



## THYROID FUNCTION CHANGES IN PEDIATRIC EPILEPSY PATIENTS: A PROSPECTIVE COMPARATIVE STUDY OF NEW VERSUS OLD ANTIEPILEPTIC DRUGS

Salma Alyaqoub<sup>1\*</sup>, Hadeel F. Anan<sup>2</sup>, Rahaf Rudda Altalhi<sup>3</sup>, Raida Albaradi<sup>4</sup>, Bahaa Alshammari<sup>5</sup>, Lama Alrabah<sup>6</sup>, Mai Alshammri<sup>7</sup>, Layaly Khattar Zeid Alshammari<sup>8</sup>, Naif Albluwi<sup>9</sup>, Faris Bandar Bdirah<sup>10</sup>, Joud Naif Alrougi<sup>11</sup>, Reem Alkahtani<sup>12</sup>

<sup>1\*</sup>Clinical pharmacist Pharmacy Affairs Admiration, Department of Clinical Pharmacy, King Fahad Specialist Hospital, Dammam. Email: salma.2342a@gmail.com

<sup>2</sup>Group manager, formulary advisory and planning Eastern Health Cluster Email: hadeelanan@yahoo.com

<sup>3</sup>Clinical pharmacy Pharmacy Affairs Admiration, Department of Clinical Pharmacy, King Fahad Specialist Hospital, Dammam. Email: Altalhirahaf@gmail.com

<sup>4</sup>Counsultanat pediatric neurologist Department of Pediatric Neurology King Fahad Specialist Hospital-Dammam Saudi Arabia. Email: raudahbaradie@moh.gov.sa

<sup>5</sup>Pharmacist Department of pharmacy at Security Forces Hospital. Email: bahaa.aljndel@gmail.com

<sup>6</sup>Pharmacist Department of Pharmacy at Medical Cities of the Ministry of Interior Email: lamaalrabah00@gmail.co

<sup>7</sup>Pharmacist Zad Aldawayiyah Pharmacy Email: maialdh1418@gmail.com

<sup>8</sup>Pharmacist Email: layaly779@gmail.com

<sup>9</sup>Pharmacist Hail PhNaifAbdulaziz@gmail.com

<sup>10</sup>Pharmacist Umm Alqura University Email: farisbdirah@gmail.com

<sup>11</sup>Final year Pharm.D student Hail university Email: jood.n.d@hotmail.com

<sup>12</sup>Pharmacist Department of Pharmacy at Security Forces Hospital Email: Reemalkahtani1@gmail.com

**\*Corresponding Author:** Salma Alyaqoub

<sup>\*</sup>Clinical pharmacist Pharmacy Affairs Admiration, Department of Clinical Pharmacy, King Fahad Specialist Hospital, Dammam. Email: salma.2342a@gmail.com

---

### Abstract:

**Background:** Epilepsy is a persistent neurological condition that requires prolonged treatment with antiepileptic drugs (AEDs). However, these medications can lead to other undesirable consequences, such as thyroid disorders.

**Aim:** To evaluate the impact of old versus new antiepileptic medications on thyroid function in children with epilepsy.

**Methods:** This prospective cohort study included epilepsy patients from the King Fahad Specialist Hospital in Dammam. Thyroid function tests (TSH, FT4, and FT3) were performed at baseline and one year after therapy. Statistical analysis included descriptive statistics, chi-square tests, independent-sample t-tests, and paired t-tests.

**Results:** The study included 142 pediatric epilepsy patients (age range, 1–15 years), equally divided between new (50%) and old (50%) AED treatments. After one year of treatment, patients on newer

AEDs showed significantly higher changes from a baseline in TSH (9.1764 vs. 4.0474 mIU/L,  $p = 0.001$ ) and FT4 (11.5453 vs. 10.6243 pmol/L,  $p = 0.003$ ) levels than those on older AEDs. Regardless of medication type, all patients experienced significant changes in all three crucial thyroid function indicators from baseline to one year post-treatment ( $p < 0.001$ ). TSH levels increased from 2.9726 to 6.5573 mIU/L, whereas FT4 and FT3 levels decreased (FT4: 11.8985 to 11.0783 pmol/L; FT3: 4.6999 to 4.2736 pmol/L). Furthermore, the New Medication Group has a significantly higher prevalence of Subclinical Hypothyroidism (66.2%) compared to the Old Medication Group (11.3%). The most common AEDs administered at baseline were sodium valproate (31.0%), levetiracetam (25.4%), carbamazepine (14.1%), and topiramate (12.7%). The medication groups had no significant differences regarding age, weight, height, and baseline thyroid function test results.

