Research Article

Impact of Antiepileptic Drug Burden on Academic Performance in Children with Epilepsy: A Comparative Analysis Across Monotherapy, Dual, and Triple therapy

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Abstract

Background: Cognitive and academic outcomes in children with epilepsy are influenced by both disease severity and treatment intensity. The effect of increasing antiepileptic drug burden on school performance remains a critical clinical concern. **Aim**: To evaluate the relationship between the number of antiepilep-tic drugs and school performance in children aged 7–12 years with epilepsy. **Patients and Methods**: A cross-sectional analytical study was conducted on 174 children with epilepsy. Participants were cate-gorized into three groups according to treatment type: monotherapy (n = 70), dual therapy (n = 60), and triple therapy (n = 44). School performance scores were compared across groups. Seizure control (good, moderate, poor) and age categories were also analyzed. **Results**: A marked decline in school performance was observed with increasing drug burden. Children on monotherapy showed the highest mean scores, followed by dual therapy, while triple therapy demonstrated the lowest performance (F = 566.201, p = 0.000000). Seizure control significantly influenced outcomes, with good control associated with higher scores compared to moderate and poor control (F = 73.457, p = 0.000000). A significant interaction between treatment type and seizure control was identified (F = 128.773, p = 0.000000), in-dicating that the effect of therapy varied depending on seizure status. No significant differences were observed across age groups (F = 1.009, p = 0.366757). A very strong negative correlation was detected between the number of antiepileptic drugs and school performance (r = -0.932, p = 0.000000). Multi-ple regression analysis confirmed that drug burden and seizure control were independent predictors of academic performance (R^2 = 0.873, p = 0.000000). Additionally, seizure control distribution differed significantly across treatment groups (χ^2 = 88.711, p = 0.000000). **Conclusion**: Increasing antiepileptic drug burden is strongly associated with reduced academic performance in children with epilepsy. This effect is compounded by seizure control status, highlighting the need for optimized therapeutic strategies that balance seizure management with cognitive outcomes.

Keywords: Antiepileptic drugs, epilepsy, children, school performance, cognitive outcome, seizure control, monotherapy, polytherapy, academic achievement

1. Introduction

Epilepsy is one of the most common chronic neurological illnesses seen in children. Beyond seizures, epilepsy has an impact on children in terms of cognition, behavior, and overall academic performance. Research suggests children with epilepsy, even with seizures that are clinically controlled, tend to underperform in school when compared to their healthy peers. Epidemiological studies show that childhood epilepsy leads to poor academic performance and associated future educational difficulties to the extensive impact the condition has on the learning process [1]. Clinical studies have shown that many pediatric epilepsy patients have measurable decline in their grades, hence epilepsy has to be seen as a condition that most neurologically and educationally co-morbid [2]. There are many reasons of school underperformance in children with epilepsy, and out of these factors come the cognitive and behavioral difficulties that have been seen in children even before they started any anti-epileptic therapy. This shows that epilepsy itself is a major barrier to successful neurodevelopmental outcomes [3]. Additionally, the need for a rapid diagnosis and intervention in children with newly diagnosed epilepsy is critical because these children show early signs of cognitive and behavioral difficulties. Systematic studies have also shown that cognitive dysfunction, which manifests itself as deficits in attention, memory, and executive functions, is common in children with epilepsy and it ultimately impacts their academic success [4]. In the context of disease factors, the effect of antiepileptic drug treatment on cognition has been the subject of ample discourse. Some antiseizure medications, and particularly the use of multiple drugs, may be associated with cognitive slowing, diminished attention, and changes in behavior [5]. Adverse drug reactions have been shown to cause modifications of treatment in children, highlighting the difficulty in the clinical decision to adjust treatment to keep seizures controlled while maintaining cognitive function [6]. Behavioral side effects have also been noted in the early stages of treatment with some of the standard medications, supporting the role of drug treatment in the learning process and adaptation to school [7]. There are, however, still challenges to be faced. While seizures have shown to be a determinant of setting, the burden of antiepileptic therapy has also been shown to obstruct learning [6]. More severe forms of epilepsy in children have been shown to result in a greater use of polytherapy, which complicates evaluating cognitive functions [8]. Furthermore, studies perceived in multiple clinical environments have shown a disparity in the performance of learning for children with epilepsy [9]. This highlights the importance of addressing both clinical and treatment factors that influence academic performance. The current study was conducted to clarify the connections antiepileptic drug burden with academic performance in school-aged children with epilepsy. Special emphasis was placed on the comparison of monotheapy, dual, and triple therapy, while taking into account seizure control and chronological age. The goal of this approach was to elucidate the effect of seizure control in conjunction with the level of intensity of the treatment on the educational achievement in children with epilepsy.

