

FREQUENCY OF HYPOTHYROIDISM IN PATIENTS WITH EPILEPSY IN PEMH

Original Research

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ABSTRACT

Background: Epilepsy is a common neurological disorder requiring long-term antiepileptic drug (AED) therapy, which is known to impact various body systems, including thyroid function. Thyroid dysfunction, particularly hypothyroidism, has been reported in patients undergoing AED treatment, but the prevalence and extent of this comorbidity remain underexplored. This study aims to determine the frequency of hypothyroidism in epilepsy patients at a tertiary care hospital.

Objective: To determine the frequency of hypothyroidism in patients with epilepsy reported to PEMH using Blood thyroid Levels.

Methods: This prospective cross-sectional study was conducted at Pakistan Emirates Military Hospital from February 2024 to July 2024. A total of 385 epilepsy patients were selected through simple random sampling based on predefined inclusion and exclusion criteria. Blood samples were collected to assess thyroid levels, and the frequency of hypothyroidism was determined. Data was collected, entered, and analyzed using SPSS version 26.0.

Results: Out of 385 patients, 195 (50.64%) were male and 190(49.3%) were female. Mean age was 39.41± 2.28. 295 (76.66%) of epileptic patients had hypothyroidism. More than 2/3rd of the patients had hypothyroidism.

Conclusion: The study concludes that there is a significant prevalence of hypothyroidism among epilepsy patients, particularly those on long-term antiepileptic drug therapy and polytherapy regimens. The findings highlight the importance of regular thyroid function monitoring in this population to manage and mitigate the risk of thyroid dysfunction effectively.

Keywords: Epilepsy, Hypothyroidism, Anticonvulsants, Thyroid Function Tests, Prevalence, Cross-Sectional Studies, Comorbidity

INTRODUCTION

Epilepsy is a neurological condition that is frequently encountered and is characterized by a disruption in the electrical activity of the brain that can be attributed to a variety of factors. The subject matter encompasses a diverse array of seizures, each with its unique intensity, characteristics, causes, effects, and treatment options (1). Anti-epileptic medications (AEDs) are necessary for the protracted treatment of this persistent condition. However, even after getting therapy, seizures in many people do not respond to antiepileptic medicines (AEDs), therefore long-term medication is often required (2).

The prolonged use of AEDs is linked to an elevated risk of adverse events, including medication interactions, cognitive impairment, behavioral alterations, and metabolic or endocrine disturbances, with a particular emphasis on thyroid malfunction (3). The metabolism of several tissues is regulated by thyroid hormones. Thus, thyroid hormone disruption significantly affects overall health (4). This health transformation is accompanied by a significant change in the activity of the metabolic, cardiovascular, central nervous, musculoskeletal, hematological, reproductive, dermatological, and gastrointestinal systems (5). Different outcomes have been observed in the literature as a consequence of the impact of antiepileptic medications on thyroid function assays (6). Studies have found that carbamazepine, phenytoin, phenobarbital, and clonazepam therapy resulted in a substantial decrease in free thyroxine (fT4) levels, while free triiodothyronine (fT3) and thyroid stimulating hormone (TSH) levels remained unaffected. Meanwhile, VPA therapy did not affect hormone levels (7-9). Additionally, it was reported that VPA therapy resulted in a subclinical increase in TSH levels (10). In Pakistan, there is a lack of research on the long-term effects of newer AED treatment, despite the fact that international studies indicate that patients treated with AEDs have an elevated risk of hypothyroidism. Therefore, the objective of this investigation was to evaluate the prevalence of hypothyroidism in patients with epilepsy who had been diagnosed with PEMH.

METHODS

We conducted a prospective cross-sectional study to explore the frequency of hypothyroidism among patients with epilepsy. The study was designed as a prospective observational study, encompassing data collection over two years, from February 2024 to July 2024, at the Pakistan Emirates Military Hospital (PEMH). The study population included epilepsy patients who were undergoing treatment at the neurology department of the respective hospital. We employed purposive sampling for convenience. We included patients of any age diagnosed with epilepsy, who were receiving treatment at Pakistan Emirates Military Hospital, with at least one year of documented epilepsy history and stable management under their current treatment regimen for the past six months. Informed consent was obtained from all participants or their guardians. We excluded patients with a prior history of thyroid disorders, other autoimmune diseases, pregnant women, those non-compliant with treatment or follow-ups, and individuals with severe comorbid conditions like advanced cardiac or renal disease that could confound the study results.

