IOSR Journal of Pharmacy and Biological Sciences (IOSR-JPBS)
e-ISSN: 2278-3008, p-ISSN:2319-7676. Volume 9, Issue 2 Ver. II (Mar-Apr. 2014), PP 165-169
www.iosrjournals.org

Correlation of Thyroid Hormone Levels with Radioactive ^{99m}*Tc*Thyroid Uptakes

Waddah M. Ali[1]*,Mohamed Yousef[2,3], Mohammed A. Ali Omer [3, 4],
M. E. M. Gar-alnabi [3],Bushra Ahmed[1]

[1]*College of Radiologic Technology, The National RibatUniversity,Khartoum Sudan*
[2]*College of Applied Science, Taibah University, Almadinah Almunawarah, KSA*
[3]*College of Medical Radiologic Science, Sudan University of Science and Technology, Khartoum-Sudan.*
[4]*College of Applied Medical Science, Qassim University, Buraydah-KSA.*

Abstract
Objective: *This study aimed to study the relationship between thyroid function test and thyroid uptake using* ^{99m}*Tc and to determine of the normal range of the thyroid uptake in Sudanese as well as the possibility of replacing the TFT test by thyroid uptake.*
Methods: *Out of the 77 patients (6.2%)males and (93.5%) females who referred to the department of nuclear medicine at radio isotope center Khartoum (RICK) for thyroid function test and thyroid scan in the period fromMay to Aug 2009, were included in this study.Simple sensitive RIA wasused for the measurement of thyroid related hormones (T4, T3and TSH), and thyroid uptake value in the gamma camera (mediso).*
Results: *The results showed that mean±SD values for T3, T4, TSH and thyroid uptake were 5.6±3.6, 79.8±6.5, 6.7±0.8 and 6.3±2.4 respectively. The normal range for thyroid uptake in this study was ranged from 5.78 to 6.12% at 20 min after injected with a dose of 3mCi 99mTc. As well as the results showed that there is strong and significant correlation at p = 0.05 between the thyroid uptake versus T3 and T4. Whereas in low uptake the correlation coefficient r = 0.87 and 0.81 for T4 and T3 respectively, and in elevated group r = 0.94 for T4 and 0.96 for T3. While in the normal uptake group r = 0.99 and 0.88 for T4 and T3 respectively. This study concluded that there was relationship between thyroid uptake and the level of the thyroid related hormones The percentage of thyroid uptake was ranging between 1.2 and 8.0*
Conclusion: *There were possibilities of using thyroid uptake only as a diagnostic tool for thyroid activity*
Key words: *Thyroid uptake, thyroid function test (TFT), thyroxin hormone (T4), triiodotyrosin hormone(T3), thyroid stimulating hormones (TSH), radioactive technetium (*^{99m}*Tc), radioimmunoassay (RIA).*

I. Introduction:

Over the past forty years, improvements in the sensitivity and specificity of thyroid testing methodologies have dramatically impacted clinical strategies for detecting and treating thyroid disorders. In the 1950s, only one thyroid test was available – an indirect estimate of the serum total (free + protein-bound) thyroxine (T4) concentration, using the protein bound iodine (PBI) technique (1,2). Since 1970, technological advances in radioimmunoassay (RIA) and more recently immunometric assay (IMA) and tandem mass spectrometry methodologies have progressively improved the specificity, reproducibility and sensitivity of thyroid testing methods (3-10). Currently, serum-based immunoassay and tandem mass spectrometric methods are available for measuring both total T4 (T4) and total triiodothyronine (TT3) concentrations as well as the free hormone moieties (FT4 and FT3) (11-13). In addition, measurements can be made of the thyroid hormone binding proteins, Thyroxine Binding Globulin (TBG), Transthyretin (TTR)/Prealbumin (TBPA) and Albumin, as well as for the pituitary thyroid stimulator, Thyrotropin (thyroid stimulating hormone, TSH) and the thyroid hormone precursor protein, Thyroglobulin (Tg) (14-16). The recognition that autoimmunity represents a major cause of thyroid dysfunction has led to the development of tests for the detection of thyroid autoautoantibodies such as thyroid peroxidase antibodies (TPOAb), thyroglobulin antibodies (TgAb) and TSH receptor antibodies (TRAb) (17-19). Currently, these thyroid tests are performed on serum specimens using either manual or automated methods employing specific antibody reagents directed at these ligands (6,20). However, sensitivity, specificity andstandardization issues still result in substantial between-method variability for many of these tests (21-23). To address this issue, new performance standards are being established by the professional organizations as well as technological advancements undertaken by instrument manufacturers (24-26)