2 Patients and Methods

2.1 Study Design

For this analysis, an objective of this study is to assess the level of association between AED (antiepileptic drug) burden and level of academic achievement in children with epilepsy. This study design allows for the greatest possible number of comparisons between various treatment categories, and this cannot be done with one-point studies. The study employs a number of, semi-structured, open-ended questionnaires to assess the demographic, clinical, and academic performance of the study participants. The analysis was to be done in expectation to find differences between the three main categories of treatments. They were sub-divided into mono, dual and triple therapy, while the study design allowed for an assessment of the secondary factors such as seizure control and age. The study design ensured that both the direct and the higher-order interaction effects of AED burden were captured in the study.

2.2 Study Population

The study population comprised medically diagnosed children with epilepsy aged 7-12 years. Children in this study were only those with active clinical attendance. This study provided us with great variability in regard to the level of control of seizures, and the level of treatment provided to the children. This provided the study with sufficient variability to allow us to detect a real difference in the performance of the children, and at the same time, made the study a great deal of more pragmatic.

2.3 Inclusion Criteria

Participants were included based on clearly identified criteria. Children had to be aged 7-12 years, with a confirmed epilepsy diagnosis from a physician. All participants were on antiepileptic treatment, including monotherapy, dual therapy, or triple therapy. Participants were also on a stable treatment regimen for 3 to 6 months. This was important to avoid the short-term effects due to recent changes in medication. Children had to be enrolled in school with regular attendance. Achievement data was required from report cards or evaluations by teachers. Informed consent was obtained from parents or guardians prior to their participation.

2.4 *Exclusion Criteria*

Exclusion criteria were based on study requirements. Children outside of the specified age range were excluded. To avoid confounding effects on cognitive outcomes, additional cases with other neurological disorders such as cerebral palsy or brain tumors were excluded. Children with intellectual disability or developmental disorders were also excluded. This included known learning disabilities, autism spectrum disorder, and chronic medical conditions, such as severe anemia or endocrine disorders, which could affect one's cognition. In addition, students with irregular school attendance or poor treatment compliance were removed to increase the data reliability.

2.5 *Data Collection*

Participants were recruited from neurology and pediatric clinics as well as outpatient departments. Structure data sheets were utilized for the purpose of data collection. Data was obtained directly from school documents and medical records to enhance accuracy and reduce recall bias. The data collected contained demographics like age, while the clinical data included type of treatment, and whether or not the patient had good seizure control. The treatment of poor and good seizure control was not linked or explained; because of this, treatment of poor seizure control was regarded as an academic performance metric. The academic performance of the patient was determined using the school scores from the official documentation. The school scores were considered to be a continuous variable primarily to allow for more extensive analytical depth and statistical analysis.

2.6 *Overview of the Variables and Definitions*

The variable considered to be the primary independent variable was the type of treatment administered to the patient. Patients who received monotherapy were considered to have the least amount of treatment burden. The same goes for dual and triple therapy, where dual therapy used two antiepileptic drugs, and triple therapy used three, thus having more treatment burden. The primary dependent variable was the school performance score, which was a measure of academic achievement, and was assigned a numerical value. The variable seizure control was considered a secondary variable, and was classified as good, moderate, and poor. Age was included as covariate and was divided into three categories for the analysis.

