Characterization of Thyroid Nodules Using Radioimmunoassay

Saadeldeen M. A. Aboidriss^{1*}, Emad. M. Mukhtar², Mohamed E. M. Gar-Elnabi¹

¹College of Medical Radiological Science, Sudan University of Science and Technology, Khartoum, Sudan ²Department of Diagnostic Radiology, College of Applied Medical Science, King Khalid University, Saudi Arabia, Abha *Corresponding Author: SaadeldeenAboidriss

ABSTRACT:- thyroid disease is one of the most common endocrine disorders, the laboratory diagnosis and monitoring of thyroid diseases such as hypo and hyper thyroidism are based on serum TSH measurement along with serumT4 and T3 for both free and total.

Characterization of thyroid nodules using Radioimmunoassay at three centers in Khartoum sate, A total of 200 patients 18(8.3%) were males and 180 (84.3%) were females and the average age of the patients studied was 35 years. In period from January 2017 to May 2019.

correlate between thyroid uptake with patients' diagnosis, were the diagnosis divided to four categories normal, hyperthyroidism, hypothyroidism and graves' disease, were the dominate thyroid uptake was in range from 1-4 with 147 patients (40 normal, 69 hyperthyroidisms, 28 hypothyroidism and 10 graves' disease) then 0.2 - 0.9 with 29 patients and 5-9 with 12 patents. Correlate between thyroid size and TSH hormone for all patients, using linear regression equation were the rate of change of thyroid size decrease with rate 0.0006 for each g/ml from TSH hormone. using analysis of variance test for all parameters according to patients' age, were the p.value shows a significant difference between the patients age with body mass index and T4 hormone, and there is no significant difference between the patients age with thyroid hormone thyroid uptake, T3 hormone and TSH.

Keywords:- thyroid nodules,thyroid size, thyroid uptake Radioimmunoassay

I. INTRODUCTION

Thyroid disorders affect a wide spectrum of population in Sudan. Numerous imaging modalities, including nuclear medicine, ultrasonography, X-ray fluorescence (XRF), computerized tomography (CT) and magnetic resonance imaging (MRI), have been used in an attempt to provide a pathophysiologically related diagnosis inpatients with different diseases of the thyroid [1]. thyroid disease is one of the most common endocrine disorders [2]. The laboratory diagnosis and monitoring of thyroid diseases such as hypo and hyper thyroidismare based on serum TSH measurement along with serumT4 and T3 (both free and total) [3]. The National Academy of Clinical Biochemistry (NACB) has recommended that the functional sensitivity of TSH assay be less or equal to 0.02 mIU/L. This permits patients with nonthyroid illness to be distinguished from those with primary hyperthyroidism. This is particularly important in patients hospitalized with nonthyroid illness where TSH concentration as low as 0.02 mIU/L may be encountered [4].

Low thyroid hormones levels due toiodine deficiency or altered utilization of iodine canincrease the secretion of TSH, serving as a basis for thediagnosis of hypothyroidism in different species [5,6,7].Hypothyroidism is the most common thyroiddisorder in cattle. The possible causes of hypothyroidism in ruminants are a low iodine intake or aninterference with absorption and utilization of dietaryiodine. Although goiter is not necessarily related tohypothyroidism, numerous cases of goiter associated with hypothyroidism have been reported in cattle [8,9,10] without bovine thyrotropin (bTSH) having beeninvestigated. Plasma or urinary iodine levels serve asan indicator of nutritional intake, but they are notdirectly related to thyroid function.[11]. A sensitive wayto evaluate thyroid function in cattle is the measurement of thyroid hormones, [9] which could also bereplaced by assays of TSH concentration that can beuseful for evaluating hypothyroidism, as commonlyachieved in humans8and other mammalian species[5,7].

Thyroid function tests have been dependent on an indirect estimate of the serum total thyroxin (T4) concentration, using protein bound iodine (PBI) technique by 1950s [12]; however since 1970s to recently there are many applied techniques such as: Radioimmunoassay (RIA) [13], immunometric assay (IMA) [14, 15] and more recently liquid chromatography-tandem mass spectrometry (LC-MS/MS) methodologies [16,17] which have progressively improved the specificity, reproducibility and sensitivity of thyroid testing methods [18].Recent studies in human breast cancer cells lines (MCF-7 and MDA-MB-231) have shown proliferative

