Sudan University of Science & Technology

Collage of Graduate Studies

Assessment of Iodine 131 Treatment for Hyperthyroidism (Sudan)

تقويم استخدام اليود- 131 في علاج فرط النشاط الدرقي

A Study Submitted for Partial Fulfillment of the Requirements of M.Sc Degree in Nuclear Medicine Technology

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الآية

بسم الله الرحمن الرحيم

قال تعالى:

(اقرأ و ربك الاكرم (3) الذي علم بالقلم(4))

صدق الله العظيم,,,

سورة العلق

Dedication

To

My parents...

My sisters...

My brothers...

My friends …

And my teachers …

And to all those who encouraged me to do this research, I dedicate this work.

Acknowledgment

First of all I thank god, the Almighty for enabling me to complete this study.

I sincerely thank Dr. Awad AbdallahAdlan for his continuous help, supervision and guidance.

I greatly thank all those who supported and helped me to complete this research. I am very grateful to all my teachers in all educational levels.

Very much thanks to the staff of Radiation and Isotopes Center of Khartoum, especially the staff of Information's and statistics department for their help and cooperation to achieve my gall.

Abstract

The main objective of this research is to study the outcome of treatment of hyperthyroidism with radioactive iodine (RAI). The study population was 55 patients come to Radiation and isotopes center of Khartoum with hyperthyroidism during 2013-2015. Data of measurements of thyroid uptake before treatment, and determination of thyroid hormones before and after Iodine-131 therapy were taken. Over a period of 2-3 months of follow up 46 of patients (84%) respond to RAI therapy, and showed marked decrease in thyroid hormones.

The mean level of TSH, T_3, T_4 before RAI treatment were 0.2IU/ml, 5.55nmol/l and 180nmol/l respectively, while the mean level after treatment (2-3 months later) was 2.31IU/ml,2.24nmol/l and 107nmol/l respectively. Normal TSH values (0.27-4.2IU/ml), the normal T_3 values (1-3.3 nmol/l) and the normal T_4 values (55-177nmol/l) and the mean thyroid uptake level before RAI treatment was 18.29%, while the normal uptake value was (.4-4%) which indicates hyperthyroidism.

The mean RAI dose given to the patients was 14.7mCi. And the dose ranged from (8-30)mCi.

During 2-3 month follow-up after RAI therapy, only 9 patients (16.4%) from the total number of patients showed no response to RAI therapy.

During 3-6 months follow-up only 5 patients (9%) from the total number of patients need further RAI dose,7 patients (12.7%) were supported with anti-thyroid drugs and 9 patients(16.4%) from the total population showed hypothyroidism.

during one year follow-up 7 patients (13%)suffered from hypothyroidism as a side effect of RAI therapy.

المستخلص

الهدف الاساسي من هذه الدراسة هو دراسة مدى فعالية استخدام اليود المشع في علاج فرط نشاط الغدة الدرقية. عدد المرضى الذين شملتهم الدراسة 55مريضا و مريضة ممن يعانون من فرط نشاط الغدة الدرقية بمركز الخروطوم القومي لعلاج الاورام خلال عام 2013-2015.

البيانات المتضمنة في الدراسة هي تحديد نسبة امتصاص الغدة لليود قبل العلاج باليود - 131 المشع و تحديد مستوى هرمونات الغدة الدرقية قبل و بعد العلاج باليود-131.

بعد مرور 2-3 اشهر من العلاج و المتابعة استجاب 46مريضآ (84%) للعلاج, و اظهرت نتائجهم نقصان ملحوظ في معدل هرمونات الغدة الدرقية .

متوسط مستويات هرمونات الغدة الدرقية قبل العلاج كانت علي النحو التالي: الهرمون المحفز للغدة الدرقية (TSH), الثايرونين ثلاثي اليود (T3) و الثايروكسين(T4) قبل العلاج يعادل 0.2IU/ml, 5.55nmol/l و180nmol/l علي التوالي. بينما متوسط مستواها بعد العلاج خلال (2-3 اشهر) كان2.31IU/ml, 2.24nmol/l و 107nmol/l على التوالي, علماً بأن المعدل الطبيعي للهرمون المحفز للغدة الدرقيةTSH (0.27 - 4.2IU/ml)و المعدل الطبيعي لهرمون الثايرونين ثلاثي اليود يتراوح بين (1-3.3nmol/l) و المعدل الطبيعي لهرمون الثايروكسين يتراوح بين(55-177nmol/l).

و قد خلصت الدراسة الى أن متوسط نسبة إمتصاص الغدة الدرقية قبل العلاج يعادل 18.29% حيث ان نسبة الإمتصاص الطبيعي للغدة تتراوح بين 4%-0.4 و هذا يدل على فرط نشاط الغدة الدرقية.

إن متوسط جرعة اليود-131 المشع المعطاة للمرضى تحت الدراسة تعادل 14.7 ملي كوري و جرعات المرضى تتدرج بين 8-30 ملي كوري.

خلال الفترة (2-3 اشهر) من المتابعة فقط 9 مرضي (16%) من العدد الكلي للمرضى الذين شملتهم الدراسة لم تظهر استجابتهم للعلاج بعد .

بعد مرور (3-6 شهور) من المتابعة بعد العلاج فقط 5 مرضى(9.1%) من العدد الكلي للمرضى احتاجوا الى جرعة اضافية من اليود المشع و عدد 7 مرضى (12.7%) تم امدادهم بعقاقير مضادة للنشاط الدرقي و 9 مرضى(16.4%) اصبح لديهم قصور درقي.

بعد مرور سنة من العلاج و المتابعة مازال هنالك حوالي 7(12.7%) من المرضى فقط يعانون من القصور الدرقي كأثر جانبي للعلاج باليود المشع.

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List of abbreviations

T_3	Tri-iodothyronine
T_4	Thyroxine
TSH	Thyroid Stimulating Hormone
RICK	Radiation and Isotope Center of Khartoum
RAI	Radioactive iodine
KeV	Kilo electron Volt
TPO	Thyroid peroxide
GD	Grave's Disease
ATA	American Thyroid Association
ETA	European Thyroid Association
JTA	Japanese Thyroid Association
SSKI	Strong Solution of Potassium Iodide
PTU	Propylthiouracil
USNRC	United States of Nuclear Regulatory Commission
TFT	Thyroid Function Test

Chapter 1

Chapter one

1-1Introduction:

Hyperthyroidism is the term for overactive tissue within the thyroid gland, resulting in overproduction and thus an excess of circulating free thyroid hormones: thyroxin (T_4), tri-iodothyronine (T_3), or both. Thyroid hormone is important at a cellular level, affecting nearly every type of tissue in the body. Thyroid hormone functions as stimulus to metabolism and is critical to normal function of the cell. In case of hyperactive function, it stimulates metabolism and exacerbates the effect of the sympathetic nervous system, causing speeding up of various body system and symptoms resembling an overdose of epinephrine (adrenaline). These include fast heart beat and symptoms of palpitations, nervous system tremor and anxiety symptoms, digestive system hyper-motility(diarrhea) and weight loss (Wikipedia, 2017).

The diagnosis may be suspected on history and physical examination, and is confirmed with blood tests for measuring the level of thyroid-stimulating hormone (TSH) in the blood is usually all that is required. A low TSH indicates that the pituitary gland is being inhibited by increased levels of T_4 and/or T_3 in the blood, and is therefore a reliable marker of hyperthyroidism (Wikipedia,2017).

Graves disease was the commonest cause of thyrotoxicosis accounting for 63% of patients also Toxic thyroid adenoma, Toxic multinodular goiter and Inflammation (thyroiditis) (Mir et al. 2004)

Hyperthyroidism could be treated in three ways: medical therapy with anti-thyroid drugs, radioiodine therapy and surgery (Francklyn, 1996).

In many clinics, radioiodine treatment is the most commonly used method for adult with hyperthyroidism and is generally accepted as safe convenient and of low cost (Francklyn, 1996).

Iodine is trapped and organified in thyroid gland to synthesize thyroid hormones.

However unlike stable iodine it emits two type of ionizing radiation namely 364 KeV gamma rays that are used for imaging of thyroid gland and 19 KeV beta particles, which during their limited passage (1-2 mm) in thyroid causes necrosis (thyroid tissue damage), which result in reducing mass of hyper functioning thyroid tissues (Sinclair et al, 1955).

There were over two hundred cases of hyperthyroidism per year referred to radiation isotopes centre Khartoum (RICK) for radioactive iodine treatment.

1.2 Problem of the study:

Determination of radioiodine therapy dose for hyperthyroidism is a real problem, because many factors influence the concentration of radioiodine in the thyroid tissue. There is a variety of radioiodine doses, patients response and side effects are different also.

1.3 Study Rational:

The radioactive iodine (RAI) is effective in most hyperthyroidism cases with minimal side effects.

1.4 Research Objectives:

1.4.1 General objective:

The main objective of this research is to evaluate the outcome of radioactive iodine -131 in the treatment of hyperthyroidism.

1.4.2 Specific objectives:

- To evaluate the response of hyperthyroidism to iodine therapy.
- To find the correlation between the dose given and the outcome obtained.
- To find the T-3,T-4 and TSH level before and after treatment with different radioiodine doses.
- To determine the thyroid uptake before RAI treatment and TSH level after treatment.

1.5 Research outlines

The study is presented into five chapters. Chapter one deals with introduction, problem of the study, hypothesis and objectives. chapter two highlights the literature review and previous studies, chapter three deals with material and methods, chapter four about results and chapter five shows the discussion, conclusion and recommendations.

Chapter 2

Literature Review

Chapter two

Literature Review

2.1 Background:

2.1.1 Anatomy and physiology of the thyroid gland:

The thyroid gland is one of several glands that make up the endocrine system the thyroid gland is a small, butterfly - shaped gland found just below the Adam's apple at the base of the neck, and in front of the trachea. The gland is controlled by pituitary gland makes thyroid - stimulating hormone(TSH). The TSH stimulates thyroid gland to make thyroid hormone (Rice, 2003).

The primary function of the thyroid is production of the hormones thyroxin (T_4), triiodothyronine (T_3), and calcitonin. Up to 80% of the T_4 is converted to T_3 by peripheral organs such as the liver, kidney and spleen. T_3 is about ten times more active than T_4.

High or low TSH is usually secondary to thyroid disease. in hyperthyroidism and thyrotoxicosis the TSH levels are found to be low due to the negative feedback of the excess T_3 and T_4. In hyperthyroidism the levels of TSH are high due to diminish thyroid hormone and therefore absence of the negative feedback (Van Herle et al, 1982).

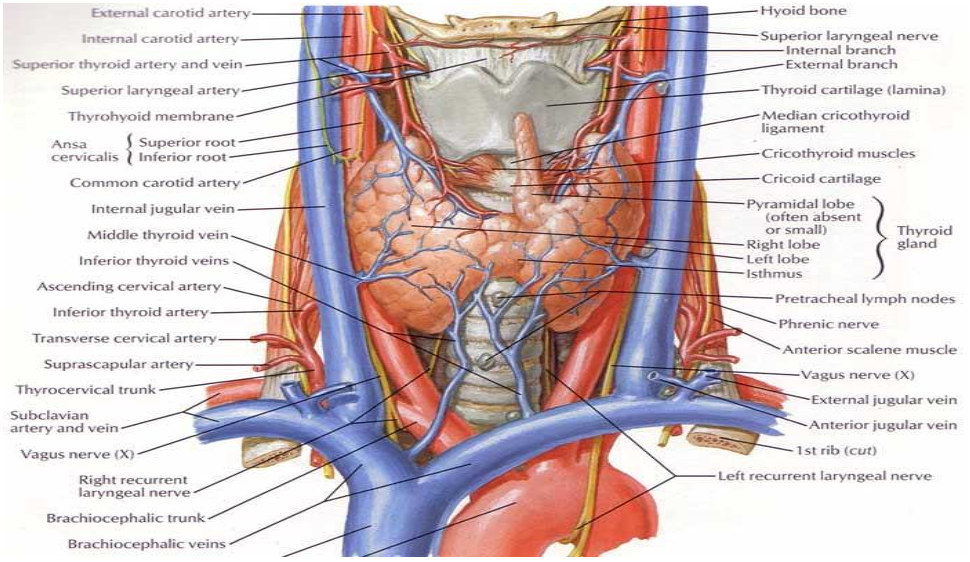

Figure 2.1 shows anatomy and blood supply of the thyroid gland

2.1.1.1 T_3 and T_4 production and Action:

Thyroxin is synthesized by the follicular cells from free tyrosine and on the tyrosine residues of the protein called thyroglobulin (TG). Iodine is captured with the " iodine trap " by the hydrogen peroxide generated by the enzyme thyroid peroxidase (TPO) and linked to the 3` and 5`sites of the benzene ring of the tyrosine residues on TG, and on free tyrosine. Upon stimulation by the thyroid - stimulating hormone (TSH), the follicular cells reabsorb TG and proteolytically cleave the iodinated tyrosine from TG, forming T_4 and T_3(in T_3 one iodine is absent compared to T_4), and releasing them into the blood. Deiodinase enzymes convert T_4 to T_3. Thyroid hormone that is secreted from the gland is about 90% T_4 and about 10% T_3.

Cells of the brain are a major target for the thyroid hormones T_3 and T_4 l. Thyroid hormones play a particularly crucial role in brain development during pregnancy (Van Herle et al, 1982)

2.1.1.2 Action of thyroid hormones:

1. Increase metabolism and protein synthesis.
2. Necessary for growth and development in children including mental development and attenuation of sexual maturity.

2.1.2 Iodine and pathology of the thyroid:

Significance of the Iodine:

In areas of the world where iodine (essential for the production of thyroxin, which contain four iodine atoms) is lacking in the diet, the thyroid gland can be considerably enlarged, resulting in the swollen necks of endemic goiter.

Thyroxin is critical to the regulation of metabolism and growth throughout the animal kingdom.

