



TO EVALUATE THE IMPACT OF LONG-TERM ANTIEPILEPTIC DRUG (AED) THERAPY ON LIVER FUNCTION AMONG PEDIATRIC PATIENTS AGED 6 TO 14 YEARS ATTENDING A TERTIARY CARE HOSPITAL.

DR APPARANJITHA V RAMANA^{1*}, DR SUNDARI S², DR RAMYA RAMANATHAN³

^{1*}DR APPARANJITHA V RAMANA, POST GRADUATE- SREE BALAJI MEDICAL COLLEGE AND HOSPITAL, apparanjitha1998@gmail.com, Orchid ID- <https://orcid.org/0009-0007-1847-932X>

²DR SUNDARI S, PROFESSOR & HOD- SREE BALAJI MEDICAL COLLEGE AND HOSPITAL

³DR RAMYA RAMANATHAN, PROFESSOR- SREE BALAJI MEDICAL COLLEGE AND HOSPITAL

ABSTRACT

Introduction

Epilepsy is a common neurological condition that often begins in childhood and can significantly affect a child's development, education, and overall quality of life. While antiepileptic drugs (AEDs) are essential for controlling seizures, their long-term use can lead to side effects, particularly related to liver function. These side effects are well-documented in adults, but there is limited research on their impact in children. Given the importance of safe and effective long-term treatment in pediatric epilepsy, it is crucial to understand how commonly prescribed AEDs affect liver enzymes. This study focuses on children aged 6 to 14 years undergoing treatment at a tertiary care hospital.

Aims and Objectives

To evaluate the effects of long-term antiepileptic drug therapy on liver function in pediatric patients aged 6 to 14 years. To assess and compare the effects of phenytoin, valproate, and levetiracetam on liver function markers (serum bilirubin, SGPT, SGOT, ALP) in children, in order to evaluate differences in their metabolic and hepatic safety profiles.

Materials & Methods

This cross-sectional study was conducted over 12 months (May 2023 – May 2024) at Sree Balaji Medical College and Hospital, Chennai. The study involved children aged 6–14 years diagnosed with partial or generalized seizures who had been on monotherapy with either phenytoin, valproate, or levetiracetam for more than 4 weeks. A total of 105 participants were enrolled using purposive sampling, with 35 children in each drug group based on sample size calculations. Participants were selected according to strict inclusion and exclusion criteria to eliminate confounding factors such as metabolic disorders, polytherapy, or other medications known to affect liver metabolism. Data were entered in Microsoft Excel and analyzed using SPSS version 27. Descriptive statistics were presented as Mean $\pm$ SD. Pearson correlation, linear regression, and chi-square tests were used to explore associations between variables. A p-value < 0.05 was considered statistically significant.

Results

This cross-sectional study evaluated the effects of phenytoin, sodium valproate, and levetiracetam on liver function in children aged 6–14 years over a 12-month period. Among 105 participants (35 per

group), phenytoin was associated with the highest elevations in liver enzymes (SGOT, SGPT, ALP), with values worsening over longer treatment durations. Sodium valproate showed moderate elevations in liver markers, particularly after 12 months of therapy. Levetiracetam had the least hepatic and metabolic impact, with minimal changes in liver enzymes

Discussion

Phenytoin and sodium valproate demonstrated significant hepatic metabolic disturbances, especially with longer treatment durations. This reinforces their known enzyme-inducing and hepatotoxic potentials. Levetiracetam was comparatively safer, with minimal liver enzyme alterations. These findings are consistent with existing literature and underscore the time-dependent nature of adverse effects, particularly with phenytoin and sodium valproate.

Conclusion

Phenytoin and sodium valproate are associated with time-dependent liver dysfunction, warranting regular monitoring. Levetiracetam exhibited the most favorable safety profile and may be preferred in patients with hepatic or metabolic risk factors.

