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Exploring the Clinical Features and Treatment Outcomes of Autoimmune Encephalitis in Pediatric Patients: A Cross-Sectional Analysis

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ABSTRACT

Background: Autoimmune encephalitis is an increasingly recognized cause of acute neurological dysfunction in children and can present with a wide spectrum of neuropsychiatric and neurological symptoms. Prompt diagnosis and treatment are important for favourable outcomes, especially in resource constrained settings. **Objectives:** This study was an objective to explore the clinical features, diagnostic profiles and treatment outcomes of pediatric patients with autoimmune encephalitis in a tertiary care hospital in Lahore, Pakistan. **Methods:** It is a cross sectional study that was carried out at a tertiary care hospital in Karachi from January to December 2024. A total of 52 children aged 1 to 18 years with confirmed autoimmune encephalitis were included. Clinical presentations, antibody subtype, neuroimaging, cerebrospinal fluid (CSF) analysis, treatment, and outcome at discharge and at three months clinic follow up were recorded. **Results:** Behavioral changes (76.9%), seizures (69.2%), altered consciousness (61.5%), and other (45.7%) were the most common presenting symptoms. The most frequent subtype was anti-NMDAR encephalitis (61.5%). EEG abnormalities were found in 80.8%, and pleocytosis in the CSF 67.3%. Corticosteroids were given to all patients and 76.9% received IVIG, 28.8% underwent plasmapheresis. Indeed, by three months, 80.8 percent of patients had full or nearly complete recovery, and 7.7 percent relapsed. Improved outcomes ($p = 0.03$) correlated with early initiation of immunotherapy. **Conclusion:** The range of symptoms seen with pediatric autoimmune encephalitis can make this entity a challenge to recognize, treat promptly, and mitigate the morbidity caused by this illness. An early diagnosis followed by aggressive immunotherapy is associated with favorable outcomes and demands heightened clinical awareness with standardization of management protocols.

INTRODUCTION

Over the past two decades, AE has become a major cause of acute and subacute encephalopathy in both adult and paediatric patients secondary to progress in antibody testing and improved clinical awareness (Santoro et al., 2024; Ancona et al., 2022). AE is characterized by immune mediated inflammation of the brain and has been reported with a broad spectrum of neurological and psychiatric symptoms including seizures, altered mental status, behavioral changes, memory deficits, movement disorders (Ford et al., 2022). Traditionally thought of as rare, recent studies have shown that AE may be as common as infectious encephalitis in children and it is important to diagnose and treat AE early especially because outcomes for AE are better when caught early.

Pediatric AE, in particular, poses unique diagnostic challenges. Children often present with non-specific symptoms such as irritability, sleep disturbances, or regression in milestones, which can delay the identification of an autoimmune etiology(Shalbafan, 2023). Among the various subtypes of AE, anti-N-methyl-D-aspartate receptor (NMDAR) encephalitis is the most commonly reported in children, especially females, and is often associated with tumors such as ovarian teratomas in older adolescents (Li et al., 2022; Joseph et al., 2024). However, pediatric cases are less likely than adults to have an underlying tumor, and the absence of such associations often complicates the diagnostic process.

Timely diagnosis is crucial because delayed treatment is associated with prolonged hospital stays, poor neurological recovery, and increased morbidity (Wright et al., 2022; Awashra et al., 2024). Diagnosis is typically based on clinical presentation, supported by investigations such as cerebrospinal fluid (CSF) analysis, magnetic resonance imaging (MRI), electroencephalogram (EEG), and antibody testing (Endres et al., 2024; Pankratz et al., 2023). However, the full diagnostic workup may not always be feasible in resource-limited settings like Pakistan due to limited access to antibody panels and neuroimaging. As a result, many children remain undiagnosed or are misdiagnosed with psychiatric or infectious disorders, delaying the initiation of immunotherapy and potentially leading to irreversible neurological damage (Kumar, Zelena, & Gautam, 2024; Flanagan et al., 2023).

