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Thyroid Disorders, Etiology and Prevalence

Alam Khan, M. Muzaffar Ali Khan and Shamim Akhtar

The major disorders (problems) of thyroid gland are hyperthyroidism and hypothyroidism, which have been reported in over 110 countries of the world with 1.6 billion people at risk and need some form of iodine supplementation. Usually hyperthyroidism is termed as thyrotoxicosis, but all hyperthyroidism may not represent thyrotoxicosis. Hyperthyroidism and hypothyroidism are due to over and under secretion of thyroid hormones. The most common causes of hyperthyroidism are diffused hyperplasia of the thyroid associated with Graves' disease, the ingestion of excess exogenous thyroid hormones, hyper functional multi nodular goiter and hyper function adenoma of thyroid. Less common causes of hyperthyroidism included certain forms of thyroiditis, thyroid stimulating hormone (TSH) secreting pituitary adenoma and the secretion of excessive amount of thyroid hormones by ectopic thyroid arising in ovarian tetramas. Hypothyroidism usually develops from iodine deficiency. However, in rare cases, it can also be a developed from chronic lymphocytic the thyroiditis, also known as Hashimoto's disease and from decreased TSH level. Iodine plays an important role in hyperthyroidism and hypothyroidism as iodine is an integral part of thyroid hormones. Availability of iodine to thyroid gland is mainly from foods and water and if these sources are deficient in iodine, then problems like hypothyroidism, cretinism and other iodine deficiency disorders can develop. Similarly, excessive iodine intake in the form of iodized oil, bread and salt can produce hyperthyroidism like iodine induced thyrotoxicosis. The prevalence of hyperthyroidism/ thyrotoxicosis and hypothyroidism vary in different countries. In Pakistan, the prevalence of hyperthyroidism and sub clinical hyperthyroidism was 5.1 and 5.8%, respectively. Similarly, the prevalence of hypothyroidism and sub clinical hypothyroidism was 4.1 and 5.4%, respectively. Prevalence of hyperthyroidism and sub clinical hyperthyroidism was higher in females than males. Similarly, the prevalence of hypothyroidism and sub clinical hypothyroidism was higher in females than males.

Key words: Thyroid problems, hyperthyroidism, thyrotoxicosis, hypothyroidism

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For further information about this article or if you need reprints, please contact:

Alam Khan
Department of Human Nutrition,
NWFP Agricultural University,
Peshawar, Pakistan

ANSInet
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Department of Human Nutrition, NWFP Agricultural University, Peshawar, Pakistan

Introduction

Thyroid problems (disorders) have been reported in over 110 countries of the world with 1.6 billion people at risk and need some form of iodine supplementation. Most of these are in developing countries, Asia, Africa and Latin America. In Pakistan about 20 million people live in iodine deficient areas, 8 million of them shows some form of iodine deficiency and at least 1 million have mental disorders (Anonymous, 1996). Thyroid disorders are due to abnormality in thyroid functions and enlargement of the thyroid gland. The major disorders of thyroid glands are over secretion (hyperthyroidism) and under secretion hypothyroidism) of thyroid hormones. Both situations lead to thyroid problems. Each thyroid problem has different manifestations and symptoms.

Thyroid hormones and their functions: Thyroid is a small gland, weighing 20-25 grams (Chandrasoma and Taylor, 1997). There are two thyroid hormones triiodothyronine (T_3) and thyroxin (T_4). Thyroxin is the major hormone secreted by the thyroid follicles. These two hormones are very much alike. Two tyrosine amino acids linked together to form these hormones. Triiodothyronine has three iodine atoms, whereas thyroxin has four iodine atoms (Elaine and Maieb, 1990). The normal thyroid gland produces about 7% triiodothyronine and about 93% thyroxin. However, the biological potency of T_3 is 3-5 fold greater than that of T_4 (Guyton and Hall, 1996). The hypothalamus produces a tripeptide-releasing hormone (TRH), which stimulates the production of TSH. Thyroid stimulating hormone also known as thyrotropin, an anterior pituitary hormone regulates the release and synthesis of triiodothyronine and thyroxin (Guyton and Hall, 1996). When circulating thyroid hormones levels falls below normal, the pituitary secretes TSH. This, in turn, acts on the thyroid gland to produce and release more thyroid hormones. When the levels of these hormones rise above normal, TSH secretion is decreased, causing the thyroid gland to decrease production and secretion of the thyroid hormones.

