SECTION I

CHAPTER 1

BACKGROUND AND REVIEW OF LITERATURE

INTRODUCTION

The prevalence and pattern of various diseases vary from country to country and also shows temporal changes over centuries. This difference is mainly because of the fact that the etiopathogenesis of most of the diseases are multi factorial i.e. they depend on race, genetic makeup, dietary habits, and lifestyle of individual as well as environmental factors which keep changing from place to place and time to time. Hence the assessment of incidence and prevalence of diseases in each country forms an important aspect of scientific research and is called epidemiology. These epidemiological data is very vital for each country as it reveals the disease pattern prevailing there, and this background information is very essential to design preventive and curative strategies and also to decide on fund allocation and priority fixation by policy makers in the health care sector in every nation.

For centuries many western countries have been maintaining excellent disease registries and still continue to generate extensive epidemiological data on the incidence and prevalence of communicable as well as non-communicable diseases prevailing in the population. Moreover many of the developed nations have been conducting periodic community health surveys of large representative samples of general population which have provided valuable data on the prevalence pattern and changing trends of many disease conditions. These data have also shed light into the causal associations and relationship between many extrinsic factors and diseases and thus provided considerable inputs into the etiological evaluation of many disease conditions.

Unlike developed countries, even after six decades of independence there is a gross lacuna of national epidemiological data from India especially on non-
communicable diseases such as diabetes mellitus, obesity, hypertension, dyslipidemia and thyroid disorders. There were only few nationwide surveys and whatever data available was from regional studies and clinic based data. Hospital based data has many limitation as the clientele of each hospital vary widely and the data may not give the true picture of the disease burden in the community. But having a national registry of various diseases, which meticulously collects disease data from every nook and corner of the country, would have provided lot of information. But unfortunately except for few communicable diseases and cancer the national registries do not exist in our country. Hence to assess the spectrum and magnitude of any disease in this country, periodic nationwide epidemiological studies are needed. This is especially important in the case of diseases which lack florid symptoms such as thyroid disorders and diabetes mellitus which are shown to be the commonest endocrine diseases seen worldwide. Though during the last decade diabetes mellitus received more attention and have been in the focus of health planning after the initiation of national non communicable disease prevention programme, thyroid disorders other than iodine deficiency have not received much attention and remains poorly studied and researched in our country.

1.1 THE THYROID GLAND

Thyroid gland is a major endocrine gland of the body situated in the front of neck. It is a butterfly shaped gland with 2 lobes connected by an isthmus, weighing 15-20gms (Fig.1.1). Basic functional unit of the thyroid gland is the follicle, a ball shaped structure composed of single layer of follicular epithelial cells surrounding a lumen filled with colloid material containing a protein, thyroglobulin, which stores the synthesized hormones till the time of release.
1.1.1 THYROID HORMONES

Thyroid gland is a major endocrine gland of the body, which secretes two hormones, Tetra iodothyronine (T4) and tri iodothyronine (T3) under the influence of trophic regulatory hormone, Thyroid Stimulating Hormone (TSH). Both T4 and T3 are synthesized in the apical border of follicular epithelial cell by iodination of tyrosine residue of thyroglobulin protein by enzyme thyroperoxidase (TPO) (Fig. 1.2). The synthesized hormones are stored in the colloid within the follicle and are released from the follicular cells as per the body demands.
Once released into blood T4 and T3 bind to Thyroxine Binding Globulin (TBG), thyroxine binding prealbumin and albumin. Only about 0.02% of the total T4 is non-protein bound and this is called Free T4 where as 0.2% of T3 is non-protein bound and is called FreeT3. Plasma FreeT4 and FreeT3 determine the tissue availability of T4 and T3 and hence considered as more reliable parameters of thyroid status than total T4 and T3 which can be influenced by the variation in concentration of transport proteins.

TSH is secreted by anterior pituitary and is regulated by the Thyrotropin Releasing Hormone (TRH) secreted from hypothalamus of the brain. The blood level of T4 & T3 influences anterior pituitary and hypothalamus in a negative feedback pattern. When the thyroid hormone level decreases it results in an increase in the TSH level to stimulate thyroid gland to synthesize and secrete more thyroid hormones whereas, if thyroid hormone levels are high it suppresses the secretion of TSH in order to reduce the synthesis and release of thyroid hormone from the gland (Fig. 1.3). Thyroid hormone is critical for growth and development of all tissues of the body especially neuronal tissue but is also essential for controlling the basal metabolic rate. It also plays an important role in thermogenesis, fuel and vitamin metabolism in the body [1].

1.1.2. THYROID DISORDERS

Diseases of thyroid gland are the second most common endocrine problem seen among human beings all over the world, first being diabetes mellitus. Thyroid diseases can be broadly classified as functional or structural or a combination of both. Functional disorders produce alterations in hormonal levels. It can be either a deficiency (hypothyroidism) or excess (hyperthyroidism) of thyroid hormones, both having profound influence on health and well-being of the affected person.

Structural disorders usually involve enlargement of the thyroid (thyromegaly or goiter) (Fig. 1.4). This can be a diffuse or nodular goiter, or can be benign or even
malignant proliferation of tissues. Goiter can present with normal or abnormal function of the gland.

Fig. 1.3 Thyroid hormone secretion is under feedback control from pituitary gland.

Fig. 1.4 Thyromegaly or Goiter
1.1.3 HYPOTHYROIDISM

Deficiency of thyroid hormones produces clinical condition called hypothyroidism. Depending on the time of occurrence of thyroid hormone deficiency, clinical manifestations of this condition vary considerably. If hypothyroidism develops in the perinatal period i.e.; in the developing fetus or infancy, it produces profound effects in the neuronal and somatic development of children and can result in major problems like growth retardation, mental retardation, and neurological deficits etc. The children affected have short stature and develop typical facial and body features as well as mental retardation i.e.: cretinism (Fig. 1.5).

In adults hypothyroidism produces subtle changes such as psychomotor slowing, depression, loss of memory, metabolic abnormalities, diffuse aches and pains, cold intolerance, hoarseness of voice, puffiness of face, edema, weight gain, high cholesterol, infertility, constipation etc (Fig.1.6). In severe cases it can lead on to heart problems such as cardiomegaly, ischemic heart disease, pericardial effusion etc. When thyroid hormone deficiency becomes very severe the subject may drift into drowsiness and develop myxoedema coma characterized by hypothermia, hyponatremia, bradycardia etc, which can be fatal.
1.1.4 HYPERTHYROIDISM

When thyroid hormones are produced in excess it can produce florid symptoms such as weight loss, palpitation, tremor, heat intolerance, restlessness, psychomotor excitation, increased catabolism, metabolic abnormalities, osteoporosis etc. It also produces fast heart rate, arrhythmias and even cardiac failure. Some forms of hyperthyroidism (Grave’s disease of autoimmune etiology) causes associated thyroid eye disease characterized by bulging of the eyes (proptosis and lid retraction) (Fig. 1.7).

