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Thyroid medications and patient adherence: understanding prescription patterns and factors influencing treatment compliance

Bhavya Poojary[1], Merlin Maria Wilson[1], Riya Jose[1], Sona P Sam[1*], Ann Elizabeth George[2]

[1]Pharm D Intern, Doctor of Pharmacy, Department of Pharmacy Practice, Bapuji Pharmacy College, Davangere, Rajiv Gandhi University of Health Sciences, Bengaluru, Karnataka, India, [2]Ex-Assistant Professor, Department of Pharmacy Practice, Bapuji Pharmacy College, Davangere, Rajiv Gandhi University of Health Sciences, Bengaluru, Karnataka, India.

ABSTRACT

Thyroid problems are common in India affecting around 42 million people. Early diagnosis and therapy play an important role in managing this endocrine disorder. Hypothyroidism and hyperthyroidism are the most common thyroid disorders and are treated with thyroid hormone replacement therapy and antithyroid drugs. However, medication adherence, side effects, and misunderstanding of the importance of medication lead to inconsistent intake. This study aimed to evaluate the pattern of prescribing and adherence to thyroid medication. This cross-sectional study was conducted over 6 months in a tertiary care hospital, involving 188 patients with thyroid disorders. Data was collected using a validated form and medication adherence rating scale. The collected data, including MARS scores, were entered into Microsoft Excel and analyzed using IBM SPSS Version 25. Quantitative data were analyzed using the mean and standard deviation, while categorical data were summarized using frequencies and percentages. The Chi-square test was used to evaluate associations, with a significance level of $p < 0.05$. In our study, 163 participants diagnosed with hypothyroidism exhibited a notable adherence rate of 89.57%. The 25 hyperthyroid patients showed strong adherence to the recommended drugs, with those provided methimazole having the highest adherence rate (52.0%). No statistically significant connections were found when examining the variables affecting drug adherence. Levothyroxine and methimazole were the preferred medications for managing hypothyroidism and hyperthyroidism, respectively. A high adherence rate among patients indicates heightened awareness and understanding of their condition, as well as consistent adherence to the medication schedule. These findings emphasize the importance of early diagnosis, appropriate prescription patterns, and patient adherence in effectively managing thyroid disorders.

INTRODUCTION

Thyroid issues are a sizable subset of the endocrine illnesses that are prevalent in the Indian population.[1,2] Globally, as well as in India, thyroid disorders are the second commonest disease, and now they are referred to as a chronic, non-communicable disease that affects females more than males. Currently, it is diagnosed more frequently due to increased awareness regarding the disease and its consequences.[3] It has been estimated that 42 million people in India suffer from thyroid problems and the core of management still entails early diagnosis and therapy.[4]

Levothyroxine has been regarded as the gold standard treatment for hypothyroidism for many years. It is

*corresponding author: sonapsam@gmail.com

administered orally and has a prolonged half-life in the bloodstream, allowing for once-daily dosing. In the majority of patients, levothyroxine effectively resolves the symptoms associated with hypothyroidism, leading to improved health. However, a minority of individuals undergoing levothyroxine therapy for hypothyroidism feel that it does not adequately restore their optimal well-being.[5] When it comes to treating hyperthyroidism, there are several options available. These include antithyroid medications (such as methimazole and propylthiouracil), radioactive iodine ablation of the thyroid gland, or surgical thyroidectomy. The underlying diagnosis, any restrictions on a particular course of treatment, the degree of hyperthyroidism, and the patient's personal preferences are all taken into consideration when choosing a course of treatment.[6] Incomplete adherence is widely recognized as a crucial impediment to the effectiveness of treatments and continues to present one of the foremost challenges for healthcare professionals.[7]