Abnormalities in TSH concentrations occur in various thyroidal and non-thyroidal diseases. Serum TSH is raised in primary hypothyroidism in which T_3 and T_4 are low. But in mild hypothyroidism T_4 may be normal but TSH will be raised (Evered *et al*., 1973). In hyperthyroidism T_3 and T_4 are elevated and TSH is suppressed due to negative feedback mechanism. (Caldwell *et al*., 1985). Except for the adult brain, spleen, testes, uterus, and the thyroid gland itself, thyroid hormones affects virtually every cell in the body. Generally, they stimulate enzymes concerned with glucose oxidation and increase the basal metabolic rate and body heat production. The thyroid hormones promote growth and development of the brain during fetal life and for the first few years of postnatal life (Elaine and Maieb, 1990). The basal metabolic rate is increased as much as 60 to 100% above normal when large quantities of the hormones are secreted. The rate of utilization of foods for energy, rate of protein synthesis and rate of protein catabolism are also increased. The mental processes are excited and the activity of many other endocrine glands is often increased. Hyperthyroidism causes excessive skeletal growth in children, making them considerably taller. On the other hand, hypothyroidism greatly reduces the growth rate in children. These children will remain mentally deficient throughout the life, if thyroid therapy is not given within days or weeks after birth. Besides these, the thyroid hormones have their specific effects on other body mechanisms (Guyton and Hall, 1996).

Role of iodine in thyroid problems: Iodine plays an important role in hyperthyroidism, thyrotoxicosis, hypothyroidism and other iodine deficiency disorders. As iodine is an integral part of thyroid hormones so, its availability to the thyroid gland affects the production of the thyroid hormones. Iodine is mainly available through food, water and if these sources are deficient in iodine, then iodine supplementation in the diet is required. If food and water are deficient in iodine and the element is not supplemented, hypothyroidism problems like cretinism and other iodine deficiency disorders can develop. Similarly excessive iodine intake in the form of iodized oil, bread and salt can produce hyperthyroidism /thyrotoxicosis like iodine induced thyrotoxicosis. Rapid introduction of even ordinary amount of iodine to a severely deficient population has induced hyperthyroidism in older population with nodular goiter (Anonymous, 1996).

Similarly, in coastal and plain areas, the intake of iodine is usually higher than the intake of iodine in the mountain regions. Also, iodine rich compounds are used as disinfectant in the milk processing plants and in water storage tanks, which may increase iodine content in milk and drinking water. In livestock, feed ingredients may also contains iodine, which may enhance iodine in the consumer's food. The amount of iodine mixed in the salt by commercial salt producers is highly variable. Some salt producers add it abundantly without knowing the exact amount needed to be mixed and some do not add at all. Generally, salt producers do not have even proper mixing arrangement. So, it is feared that the total intake of iodine may be less or more than the normal for some people.

Human beings can tolerate high levels of iodine, however, some individuals are sensitive to high iodine levels and when these individuals are given iodine in greater amount, they may develop untoward reactions. Therefore, iodine supplementation is contra-indicated in individuals, who are sensitive to higher intakes of iodine and in those who are suffering from thyrotoxicosis (Welt and Blythe, 1970). Like human, iodine deficiency also affects growth and development of animals. Reproductive failures, birth of weak, dead, or hairless young's have been noted in goitrous areas. Iodine supplementation has greatly reduced the prevalence of iodine deficiency disorders in both human and animals in developed countries (Mannar and Dunn, 1995). Iodine is essential for normal synthesis of the thyroid hormones. So the knowledge of iodine distribution in nature, its metabolism, its recommended daily allowances and its supplementation will help to understand the problems of the thyroid hormones.

