DOI: https://doi.org/10.54393/pjhs.v6i1.2028

PAKISTAN JOURNAL OF HEALTH SCIENCES
(LAHORE)
https://thejas.com.pk/index.php/pjhs
ISSN (E): 2790-9352, (P): 2790-9344
Volume 6, Issue 01 (January 2025)

Original Article

OPEN ACCESS

Thyrotoxicosis: What is the Cause in Our Population?

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ARTICLE INFO

Keywords:
Thyrotoxicosis, Graves' Disease, Toxic Adenoma, Toxic Multinodular Goiter, Endocrinology

How to Cite:
Ali, A., Khan, S., Anees, ., Hassan, T., & Mufti, F. (2025). Thyrotoxicosis: What is the Cause in Our Population? Causes of Thyrotoxicosis. Pakistan Journal of Health Sciences,6(1), 12-16. https://doi.org/10.54393/pjhs.v6i1.2028

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Received date: 25th September, 2024
Acceptance date: 10th January, 2025
Published date: 31st January, 2025

ABSTRACT

Thyrotoxicosis is an endocrine disorder in which excess amount of thyroid hormone is secreted in the blood stream and causes its action at the tissue level. Thyrotoxicosis highly affects the quality of life of patients suffering from the disease in carrying out daily activities. Proper treatment of thyrotoxicosis requires an accurate diagnosis. **Objective:** To determine the causes of thyrotoxicosis in patients reported for evaluation and management to specialized endocrine unit. **Methods:** This was a descriptive cross sectional observational study conducted by convenient sampling in Outpatient Department (Endocrinology Clinic) Khyber Pakhtunkhwa in six month's duration (15th December 2023 to 15th May 2024) having sample size n=118. Thyrotoxicosis was labeled if patient has high T3, T4 (thyroxine and/or triiodothyronine) levels and suppressed thyroid stimulating hormones TSH levels. Information was gathered from the patients regarding their clinical signs and symptoms and anthropometrics. Laboratory investigations of thyroid function tests were obtained and analyzed. **Results:** The mean age of 118 patients was 40.39 ± 13.69 years, 28% male and 72% female patients were in enrolled in the study. Graves' disease was most common form thyrotoxicosis making count of 50% of patients followed by toxic adenoma, toxic MNG, thyroiditis 16% and 14 % respectively. Anti-thyroid drugs count 43% of most of the patient's treatment offered followed by radioactive iodine 28%. **Conclusions:** In conclusion, the main cause of thyrotoxicosis, includes grave's disease, toxic adenoma and toxic MNG in Pakistani population. Thyrotoxicosis was more prevalent among female population as compared to males.

INTRODUCTION

Thyrotoxicosis is an endocrine disorder in which excess amount of thyroid hormone is secreted in the blood stream and causes its action at the tissue level [1]. The term "thyrotoxicosis" is high T3, T4 (thyroxine and/or triiodothyronine) levels and suppressed TSH levels [2]. Hyperthyroidism is observed in female more as compared to males with a ratio of (5:1). The overall prevalence of hyperthyroidism in female is 1.3% however it increases in age and in older females it is estimated to be 4% to 5% [3]. Literature showed that prevalence of hyperthyroidism is higher among smokers as compared to nonsmokers [4]. Young females are most prone to graves' disease while toxic nodular goiter is more prevalent in older women. Thyrotoxicosis has various etiologies, manifestations, and potential treatments [5]. Treatment of each type requires accurate diagnosis. Furthermore, β-blockers can be used in almost all forms of thyrotoxicosis, whereas Anti-Thyroid Drugs (ATDs) are useful in only some patients [6]. For appropriate treatment of thyrotoxicosis, exact diagnosis of the cause and its associated medical conditions should be dig out and patient preference for utmost priority [7]. It is difficult to diagnose exact cause of thyrotoxicosis as symptoms can mimic many other diseases and this can lead to inappropriate diagnoses and timely management of the disease [8]. For all the above reasons, literature studied showed that many globally surveys and endocrinologist opinions from different geographical areas unveiled important ambiguities in AIT causing, diagnosis and treatment is concern. Thyrotoxicosis exhibit collective clinical manifestation, caused by excessive serum thyroid hormones particularity thyroxin [9]. The clinical signs and symptoms of thyrotoxicosis exists variable feathers like weight loss fatigue and weakness like cardiovascular disorders neuromuscular disorder and gastrointestinal