Thyroid gland function and structure can be evaluated using uptake and scintigraphy studies. ^{131}I-iodide, which was introduced in the late thirties, was the first radiopharmaceutical used for measuring thyroid uptake, and for many years it was the main study agent used in the evaluation of thyroid function.(27) Despite the fact that the sensitivity and specificity of *in vitro* tests for evaluation of thyroid function have evolved, thyroid uptake and scintigraphy still play an important role in various clinical situations, such as the detection of ectopic

thyroid tissue in neck masses, functional assessment of single or multiple nodules, increasing the likelihood of detecting hyperthyroidism in difficult cases, identification of other causes of thyrotoxicosis and calculation of therapeutic doses of ^{131}I-iodide.(28)Studies with ^{131}I-iodide have the serious disadvantage of high radiation doses to the gland (1¾3 rad/mCi administered) caused by its long half-life and b^{-} particle emission. Its main gamma photon has high energy (364 keV) that is inadequately collimated by most conventional scintillation cameras, and therefore poor quality images are produced. In the United States, the use of ^{131}I-iodide for thyroid imaging has been prohibited and its use restricted to staging and follow-up of patients with differentiated thyroid carcinoma.(29)Iodine-123 is a good substitute for iodine-131 because it has a shorter half-life (13 hours), a gamma photon suitable for imaging using conventional scintillation cameras (159 keV) and no b^{-} radiation. However, its main limitations are its high cost and reduced availability, due to its expensive and complex production in a cyclotron. In addition, depending on the production process chosen, contaminants such as ^{124}I-iodide and ^{125}I-iodide may be formed increasing the dosimetry and image degradation.(30,31)Technetium¾99m, in the chemical form of pertechnetate ($^{99m}TcO_4^-$), is also used for thyroid scintigraphy and uptake.(32) The similarity of volume and charge between the iodide and pertechnetate ions is the explanation for the uptake of ^{99m}Tc-pertechnetate by the thyroid gland.(33,34) ^{99m}Tc-pertechnetate has been used worldwide to study the thyroid function because of a number of advantages, such as a short half-life (6 hours), short retention in the gland, and no b^{-} radiation, thus providing low dosimetry to the thyroid gland (10,000 times less than that of ^{131}I-iodide),as well as to the body as a whole. Its gamma photon of 140 keV is ideal for imaging using scintillation cameras and in addition it has low cost and is readily available(35).There is an international consensus that the radiopharmaceuticals of choice for thyroid gland imaging are ^{99m}Tc-pertechnetate or ^{123}I-iodide. Although the thyroid does not organify ^{99m}Tc-pertechnetate, in the majority of cases the uptake and imaging data provide all the information needed for accurate diagnosis.(37) In rare instances,^{123}I-iodide can subsequently be used for assessment of organificationdefects.Despite these recommendations, most nuclear medicine laboratories in Brazil choose the radiopharmaceutical ^{131}I-iodide to study the thyroid gland. This practice can in part be explained by the fact that there is a lack of standard values for ^{99m}Tc-pertechnetate uptake by the thyroid gland.
This study aimed to study the relationship between thyroid function test and thyroid uptake using ^{99m}Tc and to determine of the normal range of the thyroid uptake in Sudanese as well as the possibility of replacing the TFT test by thyroid uptake