Recommended daily allowances of iodine: The nutritional requirements of iodine depends on growth, body weight, sex, age, nutrition, climate and disease. For a normal adult, 150 μg of iodine is required daily, about 50 mg each year and one teaspoon of iodine for the whole life, to manufacture adequate quantities of thyroid hormones. The intake of iodine in the range of 50-1000 μg is considered as safe for a normal individual (Matovinovic, 1984). Iodine requirement for children increases with age. The minimum mean requirements of iodine for normal individuals in different age groups are given in Table 1 (Anonymous, 1993).

Table 1: Recommended daily intake of iodine.

Age	Intake (μg day^{-1})
0-6 months	40
6-12 months	50
1-10 years	70-120
11 years -adulthood	120-150
Pregnancy	175
Lactation	200

Hyperthyroidism: Hyperthyroidism is usually referred to a raised level of circulating thyroid hormones. The elevated level of circulating thyroid hormones is due to endogenous or exogenous reasons. The endogenous reasons of hyperthyroidism are the abnormalities developed with in thyroid gland like autoimmunity against the thyroid cells that stimulate over secretion of thyroid hormones. Graves' disease and certain kinds of adenoma in the thyroid glands are the example of endogenous reasons. The exogenous reasons for hyperthyroidism includes ingestion of excessive amount of thyroid hormones and intake of excessive amount of iodine. Usually hyperthyroidism is termed as thyrotoxicosis, but all hyperthyroidism may not represent thyrotoxicosis. It is the most common endocrine disease of middle age. In hyperthyroidism/thyrotoxicosis, entire thyroid gland is

hyperplastic and is increased 2-3 times normal size. Each cell increases its rate of secretion of hormones by 5-15 times more than the normal secretion. Low or almost zero plasma TSH concentration has been observed. Symptoms of hyperthyroidism/thyrotoxicosis are weight loss even with increased hunger, weakness, tremors of hands, increased heart rate, nervousness, goiter, loose stools, irritability and anxiety, bulging eyes (exophthalmos), increased sweating and intolerance of heat and warm and moist skin. (Guyton and Hall, 1996; Chandrasoma and Taylor, 1997; Mann *et al.*, 1995). Thyrotoxicosis is hypermetabolic state caused by the elevated circulating levels of free T_3 and T_4. Because it is mostly caused by hyperfunction of the thyroid gland, it is often referred to as hyperthyroidism. However, in certain conditions, like in some types of thyroiditis, the high concentration of the hormones is related to excessive release of preformed thyroid hormones and not hyperfunction of the gland. So, strictly speaking, hyperthyroidism is only one category of thyrotoxicosis. The term primary and secondary hyperthyroidism are some time used to designate hyperthyroidism arising from an intrinsic thyroid abnormality, and that arising from disorders outside of the thyroid, such as TSH secreting pituitary tumor but the latter is uncommon.

The most common causes of hyperthyroidism are diffused hyperplasia of the thyroid associated with Graves' disease, the ingestion of excess exogenous thyroid hormones, hyperfunctional multinodular goiter and hyperfunction adenoma of the thyroid. Less common causes of hyperthyroidism include certain forms of thyroiditis, TSH secreting pituitary adenoma and the secretion of excessive amount of thyroid hormones by ectopic thyroid arising in ovarian tetramas (Kumar *et al.*, 1997). In Graves' disease, antibodies are formed against thyroid to produce abnormally high levels of thyroid hormones, making normal feed back mechanism inefficient, that should otherwise slows down the thyroid secretion (Suarez, 1997). Immunoglobulin antibodies acting like TSH have been noted in the blood of 50-80 % thyrotoxic patients. These antibodies develops as a result of autoimmunity against thyroid tissues. Genetic factors are also involved since both Graves' disease and Autoimmune thyroiditis occur among the members of the same families (Foley, 1992). Excessive iodine ingestion also induces hyperthyroidism or thyrotoxicosis in iodine deficient individuals. This toxic effects of iodine is known as iodine induced thyrotoxicosis (IIT) or Jod-basedow. This is more common in old age (above 40 years) that has been iodine deficient since birth. It can be totally prevented in the next generations by correcting iodine deficiency (Anonymous, 1997).