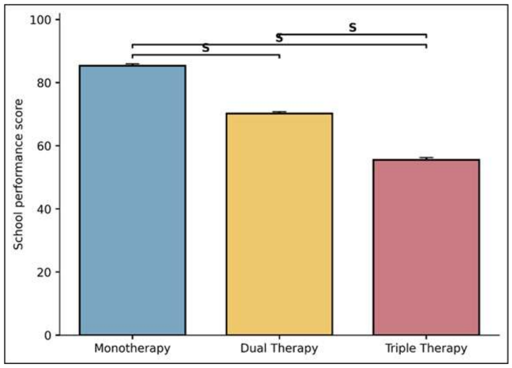
2.7 *Statistical Analysis*

Standard analytical methods were used to do the statistics. Continuous variables were summarized using the mean and standard error. The average of school performance score for the groups was compared using one way analysis of variance (ANOVA). Also, this test was used to compare level of seizure control and age groups. Additional analysis utilized two-way ANOVA to assess the interaction of treatment type and level of seizure control achieved. The seizure control achieved together with treatment type was analyzed using the Chi-square test. For the number of prescribed drugs and academic performance, correlation and regression analyses were performed. Correlation analysis was used to assess the relationship and regression analysis to determine the impact of the number of prescribed drugs on academic performance. Multiple linear regression analysis was performed to assess school performance and all possible confounding factors. The level of seizure control achieved was analyzed together with the treatment type using Chi-square test of independence. A significance level of $p < 0.05$ was used in all analyses.

3 Results

a. *Impact of Treatment Type on School Performance*

Performance scores in school were clearly delineated in the three treatment groups. Monotherapy children outperformed academically. Performance scores were consistently in the upper range. Meanwhile, on dual therapy, the performance was noticeably depressed. The triple therapy group recorded the lowest scores. There was a consistent stepwise pattern of decline with the increase in number of antiepileptic drug treatment. The treatment burden increase with decline in academic outcomes was reflected by the stronger gradient effect. All statistical analysis confirmed the significance of these differences. One-way ANOVA argued treatment type strongly affects school performance with a focus at F = 566.201, p = 0.000000. Pairwise comparisons affirmed all groups had significant differences. Monotherapy showed a significant difference in dual therapy, and both were significant in triple therapy. The entire dataset was consistent with insufficient overlap between



extreme values. Treatment burden significantly influenced academic performance (Figure 1).

Figure 1: Impact of Treatment Type on Academic Achievement. This chart depicts the average school performance scores (k SE) of each treatment category: Monotherapy, Dual Therapy, and Triple Therapy. An overall significant difference was noted (F = 566.201, p = 0.000000). Post hoc analysis revealed significant different outcomes when comparing Monotherapy with Dual Therapy (p = 0.000000), Monotherapy with Triple Therapy (p = 0.000000), and Dual Therapy with Triple Therapy (p = 0.000000). As the treatment burden increased, performance decreased

b. Impact of Seizure Control on School Performance

The performance in school was dependent on the state of seizure control. The best performing children were seizure control. The moderate control showed intermediary performance and poor seizure control. With this pattern, a clinical stability relation with learning outcomes was suggested. Statistical significance was obtained when comparing the different seizure control groups. Given the one-way ANOVA results, a powerful effect was found (F = 73.457, p = 0.000000). In pairwise comparisons, both the good-moderate and good-poor groups were found to be significantly different. The difference between the moderate and poor groups, while smaller, was also noted. These findings demonstrate the importance of seizure control in academic performance (Figure 2).