**Conclusion:** New AEDs have a more significant influence on thyroid function in pediatric patients than old AEDs. Regular thyroid function monitoring is critical for all epilepsy patients undergoing long-term AED therapy, especially for those taking newer medicines. More studies are needed to understand better the underlying processes and long-term clinical consequences of medication-induced thyroid alterations.

## Introduction

Epilepsy is a chronic neurological disorder characterized by recurrent, unprovoked seizures, affecting millions of individuals worldwide, including children. Effective management of epilepsy necessitates long-term treatment with antiepileptic drugs (AEDs), which help control seizure activity and improve patients' quality of life. However, despite their therapeutic benefits, AEDs are associated with several systemic side effects, including potential alterations in thyroid function. Given the critical role of thyroid hormones in growth, metabolism, and neurological development, understanding the impact of AEDs on thyroid function is essential, particularly in pediatric patients (Han et al., 2020).

Historically, older-generation AEDs such as carbamazepine, sodium valproate, and phenobarbital have been widely used in epilepsy management. These drugs, while effective, have been linked to various endocrine disturbances, including alterations in thyroid hormone levels. More recently, newer-generation AEDs like levetiracetam, topiramate, and lamotrigine have emerged as alternatives, with purported advantages in efficacy and safety. However, the extent to which these newer AEDs affect thyroid function remains an area of ongoing investigation, necessitating comparative studies to evaluate their endocrine effects (Elshorbagy et al., 2020).

The thyroid gland plays a vital role in maintaining homeostasis by regulating metabolic processes, growth, and brain function. Thyroid function is assessed primarily through serum levels of thyroid-stimulating hormone (TSH), free thyroxine (FT4), and free triiodothyronine (FT3). Dysregulation in these markers can lead to conditions such as hypothyroidism, subclinical hypothyroidism, or hyperthyroidism, potentially exacerbating neurological and developmental issues in pediatric epilepsy patients. The potential interplay between epilepsy, AED therapy, and thyroid dysfunction underscores the importance of this research (Lee et al., 2017).

This study aims to evaluate the impact of old versus new AEDs on thyroid function in children with epilepsy. By conducting a prospective comparative analysis, we seek to identify whether newer AEDs exhibit a more significant influence on thyroid function compared to their older counterparts. Additionally, we aim to determine the prevalence of thyroid dysfunction, particularly subclinical hypothyroidism, among pediatric epilepsy patients undergoing long-term AED therapy (Nishiyama et al., 2019).

The study was conducted at King Fahad Specialist Hospital in Dammam, where pediatric epilepsy patients receiving either new or old AEDs were monitored over one year. Baseline thyroid function tests (TSH, FT4, and FT3) were performed at the start of treatment and reassessed after one year to determine changes attributable to AED therapy. Statistical analyses, including descriptive statistics, chi-square tests, independent-sample t-tests, and paired t-tests, were employed to assess differences between the two medication groups (Kose et al., 2017).

Our findings reveal significant thyroid function changes in pediatric epilepsy patients undergoing AED therapy. Specifically, patients on newer AEDs exhibited more pronounced increases in TSH levels and reductions in FT4 levels compared to those on older AEDs. Furthermore, the incidence of subclinical hypothyroidism was markedly higher among patients receiving newer AEDs, raising concerns about the long-term endocrine impact of these medications (Rafik et al., 2024).

Given these findings, routine thyroid function monitoring should be considered an integral part of epilepsy management, particularly for children on long-term AED therapy. Early detection of thyroid dysfunction can facilitate timely intervention, potentially mitigating adverse developmental and metabolic consequences. Healthcare providers should remain vigilant in assessing thyroid health in pediatric epilepsy patients and tailor treatment strategies accordingly (Park et al., 2022).

Despite the significant insights gained, this study underscores the need for further research to elucidate the underlying mechanisms by which AEDs influence thyroid function. Longitudinal studies with larger sample sizes and mechanistic investigations may provide a deeper understanding of medication-induced thyroid alterations, ultimately contributing to more personalized and safer epilepsy treatment regimens (Yilmaz et al., 2021).

In conclusion, this research highlights the crucial interplay between epilepsy treatment and thyroid health in pediatric patients. While newer AEDs may offer advantages in seizure control, their potential endocrine effects warrant careful consideration. By advancing our knowledge in this area, we can optimize epilepsy management while safeguarding the overall well-being of pediatric patients, ensuring a balanced approach to neurological and endocrine health (Han et al., 2020).

## **Methodology**

### **Study Design**

This study is a prospective cohort study designed to evaluate the impact of old versus new antiepileptic drugs (AEDs) on thyroid function in pediatric epilepsy patients. The research was conducted at King Fahad Specialist Hospital in Dammam and involved monitoring patients over a one-year period.

