ORIGINAL ARTICLE

INCIDENCE OF TOXIC GOITERS, PYRAMIDAL LOBE, ANTITHYROID ANTIBODIES AND PREFERENCE OF FIXED DOSES OF I-131 FOR ABLATION OF VARIOUS TOXIC GOITERS IN KARACHIITES

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ABSTRACT

BACKGROUND: Hyperthyroidism has variable incidences depending upon the regional iodine status and thyroid imaging is used to ascertain type of toxic goiters. Radioioidine-131 (RAI) therapy is considered an effective therapeutic option with variable utilization in different parts of world. Aim of this study was to find out the incidence of toxic goiters, various clinical and scintigraphic parameters and preference of RAI treatment in different types of toxic goiters. **MATERIALS AND METHODS:** This was a retrospective observational study conducted at Nuclear Medicine sections of Aga Khan University Hospital (January 2012 till August 2014) and Dr. Ziauddin Hospital Karachi (April 2013 till August 2014). Records of all patients who were referred for thyroid scan during the study period were reviewed. Patients who were diagnosed with toxic goiters and later on had had RAI were reviewed for demographic data, type of toxic goiters, scintigraphic patterns (% uptake and pyramidal lobe), thyroid antibodies and administered dose of RAI. **RESULTS:** The overall incidence of toxic goiter was found to be 27% (370/1365). The mean age of the patients with toxic goiters was 46 years with female: male ratio of 69%: 31%. Grave's disease was found in 317 (86%) patients followed by autonomous toxic nodule in 44 (12%) and toxic MNG in 09 (02%). Pyramidal lobe was seen in 156 (42%) predominantly with GD. Thyroid antibodies was positive in 250/370 (68%) and negative in 120/370 (32%) and mean dose of RAI administered was 15 ± 3.51 mCi. **CONCLUSION:** We conclude that incidence of toxic goiters was in accordance with published data and GD was found to be the most common cause while the TMNG as the least common despite Pakistan lies in iodine deplete region. Antithyroid antibodies as an indicator of autoimmunity were found positive in majority of patients with GD and presence of pyramidal lobe has strong correlation with GD. Fixed doses of RAI was used for ablation of toxic goiters but outcome of this approach needs to be evaluated.

Key words: Toxic goiter; incidence; Graves' disease; Pyramidal lobe; Antithyroid antibodies

Introduction

Hyperthyroidism is defined as enhanced functioning of thyroid gland resulting in increased hormone production leading to a clinical state of thyrotoxicosis. The prevalence of hyperthyroidism in women is between 0.5-2%, and it is 10 times more common in women than in men in iodine-replete areas.[1] However, higher prevalence has been documented in iodine-deplete areas.[2] The most common causes of hyperthyroidism are Grave's disease (GD), followed by multinodular goiter (MNG) and less commonly by

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an autonomous toxic nodule (ATN). Grave's disease is attributable to autoantibodies against thyroid stimulating hormone (TSH) receptors of follicular cells (TRABs).[3] In some cases of toxic nodules, TSH receptor mutation is responsible for hyperfunctioning status.[4] Management of hyperthyroidism is based on rapid ameliorations of symptoms by beta or calcium blockers and strategies to reduce hormone synthesis by thionamide, surgery or radioactive-131 (RAI) therapy. RAI is considered the treatment of choice for GD and also for toxic MNGs and ATNs depending upon patient's preference. RAI has been the therapy of choice in the United States, being selected by 60% of thyroid specialists who responded to a survey in 2011, but only 13% of European thyroid specialists[5] and lower selection in UK and Australia as well.[6,7]

Radioioidine-131 (RAI) is rapidly incorporated into the functioning thyroid tissue and its beta-emissions (Max 0.6 MeV) result in extensive local tissue damage within 2 mm. The net effect is ablation of thyroid function over a period of 6 to 18 weeks.[8] Over the last 6 decades, RAI has proven as an effective, cheap and safe treatment for toxic thyroid conditions. However, despite of its worldwide use, controversies revolve around patient's selection and selection of effective dose.[3]

Aim of this study was to find out the incidence of toxic goiters, various clinical and scintigraphic parameters and preference of RAI treatment in different types of toxic goiters.