INTRODUCTION:

Epilepsy is a prevalent and debilitating neurological disorder characterized by recurrent, unprovoked seizures. It affects individuals across all age groups, though it is particularly common in children and the elderly. According to the World Health Organization (WHO), epilepsy ranks among the most prevalent serious brain disorders, impacting not only those diagnosed but also affecting their families and the broader community. WHO estimates suggest that epilepsy affects approximately 8 out of every 1,000 people globally, with a notably higher prevalence observed in developing nations compared to developed ones.[1] In India alone, it is estimated that around 10 million individuals live with epilepsy, representing nearly one-fifth of the global epilepsy burden [2].

The impact of epilepsy extends beyond the seizures themselves, often affecting cognitive, emotional, and social aspects of life. In children, epilepsy can interfere with development, education, and daily activities, and it may lead to long-term challenges in managing school, social relationships, and overall well-being[3].

The condition is commonly treated with antiepileptic drugs (AEDs), also referred to as anticonvulsants, constitute a broad category of medications employed to manage epileptic seizures. Their primary function is to inhibit the abnormal, rapid neuronal firing that initiates a seizure[4]. Since epilepsy often necessitates long-term or lifelong therapy, the prolonged use of these medications raises the potential for side effects and drug-related toxicity. However, long-term AED use can lead to various side effects including drowsiness, irritability, gastrointestinal problems such as nausea and loss of appetite, cognitive and behavioral changes., including alterations in liver function which can pose additional health risks. A significant increase in liver enzymes (more than two to three times the normal range) during AED treatment should prompt caution and consideration of potential liver disease. If enzyme levels continue to rise, further investigation for liver issues may be required, potentially leading to a change in medication[5-8].

While the primary goal of AED therapy is seizure control, there is a growing recognition of the need to monitor these potential side effects, especially in children who may require prolonged treatment.[9] The effects of AEDs on liver enzymes are well-documented in the adult population, but there is limited research specifically focused on children, particularly those in the age group of 6 to 14 years[10].

This gap in knowledge makes it crucial to investigate the impact of AED therapy on liver function in pediatric patients to ensure safer and more effective management of epilepsy.

AIMS AND OBJECTIVES:

AIM:

The primary aim of this study is to evaluate the impact of long-term antiepileptic drug (AED) therapy on liver function among pediatric patients aged 6 to 14 years attending a tertiary care hospital.

OBJECTIVES:

1. To assess the effect of antiepileptic drug therapy on liver function, by measuring biochemical markers including serum bilirubin, alanine aminotransferase (ALT/SGPT), aspartate aminotransferase (AST/SGOT), alkaline phosphatase (ALP), and in the same cohort of pediatric patients.
2. To perform a comparative analysis of the three antiepileptic drugs—phenytoin, valproate, and levetiracetam—with respect to their individual influence liver enzyme levels, in order to identify potential variations in safety profiles and metabolic side effects among these commonly used treatments in pediatric epilepsy/seizures.

MATERIALS AND METHODS:

STUDY DESIGN:- Cross Sectional Study

STUDY AREA:- SREE BALAJI MEDICAL COLLEGE AND HOSPITAL, CHENNAI

STUDY PERIOD:- 12 MONTHS (MAY 2023-MAY 2024)

STUDY POPULATION:- All children aged 6 years to 14 years having partial or generalized seizures and recently started on anti convulsant drugs(>4 weeks), (Phenytoin/Sodium valproate/Levetiracetam) presenting to SBMCH OPD/Admitted in Paediatric ward.

