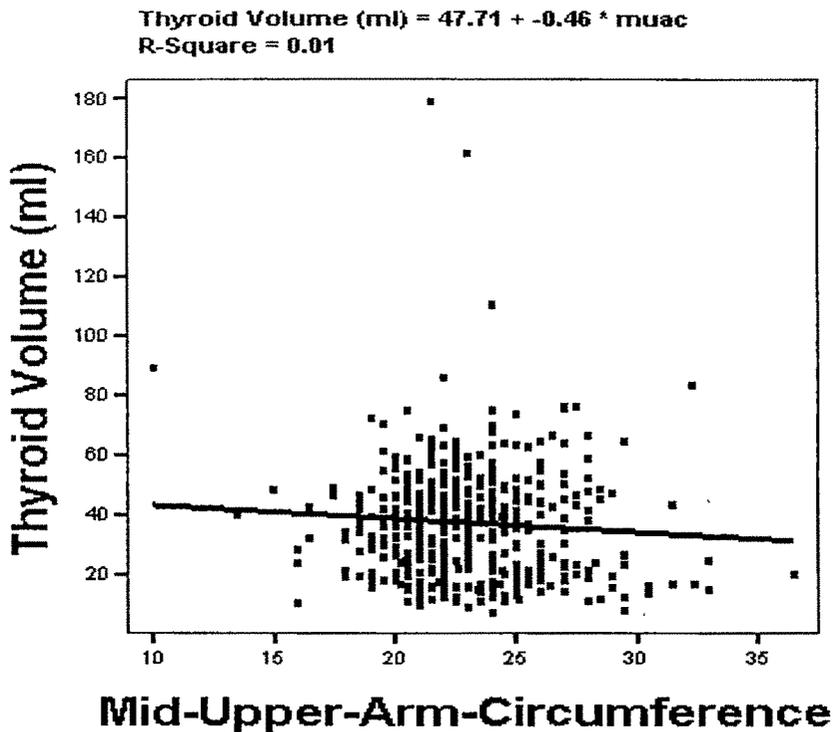


The logarithmic transformation of TV (LN-TV) was also analyzed for various regressions because of skewness and non normal distribution of data. Thus LN - TV showed a weak ( $r = - 0.11$ ) but significant ( $p = 0.009$ ) correlation with BMI. It also showed a significant correlation with HAZ and WHZ ( $p = 0.0003$  for both indices).

**7.4.2.2. ADULTS**

In adults there was a weak ( $r = 0.1$ ) but statistically significant ( $p < 0.05$ ) negative correlation between TV and MUAC (Figure 7.7.) as well as AMA, in other words poorer the protein nutrition bigger the thyroid size.

**FIGURE 7.7. REGRESSION ANALYSIS**



There was no correlation between TV and other anthropometric parameters like weight, height, BMI, BSA and TC. There was skewness and non normal distribution of data for the adult population too, hence the logarithmic transformation of TV (LN - TV) was performed and analyzed for various regressions. Thus LN - TV showed a weak but statistically significant ( $p = 0.008$ ) correlation with age, TC, MUAC and TSH ( $r = -0.20, -0.12, -0.12, 0.36$  respectively).

The best fitting multivariate linear regression models for thyroid volume using backward elimination for children is shown in chapter 5 and for adults in chapter 6.

## 7.5. DISCUSSION

The present study shows that PEM was highly prevalent in mild to moderately iodine deficient population (schoolchildren and adults) of Gujarat (Western India). Thyroid enlargement was in part related to the degree of PEM in children independent of the effect of iodine deficiency (Table 7.1.). The present study highlights the complex interplay of nutritional factors that influence the clinical expression of endemic goitre (Robinson HMP, 1986).

The extent and severity of PEM in this population group was overwhelming. About 43% of all children and 55% below ten years of age were categorised as "wasted", a symptom of acute PEM. Two-thirds of the children were "stunted", a consequence of chronic PEM. This figure is much higher than the expected proportion in developing countries. On a population basis, such high levels of stunting have been attributed to poor socio-economic conditions and endemic goitre in rural populations (Gaitan E, 1989). The weight-for-age index of our study group indicates a "worse-than-usual" for PEM (WHO, 1995). Eighty one percent of the children below 10 years of age were underweight when compared to the WHO reference (WHO, 1983). Thus the WHO percent prevalence of all the three indicators; stunting, underweight and wasting; point to a very high severity of PEM in Gujarat.

