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On

MULTINODULAR GOITRE

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CERTIFICATE

This is to certify that **"MULTINODULAR GOITRE"** is a bonafide work done by **Dr. B. ROHIT**, Post Graduate Student, Department of General Surgery, Kilpauk Medical College, Chennai - 10 under my guidance and supervision in fulfillment of regulations of The Tamilnadu Dr. M.G.R. Medical University for the award of M.S. Degree Branch I, (General Surgery) during the academic period from March 2003 to February 2006.

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CONTENTS

INTRODUCTION

Multinodular goitre is a frequently encountered problem in the surgical wards. Quite a large number of our patients reach us at a stage where the goitres are frequently massive, having perhaps contacted their private physicians, who are likely to have reassured them as to the relatively benign clinical course.

Multinodular goitres remain fairly heartening to treat, with the availability of a large number of skilled doctors to treat the disease with the least morbidity.

Controversy, however, does exist as to the best method to treat multinodular goitres adequately, especially in patients with toxic symptoms. The present study is an attempt to establish the incidence, analyse the symptomatology, modes of treatment and results in our patients.

The aim was to study the following objectives in patients admitted with a diagnosis of multinodular goiter.

AIM OF STUDY

The aim was to study the following objectives in patients admitted with a diagnosis of multinodular goiter at Government Royapettah Hospital, Chennai.

- To establish the incidence and the age preponderance.
- To estimate percentage of patients presenting with toxicity.
- To estimate the incidence of compressive symptoms.
- To analysis the sensitivity and specificity of fine needle aspiration cytology.
- To study the incidence of complications following subtotal thyroidectomy.

REVIEW OF LITERATURE

Goitre is a worldwide disease and can be sporadic or endemic, the endemic variety being particularly high in alpine areas where glacial action has leached iodine from the soil and carried it away to the sea. These endemic goitres are rarely seen in the coastal areas.

The multinodular goitre, on the often hand, occurs sporadically and tends to affect middle aged women. It may represent an acquired defect due to aging. Many multinodular goitres develop from simple goitres, especially if Iodine intake or availability is compromised. The initial diffuse hyperplastic process then becomes localized to one or several areas of disorganized thyroid metabolism in which the hyperplastic acini undergo colloid involution, while others show haemorrhage, cystic degeneration or necrosis. Fibrosis and calcification may then supervene.

Patients with longstanding multinodular goitres often develop thyrotoxicosis, the exact incidence of which is variable. Excess thyroid hormones may be produced by the nodules themselves, by the paranodular tissue or by a combination of both. Eye signs are usually absent and cardiac arrhythmias and cardiac failure are more common than in Graves disease.

APPLIED ANATOMY

The thyroid is the largest endocrine organ,weighing approximately 30 gms in average Indian adults. The potential for growth is however enormous.

The normal thyroid is made up of 2 lobes joined by a thin band of tissue, the isthmus. The latter is approximately 0.5 cm thick, 2 cm wide, 2 cm high. The individual lobes have a pointed superior pole and a poorly defined inferior pole merging medially with the isthmus. Each lobe is approximately 2 cm in thickness and 4 cm in length. Occasionally, a pyramidal lobe is discernible as a finger - like projection directed upwards from the isthmus, generally just lateral to the midline, usually on the left. The right lobe is normally more vascular than the left, is often the larger of the two, and tends to enlarge more in disorders associated with a diffuse increase in size. The lobes extend m the middle of thyroid cartilage above to the sixth tracheal ring below. Each lobe fills the space between the trachea and oesophagus medially and carotid sheath laterally. A strong condensation of an avascular connective tissue, known as the suspensory ligament of Berry, binds the gland firmly to h side of the cricoid cartilage. It is this ligament together with the tracheal fascia, which splits to invest the gland, which makes the thyroid move up and down on swallowing. The fascia, which is the false capsule, sends fibrous septa into the gland substance, dividing it into numerous lobules. Each lobule consists of 30 to 40 follicles that contain colloid.

The vascular supply is via two paired arteries; a third vessel occasionally supplies the lower pole of one or other lobe. The superior thyroid artery, the first branch of external carotid artery runs downward on the inferior constrictor

to reach the apex of the lateral lobe. The inferior thyroid artery arises from the thyrocervical trunk. Unnamed vessels arise from the oesophagus and trachea including the thyroidea ima artery, which may pass up from the aorta or brachiocephalic artery.

The venous drainage is prone to variation. The superior thyroid vein: drains into the internal jugular vein. The inferior thyroid vein drains into the internal jugular vein or the brachiocephalic veins in the anterior mediastinum. The middle thyroid vein drains into the internal jugular vein.

The lymphatic drainage from the upper part of the gland reaches the upper deep cervical lymph nodes either directly or through the prelaryngeal nodes. Lymph from the lower part of the gland drains into the lower deep cervical nodes directly, and also through the pretracheal and paratracheal nodes. G.Scott Williamson has described a very definite system of lymph vessels which leaves each lobe at the point of entrance of inferior thyroid artery, and passes directly into the lymph spaces of thymus.

Important Anatomical Relationships

1. Recurrent Laryngeal Nerves

The vagus, after entering the mediastinum, gives off the recurrent laryngeal nerve which returns to the neck after circling around the arch of aorta on the left and the right subclavian artery on the right, ascending in the tracheo-oesophageal groove. It enters the larynx posterior to cricothyroid articulation passing under or through Berry's ligament. The nerve may be non-recurrent in 0.25% cases and will be vulnerable to damage if the inferior thyroid arteries are routinely ligated laterally. The nerve supplies all the

intrinsic muscles of larynx. At the level of upper border of isthmus, the nerve often divides into two. The anterior larger branch is the motor branch, and the posterior branch is only sensory to the larynx below the level of vocal cords.

2. The Superior Laryngeal Nerve

This nerve arises from the inferior ganglion of vagus and divides at the level of thyroid into a large internal laryngeal nerve, and a smaller external laryngeal nerve, which runs close to the superior thyroid artery. It supplies the cricothyroid, which is the tensor of the ipsilateral vocal cord.

3. Parathyroid Glands

There are four parathyroids. The upper pair are situated above and medial to where the recurrent laryngeal nerve courses the inferior thyroid artery. The lower pair are situated within a 2 cm radius of the lower pole below and medial to the level where the recurrent laryngeal nerve crosses the inferior thyroid artery.

PHYSIOLOGY

The thyroid produces three hormones,, Thyroxine (T_4), Tri -Iodothyronine (T_3) and calcitonin. T_4 & T_3 are both stored in colloid, consisting primarily of thyroglobulin, which is an iodinated glycoprotein. Thyroglobulin stores are dependent on adequate dietary intake of iodine which is essential for T_4, T_3 synthesis. Iodine is derived from milk and dairy products with a small quantity coming from salt water fish and iodized salt. Iodides are absorbed by the stomach and upper gastrointestinal tract. Approximately one - third is trapped by the thyroid gland. A cytochrome reductase system generates a peroxidase enzyme which oxidizes the iodide to an active form. The activated iodide is bound covalently to tyrosine or monoiodotyro sine. Anti thyroid drugs prevent the iodide becoming trapped by inhibiting the peroxidase system within the thyroid.

The release of thyroid hormones from the colloid begins when the microvilli on the surface of thyroid cells engulf droplets of colloid. These then fuse with the lysosomes containing proteolytic enzymes, which hydrolyze the colloid. The iodotyrosines are rapidly converted to iodide and thyroxine, which enters the blood stream via the thyroid capillaries. A small quantity of

unhydrolyzed thyroglobulin returns to the circulation via the thyroid lymphatic system. The iodide released from the thyroid contributes to a much larger circulating iodide pool than the dietary iodide pool.

Thyroid stimulating hormone (TSH) produced by the thyrotrophic cells of the anterior pituitary control the complex enzymatic reactions that trap iodine,'convert it into T, T, and release them into circulation. When T3 & T, levels rise above the normal range, TSH production is shut down by a negative feedback. Release of TSH is regulated by thyrotrophin releasing hormone (TRH), which is produced by the hypothalamus.

The role of calcitonin is unclear. It may be involved in the regulation of plasma calcium and phosphate concentration.

FUNCTIONS OF THE THYROID HORMONES IN THE TISSUES

The Thyroid Hormones Increase the Transcription of Large Numbers of Genes.

The general effect of thyroid hormone is to cause nuclear transcription of large numbers of genes. Therefore, in virtually all cells of the body, great numbers of protein enzymes, structural proteins, transport proteins, and other substances increase. The net result of all this is a generalized increase in functional activity throughout the body.

Conversion of Thyroxine to Triiodothyronine and Activation of Nuclear Receptors. Before acting on the genes to increase genetic transcription, almost all the thyroxine is deiodinated by one iodide ion, thus forming triiodothyronine. This in turn has a very high binding affinity to the

intracellular thyroid hormone receptors. Consequently, about 90 per cent of the thyroid hormone molecules that bind with the receptors is triiodothyronine, and only 10 per cent, thyroxine.

The thyroid hormone receptors are either attached to the DNA genetic strands or in proximity to them. On binding with thyroid hormone, the receptors become activated and initiate the transcription process. Then large numbers of different types of messenger RNA are formed, followed within another few minutes and hours by RNA translation on the cytoplasmic ribosomes to form hundreds of new types of proteins. However, not all proteins are increased by similar percentages - some only slightly and others at least as much as sixfold. lt is believed that most, if not all, of the actions of thyroid hormone results from the enzymatic and other functions of these new proteins.

Important Types of Increased Cellular Metabolic Activity

The thyroid hormones increase the metabolic activities of all or almost all the tissues of the body. The basal metabolic rate can increase to 60 to 100 percent above normal when large quantities of the hormones are secreted. The rate of utilization of foods for energy is greatly accelerated. Although the rate of protein synthesis is increased, at the same time the rate of protein catabolism is also increased. The growth rate of young people is greatly accelerated. The mental processes are excited, and the activity of most of the endocrine glands is increased.