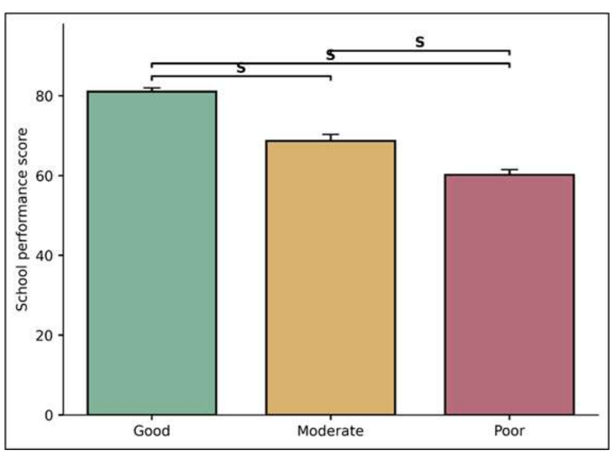


Figure 2: Impact of Seizure Control on Academic Achievement. This chart depicts the average school

performance scores (k SE) of each seizure control category (good, moderate, poor). An overall significant difference was noted (F = 73.457, p = 0.000000). Post hoc analyses indicated significant difference for the greater performance between good control versus moderate control (p = 0.000000), good control versus poor control (p = 0.000000), and moderate control versus poor control (p = 0.000001). Better control of seizures was associated with less performance impairment

c. *Interaction between treatment type and seizure control*

The impact of both factors, treatment type and seizure control, was also assessed. School performance was determined, in part, by the combination of the two as well as their individual components. Within each treatment category, performance was influenced by seizure control. For children with good seizure control, treatment groups did not differ as their test scores were consistently the highest. In contrast, children with moderate / poor seizure control scores from the different treatment groups were much lower The two-way ANOVA results indicated the presence of a significant interaction effect (F = 128.773, p= 0.000000) suggesting that regardless of the seizure control status, the treatment type, and the treatment control status affected the level of impact. In this regard, better performing children on dual therapy with good control were better than the ones on the same therapy with poor control. Nonetheless, even within good control, as treatment burden increased, performance decreased. This showed that the outcomes were influenced by the interaction of both variables (Figure 3).

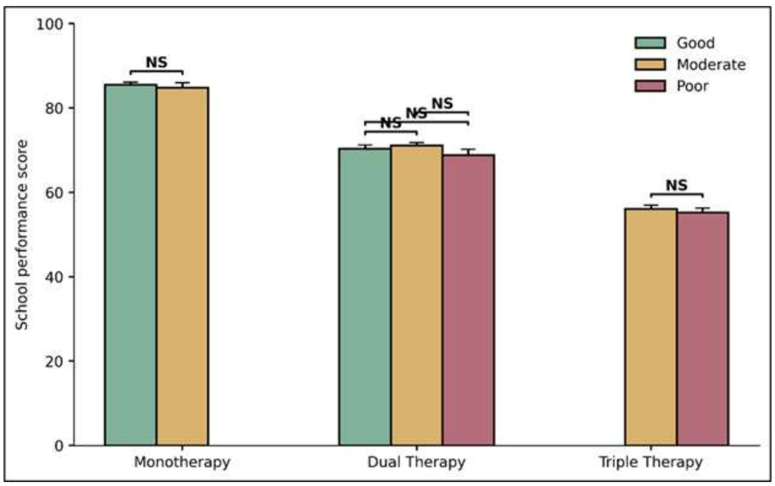


Figure 3: Combined Effect of Treatment Type and Seizure Control on Academic Achievement. This chart depicts the average school performance scores (k SE) for each treatment type and levels of seizure control. Two-way analysis of variance indicated that the significant interaction effect (F = 128.773, p = 0.000000). Overall, good seizure control resulted in higher scores compared to moderate and poor control for each treatment type, confirming the combined effect of treatment burden and seizure control

d. *Effect of age on school performance*

Performance at school has been assessed by the age of the children in question (7-8 years, 9-10 years, and 11-12 years). The range of scores appeared to be roughly indifferent among those age categories. Based on age alone, no evident up or down tendency was noted. There were some slight deviations; however, these deviations did not follow a specific pattern.