Material and Method

This was a retrospective observational study conducted at Nuclear Medicine sections of Aga Khan University Hospital (January 2012 till August 2014) and Dr Ziauddin Hospital Karachi (April 2013 till August 2014). Records of all patients who were referred for thyroid scan during the study period were reviewed. Patients who were diagnosed with toxic goiters based on their thyroid function tests and later on had had RAI were reviewed for demographic data, type of toxic goiters (as appeared on thyroid scan), scintigraphic patterns (% uptake and pyramidal lobe), thyroid antibodies and administered dose of RAI.

Thyroid scintigraphy was performed with 3-5 mCi of Technetium-99m pertechnetate (^{99m}Tc) injected intravenously and after 20 minutes multiple static images were acquired under single or dual head gamma cameras fitted with low energy high resolution collimators (Siemens, Germany). Thyroid uptake was calculated by using commercial software and a value of 0.5-3.5% was considered normal. All scans were reported by qualified nuclear physician with more than 06 year experience.

Radioiodine-131 (RAI) treatment was administered in liquid form in a fixed dose (10-30 mCi) depending upon the size and type of toxic goiters as American Thyroid Association (ATA) and American Association of Clinical Endocrinology (AACE) guidelines.[9] Patients were advised to stop antithyroid medication 3-5 days prior the RAI and restart 5 days later (as per physician's advice) and follow the measures to minimize radiation exposure to general public and family members.

Results

During the study period 1365 thyroid scans were performed and out of these 370 were found to have toxic goiters who also received RAI. The overall incidence of toxic goiter was found to be 27%. The mean age of the patients with toxic goiters was 46 years with female: male ratio of 69%: 31%. Grave's disease was found in 317 (86%) patients followed by autonomous toxic nodule in 44 (12%) and toxic MNG in 09 (02%) (Fig. 1). Thyroid scans of these

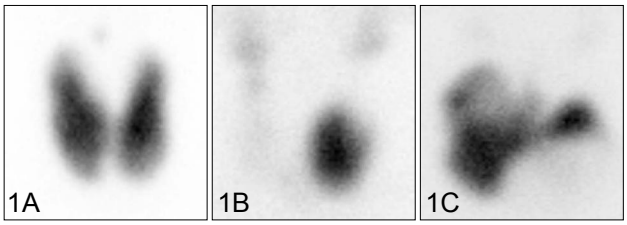

Figure 1: Tc-99m pertechnetate thyroid scans anterior views in three patients; (a) diffuse toxic goiter (Grave's disease); (b) left sided autonomous toxic nodule with suppressed right lobe; (c) toxic multinodular goiter.

patients with toxic goiters revealed pyramidal lobe in 156 (42%) predominantly with GD and thyroid uptake ≥ 3.5% in 362 (98%) and <3.5% in remaining 08 (02%) patients. Thyroid antibodies was positive in 250/370 (68%) and negative in 120/370 (32%) and mean dose of RAI administered was 15 ± 3.51 mCi (Tab. 1).

On intergroup analysis, patients with GD were found to significantly younger than ATD and TMNG (Fig.2) with no significant gender preference among them. Incidence of Pyramidal lobe and raised thyroid uptake was significantly higher in GD than ATD and TMNG. Presence of thyroid antibodies was significantly higher in GD proving the autoimmune status of GD. Mean fixed dose used to ablate toxic goiter was 15 mCi in GD and TMNG while a mean dose of 20 mCi was used to treat ATD (P< 0.0001) (Tab. 2), (Fig. 3).

Variables	Values
Incidence of toxic goiter	370/1365 (27%)
Age (mean ± SD) yrs	46 ± 14
Male	115 (31%)
Female	255 (69%)
Types of toxic goiter	
Grave's disease	317 (86%)
Autonomous	44 (12%)
Multinodular	09 (02%)
Incidence of pyramidal lobe	156 (42%)
Thyroid uptake	
≥3.5%	362 (98%)
<3.5 %	08 (02%)
Mean ± SD	15.943 ± 9.670%
	(range:2.0----59%)
Thyroid antibodies	
Positive	250 (68%)
Negative	120 (32%)
Dose of I-131 received	
Mean ± SD	15 ± 3.51 mCi
*P<0.05	

Table 1: Patients' Demographic; toxic goiter (n=370/1365)