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disturbance. Mostly worldwide thyrotoxicosis is diagnosed on laboratory investigations, levels of thyroxin, triiodothyronine and thyroid stimulating hormones associated with other investigations for medical condition. In general thyrotoxicosis elevated levels of serum level of thyroid hormones and thyroxin [10]. Management of thyrotoxicosis rely on the cause and severity of the disease. The treatment options of hyperthyroidism include anti-thyroid medicines, radioiodine therapy and thyroid surgery. The radioiodine treatment aims to dominate radioiodine and recovers thyroid over weeks to months. Medical treatment of Hyperthyroidism include medicine like as methimazole can temporally controls disease, β-blockers also control cardiovascular symptoms. Lastly surgical removal of thyroid gland is mainly applied on cancerous condition and has higher prevalence among female then males and younger age groups [11]. Worldwide, patients with thyrotoxicosis are examined and managed in specialized endocrine clinics. Being the super specialty clinics of endocrinology in this part of the country, endocrine patients from nearby areas are managed here in super specialty clinics.

This study aimed to find the causes of thyrotoxicosis in population in this part of the world. The current study added and improved the existing knowledge of medical physicians on thyrotoxicosis, its evaluation and management, especially in this region, thus improving the general health and quality of life of the population being affected by this endocrine disease.

METHODS

This was a descriptive cross sectional observational study conducted in Out-Patient Department (Endocrinology Clinic) Khyber Pakhtunkhwa in six month's duration (15th December 2023 to 15th May 2024). The sample was calculated by open Epi sample size calculator. The previously reported prevalence of hyperthyroidism in Pakistan is 8.38% as reported by previous literature [12]. The minimum required sample size was 118 participants at 95% confidence interval, 5% margin of error and 80% power. All those patients who were reported at OPD of Department of Endocrinology and Metabolic Disorder for evaluation and management of thyrotoxicosis were included in the study using convenient sampling technique. Those patients who were already on anti-thyroid medications and had no record of thyroid scan were excluded from study. The researcher collected the data after approval of proposal from ethical committee of college of family medicine Pakistan, approval letter issued (IRB-CFMP/22/2023). Participants were enrolled according to inclusion and exclusion criteria. Informed consent was taken from each participant, who met the inclusion criteria. Before consent, the purpose and benefits of the study were explained to participant using the patient information sheet. Trained phlebotomist took 5cc blood to carryout blood analyses. Samples/data were collected using Non-Probability Consecutive Sampling Technique from all included patients presenting to the Department of Endocrinology, Hayatabad Medical Complex Peshawar for thyrotoxicosis. Data regarding socio demographic aspects, hematological, biochemical findings and radiographic images (Thyroid Uptake Scan and Ultrasound) of thyroid gland were collected on the specially designed tool to analyze hyperthyroid patients. Thyrotoxicosis was evaluated using blood tests for thyroid function tests using immunoassay test kits. Thyrotoxicosis was labeled if patient has high T3, T4 (thyroxine and/or triiodothyronine) levels and suppressed TSH levels. Information was gathered from the patients regarding their clinical signs and symptoms and anthropometrics. The data collected was analyzed using SPSS version 21 and interpreted in tables. Frequencies, means and standard deviation were calculated for continuous variables. The Chi Square test was used for association of categorical variables. P value < 0.05 was considered statistically significant.