In iodine induced hyperthyroidism (IIH) mutational events occur in thyroid cells, making them autonomous. When these cells become sufficient and iodine supply is increased, the subject becomes thyrotoxic (Stanbury *et al.*, 1998). Hashimoto's thyroiditis is a painless defuse enlargement of thyroid gland in young or middle aged women. It is also known as lymphocytic thyroiditis, chronic thyroiditis and autoimmune thyroiditis (DeGroot and Stanbury, 1975). Increased prevalence of Hashimoto's thyroiditis has been observed in iodine deficient areas, where iodine supplementation has been introduced (Gaitan, 1975; McColahey, 1972; Perinetti *et al.*, 1971; Weaver *et al.*, 1966; 1969). Causative factors in the development of Hashimoto's thyroiditis may be thyroid hyperplasia (induced by iodine deficiency) and iodine repletion or excess . Hashimoto's thyroiditis is believed to be autoimmunity against the thyroid. Most of the patients have autoantibodies in their serum. Lymphocytic infiltration of thyroid gland destroys thyroid cells. However, most patients are euthyroid or mild hypothyroid and rarely hyperthyroid (Chandrasoma and Taylor, 1997). Hyperthyroidism/thyrotoxicosis can also occur after using iodine-containing topical antiseptics, medicines, or diagnostic materials such as radio contrast dyes, water purification tablets, various vitamin preparations, iodine containing kelp, and amiodarone (Anonymous, 1998). Hyperthyroidism/thyrotoxicosis is also due to localized adenoma (a tumor) that develops in the thyroid tissue and secretes large quantities of thyroid hormones (Guyton and Hall, 1996).

Prevalence of hyperthyroidism/thyrotoxicosis: Thyrotoxicosis is not a common condition in Pakistan. However, cases of Hyperthyroidism/thyrotoxicosis have been reported in patients with thyroid related problems. For better health care planning, the knowledge of prevalence of the disease and its relation with iodized salt intake and the thyroid hormone levels is important. To study the pattern of thyroid diseases, 373 thyroid patients, reported to an endocrine clinic in Ethiopia, were investigated. Thyrotoxicosis was observed in 43.9% of the patients followed by euthyroid solitary nodules (23.6%) and simple goiter (22.3%). Euthyroid multinodular goiter was seen in 6.7%. Graves' disease was the main cause (41.7%) of thyrotoxicosis followed by toxic multinodular goiter (31.9%), toxic solitary nodule (22.1%), Basedow's goiter (3.1%) and thyroiditis (1.2%) (Mengistu, 1993). Hyperthyroidism/thyrotoxicosis was also observed in Zimbabwe, after salt iodization. A 10 fold increase in urinary iodine concentration (from 20 $\mu g\ L^{-1}$ in 1983 to 283 $\mu g\ L^{-1}$ in 1994) was observed. The number of patients coming with toxic nodular goiter increased after iodization and most of them were above 40 year old (Anonymous, 1998). Kelly (1960), also observed mortality due to thyrotoxicosis during 1931-1940 in Britain. The disease was highest in areas of endemic goiter. He concluded that increase in dietary intake of iodine benefited the young population but induced thyrotoxicosis in older subjects. In Michigan, Miller and Block (1970), studied thyroid function in 70 subjects with large multi-nodular goiters. They concluded that gradual increase in autonomous tissues with age led to transition from euthyroid to hyperthyroid state.