Effect of Thyroid Hormones on Mitochondria

One of the principal functions of thyroxine might be simply to increase the number and activity of mitochondria, and they in turn increase the rate of formation of adenosine triphosphate (ATP) to energize cellular function. However, the increase in the number and activity of mitochondria could be the result of increased activity of the cells as well as the cause of the increase.

When extremely high concentrations of thyroid hormone are administered, the mitochondria swell inordinately, and there is then uncoupling of the oxidative phosphorylation process with production of large amounts of heat but little ATP. Under natural conditions, it is questionable whether the concentration of thyroid hormones ever becomes high enough to cause this effect even in people who have thyrotoxicosis.

Effect of Thyroid hormone in Increasing Active Transport of Ions through Cell Membranes. One of the enzymes that becomes increased in response to thyroid hormone is Na, K-ATPase. This in turn increases the rate of transport of both sodium and potassium through the cell membranes of some tissues. Because this process uses energy and increases the amount of heat produced in the body, it has been suggested that this might be one of the mechanisms by which thyroid hormone increases the body's metabolic rate. In fact, thyroid hormone also causes the cell membranes of most cells to become leaky to sodium ions, which further activates the sodium pump and further increases heat production.

Effect of Thyroid Hormone on Growth

Thyroid hormone has both general and specific effects on growth. For instance, it has long been known that thyroid hormone is essential for the

metamorphic -change of the tadpole into the frog. In the human being, the effect of thyroid hormone on growth is manifest mainly in growing children. In those who are hypothyrold, the rate of growth is greatly retarded. In those who are hyperthyroid, excessive skeletal growth often occurs, causing the child to become considerably taller at an earlier age. However, the bones also mature more rapidly and the epiphyses close at an early age, so that the duration of growth and the eventual height of the adult may actually be shortened.

An important effect of thyroid hormone is to promote growth and development of the brain during fetal life and for the first few years of postnatal life. If the fetus does not secrete sufficient quantities of thyroid hormone, growth and maturation of the brain both before birth and afterward an greatly retarded and the brain remains smaller than normal. Without specific thyroid therapy within days or weeks after birth, the patients remain mentally deficient throughout life.

Effects of Thyroid Hormone on Specific Bodily Mechanisms

Effect on Carbohydrate Metabolism. Thyroid hormone stimulates almost all aspects of carbohydrate metabolism, including rapid uptake of glucose by the cells, enhanced glycolysis, enhanced gluconeogenesis, increased rate of absorption from the gastrointestinal tract, and even increased insulin secretion with its resultant secondary effects on carbohydrate metabolism.

Effect on Fat Metabolism. Essentially all aspects of fat metabolism are also enhanced under the influence of thyroid hormone. Because fats are the major source of long-term energy supplies, the fat stores of the body are depleted to a greater extent than are most of the other tissue elements. In

particular, lipids are mobilized from the fat tissue, which increases the free fatty acid concentration in the plasma; thyroid hormone also greatly accelerates the oxidation of free fatty acids by the cells.

Effect on Plasma and Liver Fats. Increased thyroid hormone decreases the quantity of cholesterol, phospholipids, and triglycerides in the plasma, even though it increases the free fatty acids.

Effect on Vitamin Metabolism. Because thyroid hormone increases the quantities of many of the enzymes and because vitamins are essential parts of some of the enzymes and coenzymes, thyroid hormone causes increased need for vitamins. Therefore, a relative vitamin deficiency can occur when excess thyroid hormone is secreted unless at the same time increased quantities of vitamins are available.

Effect on Basal Metabolic Rate. Because thyroid hormone increase metabolism in almost all cells of the body, excessive quantities of the hormone can occasionally increase the basal metabolic rate to 60 to 100 per cent above normal. On the other hand, when no thyroid hormone is produced, the basal metabolic rate falls almost to one half normal; that is, the basal metabolic rate becomes - 30 to - 50. Extreme amounts of the hormones are required to cause high basal metabolic rates.

Effect on Body Weight. Greatly increased thyroid hormone almost always decrease the body weight, and greatly decreased hormone almost always increases the body weight; these effects do not always occur because

thyroid hormone increases the appetite, and this may overbalance the change in the metabolic rate.

Effect on the Cardiovascular System

Blood Flow and Cardiac Output. Increased metabolism in the tissues causes more rapid utilization of oxygen than normal and greater than normal quantities of metabolic end products to be released from the tissues. These effects cause vasodilatation in most of the body tissues, thus increasing blood flow. The rate of blood flow in the skin especially increases because of the increased need for heat elimination.

As a consequence of the increased blood flow, cardiac output also increases, sometimes rising to 60 per cent or more above normal when excessive thyroid hormone is present and falling to only 50 per cent of normal in severe hypothyroidism.

Heart Rate. The heart rate increases considerably more under the influence of thyroid hormone than would be expected from the increase in cardiac output. Therefore, thyroid hormone probably has a direct effect on the excitability of the heart, which in turn increases the heart rate. This effect is of particular importance because the heart rate is one of the sensitive physical signs that the clinician uses in determining whether a patient has excessive or diminished thyroid hormone production.

Strength of Heartbeat. The increase enzymatic activity caused by increased thyroid hormone production apparently increases the strength of the heart when only a slight excess of thyroid hormone is secreted. This is

analogous to the increase in strength of heartbeat that occurs in mild fevers and during exercise. However, when thyroid hormone is increased markedly, the heart muscle strength becomes depressed because of excessive protein catabolism. Indeed, some severely thyrotoxic patients die of cardiac decompensation secondary to myocardial failure and increased cardiac load imposed by the increased output.

Blood Volume. Thyroid hormone causes the blood volume to increase slightly. The effect probably results at least partly from vasodilatation, which allows increased quantities of blood to collect in the circulatory system.

Arterial Pressure. The mean arterial pressure usually is unchanged. However, because of the increased blood flow through the tissues between heartbeats, the pulse pressure is often increased, with the systolic pressure elevated in hyperthyroidism 10 to 15 mm Hg and the diastolic pressure reduced in a corresponding manner.

Effect on Respiration. The increased rate of metabolism increases the utilization of oxygen and the formation of carbon dioxide; these effects activate all the mechanisms that increase the rate and depth of respiration.

Effect on the Gastrointestinal Tract. In addition to increased appetite and food intake, thyroid hormone increases both the rate of secretion of the digestive juices and the motility of the gastrointestinal tract. Diarrhea often results. Lack of thyroid hormone can cause constipation.

Effect on the Central Nervous System. In general, thyroid hormone increases the rapidity of cerebration but also often dissociates this; on the other hand, lack of thyroid hormone decreases this function. The hyperthyroid individual is likely to have extreme nervousness and many psychoneurotic tendencies, such as anxiety complexes, extreme worry, and paranoia.

Effect on the Function of the Muscles. Slight increase in thyroid hormone usually makes the muscles react with vigor, but when the quantity of hormone becomes excessive, the muscles become weakened because of excess protein catabolism. On the other hand, lack of thyroid hormone causes the muscles to become sluggish, and they relax slowly after a contraction.

Muscle Tremor. One of the most characteristic signs of hyperthyroidism is a fine muscle tremor. This is not the coarse tremor that occurs in Parkinson's disease or in shivering because it occurs at the rapid frequency of 10 to 15 times per second. The tremor can be observed easily by placing a sheet of paper on the extended fingers and noting the degree of vibration of the paper. This tremor is believed to be caused by increased reactivity of the neuronal synapses in the areas of the cord that control muscle tone. The tremor is an important means for assessing the degree of thyroid hormone effect on the central nervous system.

Effect on Sleep. Because of the exhausting effect of thyroid hormone on the musculature and on the central nervous system, the hyperthyroid subject often has a feeling of constant tiredness, but because of the excitable effects of thyroid hormone on the synapses, it is difficult to sleep. On the other hand,

extreme somnolence is characteristic of hypothyroidism, with sleep sometimes lasting 12 to 14 hours a day.

Effect on Other Endocrine Glands. Increased thyroid hormone increases the rates of secretion of most of the tissues for the hormones. For instances, increased thyroxine secretion increases the rate of glucose metabolism everywhere in the body and therefore causes a corresponding need for increased insulin secretion by the pancreas. Also, thyroid hormone increases many metabolic activities related to bone formation and, as a consequence, increases the need for parathyroid hormone. Finally, thyroid hormone increases the rate at which adrenal glueocorticoids are inactivated by the liver. This leads to feedback increase in adrenocorticotropic hormone production by the anterior pituitary and, therefore, increased rate of glucocorticoid secretion by the adrenal glands.

Effect of Thyroid Hormone on Sexual Function. For normal sexual function, thyroid secretion needs to be approximately normal. In men, lack of thyroid hormone is likely to cause loss of libido; on the other hand, great excesses of the hormone frequently cause impotence. In women, lack of thyroid hormone often causes impotence. In women, lack of thyroid hormone often causes menorrhagia and polymenorrhea, that is, respectively, excessive and frequent menstrual bleeding. Yet, strangely enough, in other women thyroid lack may cause irregular periods and occasionally even amenorrhea. A hypothyroid woman, like a man, is likely to have greatly reduced libido. In the hyperthyroid women, oligomenorrhea, which means greatly reduced bleeding is common, and occasionally amenorrhea results.

The action of thyroid hormone on the gonads cannot be pinpointed to a specific function but probably results from a combination of direct metabolic effect on the gonads and excitatory and inhibitory feedback effects operating through the anterior pituitary hormones that control the sexual functions.

PHARMACOLOGY OF THYROID

A large number of compounds are capable of interfering, directly or indirectly, with the synthesis, release, or action of thyroid hormones. The major inhibitors may be classified into four categories: (1) antithyroid drugs, Which interfere directly with the synthesis of thyroid hormones; (2) ionic inhibitors, which block the iodide transport mechanism; (3) higher concentrations of iodine itself, which decrease release of thyroid hormones from the gland and also may decrease hormone synthesis; and (4) radioactive iodine, which damages the gland with ionizing radiation.

Antithyroid Drugs

The antithyroid drugs that have clinical utility are the thioureylenes, which belong to the family of thionamides. Propylthiouracil may be considered as the prototype.