### **Study Population**

The study included pediatric epilepsy patients aged 1 to 15 years who were prescribed either old or new AEDs. Patients were recruited from the neurology department of the hospital. Inclusion and exclusion criteria were as follows:

#### **Inclusion Criteria:**

- Pediatric patients diagnosed with epilepsy
- Patients aged 1–15 years
- Patients receiving either old or new AEDs for at least one year
- No prior history of thyroid disease

#### **Exclusion Criteria:**

- Patients with pre-existing thyroid dysfunction
- Patients with other significant endocrine disorders
- Patients who changed or discontinued their AEDs during the study period
- Patients with significant systemic illnesses affecting thyroid function

### **Sample Size**

A total of 142 pediatric epilepsy patients were enrolled in the study, with an approximately equal distribution between those receiving new (49.3%) and old (50.7%) AEDs. The sample size was

determined based on power calculations to detect significant differences in thyroid function tests between groups.

### Data Collection

Baseline sociodemographic and clinical data were collected, including age, sex, weight, height, type of epilepsy, and AED regimen. Thyroid function tests, including serum levels of Thyroid-Stimulating Hormone (TSH), Free Thyroxine (FT4), and Free Triiodothyronine (FT3), were measured at the beginning of the study and after one year of treatment.

### Laboratory Measurements

Blood samples were collected from each participant at baseline and after one year of AED therapy. The samples were analyzed for:

- **TSH (mIU/L)** – Indicator of thyroid function
- **FT4 (pmol/L)** – Measures free thyroxine hormone
- **FT3 (pmol/L)** – Measures free triiodothyronine hormone

All samples were analyzed in the hospital's central laboratory using standardized immunoassay techniques.

### Statistical Analysis

Data analysis was performed using SPSS software (version X.X). Descriptive statistics (mean, standard deviation) were used to summarize continuous variables, while categorical variables were expressed as frequencies and percentages. Statistical tests included:

- **Chi-square tests** to compare categorical variables
- **Independent sample t-tests** to compare means between the two medication groups
- **Paired t-tests** to assess changes in thyroid function within each group over time
- **Multivariate regression analysis** to adjust for potential confounders influencing thyroid function changes

### Ethical Considerations

Ethical approval was obtained from the hospital's institutional review board (IRB). Informed consent was obtained from parents or guardians of all participating children. Confidentiality was maintained by anonymizing patient data and securely storing all study-related information.

### Results:

A total of 142 patients were included in the study, with a somewhat higher percentage of males (52.8%) than females (47.2%). Participants ranged from 1 to 15 years, with an average age of 9.38 (SD = 3.957). The weight ranged widely from 10.2 to 141.0 kg, with a mean of 34.85 kg (SD = 16.51). The range of height measurements was 80.0 to 171.0 cm, with an average of 132.80 cm (SD = 18.87). The participants were split almost equally between new (57.3%) and old (50.7%) therapies regarding medication. Sodium valproate (31.0%), levetiracetam (25.4%), carbamazepine (14.1%), and topiramate (12.7%) were the most frequently prescribed baseline medications. The percentages of other drugs used less often ranged from 0.7% to 5.6%. Average TSH levels were 2.97 pmol/L (SD = 1.00), FT4 levels were 11.90 pmol/L (SD = 1.48), and FT3 levels were 4.70 pmol/L (SD = 0.77) according to baseline thyroid function testing. These tests had the following ranges: 0.50–5.00 pmol/L, 9.01–18.10 pmol/L, and 2.10–6.87 pmol/L, in that order. With a 35–70  $\mu$ mol/L range, the mean creatinine level was 46.94  $\mu$ mol/L (SD = 5.00).