We used a universal sample estimation method based on 50% prevalence. The sample was estimated using an online sample size calculator. By applying a confidence level of 95% and a margin of error of 5%, we estimated that a minimum of 385 participants would be needed to achieve statistical significance. A comprehensive data collection Performa was designed. This Performa was structured to capture essential patient details, including demographic information, epilepsy characteristics, and thyroid function test results. Hypothyroidism among the patients in our study was diagnosed through a systematic evaluation of thyroid function. Blood samples were collected from each participant at the Pakistan Emirates Military Hospital (PEMH) during routine clinical visits. Samples were analyzed in the hospital's central laboratory, where thyroid function tests, including the measurement of Thyroid Stimulating Hormone (TSH) and free thyroxine (FT4) levels, were conducted. The enzyme-linked immunosorbent assay (ELISA) method was employed to quantify these hormone levels, ensuring precision and reliability. A diagnosis of hypothyroidism was confirmed if the TSH levels were elevated above the normal reference range, accompanied by low FT4 levels, in accordance with established clinical guidelines.

Data analysis for the study was conducted using SPSS v.26. Descriptive statistics were used to describe the demographic and clinical characteristics of the study sample. The prevalence of hypothyroidism was presented as frequency and percentage. The Chi-square test was applied to assess the association between hypothyroidism and patient characteristics of the study sample. A p-value of <0.05 was considered a significant association.

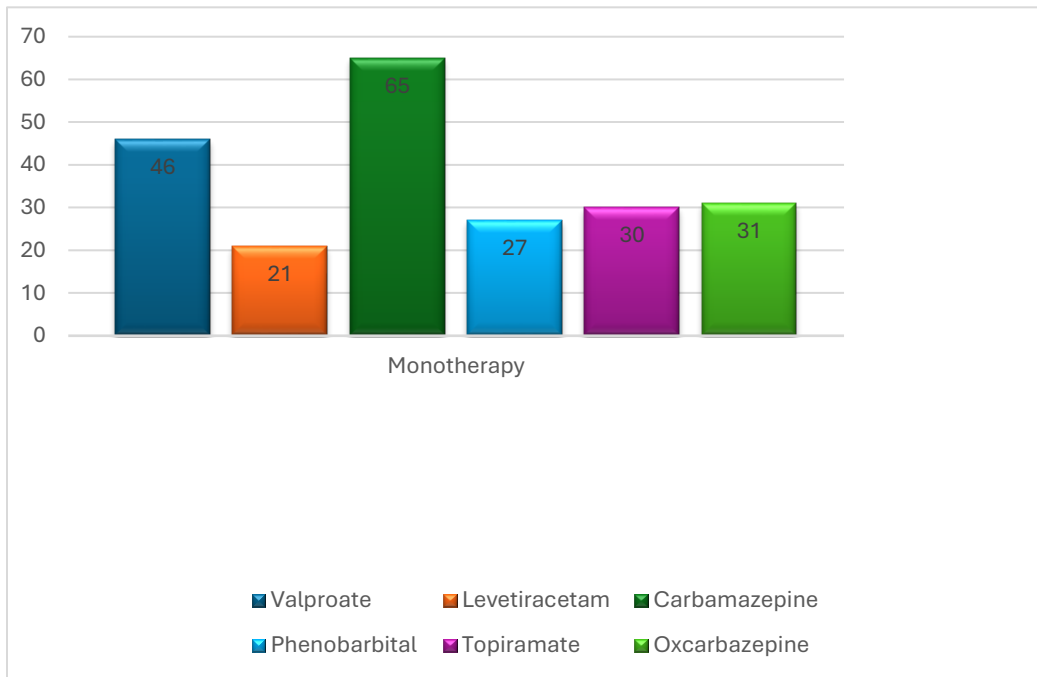
RESULTS

The study results revealed that out of the 385 epilepsy patients included, 63.64% (n=245) were diagnosed with hypothyroidism, highlighting a significant prevalence of thyroid dysfunction among the sample. Demographically, there was a near equal distribution of gender (50.64% male and 49.36% female) with a mean age of 39.41 years. The prevalence of hypothyroidism was significantly higher in females (48.98%) than males ($p = 0.03$). Patients with a duration of epilepsy exceeding 10 years showed a higher likelihood of hypothyroidism (40.82%) compared to those with shorter durations ($p = 0.05$). Moreover, a significant association was found between hypothyroidism and a positive family history of epilepsy ($p = 0.01$). Polytherapy was also linked to a higher prevalence of hypothyroidism (46.94%) compared to monotherapy ($p = 0.04$), indicating that the complexity of epilepsy management may influence thyroid function.

