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(RESEARCH ARTICLE)

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A multicentric, hospital survey to evaluate the possible adverse drug reactions associated with thyroid medication

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Abstract

This study was conducted to identify and report the Adverse drug reactions (ADRs) associated with use of thyroid medications drugs pediatric and medicine Departments in a Tertiary Care hospital of Vidarbha Maharashtra. A multicentric hospital study was conducted for 4 months in-patient at a tertiary care teaching hospital. We enrolled the patients based on Inclusion criteria and data was analyzed with the help of MS excel 7 and Graph pad Prism. Further, the assessments of type, severity, and preventability of reported ADRs were done using Wills and Brown classification, modified Schumock and Thornton severity scale, modified Hartwig and Siegel Preventability scale. Data were collected from a total of 50 (100%) patients of which 19 (38%) patients were affected with ADRs. Among twelve Patients, females (24%) were more affected with ADRs when compared to males (14%). Based on the type of ADRs, Type D ADRs (58%) were more observed followed by Type A (23%) and Type B (5%). We reported more prevalence of female patients experiencing ADRs associated with use of antithyroid drugs as compared to Male patients.

Keywords: Hypothyrodism; Thyroid medication; ADRs; Wills and Brown classification scale; Modified Schumock and Thornton severity scale; Modified Hartwig and Siegel Preventability scale**.**

1. Introduction

Hypothyroidism is the result of reduced thyroid hormone levels with different etiologies and severity. A distinction is made primarily between primary and secondary (i.e. central) hypothyroidism. In primary hypothyroidism, the thyroid gland fails to produce sufficient amounts of thyroid hormone. Less commonly, secondary or central hypothyroidism occurs when the thyroid gland is functioning normally. However, hypothyroidism is the result of abnormal functioning of the pituitary gland or hypothalamus. Autoimmune thyroiditis and iodine deficiency are the most common causes of the disease. Central hypothyroidism is rare. [1] The risk of developing Hashimoto's thyroiditis can be influenced by genetics, pregnancy, certain medications, age, sex, infections, and exposure to radiation. [2]

Hypothyroidism affects up to 5% of the general population, with another estimated 5% undiagnosed. Over 99% of affected patients suffer from primary hypothyroidism. Globally, environmental iodine deficiency is the most common cause of all thyroid disorders, including hypothyroidism, but in iodine-sufficient areas, the most common cause of thyroid failure is Hashimoto's disease (chronic autoimmune thyroiditis). [2]

Hypothyroidism, specifically, is the most common thyroid disorder in Indian adults. However, in spite of this dismal situation of the country has no effective and scientifically constructed policy of control disease. Prevalence of hypothyroidism in India is 11% compared to only 2% in the UK and 4.6% in the UK USA. Compared to coastal cities (e.g. Mumbai, Goa and Chennai), inland cities (e.g. Calcutta, Delhi, Ahmedabad, Bangalore and Hyderabad) have a higher

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prevalence (11.7% vs. 9.5%) and the reason for the higher average thyroid stimulating hormone concentration and scope in India compared to western countries is possibly associated with long-term lack of iodine in the country, which was only partially repaired over the past 20 years. The highest prevalence of hypothyroidism (13.1%) occurs in people aged 46–54 years,with people aged 18-35 less affected (7.5%). [3]

Hypothyroidism is diagnosed biochemically; it is overt primary hypothyroidism defined as a serum thyroid-stimulating hormone (TSH) concentration above the normal reference range and a thyroxine concentration below the normal reference range. Symptoms of hypothyroidism are nonspecific and include mild to moderate weight gain, fatigue, poor concentration, depression, and menstrual cycle disturbances, while the consequences of untreated or untreated hypothyroidism include cardiovascular disease and increased mortality. Levothyroxine has long been a mainstay in the treatment of hypothyroidism and is one of the most commonly prescribed drugs worldwide. In adults with overt hypothyroidism, levothyroxine is usually prescribed at an initial dose of 1.6 μg/kg/day, which is then titrated to achieve optimal TSH levels (0.4–4.0 mIU/L) according to the therapeutic goal.[2]

The present study primarily aims to determine the prevalence of hypothyroid patients, to assess ADRs (ADRs) associated with thyroid medications using a hospital survey, and to classify the number of ADRs according to the Wills and Browns classification. Secondary objectives include assessing the potential number of ADRs that would require discontinuation of thyroid medication or treatment, to assess the number of patients with mild, moderate, and severe ADRs using the Hartwig severity rating scale distribution, and to determine the percent preventability of ADRs using the Schumock and Thornton scale.

