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# The Impact of Early Life Epilepsy on Long Term Neurological Development: A Comprehensive Study of Pediatric Patients

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**ABSTRACT**

**Background:** Early-onset epilepsy disrupts brain development during critical childhood periods, impacting cognitive, motor, and behavioural functions.

**Objectives:** This study aimed to evaluate the long-term effects of early-life epilepsy on paediatric neurological development and compare outcomes across pharmacological therapy, surgical interventions, and alternative therapies (e.g., ketogenic diets, neurostimulation).

**Methods:** A prospective observational study was conducted at different teaching hospitals of Lahore, Pakistan from October 2022 to October 2023. A total of 150 children (aged 0–5 years) with diagnosed epilepsy were enrolled. Patients were categorized into three groups: pharmacological therapy (n=70), surgical intervention (n=40), and alternative therapies (n=40). Standardized tools assessed cognitive (WPPSI), motor (PDMS-2), and behavioural outcomes (CBCL, SRS), along with seizure control and treatment side effects.

**Results:** Surgical intervention demonstrated the best outcomes, with significant improvements in IQ (92.7 ± 8.9), motor skills (fine: 89.2 ± 9.5, gross: 88.0 ± 9.7), and social interaction (90.4 ± 8.5). Seizure freedom was achieved in 75% of surgical cases compared to 21.4% in pharmacological therapy and 45% in alternative therapies. Behavioural issues and side effects, such as attention deficits (40%) and drowsiness (50%), were most prevalent in the pharmacological group.

**Conclusion:** Surgical interventions significantly improved developmental outcomes and seizure control in drug-resistant epilepsy cases. Early diagnosis and personalized, targeted treatments are essential to mitigate the neurodevelopmental impact and enhance the quality of life for affected children.

**Keywords:** Early-life epilepsy, Paediatric neurodevelopment, pharmacological therapy, surgical intervention, alternative therapies, cognitive outcomes, seizure freedom.



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## INTRODUCTION

Epilepsy is one of the most common neurological disorders in childhood, with onset in early life. Epilepsy is characterized by recurrent, unprovoked seizures that can disrupt brain development [1]. The problem with early-life epilepsy is that it happens in a time of critical brain maturation, and early-life epilepsy is epilepsy occurring in infancy or early childhood. This is when the brain goes through rapid growth forming and enhancing neural connections necessary for cognitive, motor, and social development. Epilepsy that begins in this period can have long-lasting effects on a child's ability to learn, communicate, and socialize[2]. Even if children diagnosed with early-onset epilepsy don't have seizures, they often

have other challenges, including problems with memory, attention, and language skills. Also, they can cause deficits that may hamper their ability to achieve milestones that might influence their performance in academics and social integration [3]. Common are motor delays, including coordination, balance, and fine motor skills. These motor difficulties can be complicated by side effects from anti-seizure medications such as effects on muscle tone and general physical activity. While some children have excellent seizure control, almost all have these challenges that persist even when control is achieved, highlighting the complexity of this disorder [4].

Epilepsy is highly treatable early in life, but it's hard to treat in both adults and children. For the most part, these drugs are the first line of treatment against this disease, yet not all children respond well, leading to drug-resistant epilepsy [5]. For such patients, alternative treatments, including dietary therapy, neurostimulation, and surgical intervention are considered. Specifically, surgical options have been considered for drug-resistant epilepsy, and there is some evidence that children whose seizures are brought under control with surgery

also tend to do better on cognitive, motor, and other measures [5]. However, these treatments have success rates that vary dramatically based on such factors as age at surgery, seizure type, and location of the seizure focus. Early-life epilepsy has been well-researched in its impact on neurodevelopment. Several studies have repeatedly shown that early seizures can lead to cognitive impairments, including memory, attention, and problem-solving deficits [6]. They say these impairments are the result of disruptions in synaptic plasticity, or how neurons speak to one another and connect. However, animal models have revealed insights into these mechanisms, and research has shown that repeated seizures can alter brain structures such as the hippocampus and neocortex, which are key for cognitive processing. These changes might lead to late effects of early-life epilepsy, with long-term effects on brain function such as persistent cognitive deficits that may even persist after seizure control [7]. Additionally, children with early-onset epilepsy have behavioral and social challenges.