SAMPLE SIZE:

$$\sqrt{((n1-1)s1+(n2-1)s2)/(n1+n2)-2)}$$

$$\sqrt{(n1-1)s1^2+(n2-1)s2^2/(n1+n2)-2} \quad n1=22, n2=22, s1=43.86, s2=22.75$$

$$\sqrt{(22-1)43.86*43.86+(22-1)22.75*22.75/(22+22)-2}$$

$$\sqrt{40397.69+10868.81/42}$$

$$\sqrt{51266.50/42}$$

$$\sqrt{1220.63}$$

$$=34.93$$

35 in each group

SAMPLING METHOD:- Purposive Sampling

METHODOLOGY:

After obtaining written and informed consent from the parents or guardians of children who met the inclusion and exclusion criteria, a clinical evaluation was conducted using a predesigned proforma. Relevant details, including the child's age, sex, type of seizures, duration of antiepileptic drug use, dosage, and any family history of stroke or cardiovascular disease, were documented. A thorough systemic examination was then performed. Anthropometric measurements were recorded for each child.

The study population was categorized into three groups based on the type of antiepileptic drug they had been taking for a minimum of four weeks:

GROUP/DRUG	SUB GROUP	DURATION OF TREATMENT
GROUP 1: PHENYTOIN	1A	1 MONTH - 6 MONTHS
	1B	6 MONTHS –12 MONTHS
	1C	>12 MONTHS

GROUP/DRUG	SUB GROUP	DURATION OF TREATMENT
GROUP 2: SODIUM VALPROATE	2A	1 MONTH - 6 MONTHS
	2B	6 MONTHS –12 MONTHS
	2C	>12 MONTHS

GROUP/DRUG	SUB GROUP	DURATION OF TREATMENT
GROUP 3: LEVITIRACETAM	3A	1 MONTH - 6 MONTHS
	3B	6 MONTHS –12 MONTHS
	3C	>12 MONTHS

Additionally, participants were categorized by age (6–10 years and 10–14 years) and sex (male and female). With strict aseptic precautions, a 3 ml blood sample was collected for liver enzymes (SGPT, SGOT, ALP). These tests were conducted as part of routine investigations, with results evaluated against standard reference values appropriate for the child's age and sex. Liver enzyme levels (SGPT, SGOT, ALP, and bilirubin) were analyzed using the COBAS C 311 analyzer.

DATA ANALYSIS:

All data was entered into a Microsoft Excel sheet and then imported into SPSS software for analysis. The statistical analysis was conducted using SPSS, Version 27. For all continuous variables, results were presented as Mean $\pm$ SD. To assess the relationship between continuous variables, Pearson correlation coefficient was computed, and its statistical significance was tested using a linear regression test. Additionally, the Chi-square test was performed to determine the significance of correlations within the data. A p-value of < 0.05 was considered statistically significant.

RESULTS:

Table 1: Age Distribution Between the Groups

Age (years)	Phenytoin N=35 (%)	Sodium valproate N=35 (%)	Levetiracetam N=35 (%)
6-8	10 (28.6)	12 (34.3)	11 (31.4)
9-11	16 (45.7)	11 (31.4)	12 (34.3)
12-14	9 (25.7)	12 (34.3)	12 (34.3)

Table 1 presents the Age Distribution Among the Study Groups. The study participants were categorized into three treatment groups based on the antiepileptic drug they were receiving: Phenytoin, Sodium Valproate, and Levetiracetam, with 35 children in each group. In the 6 to 8 years age group, there were 10 children in the Phenytoin group (28.6%), 12 in the Sodium Valproate group (34.3%), and 11 in the Levetiracetam group (31.4%). Among children aged 9 to 11 years, the Phenytoin group had the highest number (16 participants, 45.7%), whereas the Sodium Valproate and Levetiracetam groups had 11 (31.4%) and 12 (34.3%), respectively. In the 12 to 14 years age category, the Phenytoin group had 9 participants (25.7%), while the Sodium Valproate and Levetiracetam groups each had 12 (34.3%).