In humans, children born with thyroid hormone deficiency will have physical growth and development problems, and brain development can also be severely impaired, in the condition referred to as cretinism. Newborn children

in many developed countries are now routinely tested for thyroid hormone deficiency as part of newborn screening by analysis of a drop of blood. Children with thyroid hormone deficiency are treated by supplementation with synthetic thyroxine, which enables them to grow and develop normally (Van Herle et al, 1982).

Iodine is a requisite substrate for the synthesis of thyroid hormones. The minimum daily requirement of iodine is 50 micrograms. There is an auto regulatory mechanism within the thyroid gland which protects us from the consequences of iodine deficiency and excess. The consequences of iodine deficiency in the body include Endemic goiter, hypothyroidism, cretinism, increased incidences of neuromotor disabilities and increased infant mortality.

Excessive Iodine in the body leads to Hypothyroidism (defective auto regulation), Hyperthyroidism (absence of autoregulation), Autoimmune thyroid disease, Fetal / neonatal goiter with or without hypothyroidism.

Environmental iodine deficiency continues to be a significant public problem worldwide. The implementation of iodination programs prevents endemic cretinism and reduces the frequency of the other pathological consequences of iodine deficiency.

Iodine excess results principally from the use of iodine - containing medicinal preparations or radiographic contrast media (Table2.1). The pathological consequences of iodine excess will ensure only when thyroid auto regulation is defective or absent (Van Herle et al, 1982).

Table (2.1):Shows common iodine containing preparations

Route of administration	preparations	concentration
A. Topical	Betadine	10mg/ml
	Tincture of iodine	20mg/ml
	Iodosorb powder	0.9%
B.Oral	SSKI	47mg/dro

	Amiodarone	75mg/200mg tablet
	Lugal,s solution	130 mg/ml
C. Injectable	Iopanoate(Telepaque)	335mg/500 mg tablet
	Diatrizoate (Urografin - 325)	325 mg/ ml
	Iothalamate(Conray - 420)	420 mg/ml

Particular attention should be drawn to the cardiac drug amiodarone, which has very high iodine content. Storage in adipose tissue is a particular problem in clinical practice as its release may be prolonged for months after stopping. Amiodarone can cause hypothyroidism or hyperthyroidism which may be result in a diagnostic dilemma.

Apart from iodine being the cornerstone of the treatment of endemic goiter and cretinism, iodine has an important role as adjunctive therapy for hyperthyroidism. It produces a prompt slowing of thyroid hormone secretion by inhibiting the proteolytic degradation of thyroglobulin into its constituent amino acids. This effect is exploited in the treatment of thyrotoxic crisis and severe thyrocardiac disease. Iodine also reduces the vascularity of the thyroid gland, and is used in the pre-operative preparation of thyroidectomy (Van Herle et al, 1982).

2.1.2.1 Causes of Hyperthyroidism:

There are several causes of hyperthyroidism. Most often, the entire gland is overproducing thyroid hormone. This is called Grave's disease. less commonly, a single nodule is responsible for the excess hormone secretion, " hot" nodule. Thyroiditis (inflammation of the thyroid) can also cause hyperthyroidism.

The most common underlying cause of hyperthyroidism is graves, disease, a condition named for an Irish doctor who first described the condition. This condition can be summarized by noting that an enlarged thyroid (enlarged thyroids are called goiters) is producing too much thyroid hormone. (Remember that only a small percentage of goiters produce too much thyroid hormone; the majority of thyroid goiters actually become large because they are not producing enough thyroid hormone).

Grave's disease is classified as an autoimmune disease, a condition caused by the patient's own immune system turning against the patient's own thyroid gland. The hyperthyroidism of Grave's disease, therefore, is caused by antibodies that the patient's immune system makes. The antibodies attach to specific activating sites on the thyroid gland, and that in turn causes the thyroid to make more hormones.

Most patients with Grave's disease, however, have no obvious eye involvement. Their eyes may feel irritated. About one out of 20 people with Grave's disease will suffer more severe eye problems, which can include bulging of the eyes, severe inflammation, double vision, or blurred vision. If these serious problems are not recognized and treated, they can permanently damage the eyes and even cause blindness (Norman, 2009).

There are actually three distinct part of Grave's disease: Over activity of the thyroid gland (hyperthyroidism),Inflammation of the tissues around the eyes, causing swelling and Thickening of the skin over the lower legs (pretibial myxedema) (Norman,2009).

2.1.2.2 Characteristics of Grave's disease:

- Grave's disease affects women much more often than men (about 8:1 ratio, thus 8 women get Grave's disease for every man that gets it).

- Grave's disease is often called diffuse toxic goiter because the entire thyroid gland is enlarged, usually moderately enlarged, and sometimes quite big.
- Grave's disease is uncommon over the age of 50 (more common in the 30s and 40s).
- Grave's disease tends to run in families (not known why) (Norman, 2009).

2.1.2.3 Other less Common Causes of Hyperthyroidism:

Hyperthyroidism can also be caused by a single nodule within the thyroid instead of the entire thyroid. Thyroid nodules usually represent benign (non-cancerous) lumps or tumors in the gland. These nodules sometimes produce excessive amounts of thyroid hormones. This condition is called " toxic nodular goiter."

Inflammation of the thyroid gland, called thyroiditis, can lead to the release of excess amounts of thyroid hormones that are normally stored in the gland.

In sub- acute thyroiditis, the painful inflammation of the gland is believed to be caused by a virus, and the hyperthyroidism lasts a few weeks.

Amore common painless form of thyroiditis occurs in one out of 20 women, a few months after delivering a baby and is therefore, known as postpartum thyroiditis.

Hyperthyroidism can also occur in patients who take excessive doses of any of the available forms of thyroid hormone. This is a particular problem in patients who take forms of thyroid medication that contain T_3, which is normally produced in relatively small amounts by the human thyroid gland. Other forms of hyperthyroidism are even rarer (Norman, 2009).

2.1.2.4 Common tests used to diagnose hyperthyroidism:

Thyroid-stimulating hormone (TSH) produced by the pituitary will be decreased in hyperthyroidism. Thus the diagnosis of hyperthyroidism is nearly

always associated with a low (suppressed) TSH level. If the TSH levels are not low, then other tests must be run.

Thyroid hormones themselves (T_3, T_4) will be increased. For a patient to have hyperthyroidism, they must have high thyroid hormone levels. sometimes all of the different thyroid hormones are not high and only one or two of the different thyroid hormone measurements are high. This is not too common, as most people with hyperthyroidism will have all of their thyroid hormone measurements high (except TSH).

Iodine thyroid scan will show if the cause is a single nodule or the whole gland (Norman 2009).

2.1.2.5 symptoms and signs of hyperthyroidism:

The patients usually complains of loss of weight, although she / he have a good appetite and complains of weakness and tiredness after slight exertion. The patients nervous, anxious and easily excited and may often quarrel with family and children. There is a fine tremor which can be seen in the outstretched hand.

The eyes may be protruding (exophthalmoses) and the upper eyelids may be retracted with the white sclera seen above the camera, which gives the patient star-led look the exophthalmos is due to accumulation of mucopolysaccharides. Fat and fluid behind the eyeball, the lid retraction is caused by increased tone in the levator muscle of the eyelid. due to potentiating of sympathetic activity by thyroid hormones. The syndrome of hyperthyroidism associated with exophthalmos and enlargement of the thyroid is known as Grave's disease or exophthalmos goiter.

Patients commonly complain of palpitation. The heart rate, the stroke volume and the cardiac output are all increased. the systolic blood pressure may fall due to vasodilatation. This may lead to high cardiac output failure. In some

patients cardiac symptoms may be the only manifestation of thyroid disease. This should be remembered before they are referred to the cardiologist.

Thyrotoxic patients usually have a wet, warm skin, the palm are wet and warm. In contrast, nervous sweating is associated with cold hands. Menstrual disturbances are frequent and diarrhea is a common complain (Van Herle et al, 1982)

2.1.2.6 Treatment policy:

1- Anti-thyroid drugs:

The following are anti-thyroid drugs: Methimazole, carbimazole, and propylthiouracil are the mainstays of anti-thyroid drugs therapy. Their principal action is to inhibit the organification of iodide and coupling of iodothyronines, and hence the synthesis of thyroid hormones. propylthiouracil also inhibits the peripheral monodeiodination of thyroxine to triiodothyronine (Franklyn, 1994).

Indications for Anti-thyroid drugs Therapy and Treatment Regimens:

The three main drugs are prescribed for Grave's hyperthyroidism in the hope that the patient will have a remission of Grave's disease during therapy or to achieve euthyroidism before treatment with radioiodine or Surgery. The policy is to give an anti-thyroid drug in the hope of achieving remission in young patients (those 40 years old or younger) with a first episode of Grave's hyperthyroidism. In the case of older patients and young patients with relapse after a period of anti-thyroid drug therapy, give one of these drugs for only a short time before treating them with radioiodine.

If compliance is good, anti-thyroid drugs are highly effective in controlling hyperthyroidism. Methimazole(But not propylthiouracil) is effective if administered once daily, and serum thyroxine and triiodothyronine concentrations decrease more rapidly in patients treated with methimazole than in those treated with propylthiouracil. These differences are slight, but

because methimazole in moderate doses poses a lower risk of agranulocytosis, this drug is preferable to propylthiouracil.

Treatment is generally started with 10 to 20 mg of methimazole once a day or 75 to 100 mg of propylthiouracil three times a day. The dose should be reduced after four to six weeks as clinical and biochemical improvement occurs, and then adjusted every four to six weeks to maintain normal thyroid secretion until the maintenance dose is reached (methimazole, 5 to 10 mg a day propythiouracil, 50 to 100 mg a day) after approximately three months. The interval between follow-up visits can then be extended to three months (Franklyn, 1994).

Side effects of anti-thyroid drugs:

Serious side effects occur in approximately 3 of every 1000 patients, whether they receive methimazole or propylthiouracil. although a low dose of methimazole may be safer than either a high dose of methimazole or propylthiouracil with respect to agranulocytosis. Agranulocytosis (indicated by a granulocyte count below 500 per cubic millimeter) is an idiosyncratic reaction to these drugs. It is more common among patients over 40 years old, although this side effect is rarer among patients receiving less than 30 mg of methimazole patients who have agranulocytosis commonly presented with a fever or sore throat; patients should therefore be instructed to discontinue therapy and report these symptoms promptly if they occur. Agranulocytosis is an absolute contraindication to further anti-thyroid-drug therapy, and treatment with radioiodine should be given. Jaundice, hepatitis or vasculitis, and lupus-like syndromes are other rare but serious complications that make the discontinuation of therapy mandatory.

The incidence of minor side effects such as pruritus and rash is similar with both methimazole and propylthiouracil; these problems may resolve despite continued therapy. If they are severe enough to alter treatment, methimazole can be substituted for propylthiouracil and vice versa (Franklyn, 1994).

2- Adrenergic-Antagonist Drugs:

Adrenergic-antagonist drugs are useful adjunctive agents in patients with Grave's hyperthyroidism, in that they ameliorate some of the symptoms and signs of the disease, such as tremor, anxiety, and palpitations, more rapidly than does anti-thyroid drug therapy. They need not be given unless symptoms are moderate or severe, and should be discontinued as the patient becomes euthyroid. These drugs do not affect the synthesis and secretion of thyroid hormones and therefore should not be used alone except for short periods before radioiodine or surgical therapy. Despite their different pharmacologic characteristics, propranolol, metoprolol, atenolol, and nadolol are all effective in patients with hyperthyroidism.

Compliance may be improved by using nadolol (80 mg a day) or atenolol (50 to 100 mg a day). because these drugs can be given only once a day. Caution must be exercised in treating patients with asthma or heart failure, even if it is related to hyperthyroidism(Franklyn, 1994).

3- Inorganic Iodide:

Iodine given in pharmacologic doses (as Lugol's solution or as a saturated solution of potassium iodide) inhibits the release of thyroid hormones for a few days or weeks, after which its anti-thyroid action is action is lost. For this reaction it is not used routinely, but short-term iodine therapy is useful in the preparation of patients for surgery (Franklyn, 1994).

4- Radioiodine Therapy:

Radioiodine is increasingly used as first-line therapy for Grave's hyperthyroidism, and is the treatment of choice for recurrent hyperthyroidism for after anti-thyroid drug therapy. The objective of radioiodine therapy is to destroy sufficient thyroid tissue to cure hyperthyroidism(Franklyn, 1994)

5- subtotal thyroidectomy:

among patients with graves' hyperthyroidism, subtotal thyroidectomy is appropriate treatment only for those who refuse radioiodine therapy and for

the few with large goiters who have symptoms of compression or cosmetic concerns.

Any patients with hyperthyroidism scheduled to undergo surgery should be treated with methimazole until he or she is euthyroid.

damage to the recurrent laryngeal nerve, hypoparathyroidism, and bleeding into the neck are recognized but uncommon adverse effects of subtotal thyroidectomy. The mortality rate for elective surgery is close to zero, and the rate of complications is reported to be less than 4 percent(Franklyn, 1994).

2.1.3 Iodine-131 Radiotherapy for hyperthyroidism:

Thyrotoxicosis is the term used to describe condition that result from high level of circulating thyroxine (T_4) and triiodothyronine (T_3).

The main signs and symptoms of hyperthyroidism are palpitation, sweating, weight loss, tremor, and tachycardia (Murray et al, 1980)

Radiotherapy with radioactive iodine-131 (RAI) has been used to treat benign thyroid diseases for over 50 years (Becher and Sawin, 1996).

Disease of thyroid hyper function that can be treated with RAI include Grave's disease (GD), solitary hyper functioning nodule, and toxic multinodular goiter. RAI may also benefit patients with subclinical hyperthyroidism, particularly patients at risk for cardiac or systemic complications. RAI is used less frequently for the treatment of euthyroid goiters.

The preferred method for treating hyperthyroidism varies in different countries. In a survey of American Thyroid Association (ATA), European Thyroid Association (ETA), and Japanese Thyroid Association (JTA) members 65%, 22% and 11% of respondents, respectively, chose RAI as the therapy of choices for an index patient with GD.