II. Materials and methods:

This study was conducted in Nuclear Medicine Department, Radiation and Isotope Center of Khartoum (RICK)from 2007 to 2010. A total of 77 patients (6.5%) were males and (93.5 %) were females and the average age of the patients studied was 20 years. The peak incidence was among the age between 21-30 years of age presenting the percent of (52%) referred to the department for thyroid scan from march to July 2009were included in this study, correlated with thyroid function tests. The scintigraphies were all obtained by using Nucline gamma camera computer system (planer and dual head whole body SPECT) with general purpose collimators made in Hungary. Generator UltraTechneKow ® FM DRN 432999Mo/ 99mTc Generator Composition (elute) 99Mo content < 25 Bq/MBq 99mTc. Specifica1tions are within the guidlines described by monographs of the U.S.A. and the European Pharmacopoeia PH 5.0 – 7.0 ,10-20 minutes after intravenous injection of 37-111MBq of sodiumpertechnetateTc 99m. All radioimmunoassay using RIA instrument which include SOURCERER RIA gamma counter, manufactured by OAKFIED Company, England in 1992 and specific reagents for the measurement of thyroid hormones were obtained from China Institute for Atomic Energy (CIAE), Department of Isotopes (Beijing China).used in RIA were including Adjustable micropipettes. (10-200µl), Polystyrene test tubes (disposable), Vortex mixer (single and multi-tubes), Multidose micropipette (Eppendorff), 25µl and 250 µl, magnetic base, Incubator, Centrifuge and Gamma counter (connected with computer. Five ml of blood sample were drowning from the patient in RIA laboratory for thyroid related hormones (T4, T3 and TSH) assay using Gamma counter. Then the patients were divided into three groups according to their thyroid hormones assay results. Group I consisted of 42 patients whose hormones levels were normal. Group II contained of 18 patients with low thyroid hormones level, and Group III consisting of 17 patients with high thyroid hormones level.Ultimately all the patients were enrolled in nuclear thyroid uptake test; where patients were injected with 3 to 5 mCi pure technetium pertechnetate, followed by full and empty syringe image for one minute to measure the net amount of activity entered to the patient's blood stream, 15 to 20 minute later the patient positioned supine in the gamma camera table with 15 to 30 cm distance using gamma camera fitted with LEGP collimators and anterior image for one minute were taken, then by using DIAG program the amount of thyroid uptake were calculated.

III. Result:

The result of this study showed that, there was a direct relationship between thyroid uptake and the level of the thyroid related hormones (for individual). There is strong and significant correlation at p = 0.05 between the thyroid uptake versus T3 and T4. The percentage of thyroid uptake for the subjects included in the study was ranging between 5.78 and 6.12.