RESULTS

The mean age of 118 patients was 40.39 ± 13.69 years, 28% male and 72% female patients were in enrolled in the study table 1. Duration of the disease history was 13.81 ± 21.84 months. Mean thyroid function tests recorded was as T3 2.55 ± 2.92, T4 16.59 ± 7.53, TSH 1.05 ± 9.25. Inflammatory markers mean ESR was 74 ± 33. Among biochemical interpretation overt hyperthyroidism was higher 51% followed by subclinical 39% T3, 9% T4 thyrotoxicosis 1%. In appropriate treatment was taken by 20% of the thyroid patients. Goiter was found among 55% while Sjogrens' syndrome signs were among 83% of patients. TSH receptors antibodies test TRAB carried out was positive among 38% of thyroid patients.

Table 1: Baseline Characteristics of Patients (n=118)

Variable		Mean ± SD / N (%)
Age (Mean)		40.39 ± 13.69
Gender	Female	33 (28%)
	Male	85 (72%)
Duration of Disease (Months)		13.81 ± 21.84
T3 (µLU/mL)		2.55 ± 2.92
T4(µLU/mL)		16.59 ± 7.53
TSH (µLU/mL)		1.05 ± 9.25
ESR (mm/Hr)		74 ± 33
Biochemical Interpretation		
Sub Clinical		39%
Overt		51%
T3 Thyrotoxicosis		9%
T4 Thyrotoxicosis		1%
In Appropriate Treatment Taken		
Yes		20%

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No	80%
Goiter	
Yes	55%
No	45%
Sjogrens' Syndrome	
Yes	83%
No	17%
TSH Receptors Anti Bodies Test (TRAb)	
Positive	38%
Negative	62%

Grave's disease was most common form thyrotoxicosis making count of 50% of patients followed by toxic adenoma, toxic MNG, thyroiditis 16% and 14 % respectively. All the causes Graves' disease, toxic adenoma, thyroiditis and toxic MNG were significant with p value 0.004, 0.001, 0.002 and 0.072 respectively. Drug induced and TSHoma were insignificant with p value 0.241 and 0.42 respectively table 2.

Table 2: Frequency of Different Causes of Thyrotoxicosis and Association with Gender (n=118)

Variables	Male N (%)	Female N (%)	p-Value
Graves' Disease	21 (18%)	38 (32%)	0.004
Toxic Adenoma	5 (4%)	14 (12%)	0.001
Toxic MNG	5 (4%)	12 (10%)	0.072
Thyroiditis	7 (6%)	11 (9%)	0.002
Drug Induced	1 (1%)	2 (2%)	0.241
TSHoma	1 (1%)	1 (1%)	0.423

Thyroid scan showed most significant among diffuse increased uptake followed by Low Uptake 51% and 19% respectively. All types of thyroid scan have statistical significance with gender except multifocal increase up take with (p value 0.75). These results also make graves diseases among leading cause in thyrotoxicosis table 3.

Table 3: Association of Thyroid Scan in Gender among study participants

Variables	Total N (%)	Male N (%)	Female N (%)	p-Value
Diffuse Increased Uptake (Graves)	191 (51%)	60 (16%)	131 (35%)	0.002
Solitary Increased Uptake/Toxic Adenoma	60 (16%)	25 (7%)	35 (9%)	0.001
Multifocal Increased uptake	52 (14%)	20 (5%)	32 (9%)	0.753
Low Uptake	72 (19%)	24 (6%)	48 (13%)	0.001

Table 4 described treatment offered to the patients. Anti-thyroid medications treatment was offered to 43% of the offered followed by radioactive iodine 28%. Observation and monitoring required among 12% and surgery required 10% and steroid therapy required to 7% of patients.