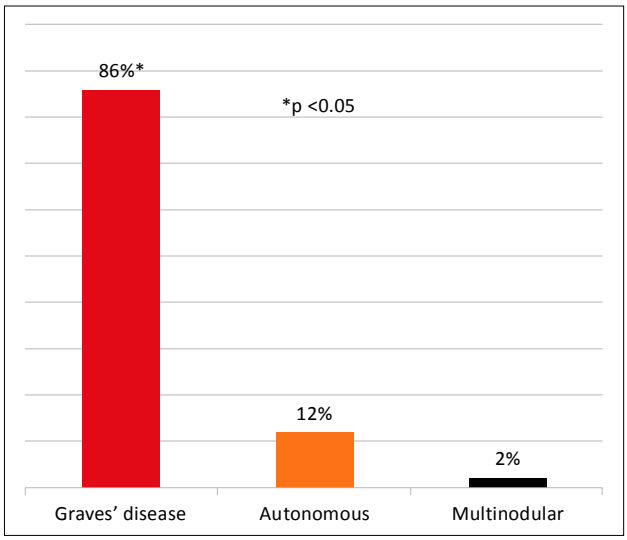

Figure 2: Comaparative incidence of toxic goiter.

Variables	Graves' Disease 317 (86%)	Autono-mous 44 (12%)	Multi-nodular 09 (02%)	t-test/X^2 (±95% CI)	P value
Age in yrs (mean ± SD)	44 ± 14*	53 ± 16	48 ± 12	3.925 (4.5-13.5)	<0.0001*
Female: Male	213:104 (67%:33%)	33:11 75%: 25%	09:00 100%:00%	0.798 (-8.2—21%)	0.371
Pyramidal Lobe	148 (47%)*	07 (16%)	01 (11%)	3.374 (0.2-18.3%)	<0.0001*
Thyroid uptake Mean ± SD Range	15 ± 9.665%* (3.0---59%)	10 ± 9.788% (2.0---35%)	10 ± 5.160% (3.8---15%)	-3.211 (-8.06- 1.93)	<0.0001*
Thyroid antibodies Positive	248 (78%)*	01(02%)	01 (11%)	18.099	
Negative	69 (22%)	43 (98%)	08 (89%)	(29-79%)	<0.0001*
Dose of I-131 received Mean ± SD	15 ± 3.428 mCi	20 ± 3.284*	15 ± 5.0	9.111 mCi (3.92-6.09)	<0.0001*
*P<0.05					

Table 2: Demographic comparison of Grave's disease, autonomous and multinodular goiter

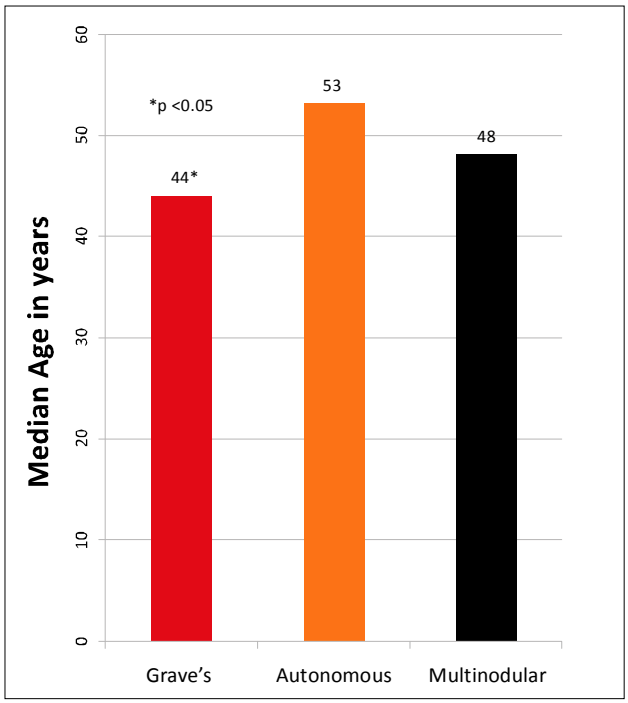

Figure 3: Comparative median age of incidence of toxic goiter among Grave's, autonomous and mutinodular goiter.