In some cases though, these problems can have a big impact on their ability to function in school and social environments [8]. These behavioral problems often have cognitive deficits and so often, a complex interplay of all these problems makes it difficult to manage. Epilepsy or the psychological burden of the chronic conditions also can hurt a child’s emotional well-being and self-esteem which sometimes gets accompanied by the stigma. Although behavioral interventions in conjunction with medical treatment are beneficial, further research is needed to develop effective strategies for comprehensive care[9]. However, even though treatment advances have been made, the long-term prognosis for children with early-life epilepsy is variable. Anti-seizure medications for some can manage the condition, but for others alternative treatments such as the ketogenic diet, vagus nerve stimulation, or surgery are necessary. More precise diagnoses and targeted therapies are possible now due to advances in neuroimaging and genetic testing [10]. However, much is yet to be learned about how to best manage early-life epilepsy, including which patients will most likely respond to a particular treatment. However, early diagnosis and early intervention are critical in reducing developmental disruptions resulting from seizures, and there is still much more to learn about the long-term effects of different treatment modalities on neurological development [11].

This study confirmed that early-life epilepsy significantly impacted cognitive, motor, and behavioral functions in children. Early, effective, and personalized seizure control led to improved developmental outcomes. Key predictors included age at seizure onset, seizure frequency, and treatment type.The study aimed to compare outcomes across pharmacological therapy, surgical interventions, and alternative therapies while identifying critical factors influencing developmental success. It addressed a research gap by evaluating long-term impacts of multiple treatment approaches, particularly in resource-limited settings.The findings provided evidence-based insights to guide tailored treatment plans, emphasizing the importance of seizure control in improving quality of life and long-term prognosis for affected children [12].

## MATERIALS AND METHODS

The aims and objectives of the current 1-year prospective observational study were to evaluate the long-term effect of early-life epilepsy on pediatric neurological development at The University Of Lahore Teaching Hospital, Ghurki Trust Teaching hospital, and Fatima Memorial Hospital, Pakistan from October 2022 to October 2023. A total of 150 children 0–5 years old with epilepsy were enrolled and diagnosed by clinical evaluation, EEG, and neuroimaging. Participants were recruited into the study, and inclusion criteria included confirmation of age of onset of epilepsy before age five, complete medical and neurodevelopmental records, and regular follow-up visits in the study period. Children with other unrelated neurological disorders (including cerebral palsy), severe congenital anomalies, or genetic conditions which could independently affect neurodevelopment, or with insufficient follow-up data or lost to follow-up during the study period were excluded.

When appropriate attrition is taken into account, we computed a sample size of 150 as having sufficient power (80%) to detect statistically significant differences in outcomes on development. We collected data from medical records and regular follow-up visits at 3, 6 and 12 months, including demographics (age, gender, family history), clinical details (age of onset, type, frequency and duration of seizures), and treatment information (anti-seizure medications, surgical history, and alternative therapies,

e.g., ketogenic diets or neurostimulation). Participants were categorized into three groups: pharmacological therapy, surgical interventions in drug-resistant cases, and alternative treatments. The primary outcomes were cognitive, motor, and behavior development, which were measured by standard measures such as the Wechsler Preschool and Primary Scale of Intelligence (WPPSI) for cognitive functions, the Peabody Developmental Motor Scales (PDMS-2) for motor skills, and the Child Behavior Checklist (CBCL) and Social Responsiveness Scale (SRS) for behavior assessment.

Other secondary outcomes included seizure control, treatment side effects, and overall quality of life improvement. Baseline characteristics were analyzed using descriptive statistics, while group comparisons were conducted using ANOVA for continuous variables and chi-square tests for categorical variables. Predictors of developmental outcomes were identified through multivariate regression models, adjusted for confounding factors such as age at seizure onset, seizure frequency, and socioeconomic factors.