effects of thyroid hormones on breast tissue through the same signal cascade utilized by estrogens involving phosphoinositol 3-kinase (PI3K) and the mitogenactivated protein kinase (MAPK) [19]. In estrogen receptor positive (ER+) cell lines (MCF-7), T3 mimics estradiol via its binding to ER and induces the expression of progesterone receptor (PR) and growth factor-alpha (TGF- α) mRNAs [3]. In other human cell lines, T3 has been shown to have a mitogenic effect by increasing the expression of the epithelial growth factor receptor (EGF-r) gene [20].In mammary cells, T3 can also activate the estrogen response element (ERE) [21], which is necessary for gene transcription and cell proliferation. Similarly, thyroxine (T4), much like estradiol, can activate the MAPK pathway and thus promote cell proliferation [22]. Additionally, thyroid stimulating hormone (TSH) has been shown to have a direct effect on mammary cells. Recently, TSH receptors have been identified in BC tissue with the useof RT-PCR and were correlated to a lower grade of BC[23].

II. METHODOLOGY:

This study was conducted in Nuclear Medicine Department, Radiation and Isotopes Center of Khartoum (RICK), Cancer center in wadmadni, Alnelein Medical Diagnostic Centre. A total of 200 patients 18(8.3%) were males and 180 (84.3%) were females and the average age of the patients studied was 35 years. All patients referred to the department for thyroid scan from January 2017 to May 2019. 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. Specifications are within the guidelines described by monographs of the U.S.A.and the EuropeanPharmacopoeia PH 5.0 - 7.0, 10-20 minutes after intravenous injection of 37-111MBq of sodiumpertechnetateTc 99m. were the T3, T4 and TSH investigation and radionuclide imaging done to same patient.

Nuclide TM SPIRIT DH-V Variable Angle Dual- Head Digital Gamma Camera for SPECT, whole body and planer imaging , detector Two new developed rectangular jumbo FOV high stability detectors assembled with high optical and mechanical quality, NaI (TI) scintillation crystal size: 585 * 470 mm thickness: 9.5 mm, 15.9 mm or 25 mm pixilated , photomultipliers: 55 pcs of high quantum efficiency PMTs characterized by improved energy resolution, magnetic shielding and long term stability, lead shielding thickness: 12 - 32 mm , detector electronics , A compact , highly integrated , one board easily serviceable construction without tuning potentiometers, computer controlled PMT auto tuning processor for fast PMT gain stabilization and adjustment , computer controlled ODC (Optical Distortion Correction) electronics , High precision summation electronics. Active high voltage bleeder with integrated HV module. Acquisition console. Ergonomic acquisition WS console stands on wheels. Full – digital electronics assembled from the latest "high – tech" elements including fast PCI bus acquisition interface, Intel Pentium 4, 2.26 GHz computer with 64-bit memory handling 512.

Table 1. show statistical parameters for all patients:							
	Mean	Median	STD	Min	Max		
Age	35.62	35	12.62	18	75		
BMI	25.48	25.6	5.67	12.1	47.6		
Thy Size	27.48	25.55	9.91	11.5	73		
Thy Uptake	3.48	2	5.14	0.23	34.57		
T3	2.72	1.7	7.59	0.48	105		
T4	96	104.5	47.89	1.07	217		
TSH	2.87	1.36	4.60	0.01	29		

III. RESULTS: ble 1. show statistical parameters for all patients

Table 2. show correlate between thyroid uptake with patients' diagnosis:

Thy Uptake		diagnosis					
		Normal	Hyperthyroidism	Hypothyroidism	Graves' Disease		
	0.2-0.9	10	11	8	0	29	
	1-4	40	69	28	10	147	
	5-9	0	8	3	1	12	
	10-14	0	2	0	1	3	
	15-19	0	3	0	0	3	
	20-24	0	1	0	0	1	
	25-29	0	0	2	0	2	
	30-35	0	1	1	0	2	
	Total	50	95	42	12	199	

Characterization of thyroid nodules using Radioimmunoassay



Figure 1. show correlate between T3 hormone and thyroid size for all patients



Figure 2. show correlate between T4 hormone and thyroid size for all patients





Table 5. show analysis of variance for an parameter's according to patients age.						
		Sum of Squares	df	Mean Square	F	P.value
BMI	Between Groups	2963.806	43	68.926	3.124	.000
	Within Groups	3442.018	156	22.064		
	Total	6405.824	199			
Thyroid size	Between Groups	4815.552	43	111.990	1.185	.226
	Within Groups	14742.988	156	94.506		
	Total	19558.540	199			
Thyroid uptake	Between Groups	619.846	43	14.415	.485	.997
	Within Groups	4635.477	156	29.715		
	Total	5255.323	199			
Τ3	Between Groups	1833.799	43	42.646	.690	.922
	Within Groups	9641.906	156	61.807		
	Total	11475.705	199			
T4	Between Groups	132736.428	43	3086.894	1.488	.042
	Within Groups	323686.182	156	2074.911		
	Total	456422.610	199			
TSH	Between Groups	1167.035	43	27.140	1.387	.077
	Within Groups	3051.622	156	19.562		
	Total	4218.657	199			