2. Methodology

2.1. Study Design and study conduct

A Multicentric, Hospital Survey were conducted to assess the prevalence of patients living with ADRs associated with the use of thyroid medications. The total duration of study was 4 months. Patients were approached for the survey by they were undergoing treatment for active thyroid disease, had Grave's Disease or any other autoimmune disease related to the thyroid, were aged between 10 and 60 years, and included both male and female patients. Patients were excluded from the study if they were above 60 years of age, had cancer of the thyroid gland, or had a chronic illness. A survey was conducted on a total of 50 patients, among whom 17 showed ADRs (ADRs).

2.2. Description of study activities

Patients with a diagnosis of hypothyroidism were approached. Eligible patients who willingly agreed to participate in the study were enrolled in this study. Patients responded the survey questionnaire after a full explanation about the participation in this study and after meeting the eligibility criteria During initial appointments, assessments included recording patients with hypothyroidism, their medical history, demographic data, vital signs, symptoms, severity scale, and any adverse effects. In second appointment (2-month follow-up/telephonic visit), severity evaluation, concomitant medication, and vital signs were recorded. On third appointment of study, adverse effects and their types were documented to assess patient responses throughout the study. [4-6]

3. Result

3.1. Demographics and Other Baseline Characteristic

Table 1 Demographics and Other Baseline Characteristics

Demographics	N	Values mean	Values median	Range min- max
Age (In Years)	50	25.14	22.5	13.0-48.0
Gender	50	Nan	Nan	Nan
Male	18	Nan	Nan	Nan
Female	32	Nan	Nan	Nan
Weight	50	55.68	53.5	40.0-79.2

Table 1 represents the patients demographics and other baseline characteristics. The average age of the patients is approximately 25 years, with A standard deviation of 9 years. The ages ranges from 13 to 56 years. The mean weight was about 55.7 KG, with a standard deviation of 10.8 KG. Weights range from 40 to 79.2 KG.

3.2. Vitals Distribution: Systolic Blood Pressure (SBP) Distribution

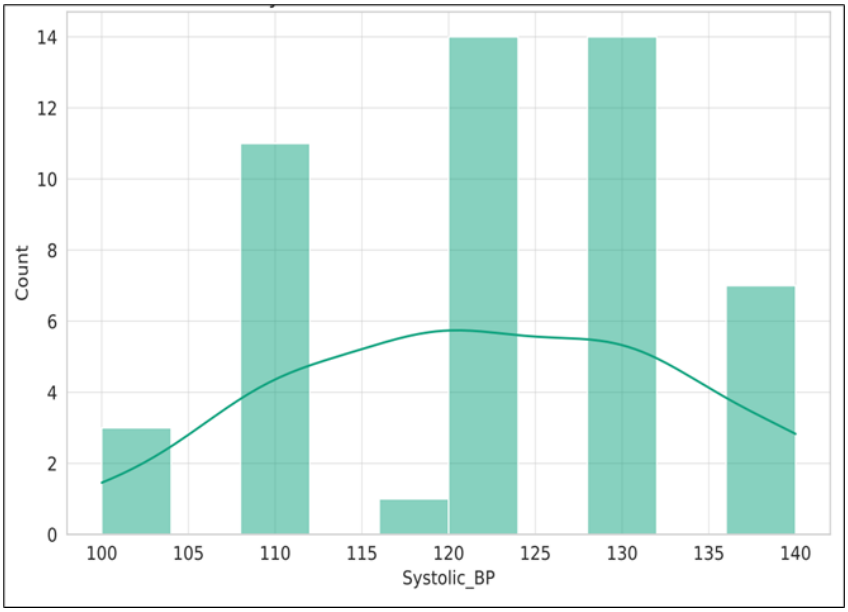

Figure 1 Systolic Blood Pressure (SBP) Distribution

Vital monitoring is crucial. The average systolic blood pressure was reported to be 122.12 mm Hg, Ranging from 100 to 140 mm Hg. (fig .1)

