Thyroid Diseases: A Brief Review

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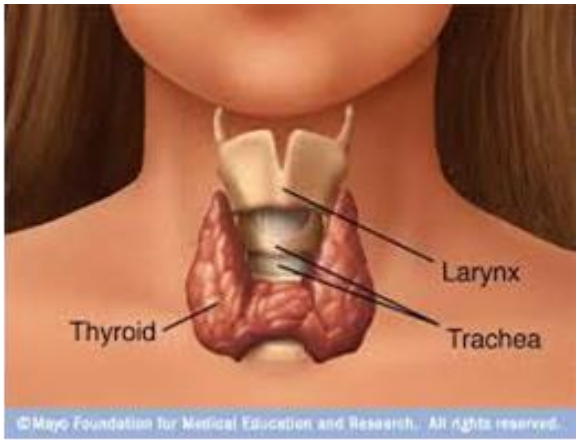
Abstract: Thyroid diseases are common worldwide. In India too, there is a significant burden of thyroid diseases. According to a projection from various studies on thyroid disease, it has been estimated that about 42 million people in India suffer from thyroid diseases. This review focuses on common diseases of thyroid and their epidemiology in India.

Key Words: Thyroid Diseases, India and Epidemiology



Thyroid disease is being increasingly diagnosed with greater awareness and is one of the chronic non-communicable disease affecting women more, though male population is not spared of the ailment. Thyroid is a butterfly-shaped gland in the neck region, just above collarbone. It is one of the endocrine glands, which make hormones. The thyroid hormones, thyroxine(T4) and triiodothyronine (T3) are tyrosine-based hormones produced by the thyroid gland primarily to regulate metabolism

An important component in the synthesis of thyroid hormones is iodine. The major form of thyroid hormone in the blood is thyroxin (T4). The thyroid also produces the hormone calcitonin, which plays a role in calcium homeostasis. Thyroxine increases cardiac output, heart rate,basal metabolic rate, ventilation rate, potentiates brain development, and potentiates the effects of catecholamines (i.e. increases sympathetic activity),and thickens the endometrium in females. These hormones also regulate protein, fat, and carbohydrate metabolism, to see human cells using their energetic compounds. They also stimulate vitamin metabolism. Numerous physiological and pathological stimuli influence thyroid hormone synthesis. Both excess (hyperthyroidism) and deficiency (hypothyroidism) of thyroxine can cause disorders. Hyperthyroidism is the clinical syndrome caused by an excess of circulating free thyroxin, free triiodothyronine, or both.

The symptoms of hyperthyroidism are fast heart rate, nervousness, increased perspiration, muscle weakness, trembling hands, weight loss, hair loss, skin changes, increased frequency of bowel movements, decreased menstrual flow and less frequent menstrual flow, goiter and exopthalmus. [N. Kochupillai;2000, Hueston WJ; 2001]

Hypothyroidism is the case where there is a deficiency of thyroxin, triiodiothyronine, or both. The symptoms of hypothyroidism are feeling slow or tired, cold, drowsy, slow heart rate,poor memory, difficulty in concentrating ,muscle cramps, weight gain, husky voice, thinning hair, dry and coarse skin, feeling depressed, heavy menstrual flow, milky discharge from the breasts and infertility[N. Kochupillai;2000]

Thyroid diseases are, arguably, among the commonest endocrine disorders worldwide. India too, is no exception. According to a projection from various studies on thyroid disease, it has been estimated that about 42 million people in India suffer from thyroid diseases. (Ambika Gopalakrishnan Unnikrishnan and Usha V Menon; 2011). Thyroid diseases are different from other diseases in terms of their ease of diagnosis, accessibility of medical treatment, and the relative visibility that even a small swelling of the thyroid offers to the treating physician. Early diagnosis and treatment remains the cornerstone of management.