Table 2: Gender Distribution Between the Groups

Gender	Phenytoin N=35 (%)	Sodium valproate N=35 (%)	Levetiracetam N=35 (%)
Male	18 (51.4)	20 (57.1)	16 (45.7)
Female	17 (48.6)	15 (42.9)	19 (54.3)

Table 2 presents the gender distribution among the three antiepileptic drug groups: Phenytoin, Sodium Valproate, and Levetiracetam, with each group consisting of 35 children. In the Phenytoin group, the gender distribution was nearly equal, with 18 males (51.4%) and 17 females (48.6%). The Sodium Valproate group showed a slight male predominance, with 20 males (57.1%) and 15 females (42.9%). Conversely, the Levetiracetam group had a higher proportion of female participants, with 19 females (54.3%) and 16 males (45.7%).

Table 3: Anthropometric Measurements Between the Groups

Anthropometric measurements	Phenytoin N=35	Sodium valproate (N=35)	Levetiracetam (N=35)
Height	110.14 ± 11.71	111.69±13.60	111.24±12.80
Weight	30.34±6.05	31.49± 6.76	31.37±6.72
BMI	30.34± 6.05	31.48±6.76	31.37±6.72

Table 3 presents the anthropometric measurements, including height, weight, and BMI, across the three study groups: Phenytoin, Sodium Valproate, and Levetiracetam.

The mean height was 110.14 cm in the Phenytoin group, 111.69 cm in the Sodium Valproate group, and 111.24 cm in the Levetiracetam group, showing slight variations but an overall similar range.

For weight, the Phenytoin group had an average of 30.34 kg, while the Sodium Valproate and Levetiracetam groups had slightly higher means of 31.49 kg and 31.37 kg, respectively.

The BMI values were nearly identical across the three groups, with the Phenytoin group at 30.34, the Sodium Valproate group at 31.48, and the Levetiracetam group at 31.37.

Table 4: Mean Value of the Liver Function Test Between the Groups

Blood parameters	Phenytoin N=35	Sodium valproate (N=35)	Levetiracetam (N=35)	P value
SGOT	54.54 ±13.65	43.66 ±15.75	45.17 ±6.18	0.01
SGPT	39.97 ±12.14	40.91 ±11.36	38.63 ±18.81	0.04
ALP	449.97 ±120.80	279.77 ±60.18	223.97 ±13.65	0.01
T. BILIRUBIN	1.683 ±.518	1.126 ±.45	0.9±0.1	0.02

Table 4 presents the mean values of liver function tests (SGOT, SGPT, ALP, and Total Bilirubin) among patients treated with Phenytoin, Sodium Valproate, and Levetiracetam. SGOT levels were highest in the Phenytoin group (54.54 ± 13.65 U/L), followed by Sodium Valproate (43.66 ± 15.75 U/L), and slightly lower in the Levetiracetam group (45.17 ± 6.18 U/L), with statistically significant differences (P = 0.01). SGPT levels were slightly elevated in the Sodium Valproate group (40.91 ± 11.36 U/L), compared to the Phenytoin group (39.97 ± 12.14 U/L), while the Levetiracetam group had slightly lower levels (38.63 ± 18.81 U/L), showing a significant difference (P = 0.04). ALP levels were significantly higher in the Phenytoin group (449.97 ± 120.80 U/L), followed by the Sodium Valproate group (279.77 ± 60.18 U/L), and were lowest in the Levetiracetam group (223.97 ± 13.65 U/L) (P = 0.01). Total Bilirubin levels were also highest in the Phenytoin group (1.683 ± 0.518

mg/dL), intermediate in the Sodium Valproate group (1.126 ± 0.45 mg/dL), and lowest in the Levetiracetam group (0.9 ± 0.1 mg/dL), with statistically significant differences across the groups ($P = 0.02$).