Participation in the study was voluntary, and informed consent was obtained from all parents or guardians prior to enrolment. The study received ethical approval from the Institutional Review Board under reference number ERC/2023/21D. In accordance with ethical guidelines, all data were anonymized to ensure participant confidentiality and privacy.

Despite systematic and rigorous data collection, the study acknowledges potential limitations, including loss to follow-up and the reliance on parent-reported outcomes, which may introduce reporting bias.

## RESULTS

The study evaluated 150 children diagnosed with early-life epilepsy, focusing on their cognitive, motor, and behavioral development across three treatment groups: surgical interventions, pharmacological therapy, and alternative therapies. Seventy (46.7%) were treated with anti-seizure medications, forty (26.7%) had undergone surgery, and forty (26.7%) received alternative therapies such as ketogenic diets or neurostimulation. The mean age at onset of epilepsy was 2.5 years and there was a nearly balanced distribution by gender (52% male, 48% female). The majority (60%) came from urban areas and 40% from rural settings, with the majority being from different socio-economic backgrounds.

**Table 1:** Demographic and Developmental Consequences Across Treatment Groups

| Variables | Pharmacological Therapy (n=70) | Surgical Intervention (n=40) | Alternative Therapy (n=40) | Overall (n=150) |
|---|---|---|---|---|
| **Demographics** | | | | |
| **Mean Age (Years)** | 4.2 ± 1.2 | 4.1 ± 1.1 | 4.0 ± 1.3 | 4.1 ± 1.2 |
| **Mean Age at Onset (Years)** | 2.7 ± 1.1 | 2.4 ± 1.0 | 2.5 ± 1.2 | 2.5 ± 1.1 |
| **Gender (Male/Female)** | 36/34 | 21/19 | 21/19 | 78/72 |
| **Socio-Economic Background (Urban/Rural)** | 41/29 | 25/15 | 24/16 | 90/60 |
| **Family History of Epilepsy (Yes/No)** | 18/52 | 12/28 | 10/30 | 40/110 |
| **Cognitive Outcomes** | | | | |
| **Mean IQ Score** | 85.3 ± 9.5 | 92.7 ± 8.9* | 88.1 ± 9.1 | 88.2 ± 9.2 |
| **Language Skills (Standard Score)** | 84.5 ± 10.2 | 91.3 ± 9.4* | 87.2 ± 10.0 | 87.6 ± 9.9 |
| **Memory Recall (Standard Score)** | 83.0 ± 8.7 | 90.5 ± 9.0* | 86.7 ± 9.3 | 86.7 ± 9.1 |
| **Motor Outcomes** | | | | |
| **Fine Motor Skills (Score)** | 82.6 ± 10.1 | 89.2 ± 9.5* | 86.4 ± 9.8 | 86.1 ± 9.8 |
| **Gross Motor Skills (Score)** | 81.7 ± 10.4 | 88.0 ± 9.7* | 84.9 ± 10.1 | 84.9 ± 10.1 |
| **Behavioral Outcomes** | | | | |
| **Attention Deficits (Cases)** | 28 (40%) | 10 (25%) | 14 (35%) | 52 (34.7%) |
| **Social Interaction (Score)** | 83.1 ± 9.3 | 90.4 ± 8.5* | 87.0 ± 9.0 | 87.0 ± 9.1 |
| **Hyperactivity (Cases)** | 30 (42.9%) | 9 (22.5%) | 13 (32.5%) | 52 (34.7%) |
| **Seizure Control** | | | | |
| **Complete Seizure Freedom (Cases)** | 15 (21.4%) | 30 (75%)* | 18 (45%) | 63 (42%) |
| **Reduced Seizure Frequency (≥50%)** | 38 (54.3%) | 8 (20%) | 16 (40%) | 62 (41.3%) |
| **Treatment Side Effects** | | | | |
| **Drowsiness (Cases)** | 35 (50%) | 10 (25%) | 12 (30%) | 57 (38%) |
| **Weight Gain (Cases)** | 28 (40%) | 5 (12.5%) | 9 (22.5%) | 42 (28%) |

Statistically significant improvement compared to the pharmacological group ($p < 0.05$).