Table 1 Demographic and clinical characteristics

Characteristic	Frequency (n = 385)	Percentage (%)
Gender		
Male	195	50.64
Female	190	49.36
Mean Age (years)	39.41 ± 2.28	-
Duration of Epilepsy		
< 5 years	90	23.38
5-10 years	150	38.96
> 10 years	145	37.66
Type of Epilepsy		
Generalized Seizures	230	59.74
Focal Seizures	155	40.26
Family History of Epilepsy		
Yes	120	31.17
No	265	68.83
Type of Antiepileptic Drugs		
Monotherapy	220	57.14
Polytherapy	165	42.86

Out of the 385 patients included in the study, there was a nearly equal distribution of gender, with males representing 50.64% (n=195) and females accounting for 49.36% (n=190) of the cohort. The mean age of the participants was 39.41 years (± 2.28). In terms of the duration of epilepsy, 23.38% (n=90) of the patients had a disease history of less than 5 years, while 38.96% (n=150) had been living with epilepsy for 5 to 10 years, and 37.66% (n=145) for over 10 years. In terms of treatment, 57.14% (n=220) of the patients were managed with monotherapy, while 42.86% (n=165) were on polytherapy regimens. Demographic and other clinical characteristics of the study sample is shown in table 1.



Various antiepileptic drugs (AEDs) were used in monotherapy. The most commonly prescribed AED was Carbamazepine, used by 65 patients, which accounts for 29.55% of the monotherapy group. Valproate was used by 46 patients, representing 20.91% of the group. Oxcarbazepine and Topiramate were prescribed to 31 (14.09%) and 30 (13.64%) patients, respectively. Phenobarbital was used by 27 patients, accounting for 12.27% of the monotherapy group, and Levetiracetam was the least used, prescribed to 21 patients, representing 9.55% of those on monotherapy (Figure 1.).

Figure 1 Frequency of different Monotherapy AEDs used by the study sample

In the polytherapy group, different combinations of antiepileptic drugs (AEDs) were used to manage epilepsy in the study population. The most common combination was Valproate + Topiramate, used by 42 patients (25.45%). This was followed closely by Levetiracetam + Oxcarbazepine, prescribed to 41 patients (24.85%). The combination of Levetiracetam + Valproate was used by 26 patients (15.76%), while Phenobarbital + Carbamazepine was administered to 20 patients (12.12%). The Levetiracetam + Carbamazepine, Levetiracetam + Phenobarbital and the Levetiracetam + Phenobarbital were less common (Figure 2.)