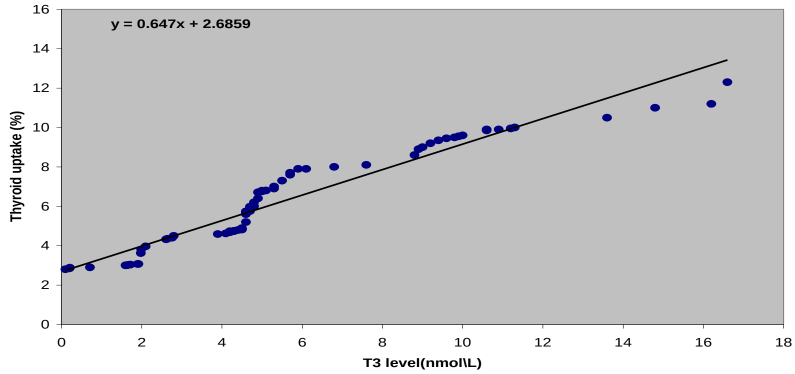

Figure (1) shows the relationship between T3 and thyroid uptake

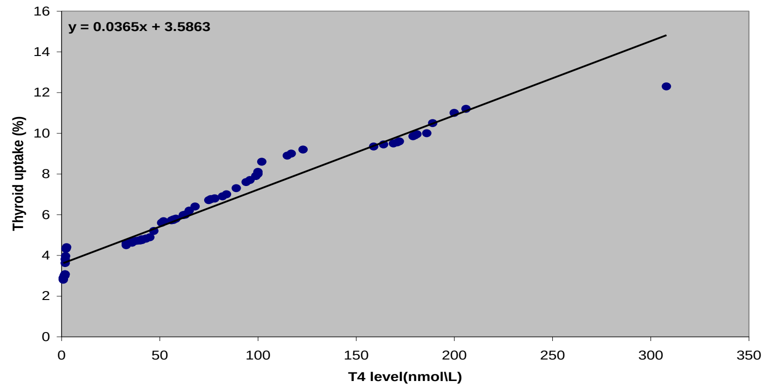

Figure (2) shows the relationship between T4 and thyroid uptake

Table 1 shows the mean and standard deviation for all groups

variables	Mean ±SD Normal group	Mean ±SD High group	Mean ±SD Low group
uptake	5.9± 0.2	10 ± 0.2	3.45 ± 0.1
T3	4.8± 0.1	8.8 ±0.6	1.5 2± 0.2
T4	61.6 ± 3.2	172.3 ± 10.7	1.65 ±0.1
TSH	1.4 ± 0.1	0.74 ± 0.2	1.1 ± 0.2

IV. Discussion:

The radiopharmaceuticals currently chosen are 99mTc-pertechnetate has become the tracer of choice, since it is readily available and has a low cost. Its uptake is similar to that of iodide, although ion organification is absent. [37.38]. The maximum thyroid uptake of 99mTc-pertechnetate takes place 10 to 20 minutes after intravenous injection, in contrast to 131I-iodide, which requires a 24-hour measurement period. [39,40] In the present study77 patients categorized into three groups depending on hormones level. The result of this study showed that the mean±SD values for T3, T4, TSH and thyroid uptake were 5.6±3.6, 79.8±6.5, 6.7±0.8 and 6.3±2.4 respectively. The normal range for thyroid uptake in this study was ranged from 5.78 to 6.12% at 20 min after injected with a dose of 3mCi ^{99m}Tc. As well as the results showed that there is strong and significant correlation at p = 0.05 between the thyroid uptake versus T3 and T4. Whereas in low uptake the correlation coefficient r = 0.87 and 0.81 for T4 and T3 respectively, and in elevated group r = 0.94 for T4 and 0.96 for T3. While in the normal uptake group r = 0.99 and 0.88 for T4 and T3 respectively.The strong and significant correlation between the T3, T4 and thyroid uptake was expected because the uptake of thyroid gland physiologically, have direct proportionality with the amount of thyroid hormones syntheses by the thyroid gland. Therefore in case of low hormones level the uptake of thyroid is low due to the smallest number of thyroid gland cells act in trapping and syntheses of thyroid hormones, while at elevated hormones level mean that the number of thyroid cell act as syntheses increase so the uptake was increased.There were insignificant correlation between the thyroid uptake and TSH level; this is because a lot of patients have no problem in thyroid stimulating hormones TSH but the problem within thyroid cells mainly due to iodine deficiency. In most cases the patients have normal TSH but have problem in the other hormones as well as the uptake result; this mean that the TSH does not reflect the status of the thyroid disorder. Therefore there is no obvious linear association between TSH and uptake, as the one shown by T3 and T4.The linear relationship between thyroid uptake and T3 showed a coefficient equal to 0.65 uptake%/(nmol\L) and a constant equal to 2.6 as shown in the following equation: uptake% = 0.647 T3 + 2.6859. In case of T4 the coefficient equal to 0.04 uptake%/(nmol\L) with a constant equal to 3.6 as shown by the following equation: uptake% = 0.0365 T4nmol\L + 3.5861. From the above result, thyroid uptake test can be used to diagnosis and evaluate the thyroid disorder because the uptake result gives an accurate indication about the thyroid hormones status in low, normal or elevated thyroid hormones level, without the use of TFT, so that we can decrease both the time for diagnosing the patient and the cost. In summary the study showed that TFT result can be estimated using thyroid uptake as well thyroid uptake can revel global and specific diagnostic information concerning thyroid status.