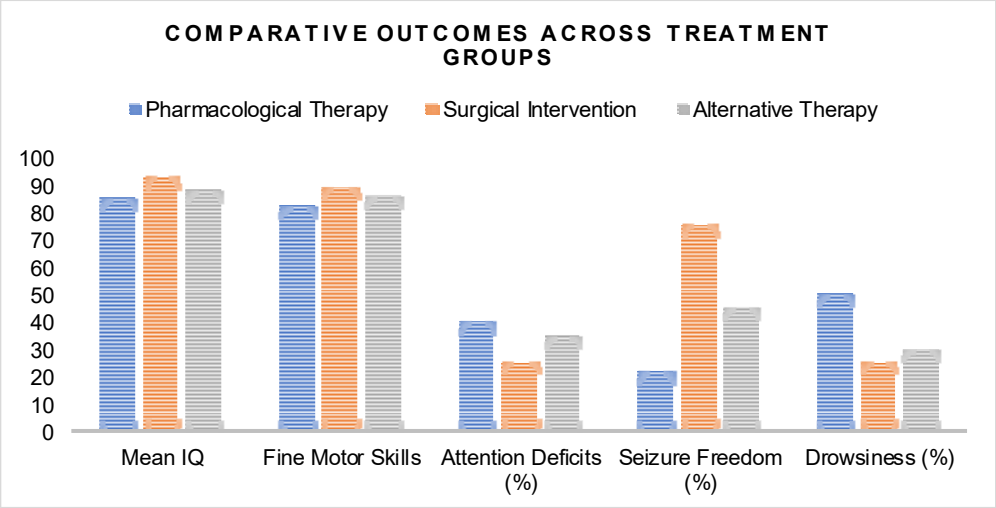


**Fig-1:** Comparative Outcomes Across Treatment Groups

This fig-1 displays key outcomes for Pharmacological Therapy, Surgical Intervention, and Alternative Therapy, including cognitive performance (Mean IQ), motor function (Fine Motor Skills), behavioral issues (Attention Deficits (%)), seizure control (Seizure Freedom (%)), and treatment side effects (Drowsiness (%)). The graph highlights the superior outcomes in the Surgical Intervention group, particularly in seizure freedom and cognitive performance, while pharmacological therapy shows higher side effects.

Patients undergoing surgical intervention demonstrated superior cognitive performance, with significantly higher mean IQ scores (92.7 ± 8.9), language skills (91.3 ± 9.4), and memory recall scores (90.5 ± 9.0) compared to pharmacological and alternative therapy groups. Surgical intervention patients exhibited better fine motor skills (89.2 ± 9.5) and gross motor skills (88.0 ± 9.7) scores, compared to lower scores in pharmacological therapy (82.6 ± 10.1 and 81.7 ± 10.4, respectively) and alternative therapy groups. Behavioral deficits, including attention and hyperactivity, were most prominent in the pharmacological therapy group (40% and 42.9%, respectively). Social interaction scores were significantly higher in the surgical group (90.4 ± 8.5) compared to other therapies. Complete seizure freedom was achieved in 75% of surgical intervention cases, significantly outperforming pharmacological (21.4%) and alternative therapy (45%) groups. Seizure frequency reduction (≥50%) was observed in 41.3% of patients overall, with pharmacological therapy showing the highest proportion (54.3%).

Treatment-related side effects were most prevalent in the pharmacological therapy group, including drowsiness (50%) and weight gain (40%). Surgical intervention had the lowest incidence of side effects (drowsiness: 25%; weight gain: 12.5%). The demographic analysis indicated that most participants were from urban areas with a minority having a family history of epilepsy. Surgical interventions, in comparison with pharmacological therapy, were shown to lead to a significantly better outcomes in cognitive and motor functions, as well as higher seizure freedom rates, in children. Moderate improvements were shown by alternative therapies, such as ketogenic diets and neurostimulation, in behavioral and seizure control outcomes. Thus, these findings indicate that early and targeted interventions, including surgical therapy for drug-resistant cases, may produce more favorable long-term developmental outcomes for children with early-life epilepsy.