In the same survey anti-thyroid drugs were regarded as initial therapy in 30.5%, 77% and 88% of ATA, ETA and JTA respondents respectively. Such variation likely stem from differences in perceived risks of prescribing radioactive treatments, differences in cost, local requirements for

hospitalization during treatment, patient compliance, response to anti-thyroid medications and natural history of autoimmune thyroid disease indifferent populations (Eary and Brenner, 2007).

2.1.4 Radiopharmaceuticals for Therapy:

Radioisotopes used in therapy require certain characteristics that differ from these of diagnostic radioisotopes. Radionuclides used in therapy are predominantly beta or alpha emitters. Pure particle emitters without any gamma component do not require special radiation safety precautions permitting out - patient treatment.

Physical and effective half-life of the radioisotope should be paired to the drug half-life in the body. Radioisotopes with very short half-lives are often not desirable because of difficulties in availability.

Before a radiopharmaceutical can be inject into patients, it needs to meet quality control standards, which include radiochemical purity, sterility and pyrogen testing.

Each radiopharmaceutical and must be assayed for each characteristic before it can be administered to the patients. Radioisotopes with high proportion of beta emission have been used clinically and represent the largest group used in therapy (Eary and Brenner, 2007).

2.1.5 Iodine-131:

Iodine-131 has convenient half-life and energy characteristics (T1/2 8.1 days, Emit beta 600 keV). Normal physiological update of iodine (and hence its radioactive form) in functioning thyroid tissue is the primary reason for its role in treating several thyroid disorders and malignancies. This fact, coupled with the energetic beta emission, has made it a treatment standard. Sodium iodide has the convenience of easy oral administration, which further improves patient compliance. Its high-energy gamma radiation (364 keV), which requires additional radiation safety measures, can be considered

advantageous for biodistribution studies and radiation-absorbed dose evaluation. Sodium iodide in liquid form is highly volatile and needs special handling in a fume hood with exhaust system to avoid inhalation of the iodide vapor during labeling. It also means that personnel handling the radiopharmaceutical should be subjected to periodic assays to exclude uptake in their thyroid glands. However, I-131 remains the most commonly used therapy radionuclide in nuclear medicine. When used for treating non thyroid malignancies, unwanted uptake of I-131 in normal thyroid gland needs to be blocked by administering elemental iodide, in the form of Lugol's iodine or strong solution of potassium Iodide (SSKI) (Eary and Brenner 2007).

2.1.6 Capsule versus Liquid dosage form:

Radioiodine is available in liquid solution or capsules are more convenient, but have generally been more expensive. Liquid formulation require extra measures to minimize radiation contamination at the time of administration.

RAI in capsules and liquid are generally believed to be equivalent in efficacy, although there has been some concern regarding a reduction in RAI bioavailability from capsules, because of incomplete dissolution related to the amount of magnesium serrate in the capsule (Yu et al, 2002).

2.1.7 Biological basis of iodine accumulation in thyroid tissue:

Iodine is the precursor of thyroxine and is taken up in to the follicular cells of the thyroid. Iodine is taken up by an active transport mechanism through the stimulation of thyroid stimulating hormone (TSH), the iodine pump increases in the presences of iodine deficiency. The retention of iodine in the follicular cell is dependent on the metabolic activity of the cell, and in the thyrotoxic patient the biological half life of iodine will be shorter than in euthyroid patient.

As the path length of the beta particle is about 0.5 mm, the toxic effects are limited to the thyroid with sparing of adjacent tissue (Murry et al, 1980).

The ensuing inflammation caused by radiation is followed by fibrosis, resulting in the reduction of the synthetic capacity of the thyroid gland (Eary and Brenner, 2007).

2.1.8 Contraindication to Radioactive Iodine Therapy:

A patient who is pregnant should not be treated with RAI. RAI crosses freely into the placenta, and the fetal thyroid tissue is capable of accumulating iodine after the 12th week of gestation. Administration of RAI during this period may result in severe neonatal hypothyroidism. Fetal and neonatal thyroid irradiation may also increase the risk of developing thyroid cancer later. Retained activity in the maternal bladder may also increase the risk of malignancy by direct radiation exposure to the fetus.

Women who are actively lactating or nursing also should not receive RAI as the iodine is excreted in breast milk.

RAI has no role for the treatment of hyperthyroid conditions unless it is classified as nodular goiter (single /multi) and grave's diseases while the contra-indicated cases are silent, sub acute and postpartum thyroiditis in addition to factitious thyroid disease (Eary and Brenner, 2007).

2.1.9 Thyroid function tests

Thyroid function tests should confirm results that are consistent with the disease to be treated. Women of childbearing age should have documentation that they are not pregnant at the time of treatment. Routine pregnancy testing should be offered prior to RAI therapy (Eary and Brenner, 2007).

Traditionally, RAI uptake measurements have been used to determine the amount of radioactivity to administer for treatment. However, this amount may also be empirically determined. Regardless of the method for dose selection, uptake measurements are useful for confirming increased thyroid gland function prior to treatment. This helps avoid inappropriate treatment of hyperthyroid conditions not associated with increased thyroid function, such

as silent thyroiditis or factitious hyperthyroidism. RAI uptake measurements can also help exclude a hyperfunction gland with "blocked" uptake, which will significantly reduce the effectiveness of RAI treatment also exogenous iodine exposure, such as from intravenous contrast agents. Also other substances which may contain large amounts of iodine include expectorants, kelp, carrageen, Lugol's solution, potassium iodide solutions, and drugs, such as amiodarone (Eary and Brenner, 2007).

Scanning is useful for the confirmation of hyperfunctioning nodules and the exclusion of cold nodules which need to be further evaluated. Although it is debatable whether a thyroid scan adds information that would alter the management of GD, scanning does provide confirmation of the diagnosis of GD while excluding the rare possibility of incidental thyroid cancer, which may manifest as a hypofunctioning nodule. Such nodules should be evaluated for possible malignancy prior to treatment with RAI (Eary and Brenner, 2007).

2.1.10 Patient preparation and adjuncts to treatment:

Pretreatment with anti-thyroid drugs have been shown to attenuate transient increases in thyroid hormone levels following treatment. Beta blockers may reduce symptoms related to hyperthyroidism.

Beta blocker medications, such as propranolol, 80-160 mg/day, or 50-150 mg/day atenolol, can be considered in patients without significant contraindications to this class of medication. Beta blockers may be continued during RAI treatment, to reduce morbidity from hyperthyroidism and prevent worsening of symptoms before the effects of radioiodine are realize, patients may also be given antithyroid medications several days before or after RAI treatment. If given, such medications should be discontinued three to five days prior to RAI administration. these drugs generally can be resumed 3 to 10 days following treatment, or earlier, if clinically necessary.

Pretreatment with propylthiouracil (PTU), with discontinuation up to one week prior to treatment, may increase the failure rate of radioiodine treatment PTU interferes not only with iodine organification, but also may cause an iodide diuresis. For this reason some have advocated higher doses (e.g. increase by 25%) for patients receiving antithyroid medications shortly before or after RAI treatment. Compared with PTU, pretreatment with methimazole may have a lesser effect on the failure rate of RAI treatment (Eary and Brenner, 2007).

2.1.11 Dose for Grave's disease:

The amount of RAI to be administered for treating hyperthyroidism related to GD may be selected empirically or determined by a dose calculation based on the assessments of thyroid mass and function. Standard treatment usually involves a single administration of RAI. The administration of small amounts of activity (e.g. 2mci)at frequent intervals is not recommended because it allows patients to remain hyperthyroid for longer periods of time and has not been proven superior at preventing iatrogenic hypothyroidism.

To deliver a specific dose to the thyroid, it is necessary to know the gland size, maximal uptake, and effective half-life of iodine in the targeted thyroid tissue. It may be assumed that the effective biological half-life of RAI is four to six days in the majority of patients with GD (Eary and Brenner, 2007).

2.1.12 Calculation of administered activities for treatment of benign thyroid disease:

Use the following equation to correct for 24-hour RAI uptake in target thyroid tissue:

Administered activity = Thyroid tissue mass(g) x Activity per g tissue / RAI uptake at 24 hours with RAI uptake expressed as a fraction of 100% uptake, (e.g. 30% uptake is 0.30).

2.1.13 Typical activities per gram for various hyperthyroid diseases:

Grave's disease: 2.96-7.4 MBq

Solitary hyperfunctioning nodule: 7.4 MBq

Toxic multinodular goiter: 3.7-7.4MBq

Euthyroid goiter: 3.7 -4.625 MBq

Although it may be possible to estimate thyroid mass by palpation, it is difficult to estimate the degree of thyroid hyperfunction i.e., thyroid uptake on the basis of clinical findings alone.

Thus, most methods for calculating administered activity will require thyroid RAI uptake measurements, typically at 24 hours. A more complicated, but potentially efficacious approach has been the use of late RAI uptake measurements to allow the estimation of physiologic half-life of RAI (Bajanok et al, 1999).

Lower doses may reduce the incidence of hypothyroidism following treatment, but will increase the likelihood that a second treatment will be needed. Administration of 5.5 MBq (150 mCi) per gram will yield a dose of approximately 120 Gy to the thyroid. Larger doses can increase the likelihood of developing hypothyroidism in the post-treatment period, but should reduce morbidity related to prolonged hyperthyroidism. If a high success rate is the primary goal, doses between 200 and 300 Gy may be used occasionally, patients with GD may demonstrate RAI uptake more at four to six hours than at 24 hours. This condition of "rapid turnover" may necessitate the administration of larger amounts of radioactivity (5.5-7.4 MBq/g), owing to the shorter physiologic half-life of iodine in this situation.

Patients with persistent hyperthyroidism following a first treatment with RAI may benefit from additional treatments. Higher doses are often used for re-treatments which are typically given three to six months after the initial treatment.

Although treatments based on dose calculations appear efficacious, they have not proven superior to the use of empirically selected administered activities.

The advantages of using a fixed administered activity for treating hyperthyroidism are its simplicity and successful outcome in an acceptable number of patients (Eary and Brenner, 2007).

2.1.14 Dose for Toxic Nodular Goiter:

In addition to GD, thyrotoxicosis can also result from a single hyperfunctioning nodule, or multiple hyperfunctioning nodules(i.e. toxic multinodular goiter).

Although antithyroid drugs can ameliorate hyperthyroidism, definitive treatment is more commonly accomplished with RAI or surgery.

An initial course of antithyroid drugs may be considered in order to render the patient euthyroid before surgical or radioiodine treatment.

Nodular goiters are believed to be more radio resistant than the diffuse goiter of GD.

A calculated administered activity of 7.4 MBq per gram to the nodule, corrected for 24-hour uptake, has been used successfully (Eary and Brenner, 2007).

Radiation exposure to normal thyroid tissue in the setting solitary toxic nodules has never been shown to increase the incidence of thyroid cancer. This is likely because uptake in the normal thyroid tissue is suppressed. Nevertheless suppressed thyroid tissue may still receive a dose. However hypothyroidism following RAI treatment does seem to occur less frequently for solitary hyperfunctioning nodules compared with GD or multinodular goiter.

For toxic multinodular goiters, doses of 150 Gy may be adequate to resolve hyperthyroidism.

Fixed administered activities (e.g. 110 MBq) have also been used. Not uncommonly, patients with toxic multinodular goiters may have large glands and 24-hour uptake RAI measurements that are not significantly elevated. This may necessitate the administration of relatively large amounts of radioactivity (Eary and Brenner, 2007).

2.1.15 Goals and expected outcomes of treatment:

With adequate doses of radioactivity, an 80% response rate should be expected. A primary goal of treatment is to resolve hyperthyroidism in as short a time as possible.

However, with RAI doses calculated to achieve this goal in the majority of patients, a significant number of patients will ultimately become hypothyroid.

With more conservative doses of RAI, the incidence of hypothyroidism may be lower, although, the availability of close follow-up, and potential risks from persistent hyperthyroidism should be considered when deciding between more definitive treatment with higher doses and the use of more conservative doses.

Some authorities have maintained that hypothyroidism, which is easily and inexpensively treated with thyroid hormone supplementation, is preferable to persistent hyperthyroidism, which if not optimally treated, may produce significant morbidity.

It is also commonly believed that hypothyroidism may be a frequent long-term consequence of autoimmune thyroid disease. This has led to the recommendation for higher treatment doses to reduce the need for additional treatments in patients who do not respond to initial treatments.

If hypothyroidism is regarded as a potential therapeutic endpoint, patients should be given the understanding that will likely require life-long thyroid hormone supplementation to maintain normal function in the future (Eary and Brenner,2007).

The incidence of hypothyroidism was estimated at 20% to 40% of one year after RAI therapy (Hagen et al, 1967).

2.1.16 Side effects of RAI:

Side effects of RAI given at doses to treat benign thyroid disease are generally mild, infrequent, and self-limiting. These include thyroid tenderness, salivary gland swelling and nausea.

In addition to permanent hypothyroidism, transient hypothyroidism may also occur.

Ophthalmopathy may be particularly severe in 3% to 5% of patients with GD. The ocular manifestations of GD appear more frequently in women than in men (Eary and Brenner,2007).

2.1.17 Cancer Risk from Radioactive Iodine Therapy:

The possibility of an increased risk of cancer following radioiodine therapy for hyperthyroidism remains controversial despite numerous studies supporting the safety of RAI for this indication. Radioiodine treatment was not associated with excess total cancer deaths, or to any particular cancer with the exception of thyroid cancer, where there was a slight increase in thyroid cancer mortality following radioiodine therapy, although the underlying thyroid disease was suggested to have played a role.

A370-MBq(10mci) dose of iodine-131 is estimated to deliver a dose of approximately 0.01-0.03 Gy to the ovaries, mostly from excreted RAI in the bladder.

Radiation dose can be minimized with hydration and frequent voiding following treatment (Eary and Brenner, 2007).

2.1.18 Treatment of children with hyperthyroidism:

Grave's disease is the most common cause of hyperthyroidism in childhood. As in adult, there are a number of options regarding the treatment of

hyperthyroidism in children. The three most common treatment options are medical therapy with antithyroid drugs, treatment with RAI, and surgery.