According to the World Health Organization (WHO), adherence is defined as the degree to which the patient accepts and follows the treatment organized by health care professionals.[8] It signifies the degree of adherence exhibited by patients in following the recommended treatment plan, which includes medication adherence, dietary modifications, and lifestyle adjustments.[9] To achieve the best therapeutic results in chronic diseases, it is typically necessary for patients to adhere to their medication regimen at a rate of 80% or higher, which is influenced by five key factors: i) social and economic factors; ii) health care team and system-related factors; iii) condition-related factors; iv) therapy-related factors; and v) patient-related factors. These factors collectively shape a patient's ability and willingness to adhere to their prescribed treatment regimen.[10] The fact that only 50% of patients with chronic illnesses follow their prescribed treatment in developed countries is concerning, as it poses a significant challenge and frequently prevents patients with long-standing chronic conditions from achieving the expected outcomes. Non-adherence may be somewhat understandable in developing countries where resources are limited and healthcare systems are unequal.[8,9] This highlights the urgent need for heightened awareness and targeted interventions to address non-adherence issues and enhance patient outcomes.[9] By identifying and understanding the barriers that exist within each factor, healthcare providers can develop strategies to improve adherence and facilitate positive clinical outcomes. Such efforts not only enhance patients' quality of life but also contribute to their overall well-being and treatment effectiveness.[10]

Thyroid conditions also significantly impact the community as a whole, particularly in India. The country faces a significant challenge in dealing with the prevalence of thyroid conditions. However, there is a shortage of comprehensive data regarding the extent of thyroid diseases. Limited resources hinder the feasibility of widespread screening for thyroid diseases among the general population due to cost-effectiveness concerns.[11] Thyroid disorders also impose a significant socioeconomic burden in India.[4] They encompass a range of physical and mental symptoms that significantly affect various facets of an individual's life. However, the effects of these conditions extend well beyond the physical aspect, influencing emotional, social, and occupational dimensions for those impacted. When considered within the framework of health and limitations, these conditions result in challenges linked to health that impede an individual's full engagement in daily activities and societal roles, including their work-related endeavours, which can potentially lead to outcomes such as unemployment, periods of absence due to illness, or the need for external support.[12] Thus, examining thyroid treatment adherence becomes imperative in the

Indian context due to the substantial socioeconomic burden on patients. These burdens, encompassing healthcare costs, reduced productivity, and compromised quality of life, can potentially hinder consistent medication adherence. Thus, understanding the intricate relationship between the socioeconomic impact of thyroid disorders and patient's adherence to prescribed medications is crucial. Conducting such studies in India is necessary to unveil the specific challenges faced by patients, address the factors influencing adherence, and develop tailored interventions. By comprehensively exploring these dynamics, researchers can contribute to improved patient outcomes, enhanced healthcare strategies, and more effective resource allocation, ultimately alleviating the economic and health-related strains thyroid disorders pose on individuals within the country. These combined factors make the study of thyroid treatment adherence essential in India. Despite several studies attempting to analyse drug utilization patterns and adherence to thyroid medications, there is a lack of substantial data regarding the factors that influence patient's adherence. This study aimed to evaluate the drug utilization pattern and adherence to thyroid medications in thyroid patients.

MATERIAL AND METHODS

Design of study and subjects

A cross-sectional study was conducted for six months at a tertiary care teaching hospital situated in the Davangere region, with the selection of the study site being influenced by the author's affiliation with the hospital. The study was aimed to assess the drug utilization pattern and adherence to thyroid medications in thyroid patients. The study obtained approval from the institutional ethics committee (BPC/IEC/75/2021-22) to ensure ethical considerations were met. Patients receiving thyroid medication for hypothyroidism and hyperthyroidism were chosen from both outpatient and inpatient department based on our convenience, with their daily medication usage taken into account during selection. Additionally, informed consent was obtained from each patient participating in the study through an informed consent form.