Typically, therapeutic strategies for AE involve immunosuppressive treatments, such as corticosteoroids, intravenous immunoglobulin (IVIG), and plasmapheresis, which are referred to as first-line therapies (Dinoto et al., 2022; Mahadeen et al., 2024). Second line agents like rituximab or cyclophosphamide may be used in refractory cases or relapses (Kanters et al., 2023; Nguyen & Wang, 2023). However, existing literature consistently demonstrates that for immunotherapy the earlier the better, and patients treated early, preferably in the first four weeks after symptom onset, have significantly better functional outcome and fewer long term cognitive deficits. Outcomes vary widely based on the type of antibody involved, the initial severity of presentation and, in the case of severe disease, when treatment starts. Overall, most children do better than adults.

In the context of Pakistan, data on pediatric AE is extremely limited, with few studies documenting its prevalence, clinical presentation, or response to treatment. Given the challenges in diagnostic resources and the scarcity of standardized treatment protocols in local settings, there is a pressing need to better understand the disease spectrum in children to guide clinical decision-making. Moreover, most international data may not be directly applicable due to differences in healthcare infrastructure, accessibility to advanced diagnostics, and sociocultural factors that may delay seeking medical care.

METHODOLOGY

This study was conducted as a cross section at a tertiary care hospital in Karachi from January to December 2024. The objective was to evaluate the clinical features and outcome of the treatment in autoimmune encephalitis among pediatric patients. Children 1 to 18 years old with an established clinical diagnosis of autoimmune encephalitis and appropriate neuroimaging, cerebrospinal fluid analysis, and relevant autoimmune antibody panels were included in the study population. Exclusion criteria included patients with infectious encephalitis, metabolic disorder, or known genetic syndromes to allow maximal diagnostic specificity.

All eligible patients presenting to the hospital during the study period were enrolled consecutively after obtaining informed consent from their parents or legal guardians. Data were collected using a structured proforma, which included demographic details, clinical presentation, duration of illness prior to diagnosis, types of autoimmune encephalitis (anti-NMDAR, anti-GAD, etc.), laboratory and imaging findings, therapeutic interventions (including immunotherapy, corticosteroids, intravenous immunoglobulin, and plasmapheresis), and short-term outcomes at discharge and at a three-month follow-up. Outcomes were assessed in terms of clinical improvement, residual neurological deficits, and relapse rates. Statistical analysis was performed using SPSS version 26.0, with descriptive statistics used to summarize the data and chi-square tests applied to determine associations between clinical variables and outcomes, with a significance level set at $p < 0.05$.

RESULTS

During the study period from January to December 2024, a total of 52 pediatric patients were diagnosed with autoimmune encephalitis at General Hospital Lahore and met the inclusion criteria. The cohort consisted of 30 males (57.7%) and 22 females (42.3%), with a mean age of 10.2 ± 3.6 years (range: 2–17 years). The majority of patients (63.5%) were between 6 and 12 years old.

The most common presenting symptom was behavioral changes (76.9%), followed by seizures (69.2%), altered consciousness (61.5%), and movement disorders (46.2%). Less commonly reported features included speech disturbances (34.6%), autonomic instability (28.8%), and psychosis (17.3%). Fever at onset was reported in 40.4% of cases.

Table 1

Frequency of Presenting Symptoms in Pediatric Autoimmune Encephalitis (n = 52)

Symptom	Frequency (n)	Percentage (%)
Behavioral changes	40	76.9
Seizures	36	69.2
Altered consciousness	32	61.5
Movement disorders	24	46.2
Speech disturbances	18	34.6
Autonomic instability	15	28.8
Fever	21	40.4
Psychosis	9	17.3

Anti-NMDAR encephalitis was the most commonly identified subtype (61.5%), followed by anti-GAD (15.4%), anti-LGI1 (7.7%), and seronegative autoimmune encephalitis (15.4%). MRI abnormalities were detected in 30 patients (57.7%), most commonly involving temporal lobe hyperintensities. CSF

pleocytosis was found in 35 patients (67.3%), and EEG abnormalities were present in 42 patients (80.8%).

Table 2
Diagnostic Markers in Pediatric Autoimmune Encephalitis

Diagnostic Parameter	Positive Cases (n)	Percentage (%)
MRI Abnormalities	30	57.7
CSF Pleocytosis	35	67.3
EEG Abnormalities	42	80.8
Anti-NMDAR Antibodies	32	61.5
Anti-GAD Antibodies	8	15.4
Anti-LGI1 Antibodies	4	7.7
Seronegative Cases	8	15.4

All patients received first-line immunotherapy. High-dose intravenous corticosteroids were administered to 100% of patients, while 76.9% received intravenous immunoglobulin (IVIG). Plasmapheresis was used in 15 patients (28.8%), mainly in severe or refractory cases. Second-line immunotherapy (rituximab) was required in 10 patients (19.2%).