Fig. 1.6: Facial features of hypothyroidism

Fig. 1.7: Typical facial features of hyperthyroidism
In severe cases of hyperthyroidism patient can rarely develop a worsening of thyrotoxicosis with multi organ dysfunction resulting in a very serious condition called ‘Thyroid Storm’ characterized by fever, cardiac arrhythmias, heart failure, jaundice, delirium etc. This condition has a very high chance of mortality and needs urgent expert treatment.

1.1.5 SUBCLINICAL THYROID DYSFUNCTION

After the wide spread availability of biochemical assessment of thyroid by thyroid function tests, other than the overt thyroid dysfunction hypo and hyperthyroidism, there are subclinical thyroid disease conditions, where blood levels of T4 and T3 are within normal limits but TSH is either high (subclinical hypothyroidism) or low (subclinical hyperthyroidism). Both of these conditions are basically biochemical abnormality detected only on testing usually remain asymptomatic, but appears to have long term health implications [2] such as cardiovascular disease and osteoporosis.

1.2 ETIOLOGY OF THYROID DISORDERS

Multiple etiological factors are suggested for thyroid disorders [3]. These include nutritional factors such as deficiency or excess of iodine, autoimmunity marked by the presence of antibodies to thyroperoxidase and thyroglobulin antigens in the gland and genetic factors leading to defects of enzymes involved in hormone synthesis, or increasing susceptibility to autoimmunity. Moreover there are many other environmental chemicals which can affect the thyroid gland. Some of them such as thiocynate cause goiter [4] whereas some others cause functional as well as structural alterations e.g. persistent organic pollutants, bisphenol, perchlorate etc [5]. Unlike other endocrine gland disorders, the pattern of thyroid disorders in any country is largely decided by the presence or absence of various factors in the community and environment. Hence it is very important to assess the epidemiology
of thyroid disorders periodically in order to assess the prevalence of these factors and its impact on thyroid diseases in the population.

1.2.1 THYROID AUTOIMMUNITY

Autoimmunity is the process of abnormal immune response occurring in the body against auto antigens resulting in damage to specific organs or organ systems leading to variety of diseases. It is a common cause of endocrine diseases and thyroid autoimmunity is most frequent [6]. Thyroid autoimmunity involves both T and B lymphocyte mediated immune response and it produces diffuse inflammation and T cell infiltration of the thyroid gland either focally or diffusely (Fig.1.8). This is called autoimmune thyroiditis and it can manifest in a wide range of disease states such as focal thyroiditis without goiter, Hashimoto’s goitrous thyroiditis with or without hypothyroidism, atrophic nongoitrous thyroiditis, silent and postpartum thyroiditis (with initial transient thyrotoxicosis followed by later hypothyroidism) to Graves disease with hyperthyroidism and associated ophthalmopathy [6].

![Autoimmune mechanism of thyroid disease](image)

Fig. 1.8 Autoimmune mechanism of thyroid disease
Autoimmune thyroid disease is hallmarked by the presence of autoantibodies against thyroperoxidase enzyme (TPO) (located at the apical border of thyroid follicular cell which is responsible for iodination and coupling to form thyroid hormone) and Thyroglobulin (TG) (which is secreted by thyroid cell as a storage form of thyroid hormone in the colloid) within the thyroid gland and in the peripheral circulation. Prevalence of these auto antibodies had been reported as 7-20% from various countries. These antibodies are seen in 95-100% of autoimmune hypothyroidism and 80-90% of Graves’s hyperthyroidism. Positive antibodies are also seen in 10-15% of multinodular goiter and 30-40% of thyroid cancers. When these antibodies are present without thyroid dysfunction, the positive predictive value of future thyroid dysfunction is 40-60% [7, 8]. The exact etiology of this autoimmune disease is not clear though it is widely believed that genetic factors can predispose and environmental factors can trigger autoimmunity.

1.2.2 IODINE AND THYROID GLAND

Thyroid gland is quite different from other endocrine glands in the fact that its function depends heavily on an external element procured through diet. The trace element iodine is the main raw material needed for thyroid hormone synthesis. Hence iodine is considered as an essential micronutrient required for adequate mental and physical functioning of the human body [9]. Daily iodine requirement for human beings is approximately 150 microgram for adults (aged above 12 years) but the allowance is more for pregnant ladies and lactating mothers [10, 11] (Table 1.1).

1.2.3 SOURCES OF IODINE

Iodine is obtained solely from dietary sources. Iodine (as iodide) is widely but unevenly distributed in the earth’s environment with maximum concentration found in the seawater (about 50 microgram/L). Iodide ions in seawater oxidize to form elemental iodine, which is volatile and evaporates into the atmosphere and returns to the soil by rain, completing the cycle.
Table 1.1 WHO Recommendation of daily Iodine intake

<table>
<thead>
<tr>
<th>Age group</th>
<th>Daily recommended Iodine intake</th>
</tr>
</thead>
<tbody>
<tr>
<td>Children 0-5years</td>
<td>90mcg</td>
</tr>
<tr>
<td>Children 6-12years</td>
<td>120mcg</td>
</tr>
<tr>
<td>Children &gt;12years and adults</td>
<td>150mcg</td>
</tr>
<tr>
<td>Pregnant females</td>
<td>250mcg</td>
</tr>
<tr>
<td>Lactation</td>
<td>250mcg</td>
</tr>
</tbody>
</table>

However, the cycle of iodine in many regions is slow and incomplete. The frequent floods and heavy rains wash away the iodine, making soils and groundwater deficient in iodine. Crops grown in these soil will be low in iodine concentration, and man and animals consuming food grown in these soil also become deficient in iodine [12]. Iodine concentration in plants grown in iodine deficient soils might be as low as 10 microgram/kg of dry weight, compared with about 1 mg/kg in plants from iodine-sufficient soil.