Mechanism of Action

Antithyroid drugs inhibit the formation of thyroid hormones by interfering with the incorporation of iodine into tyrosyl residues of thyroglobulin; they also inhibit the coupling of these iodotyrosyl residues to iodothyronines. This implies that they interfere with the oxidation of iodide ion and iodotyrosyl groups. Taurog (1976) proposed that the drugs inhibit the

peroxidase enzyme, thereby preventing oxidation of iodide or iodotyrosyl groups to the required active state.

Over a period of time, the inhibition of hormone synthesis results in the depletion of stores of iodinated thyroglobulin as the protein is hydrolyzed and the hormones are released into the circulation. Only when the preformed hormone is depleted and the concentrations of circulating thyroid hormones begin to decline do clinical effects become noticeable.

In addition to blocking hormone synthesis, propylthiouracil inhibits the peripheral deiodination of thyroxine to triiodothyronine.

The antithyroid compounds are propylthiouracil and methimazole. Carbimazole (Neo-Mercazole), a carbethoxy derivative of methimazole, is available, and its antithyroid action is due to its conversion to methimazole after absorption.

Untoward Reactions

The most serious reaction is agranulocytosis. Agranulocytosis usually occurs during the first few weeks or months of therapy but may occur later. Patients should immediately report the development of sore throat or fever, which usually heralds the onset of this reaction. Agranulocytosis is reversible upon discontinuation of the offending drug, and the administration of recombinant human granulocyte colony - stimulating factor may hasten recovery. Other less frequent complications are pain and stiffness in the joints, paresthesias, headache, nausea, skin pigmentation, and loss of hair. Drug fever,

hepatitis, and nephritis are rare, although abnormal liver functions tests are not infrequent with higher doses of propylthiouracil.

Ionic inhibitors

The term ionic inhibitors designates the substances that interfere with the concentration of iodide by the thyroid gland. The effective agents are themselves anions that in some ways resemble iodide; they are all monovalent, hydrated anions of a size similar to that of iodide. Thiocyanate, in large amounts inhibits the organification of iodine.

Mechanism of Action

Acute inhibition of the synthesis of iodotyrosines and iodothyronines by iodide is well known (the *Wolff - Chaikoff effect).* With time there is "escape" from this inhibition that is associated with an adaptive decrease in iodide transport and a lowered intracellular iodide concentration. The mechanism of the Wolff Chaikoff effect may involve inhibition of inositol phosphate signaling pathways within the thyrocyte.

A very important clinical effect of high plasma iodide concentration is an inhibition of the release of thyroid hormone. This action is rapid and efficacious in severe thyrotoxicosis. The effect is exerted directly on the thyroid gland, and it can be demonstrated in the euthyroid subject.

Response to iodide in hyperthyroidism

The response to iodides in patients with hyperthyroidism is often striking and rapid. The effect is usually discernible within 24 hours, and the basal

metabolic rate may fall at a rate comparable to that following thyroidectomy. This provides evidence that the release of hormone into the circulation is rapidly blocked. After a variable period of time, the beneficial effect disappears. With continued treatment, the hyperthyroidism may return in its initial intensity or may become even more severe than it was at first. It is for this reason that, when iodide was the only agent available for the treatment of hyperthyroidism, its use was usually restricted to preparation of the patient for thyroidectomy.

Therapeutic Uses

Prior to surgery iodide is sometimes employed alone, but more frequently it is used after the hyperthyroidism has been controlled by an antithyroid drug. It is then given during the 7 to 10 days immediately preceding the operation. Optimal control of hyperthyroidism is achieved if antithyroid drugs are first given alone. If iodine also is given from the beginning, variable responses are observed; sometimes the effect of iodide predominates, storage of hormone is promoted, and prolonged antithyroid treatment is required before the hyperthyroidism is controlled. *Strong iodine solution (Lugol's solution) is* widely used and consists of 5% iodine and 10% potassium iodide, which yields a dose of 6.3 mg of iodine per drop. The iodine is reduced to iodide in the intestine before absorption. *Saturated solution of* p0assium iodide also is available, containing 38 mg per drop. Typical doses include 3 to 5 drops of Lugol's solution or 1 to 3 drops of saturated solution of potassium iodide 3 times a day.

Untoward Reactions

Unpleasant brassy taste and burning in the mouth and throat, as well as soreness of the teeth and gums. Increased salivation is noted. Coryza, sneezing, and irritation of the eyes with swelling of the eyelids are common. Skin lesions are common, and vary in type and intensity. They usually are mildly acneform. and distributed in the seborrheic areas

Radioactive iodine

Chemical and Physical Properties. Although iodine has several radioactive isotopes, greatest use has been made of ^{131} I. It has a half-life of 8 days, and, therefore, over 99% of its radiation is expended within 56 days. Its radioactive emissions include both y rays and P particles originate within the follicle and act almost exclusively upon the parenchymal cells of the thyroid with little or no damage to surrounding tissue. When small tracer doses of^{131} I are administered, thyroid function is not disturbed. However, when large amounts of radioactive iodine gain access to the gland, the characteristic cytotoxic actions of ionizing radiation are observed. Pyknosis and necrosis of the follicular cells are followed by disappearance of colloid and fibrosis of the gland.

Therapeutic Uses

Sodium iodide I "' is available as a solution or in capsules containing essentially carrier – free^{131} I suitable for oral administrations. *Sodium iodide* I^{131} is available for scanning procedures. Radioactive iodine finds its widest use in the treatment of hyperthyroidism and in the diagnosis of disorders of thyroid function.

Indications

The clearest indication for this form of treatment is hyperthyroidism in older patients and in those with heart disease. Radioactive iodine is indicated in patients with toxic nodular goitre, since the disease does not go into spontaneous remission. The risk of inducing hypothyroidism is less in nodular goitre than in Graves' disease, perhaps because of the normal progression of the latter and the preservation of nonautonomous thyroid tissue in the former. Usually, larger doses of radioactive iodine are required in the treatment of toxic nodular goitre than in the treatment of Graves' disease.

The use of radioactive iodine during pregnancy is contraindicated; after the first trimester the fetal thyroid would concentrate the isotope and thus suffer damage, but even during the first trimester radioactive iodine is best avoided because there may be adverse effects of radiation on fetal tissues.

Diagnostic Uses. Tracer studies with radioactive iodine have found wide application in studies of disorders of the thyroid gland. Measurement of the thyroidal accumulation of a tracer dose is helpful in the diagnosis of the thyroid to TSH or to suppression by thyroid hormone.

PATHOPHYSIOLOGY OF MULTINODULAR GOITRES

Any comprehensive theory concerning the pathogenesis of multinodular goitres must take into account the pathogenesis and pathophysiology of simple goitres.

These goitres probably represent a response to any of the several factors that impair the efficiency of thyroid in manufacturing adequate quantities of

hormones. There is a hypersecretion of TSH leading to stimulation of thyroid growth and increase in the activity of the processes concerned with hormone biosynthesis that are capable of response. As a result of the increase in the thyroid mass and unit functional activity, a normal rate of hormone secretion is restored and the patient is eumetabolic but goitrous, associated perhaps with factors inhibiting normal iodine usage. Hyperstimulation or cycles of hyperstimulation and involution could lead to the emergence of areas of hyperplasia, possibly associated with functional autonomy, coupled with areas of exhaustion atrophy (involution), the whole mass made more heterogenous by areas of localized hemorrhage, fibrosis and sometimes calcification. This is perhaps due to local variations in thyroid microcirculation, as well as clonal differences between cells that give rise to thyroid follicles, some being more and some less responsive to TSH, and some autonomous from the outset.

With the passage of time, the quantity of autonomous functional tissue is sufficient to suppress the TSH-secretory mechanism. Initially this is manifest by subnormal response to TRH or lack of thyroid suppression during administration of exogenous hormone. Ultimately autonomous hyperfunction may be sufficient to produce thyrotoxicosis.

In general, two patterns are seen. The first is a diffuse but somewhat uneven distribution of radioisotope that is altered little by the administration of exogenous thyroid hormone. Histopathological examination reveals multiple aggregates of small follicles with hyperplastic epithelium interspersed with variably sized nodules that appear as if they should be inactive. The second type of toxic multinodular goitre is also distinguished by its functional pattern. Here radioiodine becomes localized in one or more discrete nodules, while

iodine accumulation in the remainder of the gland is suppressed. No further suppression is produced by exogenous thyroid hormone but TSH stimulates accumulation of iodine in the areas previously inactive. Histopathologically, the functioning areas resemble adenomas in being reasonably well demarcated from the surrounding tissue, consisting of large follicles consisting of hyperplastic epithelium, but the correlation of architecture with functional state is not good. The remaining issue appears inactive and zones of demarcation are present in both the functioning and non functioning areas suggesting that the areas that are functioning can do so without TSH and that the remaining areas retain their dependence on TSH, their function being suppressed as a consequence of hyperfunction of the autonomous zones. The extent of overproduction of T_3 and T_4 in toxic multinodular goitres is however, only mild. The radioiodine uptake is not greatly increased and may even be normal, and the Serum T_3 and T^4, levels are only marginally increased.

PATHOLOGY

Grossly, the thyroid in enlarged and its shape is distorted, one lobe being frequently larger than the other. The thyroid capsule is stretched but intact.

Cross-section reveals multiple nodules, some surrounded by a partial or complete capsule. Secondary changes in the form of haemorrhage, calcification, cystic degeneration are common.

Microscopically, there is a wide range of appearances. Some nodules are composed of huge follicles lined by flattened epithelium; others are extremely cellular or hyperplastic, and still others are predominantly or exclusively lined by Hiirthle cells. Some of the dilated follicles have a conglomerate of small

active follicles at one pole (so called Sanderson's pollsters). Others have papillary projections facing the lumen of a cystic follicle, a feature that may lead to confusion with papillary carcinoma.

It is not unusual to find within a nodule predominantly composed of large dilated follicles, sharply outlined solid or microfollicular clusters of follicular cells. It has been suggested that nodular goitres grow by episodic replication of these clusters which have been found to express immunohistochemically the P21 proto-oncogene product. The proliferative activity of these nodules can be estimated by immunostaining the sections with monoclonal antibody MIB-1.