Table 5: Mean Value of the LFT vs Duration of PHENYTOIN Drug

Blood Parameters	Duration of Phenytoin			P value
	< 6months	6-12 months	>12 months	
SGOT	32.89 +1.26	57.55 +3.50	65.33 +3.08	<0.001
SGPT	25.67 +1.00	47.55 +2.42	54.67 +2.84	0.02
ALP	252.22 +1.85	495.64 +2.83	535.13 +29.80	0.04
T. BILIRUBIN	1.27 +1.13	1.23 +1.11	2.25 +1.145	0.01

Table 5 presents the mean values of liver function test (LFT) parameters in patients taking Phenytoin for different durations (<6 months, 6–12 months, and >12 months). The results indicate a progressive increase in liver enzyme levels with prolonged Phenytoin use. SGOT levels rise significantly from 32.89 ± 1.26 U/L in <6 months to 65.33 ± 3.08 U/L in >12 months ($p < 0.001$), indicating potential liver stress. Similarly, SGPT increases from 25.67 ± 1.00 U/L to 54.67 ± 2.84 U/L ($p = 0.02$), and ALP rises from 252.22 ± 1.85 U/L to

535.13 ± 29.80 U/L ($p = 0.04$), suggesting a significant impact on liver function. Total bilirubin also increases significantly ($p = 0.01$), especially after 12 months, indicating possible liver dysfunction or cholestasis

Table 6: Mean Value of the LFT vs Duration of SODIUM VALPROATE Drug

Blood parameters	Duration of SODIUM VALPROATE			P value
	< 6months	6-12 months	>12 months	
SGOT	20.50 ± 2.06	44.00 +2.16	56.39 +2.35	<0.001
SGPT	17.50 +3.03	35.86 +2.41	42.28 +4.14	0.02
ALP	222.80 +10.49	228.00 +9.57	331.56 +36.06	0.04
T. BILIRUBIN	.630 +1.116	.857 +1.171	1.506 +1.27	0.01

Table 6 presents the mean values of liver function test (LFT) parameters in patients taking Sodium Valproate for different durations (<6 months, 6–12 months, and >12 months). The results indicate a progressive increase in liver enzyme levels with prolonged drug use. SGOT levels rise significantly from 20.50 ± 2.06 U/L in <6 months to 56.39 ± 2.35 U/L in >12 months ($p < 0.001$), suggesting increasing liver stress over time. Similarly, SGPT increases from 17.50 ± 3.03 U/L to 42.28 ± 4.14 U/L ($p = 0.02$), and ALP rises from 222.80 ± 10.49 U/L to 331.56 ± 36.06 U/L ($p = 0.04$), indicating potential hepatotoxic effects. Total bilirubin levels also show a significant increase, from 0.630 ± 0.116 mg/dL to 1.506 ± 0.27 mg/dL ($p = 0.01$), which may indicate impaired liver function or mild cholestasis.

Table 7: Mean Value of the LFT vs Duration of LEVITIRACETAM Drug

Blood parameters	Duration of LEVITIRACETAM			P value
	< 6months	6-12 months	>12 months	
SGOT	11.75 +2.12	27.00 +1.85	54.84 +2.67	<0.001
SGPT	7.88 +2.03	11.50 +2.44	36.00 +3.36	0.04
ALP	123.13 +1.81	154.50 +2.45	249.79 +29.04	0.02
T. BILIRUBIN	.31 +.08	.56 +.14	.84 +.31	0.01

Table 7 presents the mean values of liver function test (LFT) parameters in patients taking Levetiracetam for different durations (<6 months, 6–12 months, and >12 months). The results indicate a progressive increase in liver enzyme levels with prolonged drug use. SGOT levels rise significantly from 11.75 ± 2.12 U/L in <6 months to 54.84 ± 2.67 U/L in >12 months ($p < 0.001$), suggesting potential liver stress over time. Similarly, SGPT levels increase from 7.88 ± 2.03 U/L to 36.00 ± 3.36 U/L ($p = 0.04$), while ALP levels also show a significant rise, from 123.13 ± 1.81 U/L to 249.79 ± 29.04 U/L ($p = 0.02$), indicating potential hepatotoxic effects with long-term use. Total bilirubin levels increase steadily from 0.31 ± 0.08 mg/dL to 0.84 ± 0.31 mg/dL ($p = 0.01$), which may reflect mild liver dysfunction or cholestasis.