References

[1]. Chaney AL 1958 Protein-bound iodine. AdvClinChem 1:82-89

[2]. Benotti J, Benotti N 1963 Protein-bound iodine, total iodine and butanol extractable iodine by partial automation. ClinChem 9:408-416

[3]. Chopra IJ 1972 A radioimmunoassay for measurement of thyroxine in unextracted serum. J ClinEndocrinolMetab 34:938-947

[4]. Ekins RP 1998 Ligand assays: from electrophoresis to miniaturized microarrays. ClinChem 44:2015-2030 Spencer CA, LoPresti JS, Patel A, Guttler RB, Eigen A, Shen S, Nicoloff JT 1990 Applications of a new chemiluninometricthyrotropin assay to subnormal measurement. J ClinEndocrinolMetab 70:453- 460

[5]. Baloch Z, Carayon P, Conte-Devolx B, Demers LM, Feldt-Rasmussen U, Henry JF, LiVosli VA, Niccoli-Sire P, John R, Ruf J, Smyth PP, Spencer CA, Stockigt JR 2003 Laboratory Medicine PracticeGuidelines: Laboratory Support for the Diagnosis and Monitoring of Thyroid Disease. Thyroid 13:5767

[6]. Spencer CA, Bergoglio LM, Kazarosyan M, Fatemi S, LoPresti JS 2005 Clinical Impact ofThyroglobulin (Tg) and Tg autoantibody Method Differences on the Management of patients withDifferentiated Thyroid Carcinomas. J ClinEndocrinolMetab 90:5566-5575

[7]. Thienpont LM, Beastall G, Christofides ND, Faix JD, Ieiri T, Jarrige V, Miller WG, Miller R, NelsonJC, Ronin C, Ross HA, Rottmann M, Thijssen JH, Toussaint B 2007 Proposal of a candidateinternational conventional reference measurement procedure for free thyroxine in serum. ClinChemLab Med 45:934-936

[8]. Kahric-Janicic N, Soldin SJ, Soldin OP, West T GJ, Jonklaas J 2007 Tandem mass spectrometryimproves the accuracy of free thyroxine measurements during pregnancy. Thyroid 17:303-311

[9]. Dufour DR 2007 Laboratory tests of thyroid function: uses and limitations. EndocrMetabClinNorth Am 36:155-169

[10]. Nelson JC, Wilcox RB 1996 Analytical performance of free and total thyroxine assays. ClinChem42:146-154

[11]. Stockigt JR 2001 Free thyroid hormone measurement. A critical appraisal.EndocrinolMetabClinNorth Am 30:265-289

[12]. Thienpont LM, Van Uytfanghe K, Marriott J, Stokes P, Siekmann L, Kessler A, Bunk D, Tai S 2005Feasibility study of the use of frozen human sera in split-sample comparison of immunoassays withcandidate reference measurement procedures for total thyroxine and total triiodothyroninemeasurements. ClinChem 51:2303-2311

[13]. Robbins J 1996 Thyroid hormone transport proteins and the physiology of hormone binding .

[14]. Spencer CA, Takeuchi M, Kazarosyan M 1996 Current Status and Performance Goals for Serum Thyroglobulin Assays. ClinChem 42:164-173

[15]. Spencer CA, Takeuchi M, Kazarosyan M 1996 Current status and performance goals for serum thyrotropin (TSH) assays. Clinical Chemistry 42:141-145

[16]. Feldt-Rasmussen U 1996 Analytical and clinical performance goals for testing autoantibodies to thyroperoxidase, thyroglobulin and thyrotropin receptor. ClinChem 42:160-163

[17]. Kamijo K 2007 TSH-receptor antibodies determined by the first, second and third generation assays and thyroid-stimulating antibody in pregnant patients with Graves' disease. Endocr J 54:619-624

[18]. Ajjan RA, Weetman AP 2008 Techniques to quantify TSH receptor antibodies. Nat ClinPractEndocrinolMetab 4:461-468

[19]. Demers LM 1999 Thyroid function testing and automation. J Clin Ligand Assay 22:38-41

[20]. Steele BW, Wang E, Klee GG, Thienpont LM, Soldin SJ, Sokoll LJ, Winter WE, Fuhrman SA, Elin RJ 2005 Analytic bias of thyroid function tests: analysis of a College of American Pathologists freshfrozen serum pool by 3900 clinical laboratories. Arch Pathol Lab Med 129:310-317

[21]. Beckett G, MacKenzie F 2007 Thyroid guidelines – are thyroid-stimulating hormone assays fit forpurpose? Ann ClinBiochem 44:203-208