Iodine excess is toxic and may lead to thyrotoxicosis. Families with the history of thyrotoxicosis should avoid unnecessary iodine supplementation in their diets. Many workers have suggested that a normal healthy individual must not take iodized salt until and unless prescribed by a doctor (Kelly, 1960; Anonymous, 1998). Gomez *et al.* (1993) conclude a six years study of 110 patients with thyroid nodular disease. They found an incidence of 0.4 per 1000 population per year. Out of 110 patients, 58.2% had hyperthyroidism (53.1% of which were T_4 thyrotoxicosis, 12.5% T_3 thyrotoxicosis, and 34.4% had subclinical hyperthyroidism) and 8.2% of patients had iodine induced hyperthyroidism. Lavard *et al.* (1994) confirmed thyrotoxicosis in 56 (48 girls and 8 boys) children under 15 years of age in Denmark, during the years 1982-1988. The prevalence rate of thyrotoxicosis was 0.79/100,000 population. They considered thyrotoxicosis a rare problem, which increased with age. Female showed higher tendency (6.7:1) of hyperthyroidism in the study.

Galofre *et al.* (1994) studied thyrotoxicosis before and after dietary iodine supplementation in Vigo, Span. After the introduction of mandatory iodized salt, the prevalence of thyrotoxicosis was increased in the area and it was more prevalent in women than man. Wolff (1969) studied the prevalence of dietary iodine induced goiter in Hokkaido, an Island of Japan. The residents of the Island were consuming large amounts of iodine-rich seaweed. He reported that the prevalence of iodine induced goiter was 6 to 12% among the coast dwellers of the Island. Fisher and Carr (1974) did not find any increase in the prevalence of iodine toxicity or hypersensitivity due to increased ingestion of iodine.

Connolly (1971, 1973), Stewart *et al.* (1971) and Vidor *et al.* (1973) have reported iodine-induced thyrotoxicosis in Tasmania, Australia. Iodine supplementation of bread in Tasmania was initiated in 1966 to correct moderate iodine deficiency. After iodine supplementation they observed an increase in the prevalence of thyrotoxicosis in the area. They further noted that the increase in the prevalence of thyrotoxicosis involved primarily middle-aged to older individuals, who lived in iodine deficient sections of Tasmania and had histories of long standing nodular goiters. They suggested that iodine was a regulator of thyroxine production in the autonomous tissues and that increased dietary intake resulted in increased hormonal production. They concluded that because of the development of autonomous tissue was correlated with aging, a population with a significant number of individuals of 40 to 50 years old or above could be at risk of epidemic thyrotoxicosis if

iodine intake was increased. A prospective study of 242 patients with non-toxic nodular goiter was conducted in an area with normal iodine intake. The high prevalence of subclinical hyperthyroidism (75%), in patients with clear cut autonomous areas, were observed. The patients without autonomous tissues had low subclinical hyperthyroidism (17.2%). This indicates a relationship of high prevalence of subclinical hyperthyroidism with autonomous tissues (Rieu *et al.*, 1993).

Autoimmune thyroiditis (Hashimoto's disease) also occurs in areas of iodine deficiency after iodine supplementation in susceptible individuals. Foley (1992) observed that the disease was less common in susceptible individuals, who lived in the regions with dietary iodine deficiency. The autoimmune disease particularly thyroiditis increased after the therapeutic administration of iodized salt, bread and oil. Lymphocytic infiltration of the thyroid occurred after dietary iodine supplementation. Thyroid antibodies were not detected in serum from patients with endemic goiter, but 43% subjects became positive after therapy with iodized oil and hyperthyroidism developed. Also these medication and diet containing iodine increased the frequency and severity of autoimmune thyroid diseases. Thyrotoxicosis had also been observed during the treatment of goiter with lugol's iodine. Iodine was found to be a sole source of thyrotoxicosis (Paindakhel *et al.*, 1980). Oakley (1973) reported enlargement of thyroid after prolonged use of drugs such as lugol's and hydroxyquinoline iodine. Roti *et al.* (1993) also noted that thyrotoxicosis after ingestion of amiodarone, which is an iodine rich drug.