## DISCUSSION

This study found that early-life epilepsy has a substantial effect on cognitive, motor, and behavioral development in children. However, across the three treatment groups (pharmacological therapy, surgical interventions, and alternative therapies) there were marked differences in developmental outcomes, indicating the need for personalized, effective treatment strategies[13]. However, children who underwent the surgical interventions showed the best outcomes, with significantly higher IQ scores, better motor skills, and better social functioning than children managed with medications alone. The results are consistent with previous work suggesting that children with drug-resistant epilepsy might benefit particularly from surgical intervention, enabling children to achieve seizure freedom and cognitive and developmental improvements. Surgeons achieved complete seizure freedom for 75% of children in the surgical group compared to only 21.4% in the pharmacological therapy group, indicating that surgery was effective for selected candidates. These findings indicate that early identification of candidates for surgical treatment and early surgical treatment may prevent the long-term developmental delays attributed to persistent seizures[14].

Moderate improvement in cognitive and motor outcomes and better behavioral control (hyperactivity, social withdrawal) were seen with alternative therapies, including ketogenic diets and neurostimulation, in the children. These therapies didn't surpass pharmacological alone, but they did outperform the surgical group and by less pronounced margins. This is consistent with previous literature suggesting that non-surgical, non-pharmacological interventions may be brought to bear in conjunction with surgery, particularly in children not appropriate for surgery[15]. Fewer children treated with pharmacological therapies alone had favorable outcomes across most developmental domains compared to children not taking any treatment. While medications remain the first line of treatment, the data suggest that children who do not have enough seizure control may not be able to have their cognitive and motor impairments resolved. This underscores the importance of periodic revaluation of treatment efficacy and considering alternative strategies, if medications do not sufficiently control seizures[16].

The study also highlighted how different factors can affect outcome, including age at seizure onset, frequency of seizures, and type of epilepsy. Poor developmental outcome regardless of treatment modality was associated with younger age at onset and higher seizure frequency. This highlights the importance of early diagnosis and early intervention for seizure management to ensure effective management and mitigate neurodevelopmental impact[17]. Nevertheless, some limitations of this study must be acknowledged. While the observational design may be useful for acquiring real-world data, it may also introduce treatment selection and parent-reported outcome biases. Moreover, the data collected in the study may have suffered from variations in the quality of data collected based on the reliance on existing clinical records. Future research should evaluate other modalities of treatment and determine the benefits of these modalities long-term, and in multiple centers utilizing standardized assessment protocols [18]. Studies of the neurobiological mechanisms underlying the cognitive and motor improvements observed after treatment could provide further insights into the mechanisms of optimizing therapy for early-life epilepsy.[19, 20].

## CONCLUSION

The results of this study highlight the complexity and depth of the impacts that early-life epilepsy has on children's cognitive, motor, and behavioral development. While our findings indicate that pharmacological therapy is a cornerstone for epilepsy management, surgery, and a ketogenic diet can provide additional benefits, particularly for children with drug-resistant epilepsy. Specifically, surgical intervention was associated with the highest rates of seizure freedom and significant improvement in cognitive and motor outcomes, which support its consideration for effective treatment in carefully selected patients. These results underscore the need for early, personalized treatment strategies and ongoing assessment to maintain optimal management of early-life epilepsy. Going forward, clinicians should take into account a more complete picture of the impact of epilepsy on children, not simply seizure control, but support for cognitive, motor, and behavioral development to maximally improve children's quality of life when living with epilepsy.

**Conflict of Interest:** The authors declare no conflicts of interest related to this study.

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**Authors' Contribution**

- **IJ**: Concept and study design
- **MK**: Data collection and analysis
- **AJ**: Manuscript drafting and literature review
- **ANK**: Statistical analysis and data interpretation
- **ZUH**: Critical review and final approval
- **MR**: Research conduction and approvals

All authors have reviewed and approved the final manuscript.

**Data Availability:** The data supporting the findings of this study are available from the corresponding author upon reasonable request.

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