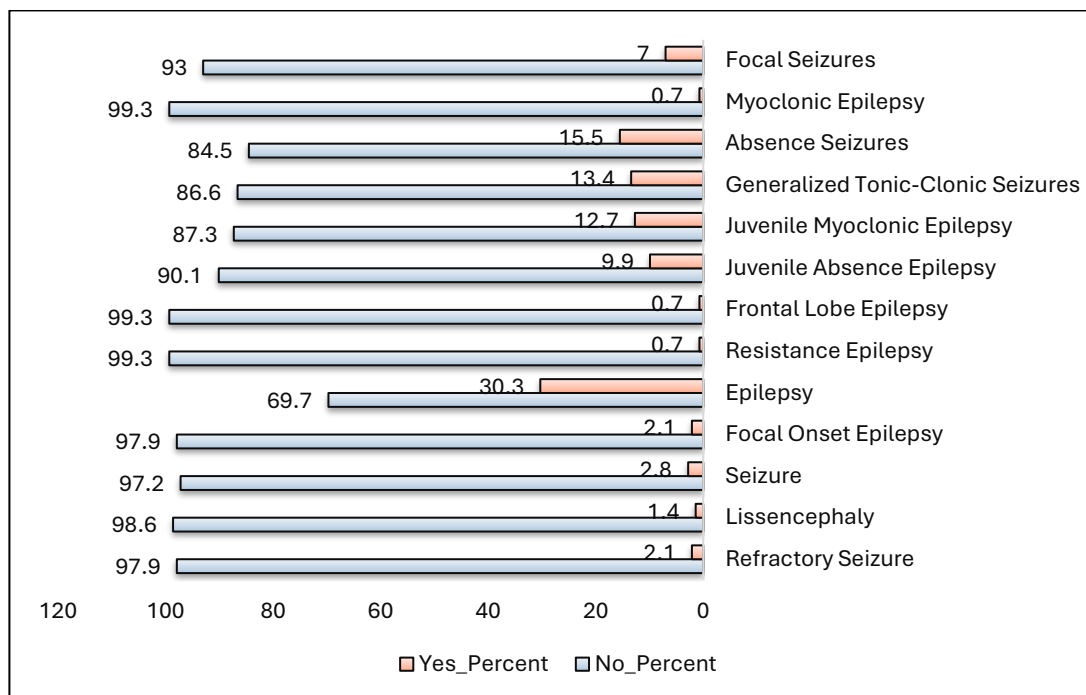
**Table 1: Sociodemographic characteristics and baseline measurements of participants (N = 142)**

Characteristic		N (%)
Gender	Female	67 (47.2%)

	Male	75 (52.8%)
Age (years); Mean (SD) / Range		9.38 (3.957) / 1-15
Weight (kg); Mean (SD) / Range		34.85 (16.51) / 10.2-141.0
Height (cm); Mean (SD) / Range		132.80 (18.87) / 80.0-171.0
Medication	New	70 (49.3%)
	Old	72 (50.7%)
Baseline Medications	Levetiracetam	36 (25.4%)
	Topiramate	18 (12.7%)
	Vigabatrin	3 (2.1%)
	Oxcarbazepine	2 (1.4%)
	Lamotrigine	8 (5.6%)
	Locosamide	1 (0.7%)
	Phenobarbital	2 (1.4%)
	Perampanel	1 (0.7%)
	Ethosuximide	1 (0.7%)
	Sodium Valproate	44 (31.0%)
	Carbamazepine	20 (14.1%)
	Clonazepam	2 (1.4%)
	Clobazam	4 (2.8%)
(Baseline) TSH (pmol/L); Mean (SD) / Range		2.97 (1.00) / 0.50-5.00
(Baseline) FT4 (pmol/L); Mean (SD) / Range		11.90 (1.48) / 9.01-18.10
(Baseline) FT3 (pmol/L); Mean (SD) / Range		4.70 (0.77) / 2.10-6.87
Creatinine (umol/L); Mean (SD) / Range		46.94 (5.00) / 35-70

*N: Frequency, %: Percentage, SD: Standard deviation*

The features of epilepsy and seizures are depicted in Figure 1, revealing various situations. Epilepsy was the most common ailment, accounting for 30.3% of the people under investigation. With 15.5% of the population experiencing absence seizures, they were the most prevalent form of seizures, closely followed by generalized tonic-clonic seizures (13.4%). Juvenile myoclonic epilepsy was detected in 12.7% of cases, whereas 9.9% of patients had juvenile absence epilepsy. Focal seizures occurred in 7.0% of patients. Refractory seizures and focal-onset epilepsy, which each affect 2.1% of people, are less prevalent than general seizures, which affect 2.8% of instances. Approximately 1.4% of people have an unusual brain deformity known as licensephaly. The research also discovered several disorders, such as frontal lobe epilepsy, myoclonic epilepsy, and resistance epilepsy, with a lower prevalence rate of 0.7%. The distribution of seizure and epilepsy types provides essential information on the neurological conditions of the study population.



**Figure 1:** Features of epilepsy and seizures among patients

A study that examined the relationship between several sociodemographic and diagnostic characteristics and the type of medicine (new vs. old) in individuals with epilepsy produced some intriguing results. The distribution of genders was comparatively balanced, and there was no discernible difference ( $p = 0.507$ ) between the treatment groups. No statistically significant differences were found for conditions like juvenile absence epilepsy, refractory seizures, Lissencephaly, general seizures, focal onset epilepsy, epilepsy, resistance epilepsy, frontal lobe epilepsy, juvenile myoclonic epilepsy, generalized tonic-clonic seizures, absence seizures, and myoclonic epilepsy ( $p > 0.05$ ), the prevalence of most epilepsy types and seizure disorders was similar between the two medication groups.