Braverman *et al.* (1971), found that iodide goiter, with or without hypothyroidism could occurs in patients on prolonged treatment with iodide or iodide-generating compounds. Iodide goiter could be developed in normal individuals, whose diets contain excessive amounts of iodine. Excess iodine in medication caused iodine induced thyrotoxicosis in ten patients, who were euthyroid with no thyroid abnormalities before taking iodine-containing drugs. However, after cessation of iodine medication, they returned to euthyroid status (Savoie *et al.*, 1975). Thyrotoxicosis has been reported after an oral dose of 180 mg of potassium iodide daily for eight to ten weeks in four out of eight non-toxic goiter patients who lived in the Boston, Massachusetts area where concentration of iodine in the diet was sufficient. Large doses of iodine are therefore not advisable to patients with goiter or any thyroid disease except in known iodine deficiency (Vagenakis *et al.*, 1972). Livadas *et al.* (1977) noted progressive increase in the serum T_4 level of the patients having toxic adenoma after giving potassium iodide. In Bangladesh pregnant rural women were examined to determine the contributing factors of goiter before instituting iodine supplementation. Total goiter prevalence was 99%. Urinary iodine levels indicated only moderate iodine deficiency. Dietary factors, which contributed to goiter, were not found. They concluded that higher goiter prevalence can occur even in the absence of severe iodine deficiency and iodine supplementation may not completely solve the community goiter problem (Filteau *et al.*, 1994).

Recently Akhtar *et al.* (2001) determined the frequencies of thyroid problems in different age groups, sex and indifferent seasons. They reported that hyperthoidism and subclinical hyperthyroidism in all age groups were 5.1 and 5.8%, respectively. Prevalence of hyperthyroidism was higher in females (3.85) than males (1.2%). Prevalence of subclinical hyperthyroidism was also higher in females (4.3%) than males (1.5%).

Hypothyroidism: Hypothyroidism stands for the low level of circulating thyroid hormones. Like hyperthyroidism, the low circulating level of thyroid hormones in hypothyroidism is also due to endogenous or exogenous reasons. The endogenous reason is again autoimmunity developed against the thyroid gland, but in this case destruction of the gland occurs rather than stimulation. Hashimoto's disease is the example of hypothyroidism due to endogenous reasons. The exogenous reason for hypothyroidism is the low intake of iodine. The endemic goiter is an example of hypothyroidism due to exogenous reason (Guyton and Hall, 1996). Hypothyroidism is a condition where the thyroid gland is not producing enough hormones. The thyroid gland needs iodine for normal production of thyroid hormones. When iodine is not available to the thyroid gland, hypothyroidism will develop. Hypothyroidism usually develops from iodine deficiency. However, in rare cases, it can also be developed from chronic lymphocytic thyroiditis, also known as Hashimoto's disease and from decreased TSH level. The decreased TSH level may results due to the defects in pituitary gland and due to administration of antithyroid drugs.

The individual, in early stage of iodine deficiency, feels tiredness, weakness, constipation, dry and coarse skin, intolerance to cold, reduced and slow metabolic rate (Suarez, 1997). The most common psychological symptom with hypothyroidism is depression (Gadde and Krishnan, 1994). These symptoms were observed in almost all the patients with severe hypothyroidism (Haggerty and Prange, 1995). When iodine deficiency remains for a long time, the thyroid gland cannot manufacture thyroid hormones. This leads to increase production of TSH by anterior pituitary gland. In efforts to get iodine from the blood TSH continuously stimulates the thyroid gland, which results in increase in size to as large as 300-500 grams or more. In some areas of the world, insufficient iodine is present in soil and water and hence food, and feeds grown on that soil are deficient in iodine. So, people residing in those areas do not get enough iodine and develop large goiter called endemic goiter (Stanbury and Hetzel, 1980).