3.3. Diastolic Blood Pressure (DBP) Distribution

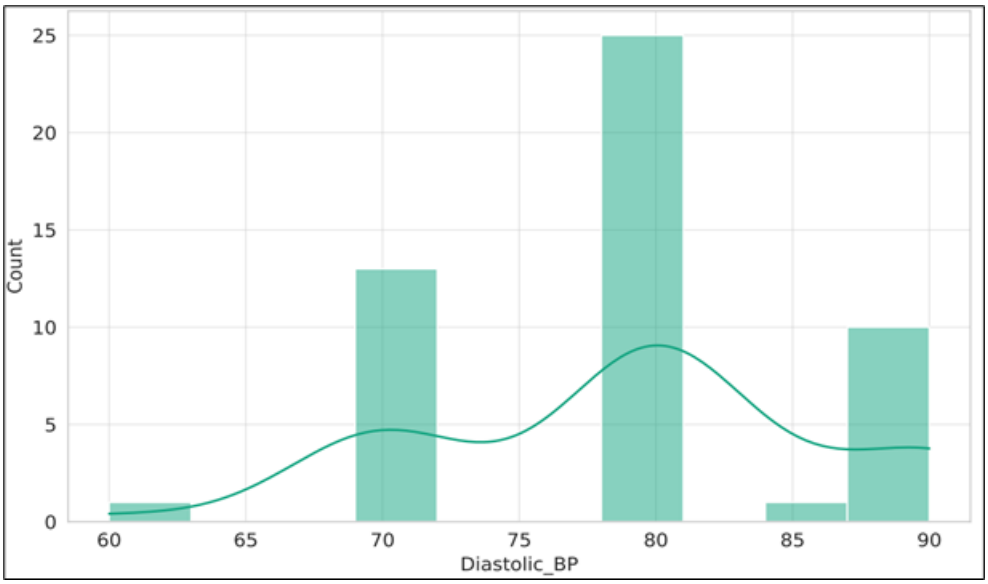

Figure 2 Diastolic BP

The average diastolic blood pressure was reported to be 79.10 mm Hg, ranging from 60 to 90 mm Hg.

3.4. Hartwig's Severity Assessment Scale Distribution [5]

Out of total 50 (100%) patients 17(38%) Persons show ADR of which 9 (53%) population were found to experience mild type of ADR , 6(35%) population shows Moderate type of ADR And 2 (12%) show severe type of ADR.