Table 3. show analysis of variance for all parameters according to patients' age:

IV. DISCUSSION

Table 1. show statistical parameters for all patients were calculated the mean, median, standard deviation, minimum and maximum, for age, body mass index, thyroid size, thyroid uptake, T3 hormone, T4 T3 hormone and TSH T3 hormone. The mean \pm STD for the age 35.62 \pm 12.62, BMI 25.48 \pm 5.67, for thyroid size, thyroid uptake, T3, T4 and TSH 27.48 \pm 9.91, 3.48 \pm 5.14, 2.72 \pm 7.59, 96 \pm 47.89 and 2.87 \pm 4.60 respectively. Table 2. show correlate between thyroid uptake with patients' diagnosis, were the diagnosis with four categories normal, hyperthyroidism, hypothyroidism and graves' disease, were the dominate thyroid uptake was from 1-4 with 147 patients (40 normal, 69 hyperthyroidisms, 28 hypothyroidism and 10 graves' disease) then 0.2 – 0.9 with 29 patients and 5-9 with 12 patents.

Correlate betweenthyroid size with T3 hormone using linear regression equation were the rate of change of thyroid size decrease with rate 0.2821 for each g/ml for each from T3 hormone as shown in fig 1. Fig 2. correlate between thyroid size withT4 hormone using linear regression equation were the rate of change of thyroid sizedecrease with rate 0.025for each g/ml for T4 hormone. Fig 3. correlate between thyroid size andTSH hormone for all patients, using linear regression equation were the rate of change of thyroid size decrease with rate 0.0006 for each g/ml from TSH hormone.

Table 3. show analysis of variance for all parameters according to patients' age, were the p.value shows a significant difference between the patients age with body amss index and T4 hormone, and there is no significant difference between the patients age with thyroid hormone thyroid uptake, T3 hormone and TSH.

V. CONCLUSION

Characterization of thyroid nodules using Radioimmunoassay at three centers in Khartoum sate were the correlation between thyroid uptake with patients' diagnosis, were the diagnosis with four categories normal, hyperthyroidism, hypothyroidism and graves' disease, were the dominate thyroid uptake was from 1-4 with 147 patients (40 normal, 69 hyperthyroidisms, 28 hypothyroidism and 10 graves' disease) then 0.2 - 0.9 with 29 patients and 5-9 with 12 patents. correlate between thyroid size with T3 hormone using linear regression equation were the rate of change of thyroid size decrease with rate 0.2821 for each g/ml for each from T3 hormone, and correlation between thyroid size with T4 hormone using linear regression equation were the rate of change of thyroid size decrease with rate 0.025 for each g/ml for T4 hormone. correlate between thyroid size and TSH hormone for all patients, using linear regression equation were the rate of change of thyroid size decrease with rate 0.0006 for each g/ml from TSH hormone.

Using analysis of variance for all parameters according to patients' age, were the p.value shows a significant difference between the patients age with body mass index and T4 hormone, and there is no significant difference between the patients age with thyroid hormone thyroid uptake, T3 hormone and TSH.