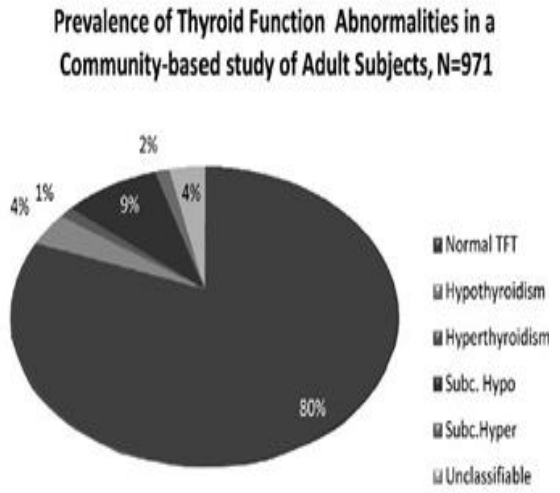
Hypothyroidism

Among the various varieties of hypothyroidism, congenital hypothyroidism is probably the most important, as it is requires an early diagnosis, which is usually followed by appropriate therapy that can prevent the onset of brain damage. Studies from Mumbai have suggested that congenital hypothyroidism is common in India, the disease occurring in 1 out of 2640 neonates, when compared with the worldwide average value of 1 in 3800 subjects. (Desai PM;1997)There is often a delay in the diagnosis of congenital hypothyroidism in the country. This delay is attributable to the lack of awareness about the illness, as well as the lack of facilities available or screening program in place to comprehensively screen and test newborns for this illness.

In childhood too, hypothyroidism can occur. In a clinic-based study from Mumbai, out of 800 children with thyroid disease, 79% had hypothyroidism. Common causes of hypothyroidism in these children were thyroid dysgenesis, dyshormonogenesis, and thyroiditis. (Desai PM;1997)

Among adult people in India, the prevalence of hypothyroidism has been recently studied. In this population-based study done in Cochin on 971 adult subjects, the prevalence of hypothyroidism was 3.9%. (Usha Menon V ;2009).The prevalence of subclinical hypothyroidism was also high in this study, the value being 9.4%. In women, the prevalence was higher, at 11.4%, when compared with men, in whom the prevalence was 6.2%. The prevalence of subclinical hypothyroidism increased with age. About 53% of subjects with subclinical hypothyroidism were positive for anti-TPO antibodies. This was a population-based study, which used cluster sampling strategy. (Usha Menon V;2009) In this study, Urinary Iodine Status was studied in 954 subjects from the same population sampled, and the median value was 211 µg/l; this suggested that this population was iodine sufficient.

Hyperthyroidism



The prevalence of hyperthyroidism has been studied in several studies. In an epidemiological study from Cochin, subclinical and overt hyperthyroidisms were present in 1.6% and 1.3% of subjects participating in a community survey. (Usha Menon V;2009) In a hospital-based study of women from Pondicherry, subclinical and overt hyperthyroidisms were present in 0.6% and 1.2% of subjects. (Abraham R *et al*;2009) More than a third of community-detected hyperthyroid cases have positive anti-TPO antibodies, and about 39% of these subjects have a goiter **(Usha Menon V;2009)**

Place of study	Reference	Age (in years)	Sex (%)		Number	Prevalence %			TSH Cut off (µIU/mL)
			M	F		Total	M	F	
Wickham	Tunbridge *et al.*[3]	18+	33	77	2779	8.9	2.8	7.5	>6
Sweden	Nystrom *et al.*[22] (1981)	44+	0	100	1283	5.1	-	5.1	>8
Farmingham	Sawin *et al.*[4]	60+	41	59	2139	10.3	5.6	13.5	>5
Birmingham	Parle *et al.*[24] (1990)	60+	41	59	1210	8.3	2.9	11.6	>5
U.S.A.	Bauer *et al.*[23] (1998)	65+	0	100	279	6.8	-	6.8	>5 .5
Rotterdam	A.E. Hak *et al.*[12] (2000)	55+	0	100	1149	10.8	-	10.8	>4.0
U.S.A.	Canaris *et al.*[14]	70-79	49	51	2799	3.9	-	11.1	>5.5
Colorado	Kanaya *et al.*[18] (2002)	18+	44	56	2336	9.5	-	-	>5.1