The mechanism of goitre in the setting of PEM is probably multi-factorial. In PEM children, negatively charged iodide is less efficiently absorbed against the electrochemical gradient (Gaitan E, 1983). In populations with pre-existing iodine deficiency as in Gujarat these processes will lead to exaggerate iodine deficiency (Gaitan E, 1985). In addition, iodide

concentrating ability of the thyroid gland in PEM is decreased due to depressed iodide clearance and uptake, and is related to the duration of protein deficiency (Robinson, 1986). Thus PEM indirectly results in alterations in iodine metabolism that may lead to thyroid hyperplasia that may further decrease circulating thyroid hormones. Furthermore, PEM may contribute to goitrogenesis directly through a lack of substrate availability, in particular the lack of essential amino acids (Vadivel V, 2000). In the community of Gujarat, where most of the population consumes a vegetarian diet, these substrate deficiencies are probably exaggerated.

Thyroid size in children was positively correlated to weight, height and body surface area, as well as to other measures of growth such as MUAC, TC, and HAZ. These relationships have been defined by other investigators and indicate that the thyroid gland increases in size according to other markers of development. However, markers of undernutrition were associated with larger thyroid glands in children. A negative correlation was found between TV and variables of BMI, TSF and Z-scores weight for height (wasting which is the preferred index for thinness in children) (Fig 7.6.). This would appear to suggest that in these very nutritionally deficient children thyroid homeostatic compromise is present. Thyroid function in this group is described in chapter 6. The negative relationship of thyroid size to BMI is probably artefactual and is skewed by the abnormally high BMI values from children from Baroda. In this population the high BMI values are explained by stunting of growth and not by obesity.

Adults were also malnourished. They showed a very high prevalence of low BMI (a critical situation) with almost 54% of the population having BMI < 18.5 kg/ m<sup>2</sup> based on the classification of the public health problem of low BMI amongst adults suggested by the WHO Expert Committee on Nutrition (1995) (WHO, 1995). The entire adult population had prolonged protein malnutrition as evident from smaller mean and median MUAC and AMA (Polge A, 1997). Generally thyroid size in normal adults correlates

well with body weight (Ivarson SA, 1989) but the correlation in this study was weaker because of the tighter range of body weight and the generalized increase in thyroid size. In those adults with poorer nutrition (as measured by MUAC and AMA; Figure 7.7.) thyroid size was greater reflecting underproduction of thyroid hormones with resultant thyroid hyperplasia.

The greatest public health concern of the present findings is the potential impact of PEM not on the development of goitre per se, but the effects on brain development of the fetus and neonate. Recently, maternal hypothyroidism alone has also been shown to impact the neurological outcome of the offspring. Although, we did not measure thyroid function in this population because it is a less sensitive prevalence indicator and not usually recommended for monitoring iodine nutrition (Dunn J, 1999), changes in circulating thyroid hormone levels are to be expected in children and adults for several reasons. Apart from the effects of nutrition on thyroid hormone production and secretion, there are also potential effects of poor nutrition on central and peripheral thyroid hormone homeostasis. Dietary treatment can normalise the indices of thyroid function due to high potential of pituitary-thyroid axis that is usually suppressed by PEM (Gaitan E, 1986). Finally, the well-described effects of poor nutrition on 5' deiodinase activity and the development of the sick euthyroid state also contribute to peripheral thyroid hormone economy.

In summary, the present study conducted in subjects with severe PEM in the setting of iodine deficiency has demonstrated that there is an impact of PEM on thyroid volume as measured by ultrasonography.

## 7.6. CONCLUSIONS

- (i) The severity of acute (wasting) and chronic (stunting) PEM along with underweight was very high amongst children (>40% of subjects) as per WHO classification. The Waterlow based threshold shows that children are stunted or wasted or both stunted and wasted or stunted and obese. Gujarati adults are thin with low protein and fat reserves as evidenced from their lower BMI, MUAC, AMA, AFA and TSF values when compared to USA and British values.
- (ii) Anthropometric parameters showed a statistically significant ( $p < 0.001$ ) correlation with thyroid size in children and adults.
- (iii) Higher prevalence of goitre (100% in children and 82% in adults) may be due to macronutrient malnutrition (PEM) on the face of already existing micronutrient malnutrition.