When the hormones deficiency occurs during adulthood, myxedema is developed. Myxedema is characterized by edematous appearance throughout the body (Guyton and Hall, 1996). Rough skin, hoarseness of voice (also observed in children in severe hypothyroidism), and cardiac enlargement are commonly observed in myxedematous patients (Chandrasoma and Taylor, 1997). Causes of myxedema are Hashimoto's, Autoimmune thyroiditis, where the thyroid tissue are destroyed by the autoimmunity, decreased TSH levels due to a defect in the pituitary gland, administration of antithyroid drugs or ablation of the gland by surgery and failure of thyroid hormones synthesis due to extreme dietary iodine deficiency (Chandrasoma and Taylor, 1997). Severe hypothyroidism during fetal life and infancy is called cretinism, and prompt diagnosis soon after birth can prevent its severe effects. In areas of wide spread iodine deficiency, it is called as endemic cretinism. Cretinism could be developed because of failure of thyroid development, failure of hormones synthesis due to severe iodine deficiency, failure of hormones synthesis due to dietary goitrogen and failure of hormones synthesis due to autosomal recessive enzyme deficiency (sporadic cretinism). The child with cretinism has a short, stocky body, a thick tongue and neck, and is mentally retarded. This condition is not reversible and should be prevented before occurrence (Elaine and Maieb, 1990).

A condition called iodide goiter with or without hypothyroidism is developed after chronic use of excess iodide or iodide containing compounds (Braverman *et al.*, 1971; Wolff, 1969). Enlarged goiter has been reported in school age children in four cities of America, having adequate intake of iodine. The prevalence of iodide goiter was 5-10% (Stanbury *et al.*, 1980). Iodide goiter is common in patients with respiratory diseases. However, it is reported rarely and associated with the presence of thyroid dysfunction (Larsen and Ingbar, 1992).

Diffused and multinodular goiter are not common. These are not endemic goiters caused by ingestion of substances interfering with thyroid hormones synthesis. These are caused by inborn enzymatic defects. However, in most cases, causes are not known. Sometimes, both of these goiters are considered as different stages of the same pathological process. Diffused goiter is symmetrical with diffused radio uptake, while multinodular goiter is asymmetrical with irregular uptake (Kumar *et al.*, 1997). Deficiency of iodine in soil and thus in foods is the major cause of hypothyroidism. Deficiency usually occurs during growth periods, when inadequate iodine is supplied in the diet. Pregnant mothers and baby before and after birth are affected. In chronic lymphocytic thyroiditis also known as Hashimoto's disease, the thyroid hormones production is decreased due to destruction of

thyroid cells. Removal of thyroid gland for treatment of cancer and partial thyroidectomy in hyperthyroidism can make the patient hypothyroid. Inflammation of the thyroid during pregnancy, viral illness and goitrogenic substances found in some plants such as cassava, turnip, cabbage, rape seeds, mustard and in drinking water can develop goiter (Matavonovic, 1984). Some antithyroid drugs used for treatment of hyperthyroidism for instance propylthiouracil, thiocynates and high concentration of inorganic iodide can cause goiter (Guyton and Hall, 1996). Hypothyroidism can occur due to pituitary failure (secondary hypothyroidism), but is uncommon (Chandrasoma and Taylor, 1997). Inborn errors of iodine metabolism, increase production of TSH, defects of thyroid hormone receptor, malignancy and autoimmunity of the thyroid gland are rare causes of goiter. More than 90% of the patients with goiter are iodine deficient. Untreated thyroid diseases can produce serious effects in other parts of the body (Jockenhovel and Olbricht, 1993).

Prevalence of hypothyroidism: Hypothyroidism, which is the most common manifestation of iodine deficiency, is very common. The prevalence of Hypothyroidism in some areas reaches from 5-15% of the population. In North West Frontier Province of Pakistan, 70% of the rural and above 50% of the urban population is facing iodine deficiency disorders (IDD). According to a survey conducted in the public schools of Peshawar, the prevalence of initial stage goiter in children of under 10 year of age was 59% (The News, 1995). In Kalam and North Kalam, the prevalence of palpable goiter was reported as 21.18% in the 5-11 years age group (Paindakhel, 1981). Iodine Deficiency Disorders is a big problem in NWFP, generally in Hazara and Malakand division, and specifically in Chitral district (Malik, 1993). Severe iodine deficiency was also reported in Islamabad where goiter prevalence in school children was 62.1%. The children examined clinically having goiter of grade-1 and grade-2 were 39.27% (Zaffar, 1994). In areas of endemic goiter and cretinism in Southern China occult impaired hearing was found due to severe iodine deficiency in 120 apparently normal school children 7 to 11 years old and was corrected by iodized salt (Wang and yang, 1985). Chiovato *et al.* (1994) reported transient neonatal hypothyroidism due to iodine deficiency in the Third world, Europe and particularly in Italy.