Nonetheless, a noteworthy distinction was observed in the frequency of focal seizures between the two drug groups ( $p = 0.001$ ). Remarkably, none of the patients in the new medicine group reported having focal seizures, but 13.9% of the patients in the old medication group did. This study raises the possibility of a link between the type of medicine used and the incidence of focal seizures, which might impact patient care and treatment plans. Except for focal seizures, the study showed that the decision between new and old drugs did not affect most epilepsy and seizure types.

**Table 2: Association between medication type, sociodemographic, and diagnosis type 2**

Sociodemographic and diagnosis type			Medication		P-Value
			New	Old	
Gender	Female	Count	35	32	0.507
		%	50.0%	44.4%	
	Male	Count	35	40	
		%	50.0%	55.6%	
Juvenile Absence epilepsy	No	Count	62	66	0.536
		%	88.6%	91.7%	
	Yes	Count	8	6	
		%	11.4%	8.3%	
Refractory seizure	No	Count	68	71	0.617
		%	97.1%	98.6%	
	Yes	Count	2	1	
		%	2.9%	1.4%	
Lissencephaly	No	Count	69	71	1.000

	Yes	%	98.6%	98.6%	0.620
		Count	1	1	
		%	1.4%	1.4%	
Seizure	No	Count	69	69	0.572
		%	98.6%	95.8%	
		Count	1	3	
Focal onset epilepsy	Yes	%	1.4%	4.2%	0.572
		Count	69	70	
		%	98.6%	97.2%	
Epilepsy	No	Count	1	2	0.943
		%	1.4%	2.8%	
		Count	49	50	
Resistance epilepsy	Yes	%	70.0%	69.4%	0.493
		Count	21	22	
		%	30.0%	30.6%	
Frontal lobe epilepsy	No	Count	69	72	0.493
		%	98.6%	100.0%	
		Count	1	0	
Juvenile Myoclonic Epilepsy	Yes	%	1.4%	0.0%	0.115
		Count	58	66	
		%	82.9%	91.7%	
Generalized Tonic-Colonic Seizures	No	Count	12	6	0.421
		%	17.1%	8.3%	
		Count	59	64	
Absence Seizures	Yes	%	84.3%	88.9%	0.695
		Count	11	8	
		%	15.7%	11.1%	
Myoclonic epilepsy	No	Count	10	12	1.000
		%	14.3%	16.7%	
		Count	70	71	
Focal Seizures	Yes	%	100.0%	98.6%	0.001*
		Count	0	1	
		%	0.0%	1.4%	
	No	Count	70	62	0.001*
		%	100.0%	86.1%	
		Count	0	10	
	Yes	%	0.0%	13.9%	0.001*
		Count	0	10	
		%	0.0%	13.9%	

\* $p < 0.05$ , significant

A comparison of drug type (new vs. old) with different sociodemographic factors and thyroid function in patients yielded some exciting results, as shown in Table 3. Age, height, and weight were among the sociodemographic variables that did not differ significantly between the two groups. Both groups' mean ages (new: 9.43 years, old: 9.33 years,  $p = 0.887$ ) were comparable. Additionally, there were no statistically significant changes in height or weight ( $p = 0.881$  and  $p = 0.485$ , respectively). TSH, FT4, FT3, and creatinine levels did not change substantially between the two groups ( $p > 0.05$ ). However, following a year of therapy, notable variations were observed in a few thyroid function tests. TSH levels in the new medication group were significantly higher than in the old medication

group (9.1764 vs. 4.0474 pmol/L,  $p = 0.001$ ). In the same way, the new medicine group's FT4 levels were considerably higher ( $p = 0.003$ ) at 11.5453 vs. 10.6243 pmol/L. After a year, there was a trend toward greater FT3 levels in the group using the new medicine, but the difference was not statistically significant ( $p = 0.077$ ).

These results imply that while the decision between new and old drugs has no discernible effects on baseline laboratory measurements or sociodemographic characteristics, it may eventually significantly influence thyroid function. After a year of therapy, the new medicine group had greater TSH and FT4 levels, which calls for more research to determine the underlying processes and therapeutic consequences.