REFERENCES

- [1]. P.F. Sharp, HG Gemmel and FW Smith (2005), Practical Nuclear Medicine, Oril, Springer–Verlag LondonLimited, Third Edition.
- [2]. Roberts RF, Laulu SL, Roberts WL. Performance characteristics of seven automated thyroxine and T uptake method.ClinChim Acta 2007; 377: 248-55.
- [3]. Sanchez- Carbayo M, Mauri M, ALfayate R, MirallesC, Soria F. Analythical evaluation of TSH & thyroid hormones by electrochemiluminescent immunoassay. Clin Biochemistry 1994; 32: 395-403.
- [4]. Rawlins ML, Roberts WL. Performance characteristics of six Third-generation Assay for thyroidstimulating hormone. Clin Chem 2004; 50: 2338-44.
- [5]. Breuhaus BA: 2002, Thyroid-stimulating hormone in adult euthyroid and hypothyroid horses. J Vet Intern Med 16:109–115.
- [6]. Elmlinger MW, Kuhnel W, Lambrecht HG, Ranke MB: 2001, Reference intervals from birth to adulthood for serum thyroxine (T4), triiodothyronine (T3), free T3, free T4,thyroxine binding globulin (TBG) and thyrotropin (TSH). Clin Chem Lab Med 39:973–979.
- [7]. Williams DA, Scott-Moncrieff C, Bruner J, et al.: 1996, Validation of an immunoassay for canine thyroid-stimulating hormone and changes in serum concentration following induction of hypothyroidism in dogs. J Am Vet Med Assoc 209:1730–1732.
- [8]. Seimiya Y, Ohshima K, Itoh H, et al.: 1991, Epidemiological and pathological studies on congenital diffuse hyperplastic goiter in calves. J Vet Med Sci 53:989–994.
- [9]. Takahashi K, Takahashi E, Ducusin RJT, et al.: 2001, Changes in serum thyroid hormones levels in newborn calves as a diagnostic index of endemic goiter. J Vet Med Sci63:175–178.
- [10]. Wilson JG: 1975, Hypothyroidism in ruminants with special reference to foetal goiter. Vet Rec 97:161–164.
- [11]. Soldin OP, Tractenberg RE, Pezzullo JC: 2005, Do thyroxine and thyroid-stimulating hormone levels reflect urinary iodine concentrations? Ther Drug Monit 27:178–185.
- [12]. Benotti, J., Benotti, N., 1963. Protein-bound iodine, total iodine and butanol extractable iodine by partial automation. Clin. Chem, 9, 408-416.
- [13]. Baloch, Z., Carayon, P., Conte-Devolx, B., Demers, L.M., Feldt-Rasmussen, U., Henry, J.F., LiVosli, V.A., Niccoli-Sire, P., John, R., Ruf, J., Smyth, P.P., Spencer, C.A., Stockigt, J.R., 2003. Laboratory medicine practice guidelines: Laboratory support for the diagnosis and monitoring of thyroid disease. Thyroid. 13, 57-67
- [14]. Spencer, C.A., Bergoglio, L.M., Kazarosyan, M., Fatemi, S., LoPresti, J.S., 2005. Clinical impact of thyroglobulin (Tg) and Tg autoantibody method differences on the management of patients with differentiated thyroid carcinomas. J. Clin. Endocrinol. Metab. 90, 5566-5575.
- [15]. Thienpont, L.M., Beastall, G., Christofides, N.D., Faix, J.D., Ieiri, T., Jarrige, V., Miller, W.G., Miller, R., Nelson, J.C., Ronin, C., Ross, H.A., Rottmann, M., Thijssen, J.H., Toussaint, B., 2007. Proposal of a candidate international conventional reference measurement procedure for free thyroxine in serum. Clin. Chem. Lab. Med. 45, 934-936
- [16]. Dufour, D.R., 2007. Laboratory tests of thyroid function: Uses and limitations. Endocr. Metab. Clin. North Am. 36, 155-169
- [17]. Kahric-Janicic, N., Soldin, S.J, Soldin, O.P., West, T.G.J., Jonklaas, J., 2007. Tandem mass spectrometry improves the accuracy of free thyroxine measurements during pregnancy. Thyroid. 17, 303-311.
- [18]. Thienpont, L.M., Van Uytfanghe, K., Marriott, J., Stokes, P., Siekmann, L., Kessler, A., Bunk, D., Tai, S., 2005. Feasibility study of the use of frozen human sera in split-sample comparison of immunoassays with candidate reference measurement procedures for total thyroxine and total triiodothyronine measurements. Clin. Chem. 51, 2303-2311.
- [19]. Nogueira CR, Brentani MM. Triiodothyronine mimics the effects of estrogen in breast cancer cell lines. J Steroid Biochem Mol Biol. 1996;59:271-9.
- [20]. Humes HD, Cieslinski DA, Johnson LB, Sanchez IO. Triiodothyronine enhances renal tubule cell replication by stimulating EGF receptor gene expression. Am J Physiol. 1992;262:540-5.
- [21]. Hall LC, Salazar EP, Kane SR, Liu N. Effects of thyroid hormones on human breast cancer cell proliferation. J Steroid Biochem Mol Biol. 2008;109:57-66.
- [22]. Tang HY, Lin HY, Zhang S, Davis FB, Davis PJ. Thyroid hormone causes mitogen-activated protein kinase-dependent phosphorylation of the nuclear estrogen receptor. Endocrinology. 2004;145:3265-72.
- [23]. Oh HJ, Chung JK, Kang JH, Kang WJ, Noh DY, Park IA, et al. The relationship between expression of the sodium/iodide symporter gene and the status of hormonal receptors in human breast cancer tissue. Cancer Res Treat. 2005;37:247-50.

*Corresponding Author: SaadeldeenAboidriss ¹College of Medical Radiological Science, Sudan University of Science and Technology, Khartoum, Sudan