Mengreli *et al.* (1994) reported that in Greece, 1979, 1274000 neonates were screened and 377 cases of congenital hypothyroidism were detected. The occurrence of congenital hypothyroidism was different from North and South. Shankar *et al.* (1994) carried out a prospective study in an environmentally iodine deficient area of North India to find a cause of hypothyroidism in children. The group was consisted of 45 children with mean age of 4-5 years. They reported that significant growth retardation in 54% of children below 5th percentile of India standard. The concentration of serum T_4 was significantly low and dysgenesis of the thyroid was the most common type of childhood hypothyroidism in iodine deficient endemias.

Akhtar *et al.* (2001) has reported 4.0% hypothyroidism and 5.4% subclinical hypothyroidism in thyroid patients in Pakistan. They reported 1.3% hypothyroidism in males and 2.75 in females. Similarly, they reported 1.5% subclinical hypothyroidism in males and 3.9% in females. Foo *et al.* (1994) conducted a survey of 974 villagers in the Lemanak and Ai river villages of Sarawak to know the prevalence of goiter. According to the degree of iodine deficiency in the soil, the high prevalence (36.9%) was observed in the more interior Ai river area than Lemanak river (26.5%). Also the prevalence was high in young women than older (75.4 vs 49.1%). The median urinary iodine excretion for the Ai river villagers was also low (22.1 μg L^{-1}) as compare to Lemanak river subjects (72.9 μg L^{-1}). Iodine deficiency can be easily prevented by iodination of irrigation water. This method has been applied in Southern Xinjian province, China and has increased the iodine content of soil crops, animal and human beings. Median urinary iodine excretion in children increased from 18 to 49 μg L^{-1}. Iodination of water is an advantageous and cost effective method and may be useful in other areas (Cao *et al.*, 1994). Iodine deficiency has been documented in British before the second world war. But its prevalence was reduced accidentally after the war due to large consumption of milk and dairy produce contaminated with iodine. This was the main reason for this decline.

Iodine supplementation: Iodine supplementation is the only way to prevent iodine deficiency disorders (IDD). As iodine cannot be stored for a long period in the body, it must be supplied regularly in the diet. The iodization of salt is the most common, long-term method of iodine supplementation. As this method takes time for full implementation, iodized oil in the form of capsules is recommended for short time intervention in areas of severe iodine deficiency. In the past various other food items such as bread, sweats, milk, sugar and water were tested as vehicles for iodine supplementation. But salt has become the most commonly accepted because of its universal consumption by almost all section of community irrespective of economic level and used throughout the year (Mannar and Dunn, 1997). Due to dangerous effects of iodine deficiency, the government of Pakistan is trying to eliminate IDD through universal salt iodization. For this purpose National Assembly has approved legislation in 1995, through which iodization of table salt is mandatory for all manufacturers. The recommended concentration of iodine usually in the form of sodium iodide or iodate is 70 ppm. But according to a research study the iodized salt does not contain the recommended levels of iodine (Anonymous, 1998).

Syrenicz *et al.* (1993) conducted a study in children of 6 to 13 years old to find salt consumption, urinary iodine concentration and incidence of goiter in four districts of North-West Poland. They reported that only 11.2% of children consumed iodized salt. Mean iodine concentration in children consuming and not consuming iodized salt was 76.2 μg L^{-1} and indicating mild deficiency of iodine. The incidence of goiter was found 12.9%. In Tuscan Appennines, Italy, the efficacy of iodized salt was determined in 1981 and 10 years later 1991. In 1981, mean urinary iodine excretion was 47.1 $\pm$ 22.4 mg Kg^{-1} creatinine and goiter prevalence was 60%. While in 1991 mean urinary iodine excretion increased to 129.7 $\pm$ 73 mg Kg^{-1} creatinine and goiter prevalence dropped to 8.1% (Lombardi, 1993).

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