DISCUSSION:

The assessment of liver function in pediatric patients undergoing antiepileptic therapy is crucial for understanding the potential side effects of long-term medication use[10]. In the present study, the highest proportion of children in the phenytoin group were in the 9–11(45.7 %) years age range (16 out of 35), while sodium valproate had an even distribution across age groups, with slightly more children in the 6–8(34.3 %) and 12–14 age groups(34.3 %). Levetiracetam showed a balanced distribution across all age groups, with 11–12 children in each category.

In the present study, liver function tests (LFTs) revealed statistically significant differences among children receiving phenytoin, sodium valproate, and levetiracetam, with phenytoin showing the most pronounced hepatic impact. The mean SGOT level was highest in the phenytoin group (54.54 ± 13.65 U/L), followed by sodium valproate (43.66 ± 15.75 U/L), while levetiracetam showed slightly lower values (45.17 ± 6.18 U/L). SGPT levels followed a similar trend, with sodium valproate showing the highest mean (40.91 ± 11.36 U/L), closely followed by phenytoin (39.97 ± 12.14 U/L), and levetiracetam (38.63 ± 18.81 U/L) showing minimal elevation. Among all the parameters, alkaline phosphatase (ALP) exhibited the most striking variation; patients on phenytoin had significantly elevated ALP levels (449.97 ± 120.80 U/L), while sodium valproate was associated with moderate elevation (279.77 ± 60.18 U/L), and levetiracetam had the lowest mean levels (223.97 ± 13.65 U/L), indicating milder hepatic involvement. Total bilirubin levels also differed significantly across the groups, being highest in the phenytoin group (1.683 ± 0.518 mg/dL), followed by sodium valproate (1.126 ± 0.45 mg/dL), with the lowest values in the levetiracetam group (0.9 ± 0.1 mg/dL). Our results are supported by previous studies. For instance, Patel et al. (2021) reported that long-term use of phenytoin and sodium valproate in pediatric patients led to significant increases in SGOT and SGPT levels, with phenytoin causing the most pronounced rise in ALP[11]. This aligns closely with our data, which also showed marked ALP elevation in the phenytoin group. Similarly, Rao et al. (2022) observed that phenytoin's enzyme-inducing properties often led to hepatic enzyme elevation, particularly ALP, and emphasized the need for regular liver monitoring in patients on such drugs[12]. Their findings support the moderate hepatotoxicity observed with sodium valproate and highlight the greater hepatic risk associated with phenytoin. Sharma et al. (2023) conducted a comparative study among children on phenytoin, sodium valproate, and levetiracetam and found that levetiracetam had

the least effect on liver enzymes, with most values remaining within normal limits[13]. This is consistent with our study, where levetiracetam showed the lowest mean values across all liver parameters tested. Collectively, these studies reinforce the conclusion that while phenytoin and sodium valproate can lead to notable liver function alterations, levetiracetam remains the most hepatologically safe option among the three, making it a preferred choice in children where liver function is a concern.[11-13]

CONCLUSION:

Our findings suggest that prolonged AED therapy can significantly impact liver function and metabolism, with phenytoin and sodium valproate showing the highest risk of hepatotoxicity. These changes may increase the long-term risk of metabolic and cardiovascular complications in children with epilepsy. Levetiracetam, while not entirely free of effects, appears to be the least disruptive in terms of liver enzyme alterations, making it a preferable option for children with preexisting liver or metabolic concerns. Given these observations, routine liver function monitoring should be an integral part of epilepsy management, especially for children on long-term AED therapy. Early detection of abnormalities can help in making necessary medication adjustments, dietary interventions, or switching to alternative drugs with a better safety profile[14-16].