Seafood is usually a good source but iodine content of the freshwater fish depends on the iodine content of the water they live in. In all animals and human, the mammary gland concentrates iodine and during lactation lot of iodine is secreted into breast milk to provide for the offspring. Hence dairy products are usually a good source, but only if those cattle are iodine sufficient. Similarly the meat or other products from animals fed on iodine-deficient plants also become poor sources of iodine in the diet. Iodine-deficient soils are common in inland regions, mountainous areas, and places with frequent flooding, but can even occur in coastal regions [11, 13].

1.2.4 IODINE ABSORPTION AND EXCRETION

Almost all of the iodine absorbed from the gut is trapped by the thyroid gland under the influence of TSH. Iodate, is reduced in the gut and absorbed as iodide
Organically bound iodine is typically digested and the released iodide is absorbed. Iodide is rapidly and nearly wholly absorbed (>90%) in the stomach and duodenum. Thyroid clearance of circulating iodine varies with iodine intake: in situations with adequate iodine supply, 10% or less of absorbed iodine is taken up by the thyroid. In chronic iodine deficiency, this percentage can exceed 80% [12].

Table 1.2 Iodine status - Urine iodine levels and iodine status

<table>
<thead>
<tr>
<th>Median Urinary Iodine Concentration (mcg/L)</th>
<th>Corresponding Approximate Iodine Intake (mcg/day)</th>
<th>Iodine Nutrition</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;20</td>
<td>&lt;30</td>
<td>Severe deficiency</td>
</tr>
<tr>
<td>20-49</td>
<td>30-74</td>
<td>Moderate deficiency</td>
</tr>
<tr>
<td>50-99</td>
<td>75-149</td>
<td>Mild deficiency</td>
</tr>
<tr>
<td>100-199</td>
<td>150-299</td>
<td>Optimal</td>
</tr>
<tr>
<td>200-299</td>
<td>300-449</td>
<td>More than adequate</td>
</tr>
<tr>
<td>&gt;299</td>
<td>&gt;449</td>
<td>Possible excess</td>
</tr>
</tbody>
</table>

Plasma half-life of iodine is 10 hours but this can be reduced in iodine deficiency. The body of a healthy adult contains 15–20 mg of iodine, of which 70–80% is in the thyroid [13]. In chronic iodine deficiency, the iodine content of the thyroid might fall to less than 20 micrograms. In iodine-sufficient areas, the adult thyroid traps about 60 microgram of iodine per day to balance losses and maintain synthesis of thyroid hormone. The sodium/iodide symporter transfers iodide into the thyroid at a concentration gradient 20–50 times that of plasma. Iodine consists of 65% and 59% of the weights of thyroxine (T4) and tri-iodothyronine (T3), respectively. Turnover is slow: the half-life of T4 is about 5-7 days and for T3, 1.5–3 days. The released iodine enters the plasma iodine pool and can be taken up again by the thyroid or excreted by the kidney. More than 90% of ingested iodine is ultimately excreted in the urine [15].
1.2.5 IODINE DEFICIENCY DISORDERS

The effect that iodine deficiency has upon human life in terms of health costs, quality of life and economic productivity is immeasurable. Deficiency of iodine generally produces hypo function of thyroid and thyromegaly (goiter) [13] and such diseases are categorized as Iodine Deficiency Disorders (IDD). Iodine deficiency in the perinatal period is the single most important preventable cause of brain damage (especially in children) worldwide [16]. People living in areas affected by severe iodine deficiency may have an intelligence quotient (IQ) of up to 13.5 points below that of those from comparable communities in areas where there is no iodine deficiency. This is because maternal iodine deficiency leading to maternal and fetal hypothyroxinaemia occurring during gestation and post natal period adversely affect the neuronal migration and myelination and result in irreversible brain damage. This produces cretinism which can be of either neurological or myxedematous variety (Fig. 1.8) [17].

Neurological cretinism shows three characteristic features: severe mental deficiency together with squint, deaf mutism, and motor spasticity of the arms and legs. The thyroid gland is present, and frequency of goiter and thyroid dysfunction is similar to that noted in the general population. The characteristic features of myxoedematous cretinism are severe mental retardation, short stature, incomplete maturation of the face with wide-set eyes, mild strabismus, saddle-nose deformity, mandibular atrophy, thickened, dry skin and hair along with profound primary hypothyroidism. The thyroid typically shows atrophic fibrosis (Fig.1.9).

Whether mild to moderate maternal iodine deficiency causes more subtle impairment of cognitive or neurological function in offspring is still a matter of debate. Though correcting iodine deficiency of mother had been shown to reduce thyroid size and TSH levels in mothers and newborns, the impact on neurological function of offspring is poorly studied. The maternal subclinical hypothyroidism has been shown to reduce the IQ of the offspring by about 7 points compared to mothers
with normal thyroid function. This mental deficiency has an immediate effect on child learning capacity, women’s health, the quality of life in communities, and economic productivity.

Fig. 1. 9 (A) Neurological cretinism in a 9-year-old girl (photograph, 2007) and (B) Myxoedematous cretinism in a 7-year-old girl (photograph, 2008) from western China [12].

Fig. 1.10 Large multinodular goiter [12]
Iodine deficiency in adults leads to diseases such as goiter and its associated complications of impaired mental function and hypothyroidism [12]. As the iodine intake falls, secretion of thyroid-stimulating hormone (TSH) increases in an effort to maximise uptake of available iodine, and TSH stimulates thyroid hypertrophy and hyperplasia. Initially, goiters are characterised by diffuse, homogeneous enlargement, but over time nodules often develop (Fig. 1.10) [12]. Over the time some of these nodules become autonomous and thus iodine deficiency is associated with a high occurrence of multinodular toxic goiter, mainly seen in women older than 50 years. In areas of chronic moderate to severe deficiency it produces increased hypothyroidism where as in areas of mild to moderate deficiency it produces less hypothyroidism.

1.2.6 IODINE EXCESS

As low levels of iodine can result in IDD, more than adequate iodine intake can produce thyroid problems ranging from goiter, hypothyroidism to iodine induced hyperthyroidism [18]. Most people who are iodine sufficient are remarkably tolerant to high dietary intakes of iodine. Iodine intakes of up to 1000μg per day are well tolerated by most adults, since the thyroid is able to adjust to a wide range of intakes and regulates the synthesis and release of thyroid hormones. In children, chronic intakes of 500μg per day or more are associated with increased thyroid volume, which is an early sign of thyroid dysfunction.

An increase in iodine intake in populations with chronic iodine deficiency might precipitate iodine induced hyperthyroidism. Transition phase from iodine deficiency to sufficiency can also result in increase in thyroid autoimmunity in some but not all populations [19-21]. Hence it is well accepted that the pattern of thyroid disorders in any part of the world depends on the iodine status of that population.