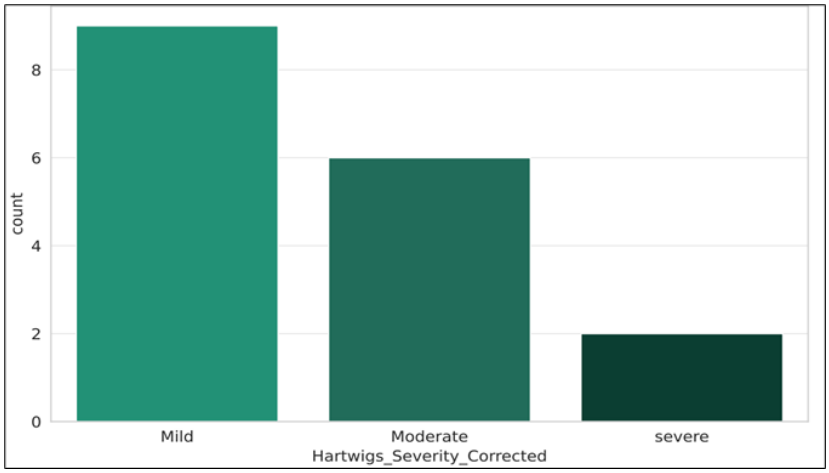

Figure 3 Hartwig's Severity Assessment Scale Distribution

3.5. Preventability Analysis (Schumock And Thornton Scale) [6]

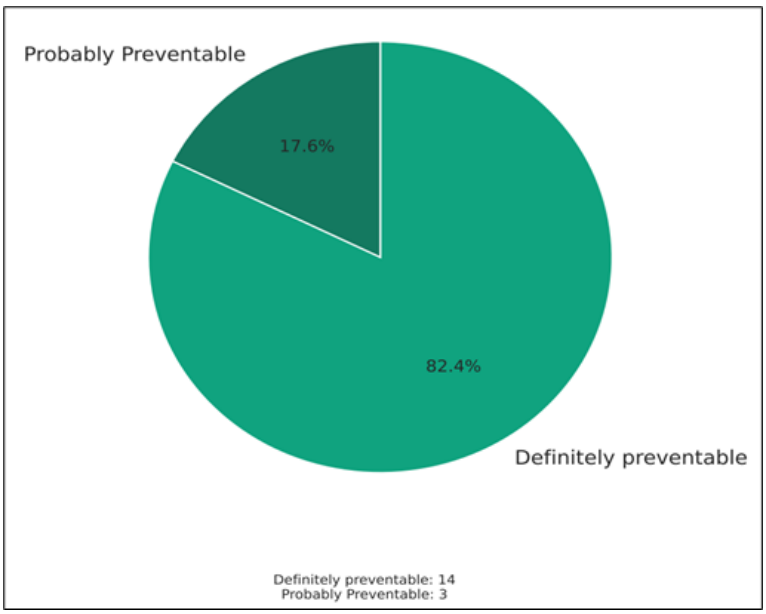

Figure 4 Preventability Analysis (Schumock and Thornton Scale)

Out of 50 (100%) patients, 17 patients shows ADR's out of Which 14 (82.4%)are definitely preventable ADR's and 3 (17.6%) are probably preventable ADR's .

3.6. Concomitant Medications

Majority of patient were on various concomitant medications. We reported 11(22%) patients were given antidiabetic drugs as Concomitant medications. Similarly, 5 (10%) patients are given antibiotic drugs, 9(18%) were Given probiotics, 2(4%) were given antiplatelate drugs , 11(22%) were given multivitamins , 3(6%) were given antipyratic drugs , 24(48%) were given beta blockers , 18(36%) were given Antiinflamatory drugs , 2(4%) were given proton pump inhibitors , 10 (20%) were given Vitamin D and supplements .

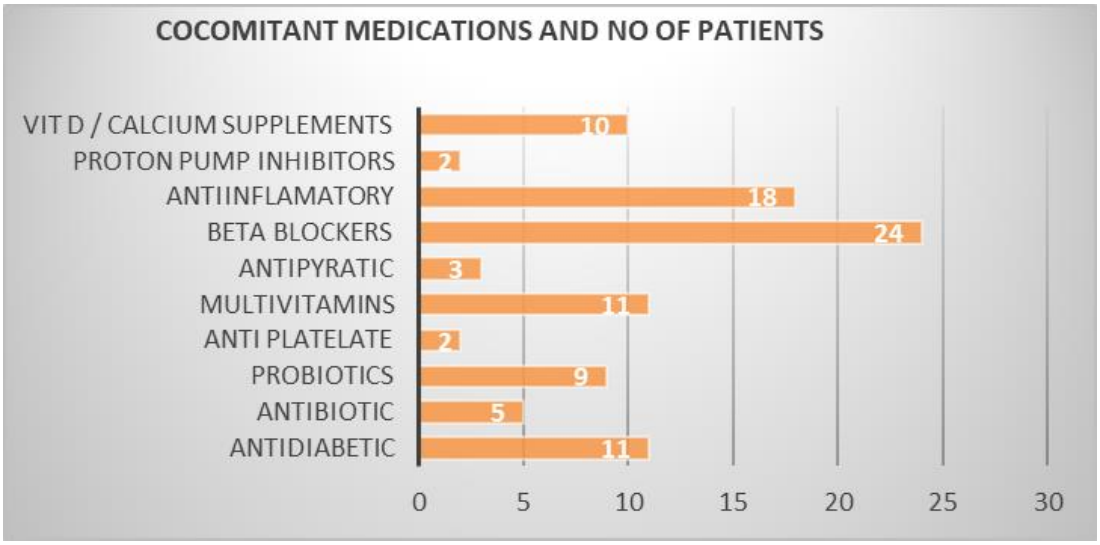

Figure 5 Concomitant Medications

4. Discussion

Thyroid if untreated, can be lethal. It still presents a risk of death even with quick treatment. Based on statistical data, the survival rate for thyroid storm patients is estimated to be between 10% and 30%.[7]