Surgery for hyperthyroidism may have the highest cure although RAI is effective.

Because of radiation concerns, RAI therapy is often considered as second line therapy in children. RAI remains efficacious in treating patients who have not responded to other therapies (Eary and Brenner, 2007).

2.1.19 Patients instructions, Precautions, and follow-up:

Following the administration of therapeutic dose of RAI, contamination from excretion of RAI in urine, perspiration, breast milk, and saliva, can be associated with internal accumulation of RAI by others who come in contact with the patient.

Potential avenues of radiation exposure to others include ingestion of iodine-131 excreted by the patient, and from emitted gamma rays from iodine-131. Although there is little evidence to suggest that small amounts of radiation from iodine-131 treated patients can cause significant problems to others, guidelines have provided simple recommendations to reduce unnecessary radiation exposure, especially to pregnant women, infants, and children. It is requirement of the United States Nuclear Regulatory Commission to give patients verbal and written instructions prior to treatment with RAI.

- The Society of nuclear medicine has recommended that patients sleep alone for the first few days after treatment.
- For the first 72 hours, patients should not prolonged periods of time closer than three feet to any adult or within the same room as any child. An easy to follow guideline is to maintain a distance of one arm's length between treated person and others.

- Short periods of contact are acceptable if caring for an infant, patients should minimize the amount of time spent in close proximity with the infant during this time.
- Specially, infants should not be held for prolonged periods because of proximity to the thyroid or bladder.
- It is also recommended that time spent with pregnant women and young children be minimized for four to seven days after treatment.
- Work restrictions should be given to patients who may potentially expose pregnant women or children when performing their occupation.
- Fluid intake and frequent voiding should be encouraged for at least the first hour following treatment.
- Patients should be instructed to wake up at least 24 once the night following treatment to empty their bladder.
- The toilet should be flushed two or three times.
- Hand washing should be performed routinely and frequently.
- If patients perspire heavily, clothing should be washed separately.
- Because of contamination concerns, it is not recommended to treat women during their menses.
- Sharing food and eating utensils should be prohibited.
- Patients should wash their utensils separately or use disposable utensils.
- Lactating women who wish to be treated should be instructed to discontinue breastfeeding. Treatment should be withheld until lactation ceases. It may be possible to detect radioactivity in breast milk for several months following treatment. Patients should be instructed not to resume breastfeeding until the birth of another child.
- Women capable of childbearing should be asked to avoid pregnancy for at least six months following treatment, in order to confirm resolution of hyperthyroidism in addition to minimizing risks from radiation.
- Patients should be told that symptoms would resolve over several weeks and those they would require close follow-up, as hyperthyroidism my worsen during the intervening time.

- Symptoms of uncontrolled hyperthyroidism should be described, and patients should be informed to seek medical attention if such symptoms occur.
- They should also be made aware of the probable need for thyroid hormone supplementation in the future. The risk of persistent hyperthyroidism and myxedema following treatment necessitates close follow-up that includes clinical examination and thyroid function tests.
- Patients with GD should be made aware that ophthalmopathy may occur or worsen (Eary and Brenner, 2007).

2.2 Literature review:

Evaluation of RAI treatments for hyperthyroidism:

2.2.1 Research which was done by Khan SH, et al, in Khashmir institute of medical sciences, India. which was published by world journal of nuclear medicine, April 2006.Reported that the outcome of iodine131 in children and adolescents with Grave's disease as related to the dose resulted in a response rate at 3 months of 62.16% for low dose of I-131 (185 MBq) and 92.85% for the high dose (370 MBq).

2.2.2 In the study carried by Abdurrahman, (2009), about TFTs revealed that Grave's disease was the most common underlying cause of hyperthyroidism.

Symptoms of hyperthyroidism improved after one month only in 11 patients of 216 patients but other patients required anti thyroid medication for two months following RAI.

2.2.3 In the study carried by Alsiddig, (2010), to measure the outcomes of RAI therapy in hyperthyroidism among 53patients. And the study revealed that the radioactive iodine is effective in the treatment of hyperthyroidism with occurrence of hypothyroidism in 13 patients(24.5%) as main side effect during one year after RAI therapy.

Chapter 3

Material and Methods

Chapter Three

Material and Methods:

3.1 Materials:

The study group comprised of 55 patients suffering from hyperthyroidism and referred to Radiation and Isotopes center-Khartoum (RICK) for radioactive iodine therapy(RAI) during 2013-2015.The study group comprised adult males and females, suffering from (diffuse toxic goiter, thyrotoxicosis, toxic multinodular goiter, grave's disease, toxic nodular goiter and hyperthyroidism).

The radioactive iodine was administered to the study patients in liquid form (injection) and some of them take their dose orally (capsules or solution), the doses ranged from 8 mCi to 30 mCi.

Dose Calibrator used to calculate the actual therapy doses for patients under study is an ionization chamber and one of the most essential instruments in nuclear medicine for measuring the activity of radionuclides and radiopharmaceuticals. Since it measures the current produced by activity, it does not have dead time effects. It is a cylindrically shaped, sealed chamber with a central well and is filled with argon and traces of halogen at high pressure (~5–12 atmospheres). Its operating voltage is about 150V.Because radiations of different types and energies produce different amounts of ionization (hence current), equal activities of different radionuclides generate different quantities of current. For example, the amount of the current produced by 1 mCi (37 MBq) of 99mTc differs from that produced by 1mCi (37MBq) of 131I. Isotope selectors provided on the dose calibrator

are the feedback resistors to compensate for the differences in ionization (current) produced by different radionuclides so that equal activities produce the same reading. In most dose calibrators, isotope selectors for common radionuclides are push-button type, whereas those for other radionuclides are

set by a continuous dial. An activity range selector is a variable resistor that adjusts the range of activity (mCi, mCi, Ci, or kBq, MBq, GBq) for display.

3.2 Methods:

The study is a retrospective study for hyperthyroid patients referred to (RICK) during 2013 to 2015. Prior to administration of I131 dose, for any patient the thyroid uptake and laboratory parameter of thyroid function profile (TFT) were noted including (TSH, T_3 and T_4). The thyroid function test was performed by radio immune assay.The patients were followed up for evaluation of response during 2-3 months after I131 therapy, the (TFT) i.e. TSH, T_3 and T_4 were noted.

The patients documented to have normal or reduced thyroid hormone after I131 dose were termed as well responder to RAI therapy. And the patients with elevated thyroid hormones after radioiodine therapy were termed as non responder although some patients need further I131 dose and some of them need thyroid supplementary drugs.

The thyroid uptake was obtained by the thyroid scintigraphy which is non-invasive manner that used radioisotopes as tracer to diagnosis disease, uptake is obtained by reading the syringe before and after injection

The thyroid function profile was obtained by (RIA) method which is sensitive and specific assay method that uses the competition between radio labeled and unlabeled substances in antigen antibody reaction to determine the concentrate of the unlabeled substance, it can determine antibody concentrate or to determine the concentrate of any substance against which specific antibody can be produced..

Patients preparation for Radioactive Iodine Treatment:

- Withdraw drugs which may interfere with RAI treatment: antithyroid medications for at least three days, multivitamins for one week, over-the-counter medications (expectorants, topical iodine, kelp, agar,

potassium iodide solutions) for 2-3 weeks or longer depending on the iodine content, radiographic contrast agents for 4 weeks, and amiodarone for at least three to six months.

- Review results from previous biochemical tests, RAI uptake measurements, and thyroid scintiscans.
- Confirm the appropriateness of treatment and treatment dose.
- Obtain written informed consent.
- Provide verbal and written instructions.
- Consider pretreatment with beta blockers for symptomatic control.
- Beta blockers may be continued during treatment.
- Patients who have the potential to become pregnant should undergo pregnancy testing.
- Breastfeeding patients should be instructed to stop for at least two days prior to treatment.
- Patients must be instructed not to resume breastfeeding until the birth of their next child.
- Patients identity must be confirmed immediately before treatment in accordance with institutional requirements.
- Instruction for Patients Receiving Radioactive Iodine Treatment Before treatment:
- If there is a possibility that you are pregnant, inform the physician.
- RAI treatment should not be given to pregnant women.
- If you are breastfeeding, you cannot restart breastfeeding for that child. You may breastfeed with the birth of your next child.
- Do not eat for two hours before or after receiving treatment.

For the first 72 hours after treatment:

- Drink plenty of fluid to help flush any extra radioactive iodine from your body.

- Do not spend prolonged period of time closer than 3 feet to any adult, or within the same room as any child.

For 4 - 7 days after treatment, including the first 72 hours:

- Void as often as possible. Flush toilet twice after use.
- Wash hands thoroughly and routinely.
- Do not share eating utensils or towels. Use separate or disposable eating utensils.
- Wash utensils separately or before placing in dishwasher.
- Avoid close contact with children and pregnant women (not closer than 2 feet) for long periods of time.
- Sleep in a separate bed.
- If you are caring for a child, brief contact is acceptable, but avoid prolonged close contact, such as sitting in your lap.
- Avoid kissing and sexual intercourse.

Occasionally, there may be temporary neck or gland soreness, this can treated with over-the-counter pain relievers like acetaminophen.

The data was collected by special design data collecting paper as follow

3-2.1 Data collection:

the data was collected from the patients records using the following master sheet:

Table 3-1 simple example of master data sheet

Number of case	Radioactive iodine dose	T3b	T4b	TSHb	T3a	T4a	TSHa	Thy.UP	Patient gender	Patient age
1-										
2-										
3-										

whenT3b: T3 before treatment,T4b: T4 before treatment,TSHb: TSH before treatment, T3a:T3 after treatment,T4a: T4 after treatment, Thy.Up: the thyroid uptake before RAI treatment, TSHa ;TSH after treatment.

3.2.2 Data analysis:

The data was collected and analyzed by using EXCELL software and SPSS (Statistical Package for the Social Sciences).

Chapter 4

Result

Chapter four

Results

Hyperthyroidism is a condition associated with increased T_3& T_4 and depressed TSH level. In this chapter the following results will be highlighted: frequency percent of gender involved by hyperthyroidism, ages, applied radioactive iodine dose, level of T3,T4 and TSH before and after treatment, need of further dose and hypothyroidism induction (side effect).

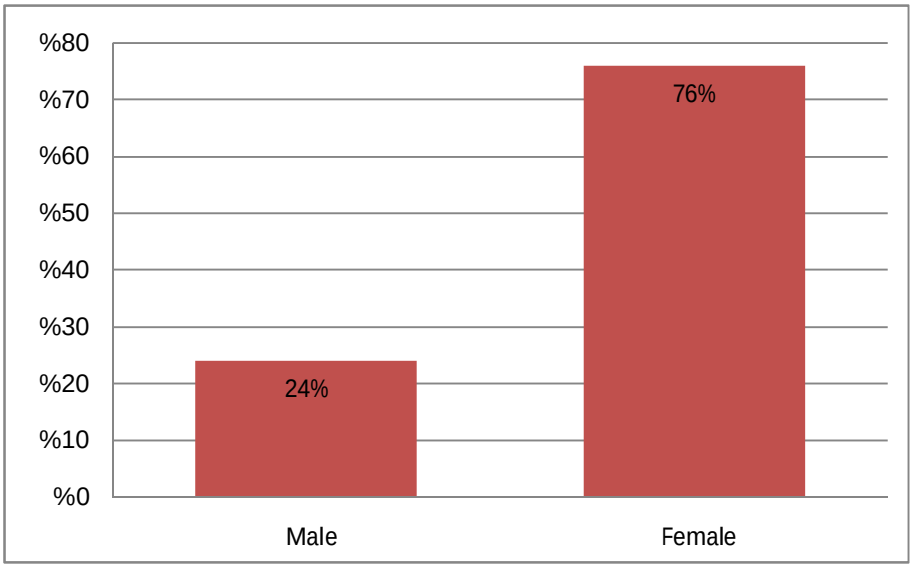

Figure 4.1: Distribution of the study population according to gender

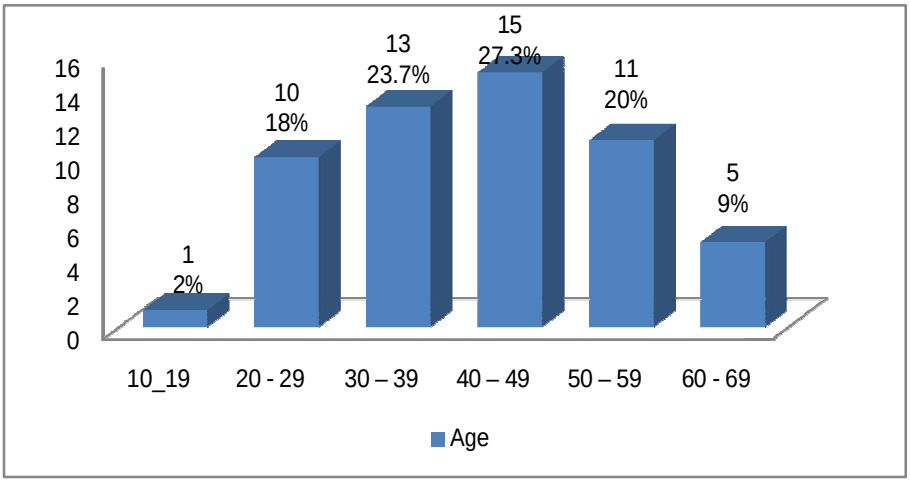

Figure 4.2: Distribution of the study population according to age

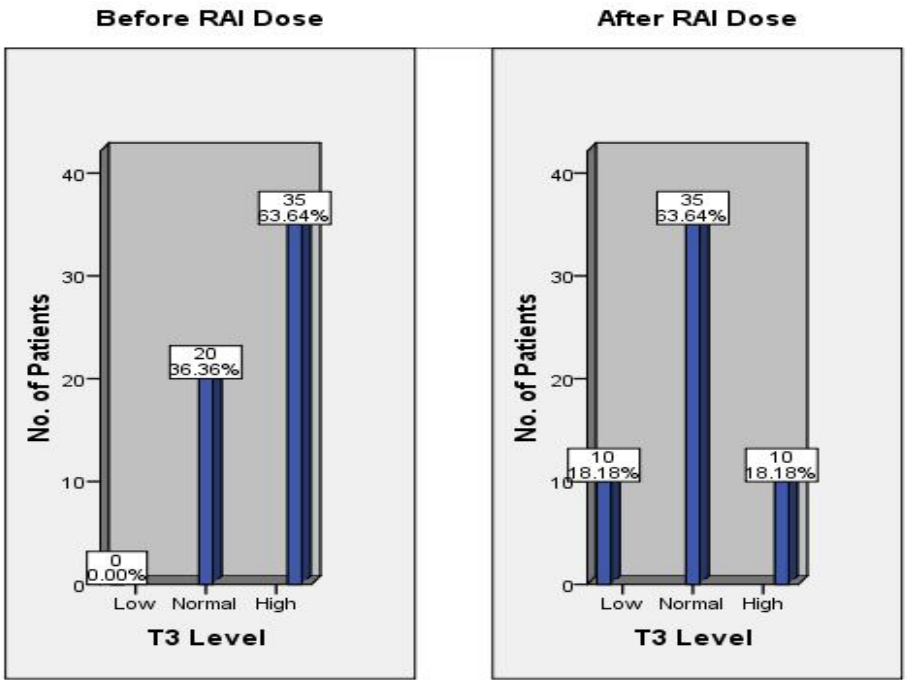

Figure 4.3: T3 levels before and after radioiodine therapy among the study population