**Table 3: Association between medication type and sociodemographic and thyroid function**

Sociodemographic and thyroid function	Medication	Mean	SD	P-Value
Age in years	New	9.43	4.020	0.887
	Old	9.33	3.922	
Weight (kg)	New	35.8357	18.08158	0.485
	Old	33.8910	14.88063	
Height (cm)	New	132.5571	20.54944	0.881
	Old	133.0336	17.21415	
TSH pmo/L (Baseline)	New	2.8223	.88507	0.081
	Old	3.1164	1.09305	
FT4 pmo/L (Baseline)	New	12.0493	1.46485	0.231
	Old	11.7519	1.48041	
FT3 pmo/L (Baseline)	New	4.7800	.85813	0.220
	Old	4.6219	.66045	
Creatinine umol/L	New	46.81	5.528	0.762
	Old	47.07	4.451	
TSH Pmol/l (After one year)	New	9.1764	4.18643	0.001*
	Old	4.0474	2.45228	
FT4 pmol/L (after one year)	New	11.5453	1.85335	0.003*
	Old	10.6243	1.80752	
FT3 pmol/L (after one year)	New	4.4661	1.07116	0.077
	Old	4.0864	1.43840	

\* $p < 0.05$ , significant

Table 3 compares thyroid function in epilepsy patients at baseline and one year post-treatment using a paired t-test analysis. Over the year, the research found that all three significant thyroid function markers had changed significantly. There was a significant increase in TSH levels from baseline to one year after therapy. One year later, the mean TSH level increased from 2.9726 pmol/L at baseline to 6.5573 pmol/L, a statistically significant increase ( $P < 0.001$ ). This significant increase in TSH levels raises the possibility that epilepsy medication may influence thyroid function.

In contrast, FT4 levels decreased significantly throughout the year. After a year, the mean FT4 level decreased ( $p < 0.001$ ) from 11.8985 pmol/L at baseline to 11.0783 pmol/L. Nevertheless, this decline in thyroid hormone levels is significant, even if it is not as significant as the TSH drop.

FT3 levels also showed a significant decline. After a year of therapy, the mean FT3 level dropped ( $p < 0.001$ ) from 4.6999 pmol/L at baseline to 4.2736 pmol/L. Together with changes in TSH and FT4 levels, this change in FT3 levels suggests a thorough change in thyroid function parameters throughout therapy.

These results emphasize how crucial it is to keep an eye on thyroid function in individuals with epilepsy receiving long-term therapy. The noteworthy alterations identified in all three thyroid indicators imply that thyroid function may be significantly affected by epilepsy medicines, which may have consequences for patient care and treatment plans.



**Table 4: Summary of Subclinical Hypothyroidism Analysis**

Statistic	New Medication Group	Old Medication Group
Total Patients	71	71
Cases of Subclinical Hypothyroidism	47	8
Prevalence	66.2%	11.3%
Chi-square statistic ( $\chi^2$ )	45.32	
Degrees of freedom	1	
p-value	< 0.00001	

There is a statistically significant difference in the occurrence of Subclinical Hypothyroidism between the New Medication Group and the Old Medication Group. The New Medication Group has a significantly higher prevalence of Subclinical Hypothyroidism (66.2%) compared to the Old Medication Group (11.3%).

This analysis suggests that the new medication is associated with a higher risk of Subclinical Hypothyroidism. However, it's important to note that while this analysis shows a strong association, it doesn't prove causation. Other factors could be influencing this relationship, and further research would be needed to establish a causal link.

**Table 5: Paired T-test to assess thyroid function changes from baseline and after one year**

Laboratory measures	Mean	SD	P-Value
TSH (Baseline) pmo/L	2.9726	1.00683	<0.001
TSH (After one year) Pmol/l	6.5573	4.26418	
FT4 pmo/L (Baseline)	11.8985	1.47509	<0.001
FT4 pmol/L (after one year)	11.0783	1.88138	
FT3 (Baseline) pmo/L	4.6999	.76570	<0.001
FT3 pmol/L (after one year)	4.2736	1.28047	

## Discussion

The findings of this study provide critical insights into the effects of antiepileptic drugs (AEDs) on thyroid function in pediatric patients. The significant alterations observed in thyroid hormone levels, particularly among patients receiving newer AEDs, emphasize the importance of routine thyroid function monitoring in children undergoing epilepsy treatment. These findings align with previous research highlighting the endocrine effects of AEDs and their implications for patient management (Han et al., 2020).

The study demonstrated that patients on newer AEDs exhibited a greater increase in thyroid-stimulating hormone (TSH) levels and a significant decrease in free thyroxine (FT4) levels after one year of treatment compared to those on older AEDs. This is consistent with research by Elshorbagy et al. (2020), who also found that newer AEDs led to more pronounced thyroid function disturbances. The increase in TSH levels suggests that newer AEDs may interfere with thyroid hormone synthesis or metabolism, leading to a compensatory response by the pituitary gland.