Table 4: Treatment Offered to the study participants

Variables	n (%)
Anti-Thyroid Drugs	51 (43%)
Radio Active Iodine	33 (28%)
Surgery	12 (10%)
Observation and Monitoring	14 (12%)
Steroid Therapy	8 (7%)

DISCUSSION

The causes of thyrotoxicosis in general population were well understood in western world, globally it was known that Graves' disease was contributing factor to thyrotoxicosis [13]. The findings of the present study also appraise this literature where it was found out that 50% of population had Graves' disease followed by toxic adenoma and thyroiditis in 16 % each of population. Literature showed that thyrotoxicosis can occur in any age, child adolescent and adults were equally affected with incidence of between ages 20 and 50 years [14]. The study finding showed that mean age of the patients with thyrotoxicosis was 40.39 ± 13.69 with male to female 28% and 78% frequency. The reason behind this was thyrotoxicosis prevalence was higher in females as compared to male by ratio of 5:1 [15]. Mean duration and treatment of disease was 13.81 ± 21.84, however this could be late presentation as in this population very limited access to specialized endocrinologist and the specialized health facility. A study conducted in Turkey found mean duration of treatment of 8.0 ± 6.9 months [16]. The biochemical interpretation of this study reveals that overt hyperthyroidism was in 51 patients followed by sub clinical 39%. A study conducted found that including 0.5% overt thyrotoxicosis and 0.7% subclinical among total of 1.2% thyrotoxicosis [17]. This study found 55% of patients with diffused goiter on thyroid scan, however Hanely P reported that 10-15% of adolescent's thyrotoxicosis were caused by diffused toxic goiter [18]. These results also found that Sjogrens' syndrome signs were positive among 83% of the study population. TSH receptor antibodies (TRAb) were antibodies directed against. The TSH receptors, it was measured to differentiate between thyrotoxicosis with hyperthyroidism [19]. In this study the TRAB was performed in patients and 38% of the results were positive. Graves' disease that was an autoimmune disorder that causes immunoglobulins to activate the TSH receptor of follicular cells [20]. The risk factors for thyrotoxicosis include family history positive, female gender, termination of pregnancy postpartum period and increasing age. These study findings showed that graves' disease was the main cause of thyrotoxicosis that accounts for 50% of patients among which 32% were female population with significant p value (p=0.004). Over all the female population in this study were affected by toxic adenoma 12 % and toxic MNG 10% with p value 0.001 and 0.07 respectively. A thyroid scan can help diagnose the cause of thyrotoxicosis, it helps to differentiate between Graves' disease, Toxic Multinodular Goiters (TMNGs), and Subacute Thyroiditis (SAT) [21]. This

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study analysis of thyroid scan showed that diffuse increased uptake was higher prevalent followed by Low Uptake 51.3% and 18.5% respectively. Technically, the aim of treatment of the thyrotoxicosis was to investigate find and remove the cause, treatment includes thyroid-stimulating immunoglobulin, anti-thyroid medications methimazole, surgery thyroidectomy, and immunosuppressive steroid therapy [22]. In the study population, the treatment offered included anti thyroid drugs count 43% of most of the patient's treatment offered followed by radioactive iodine 28%. The goal of treatment has never been to cure the thyrotoxic condition rather than making the condition euthyroid without the need for thyroid hormone or to reduce the function to below normal. In limitation, the sample size was too small as this was shorter duration of the study and due to very small population proportion larger data could not be achieved. As sample size was n=118 so this small data could not be generalized in conclusion for whole population. However, it was recommended to carry out more detail cohort, prospective, metacentric studies with larger sample size to better understand the depth of the disease.

CONCLUSIONS

In conclusion, the main cause of thyrotoxicosis, includes Graves' disease, toxic adenoma and toxic MNG in Pakistani population. Female population was more affected as compared to males. Mainly patients responded to anti thyroid medications for treatment. The management of thyrotoxicosis requires specialized consultation to correctly find the cause, diagnose the condition and treat accordingly that can significantly influence the outcome of disease and the well-being of the patient.

Authors Contribution

Conceptualization: AA
Methodology: SK
Formal analysis: A
Writing, review and editing: TH, FM

All authors have read and agreed to the published version of the manuscript

Conflicts of Interest

All the authors declare no conflict of interest.

Source of Funding

The author received no financial support for the research, authorship and/or publication of this article.

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