Table (4.1): Paired Samples distribution for T3 (before and after dose):

	Mean	No. of pts.	Std. Deviation	Std. Error Mean
T3 before	5.5462	55	6.40581	.86376
T3 after	2.2362	55	1.88418	.25406

Table (4.2): Paired Samples test of mean difference between T3 (before and after dose):

	Paired Differences			t	df	Sig. (2-tailed)
	Mean	Std. Deviation	Std. Error Mean			
T3 before - T3 after	3.31000	6.40841	.86411	3.831	54	.000

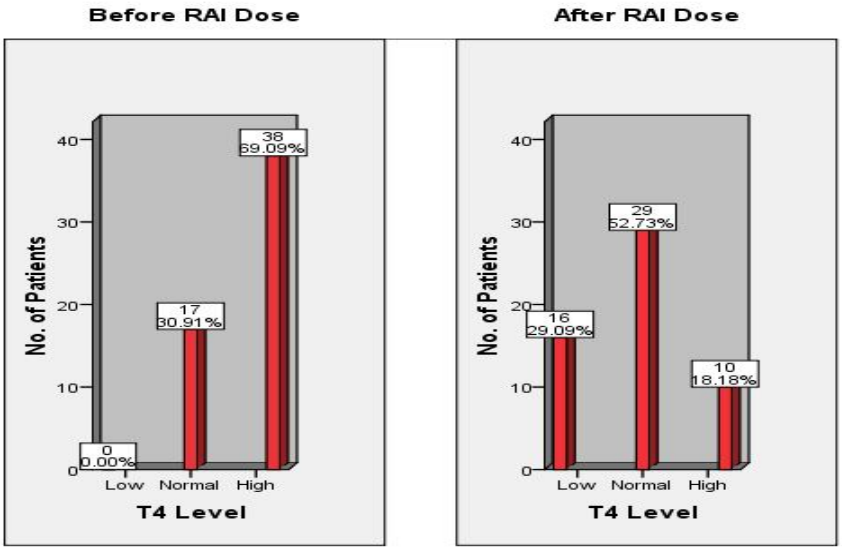

Figure 4.4: T4 level distribution before and after RAI therapy among the study population

Table (4.3): Paired Samples distribution for T4 (before and after RAI therapy)

	Mean	N	Std. Deviation	Std. Error Mean
T4 before	179.75	55	65.64516	8.85159
T4 after	106.94	55	78.62012	10.60113

Table (4.4): Paired Samples test of mean difference between T4 (before and after RAI therapy)

	Paired Differences			t	df	Sig. (2-tailed)
	Mean	Std. Deviation	Std. Error Mean			
T4 before – T4 after	72.8078	101.07897	13.62949	5.342	54	.000

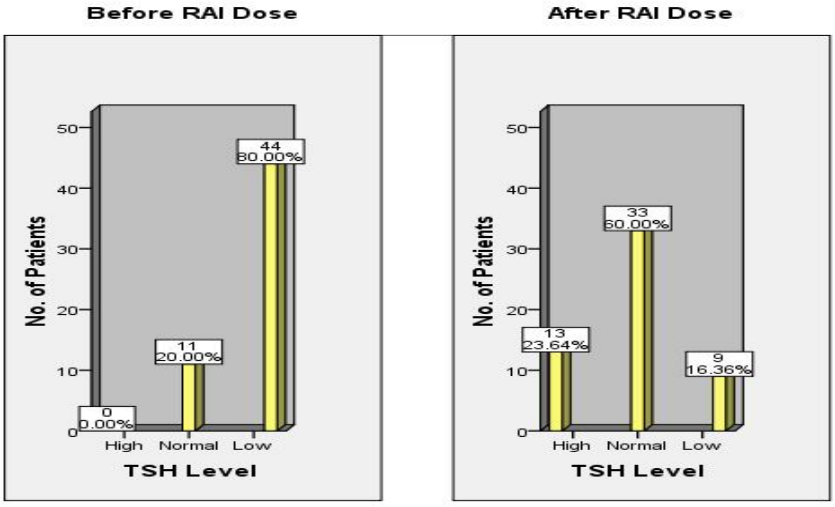

Figure 4.5: TSH level before and after RAI therapy among the study population

Table (4.5): Paired Samples distribution for TSH (before and after RAI therapy):

	Mean	N	Std. Deviation	Std. Error Mean
TSH before	.2037	55	.39355	.05307
TSH after	2.3062	55	2.28386	.30796

Table (4.6): Paired Samples test of mean difference between TSH (before and after RAI therapy):

	Paired Differences			t	df	Sig. (2-tailed)
	Mean	Std. Deviation	Std. Error Mean			
TSH before – TSH after	-2.10245	2.37355	.32005	-6.569	54	.000

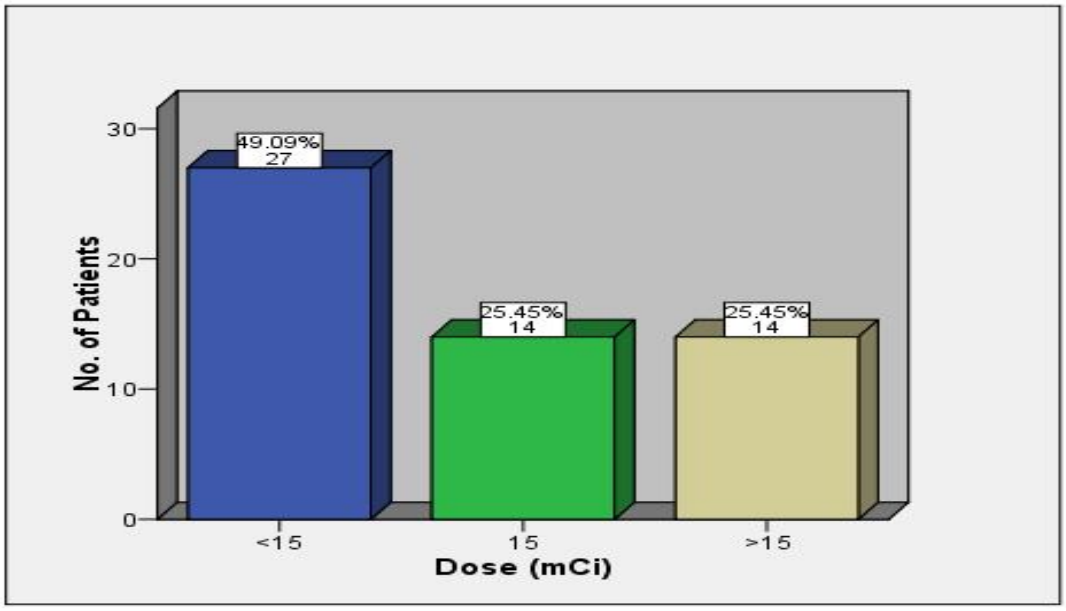

Figure 4.6: distribution of study population according to RAI dose given(mCi)

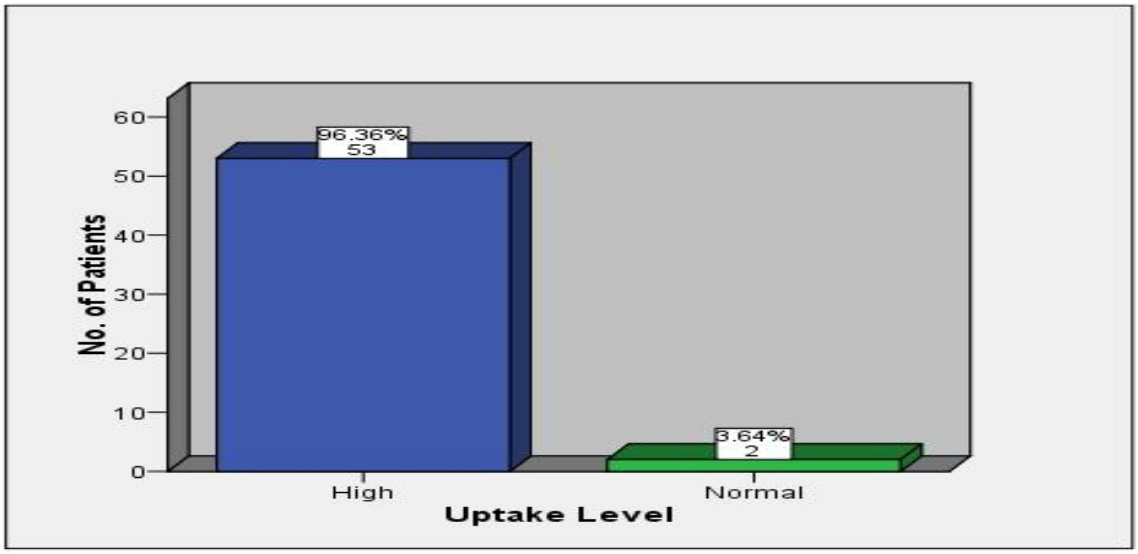

Figure 4.7: distribution of population according to thyroid Uptake level(%)

Table (4.7): Mean Uptake:

	N	Mean	Std. Deviation
Uptake	55	18.2944	14.89638

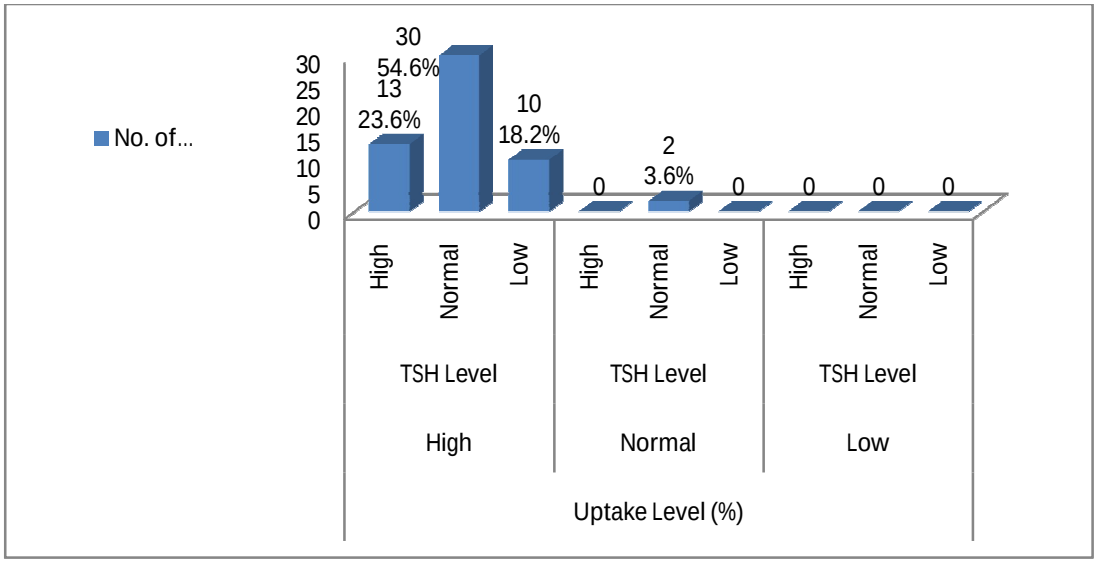

Figure 4.8: TSH level (2-3 months)after RAI therapy versus uptake level

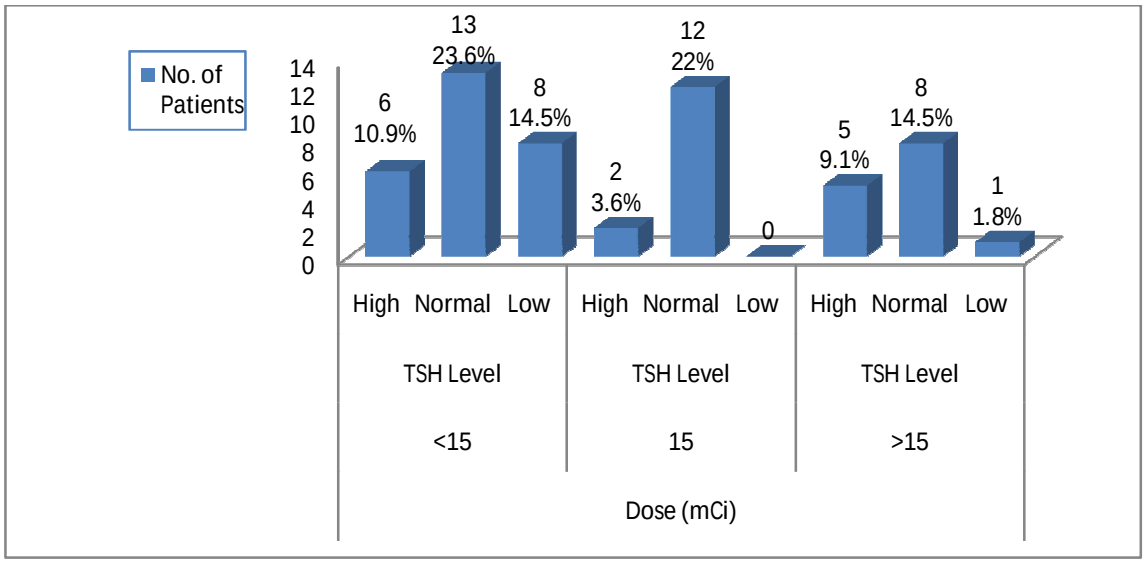

Figure 4.9: TSH level after RAI therapy(2-3 months) distribution according to dose level

