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# Metabolic Syndrome in Epileptic Children on Sodium Valproate Therapy

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***Abstract:***
***Background:*** *Epilepsy is one of the most common neurological disorders in the world with more than 50 million affected. Valproate, is one of the most frequently prescribed antiepileptic drugs (AEDs) [1], with more than one million people around the world estimated to be taking VPA every day. This study is being conducted to assess the parameters of the metabolic syndrome in Indian children with epilepsy on valproate therapy for more than 1year, so that early reorganization and timely intervention can be employed to prevent /manage metabolic syndrome.*
***Materials and Methods:*** *This Cross sectional study recruited 100 patients (50 patients of epilepsy on valporate therapy more than 1yr attending the outpatient department of Pediatrics and Neurology and admitted in the Department of Pediatrics, RKMSP constitute the study population and another 50 healthy control subjects, who attended OPD for routine checkup). All consecutive children diagnosed with epilepsy as per International League against Epilepsy definition aged 3–18 years on valproate monotherapy for at least 12 months were enrolled at our hospital. After clinical and anthropometric evaluation (including BMI and waist circumference), the blood samples were analyzed for fasting serum glucose, total cholesterol, HDL, and serum triglyceride.*
***Results:*** *We found that BMI ($p<0.0001$), abnormal triglyceride ($p=0.0004$), cholesterol level was more in cases compared to control which was statistically significant in children on valoproate.*
***Conclusion:*** *In this present study we found that the risk of metabolic syndrome is greater in patients with epilepsy who had received VPA treatment than in the general population. This study helps us early recognition and timely intervention of valproate related metabolic syndrome.*
***Key Word:*** *Epilepsy, Valproate, Indian children, Metabolic syndrome*

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## I. Introduction

The incidence of epilepsy in children worldwide ranges between 40 – 187 /100000 children /year. Among the commonly used anti epileptic drug sodium valproate has a broad spectrum activity against both generalized and partial seizures .The long term use of this drug in children raises the importance of evaluating its safety. One of the most common problem is weight gain along with a number of endocrine and metabolic side effects. Childhood obesity when tracked into adulthood increases the risk of complications like dyslipidemia , diabetes mellitus and coronary artery disease . With this in background we conducted a cross sectional study of children with epilepsy on valprote for more than a year.

## II. Material And Methods

**Place of Study**: Department of paediatric medicine and neuromedicine ,Vivekananda Institute of medical sciences , Kolkata.
**Period of Study**: March 2019 to March 2020
**Sample population**: 50 patients and 5O age matched and sex matched healthy controls.

**Inclusion criteria**:
1. Patients of epilepsy on valproate monotherapy for more than one year.
2. Age between 2 – 12 years.

**Exclusion criteria**:
1. History of intake of multiple anti epileptic drugs or drugs which may alter lipid profile or blood glucose for example, steroids, statins, insulin etc.
2. Children having endocrinopathies, dyslipidemia , chronic liver or renal disease , obesity, hypertension or glucose intolerance.
3. Children having family history of diabetes, hypertension, obesity, dyslipidemia.

**Procedure Methodology**

After taking detailed history and clinical examination anthropometric measurements were done [Body Mass Index &Waist circumference]. BMI was calculated = weight in kg/height in square meter. The waist circumference was measured midway between symphysis pubis and xiphisternm. Obesity is defined as BMI more than 95 th percentile and waist circumference more than 90 th percentile according to WHO criteria. Blood pressure was measured using an appropriate sized cuff. Fasting blood samples were analysed for serum glucose, insulin, total cholesterol, high density lipoprotein [HDL] and serum triglyceride. Serum triglyceride was estimated calorimetrically and HDL was determined using autozyme HDLC precipitating agent.

**Statistical analysis**

Data collected from the study group were tabulated and analyzed using appropriate statistical tools. Regarding age and sex of the 50 cases 18 were female and 32 were male.

## III. Result

**Association between Age: group**

| | GROUP | | |
|---|---|---|---|
| **Age** | **Case** | **Control** | **TOTAL** |
| **2-5** | 14 | 11 | 25 |
| Row % | 56.0 | 44.0 | 100.0 |
| Col % | 28.0 | 22.0 | 25.0 |
| **>5-10** | 33 | 35 | 68 |
| Row % | 48.5 | 51.5 | 100.0 |
| Col % | 66.0 | 70.0 | 68.0 |
| **>10** | 3 | 4 | 7 |
| Row % | 42.9 | 57.1 | 100.0 |
| Col % | 6.0 | 8.0 | 7.0 |
| **TOTAL** | 50 | 50 | 100 |
| Row % | 50.0 | 50.0 | 100.0 |
| Col % | 100.0 | 100.0 | 100.0 |

**Chi-square value:** .5617; **p-value:** 0.7551

In Case, 14(28.0%) patients were 2-5 years old, 33(66.0%) patients were >5-10 years old and 3(6.0%) patients were >10 years old.