1.3 GOITER AND GOITROGENS

Goiter or thyromegaly can occur with or without alteration of thyroid function (Fig. 6) and this is called euthyroid goiter. Iodine deficiency is a common cause of diffuse goiter where as it can also cause nodular goiter in later stages. (Fig. 1.11)
Fig.1.11 Schematic representation of different types of goiters (normal, diffuse enlargement, single nodule and multiple nodules).

In some areas, goiter endemicity has been reported despite adequate availability of iodine in food and water. This may be due to the dietary substances termed goitrogens, which interfere with thyroid metabolism. They include food substances like cassava, sweet potato, sorghum, cabbage, cauliflower and soy. Goitrogens in this food stuff are generally present as thioglucosides or lucosinolates. Cassava had the highest concentration (18.6 mg per 100g), of thiocyanate, a hydrolysis product of thioglucosides or glucosinolates, followed by mustard oil seed (16.2 mg/100g), cabbage (10.1 mg/100g), and cauliflower (5.7 mg/100g) [22, 23].

Industrial pollutants like perchlorate, disulphides, smoking and nutrient deficiencies like selenium deficiency, iron deficiency and vitamin A deficiency have been documented to contribute to goiter development in various studies [24, 25]. Most goitrogens do not have a major clinical effect unless there is coexisting iodine deficiency. But recently, exposure to many endocrine-disrupting chemicals like polychlorinated biphenyls, pesticides and dioxins has been described to cause of goiter [24, 26].
<table>
<thead>
<tr>
<th>Goitrogens</th>
<th>Mechanism</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Foods</strong></td>
<td></td>
</tr>
<tr>
<td>Cassava, lima beans, linseed, sorghum, sweet potato</td>
<td>Contain cyanogenic glucosides; they are metabolised to thiocyanates that compete with iodine for thyroidal uptake</td>
</tr>
<tr>
<td>Cruciferous vegetables such as cabbage, kale, caulifower, broccoli, turnips, rapeseed</td>
<td>Contain glucosinolates; metabolites compete with iodine for thyroidal uptake</td>
</tr>
<tr>
<td>Soy, millet</td>
<td>Flavonoids impair thyroid peroxidase activity</td>
</tr>
<tr>
<td><strong>Industrial pollutants</strong></td>
<td></td>
</tr>
<tr>
<td>Perchlorate</td>
<td>Competitive inhibitor of the sodium/iodine symporter, decreasing iodine transport into the thyroid</td>
</tr>
<tr>
<td>Others (eg, disulphides from coal processes)</td>
<td>Reduce thyroidal iodine uptake</td>
</tr>
<tr>
<td>Smoking</td>
<td>An important goitrogen. Smoking during breastfeeding is associated with reduced iodine concentrations in breast milk. High serum concentration of thiocyanate due to smoking might compete with iodine for active transport into the secretary epithelium of the lactating breast</td>
</tr>
<tr>
<td><strong>Nutrients</strong></td>
<td></td>
</tr>
<tr>
<td>Selenium deficiency</td>
<td>Accumulated peroxides might damage the thyroid, and deiodinase deficiency impairs thyroid hormone synthesis</td>
</tr>
<tr>
<td>Iron deficiency</td>
<td>Reduces haeme-dependent thyroperoxidase activity in the thyroid and might blunt the efficacy of iodine prophylaxis</td>
</tr>
<tr>
<td>Vitamin A deficiency</td>
<td>Increases TSH stimulation and goiter through decreased vitamin A-mediated suppression of the pituitary TSH β gene</td>
</tr>
</tbody>
</table>
1.4. ASSESSMENT OF IODINE STATUS AND THYROID FUNCTION

Iodine status of any population is usually assessed in school going children due to ease of conducting the survey and also the continuous availability of regular cohorts for follow up studies.

Assessment of iodine status is done by various methods such as estimating urine iodine excretion levels, assessing the goiter prevalence and measuring thyroglobulin (TG) level in the blood [27]. TG is a thyroid protein that is a precursor in the synthesis of thyroid hormone, and small amounts of TG can be detected in the blood of all healthy individuals. The thyroid hyperplasia and goiter, characteristic of iodine deficiency increases serum TG levels, and in this setting serum TG reflects iodine nutrition over a period of months or years [12]. These indicators are complementary, in that urine iodine concentration is a sensitive indicator of recent iodine intake (days) and thyroglobulin shows an intermediate response (weeks to months), whereas changes in the goiter rate show long-term iodine nutrition (months to years).

Biochemical assessment of thyroid function is usually done by measuring blood levels of T4 and TSH. This will classify the thyroid status as normal (euthyroid), hypothyroid (T4 is low and TSH is high), hyperthyroid (T4 is high and TSH is low) or subclinical hypo or hyperthyroid where T4 is within normal limits and TSH is either high or low.

Presence of thyroid autoimmunity is suggested by the presence of antibody to thyroperoxidase enzyme (Anti TPO) or Anti thyroglobulin antibodies (Anti TG antibody). Clinically goiter grading is done using the definition provided by the WHO/UNICEF/ICCIDD (1992) which is as follows

1. Grade 0: no goiter (Fig.1.12).
2. Grade 1: a mass in the neck that is consistent with enlarged thyroid that is palpable but not visible when neck is in normal position. It moves upward in the neck when the subject swallows. Thyroid nodules in a thyroid which is otherwise not enlarged fall into this category (Fig. 1.13).
3. Grade 2: swelling in the neck that is visible when the neck is in a normal position is consistent with an enlarged thyroid when palpated (Fig. 1.14).

Fig. 1.12 Grade 0 goiter

Fig. 1.13 Grade 1 goiter

Fig. 1.14 Grade 2 goiter
1.4.1 ULTRASOUND EVALUATION OF THYROID VOLUME

Ultrasound imaging is usually a noninvasive mode of imaging that helps physicians diagnose and treat medical conditions (Fig.1.15). Ultrasound imaging, also called ultrasound scanning or sonography, involves exposing part of the body to high-frequency sound waves to produce pictures of the inside of the body. Ultrasound examination do not use ionizing radiation (x-ray). Because ultrasound images are captured in real-time, they can show the structure and movement of the body's internal organs, as well as blood flowing through blood vessels.

An ultrasound of the thyroid produces a two dimensional picture of the thyroid gland. Ultrasound measurement is considered as the gold standard of thyroid volume measurement [28].