Rupture of follicles leads to a granulomatous reaction to the colloid with appearance of histiocytes and foreign body-type giant cells. Areas of fresh and old haemorrhage, coarse fibrous trabeculation and foci of calcification are common. Occasionally osseous metaplasia may be seen. Greatly thickened vessels with calcified media may be present at the periphery. A variable number of chronic inflammatory cells are present in the ffIxoma in many of the cases indicating the coexistence of chronic thyroiditis. It is not possible to predict on the basis of the morphological appearance whether the patient has clinical or laboratory evidence of hyperthyroidism.

Clinical Picture

The clinical features of a non toxic goitre are those that result from thyroid enlargement. Most commonly, the effect is either merely disfiguring or is felt on a tightening of garments worn about the neck. With larger goitres, displacement or compression of oesophagus or trachea may occur, leading to dysphagia, a choking sensation or inspiratory stridor. Compression of the

recurrent laryngeal nerve leading to hoarseness is unusual and would suggest carcinoma. Haemorrhage into a nodule or cyst produces acute painful enlargement locally, and if appropriately situated can enhance or induce symptoms of obstruction. Narrowing of the thoracic inlet may compromise the venous return from the head, neck and upper limbs sufficiently to produce venous engorgement, accentuated when the patient's arms are raised.

Toxic multinodular goitre is a common complication of its nontoxic precursor, but its precise incidence in the latter disorder is unknown . It usually occurs after the age of 50 years in patients who have had multinodular goitre for many years. It is many more times more common among women, and is almost never accompanied by infiltrative ophthalmopathy. The clinical manifestations tend to differ from those in dffise toxic goitre. Cardiovascular manifestations tend to predominate, possibly because of the age of the patients. These may include atrial fibrillation or tachycardia, with or without heart failure. Weakness and wasting of muscles are common. Emotional lability may be pronounced. Obstructive symptoms are more common than in Graves' disease.

INVESTIGATIONS FOR THYROID DISORDERS

There is no substitute for good history taking, and careful clinical examination in the assessment of thyroid disorders. None of the available tests is infallible, and misleading results may be obtained especially if the patient is taking medicines or has altered physiology, for example - in pregnancy.

I. Tests of Circulating thyroid hormone levels:

1. Serum. Free Thvroxine (T_4) :

Normal range 55 - 150 nmol/l

This measures the total protein-bound Thyroxine, and provided that the patient is not on any drug which may affect the serum levels of binding proteins, offers a good test for thyroid function. Low levels are seen in nephrotic syndrome, and false high levels are seen in pregnancy, and in patients taking oral contraceptives.

Some drugs like salicylates, competing for protein binding, may give false low levels.

2. Serum Tri-iodothyronine (T_3)

Normal range 1.2 - 3.1 nmol/l

The serum T_3 levels are also affected by changes in the thyroid binding proteins and are therefore subject to the same limits of interpretation. Most useful for confirmation of hyperthyroidism, especially when clinical picture strongly suggests Thyrotoxicosis but the T_4 levels are normal.

3. Free Thyroxine

Normal range 8 - 26 pmol/l

Using radioimmunoassay, can be done at low cost. Levels do not vary with age or due to drugs such as salicylates, phenytoin.

4. Free tri-iodothyronine

Normal range 3 - 9 pmol/l

The Free T_3 imino radioimmunoassay has the same merit as Free T_4 assay. Best single test to assess hyperthyroidism.

II. Tests of Hypothalamic - Pituitary Function

1. Thyroid - Stimulating Hormone

(Normal range 0.5 - 5 mmol / 1)

New IRMA assays (Immunoradiometric assay) are useful to confirm both hypothyroidism and hyperthyroidism.

2. Thyrotrophin - Releasing hormone Test

Following the IV administration of 400 micrograms / 1.73 m^2 of BSA of thyrotrophin, the patient's TSH levels are measured in blood samples taken at 0,20,60 mins.

In patients with hypothyroidism, exaggerated response in seen, while in patients with hyperthyroidism, little or no response is seen.

III. Dynamic Tests of Thyroid Function

1. Radioiodine Isotope Uptake

Uptake measurement combined with thyroid scanning is helpful in identifying which part of the gland is hyperfunctioning and in identifying the patients with thyroiditis who are clinically thyrotoxic but have low uptake.

Factors that increase uptake:

a) Reflecting increased hormone synthesis.

i) Hyperthyroidisin

ii) Response to glandular hormone depletion

Recovery from thyroid suppression

Recovery from subacute thyroiditis

Antithyroid drugs

iii) Excessive hormone losses

Nephrosis

Chronic diarrhoeal states

Soyabean ingestion

b) Not reflecting increased hormone synthesis -

i) Iodine deficiency

Dietary supply

Excessive loss (dehalogenase deficiency, pregnancy)

ii) Hormone biosynthetic defects.

Factors that decrease uptake.

a) Reflecting decreased hormone synthesis.

i) Primary Hypofunction

Hashimoto's disease

Subacute thyroiditis

ii) Secondary hypofunction

iii) Exogenous thyroid hormones.

b) Not reflecting decreased hormone synthesis:

i) Increased bioavailability of iodine

Dietary or Pharmacologic supply

Cardiac or Renal insufficiency

ii) Increased hormone release

(rare) very severe hyperthyroldism

IV. Tests of Thyroid Dysfunctions

Antithyroid Antibodies

(antithyroglobulin and antimicrosomal antibodies).

Very high tires of antithyroglobulin antibodies are seen in patients with Hashimoto's thyroiditis, especially in those with long standing disease, when their presence strongly supports the diagnosis. The presence of antithyroglobulin antibodies in a hyperthyroid patient with eye signs suggests Grave's disease. The presence of antimicrosomal antibodies indicates autoimmune thyroid disease of Hashimoto's type and when found in patients who have already received thyroxine makes a presumptive initial diagnosis of thyroid failure more likely. This antibody is also seen in patients with thyroid malignancy.

Fine Needle Aspiration Cytology

This technique promoted by the Karolinska Institute has only recently gained wider acceptance. A 25 gauge disposable needle on a 10 ml syringe enables cells to be aspirated from any suspicious areas of the thyroid. The procedure can be performed quickly and painlessly in the outpatient department without the need for a local anaesthetic, providing a smeared specimen which

can be fixed and stained on a microsurgery shade. A high level of diagnostic accuracy can be achieved when the clinician and cytologist are experienced. The technique cannot distinguish benign from malignant follicular lesions since no information is available about capsular or vascular invasion.

TREATMENT

The treatment of a non toxic goitre depends on its cause and stage of development. If a pharmacological goitrogen is being given, its removal will suffice. If this is not useful, Levothyroxine may be administrated in replacement doses to interrupt the endogenous thyroid stimulation.

This is more useful in younger patients where the serum TSH levels are normal or somewhat increased. In older patients with nodular goitres, the serum TSH concentrations are often less than 0.5 MuA even though serum thyroid hormone levels may still be in the normal range. In such patients further suppression of TSH is inappropriate and may lead to thyrotoxicosis resulting from a combination of both exogenous and endogenous hormone.

(Use of iodine is to deplored as it is ineffective and has a capacity to induce thyrotoxicosis)

Indications for Surgery

Large goitres may well cause cosmetic disfigurement, pressure symptoms and discomfort. All of these are good indications for surgery, the extent of which is dependent on the size and number of nodules present. Following surgery a small dose of thyroxine reduces the risk of recurrence. In the elderly, a dose of 0.05 mg may be sufficient, to achieve an acceptable

degree of TSH suppression. In addition, the possible exacerbation of osteoporosis with excessive thyroid hormone therapy must be kept in mind.

There is considerable disagreement regarding the treatment of choice for most patients with multinodular goitre with toxicity. A marked preference for radioiodine exists in the North America, where experience indicates that the responsiveness to radioiodine of multinodular goitre differs little from that of diffuse toxic goitre, whereas it's use is more selective in United Kingdom and India. The type that responds to radioiodine may resemble diffuse toxic goitre in displaying a relatively diffuse accumulation of radioiodine. The more resistant variety, on the other hand may be associated with adenomatous hyperfunction; here the tissue previously suppressed may regain function and ultimately achieve autonomy after the hyperactive tissue has been destroyed.

Unfortunately the thyroid function of patients with large toxic multinodular goitres is often very labile during treatment with antithyroid drugs and relapse rates following withdrawal are greater than 50 percent. Radioactive iodine is also very unlikely to suit most patients as drug uptake is variable, there is minimal impact on the size of the gland, and response is slow. Surgery is best carried out sooner than later to avoid compromise of the airway and the cardiovascular system. The specific surgical procedure is subtotal thyroidectomy i.e removal of atleast 85% of the gland, notably those parts shown to be active on radioiodine scanning . Recent literature recommends a total thyroidectomy for multinodular goiters.

The definitive treatment should be preceded by a course of antithyroid therapy until a eumetabolic state in achieved. After six to eight weeks the

antithyroid drugs are gradually withdrawn, and if hyperthyroidism recurs, a second course of therapy should be given.

Preoperative Measures

Preparation is directed to ensure safe induction of anaesthesia and a trouble free intra and post operative course. Hemoglobin estimation, chest radiology and an ECG are mandatory. Blood transfusion is rarely required. Grouping and saving of serum is all that is required. The vocal cords should always be examined by indirect laryngoscopy. This is especially important when the voice is compromised, malignancy is suspected or when previous thyroid surgery has been undertaken. A small proportional of patients have unsuspected recurrent laryngeal nerve palsy. It is of medicolegal importance to both the patient and the surgeon to determine before surgery whether or not the vocal cords were moving normally.