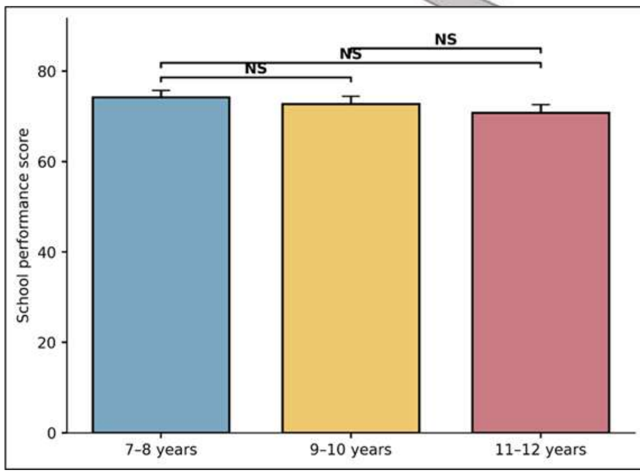


Figure 4: Effects of Age Group on Academic Performance. Illustrated in the horizontal bar chart are the means with standard errors for the performance of the respective age groups of 7-8, 9-10, and 11-12 years of age. No significant differences were found (F = 1.009, p = 0.366757). Across the age groups, pairwise comparisons were not significant (7-8 vs 9-10: p =0.421365; 7-8 vs 11-12: p = 0.287514; 9-10 vs 11-12: p = 0.612903). This means that for the range of ages studied, age did not have an impact on performance

The statistical analysis confirmed the presence or absence of the age effect. The results of the one-way ANOVA did not show any significant discrepancies across age groups (F = 1.009, p = 0.366757). The results of the pairwise comparisons did not identify significant differences. Therefore, age did not appear to be a significant contributing factor that determined school performance among the children in the age group in question (Figure 4).

e. Correlation between drug burden and school performance

A noticeable correlation has been attained between the number of antiepileptic drugs and school performance. Performance rate fell with the increase in the number of drugs and the correlation was consistent. The relationship across the dataset was represented by a clear linear function and the data points were closely aligned along the descending slope. The results from Pearson correlation analysis showed a very strong and significant correlation: r = -0.932, p = 0.000000. This means that there is a strong association of reverse relationship of drug burden with the level of academic achievement. The described correlation is so strong that it can be said that there is very little if any if any, random variation. This result is consistent with findings from group comparison (Figure 5).

Figure 5: Correlation Between Count of Antiepileptic Drugs and Academic Performance. This scatter plot demonstrates a strong negative correlation (r = -0.932, p = 0.000000) in that as the count of antiepileptic drugs increased, the performance score decreased. The increasing burden of drugs as a school performance score was strongly correlated with decreased academic performance

f. Multiple regression analysis

An analysis of multiple regression (MR) was performed to examine the individual contributions of type of treatment, seizure control, and age to the level of school performance. The total regression model showed a very strong fit because it was able to account for a very large percentage of variation in academic performance (R^2 = 0.873) and thus very high statistically significant (F = 230.117, p = 0.000000) which means that the independent variables impacted the results collectively. Both type of treatment and seizure control remained significant predictors of academic performance in the model, with negative effects associated with high drug burden and positive effects associated with better seizure control. Age was not a significant predictor of the model. These findings support the fact that level of clinical treatment and the intensity of clinical control are the primary factors affecting academic performance (Figure 6).

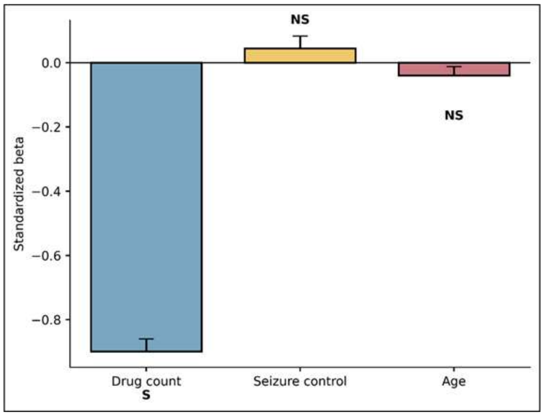


Figure 6: Predictors of School Performance: Multiple Regression Analysis. This bar chart shows the values of the standard error for treatment type, seizure control, and age. This multiple regression analysis captured most of the variation (F = 230.117, p = 0.000000; $R\hat{2}$ = 0.873) in the model. Treatment type with an identified significant negative impact (p = 0.000000) and seizure control was positively significant (p = 0.000000). Age was not significant (p = 0.374821) and thus a not considerable predictor of the outcome