Hypothyroidism impacts approximately 5% of the general population, with an additional estimated 5% going undiagnosed. More than 99% of individuals affected experience primary hypothyroidism. On a global scale, environmental iodine deficiency stands as the predominant cause of all thyroid disorders, inclusive of hypothyroidism. However, in regions with sufficient iodine levels, Hashimoto's disease (chronic autoimmune thyroiditis) emerges as the leading cause of thyroid failure.[6] In India, the prevalence of hypothyroidism is 11%, notably higher than the 2% in the UK and 4.6% in the USA. Inland cities like Calcutta, Delhi, Ahmedabad, Bangalore, and Hyderabad show a higher prevalence (11.7%) compared to coastal cities like Mumbai, Goa, and Chennai (9.5%). This disparity may be attributed to the historically insufficient iodine intake in India, only partially addressed over the past two decades, leading to higher average thyroid stimulating hormone levels compared to Western nations.[3]

Hypothyroidism, characterized by an underactive thyroid gland, has various etiologies. The most common cause is autoimmune thyroiditis, particularly Hashimoto's thyroiditis, where the body's immune system attacks the thyroid gland, leading to inflammation and impaired function. Other causes include thyroid surgery or radioactive iodine treatment for hyperthyroidism, radiation therapy to the neck area for cancer treatment, and certain medications like lithium and amiodarone. Congenital hypothyroidism can occur due to genetic defects or abnormal development of the thyroid gland in babies. Additionally, iodine deficiency in the diet, pituitary or hypothalamic disorders affecting hormone regulation, thyroiditis from infections, and certain chronic illnesses such as Type 1 diabetes and celiac disease can also contribute to hypothyroidism. Understanding these diverse causes is crucial for appropriate diagnosis and management of the condition. Hypothyroidism symptoms encompass fatigue, weight gain, sensitivity to cold, constipation, dry skin and hair, muscle and joint pain, depression, memory issues, menstrual irregularities, hoarseness, slow heart rate, swelling, hair loss, and sexual dysfunction in men. [9]

Our study investigates ADRs (ADRs) linked with antithyroid medications through a hospital survey, aiming to determine the extent of ADRs warranting the cessation of antithyroid therapy. The elevated risk of thyroid disorders in women, approximately ten times higher than in men, is often attributed to autoimmune responses, which are more prevalent in women due to hormonal fluctuations during menstruation and the influence of sex steroids on the immune system [10]. Our survey involved 50 patients, with 17 (34%) experiencing potential ADRs, notably more prevalent among females.

The predominant anomaly detected was subclinical hypothyroidism, seen in up to 20% of postmenopausal women, with 7 (14%) women in our study presenting this condition. [11] Evidence from research indicates a decline in thyroid function with age [12], with hypothyroidism most prevalent in the 46-54 age group according to AG Unnikrishnan. [13] However, our study found the highest prevalence in the 25-30 age group (50%) and the lowest in the 46-55 age group (20%), with minimal cases in those over 56 years (7%).

Among the observed ADRs, weight gain was common, particularly in females, alongside additional complications like infertility and hypertension. Thyronorm, frequently prescribed for hypothyroidism, displayed potential adverse effects such as elevated blood pressure and osteoporosis according to Bondi B *et al*, consistent with our findings where 14 (82%) patients experienced hypertension and 9 (52%) developed osteoporosis. [14] Other adverse effects included irregular menstrual cycles and minor symptoms like itching and joint pain.

In severe cases, drug therapy was discontinued in 2 (11%) instances. ADR types were categorized as 4 (23%) type A, 1 (5%) type B, 2 (11%) type C, and 10 (58%) type D. Severity assessment, using the modified Hartwig and Siegel scale, revealed 9 (53%) cases of mild, 6 (35%) cases of moderate, and 2 (12%) cases of severe ADRs. According to the Schumock and Thornton scale, 14 (82.4%) cases were deemed definitely preventable and 3 (17.6%) probably preventable, with no instances categorized as non-preventable. It is crucial to monitor patients on hypothyroidism therapy. Additionally, clinical decision impacts patients' health outcome after understanding the patient centric therapy.

5. Conclusion

Our study found that the prevalence of ADRs (ADRs) associated with Antithyroid medications, particularly among women. Subclinical hypothyroidism was a notable Finding, with variations in age distribution compared to previous studies. Common ADRs Included weight gain, hypertension, and osteoporosis. The identification of preventable ADRs Underscores the importance of proactive management strategies. Overall, our findings Emphasize the need for tailored interventions to minimize ADRs and optimize treatment Outcomes in hypothyroidism patients.

Compliance with ethical standards

Disclosure of conflict of interest

Authors declares that there is no any conflict of interest.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

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