In Control, 11(22.0%) patients were 2-5 years old, 35(70.0%) patients were >5-10 years old and 4(8.0%) patients were >10 years old.

Association of Age vs. group was not statistically significant (p=0.7551).

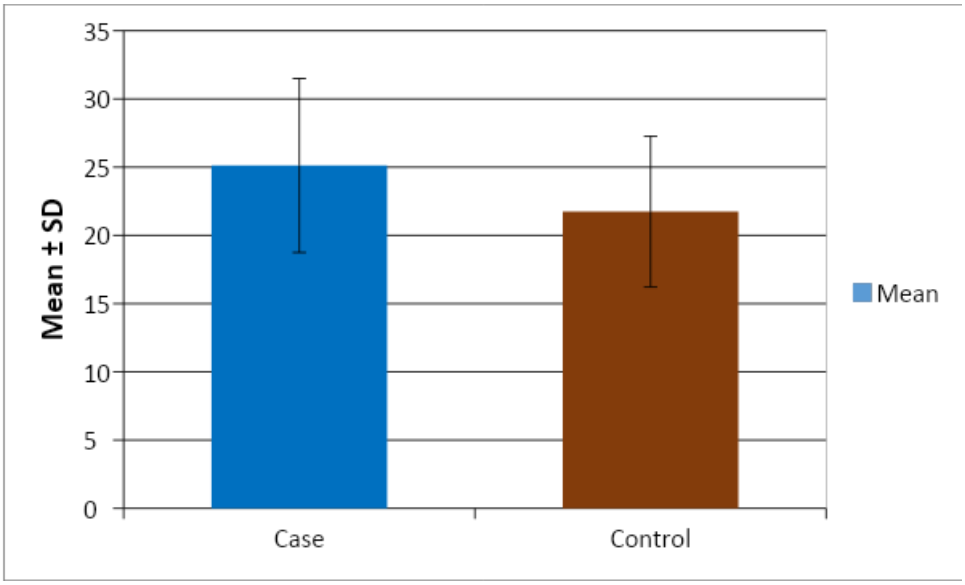
**Distribution of mean WT: Group**

| | | Number | Mean | SD | Minimum | Maximum | Median | p-value |
|---|---|---|---|---|---|---|---|---|
| **WT** | Case | 50 | 25.1200 | 6.3748 | 13.0000 | 33.0000 | 25.0000 | 0.0056 |
| | Control | 50 | 21.7400 | 5.5247 | 13.0000 | 34.0000 | 21.0000 | |

In Case Group, the mean WT (mean± s.d.) of patients were 25.1200 ± 6.3748.

In Control Group, the mean WT (mean± s.d.) of patients were 21.7400 ± 5.5247.

Difference of mean WT with both Group was statistically significant (p=0.0056).




**Distribution of mean WAIST CIR: Group**

| | | Number | Mean | SD | Minimum | Maximum | Median | p-value |
|---|---|---|---|---|---|---|---|---|
| **WAIST CIR** | Case | 50 | 64.3000 | 8.5934 | 50.0000 | 77.0000 | 64.0000 | 0.0415 |
| | Control | 50 | 61.1800 | 6.3429 | 50.0000 | 76.0000 | 61.0000 | |

In Case Group, the mean WAIST CIR (mean± s.d.) of patients were 64.3000± 8.5934.

In Control Group, the mean WAIST CIR (mean± s.d.) of patients were 61.1800± 6.3429.

Difference of mean WAIST CIR with both Group was statistically significant (p=0.0415).

**Association between BMI STATUS: Group**

| | GROUP | | |
|---|---|---|---|
| **BMI STATUS** | **Case** | **Control** | **TOTAL** |
| **NORMAL** | 41 | 48 | 89 |
| Row % | 46.1 | 53.9 | 100.0 |
| Col % | 82.0 | 96.0 | 89.0 |
| **OBESE** | 6 | 1 | 7 |
| Row % | 85.7 | 14.3 | 100.0 |
| Col % | 12.0 | 2.0 | 7.0 |
| **OVERWEIGHT** | 3 | 1 | 4 |
| Row % | 75.0 | 25.0 | 100.0 |
| Col % | 6.0 | 2.0 | 4.0 |
| **TOTAL** | 50 | 50 | 100 |
| Row % | 50.0 | 50.0 | 100.0 |
| Col % | 100.0 | 100.0 | 100.0 |

**Chi-square value:** 5.1220; **p-value:** 0.0502

In Case Group, 41(82.0%) patients were NORMAL, 6(12.0%) patients were OBESE and 3(6.0%) patients were OVERWEIGHT.

In Control Group, 48(96.0%) patients were NORMAL, 1(2.0%) patients were OBESE and 1(2.0%) patients were OVERWEIGHT.