Imaging thyroid using ultrasound can be used to assess goiter prevalence [29]. Goiter or thyromegaly is usually assessed clinically by inspection and palpation of the front of neck and graded as per WHO grading of goiter (Fig. 1.16). This can produce an error up to 50% [30]. Hence definition of goiter prevalence by ultrasound imaging is found to be more accurate. It also gives additional information on the texture of the thyroid gland such as presence of nodules.
1.5 PREVENTION OF IODINE DEFICIENCY - UNIVERSAL SALT IODIZATION PROGRAMME

According to WHO, in 2007, nearly 2 billion individuals worldwide had insufficient iodine intake, a third being of school age. Thus iodine deficiency, as the single greatest preventable cause of mental retardation, is still an important public health problem. In 1993, recognizing the importance of preventing IDD as a public health problem, WHO and UNICEF recommended universal salt-iodisation as an easy and effective way of increasing and ensuring adequate iodine intake for all population.

Every human being irrespective of the race, cast, and creed uses salt. Daily salt intake varies in different food cultures in the range of 6-12 g per day. With only a few isolated exceptions, edible salt (sodium chloride) does not naturally contain iodine. Iodine is added deliberately as one of the most efficient ways of improving iodine nutrition. Either potassium iodide or potassium iodate is used to fortify salt. The amount added varies widely in different regions. In Canada and the United States, iodized salt contains 100ppm (parts per million, same as 100 mcg/gram) as potassium iodide (equals 77ppm as iodide), so two grams of salt approximately contains the daily-recommended amount of 150 mcg iodine (Fig. 1.17).
Fig. 1.17 Iodization of salt – for preventing Iodine Deficiency

About 50% of all the salt sold in the U.S.A is iodized. In Canada, all table salt is iodized. Most other countries including India, add 10 to 40 mcg iodine per gram of salt (10-40 ppm). These statements apply only to table salt. Most edible salt is added at cooking. If present as potassium iodate, as in most countries, little iodine is lost during cooking, depending on how pure the salt is. Many people get most of their salt from processed foods, especially in developed countries, and commercial practices vary as to whether these contain iodine or not.

Many countries have tried fortification of other food stuff as a measure to increase iodine intake. Bread can be an effective vehicle for iodine intake by including baker’s salt enriched with iodine [31]. Although iodizing drinking water or irrigation water can also be effective [32, 33] the high cost and complexity of monitoring are disadvantages. Iodine-containing milk is a major adventitious source in countries such as Switzerland and USA [34] because of the use of iodophores in the dairy industry rather than the deliberate addition of iodine. In Finland iodine-fortified animal fodder has increased the iodine content of foods derived from animal source and studies have shown that it has helped in improving the iodine status of people significantly through consumption of iodine rich animal products. [12].
In some remote areas where salt iodization is impractical, iodized oil is used as a source of iodine supplement [35]. This iodized oil is prepared by esterification of the unsaturated fatty acids in seed or vegetable oils and addition of iodine to the double bonds. It can be given orally or by intramuscular injection [36]. Iodine can also be given as potassium iodine or potassium iodate as drops or tablets. Single oral doses of potassium iodide monthly (30mg) or every 2 weeks (8mg) can provide adequate iodine for school-aged children [37]. Lugol’s iodine, containing about 6mg of iodine per drop, and similar preparations are commonly available as antiseptics in rural dispensaries in developing countries and offer another simple way to deliver iodine locally.

1.6. IODINE STATUS AND THYROID DISORDERS - CURRENT SCENARIO

1.6.1 WORLD SCENARIO

As result of the ongoing efforts of WHO, many countries have made rapid strides towards the goal of universal salt iodisation, though IDD is still a major nutritional public health problem in many developing countries. In 2007, WHO estimated that nearly 2 billion individuals have an insufficient intake of iodine, including a third of all school-aged children [12, 18]. However, significant progress has been made since 2003; 12 countries have progressed to optimum iodine status and the percentage of school-aged children at risk of iodine deficiency has decreased by 5%. On the other hand, iodine intake is more than adequate, or even excessive, in 34 countries, an increase from 27 in 2003 (Fig.1. 18). In the mean time in Australia and USA, two countries that were previously iodine sufficient, the iodine intakes are falling [38, 39]. These changes emphasise the importance of regular monitoring of iodine status in countries, even after achieving iodine sufficient state in order to detect both low and excessive intakes of iodine.
Assessing the iodine status of the population is very important as the pattern of thyroid disease in a community changes with the changes in iodine status of the population [40, 41]. In areas of iodine deficiency, commonly encountered thyroid problems are endemic goiter (10-80%), endemic cretinism (10%) due to maternal iodine deficiency and thyroid carcinoma (<1%), mostly follicular and anaplastic. In iodine replete areas autoimmune thyroid disorders such as the primary hypothyroidism and hyperthyroidism, postpartum hypothyroidism as well as simple or multinodular goiter and thyroid carcinoma (<1%) (more of follicular or papillary) are commonly encountered [42].

1.6.2 EPIDEMIOLOGY OF THYROID FUNCTIONAL DISORDERS

Though iodine status of many countries has been assessed periodically by the WHO ICDIDD initiative worldwide, the spectrum of thyroid functional disorders are poorly studied in many countries. However a number of population-based studies examining the prevalence of thyroid disorders have been conducted in adult
population of developed countries. A large population-based study from UK, prevalence of overt hyperthyroidism was 19/1000 females, compared with 1.6 – 2.3/1000 males, and prevalence of overt hypothyroidism was 14/1000 females, compared with less than 1/1000 males. TSH levels above 6mu/L were associated with a significant lowering of circulating thyroxin levels, and showed a strong association with thyroid antibodies in both men and women independent of age. Three percentage of the sample (N=3538) had thyroid antibodies and TSH levels equal to or greater than 6mu/ [7]. In another large US-based study (NHANES-III) conducted between 1988 and 1994 found hypothyroidism in 4.6% of the US population (0.3% clinical and 4.3% subclinical), and hyperthyroidism in 1.3% of the population (0.5% clinical and 0.7% subclinical). The prevalence of anti-thyroid antibodies was greater in females and increased with age [42]. In a study done among 1818 Japanese adults who chose to be screened by a general health check-up system, the prevalence of abnormal thyroid function was nearly 10%. In a high percentage of these patients, abnormal thyroid function could not be detected by their history or physical examination. Just a physical examination without thyroid function tests, particularly serum TSH levels, was not adequate even when performed by a thyroid specialist [8]. These results indicated that thyroid disorders are (especially sub-clinical disease and autoimmune thyroid disease) quite prevalent in developed countries.