Goiter and Iodine Deficiency

Recent population studies have shown that about 12% of adults have a palpable goiter. (Usha Menon V;2009) Autoimmune thyroid disease is probably commoner than iodine deficiency as a cause of goiter in areas that are now iodine sufficient. However, given that iodine deficiency is a problem in India, the importance of iodine deficiency cannot be underestimated in the Indian context. The link between endemic goiter and iodine deficiency has been researched in India by several eminent researchers, and this has led to the publication of several important reports. (Karmarkar MG et al;1974, Sooch SS et al;2001, Pandav CS et al;1984) Critical research has resulted in endemic goiter being reported from all over the country and not just from the Himalayan and Sub-Himalayan regions. (Ambika Gopalakrishnan Unnikrishnan and Usha V Menon; 2011). Researchers from New Delhi had shown that this was linked to iodine deficiency and that this resulted in decompensated hypothyroidism in many cases. (Ambika Gopalakrishnan Unnikrishnan and Usha V Menon; 2011). This led to landmark studies which showed that iodine deficiency was associated with hypothyroidism in neonates, setting the scene for the now legendary salt iodization program supported by the Government of India. (Ambika Gopalakrishnan Unnikrishnan and Usha V Menon; 2011). Subsequent to this program, it was shown that in selected regions of Uttar Pradesh, the prevalence of congenital hypothyroidism had come down from 100/1000 to 18/1000. (Ambika Gopalakrishnan Unnikrishnan and Usha V Menon; 2011). Several landmark studies have been carried out in the area of iodine deficiency disorders in the country. (Karmarkar MG et al;1974, Sooch SS et al;2001, Pandav CS et al;1984)

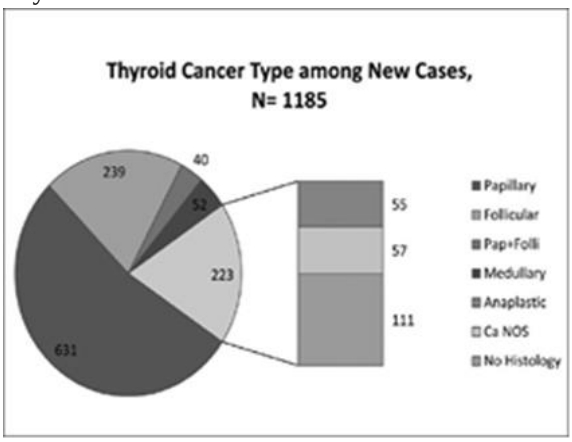
In the postiodization phase, what happens to the prevalence of goiter? This very important question was answered in an elegantly conducted study. (Marwaha RK et al;2003) About 14,762 children from all over India were studied for the following characteristics: goiter prevalence, urinary iodine and thiocyanate excretion, functional status of the thyroid, as well as serological and cytopathological markers for thyroid autoimmunity. About 23% of subjects had a goiter. A significantly higher level of median urinary thiocyanate (USCN) excretion was noted in goitrous subjects (0.75 mg/dl) when compared with controls (0.64 mg/dl; $P < 0.001$). The authors suggested that despite iodization, the prevalence of goiter has not dramatically declined. (Marwaha RK et al;2003) The researchers noted that thyroid autoimmunity could only partly explain the goiter and concluded that the role of goitrogens is an area that deserves further study.