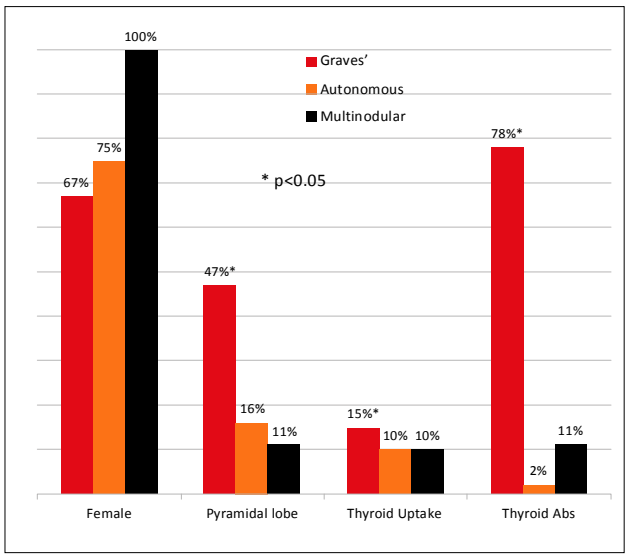

Figure 4: Comparison of female gender, pyramidal lobe, thyroid uptake and antibodies among Grave's disease, autonomous and multinodular toxic goiter.

Discussion

The overall incidence of toxic goiters in our study is 27% and this is much higher than reported incidence of 0.4-2%.[10] However, this is to elucidate that reported incidence is community based and our incidence is based on a selected patient's group and biased sampling is the sole reason for this over estimation. This is to mention that our overall incidence is close to a reported incidence of 25.8% from a single center based study from Sweden.[11] The mean age of patients with toxic goiters and female prevalence is again in concordance with published data.[12] In our study GD was found to be most common cause of toxic goiters and this is in accordance with published data.[13] ATD was the 2nd most cause of toxic goiters in our study and it correlated with published data from iodine deficient area.[14] However, in contrast to published studies, our patients were in older age group and this could be explained by an expected delayed diagnosis in our cohort. Although a study from iodine replete area has shown a rising incidence of ATD with age.[15] TMNG was the least common cause for hyperthyroidism in our cohort and again matches with reported prevalence of about 5% in iodine deficient areas.[14] However, there are reports of very high incidence of TMNG from iodine deficient Middle East.[12]

The overall incidence of PL in this study was 11.4% comparable with our published data.[16] This study also shows a significantly higher incidence of PL in patients with GD and is important for surgeon to ensure adequate thyroidectomies in patients with GD opted for surgery.

Thyroid antibodies (anti-thyroglobulin, TgAb and anti-thyroid per oxidase, TPOAb) are sensitive indicator of autoimmune thyroid disorders but may be detectable in 10-12% of healthy population as well.[1] Change in titer of these antibodies (primarily TPOAb) is used for monitoring the progression or regression of autoimmune diseases. In this study, the overall incidence of positive TAb was 68% (248/250 positive patients had GD) and was undetectable in 32% patients (69/120 had GD and 51/120 had toxic nodular goiter). Prevalence of positive Tab was 78% in GD, 02% in ATN and 11% in TMNG. These figures are in accordance with published data mentioning positivity in 50-80% patients with autoimmune based GD.[17]

We have used a fixed dose of RAI for ablating the toxic goiters and rationale for this strategy is well known higher incidence of ablation failure associated with lower doses.[9] Dose used for ablation of ATN was significantly higher (20 mCi ± 3.2) and reiterate

our goal of using maximum dose of RAI to have successful ablation. There was no significant difference between RAI dose used for GD and TMNG and this could be due to relatively smaller sizes of TMNG in our cohort. However, the outcome of this approach in terms of ablation failure or success was studied and this is a major limitation of this study.
We conclude that incidence of toxic goiters was in accordance with published data and most likely due to biased sampling. GD was found to be the most common cause while the TMNG as the least common despite Pakistan lies in iodine deplete region. Antithyroid antibodies as an indicator of autoimmunity were found positive in majority of patients with GD and presence of pyramidal lobe has strong correlation with GD. Fixed doses of RAI was used for ablation of toxic goiters but outcome of this approach needs to be evaluated.

Conflict of Interest: Authors declare no financial or institutional conflict of interest

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