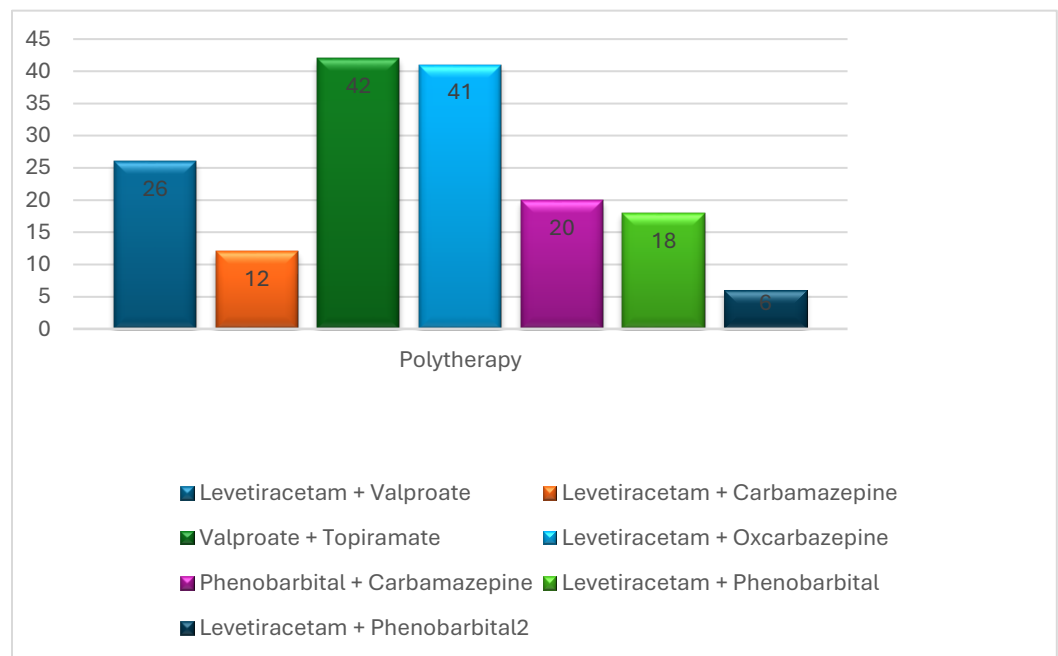


Figure 2 Frequency of combinations of AEDs used by the study sample

Figure 3. shows the distribution of thyroid function among the study population. Out of 385 patients, 245 (63.64%) were diagnosed with hypothyroidism, while 140 (36.36%) had normal thyroid function. This indicates a significant prevalence of hypothyroidism in the sample, which may be reflective of the comorbid relationship between epilepsy and thyroid dysfunction.

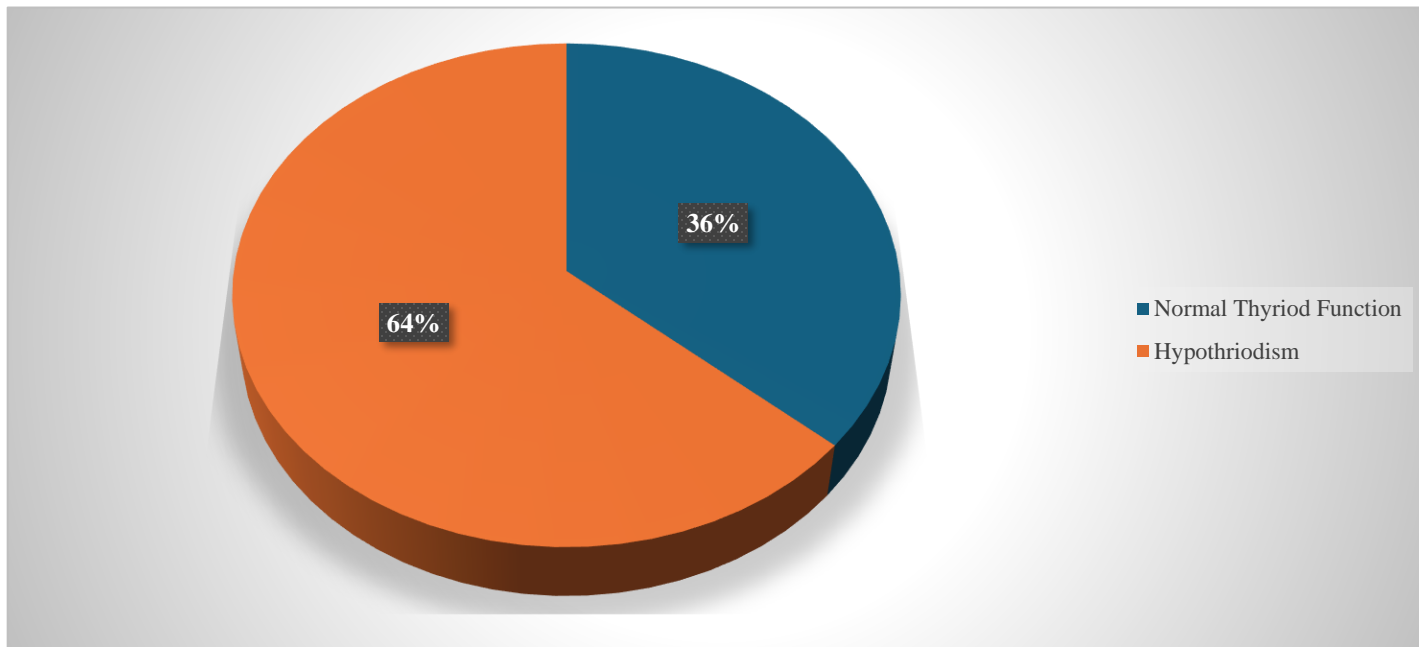


Figure 3 Distribution of Thyroid

Table 2 Association of demographic and clinical characteristics with hypothyroidism

Characteristic	Hypothyroidism Present (n=245)	Hypothyroidism Absent (n=140)	P value
Gender, Female	120 (48.98%)	70 (50.00%)	0.03*
Mean Age (years)	40.2 ± 3.1	38.5 ± 2.5	0.12
Duration of Epilepsy, > 10 years	100 (40.82%)	45 (32.14%)	0.05
Type of Epilepsy, Focal Seizures	85 (34.69%)	70 (50.00%)	0.08
Positive Family History of Epilepsy	80 (32.65%)	40 (28.57%)	0.01*
Type of Antiepileptic Drugs, Polytherapy	115 (46.94%)	50 (35.71%)	0.04*