Protocol

The study included 188 patients aged 18 to 85 already diagnosed with thyroid disorders and on medication. Critically ill and disabled hearing patients were excluded. To collect detailed data, a validated data collection form was utilized. This form contained social demographic details, personal information, and clinical profiles, including past and present medications for the participants. In addition, the Medication Adherence Rating Scale-5 (MARS-5) was used to assess medication adherence, which is a self-report questionnaire comprising five items designed to assess medication adherence. Respondents rate each item using a 5-point Likert scale. It is a validated and widely used questionnaire that measures medication adherence in various patient populations. This questionnaire comprises five items that inquire about medication-related behaviours: i) altering dosage; ii) forgetting doses; iii) temporarily stopping medication; iv) intentionally skipping doses; and v) taking less medication than prescribed. Respondents rate these items on a Likert scale ranging from 1 (always) to 5 (never). A total score of 20 serves as the cut off point on the MARS-5. Scores above 20 signify a strong adherence to medication. By utilizing the MARS-5, the study aimed to gather self-reported data on medication adherence among thyroid patients, which could help identify potential areas for intervention or improvement in clinical practice.

Statistical analysis

The collected data, including the MARS-5 scores, was entered into Microsoft Excel Professional Plus 2016 and subsequently analyzed using IBM SPSS (International Business Machine Statistical Presentation System Software) Version 25 for Windows. Quantitative data, involving numerical measurements was analyzed using the mean and standard deviation to assess average values and variability. Categorical data were summarized using frequencies and percentages to provide an overview of responses. The significance of associations between variables was evaluated using the Chi-square test, which determined whether relationships were statistically significant. A p ≤ 0.05 was considered statistically significant.

RESULT

Socio demographics and clinical profile

The study enrolled a total of 188 already diagnosed thyroid patients with a mean age of 46.14±15.86 yr based on the purpose of the study. The majority of the participants were female, accounting for 77.13% of the total sample. Most of the participants belonged to urban residential areas (56.38%), and the majority of the participants were literate (91.49%). Among the total population, 39.89% of participants had comorbid conditions (TABLE 1)

TABLE 1. Socio demographics and clinical profile

Category/variables	Hypothyroidism	Hyperthyroidism
Age (mean ± SD yr)	46.19±15.41	45.8±18.87
Gender (%)		
• Male	20.86	36.00
• Female	79.14	64.00
Residential area (%)		
• Urban	55.83	60.00
• Rural	44.17	40.00
Literacy (%)		
• Literate	91.41	92.00
• Illiterate	8.59	8.00
Job status (%)		
• Employed	39.87	68.00
• Unemployed	56.44	32.00
• Retired	3.68	0.00
Comorbidities (%)		
• Present	40.49	36.00
• Absent	59.51	64.00

Drug utilization pattern in thyroid patients

Out of 163 hypothyroid patients, all were prescribed levothyroxine replacement therapy, with varying doses based on the thyroid hormonal status and bodyweight. Among 25 hyperthyroidism patients, 15 were prescribed methimazole, 8 with carbimazole, and the remaining were prescribed two drugs namely methimazole and propylthiouracil. All the patients with comorbidities were treated with suitable drugs for their condition (TABLE 2).

Evaluation of Adherence

Medication adherence among the patients was assessed using the MARS-5. In the case of hypothyroidism patients, the evaluation revealed that the majority of them demonstrated adherence to their prescribed medication, with a rate of 89.57%. Similarly, among the hyperthyroidism

patients, 84.00% exhibited adherence to their prescribed medications (TABLE 2). The high adherence rates observed in this study are encouraging and suggest that patients are actively participating in their treatment regimens.

Association between the variables and the adherence

The study examined various factors, including age, gender, residential area, literacy, job status, comorbidities, duration of illness, and TSH levels to assess their association with the adherence status of patients towards their medication. However, the analysis revealed that none of these factors exhibited a significant association with medication adherence (TABLE 3 and TABLE 4). [Note: inadequate sample sizes in those groups prevented the assessment of the association between factors such as literacy and TSH levels in individuals aged above 60 yr (p value analysis was not feasible)].