Population studies have suggested that about 16.7% of adult subjects have anti-thyroid peroxidase (TPO) antibodies and about 12.1% have anti-thyroglobulin (TG) antibodies. In this same study of 971 subjects, when subjects with abnormal thyroid function were excluded, the prevalence of anti-TPO and anti-TG antibodies was 9.5% and 8.5%. (Usha Menon V;2009)

Autoimmune Thyroiditis in India

In a landmark study of Hashimoto's thyroiditis in India, 6283 schoolgirls from all over the country were screened. (Marwaha RK et al;2000) Among them, 1810 schoolgirls had a goiter. Among them 764 subjects underwent a fine needle aspiration cytology, and of these subjects, 58 (7.5%) had evidence of juvenile autoimmune thyroiditis (the term included both Hashimoto's thyroiditis and focal lymphocytic thyroiditis). Among fine needle aspiration cytology-confirmed cases of juvenile autoimmune thyroiditis, subclinical and overt hypothyroidisms were seen in 15% and 6.5%, respectively. (Marwaha RK et al;2000)

Thyroid Cancer and India



The Indian Council of Medical Research established the National Cancer Registry Program, and the NCRP has collected the data of more than 3,00,000 cancer patients between the periods 1984 and 1993. (Rao DN :1999).Among these patients, the NCRP noted 5614 cases of thyroid cancer, and this included 3617 females and 2007 males. The six centers involved in

the studies were at Mumbai, Delhi, Thiruvananthapuram, Dibrugarh, Chandigarh, and Chennai. Among them, Thiruvananthapuram had the highest relative frequency of cases of thyroid cancer among all cancer cases enrolled in the hospital registry, 1.99% among males and 5.71% among females. The nationwide relative frequency of thyroid cancer among all the cancer cases was 0.1%-0.2%. The age-adjusted incidence rates of thyroid cancer per 100,000 are about 1 for males and 1.8 for females as per the Mumbai Cancer Registry, which covered a population of 9.81 million subjects. The histological types of thyroid cancer were studied in a Hospital Cancer Registry of 1185 "new cases" of thyroid cancer. (Gangadharan P et al;1999). The commonest cancer type was papillary, followed by follicular cancer, and the results are summarized in Figure.

Reference Ranges of Thyroid Function in Pregnancy and Children

In the past 2 years, exciting work has been carried out to understand the thyroid in pregnancy and childhood in India. (Marwaha RK et al;2008,, Chakraborty et al;2010, Marwaha RK et al;2010) In the first article, Marwaha et al indicate the normal reference ranges of FT4, FT3, and TSH in pregnant women, and used the 5 th and 85 th percentile to define the reference ranges in the disease-free subjects. The authors report that the trimester-wise values in the first, second, and third trimesters were FT(3) (1.92-5.86, 3.2-5.73, and 3.3-5.18 pM/l), FT(4) (12-19.45, 9.48-19.58, and 11.32-17.7 pM/l), and TSH (0.6-5.0, 0.44-5.78, and 0.74-5.7 IU/ml), respectively. (Marwaha RK et al;2008) With regard to iodine deficiency during pregnancy, a hospital-based study from Kolkata has suggested that pregnant women from their center were iodine sufficient. (Chakraborty et al;2010)

In a large epidemiological study of 24,685 students from all over India published in 2010, the authors attempted to define normative data on thyroid hormone levels in healthy school children. (Marwaha RK et al;2010). Among them, the authors calculated the reference ranges from the 5343 subjects. In a separate publication in 2008, the same authors studied normative thyroid hormone ranges in 5122 school children, after excluding children who had a personal or family history of thyroid disease, used thyroid medications, had a goiter, and had hypoechogenicity/nodularity on ultrasound or positivity for serum anti-TPO antibodies. (Marwaha RK et al;2008) The authors reported that for TSH, the 97th percentile was in the range 6.01-8.4 mIU/l for boys and 5.28-8.04 mIU/l for girls. (Marwaha RK et al;2008) This, as the authors themselves suggest, offers a compelling argument against lowering the reference range of TSH in this population.

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