Association of BMI STATUS vs group was statistically significant (p=0.0502)

**Association between CHOLESTEROL STATUS: Group**

| | GROUP | | |
|---|---|---|---|
| **CHOLESTEROL STATUS1** | **Case** | **Control** | **TOTAL** |
| **ABNORMAL** | 4 | 0 | 4 |
| Row % | 100.0 | 0.0 | 100.0 |
| Col % | 8.0 | 0.0 | 4.0 |
| **BORDERLINE** | 6 | 1 | 7 |
| Row % | 85.7 | 14.3 | 100.0 |
| Col % | 12.0 | 2.0 | 7.0 |
| **NORMAL** | 40 | 49 | 89 |
| Row % | 44.9 | 55.1 | 100.0 |
| Col % | 80.0 | 98.0 | 89.0 |
| **TOTAL** | 50 | 50 | 100 |
| Row % | 50.0 | 50.0 | 100.0 |
| Col % | 100.0 | 100.0 | 100.0 |

**Chi-square value:** 8.4815; **p-value:** 0.0144
In Case Group, 4(8.0%) patients were ABNORMAL, 6(12.0%) patients were BORDERLINE and 40(80.0%) patients were NORMAL.
In Control Group, 1(2.0%) patients were BORDERLINE and 49(98.0%) patients were NORMAL.
Association of CHOLESTEROL STATUS 1 vs group was statistically significant (p=0.0144).

**Association between TRIGLYCERIDE STATUS: Group**

| | GROUP | | |
|---|---|---|---|
| **TRIGLYCERIDE STATUS** | **Case** | **Control** | **TOTAL** |
| **ABNORMAL** | 1 | 0 | **11** |
| **Row %** | 100.0 | 0.0 | **100.0** |
| **Col %** | 22.0 | 0.0 | **11.0** |
| **NORMAL** | 39 | 50 | **89** |
| **Row %** | 43.8 | 56.2 | **100.0** |
| **Col %** | 78.0 | 100.0 | **89.0** |
| **TOTAL** | **50** | **50** | **100** |
| **Row %** | **50.0** | **50.0** | **100.0** |
| **Col %** | **100.0** | **100.0** | **100.0** |

**Chi-square value: 12.3596; p-value: 0.0004**
In Case Group, 11(22.0%) patients were ABNORMAL and 39(78.0%) patients were NORMAL. In Control Group, 50(100.0%) patients were NORMAL. Association of **TRIGLYCERIDE STATUS** vs control group was statistically significant (p=0.0004).

**Association between Age in years & abnormal value Triglyceride vs. Group**

| | GROUP | | |
|---|---|---|---|
| **Age** | **Case** | **Control** | **P-Value** |
| **2-5 (n=14)** | 2 | 0 | 0.0455 |
| **5-10 (n=33)** | 8 | 1 | 0.0009 |
| **>10 (n=3)** | 1 | 0 | 0.1585 |
| **Total** | 11 | 1 | |

In Case Group, 2 patients were 2-5 years old, 8 patients were 5-10 years old and 1 patients were >10 years old.

In Control Group, 1 patients were 5-10 years old.

**Distribution of mean FBS: Group**

| | | **Number** | **Mean** | **SD** | **Minimum** | **Maximum** | **Median** | **p-value** |
|---|---|---|---|---|---|---|---|---|
| **FBS** | Case | 50 | 84.6200 | 8.1212 | 76.0000 | 95.0000 | 85.0000 | 0.7032 |
| | Control | 50 | 84.0600 | 6.4378 | 74.0000 | 95.0000 | 84.0000 | |

In Case Group, the mean FBS (mean± s.d.) of patients were 84.6200 ± 8.1212.

In Control Group, the mean FBS (mean± s.d.) of patients were 84.0600 ± 6.4378.

Difference of mean FBS with both Group was not statistically significant (p=0.7032).

**Distribution of mean INSULIN: Group**

| | | Number | Mean | SD | Minimum | Maximum | Median | p-value |
|---|---|---|---|---|---|---|---|---|
| **INSULIN** | Case | 50 | 1.2860 | .1654 | 1.1000 | 1.5000 | 1.3500 | 0.9486 |
| | Control | 50 | 1.2840 | .1434 | 1.1000 | 1.5000 | 1.3000 | |

In Case Group, the mean INSULIN (mean± s.d.) of patients were 1.2860 ± .1654.

In Control Group, the mean INSULIN (mean± s.d.) of patients were 1.2840 ± .1434.

Difference of mean INSULIN with both Group was not statistically significant (p=0.9486).