TABLE 2 Drug utilization pattern and adherence status in thyroid patients

Thyroid disorder/drug given	Total (n)	Adherent [n (%)]	Nonadherent [n (%)]
Hypothyroidism (163)			
• Levothyroxine	163	146 (89.57)	17 (10.43)
• Methimazole	15	13 (52.00)	2 (8.00)
Hyperthyroidism (25)			
• Methimazole and propylthiouracil	2	2 (8.00)	0 (0.00)
• Carbimazole	8	6 (24.00)	2 (8.00)

TABLE 3. Association between the variables and the adherence to hypo-
thyroid medications

Variable/category	Adherent [n (%)]	Nonadherent [n (%)]	Chi square value	p
Age (y.o.)				
• 18-25	16 (88.89)	2 (11.11)		
• 26-44	54 (93.10)	4 (6.90)	0.7514	0.861
• 45-59	45 (88.24)	6 (11.76)		
• ≥ 60	31(86.11)	5 (13.89)		
Gender				
• Male	31(91.18)	3 (8.82)	0.1186	0.731
• Female	115(89.15)	14 (10.85)		
Residential area				
• Urban	84 (92.31)	7 (7.69)	1.6522	0.199
• Rural	62 (86.11)	10 (13.89)		
Literacy				
• Literate	133 (89.26)	16 (10.74)	0.1771	0.674
• Illiterate	13 (92.86)	1(7.14)		
Employment status				
• Employed	60 (92.31)	5 (7.69)		
• Unemployed	81 (88.04)	11 (11.96)	1.0008	0.606
• Retired	5 (83.33)	1 (16.67)		
Comorbidities				
• Present	59 (85.51)	10 (14.49)	2.1147	0.146
• Absent	87 (92.55)	7 (7.45)		
Duration of illness (yr)				
• ≤10	134 (90.54)	14 (9.46)	1.6198	0.203
• 11-20	12 (80.00)	3 (20.01)		
TSH (≤60 yr)				
• Normal	23 (95.83)	1 (4.17)		
• Below normal	4 (80.00)	1 (20.00)	1.4808	0.477
• Above normal	91 (90.10)	10 (9.90)		
TSH (>60 yr)				
• Normal	4 (80.00)	1 (20.00)		
• Below normal	0 (0.00)	0 (0.00)	0.1078	0.743
• Above normal	24 (85.71)	4 (14.29)		

TABLE 4. Association between the variables and the adherence to hyperthyroid medications

Variable/category	Adherent [n (%)]	Nonadherent [n (%)]	Chi square value	p
Age (y.o.)				
• 18-25	3 (75.00)	1 (25.00)		
• 26-44	7 (77.78)	2 (22.22)	0.2331	0.972
• 45-59	4 (80.00)	1 (20.00)		
• ≥ 60	6 (85.71)	1 (14.29)		
Gender				
• Male	7 (77.78)	2 (2.22)	0.0434	0.835
• Female	13 (81.25)	3 (18.75)		
Residential area				
• Urban	12 (80.00)	3 (20.00)	0	1
• Rural	8 (80.00)	2 (20.00)		
Literacy				
• Literate	18 (78.26)	5 (21.74)	NA	NA
• Illiterate	2 (100.00)	0 (0.00)		
Employment status				
• Employed	13 (76.47)	4 (23.53)		
• Unemployed	7 (87.50)	1 (12.50)	0.4136	0.520
• Retired	7 (87.50)	0 (0.00)		
Comorbidities				
• Present	7 (87.50)	2 (22.22%)	0.0434	0.835
• Absent	7 (87.50)	3 (18.75%)		
Duration of illness (yr)				
• ≤10	7(87.50%)	4(19.05%)	0.0744	0.785
• 11-20	7(87.50%)	1(25.00%)		
TSH (≤60 yr)				
• Normal	7(87.50%)	2(14.29%)		
• Below normal	7(87.50%)	0(0.00%)	1.4657	0.226
• Above normal	7(87.50%)	0(0.00%)		
TSH (>60 yr)				
• Normal	7(87.50%)	0(0.00%)		
• Below normal	7(87.50%)	1(25.00%)	NA	NA
• Above normal	7(87.50%)	0(0.00%)		

NA: Not available (p value analysis was not possible)

DISCUSSION

This study aimed at assessing the prescription pattern of thyroid medications as well as adherence to those medications. It enrolled 188 already diagnosed thyroid patients, who provided consent to participate in the study. The mean age of the patients with hypothyroidism and hyperthyroidism was 46.19±15.41 and 45.8±18.87 yr, respectively, indicating that the onset of thyroid disorders in the studied population predominantly occurred during adulthood. A similar age trend and patient recruitment approach was also observed in a study conducted by Patel *et al.*,[13] which included consenting participants of both genders aged >18 y.o, all diagnosed with thyroid disorders (hypothyroid or hyperthyroid) and under treatment and the mean ages for hypothyroidism and hyperthyroidism patients were 39.34 ±13.49 and 40.03 ±13.49 yr, respectively, further supporting the notion of adult-onset thyroid disorders.