Thyrotoxic patients need to be rendered euthyroid or the peripheral effects of high circulating levels of thyroxine blocked. The majority of thyrotoxic patients referred to surgery have already been started on antithyroid drugs. 10 days prior to operation, oral propranolol is started in a dose of 30 to 120 mg every 6 to 8 hours. The dose is adjusted to keep the patients sleeping pulse at about 70 beats / min. Since the effective duration of action of propranolol is approximately 6 hrs, it is important to administer medication right up to induction of anaesthesia and to continue treatment thereafter, especially if the patient develops tachycardia. Propranolol is contraindicated in patients with bronchial asthma, sinus bradyeardia or congestive heart failure. Prompt treatment of the hyperthyroid state can often significantly reduce the

cardiovascular symptoms. In elderly patients with apathetic hyperthyroidism especially, cardiovascular symptoms predominate. These individuals are resistant to cardiac glycosides. B-blockers can be administered orally or intravenously, but must be used with caution in patients with failure, but are beneficial if the failure is accompanied by tachycardia. Correction of the basic metabolic defect requires specific therapy directed at reducing the production of thyroid hormone. Iodides, and Propylthiouracil are useful in the rapid amelioration of the hyperthyroid state. Most hyperthyroid patients escape from the effects of iodine after 10 to 14 days. Patients on anti-thyroid drugs should have their blood counts checked regularly if reduced resistance to infection is suspected.

PATIENTS AND METHODS

This study was carried out on 49 patients of multinodular goitre in surgical wards of Government Royapettah Hospital, Chennai from March 2003 – August 2005.

Initial workup included clinical examination, hematological and biochemical parameters, radiological investigations. Routine ENT examination including indirect laryngoscopy was done. Ultrasonogram of the thyroid was done in selected cases. All cases had extensive cardiac evaluation including clinical evaluation, ECG and echocardiogram. FNAC was done for all patients.

Patients were categorized into those with toxic symptoms and those without toxic symptoms. The patients with clinical and/or biochemical evidence of thyrotoxicosis were started - on antithyroid drugs viz. Tab .Carbimazole 5 mg t.d.s. and progressively increased till control of toxicity along with Tab.Propranolol 20 mg 6 hrly. All such patients had monitoring of sleeping pulses as an index of toxicity.

Surgery was recommended for all patients with large goitres which were cosmetically disfiguring, which produced obstructive symptoms over their trachea or oesophagus, which were producing toxic symptoms (once the toxicity was reduced).

The specific surgical procedure performed was Subtotal thyroidectomy. Following surgery, histopathological examination was performed on all specimens.

Postoperative adjunct treatment was given in the form of L-Thyroxine tablets 0.1 mg tablet daily. Patients with preoperative toxicity were continued postoperatively on tab. Propranolol. The postoperative complications were recorded.

Patients were followed up after discharge for evidence of toxicity or hypothyroidism, or recurrence of symptoms.

OBSERVATIONS

Epidemiology

The sex incidence of our study showed that overwhelming majority of our patients with multinodular goitre were females. The ratio was 48 :1 in favour of females.

The age incidence showed a wide variation with the youngest patient being 16 years, and the oldest being 46 years with a mean age of 31 years.

The study revealed that only 6 of the 49 patients in our study had clinical or biochemical evidence of toxicity. The youngest of these patients was 22 yrs with a mean age of 29.5 years.

Socioeconomic Status

The socioeconomic status was more or less reflective of the usual input of patients of our hospital, the majority being from semi skilled labourer class earning on an average 1000-1200 Rs. per month.

Symptoms

All the patients in our study revealed that they are aware of the lump. 39% of the patients (19/49) complained of difficulty in swallowing. 32% of the patients (16/49) complained of dyspnoea. Only 4 of the 49 patients (8%) complained of hoarseness. 17 of the 49 patient i.e. 35% of the patients complained of no symptom other than the swelling in the neck. All the six patients with toxicity had dyspnoea, palpitations.

The study of duration of symptoms of these patients revealed that some patients consulted their physicians within 4 months of onset of symptoms while others waited as long as 6 years, with the mean at 1½ years.

Past History

The past history of none of these patients was contributory to their symptoms. 2 patients had treatment for pulmonary tuberculosis, 4 of the patients were hypertensive, but were not associated with hyperthyroidism: None of the patients gave any history of irradiation to the neck.

Personal Habits

46 of these 49 patients consumed mixed diet: all of them consumed sea food.

44 patients used rock salt at home. Only 2 patients could specify that they use iodized salt.

2 patients with toxicity had disturbances of their menstrual cycles.

Signs

All the glands were found to be involved in both the lobes, the number of nodules variable. All the toxic patients exhibited tremors and tachycardia. The gland was vascular, with palpable thrill and an auscultable bruit in each of them.

Fine Needle Aspiration Cytology :

All the patients had FNAC of their thyroid swellings done. All the cytology reports revealed the cells to be from goitrous lesions.

Adjunct Investigations

Radioiodine uptake study and scanning of the thyroid was not done as a routine measure in view of its non-availability at our hospital. Only those patients who had clinical evidence suspicious of toxicity had RAIU and scanning. 6 of the 49 patients had this study,

ECG and Echocardiogram was done in all the patients. None of the patients with toxicity were in failure. There were no cases with atrial fibrillation.

USG thyroid was done in 10 of the 49 patients and identified cystic lesions in 6 of these 10 cases, none of whom were toxic.

Biochemical markers for hyperthyroidism i.e. serum T_3, T_4, TSH assays were contributory in 6 patients.

Preoperative Workup

All the patients had ENT examinations and indirect laryngoscopy was performed in all the patients. All the patients were assessed for subtotal thyroidectomy under general anesthesia. The patients with clinically or biochemically proven hyperthyroidism were started on Tab. Neomercazole 5 mg tds dosage along with Tab. Propranolol 40m g bds dosage. The dosage was adjusted to achieve a target of sleeping pulse rate around 70 beats/m. This involved an average waiting period of over eight weeks. 3 of the patients with toxicity had Lugol's iodine for 10 days preoperatively.

Operative Findings

All patients underwent subtotal thyroidectomy, under general anaesthesia.

The parathyroids were preserved in all cases.

The recurrent laryngeal nerve was identified in 30 of the thyroidectomies as a deliberate attempt to preserve it during the course of the operation.

The blood loss was found to be appreciably more in patients with toxicity. There appeared to be not much difference due to preoperative Lugol's iodine. Five of the 49 patients needed blood transfusion (including 4 of the patients with toxicity). The vocal cords were inspected routinely at the end of the operation. There was no paralysis in any case. All patients had a drain from the inferior aspect of their wound.

Postoperative Sequelae

37 of the 49 patients had uneventful postoperative periods.

Three patients developed hoarseness of voice, which corrected itself by the 2nd postoperative day in all patients.

Subcutaneous edema developed in 3 patients who had subcuticular sutures which subsided spontaneously by the 3rd postoperative day.

One patients developed toxicity on the first night after the operation, which subsided with antithyroid drugs and β-blockers.

All patients had their sutures removed by the 6th Postoperative day.

There was no mortality in our group of 49 patients. There was no wound infection.

Histopathology

All the specimens were sent for histopathological examination. 43 of 49 specimens were confirmed to be multinodular goitre.

3 specimens were reported as Hashimoto's thyroiditis.

2 specimens were reported as multinodualr goiter with foci of papillary carcinoma.

1 specimen was reported as follicular carcinoma.

Followup

All the patients were advised Tab. Eltroxin 0.1 mg, daily as a replacement dose. The patients with preoperative hyperthyroidism were asked to continue tab propranolol for 1 week post operatively. Although all the patients were advised regular followup, only 7/49 patients do so regularly.

DISCUSSION

The results of the present study reflect the pattern of multinodular goiter treated in our hospital.

The multinodular goiter showed a very definite female predilection, as with other studies. The highest incidence was found in the group of patients age 20 – 35 years. This suggests that our patient are affected atleast a decade or two earlier than the patients in Western series.

In contrast to Western literature, patients with multinodular goiter with toxicity in India tend to present at an early age. This study showed that average age of the toxicity in our study was 29 years. In West, this figure is about 50 yrs.

Majority of our patients belong to the low socioeconomic group. This may reflect the usual input of patients to our hospital. No specific factor related to the socioeconomic status of the patent appeared to be related to the appearance of multinodular goiter in our patients.

Several studies have attempted to establish the actiological role of various food items in multinodular goiters. A det rich in derivatives of the vegetables of the brassicae family viz – cabbage, has been implicated. A deficiency of iodine as the cause of the goiter has long been speculated. Diet rich in seafood has always been considered protective. Almost all our patients consumed a mixed diet, sea food being a fairly common constituent of their diet. The majority of patients however did not use iodized salt. Indeed, a large proportion were not aware of iodized salt. There was no specific increase in

consumption of the vegetables of the Brassicae family in our group which could constitute a cause for their goiters. Pharmacologic products have occasionally been implicated in the causation of goiters. Drugs like iodides, phenytoin, PAS, amiodarone are known to be goitrogenic. None of our patients however had any chronic intake of a goitrogen that could have been the cause of their symptoms.

Our study of the symptomatology revealed that all our patients were aware of the swelling in the neck, either noticed by themselves, or brought to their notice by others. Quite a few of these patients however, did not immediately seek attention; indeed some patients went for as long as 6 yrs with the enlarging swelling without consulting a doctor. Eventually when they did approach a doctor, greater than half of them had troubling symptoms such as dysphagia accompanying the goiter. The symptomatology accompanying the goiter were particularly distressing to patients with hyperthyroidism. All of them complained of palpitation and dyspnoea. Most of them had tremors and gave a history of weight loss despite adequate appetite. Hoarseness was complained of by only 4 of our patients, none of whom had any evidence of vocal cord involvement, suggesting that it was likely to be due to pressure effect. This is in keeping with the published literature, which suggests that hoarseness in more common in malignant thyroid disease.

All the patients had readily palpable goiters with nodules. The manifestation of symptoms of secondary thyrotoxicosis has been fairly impressive, all the patients with toxicity having tachycardia and high sleeping pulse rates. All these patients had glands which exhibited signs of high vascularity.

β - blockers are known to be of great advantage in decreading the signs of toxicity. The use of Tab. Propranolol helped to bring down the toxicity considerably along with the use of Tab. Neomercazole (Casrrbimazole).

The sleeping pulse rate has been found to be a reliable index of toxicity.