Additionally, the study identified a significantly higher prevalence of subclinical hypothyroidism in patients receiving newer AEDs. This finding raises concerns regarding the long-term endocrine effects of these medications, particularly in pediatric patients who rely on stable thyroid function for growth and development (Lee et al., 2017). The higher prevalence of thyroid dysfunction necessitates further research into the mechanisms through which newer AEDs influence thyroid hormone regulation.

Interestingly, the results also revealed that while all patients experienced thyroid function changes over time, those in the newer AED group had more substantial deviations from baseline

measurements. This is supported by studies such as Nishiyama et al. (2019), which reported significant endocrine disturbances in children treated with levetiracetam and carbamazepine. These findings underscore the need for individualized patient monitoring to mitigate potential adverse effects.

The observed increase in TSH levels among patients with prolonged seizure duration further supports the hypothesis that seizures themselves may contribute to thyroid dysfunction (Han et al., 2020). Seizures can trigger a stress response that influences thyroid hormone levels, potentially exacerbating the effects of AEDs. This interplay between epilepsy, AED therapy, and thyroid function warrants a more comprehensive approach to epilepsy management.

Further supporting evidence from Kose et al. (2017) suggests that metabolic changes associated with ketogenic diets may also contribute to thyroid dysfunction in children with intractable epilepsy. The combination of dietary therapy and AEDs may have compounding effects on thyroid hormone regulation, necessitating a multidisciplinary approach to treatment planning.

Another noteworthy aspect of this study is the impact of oxcarbazepine on thyroid function. Park et al. (2022) found that oxcarbazepine led to progressive changes in thyroid hormone levels over time, which is consistent with the results of the current study. These findings suggest that while oxcarbazepine may be effective in seizure control, its long-term endocrine effects require careful consideration in pediatric patients.

Moreover, the lipid profile and thyroid function interactions observed in children treated with AEDs, as reported by Garoufi et al. (2014), highlight the broader metabolic implications of epilepsy treatment. Given that thyroid hormones play a crucial role in metabolism, alterations in their levels could have cascading effects on overall health and development.

The statistical analyses in this study demonstrated clear associations between AED use and thyroid function changes. The significant differences between the new and old medication groups in terms of TSH and FT4 levels suggest that newer AEDs may have a stronger impact on the hypothalamic-pituitary-thyroid axis. These findings align with Rafik et al. (2024), who also observed substantial thyroid function changes in children receiving AED therapy.

Despite these compelling findings, several limitations should be acknowledged. The study was conducted at a single center, which may limit the generalizability of the results. Additionally, the one-year follow-up period, while sufficient to detect short-term changes, may not fully capture the long-term endocrine effects of AED therapy. Future studies with extended follow-up periods and larger sample sizes are needed to confirm these findings and elucidate underlying mechanisms.

Given the significant thyroid function changes observed, routine thyroid screening should be incorporated into the management of pediatric epilepsy patients. Early detection of subclinical hypothyroidism can facilitate timely intervention, potentially preventing more severe thyroid dysfunction and its associated complications (Yılmaz et al., 2021).

Furthermore, clinicians should consider the potential endocrine side effects when selecting AEDs for pediatric patients. While newer AEDs may offer advantages in seizure control, their impact on thyroid function must be weighed against their benefits. A personalized approach to epilepsy treatment, including periodic thyroid function assessments, is essential to ensuring optimal patient outcomes.

In conclusion, this study highlights the complex interplay between epilepsy treatment and thyroid function in children. The findings underscore the need for continuous thyroid function monitoring in pediatric epilepsy patients, particularly those receiving newer AEDs. By integrating thyroid assessments into routine epilepsy management, healthcare providers can better safeguard the overall well-being of their patients while optimizing seizure control strategies. Further research is necessary to fully understand the mechanisms driving AED-induced thyroid changes and to develop targeted interventions that minimize endocrine disruptions.

## Limitations

This study has certain limitations, including its single-center design, potential confounding factors, and reliance on a one-year follow-up period. Future research with a multi-center approach and extended follow-up periods is recommended to validate findings.