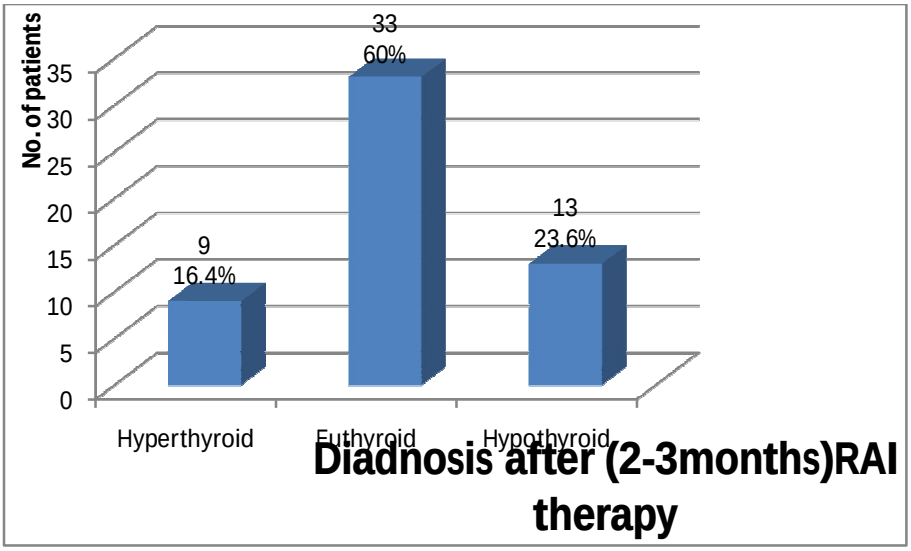

Figure 4.10 RAI therapy outcome (2-3 months) after first dose

Thyroid hormones level (3-6 months) after RAI therapy:

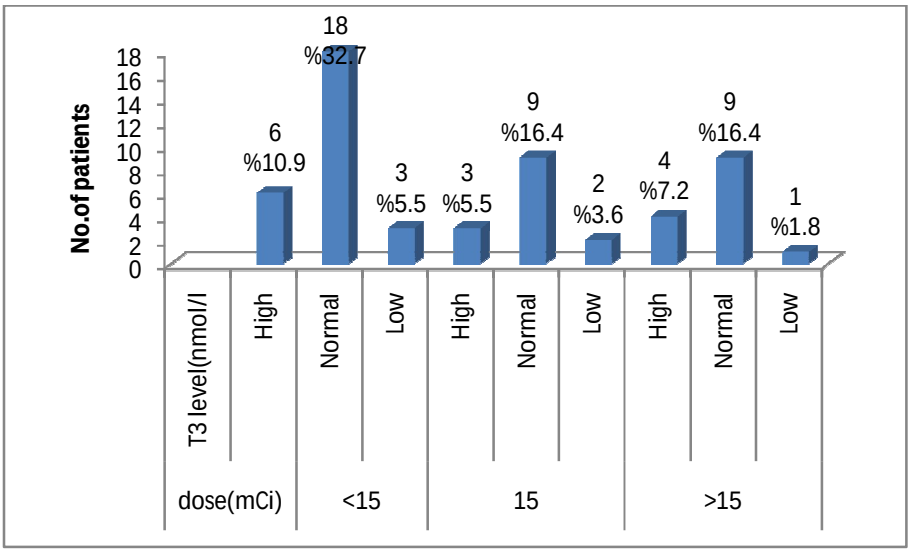

Figure 4.11: T3 level (3-6 months) after RAI therapy according to dose level

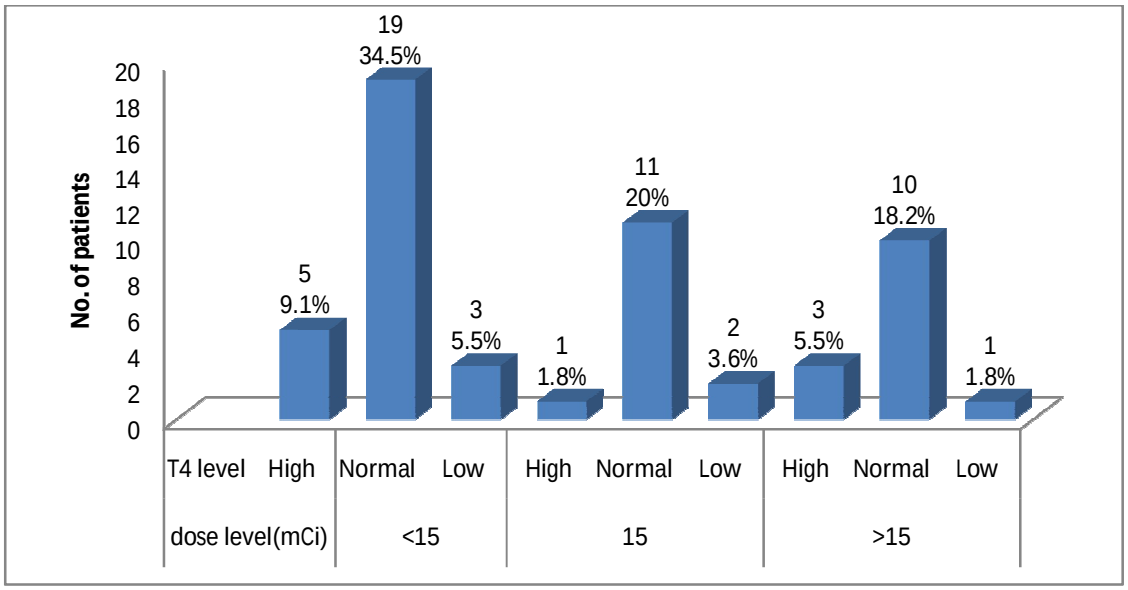

Figure 4.12: T4level(3-6 months)after RAI therapy according to dose given

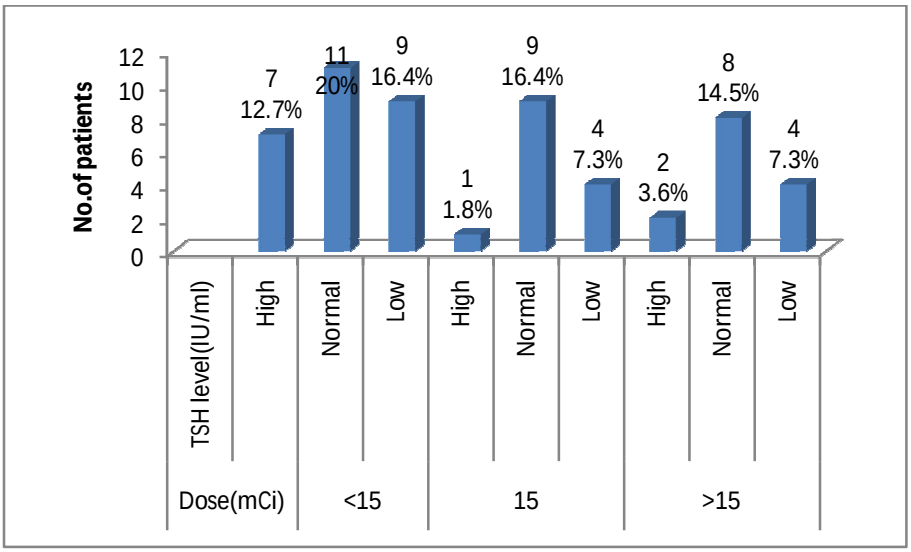

Figure 4.13: TSH level(3- 6months) after RAI therapy according to dose level

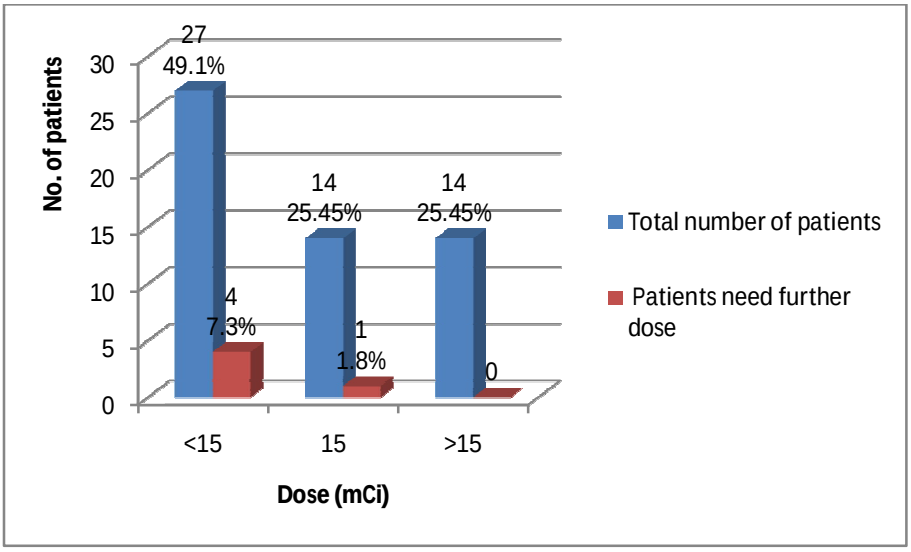

Figure 4.14: patients need further doses of RAI among the study population

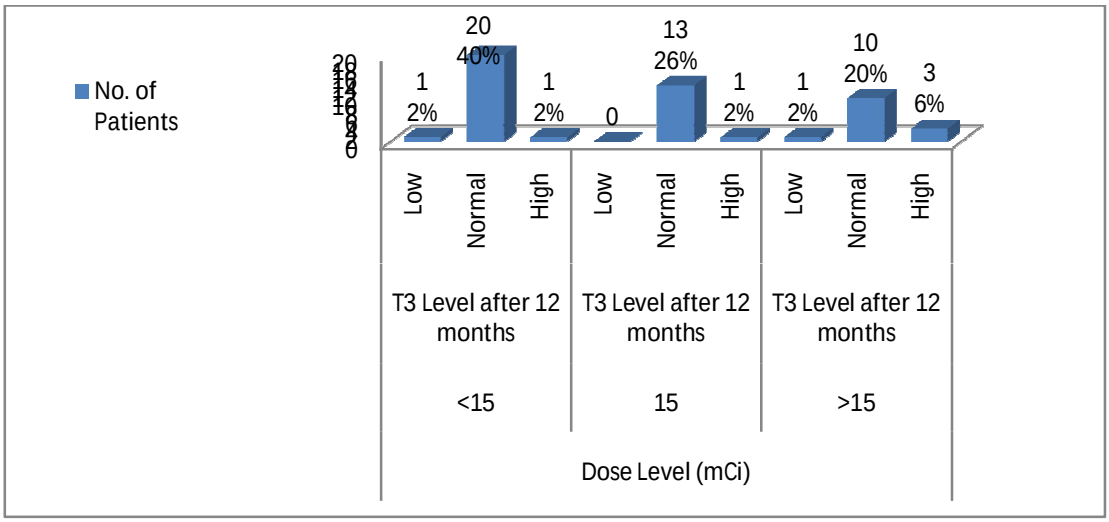

Figure 4.15: T3 level after 12 months of RAI therapy according to dose level

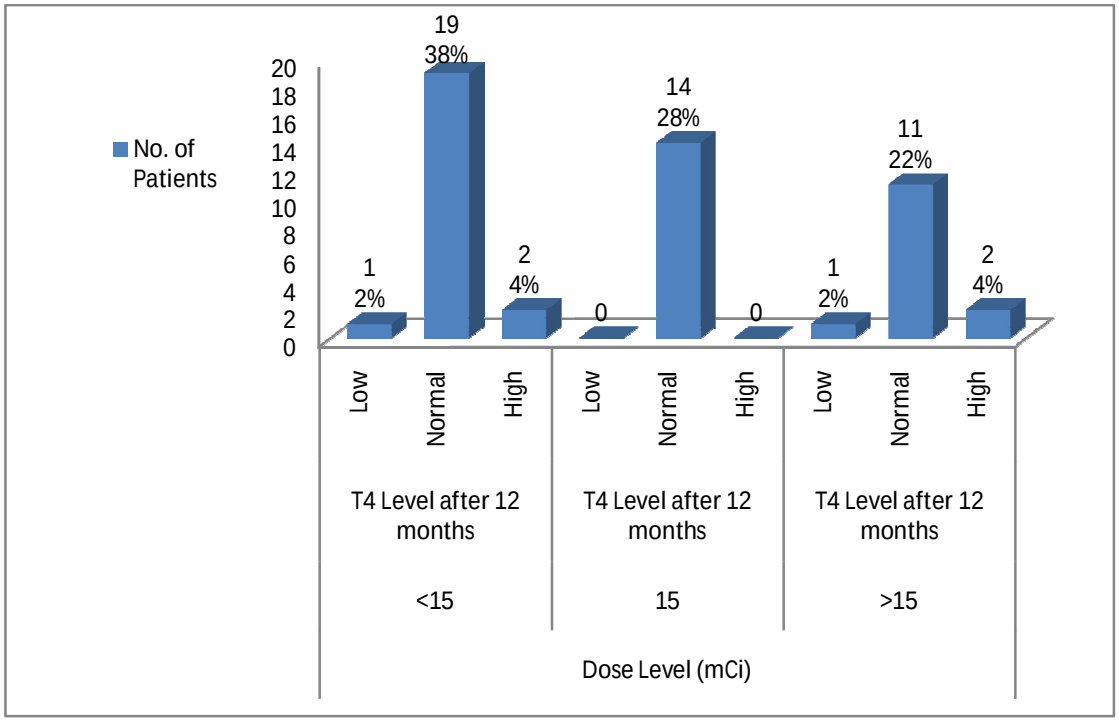

Figure 4.16: T4 level after 12 months of RAI therapy according to dose levels

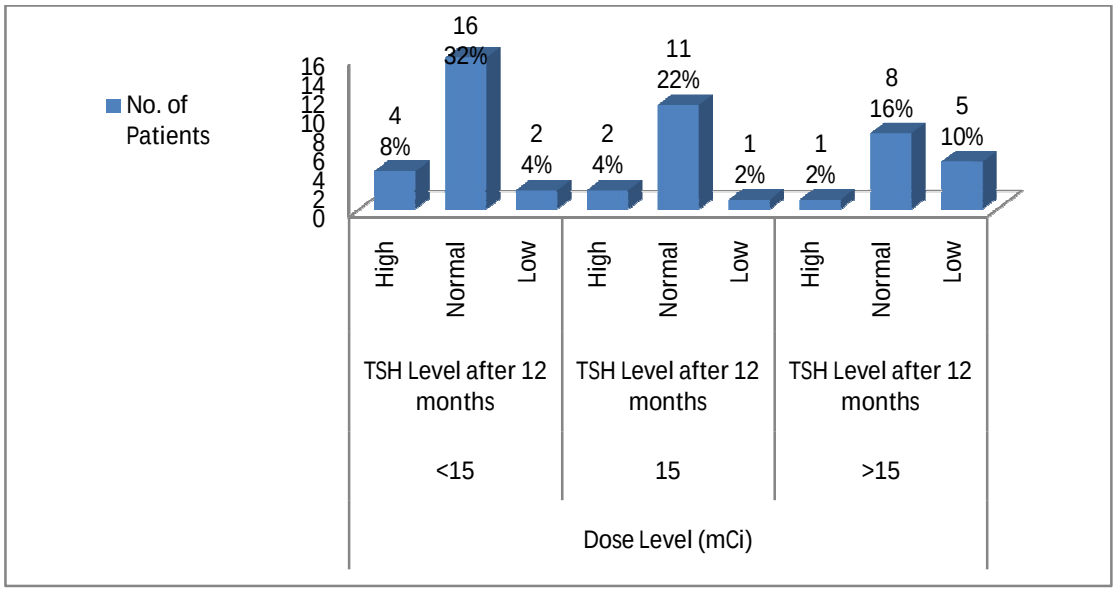

Figure4.18: TSH level after 12 months of RAI therapy according to dose levels

Chapter 5
Discussion, Conclusion and Recommendations

Chapter five

Discussion, Conclusion and Recommendations

5.1Discussion:

Distribution of the study population according to gender, which reveals that: there were 76% of the sample population were females and 24% were males. This results matched with information stated by Norman,(2009). (Grave's disease affects women much more often than men (about 8:1 ratio, thus 8women gets Grave's disease for every man that gets it) as show in Figure (4.1).

distribution of the study population according to ages. Such data reveal that: the common involved age with hyperthyroidism were the age groups of 30-59 years old with peak incidence in the range from 40-49 years. This is matched with information given by Norman2009 (Grave's disease is uncommon over the age of 50 more common in the 30 and 40 years as shown in figure(4.2).

T3 level before and after I-131 treatment among the study population. The data reveal that: the mean T3 level before RAI therapy was 5.55 nmol/l, which clearly indicate hyperthyroidism because the normal T3 levels(1-3.3nmol/l). And hyperthyroidism is associated with elevated T3 level. The mean T3 level after RAI therapy as 2.24 nmol/l, this value with significant correlation indicate that there is clearly response to RAI therapy because the normal T3 level (1-3.3 nmol/l). Among the population before RAI treatment, there was (63.6%)of patients had elevated T3 level, this percent is decreased to 18.2%after (2 -3 months) RAI therapy, while there were only 36.4% had normal T3 level before therapy dose and it raised to 53.6% after (2 - 3)RAI therapy, and there was evidence of (18.2%) low T3 level after RAI therapy as shown in Figure 4.3 and tables(4.1,2).

T4 level before and after RAI therapy among the study population, in which the mean T4 level before RAI therapy was 179.75nmol/l indicating the presence of hyperthyroidism, because the normal T4 levels(55-177nmol/l).

And hyperthyroidism is associated with elevated T4 level. The mean T4 level after RAI therapy was 106.9 nmol/l, this value with significant correlation indicate that there is a clear response to RAI therapy because the normal T4 level (55-177 nmol/l). Among the population before RAI treatment, there was (69.1%)of patients had elevated T4 level, this percent is decreased to 18.2%after (2 -3 months) RAI therapy, while there were only 30.9% had normal T4 level before therapy dose and it raised to 52.7% after (2 - 3)RAI therapy, and there was evidence of (29.1%) low T4 level after RAI therapy as shown in Figure 4.4and tables(4.3,4).

TSH level before and after RAI therapy among the study population. The data reveal that: the mean TSH level before RAI therapy was 0.204 IU/ml, which clearly indicate hyperthyroidism because the normal TSH levels(0.27- 4.2 IU/ml). And hyperthyroidism is associated with suppressed TSH level. The mean TSH level after RAI therapy within 2-3 months follow up was 2.31 IU/ml, this value with significant correlation indicate that there is a clear response to RAI therapy because the normal T3 level (0.27 - 4.2 IU/ml). Among the population before RAI treatment, there was (80%)of patients had low TSH level, this percent is decreased to 16.4% after (2 -3 months) RAI therapy, while there were only 20% had normal TSH level before therapy dose and it raised to 60% after (2 - 3)RAI therapy, and there was evidence of (23.6%) high TSH level after RAI therapy as shown in Figure 4.5and tables(4.5,6).

distribution of study population according to RAI dose given(mCi). It reveal that the mean RAI dose given to the patients was 14.7 mCi while the dose range was 10 - 30 mCi as has been applied at RICK, however the required dose which is stated by Eary and Brenner, (2007) is 1110 MBq (30) as shown in Figure 4.6.

distribution of population according to thyroid Uptake level(%) before RAI therapy among the study population. The data reveal that: the mean uptake

level before RAI therapy was 18.29%, which clearly indicate hyperthyroidism because the normal thyroid uptake levels(0.4 - 4%). And hyperthyroidism is associated with elevated thyroid uptake value as shown in Figure 4.7.

TSH level (2-3 months)after RAI therapy versus uptake level. The data reveal that: among the patients (96.4%) who were high thyroid uptake level before RAI therapy, there was 23.6% were high TSH(elevated),54.6% of them was normal TSH and 18.2% were low TSH level(hyperthyroidism). And all patients who have normal thyroid uptake(3.6%) before RAI therapy had normal TSH level after(2-3 months)RAI therapy. That means there was only 10 patients from the total number of patients who have elevated thyroid uptake level before RAI treatment suffer from decreased TSH level after (2-3 months) RAI therapy as shown in Figure 4.8.

TSH level after RAI therapy(2-3 months) distribution according to dose level. The data reveal that: among the patients (49.1%) who were received less than 15 mCi there was 10.9% were high TSH(elevated),23.6% of them was normal TSH and 14.5% were low TSH level(hyperthyroidism). And among that who received 15mCi there was 3.6% of the patients were high TSH,22% of them has normal TSH and no evidence of low TSH level in patients who received 15mCi, that mean no hyperthyroidism patients in populations of 15mCi. While the patients (25.5%) who received doses more than 15mCi there were 9.1% were high TSH level, 14.5% of them were normal TSH level and there was 1.8% has low TSH level.(still hyperthyroidism after 2-3 months from RAI therapy)as shown in Figure 4.9.

The RAI therapy outcome(2-3 months) after first dose. the data shows that during 2-3 months follow up for the patients sample, there were 83.6% having considerable response to RAI therapy, specifically 60% showed euthyroid and hypothyroid, indicate non response to first RAI dose i.e. needs further iodine dose, therefore the 83.6% of patients who response to RAI is clearly indicate the effectiveness of RAI in the treatment of hyperthyroidism such result is on

agreement with Eary and Brenner,(2007). Statement" with adequate dose of radioactivity, an80% response rate should be expected as shown in figure 4.10.

T3 level (3-6 months) after RAI therapy according to dose level. The data reveal that: among the patients (49.1%) who were received less than 15 mCi there was 10.9% were high T3(elevated),32.7% of them was normal T3 and 5.5% were low T3 level. And among that who received 15mCi there was 5.5% of the patients were high T3,16.4% of them has normal T3 and 3.6%have low T3 level. While the patients (25.5%) who received doses more than 15mCi there were 7.2% were high T3 level, 16.4% of them were normal T3 level and there was 1.8% has low T3 level. This means that there was 13 patients from the total number of patients were still suffer from elevated T3 after 3-6 months from RAI therapy as shown in Figure 4.11.

T4 level (3-6 months) after RAI therapy according to dose level. The data reveal that: among the patients (49.1%) who were received less than 15 mCi there was 9.1% were high T4(elevated),34.5% of them was normal T4 and 5.5% were low T4 level. And among that who received 15mCi there was 1.8% of the patients were high T4,20% of them has normal T4 and 3.6% have low T4 level. While the patients (25.5%) who received doses more than 15mCi there were 5.5% were high T4 level, 18.2% of them were normal T4 level and there was 1.8% has low T4 level. This means that there was 9 patients(16.4%) from the total number of patients were still suffer from elevated T4 level after 3-6 months from RAI therapy as shown in Figure 4.12.

TSH level (3-6 months) after RAI therapy according to dose level. The data reveal that: among the patients (49.1%) who were received less than 15 mCi there was 12.7% were high TSH(elevated),20% of them was normal TSH and 16.4% were low TSH level(hyperthyroidism). And among that who received 15mCi there was 1.8% of the patients were high TSH, 16.4% of them has normal TSH and 7.3% have low TSH level. While the patients (25.5%) who

received doses more than 15mCi there were 3.6% were high TSH level, 14.5% of them were normal TSH level and there was 7.3% has low TSH level. This means that there was 17 patients from the total number of patients were still hyperthyroidism after 3-6 months from RAI therapy according to TSH values) as shown in Figure 4.13.

The patients need further doses of RAI-131 among the study population sample. The data reveal that : among the patients(49.1%) ho were received less than 15mCi there was (7.3%) of the patients were in need to further iodine dose. And among those who were received 15 mCi there was (1.8%) of the patients were in needful to further iodine dose. while the patients (25.45%) who were received more than 15 mCi there were no patients needed further iodine dose as shown in figure 4.14

T3 level (12 months) after RAI therapy according to dose level. The data reveal that: among the patients (49.1%) who were received less than 15 mCi there was 2% were high T3(elevated),40% of them was normal T3 and 2% were low T3 level. And among that who received 15mCi there was 2% of the patients were high T3, 26% of them has normal T3 and no evidence of low T3 level in patients who received 15mCi. While the patients (25.5%) who received doses more than 15mCi there were 6% were high T3 level, 20% of them were normal T3 level and there was 2% has low T3 level. This means that there was only 5 patients from the total number of patients were still suffer from elevated T3 hormone level after 3-6 months from RAI therapy as shown in Figure 4.15.

T4 level (12 months) after RAI therapy according to dose level. The data reveal that: among the patients (49.1%) who were received less than 15 mCi there was 4% were high T4(elevated),38% of them was normal T4 and 2% were low T4 level. And among that who received 15mCi there was no evidence of low or high T4 levelin patients who received 15mCi, 28% of them has normal T4. While the patients (25.5%) who received doses more than

15mCi there were 4% were high T4 level, 22% of them were normal T4 level and there was 2% has low T4 level. This means that there was only 4 patients from the total number of patients were still suffer from elevated T4 hormone level after 12 months from RAI therapy as shown in Figure 4.16.

TSH level (12 months) after RAI therapy according to dose level. The data reveal that: among the patients (49.1%) who were received less than 15 mCi there was 8% were high TSH(elevated),32% of them was normal TSH and 4% were low TSH level(hyperthyroidism). And among that who received 15mCi there was 4% of the patients were high TSH, 22% of them has normal TSH and 2% have low TSH level. While the patients (25.5%) who received doses more than 15mCi there were 2% were high TSH level, 16% of them were normal TSH level and there was 10% has low TSH level. This means that there was 8 patients from the total number of patients were still hyperthyroidism after 12 months from RAI therapy according to TSH values)as shown in Figure 4.17.

At level of T3 hormone there is 10patients (18.2%) from the total number of patients under study still suffer from elevated triiodothyronine hormone after(2-3 months) RAI therapy, when there is 13patients(23.6%) have elevated T3 after (3-6 months) RAI treatment, and only 5 patients (10%) after (one year) of RAI therapy. That means the response of RAI treatment at level of T3 hormone is clearly appears after time.

At level of T4 hormone there is 10patients (18.2%) from the total number of patients under study still suffer from elevated Thyroxine hormone after(2-3 months) RAI therapy, when there is 9patients(16.4%) have elevated T4 after (3-6 months) RAI treatment, and only 4 patients (8%) after (one year) of RAI therapy. That means the response of RAI treatment at level of T3 hormone is clearly appears after time.

At level of Thyroid Stimulating Hormone there is 9 patients (16.4%) from the total number of patients under study still suffer from suppression of TSH

after(2-3 months) RAI therapy, when there is 17patients(30.9%)have low TSH level after (3-6 months) RAI treatment and only 8 patients (16%) after (one year) of RAI therapy and they were under thyroid hormone supplementation. That means the response of RAI treatment at level of Thyroid stimulating hormone is clearly appears after time.