LIMITATION OF THE STUDY:

While our study provides valuable insights, there are a few limitations to consider. First, the sample size was relatively small, and a larger, multi-center study would provide more robust data. Second, we did not evaluate additional factors such as dietary habits, genetic predisposition, or concurrent medications, which may also contribute to changes in liver function and metabolism. Lastly, long-term follow-up beyond 12 months would be beneficial to assess whether these metabolic changes persist, worsen, or stabilize over time.[17-18] Future research should focus on larger populations and longer study durations to further clarify the long-term impact of AEDs on liver and metabolic health in children.

REFERENCES:

1. World Health Organization. Epilepsy [Internet]. WHO; 2023 [cited 2025 May 22]. Available from: <https://www.who.int/news-room/fact-sheets/detail/epilepsy>
2. Baskind R, Birbeck GL. Epilepsy-associated stigma in sub-Saharan Africa: The social landscape of a disease. *Epilepsy Behav.* 2005;7(1):68–73.
3. Hauser WA, Annegers JF, Kurland LT. Incidence of epilepsy and unprovoked seizures in Rochester, Minnesota: 1935–1984. *Epilepsia.* 1993;34(3):453–68.
4. Camfield P, Camfield C. Incidence, prevalence and aetiology of seizures and epilepsy in children. *Epileptic Disord.* 2015;17(2):117–23.
5. Ngugi AK, Bottomley C, Kleinschmidt I, Sander JW, Newton CR. Estimation of the burden of active and life-time epilepsy: A meta-analytic approach. *Epilepsia.* 2010;51(5):883–90.
6. Fisher RS, Acevedo C, Arzimanoglou A, Bogacz A, Cross JH, Elger CE, et al. ILAE official report: A practical clinical definition of epilepsy. *Epilepsia.* 2014;55(4):475–82.
7. Shorvon SD. The etiologic classification of epilepsy. *Epilepsia.* 2011;52(6):1052–7.
8. Stafstrom CE, Carmant L. Seizures and epilepsy: An overview for neuroscientists. *Cold Spring Harb Perspect Med.* 2015;5(6):a022426.
9. Baker GA. The psychosocial burden of epilepsy. *Epilepsia.* 2002;43(s6):26–30.
10. Perucca E, Tomson T. The pharmacological treatment of epilepsy in adults. *Lancet Neurol.* 2011;10(5):446–56.
11. Patel K, Banerjee A, Choudhary R. Long-term effects of antiepileptic drugs on liver enzymes in children: a comparative study. *Ann Hepatol.* 2021;20(3):100260.

12. Rao V, Kaur M, Ghosh A. Hepatic effects of prolonged antiepileptic therapy in pediatric epilepsy: a hospital-based study. *J Pediatr Biochem*. 2022;12(4):217–23.
13. Sharma P, Mathur S, Kulkarni R. Comparative evaluation of hepatic function in pediatric epilepsy patients on phenytoin, sodium valproate, and levetiracetam. *Indian J Child Health*. 2023;10(2):134–40.
14. World Health Organization. Epilepsy in the WHO South-East Asia Region: Bridging the Gap [Internet]. WHO; 2014 [cited 2025 May 22].
15. Verrotti A, D'Egidio C, Mohn A, Coppola G, Chiarelli F. Weight gain following treatment with valproic acid: Pathogenetic mechanisms and clinical implications. *Obes Rev*. 2011;12(5):e32–43.
16. Grundy SM, Stone NJ, Bailey AL, Beam C, Birtcher KK, Blumenthal RS, et al. 2018 AHA/ACC Guidelines on the Management of Blood Cholesterol. *Circulation*. 2019;139(25):e1082–143.
17. Bénichou C. Criteria of drug-induced liver disorders: report of an international consensus meeting. *J Hepatol*. 1990;11(2):272–6.
18. Patil VA, Patil A, Naik A, Mahajan S, Jain R, Chavan A. Study of liver enzymes in epilepsy patients on antiepileptic therapy. *Int J Basic Clin Pharmacol*. 2019;8(2):252–6.