Fine needle aspiration cytology continues to be a very useful tool, but has its limitations. All patients with a clinical diagnosis of multinodular goiter had an FNAC preformed. All the patients who had cytology smears suggesting goitrous lesion were studied. The eventual correlation with histopathological examination indicated that FNAC was accurate in 45 of the 49 patients, but could not defect follicular neoplasm in one patient. Three others who were initially though to lave multinodular goiter turned out to have Hashimoto's disease. thus FNAC is useful in multinodular goiter to rule out the presence of the neoplasm, especially papillary, and to suggest if a particular thyroid swellings is cystic or has solid and cystic components or only solid.

In cases with borderline hyperthyroidism, investigations like radioactive iodine uptake and serum T_3, T_4, TSH may be necessary. We found the serum T_3, T_4, TSH level correlate well with the thyroid activity, and helped to rule out toxicity in two patients, and confirming toxicity in four others. The 24 hrs radioiodine uptake also correlated well with the toxicity in our patients, and was over 40% in 2 of the six patients with toxicity in whom it was done.

Surgical procedure for goiter should be based on anatomical consideration, knowledge of for natural history of the disease and specific surgical goals in each case. Our goal in doing subtotal thyroidectomy for patients without toxicity was to remove as much of the goiter as possible

including all nodular tissue. In patients with toxicity, Sibtotal thyroidectomy was done, aiming to leave behind approximately 4 – 5 gms of thyroid tissue of each lobe. The Recurrent Laryngeal nerves were identified in 30 of our patients, and not identified in 19 of our patients. None of these patients had any vocal cord involvement postoperatively, suggesting that it is not necessary to look for recurrent laryngeal nerve in every case of subtotal thyroidectomy to do a safe surgery. The blood loss was significantly higher in patients with preoperative thyrotoxicosis.

The study the of postoperative complication rates revealed that most of our patients had an uneventful postoperative period. Wound infection was not recorded even in one case, and the policy of keeping a drain appears to have its use, none of our patients ever developing a hematoma postoperatively. Transient suture line edema developed in patients with subcuticular sutures.

One patient developed transient thyrotoxicosis in the first 24 hrs postoperatively, and was managed with ice cold sponging, β - blockers and antithyroid drugs and hydrocortisone, possibly reflecting a release of performed hormone into the circulation during the handling of the gland during the operation.

Thus, the complication rates of surgery in our study are very much in line with those recorded in literature. There was no mortality, as should be expected.

The histopathology examinations confirmed our clinical impressions in most patients. Three patients turned out to have Hashimoto's disease and will require life long replacement therapy with Tab. thyroxine. Three patients with differentiated thyroid carcinoma, were referred to Dept. of Radiation Oncology for further management.

SUMMARY AND CONCLUSIONS

- Multinodular goiter occurred most commonly between the third and fifth decades of life. Over whelming majority of our patents are female. Patients consuming a diet low in iodine seem to be susceptible to this disease.

- Our patients tend to present fairly late – 3 after the onset of the symptoms. Patients with toxicity tended to present earlier.

- Most common symptoms in our study were lump, lump with dysphagia, lump with dyspnoea, lump with dysphagia and dyspnoea.

- Hoarseness was unusual as a primary symptom, and was seen in only 8% of our patients.

- Pain was unusual among our patient occurring in only 12% of the patients.

- 14% of our patients had documented hyperthyroidism. The serum T_3, T_4, TSH, and the radioiodine Isotope uptake were both useful in confirming the presence of hyperthyroidism.

- Fine Needle Aspiration Cytology is a good, inexpensive, safe investigation with a sensitivity of 93%.

- Surgery is an excellent modality of treatment, and can be performed with minimum morbidity and nil mortality.

- Patients with hyperthyroidism will need preoperative normalization of their thyroid status with antithyroid drugs and β - blockers.

- Most common histopathology examination result appears to be multinodular goiter with degenerating nodules.

- Regular follow up is essential, to look for occurrence of hypothyroidism.

Multinodular goiter is a common clinical entity. With the best of technology and skilled surgical care available today, it should be possible to relieve the patients of their symptoms with least morbidity. Surgery is an excellent modality of treatment. Regular follow up of the patient is essential after the definitive treatment.

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MULTINODULAR GOITRE - PROFORMA

Name

Age

Sex

Address

Occupation

Socioeconomic Status

I.P. No.

Symptoms

1. Duration
2. Lump in the neck
3. Discomfort on swallowing
4. Dyspnoea
5. Hoarseness of voice
6. Symptoms of hyperthyroidism or hypothyroidism sweating, tremors, sleep disturbance, appetite alteration, weight alteration, alteration in bowel motility, palpitations, proximal muscle weakness, menstrual disturbances.

Past History

Radiation

Drugs

Others

Family History

Personal History

- Diet, (including iodized salt)
- Sea food intake

General Examination

1. Nervous appearance
2. Sweaty palms
3. Tachycardia
4. Hypertension
5. Eye signs

Local Examination:

1. Bilateral Involvement
2. Palpable thrill
3. Auscultable, bruit

Systemic Examination:

1. Cardiovascular system
2. Respiratory system
3. Abdomen
4. Central Nervous system

Investigations:

1. Blood Parameters
2. Biochemical Parameters
3. X-ray chest
4. X-ray neck
5. Indirect Laryngoscopy
6. FNAC
7. ECG and Echocardiogram
8. USG thyroid
9. Serum T_3, T_4, TSH
10. RAIU

Operative :

Findings

Identification of Recurrent Laryngeal nerve

Parathyroids

Blood loss, needing transfusion.

Histopathology:

Sequelae:

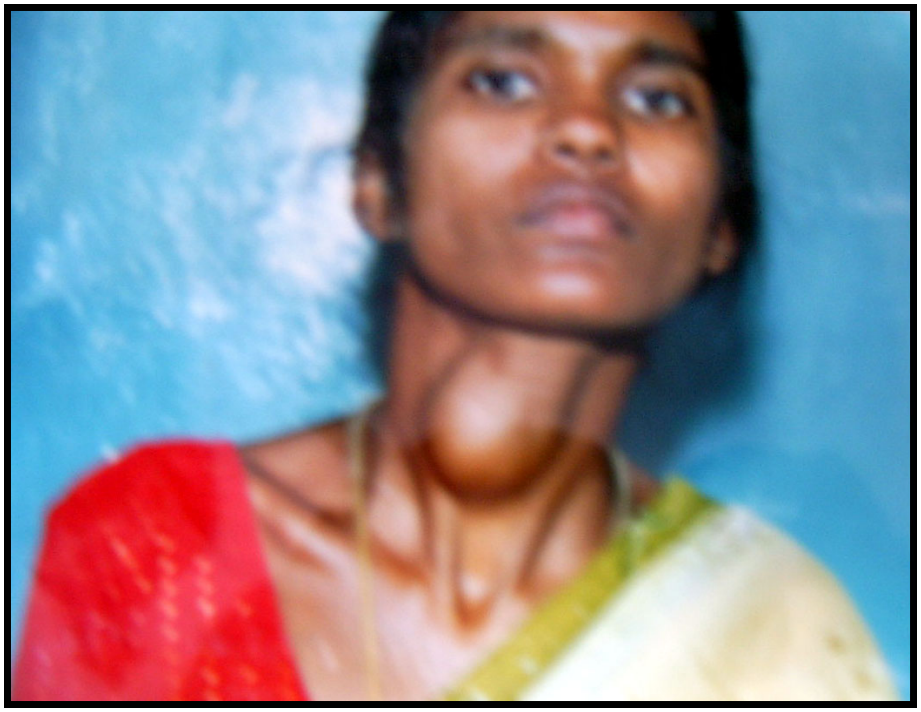
Early	1.	Hoarseness
	2.	Haematoma
	3.	Hyperthyroidism
	4.	Hypocalcemia
	5.	Mortality
Late	1.	Recurrent nodule

2. Toxicity

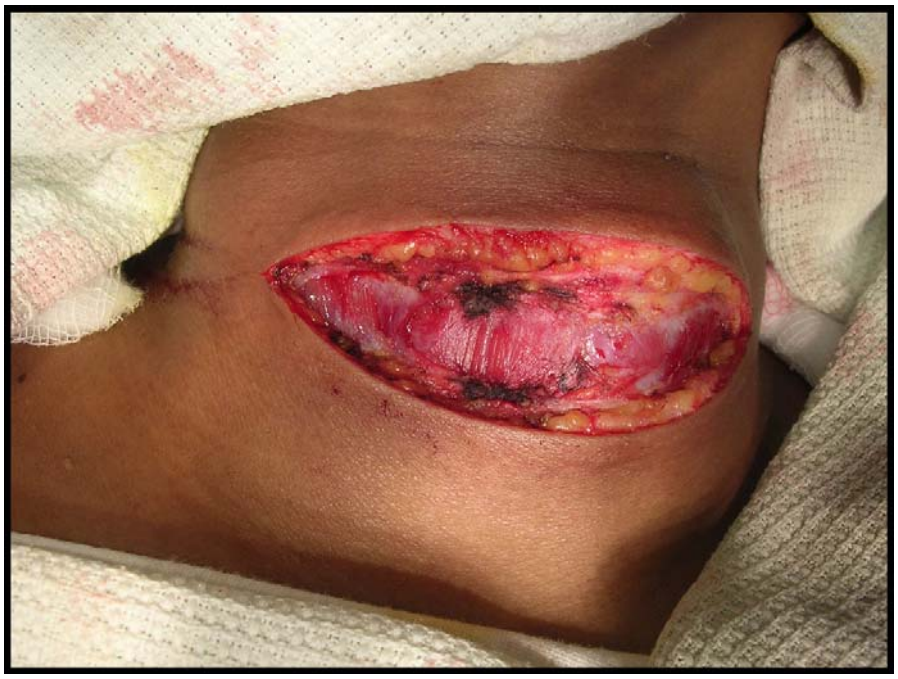
3. Hypothyroidism

Follow up:

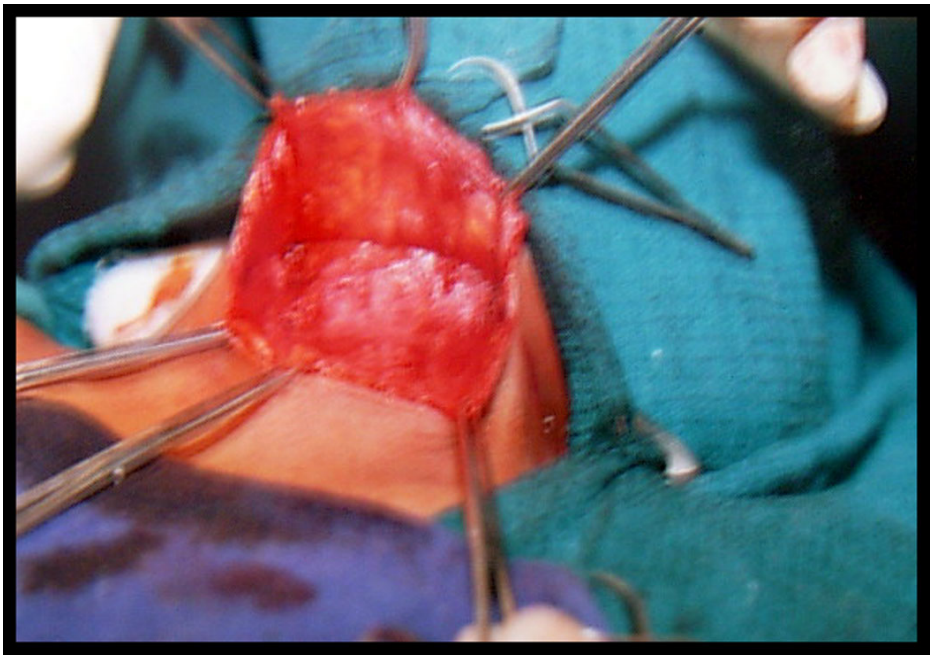
A PATIENT WITH MULTI NODULAR GOITRE



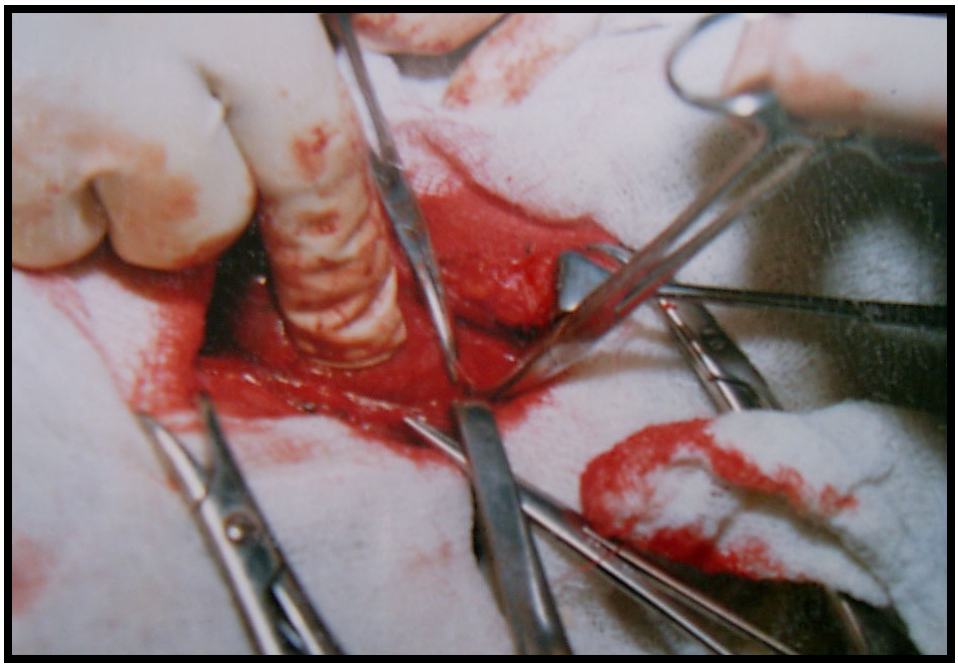
A PATIENT WITH MULTI NODULAR GOITRE



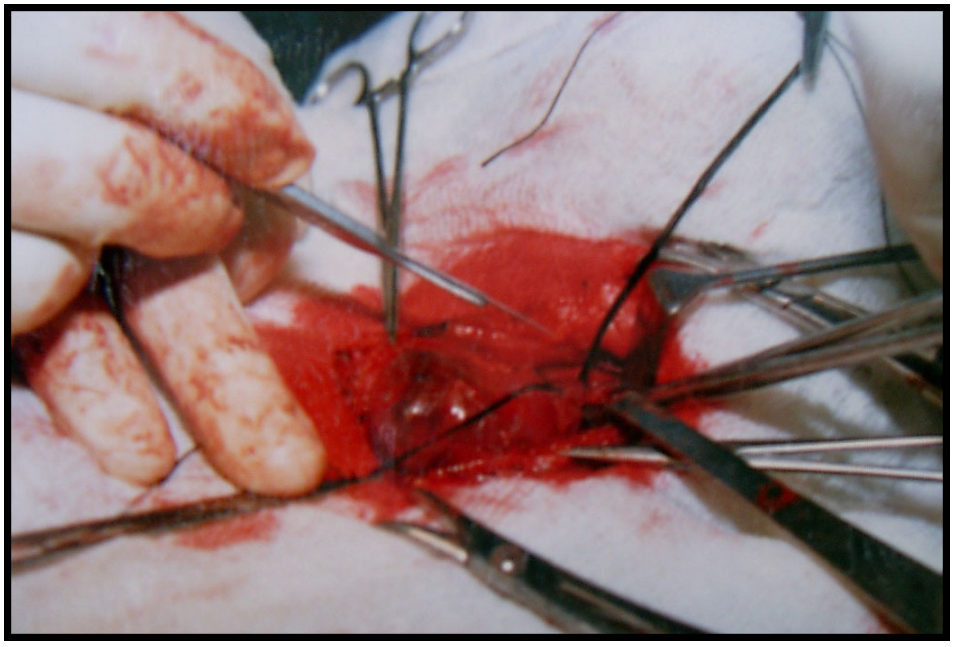
SKIN INCISION



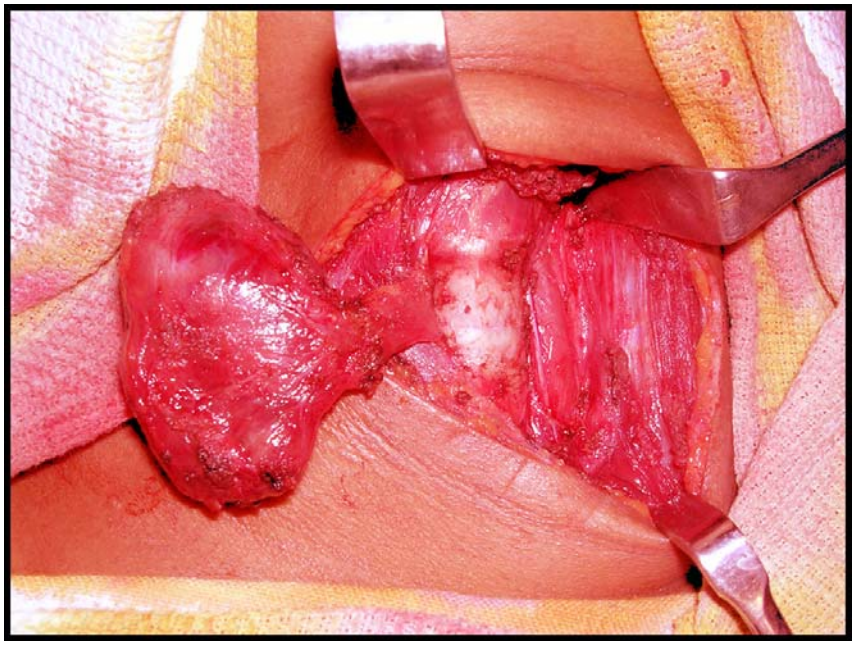
RAISING OF SUB PLATYSMAL FLAP



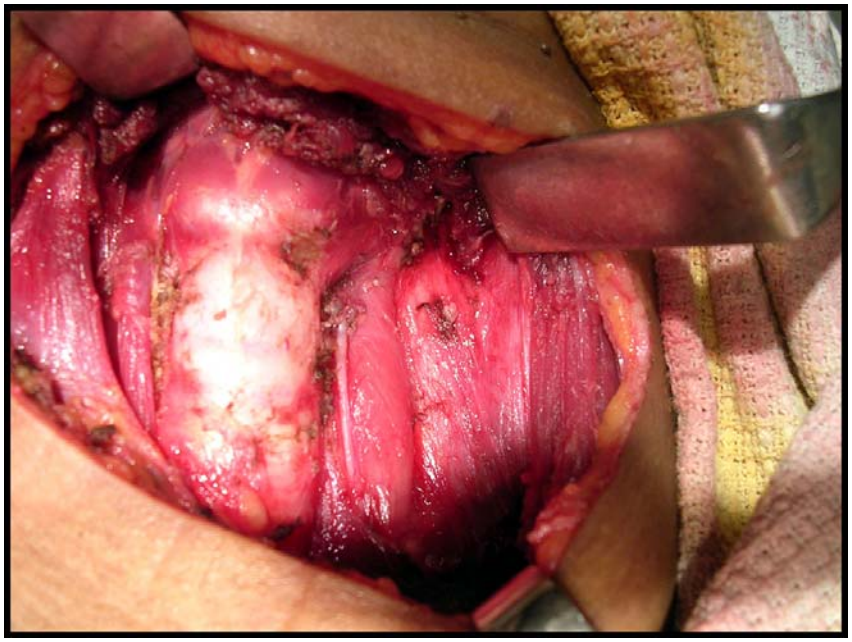
SECURING THE MIDDLE THYROID VEIN



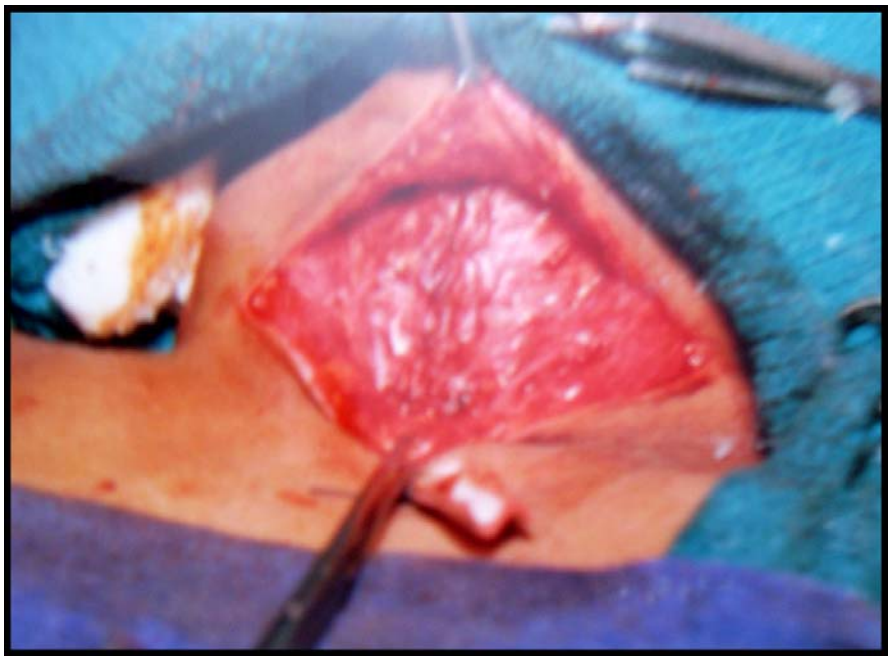
LIGATION OF SUPERIOR PEDICLE



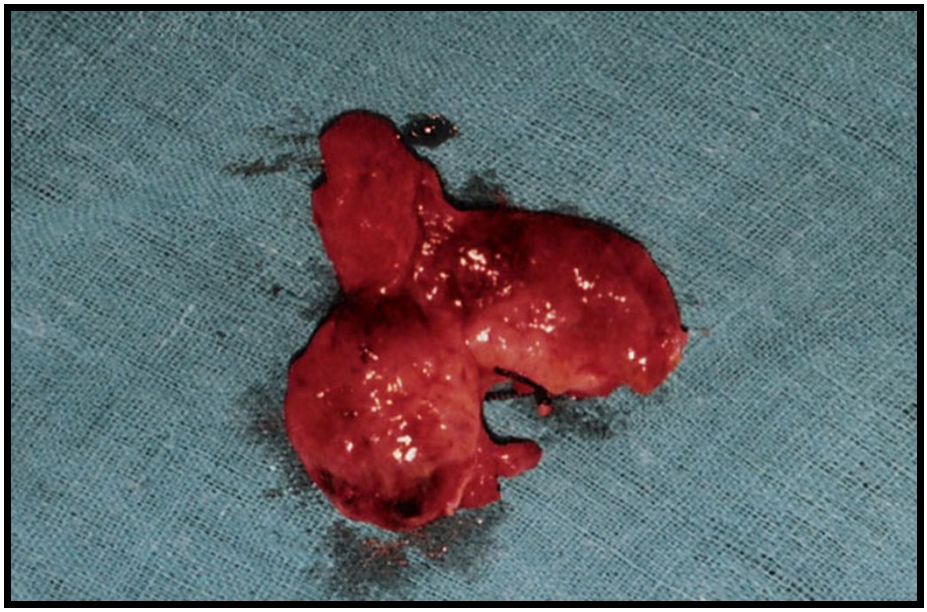
THYROIDECTOMY IN PROGRESS



POST THYROIDECTOMY - INTACT RLN



APPROXIMATION OF THE STRAP MUSCLES



SPECIMEN

MASTER CHART

S. No.	Name	Age	IP	Dur	Lump	Dysph	Dyspn	Hoarseness	Biochem	RAIU	Toxic	Treat	Postop	HPE
1	Kavitha	22	762228	6 M	+	-	-	-	-	-	-	STT	UE	MNG
2	Malar	25	765616	2 Y	+	+	-	-	-	-	-	STT	Edema	Foll. Ca
3	Selvi	24	766170	8 M	+	-	-	-	-	-	-	STT	UE	MNG
4	Shanthi	30	771781	1.5 Y	+	+	+	-	+	+	+	AT+STT	Toxicity	MNG
5	Sujatha	31	774800	6 M	+	-	-	-	-	-	-	STT	UE	MNG
6	Amudha	28	777164	10 M	+	-	-	-	-	-	-	STT	Hoarse	MNG
7	Latha	30	778109	1 Y	+	+	-	-	-	-	-	STT	UE	Degen MNG
8	Prema	32	779005	4 M	+	+	-	-	-	-	-	STT	UE	MNG
9	Sundari	35	780168	6 M	+	-	-	-	-	-	-	STT	UE	Degn MNG
10	Kalaiselvi	32	780194	2 Y	+	-	+	-	-	-	-	STT	Edema	Hashimotos
11	Raja	30	780214	4 Y	+	+	+	-	+	+	+	AT+STT	UE	Treated MNG
12	Lakshmi	22	782164	1 Y	+	-	+	-	+	+	+	AT+STT	UE	MNG
13	Gandhimathy	40	783175	4 M	+	-	-	-	-	-	-	STT	UE	MNG
14	Meena	36	784261	5 M	+	-	+	-	+	+	+	AT+STT	UE	Degn MNG
15	Panchalai	41	784316	6 Y	+	+	+	-	-	-	-	STT	UE	Degn MNG
16	Kasthuri	36	784960	2 Y	+	+	-	-	-	-	-	STT	UE	Degn MNG
17	Gayathri	24	785160	1.5 Y	+	-	-	-	-	-	-	STT	UE	MNG
18	Solai	41	786461	1 Y	+	+	-	-	-	-	-	STT	UE	MNG
19	Megala	45	787146	6 M	+	+	-	-	-	-	-	STT	UE	Degen MNG
20	Nalini	32	788106	8 M	+	-	-	-	-	-	-	STT	UE	MNG
21	Linda	26	789171	1 Y	+	+	-	-	-	-	-	STT	UE	MNG
22	Muniammal	46	789673	1.5 Y	+	-	+	-	-	-	-	STT	UE	MNG
23	Bhavani	24	790166	8 M	+	+	-	+	-	-	-	STT	UE	Hashimotos