1.6.3 IODINE STATUS AND THYROID DISORDERS -INDIAN SCENARIO

Iodine deficiency disorders were widely prevalent in Indian subcontinent especially in the ‘Himalayan and sub Himalayan belt areas’ before the era of salt iodization. [43]. ICMR study conducted in 1984-86 among 409,923 subjects in various states showed that no state or union territory is free of iodine deficiency. Overall goiter prevalence was 21% and cretinism was present in 0.7% [44]. Further detailed studies done by scientists from AIIMS among adult and children had shown that iodine deficiency can cause functional decompensation of thyroid as
well as increasing prevalence of cretinism [45, 46]. Based on all these findings in 1997, the Indian Government introduced a promulgation that banned the sale and storage of non-iodinated salt in an effort to promote universal salt iodization, with the goal of India becoming an iodine sufficient area in the foreseeable future. As a result of nation wide campaign and iodization of salt, surveys done after a decade has shown a remarkable decline in cretinism, goiter prevalence and improvement of functional thyroid status and normalization of iodine nutrition status in the community [47, 48].

Based on these evidences WHO classified India as a country with ‘optimal iodine nutrition’ (Fig. 1.19). But this is a comparative description because almost 1/3rd (31.3%) of school age children in India still have urinary iodine excretion of less than 100μg/l [49], which indicates ‘insufficient iodine intake’ and ‘mild iodine deficiency.’

Fig. 1.19 Studies on school children shows that India as a country with ‘optimal iodine nutrition’.

Hence it can be considered that though the WHO classification might be true for the country as a whole, many pockets of iodine deficiency still exist. Despite becoming iodine sufficient the total goiter prevalence amongst school age children
in India remains 17.9%, more than the recommended 5% [50] which is thought to be due to the presence of unidentified goitrogens such as thiocyanate, environmental pollutants etc.

Regarding the pattern of thyroid functional disorders in the post iodization phase, the results from previous nationwide surveys among school children have clearly showed that subclinical hypothyroidism was the commonest disorder (4.9%) whereas overt hypothyroidism (0.79%), and hyperthyroidism (1.0%) were much less common [50].

On the contrary there is not much data on thyroid disorders on the adult population of India either in the pre or post iodization period. Although there have been many studies on the prevalence of goiters and thyroid disorders in Indian school children, the magnitude thyroid problems in Indian adults is still estimated as (42 millions) an extrapolation of children’s [48]. In one small study conducted among the subjects attending a health camp in the costal district Karnataka state with iodine deficiency, the goiter prevalence was 53.8% before iodization and 50.3% 1year after iodization [51]. This study had attempted look at the thyroid dysfunction pattern in a small number of subjects (n 36) before and 1year after iodization (n 41) and showed a significant increase in hyperthyroidism and hypothyroidism. But the number of subjects in this study is too small to derive any sensible conclusion.

The nationwide survey (NFHS-3) of population 15-50 years was conducted by Ministry of Health and Welfare which has assessed the reported prevalence of goiter and other thyroid disorders in 2005-2006 [52]. The results of this survey showed wide variation in the prevalence of known thyroid problems and goiter in different parts of India. However it was higher among females than males and increased with age in females. But this is a gross underestimation of the true prevalence of thyroid problems as neither clinical and biochemical thyroid assessment nor iodine status evaluation was included in this study.
One previous study that looked at the thyroid status of adult females was done among 505 women who voluntarily attended a well woman clinic in Puduchery [53]. In this study, among subjects with no history of thyroid problems, 15.8% had thyroid dysfunction and 84.2% were euthyroid. 11.5% were hypothyroid (9.5% subclinical) and 1.8% hyperthyroid (1.2% clinical). One major drawback of this study is the lack of information of iodine status of the participants as urine iodine was not assessed. Moreover this being a clinic data it may not represent the true picture in the community. In a review paper by Prof. Kochupilla, a pioneer on Iodine studies in India, the magnitude of thyroid disease burden in Indian adults has been estimated as 42 million which is about 6% of the 720 million adults above 18 years [48]. However this is an extrapolation from children’s data and may not reflect the real magnitude. To summarize, there is a significant lack of epidemiological data on iodine status, goiter prevalence, and thyroid functional disorders among adult Indian population.

1.6.4 KERALA SCENARIO

Kerala is a small state situated in the south-western corner of India. It represents 1.18% of the total area of India, but 3.4% of the total population lives here. Kerala has highlands sloping from the Western Ghats (900 to 1,800 metres high) with major tea, coffee, rubber and cardamom plantations. The midland areas have many small hills and valleys and are utilized for cashew, coconut, cassava, banana, paddy, and sugarcane cultivation. The lowlands are mainly coastal areas adjacent to the Arabian Sea with paddy, coconut cultivation, and fishing being the main sources of income. Over the last 2-3 decades many of the younger generation have been employed in the gulf countries and this has contributed to the improvement in economic status and living standards of the state in general. Kerala has near 100% literacy and has achieved remarkable progress in improving health care and health indicators. Many of the health indices of Kerala such as maternal mortality, infant mortality birth rate etc. are comparable with that of developed countries.
Many studies have been conducted in Kerala to determine the prevalence of goiter and IDD. In 1976, Kochupillai et al undertook a study in coastal areas in Kerala to examine goiter characteristics, and reported that the prevalence of thyroid nodules was 13% in the population surveyed [54]. Surveys conducted in 14 districts in Kerala between 1989 and 1994 demonstrated goiter prevalence ranging from 4.7% to 27.3% [55]. Population in hilly areas such as Kottayam, Idukki and Wayanadu had higher prevalence of goiter i.e. 21% while coastal area Ernakulam had goiter rate of 9%. However Kerala was the only state that did not ban the sale of non-iodised salt on a state-wide level.

Subsequently, an Ernakulam-based school-district survey conducted in 1998 reported the prevalence of goiter as 1%, with a mean urinary iodine excretion (UIE) of 200microgram/L [56]. Another ICMR sponsored state-wide survey of children between 6 and 12 years of age found the prevalence of goiter to be 16.6% (n=1067). Median urinary iodine excretion was 123.3 microgram/L; while 32.5% had a urinary iodine excretion below 100 microgram/L [57]. But another recent state wide school survey of Kerala has showed Kottayam, Kasargod and Idukki still have iodine deficiency [58].