There is 5patients (9.1%)from all population under the study needs further RAI dose after (3-6 months) therapy and only 7 patients (12.7%) become hypothyroidism patients after one year of RAI therapy.

Generally RAI appear to be safe except hypothyroid which is easily manage with thyroxine supplementation.

5.2 Conclusion:

The main objective of this study is to measure the outcomes of RAI therapy of hyperthyroidism, which is collected by using special data collecting paper among 55 patients referred to RICK for therapy during 2013 -2015. The assessment has been carried out among them before and after RAI therapy, and the results could be summarizes as follow:

- The study revealed that the hyperthyroidism is associated with female gender with 76% relative to 24% among males.
- The common involved age is 40-49.
- The effective dose range for hyperthyroidism treatment is 10-30mCi
- the radioactive iodine therapy was more affective after a relatively long time.
- The induction of hypothyroidism due to RAI therapy is 12.7% during 1year follow up.
- The applied RAI dose has great impact on the treatment outcome.
- Radioactive iodine is effective in the treatment of hyperthyroidism with occurrence of hypothyroidism as main side effect.

5.3 Recommendations:

Radioactive iodine is effective in treatment of hyperthyroidism with minor side effects such as hypothyroidism. Therefore to get the most outcome benefits of the radioactive iodine therapy there some precaution, some worth mention and recommended such as:

- The patient should be retained for follow up at interval extended to years and the TFT should be noted.
- There should be written and informed consent.
- There should be written and verbal instructions, preparation, and advices.
- The patient must be given clear idea about radioactive iodine therapy procedure.
- The patient must follow the instruction of precaution for post radioactive iodine therapy.
- There should be a fixed protocol for RAI therapy and for follow up.
- The hospital should be under control of nuclear regulatory commission.

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Appendices

Appendix 1

Radiation & Isotopes Center -Khartoum (RICK)

Department of Nuclear Medicine

Patient Consent

The medical staff of (RICK) explains to me the nature of the RAI therapy and all information has been fully explained to me.

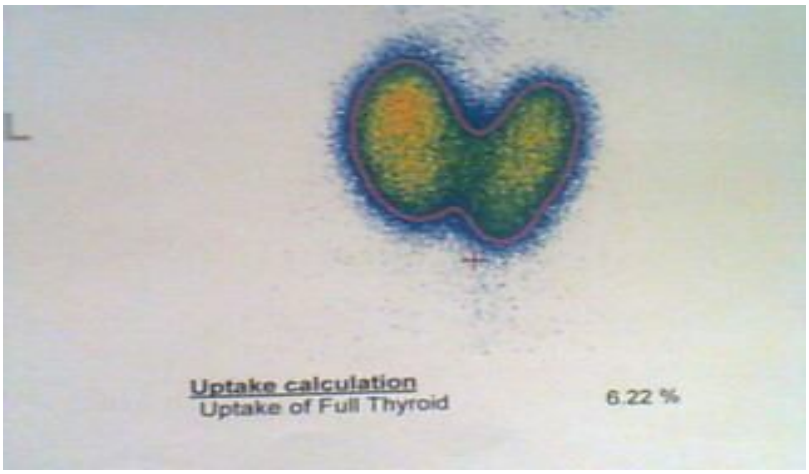
I agree to receive RAI therapy.

Patient name.....

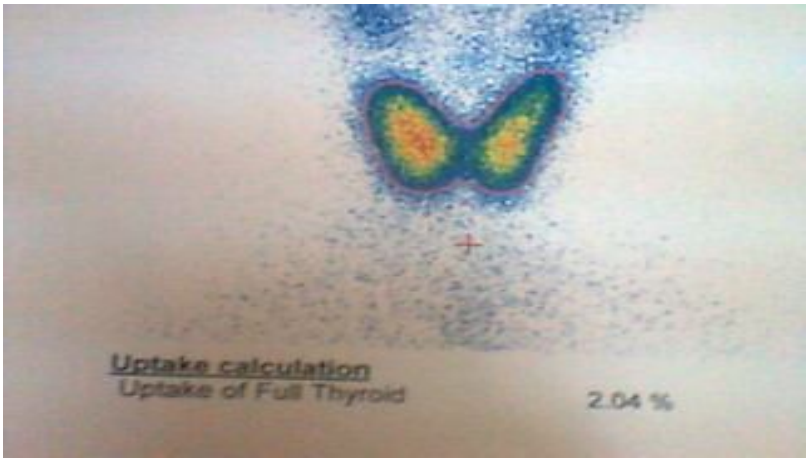
Patient signature.....

Date.....

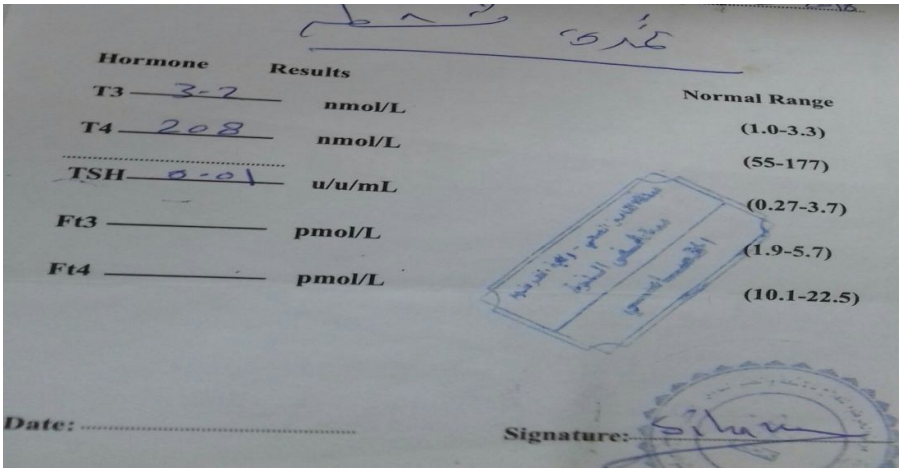
Appendix 2: Thyroid scan and uptake before and after RAI treatment



Thyroid scan and uptake after RAI treatment:



Appendix 3: Thyroid hormonal profile



Appendix 2: the table represents

The T3,T4,TSH before and after (2-3,3-6 months and year)RAI therapy and the thyroid uptake results for all patients.

								2-3months			3-6 months			1year			
NO.	Gend	Age	T_3b	T_4b	TSHb	Thy.up	RAI^{131}d	T_3a	T_4a	TSHa	T_3a	T_4a	TSHa	T_3a	T_4a	TSHa	
1	1	42	4.1	60.3	0.004	12.90%	10	3.4	182.8	0.1	9.3	187.5	0.16	0.4	54.5	22.4	12mci(2nd Capsule)
2	1	24	2.1	183	0.02	40.47%	22	1.8	58.4	0.4	3.8	199	0.1	0.68	14.4	1.98	
3	1	56	2.1	186	0.09	8.77%	20	0.7	6	4.5	6.6	190.6	0.28	1.7	174.8	0.03	
4	1	19	3.2	208	0.01	13.36%	8 I.V	0.25	46.7	0.5	1.88	173.21	4.2	2.1	172.9	0.632	
5	1	48	3.9	248	0.4	24.18%	10	1.3	56	3.3	1	99	3.3	1.5	80	8	
6	1	50	5.3	178	0.01	12.73	10	0.0	44.4	6.83	1.9	175.8	0.15	1	187	0.23	

			1			%		1				2					
7	1	27	7.86	216	0.005	42.87%	15	2.6	115	1.2	1.7	138	1.2	3.1	87	1.7	
8	1	47	3.7	58	0.08	28.87%	15	1.3	59.7	1.3	0.5	30	7.15	2.5	108	1.2	
9	1	44	5.2	178	0.06	20.70%	20	1.59	110.6	0.73	3	56	1.1	1.1	99	1.3	
10	2	45	5	180	0.01	34.86%	20	4.2	180.5	0.3	4.6	175	0.2	3.3	195	0.12	
11	1	24	4.1	201	0.08	27.55%	20	1.19	54.2	4.8	1.19	52.4	4.8	0.8	44	4.6	
12	1	30	3.6	181	0.016	5.29%	10	0.01	50	9	0.2	52	5.2	1.2	78	2.6	
13	1	45	3	175.7	0.2	20.40%	15	1.9	25	4.5	2.7	115	0.3	1.8	120	1.6	
14	1	56	4.1	179.7	0.02	22.13%	15	1.8	118	0.8	4.8	18.4	0.05	21.9	61.9	0.005	

15	1	45	3.1	188	0.9	6.22%	13	4.1	59	0.3	2.8	176.5	0.1	3.1	57.4	3.7	
16	1	50	11.5	60.5	0.05	38.46%	15	1	5.2	4.2	2.7	90	0.2	2.9	175	10.3	
17	1	58	2.68	175.8	0.005	12%	10	7.8	187.9	0.05	4.08	176.7	0.1				14mci(2nd dose)
18	1	30	4.1	190	0.05	12.60%	13	2.7	57.2	0.01	2.63	231.4	0.3	2.63	231.4	0.3	
19	1	55	14.9	297	0.9	4.30%	15	2.2	148	0.7	1	129	1.7	1.2	112	0.5	
20	1	54	10.1	207.3	0.05	9.23%	15	0.01	46.4	8.9	1.41	56.43	2.73	1.13	57.1	1.6	
21	2	52	2.7	177.5	0.03	1.99%	20	1.7	55.54	0.51	2.65	173.4	2.09	2	175.5	1.59	
22	1	70	1.9	208	0.01	16.39%	14	2.45	55.8	4.7	2.65	56.7	5.4	2.65	175.8	0.02	
23	1	37	7	187.9	0.4	25.63%	20	1.9	60.7	4.8	2.4	57.98	0.049	4.1	177.7	0.01	

24	1	32	2.2	200	0.1	56.46 %	20	2.2	378	0.1	4.06	216.7	0.05	4.7	200	0.017	
25	1	41	1.3	138	1.7	4.30%	15	2.57	52.83	1.15	3.08	174.2	2	1.24	60.34	4	
26	1	28	4.7	200	0.06	32.81 %	12	0.6	35	5.2	0.01	54.2	4.4	1.5	61.9	1.8	
27	1	30	3.3	178	0.005	7.36%	10	1.3	73	5	1	70	5	0.9	50	20	
28	2	60	2.7	60	0.3	5.07%	12	1.5	92	3	2.3	132	0.6	1.4	83	21	
29	2	42	1.5	84	0.8	6.47%	22	1.9	106	1.1	1.9	83	2	2	80	1.6	
30	2	29	1.2	55	1.9	24.22 %	20	2.12	60.7	1.4	1.79	79.35	3.9	1.6	91	3.8	
31	2	48	5.6	180.6	0.01	40.50 %	10	2.6	323	0	12.4	183.5	0.05				14mci(2nd dose)
32	1	27	3.67	172.1	0.05	12.96 %	14	3.08	96	3.66	1.58	87	2.06	2.1	80	0.7	
33	1	54	10.	207.	0.05	9.23%	20	0.0	46.4	4.9	0.8	55.2	4.9	1.1	57.1	1.76	

			1	3				1			7			3			
34	2	45	46.2	255	0.005	63.84%	15	5.92	205.46	0.8	4.2	178	0.2	3.3	177	0.29	
35	2	34	10	377	0.05	41.43%	12	0.4	13	4.1	0.7	44	2.7	2	109	2	
36	1	32	9	320	0.05	6.30%	10	1.4	99	0.9	1.4	106	7.6	1.2	91	1.1	
37	1	26	12.7	194	0	27.50%	12	1.7	138	1	1.6	155	0.3	1.5	116	0.4	
38	1	58	2.66	177.8	0.005	12%	10	4.81	187.86	0.05	2.78	175	0.01				14mci(2nd dose)
39	2	35	5.9	177	0.01	7.25%	25	0.6	51.9	4.8	1.11	57.3	0.29	2.98	160	0.05	
40	1	80	4.5	205	0	26.12%	25	1.2	56	3.5	1.5	152	2.9	1.8	137	4	
41	1	26	3.6	192	0.01	48.61%	15	10	304	0.5	2.9	79	0.02	1.4	90	1.2	
42	1	35	2.1	323	0	12.17	12	0.8	36	4.8	1.2	71	1.9	1	109	1.4	

						%											
43	1	38	3.4	55	0.01	9.97%	15	1.1	43	0.7	0.9	55	0.6	2.7	171.1	0.4	
44	1	55	2.2	123	0.09	6.46%	10	5.4	179.7	0.1	11.8	179.9	0.1	5.2	180	0.2	
45	2	60	2.7	60	0.3	5.07%	12	1.5	92	3	2.3	132	0.6	1.2	69	44	
46	2	60	3.4	236	0.16	17.43 %	15	2	172.2	3.5	2.6	57.2	1.5	1.5	112	1.5	
47	1	31	3.6	178	0.2	9.11%	12	1.6	85	3.5	1.3	171	6	1	104	2.8	
48	1	25	3.3	175	0	3.17%	12	1.7	138	1	1.6	155	0.3	1.5	116	0.7	
49	1	32	5.2	182	0.01	5.90%	12	1	158.9	1.4	1	174.7	0.6	1.9	122	0.5	
50	1	45	6.82	191.9	0.2	5.31%	10	3.5	175.1	0.1	4.2	175.8	0.01				15mci(2nd dose)
51	1	22	12.4	183.7	0.011	9.38%	15	2.9	155.5	1.6	5.8	81	0.9	2.1	94	0.9	
52	1	48	5.02	188	0.01	32.64 %	10	4.88	185.9	0.05	5.88	181.2	0.005	2.48	179.6	0.17	

53	1	41	1.3	138	0.7	4.30%	15	2.57	52.38	1.15	3.08	174.2	2	2.9	155	1.1	
54	2	34	4.2	179.9	0.21	6.35%	12	1.5	136	1	1.7	136	5.1	1.6	174	0.7	
55	2	58	3.32	175.4	0.8	4.60%	25	2.72	171.1	1.351	2	95	1.1	2.5	59.2	2.1	

1= represent female

2= represent male