**Distribution of mean HDL: Group**

| | | Number | Mean | SD | Minimum | Maximum | Median | p-value |
|---|---|---|---|---|---|---|---|---|
| **HDL** | Case | 50 | 50.4200 | 5.2102 | 41.0000 | 60.0000 | 50.0000 | 0.7827 |
| | Control | 50 | 50.1200 | 5.6302 | 36.0000 | 60.0000 | 50.0000 | |

In Case Group, the mean HDL (mean± s.d.) of patients were 50.4200± 5.2102.

In Control Group, the mean HDL (mean± s.d.) of patients were 50.1200± 5.6302.

Difference of mean HDL with both Group was not statistically significant (p=0.7827).

## IV. Discussion

One of the commonest drugs used in the long term management of childhood epilepsy, is sodium valproate. Prolonged use of valproate is associated with weight gain and a host of metabolic and endocrine abnormalities.

Our study showed that out of 50 children, who were on valproate therapy for more than 1 year, 6(12%) patients developed obesity and 3 children (6%) became overweight. When BMI of these children was compared with the control population, it was found to be statistically significant(p=0.0502) .A study by Abaci A et al(1), involving 30 children on valproate months also showed significant increase in BMI when followed up for 12 months . Similar conclusions were also drawn by Kanemura H et al (2) and Pylvanen V et al (3).

Regarding the metabolic parameters, our study revealed that there was significant differences in total cholesterol (p=0.0144) Of the 50 cases 4 had abnormal levels [ male 1 , female 3 ] . Triglyceride levels also showed significant alterations (p=0.0004) between the cases and healthy controls. The age group between 5 to 10 years showed the maximum increase in triglyceride levels (p=0.0009). However our study did not reveal any significant differences in fasting blood glucose, serum insulin and HDL levels between the cases and controls.

Similar results were echoed by Abaci A et al (1). Their study involving 30 children did not reveal any significant differences regarding fasting blood glucose, serum insulin and HDL. On the contrary, total cholesterol and LDL were significantly increased.

However studies conducted by Verrotti et al (4) and Tekgul et al (5) over 2.5 and 2 years respectively did not show any significant differences between cholesterol and triglyceride levels.

There are very few Indian studies in this subject. The most prestigious study was conducted by Aditi et al (6) in 2015, where they studied metabolic parameters on children with valproate Vs those with phenytoin . They concluded that children who were on valproate showed significant rise in triglyceride and total cholesterol, when compared to children on phenytoin. However another study by Dewan et al in 2008, when comparing the metabolic derangements caused by valproate Vs phenytoin failed to demonstrate any significant differences in triglyceride and total cholesterol between the 2 groups.

## V. Conclusion

This present study we found that the risk of metabolic syndrome greater in patients with epilepsy who had received VPA treatment than in the general population. This study helps us early reorganization and timely intervention of valproate related metabolic syndrome. Thus, the lipid abnormalities may be encountered in children on valproate therapy. Periodic screening and counseling for lifestyle modifications may be warranted. Their use should be cautious in those with pre-existing risk factors for metabolic syndrome such as family history, obesity, hypertension, dyslipidemia, or insulin resistance. Whenever used, the children should get periodic screening for cardio-metabolic risk factors. The protocol for initial and periodic screening for metabolic derangements in children on long-term valproate therapy is the area for further research proposed by our observations.

## References

[1]. Hideaki K. et al. Valproate sodium enhances body weight in patients with childhood epilepsy: A pathogenic mechanism and open label clinical trial of behaviour therapy. Seizure ; 2012 : 496 -500
[2]. Abaci A, Saygi M, Yis U, Demir K, Dirik E, Bober E. Metabolic alterations during valproic acid treatment: a prospective study. Pediatric neurology. 2009 Dec 1; 41(6):435-9.
[3]. Pylvänen V, Pakarinen A, Knip M, Isojärvi J. Insulin-related metabolic changes during treatment with valproate in patients with epilepsy. Epilepsy & Behavior. 2006 May 1; 8(3):643-8.
[4]. Verrotti A, La Torre R, Trotta D, Mohn A, Chiarelli F. Valproate-induced insulin resistance and obesity in children. Hormone Research in Paediatrics. 2009; 71(3):125-31.
[5]. Tekgul H. et al. Serum lipid profile in children receiving antiepileptic drug mono therapy: is it atherogenic? Journal of paediatric endocrinal metab.2006:19: 1151 -55.
[6]. Dhir A, Sharma S, Jain P, Bhakhri BK, Aneja S. Parameters of metabolic syndrome in Indian children with epilepsy on valproate or phenytoin monotherapy. Journal of pediatric neurosciences. 2015 Jul; 10(3):222.
[7]. Dewan P, Aggarwal A, Faridi MM. Effect of phenytoin and valproic acid therapy on serum lipid levels and liver function tests. Indian pediatrics. 2008 Oct 1; 45(10):855.

Kumar Bhattacharya, et. al. "Metabolic Syndrome in Epileptic Children on Sodium Valproate Therapy." *IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)*, 20(02), 2021, pp. 55-60.