Studies in the adult population are very few and most of them were district based surveys of goiter prevalence and iodine status. No study has looked at the thyroid function status and hence there is no data on antibody status and magnitude of thyroid disorders from Kerala.

These studies adequately demonstrated that though iodine levels are sufficient in most parts of Kerala, probably some iodine deficient pockets exists and prevalence of goiter in child population is still higher than expected for the level of iodination. As most of these studies have been conducted among school children and data from the adult population is largely missing.
As part of national health survey NFHS 3, a proportion of Kerala population (15-50years) was surveyed regarding the prevalence of known goiter and other thyroid disorders. It showed that females had higher prevalence of 5.7% thyroid problems compared to males (1.89%). It had also shown that prevalence of thyroid problems increased with increasing age in females (3.27% in 15-19yr, 5.2% in 20-34yrs and 7.23% in 35-49yrs) [52]. As mentioned earlier this study has only assessed one aspect of the problem and may represent only tip of the iceberg. These findings would be a gross underestimation of thyroid problems, as many subjects may not be aware of the presence of thyroid problems other than goiter. Hence it is very obvious that there is a gross lacuna of epidemiological data on the prevalence of various thyroid disorders among adult population. A proper study designed to address the various aspects of thyroid problem such as iodine status, pattern of thyroid disorders and autoimmunity in adults would be really helpful to understand this health problem better.

1.7 DIABETES MELLITUS

Diabetes Mellitus, another major endocrine disorder has reached epidemic proportions globally especially in developing countries like India [59]. The inevitable lifestyle changes brought about by rapid industrialization and urbanization of the Indian society is thought to be the cause for this epidemic and the solutions for tackling this problem still remain elusive and expensive. But recent studies have shown that lifestyle modifications can prevent or postpone the onset of diabetes in high-risk population [60-62]. Considering the long term impact of diabetes on morbidity and mortality of the population it is very important to assess the magnitude of this problem in every community so that preventive strategies can be implemented effectively. As diabetes can remain silent for many years screening the population for diabetes will help in early detection and better management. Detecting subjects with prediabetes (impaired fasting glucose and impaired glucose tolerance), who are having very high risk of developing diabetes provide an excellent opportunity of primary prevention of diabetes.
Type 2 diabetes is a heterogeneous disorder characterized by two interrelated metabolic defects: insulin resistance coupled with impaired insulin secretion by β-cells of the pancreas [63]. During the initial period body tries to overcome Insulin resistance by over producing insulin from the pancreatic beta cells in order to keep the blood sugar within normal limits. This hyperinsulinemic state is manifested externally as acanthosis nigricans or blackish velvety pigmentation of neck, axilla, knuckles etc, produced by the hyperkeratosis and papillomatosis of keratinocytes (Fig. 1.20). Later on the beta cells of the pancreas fail to produce adequate amount insulin and the blood sugar starts raising resulting in clinical diabetes. Hence acanthosis nigricans is considered as an important and easily identifiable clinical marker of insulin resistance [64].

![Acanthosis Nigricans in the neck](image)

Fig. 1.20 Acanthosis Nigricans in the neck

People with diabetes have a two to fourfold increased risk of developing cardiovascular disease, peripheral vascular disease, and stroke. These complications account for 65% of mortality from diabetes and, as of 2006, have made diabetes becoming the seventh leading cause of death in the United States [65]. Because of its silent nature, diabetes is often diagnosed relatively late in the course of the disease, at a point when many patients have already developed complications. In addition, management efforts are labor intensive and challenging for both patients and physicians. Furthermore, the economic burden associated with diabetes is substantial. The impact of diabetes on individuals’ health and its economic burden to society has
made its prevention a major goal of the current era. But to design any preventive strategy, the extent of the problem in that community should be assessed. As prevalence of diabetes varies from country to country and race to race, it is important to assess the prevalence in various populations.

1.7.1 Diabetes Mellitus - Ateiologic Factors

Diabetes Mellitus is defined as a chronic metabolic disorder resulting because of varying degrees of insulin secretory defects and insulin resistance. Genetic factors play a major role in the etiology of diabetes mellitus by conferring a susceptibility on which environmental factors act to precipitate diabetes. Family history of diabetes, increasing age, obesity and sedentary life style are all implicated in the etiopathogenesis of diabetes. Newer research has shown many environmental factors such as persistent organic pollutants, pesticides, toxins from plastic are all have shown as possible etiologic factors though no study has been able to show a cause and effect relationship with diabetes and the exposure to these chemicals [66].

1.7.2 Diabetes Mellitus – Global Scenario

Prevalence of diabetes mellitus is increasing worldwide (Fig. 1.21, 1.22) [67]. Studies have shown that an ever increasing aging population, life style changes brought about by the urbanisation and modernisation, change in the dietary choices preferring energy dense nonvegetarian food items may be the reasons for this increase [68].

Increase in obesity parallels with increase in diabetes all over the world. Even in countries with poverty imbalance of nutrients is leading to the double burden of undernutrition and overnutrition [69].
Fig. 1.21 ‘The number of people with diabetes will nearly double within the first quarter of this millennium’. World Health Report, 1997; Geneva: WHO.

Fig. 1.22 Global burden of diabetes in 2010 and its projected increase by 2025
1.7.3 DIABETES MELLITUS – INDIAN SCENARIO

During the last two decades, many population studies have been conducted in various parts of India looking at the prevalence of Diabetes Mellitus. In 1992, Ramachandran et al found that the prevalence of diabetes in south India was 8.2% & 2.4% in the urban and rural population respectively [70]. This was much higher than their own earlier estimates done two decades ago, which showed prevalence rates of 2.3% and 1.5% in urban and rural population respectively. The same researchers found even higher prevalence rates of 11.6% in their follow-up study conducted 5 years later [71]. A recent large survey conducted in north India [72] has shown that the age and gender standardized prevalence rates for DM and IFG in the total Indian population were 3.3 and 3.6% respectively (urban DM prevalence 4.6% versus rural DM prevalence 1.9%). This study also showed that the prevalence of newly detected diabetes was 2.4% (urban 3% and rural 1.5%). As the Indian population is heterogeneous, the pattern of disease prevalence in one area may not be similar to that in another area, hence the necessity for obtaining data through regional studies.