This study revealed a higher prevalence of thyroid disorders in females compared to males. Analysis of data from the National Health and Nutrition Survey (NHANES III) supported the findings that women have higher levels of thyroid-stimulating hormone (TSH) and a greater prevalence of antithyroid antibodies compared to men.[14] This gender disparity can be attributed, at least in part, to the autoimmune nature of many thyroid disorders. Autoimmune diseases tend to occur more frequently in women, possibly due to the influence of sex steroids on the immune system. Although the mechanisms are not fully understood, estrogen, and progesterone are believed to play a role in the development and activation of lymphocyte, as well as in triggering autoimmune responses. This suggests that hormonal factors may contribute to the observed gender difference in thyroid disorders.[15]

The study examined prescription trends for both hypothyroidism and hyperthyroidism. The predominant treatment approach for hypothyroidism was found to be levothyroxine replacement therapy, which aligns with the findings reported in a study conducted by Patel *et al.*[13] On the other hand, for hyperthyroidism, methimazole was the most commonly prescribed medication, followed by carbimazole. Interestingly, this differs from the observations in the study conducted by Patel *et al.*[13] which reported a higher prevalence of carbimazole usage compared to methimazole. These disparities signify the significance of contextual and geographical factors in influencing treatment decisions, thus highlighting the ned for localized and personalized approaches in thyroid disorder management.

It is also important to highlight that medication compliance is essential for the proper management of thyroid diseases. In contrast to the approach taken by Cappelli C *et al.*[16] our research employed the MARS-5, while they utilized the Morisky Medication Adherence Scale (MMAS-8), to evaluate patient's adherence to prescribed medications. Despite the differing scales, the shared goal of both tools is to assess adherence behavior through patient's self-reporting. MMAS-8 comprising 8 items that inquire about specific medication-taking behaviors, potentially provides a more implicate understanding of adherence challenges. Conversely, MARS-5's concise 5-item format offers a streamlined evaluation. While MMAS-8's comprehensive approach might capture a broader range of adherence complexities, MARS-5's brevity could result in improved completion rates and a general adherence overview. The decision between these scales is

influenced by considerations of required depth, participant convenience, and alignment with study objectives. However, evaluation of medication adherence revealed high adherence rate in both hypothyroidism (89.57%) and hyperthyroidism (83.00%). High adherence rate in hypothyroidism was in alignment with the study findings of Cappelli C *et al*.[16] This increased adherence pattern towards levothyroxine is possibly due to easy administration, good tolerability, and a single daily dose of the drug.[16] Similarly, the high adherence rate observed in patients with hyperthyroidism in our study is consistent with the results of a randomized trial that compared different doses of drugs used for hyperthyroidism. The trial revealed that patients receiving methimazole exhibited a compliance rate of 83.00%. These findings further support the notion that patients with hyperthyroidism are actively adhering to their prescribed treatment plans.[17] High adherence rates indicate that patients are following their prescribed treatment plans, which can contribute to better disease control and improved health outcomes. Therefore, the high adherence rates observed in this study are encouraging and suggest that patients are actively participating in their treatment regimens.