24	Ambika	26	791684	1 Y	+	-	-	-	-	-	-	STT	UE	Foll. Ca
25	Nalini	22	792614	8 M	+	+	-	-	-	-	-	STT	UE	MNG
26	Mangammal	41	792656	6 M	+	-	-	-	-	-	-	STT	UE	MNG
27	Muthammal	44	793167	1.5 Y	+	+	+	+	-	-	-	STT	UE	MNG
28	Vadivazhagi	24	794657	2 Y	+	-	+	-	-	-	-	STT	UE	T.it is

S. No.	Name	Age	IP	Dur	Lump	Dysph	Dyspn	Hoarseness	Biochem	RAIU	Toxic	Treat	Postop	HPE
29	Devaki	31	795168	3 Y	+	-	-	-	-	-	-	STT	UE	Degen MNG
30	Rani	28	796169	4 M	+	-	+	-	-	-	-	STT	Hoarse	MNG
31	Sulochana	34	796646	9 M	+	+	+	-	-	-	-	STT	UE	MNG
32	Jagadambal	42	796816	1 Y	+	+	+	+	-	-	-	STT	UE	MNGPap. Ca
33	Prameela	26	796960	1.5 Y	+	-	-	-	-	-	-	STT	UE	T. it is
34	Ranganayaki	34	797016	6 M	+	-	+	+	+	+	+	AT+STT	Hoarse	MNGPap. Ca
35	Chellammal	35	797611	2 Y	+	+	+	-	+	+	+	AT+STT	UE	Degen MNG
36	Vadivammal	40	797819	1 Y	+	-	+	-	-	-	-	STT	UE	MNG
37	Chittammal	38	799104	1 Y	+	+	-	-	-	-	-	STT	UE	MNG
38	Shakunthala	26	799690	5 Y	+	-	-	-	-	-	-	STT	Edema	Degen MNG
39	Jagadha	24	799909	1.5 Y	+	+	+	-	-	-	-	STT	UE	Hashimotos
40	Rosy	16	800691	2 Y	+	-	-	-	-	-	-	STT	UE	MNG
41	Mumtaj	34	810961	6 M	+	-	-	-	-	-	-	STT	UE	Degen MNG
42	Selvamery	26	815614	8 M	+	-	-	-	-	-	-	STT	UE	MNG
43	Sulthana Begum	40	819561	1 Y	+	-	-	-	-	-	-	STT	UE	MNG
44	Meena	25	820156	2 Y	+	-	-	-	-	-	-	STT	UE	MNG
45	Susheela	29	820619	1 Y	+	-	-	-	-	-	-	STT	UE	MNG
46	Viji	26	820118	1 M	+	-	-	-	-	-	-	STT	UE	MNG
47	Girija	30	821168	7 M	+	-	-	-	-	-	-	STT	UE	MNG
48	Punitha	31	821170	1 Y	+	-	-	-	-	-	-	STT	UE	MNG
49	Ramya	29	821179	3 Y	+	-	-	-	-	-	-	STT	UE	MNG

IP : Inpatient Number; Bio. Chem. : Serum T_3, T_4, TSH assay; RAIU : Radioiodine Uptake; STT : Subtotal thyroidectomy; AT : Antithyroid Drugs;
UE : Uneventful; HPE : Histopathology; MNG : Multinodular Gotire; Post Operative Sequel; Treat : Treatment given; Toxic : Toxicity;
Dur : Duration; Dysph : Dysphagia; Dyspn : Dyspnoea; T. itis : Lymphocytic thyroiditis; Degen MNG : Degenerating Goitre; Foll. Ca : Follicular carcinoma; Pap. Ca : Papillary Carcinoma; Hoarse : Hoarseness