1.7.4 DIABETES MELLITUS – KERALA SCENARIO

Kerala, a small south Indian state, represents 1.18% of the total land area of India and contains 3.4% of the total Indian population. During the last five decades, Kerala has achieved remarkable progress in reducing fertility and mortality [73], combating infectious diseases and poverty related illnesses [74]. Kerala has also achieved the lowest population growth rate and highest literacy rate in the country. This high literacy rate, especially among females and easy accessibility to health care are thought to be the major contributing factors to the improved health standards in Kerala.

Socio economic factors are also very different in Kerala compared to other states of India. Though the main sources of income are from agriculture, fishing and industries, many families receive income generated by family members working abroad. Over the last two decades, urbanization, westernization as well as general
improvement in economic status and living standards have led to substantial changes in diet and lifestyle of the population. This has been associated with a marked increase in the prevalence of non-communicable lifestyle related diseases such as diabetes, hypertension and coronary artery disease among the Kerala population, which now shows similar demographic features of western countries.

The National Urban Diabetes Survey conducted in 2001 was the only national study that had included a small sample population from Kerala [75] which reported a diabetes prevalence of 12.1%. Other than this study there have been only two previous regional studies looking at the prevalence of diabetes in Kerala [76, 77] and both were in South Kerala. These studies showed that 23.4% of diabetes cases are undetected in this population. A nationwide sample survey, NFHS-3 2006 revealed the prevalence of known DM as 3.08% in males and 2.55% in females. This included Kerala population also. This low rate may be an underestimation of the magnitude of diabetes due to the fact that many of the diabetic subjects are probably not aware of the existence of their disease. Prevalence of comorbidities like hypertension, obesity, dyslipidemia are also apparently increasing in Kerala. But community studies depicting the real extent of these problems in the community are largely lacking from Kerala.

1.8 DIABETES AND THYROID DISEASES

The impact of thyroid alterations on glucose metabolism has been known for a long time. Thyroid hormones exert profound effects in the regulation of glucose homeostasis. These effects include modifications of circulating insulin levels and counter-regulatory hormones, intestinal absorption, hepatic production and peripheral tissues (fat and muscle) uptake of glucose. Most recently, new pathways of thyroid hormone action at the tissue level have been unveiled and may be of relevance to the understanding of insulin resistance present both in the hypothyroid and hyperthyroid state [78]. Thyrotoxic patients usually lose their glucose control when thyroid decompensation is not promptly solved. On the contrary in hypothyroidism the
increased insulin resistance present in peripheral tissues results in impaired uptake of glucose but simultaneous decreased liver glucose output compensate for this and thereby accounting for the diminished insulin requirement for glycemic control in hypothyroid diabetic patients.

Many studies have shown that diabetic patients, who are already having higher risk of cardiovascular disease [79] were having a higher prevalence of thyroid dysfunction as compared to general population. Most of the studies on diabetes and thyroid were done in type 1diabetes. Association of these two conditions forms the autoimmune polyendocrine syndrome variant and up to 50% of type 1 diabetes patients were reported to be positive for thyroid antibodies [80] and approximately 50% of them progress to develop clinical autoimmune thyroid disease. Many studies in India and abroad have shown a significantly higher prevalence of autoimmune thyroid dysfunction in type 1diabetes patients [81-83]. This association is thought to be due to the shared genetic susceptibility between several autoimmune diseases. Despite this strong genetic association, knowledge on shared susceptibility genes for type 1 diabetes and autoimmune thyroid disease is incomplete.

But in case of type 2 diabetes and thyroid, genetic links are less well characterized. But thyroid hormones are positively associated with insulin resistance not only in clinically diagnosed diabetes but also in subjects with a normal glucose tolerance. Indices of insulin resistance as judged by the homeostatic model assessment (HOMA, which assesses the fasting and postprandial insulin resistance) are closely linked to thyroid hormone status even in euthyroid, eumetabolic subjects, where HOMA is related to the increase in thyroid hormone concentrations even within the normal range [84, 85]. Studies on thyroid problems in type 2 diabetes are fewer than those in type 1diabetes, but data from different parts of the world showed conflicting results. In a study conducted at a diabetic outpatient clinic in UK [86], the overall prevalence of thyroid disease was found to be 13.4%, and was highest (31.4%) in Type 1 diabetic females, and lowest in Type 2 diabetic males (6.9%). As a
direct result of screening, new thyroid disease was diagnosed in 6.8% (89 patients) of the population screened; the commonest diagnosis was subclinical hypothyroidism (4.8%), followed by hypothyroidism (0.9%), hyperthyroidism (0.5%), and subclinical hyperthyroidism (0.5%). The prevalence of undiagnosed thyroid disease in diabetic patients receiving community diabetes care was 5.5% [87] which was higher than non-diabetic controls. In a clinic based study in Jordan 12.5% of type 2 diabetic subjects had thyroid problem compared to 6.6% of non-diabetic controls [88]. But in a study from Israel there was no difference between female diabetic and non-diabetic population regarding thyroid function [89]. In another study done in USA among elderly subjects thyroid dysfunction was found similar in diabetic and non-diabetic subjects [90]. In a community based Fermantle study of diabetic females, subclinical hypothyroidism was found in 8.6% not found to be significantly progressing after 5 years of follow up [91]. But in India only few clinic based studies of prevalence of thyroid problems were done in type 2 diabetes and the data from a community perspective is largely lacking [92, 93].

### 1.9 HYPOTHESIS

1. Iodine deficiency and autoimmunity could be the causative factors for thyroid disorders.

2. Subjects with type 2 diabetes have higher prevalence of thyroid disorders than non diabetic subjects in our population.

### 1.10 STUDY OBJECTIVES

**Primary objectives**

1. To evaluate prevalence of thyroid abnormalities such as, goiter, sub-clinical and clinical hypo and hyperthyroidism among adult Indian population in central Kerala

2. To estimate the Iodine status by measuring urinary iodine levels and to assess its association with different thyroid abnormalities
3. To assess the prevalence of thyroid autoimmunity and to identify its relation with thyroid disorders
4. To find out the population prevalence of diabetes and co morbidities such as obesity, hypertension, dyslipidemia in adult population in central Kerala
5. To assess the coexistence of diabetes and thyroid disorders in this population

Secondary Objectives
1. To study the older female subpopulation with high prevalence of thyroid problems
2. To evaluate the iodine status and its relation with thyroid volume and other factors in this population
3. To assess the prevalence of clinical goiter and nodularity in this population using ultrasound.
4. To establish the normal thyroid volume of study subjects
5. To explore the relation between Iodine status, autoimmunity, prevalence of goiter and other thyroid disorders among the study population.

SECTION II

CHAPTER 2