*=P<0.05

The analysis of the association between hypothyroidism and various patient characteristics is shown in Table 2. The prevalence of hypothyroidism was slightly higher in females (48.98%) compared to those without hypothyroidism (50.00%), and this difference was statistically significant ($p = 0.03$). The mean age of patients with hypothyroidism was 40.2 ± 3.1 years, which was higher than those without hypothyroidism (38.5 ± 2.5 years), though this difference did not reach statistical significance ($p = 0.12$). Duration of epilepsy greater than 10 years was more common in patients with hypothyroidism (40.82%) compared to those without (32.14%), with a p-value of 0.05, indicating a potential association. Focal seizures were less prevalent in patients with hypothyroidism (34.69%) compared to those without (50.00%), but this difference was not statistically significant ($p = 0.08$). Patients with a positive family history of epilepsy were more likely to have hypothyroidism (32.65%) compared to those without (28.57%), and this association was statistically significant ($p = 0.01$). Additionally, polytherapy was more frequently used in patients with hypothyroidism (46.94%) than in those without (35.71%), with a significant p-value of 0.04, suggesting a link between polytherapy and hypothyroidism.

DISCUSSIONS

Epilepsy is associated with significant endocrinological comorbidities, according to emerging research. Despite contradictory findings on the correlation between thyroid dysfunction and adult epilepsy, several studies have lent credence to the hypothesis that hypothyroidism is more frequent in this demographic. Antiseizure medications (ASMs) constituted the backbone of therapy, and although theories about their mechanisms varied, AEDs influenced thyroid hormone levels.

In our study sample, carbamazepine was the most frequently used AED, and literature had documented its adverse effects on the endocrine system. This finding was consistent with studies on similar subjects, as most epilepsy patients used this class of drug (12). Research showed that carbamazepine induced the P-450 enzyme system and enhanced the metabolism of thyroid hormones, resulting in decreased thyroid serum concentrations (13). Another study reported thyroid hormonal abnormalities with phenobarbital, phenytoin, valproate, and oxcarbazepine, but not with lamotrigine, levetiracetam, topiramate, tiagabine, and vigabatrin (14). The results of this study confirmed the existence of a strong link between hypothyroidism and epilepsy, with gender, duration of epilepsy, and choice of treatment at the core of the issue. The prevalence of hypothyroidism in this cohort was calculated at 63.64%, with a higher rate observed in the female subgroup, consistent with prior research indicating a greater incidence of thyroid dysfunction among females with epilepsy compared to males. For instance, Bal & Senol and Schiller et al. also described a similar gender bias in thyroid disorders among epilepsy patients, possibly due to the preponderance of estrogen receptors in the thyroid gland (15,16).

Our findings also revealed that a longer duration of epilepsy, particularly beyond 10 years, increased the prevalence of hypothyroidism. This may be attributed to the cumulative effect of prolonged exposure to AEDs, especially enzyme-inducing AEDs, which were known to affect thyroid hormone levels. Over time, the extended use of these medications led to clinically significant hypothyroidism. This study also found that polytherapy, as opposed to monotherapy, was independently associated with hypothyroidism. This finding was further affirmed by other works, such as the cross-sectional studies by Bal & Senol (16) and Dabla et al. (17), which showed that polytherapy, especially with first-generation AEDs like valproate and carbamazepine, was likely to affect thyroid hormones. The reason for this might be that the concomitant use of several drugs and their influence on hepatic enzyme induction resulted in altered metabolism of thyroid hormones. Additionally, in the present study, a positive family history of epilepsy was significantly correlated with hypothyroidism. Although this association was not frequently described in the literature (18,19,20), it suggests there may be some germinal immune vulnerability that warrants further research into the implications of this link.

The findings of our study supported previous studies, highlighting the necessity of repeated thyroid function check-ups in epilepsy patients, especially those receiving long-term AED therapy or polytherapy. Further research should aim to understand the genetic basis of this association and explore how this risk can be minimized in affected patients.

CONCLUSIONS

Our study demonstrates that epilepsy significantly impacts thyroid function, with a marked association between epilepsy and the development of hypothyroidism. The findings underscore epilepsy as a major risk factor for hypothyroidism, suggesting the need for regular thyroid function monitoring in patients with epilepsy, particularly those on long-term antiepileptic drug therapy. This highlights the importance of a multidisciplinary approach in managing epilepsy, considering the potential endocrine complications that may arise over time.

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