### Conclusion:

Several significant findings were found in this prospective investigation assessing the impact of new and old antiepileptic medications on thyroid function in pediatric patients. Patients taking new antiepileptic drugs had significantly higher TSH and FT4 levels after a year of treatment than those taking older drugs, indicating a possible more significant effect on thyroid function. Furthermore, independent of the type of medicine the patient took, the study found substantial changes in all three crucial thyroid function markers (TSH, FT4, and FT3) from baseline to one year post-treatment. It is interesting to note that focal seizures were much more common among individuals taking older drugs, even though other forms of epilepsy and seizures were distributed evenly across the medication groups. These findings highlight the significance of routine assessment of thyroid function in children with epilepsy, especially in those on more recent antiepileptic medications. These results further emphasize the necessity of greater investigation to comprehend the underlying processes of medication-induced thyroid alterations and their long-term clinical consequences, which may help develop more specialized treatment plans for children with epilepsy.

### References

1. Han JY, Lee IG, Shin S, Park J. Seizure duration may increase thyroid-stimulating hormone levels in children experiencing a seizure. *J Int Med Res.* 2020 May;48(5):300060519888401. doi: 10.1177/0300060519888401. Epub 2019 Nov 27. PMID: 31774013; PMCID: PMC7265565.
2. Elshorbagy HH, Barseem NF, Suliman HA, Talaat E, AlSHOKARY AH, Abdelghani WE, Abdulsamea SE, Maksoud YHA, Azab SM, Elsadek AE, Nour El Din DM. The Impact of Antiepileptic Drugs on Thyroid Function in Children with Epilepsy: New Versus Old. *Iran J Child Neurol.* 2020 Winter;14(1):31-41. PMID: 32021626; PMCID: PMC6956958.
3. Lee YJ, Nam SO, Kim KM, Kim YM, Yeon GM. Longitudinal Change in Thyroid Hormone Levels in Children with Epilepsy on a Ketogenic Diet: Prevalence and Risk Factors. *J Epilepsy Res.* 2017 Dec 31;7(2):99-105. doi: 10.14581/jer.17015. PMID: 29344467; PMCID: PMC5767495.
4. Nishiyama M, Takami Y, Ishida Y, Tomioka K, Tanaka T, Nagase H, Nakagawa T, Tokumoto S, Yamaguchi H, Toyoshima D, Maruyama A, Nozu K, Nishimura N, Iijima K. Lipid and thyroid hormone levels in children with epilepsy treated with levetiracetam or carbamazepine: A prospective observational study. *Epilepsy Behav.* 2019 Jan;90:15-19. doi: 10.1016/j.yebeh.2018.11.003. Epub 2018 Nov 27. PMID: 30500483.
5. Kose E, Guzel O, Demir K, Arslan N. Changes of thyroid hormonal status in patients receiving ketogenic diet due to intractable epilepsy. *J Pediatr Endocrinol Metab.* 2017 Apr 1;30(4):411-416. doi: 10.1515/jpem-2016-0281. PMID: 28076316.
6. Rafik, A., Salah, N., El Khayat, N. M., Nada, M., & Abushady, E. M. (2024). Effect of anti-epileptic drugs usage on thyroid profile in Egyptian epileptic children. *The Egyptian Journal of Neurology, Psychiatry and Neurosurgery*, 60(1), 1-18. <https://doi.org/10.1186/s41983-023-00776-7>
7. Park H, Heo J, Kim MJ, Lee JH, Kim MS, Jin DK, Kim TH, Chung JH, Cho SY, Kim SW. The longitudinal effect of oxcarbazepine on thyroid function in children and adolescents with epilepsy. *Epilepsia.* 2022 Dec;63(12):3148-3155. doi: 10.1111/epi.17407. Epub 2022 Oct 1. PMID: 36073252.
8. Yılmaz Ü, Nalbantoğlu Ö, Güzin Y, Edizer S, Akışın Z, Pekuz S, Kırkgöz HH, Yavuz M, Ünalp A, Özkan B. The effect of ketogenic diet on thyroid functions in children with drug-resistant epilepsy. *Neurol Sci.* 2021 Dec;42(12):5261-5269. doi: 10.1007/s10072-021-05225-y. Epub 2021 Apr 12. PMID: 33846882.

9. Han JY, Lee IG, Shin S, Park J. Seizure duration may increase thyroid-stimulating hormone levels in children experiencing a seizure. *J Int Med Res.* 2020 May;48(5):300060519888401. doi: 10.1177/0300060519888401. Epub 2019 Nov 27. PMID: 31774013; PMCID: PMC7265565.
10. Garoufi A, Koemtziidou E, Katsarou E, Dinopoulos A, Kalimeraki I, Fotinou A, Drakatos A, Attilakos A. Lipid profile and thyroid hormone concentrations in children with epilepsy treated with oxcarbazepine monotherapy: a prospective long-term study. *Eur J Neurol.* 2014;21(1):118-23. doi: 10.1111/ene.12262. Epub 2013 Oct 1. PMID: 24118208.