The study also aimed to examine the association between medication adherence and various factors, including age, gender, residential area, literacy, job status, comorbidities, duration of illness and TSH levels. However, no significant associations were found, which could be due to several reasons. Through a comprehensive analysis of the study and its findings, we can understand why each factor did not achieve significance. Age, which is commonly assumed to correlate with adherence, may not have shown significance due to the intricate interplay of unaccounted

variables. The absence of significance for gender might arise from the complex interaction of personal, cultural, and societal influences. The insignificance of residential area could be attributed to medication adherence being molded by broader elements like healthcare access and socioeconomic status. Although literacy is often considered important, its lack of significance may be because other factors such as health education and individual attitudes possibly carrying greater weight than the singular influence of literacy. Job status, with its potential to impact routines, might not have been significant due to the intricate relationship between work demands and personal copying strategies. Surprisingly, comorbidities didn't yield significance, which challenges established presumptions, possibly originating from the specific demographics of the study population or the categorization of comorbid conditions which may not have fully captured their complexities. Similarly, the lack of significance concerning the duration of illness and TSH could be attributed to the specific demographics of the study group, potentially highlighting the need for a more diverse and expansive range of cases. Overall, this collective absence of significance underscores the complexity of medication adherence, influenced by multifaceted factors that extend beyond the scope of this study. The capacity to identify significant relationships may also have been impacted by the sample size, the characteristics of the study population, and other design limitations. It's important to acknowledge that while no significant associations were observed in this study, other variables and confounding factors not considered here may still contribute to medication adherence among thyroid patients.

The deeper motivations, obstacles, and particular nuances behind patients' adherence habits may be missed by

quantitative assessments like the MARS-5, which nonetheless provide useful numerical insights into adherence. Qualitative data, obtained through patient interviews or similar methods, can reveal essential experiential and psychosocial aspects that shape medication adherence. By delving into patient's viewpoints, challenges, and thought processes, qualitative data can provide a more comprehensive understanding of the observed patterns in MARS-5 scores. This comprehensive approach not only complements quantitative findings but also provides researchers and healthcare practitioners with a more detailed grasp of the factors influencing medication adherence. Thus, recommending the integration of patient interviews or qualitative data emerges as a well-justified suggestion, enhancing the study's overall depth and relevance.

Despite the nonsignificant results, it is important to recognize that medication adherence is a multifaceted issue that requires ongoing research and targeted interventions. Future studies could consider incorporating a broader range of variables and employing robust methodologies to gain a more comprehensive understanding of the factors influencing medication adherence among thyroid patients.

Several limitations warrant consideration in our study. Firstly, the absence of qualitative data collection, such as patient interviews, prevented a comprehensive understanding of the experiential and psychosocial factors shaping adherence behaviours. Secondly, the study's focus on a specific set of demographic variables to assess associations with medication adherence, while informative, might not encompass the full range of factors influencing adherence. Adding to this, our study faces the challenge of a comparatively limited sample size and a brief study duration. These constraints inevitably exert an influence on the scope and comprehensiveness of our findings. Lastly, the cross-sectional design of our study captures a singular moment in time, hindering the establishment of causal relationships between variables and adherence patterns over time. Future research employing longitudinal approaches can offer a more comprehensive understanding of how factors evolve and impact adherence behaviours over the longer term. These limitations underscore the importance of refining study methodologies to encompass qualitative insights, diverse variables, and more dynamic research designs to evaluate the multifaceted nature of medication adherence comprehensively.

Overall, this study has the potential to provide valuable insights into drug utilization patterns and adherence to thyroid medications, which can inform the development of effective interventions to improve patient outcomes.

CONCLUSION

The study revealed that levothyroxine was the most commonly prescribed medication for hypothyroidism, while methimazole was the preferred choice for hyperthyroidism treatment. The high adherence rate observed among the patients suggests heightened awareness and understanding of their condition, as well as consistent adherence to the prescribed medication schedule. The findings emphasize the need for healthcare providers to focus on patient education, support, and communication to optimize treatment outcomes and ensure long-term management of thyroid conditions.

The study also contributes uniquely by shedding light on the medication preferences and adherence behaviors within the context of thyroid disorders.

To deepen insights, future investigations could explore the fundamental drivers behind these preferences. This might involve examining patient choices, healthcare provider viewpoints, and the cost-effectiveness of these treatments. By addressing these aspects, researchers have the opportunity to enrich our overall understanding of thyroid disorder management, thereby informing more targeted and patient-centric healthcare strategies.

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