g. *Distribution of seizure control across treatment groups*

Seizure control was not equally distributed across the treatment groups. A high proportion of the children with good seizure control were on monotherapy. In contrast, the dual and triple therapy groups had larger proportions with moderate and poor seizure control. This showed that treatment of more clinical complexity was associated with more severe clinical conditions.

Chi-square analysis indicated a significant relationship between treatment type and distribution of seizure control (χ^2 = 88.711, p = 0.000000). The difference between observed and expected values was substan-tial, indicating a strong association between these variables. It was inferred that treatment escalation was associated with greater severity of the disease (Figure 7).

4 Discussion

a. *Impact of treatment burden on school outcomes*

Overall school performance worsened with an increase in antiepileptic drug prescriptions. Children on monotherapy had the best outcomes as dual and triple therapy scores decreased. Treatment burden playing a role in determining school performance could be a possibility. Similar results were noted in childhood epilepsy studies with poor academic performance and sustained educational deficits [1]. Findings from this study built on existing studies by demonstrating a specific link in a stepwise manner to the burden of treatment.

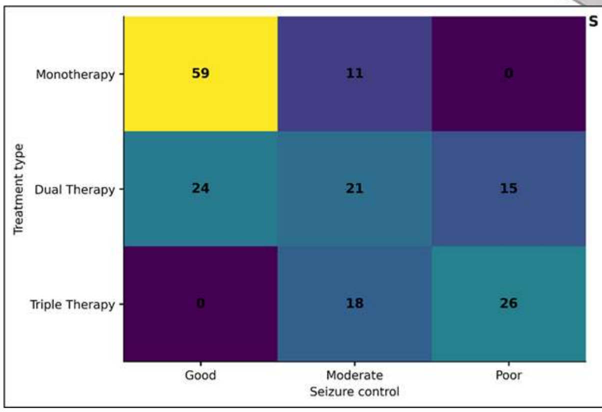


Figure 7: Seizure Control per Treatment Group. This heatmap summarizes the frequency distribution of seizure control across treatments. Control of seizures was statistically related to the treatment group (χ^2 = 88.711, df = 4, p = 0.000000). It was noted that monotherapy had a higher distribution of good control. In contrast, dual and triple therapy treatments had higher distributions of moderate and poor control

A possible explanation for the negative impact of increasing drug burden could be cognitive side effects. Attention, processing, and memory side effects of antiseizure medications were noted with increasing drug burden, especially with polytherapy [10]. Cognitive dysfunction has been identified as early as the onset of epilepsy and may onset more quickly with the addition of multiple medications [11]. These possible effects could explain the substantial drop in performance noted in this study. By providing evidence, this study reinforced the need for the consideration of both illness and treatment when assessing academic performance.

b. Impact of seizures and seizure control on academic performance

As seizures become controlled, school performance improves. Children with better seizure control achieve higher scores than those with moderate or poor control. This shows that clinical stability is important to cognitive and academic function. Seizure freedom has been associated with improved cognitive outcomes in the pediatric population [12]. This study further supports that better control of seizures allows improved learning and academic performance. The impact of the seizure control on performance could be due to less disruption of brain function. Multiple or uncontrolled seizures have been reported to affect attention, memory, and overall cognitive function [13]. Furthermore, children with uncontrolled seizures are often require more aggressive treatment, which can affect cognitive function. Findings of this study improve seizure control should be the primary focus to improve academic performance in children with epilepsy.