[22]. Fritz KS, Wilcox RB, Nelson JC 2007 Quantifying spurious free T4 results attributable to thyroxine-binding proteins in serum dialysates and ultrafiltrates. ClinChem 53:985-988

[23]. Spencer CA, Lopresti JS 2008 Measuring thyroglobulin and thyroglobulin autoantibody in patientswith differentiated thyroid cancer. Nat ClinPractEndocrinolMetab 4:223-233

[24]. Cooper DS, Doherty GM, Haugen BR, Kloos RT, Lee SL, Mandel SJ, Mazzaferri EL, McIver B,Sherman SI, Tuttle RM 2006 Management guidelines for patients with thyroid nodules anddifferentiated thyroid cancer. The American Thyroid Association Guidelines Taskforce. Thyroid16:109-142

[25]. Cooper DS DG, Haugen BR, Kloos RT, Lee SL, Mandel SJ, Mazzaferri EL, McIver B, PaciniF,Schlumberger M, Sherman SI, Steward DL, Tuttle RM, 2009 Revised American Thyroid Associationmanagement guidelines for patients with thyroid nodules and differentiated thyroid cancer. Thyroid19:1167-1124

[26]. Chapman EM. History of the discovery and early use of radioactive iodine. JAMA 1983;15:2042-4. [Links]

[27]. Cavalieri RR, McDougall IR. "In vivo" isotopic tests and imaging. In: Braverman LE, Utiger R. Werner &Ingbar. The thyroid. 7th ed. Philadelphia: Lippincott-Ranen; 1996:1-372. [Links]

[28]. Becker D, Charkes ND, Dworkin H, et al. Procedure guideline for thyroid scintigraphy. J Nucl Med 1996;37:1264-6. [Links]

[29]. Paras P, Hamilton DR, Evans C, Herrera NE, Lagunas Solar MC. Iodine-123 assay using a radionuclide calibrator. Int J Nucl Med Biol 1983;10:111-5. [Links]

[30]. Ziessman HA, Fahey FH, Gochoco JM. Impact of radiocontaminants in commercially available iodine-123: dosimetric evaluation. J Nucl Med 1986;27:428-32. [Links]

[31]. Burke G, Halko A, Silverstein GE, Hilligoss M. Comparative thyroid uptake studies with ^{131}I and $^{99m}TcO_4$. J ClinEndocrinolMetab 1972;34:630-7. [Links]

[32]. Andros G, Harper PV, Lathrop KA, McCardle RJ. Pertechnetate-99m localization in man with applications to thyroid scanning and the study of thyroid physiology.JClinEndocrinolMetab 1965; 25:1067-76. [Links]

[33]. Smith JJ, Croft BY, Brookeman VA, Teates CD. Estimation of 24-hour thyroid uptake of I-131 sodium iodide using a 5-minute uptake of technetium-99m pertechnetate.ClinNucl Med 1990;15:80-3. [Links]

[34]. Sodee DB. The study of thyroid physiology utilizing intravenous sodium pertechnetate. J Nucl Med 1966;7:564-7.[Links]

[35]. Sucupira MS, Camargo EE, Nickoloff EL, Alderson PO, Wagner HN. The role of ^{99m}Tc pertechnetate uptake in the evaluation of thyroid function.Int J Nucl Med Biol 1983;10:29-33. [Links]

[36]. Andros G, Harper PV, Lathrop KA, McCardle RJ(1965). Pertechnetate-99m localization in man with applications to thyroid scanning and the study of thyroid physiology. J ClinEndocrinolMetab; 25:1067-76.

[37]. Smith JJ, Croft BY, Brookeman VA, Teates CD(1990). Estimation of 24-hour thyroid uptake of I-131 sodium iodide using a 5-minute uptake of technetium-99m pertechnetate.ClinNucl Med;15:80-3

[38]. Schneider PB(1979). Simple, rapid thyroid function testing with 99mTc-pertechnetate thyroid uptake ratio and neck/thigh ratio. Am J Roentgenol;132:249-353.

[39]. Selby JB, Buse MG, Gooneratne NS, Moore DO(1979). The Anger camera and the pertechnetate ion in the routine evaluation of thyroid uptake and imaging.ClinNucl Med;4:233-7