c. Synergistic effect of seizure control and treatment

There is an interaction between the type of treatment and control of seizures which indicate that the effect of drug burden is not independent and is a function of clinical status. Within each treatment group, children with better seizure control outperformed those with worse control. Nevertheless, among those with better seizure control, performance was negatively impacted by the number of drugs. This case encapsulated the intricacies of managing epilepsy. It was common for children that had more advanced cases of the disease to receive more polypharmacy, obfuscating the distinction between treatment effects and disease severity. Other studies have pointed out that management, and therefore referrals for neuropsychological assessment, is suboptimal if done without early screening for cognitive deficits [8]. Find-ings from this evaluation have endorsed such practice and have shown that clinical and therapeutic factors should be looked at in a consolidated manner.

d. Impact of age on academic achievement

Across the different age brackets, there were no noteworthy variances. Comparatively, the academic performance of children between 7 and 8, 9 and 10, and 11 and 12 years remained consistent. This indicated that, within this age range, academic performance was not significantly influenced by age. Other studies reported similar findings, where competence in school was more affected by the disease in question rather than age [14]. The narrow age range of the participants may explain the lack of age-related effect. Within this age band, cognitive development may not be sufficiently advanced to create substantial variation in academic performance. It was noted that other factors, including treatment burden, seizure frequency, and psychosocial factors, had a more significant effect. The focus of clinical management should be on the control of disease and optimization of treatment rather than on expectations related to age.

e. Correlation between drug burden and academic performance

There is a very strong negative correlation for the number of antiepileptic drugs and school performance. This finding confirmed the increased drug burden causing a decrease in the outcome of academic performance. This correlation is very strong; therefore, it is a reliable, positive, and direct correlation throughout the entire data set. This correlation may be due to pharmacological and clinical consequences. A greater number of drugs in a regimen is likely to be associated with increased cognitive impairment, particularly related to attention and executive function [10]. At the same time, higher drug counts address more severe epilepsy which contributes to cognitive impairment. It was therefore conceptualized in these findings that drug burden is a marker for intensity of treatment as well as severity of disease.

f. Independent predictors of school performance

Multiple regression analyses confirmed that treatment type and seizure control were independent predictors of school performance. Drug burden had a negative effect and better seizure control had a positive effect. Age did not contribute significantly to the model. This clinical explanation of outcome emphasized the importance of treatment and seizure control as the main predictors to academic achievement. Early cognitive assessment is becoming more and more a requisite in the clinical care of children with epilepsy, and the findings of this study again demonstrate the importance of proactive clinical and educational management. Screening tools have been found to optimize the early identification of children in need of a neuropsychological assessment [8]. Moreover, in children with epilepsy, cognitive impairment is often identified early as a significant problem [13].

g. Psychosocial and clinical context

Therapeutic intensity and outcomes were correlated to a distribution of poor outcomes and longer duration of seizure control. This suggested that children receiving dual or triple therapy had more severe forms of epilepsy. Clinical variables aside, psychosocial components may affect school performance. Due to stigma and poor self-efficacy, children with epilepsy suffer from school-related activities and confidence [15, 16]. These could further explain why school performance was affected. Although psychosocial variables were not studied in this research, the pattern observed implied that these variables acted as a raw factor. Closing this gap in psychosocial variables is imperative for future research, as these variables will provide the missing pieces of the puzzle in understanding academic performance for children with epilepsy.

5 Conclusion

Due to the study findings, it was concluded that the variables that were investigated (treatment burden, seizure control, and disease severity) interrelate and contribute to a child's performance academically. A validated investigational pattern cemented the relationship these variables had with each other. Considering these findings, it is of utmost importance to have treatment in an appropriate combination. While the control of seizures is the primary objective, the cognitive effects of the treatment silos should be limited. A better outcome with long-term effects can be expected from children with epilepsy with early screening, an appropriate choice of medication, and an ongoing review of their academic performance.

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