At the time of hospital discharge, 36 patients (69.2%) had marked clinical improvement, while 10 (19.2%) had partial improvement with residual neurological deficits. Six patients (11.5%) showed minimal or no improvement. During the three-month follow-up, 42 patients (80.8%) achieved full or near-complete recovery, 6 (11.5%) had persistent neurological deficits, and 4 (7.7%) experienced relapse.

Table 3
Treatment Outcomes

Outcome	Discharge (n/%)	3-Month Follow-Up (n/%)
Full recovery	20 (38.5%)	35 (67.3%)
Near-complete recovery	16 (30.7%)	7 (13.5%)
Partial improvement	10 (19.2%)	6 (11.5%)
No improvement	6 (11.5%)	0 (0%)
Relapse	-	4 (7.7%)

Statistical analysis showed that early initiation of immunotherapy (within 10 days of symptom onset) was significantly associated with better outcomes at 3 months ($p = 0.03$). The presence of anti-NMDAR antibodies also correlated with favorable prognosis ($p = 0.04$).

DISCUSSION

This cross-sectional study provides insight into the clinical spectrum, diagnostic characteristics, treatment modalities, and short-term outcomes of autoimmune encephalitis in pediatric patients at a tertiary care center in Pakistan. The findings align with global literature in many aspects while also highlighting unique regional observations.

Increasingly, autoimmune encephalitis contributes to a significant number of pediatric encephalopathies with presentations of neuropsychiatric symptoms, seizures and altered mental status. The predominance of behavioral changes and seizures as features of presentation is consistent with previous reports, and, in particular, with anti-NMDAR encephalitis. Like in, Dalmau et al. (2011) review cites similar neuropsychiatric profiles, which could delay diagnosis because initially invoke psychiatic condition.

While the male predominance in our sample (57.7%) is slightly different from international studies which usually show a female preponderance, in particular in anti-NMDAR encephalitis, it occurs more often in parasitic encephalitis and in other diseases caused by F. heterocola. Sensitivity to this gender variation may be due to sampling bias or regional demographic trends. The onset of this period of increased susceptibility in children aged 6–12 years corresponds to established periods of increased susceptibility in other pediatric studies, which may be related to maturation of the immune system as well as exposure to triggering infections.

These studies also showed a high prevalence of abnormal EEG (abnormal in 80.8%) and CSF pleocytosis (abnormal in 67.3%) and demonstrated their utility in early diagnosis. Although MRI findings were less frequent (57.7%) , they were valuable especially when temporal lobe abnormalities were present. This study confirms that a complete diagnostic approach (combining clinical findings, CSF analysis, EEG, MRI and antibody testing) is important to accurately identify the syndrome and initiate early treatment.

Anti-NMDAR encephalitis emerged as the most common subtype, accounting for over 60% of cases, consistent with global data. The high percentage of anti-GAD and seronegative cases underlines the need for broader diagnostic panels, especially in resource-limited settings. The recognition of seronegative autoimmune encephalitis remains critical, emphasizing the role of clinical suspicion and ancillary testing even in the absence of confirmatory antibodies.

Regarding treatment, all patients received first-line immunotherapy, with corticosteroids and IVIG forming the backbone of management. Plasmapheresis was selectively employed in patients with severe or refractory symptoms, mirroring practices in other tertiary centers. The need for second-line agents such as rituximab in nearly 20% of cases reflects the refractory nature of some subtypes, particularly in delayed diagnosis or when initial treatment is suboptimal.

The short-term outcomes in our cohort were encouraging, with over 80% achieving full or near-complete recovery at three months. These outcomes are comparable to those reported by Titulaer et al. (2013), who found that early and aggressive immunotherapy leads to better neurological recovery in pediatric autoimmune encephalitis. Importantly, our data revealed that early initiation of treatment—within 10 days of symptom onset—was significantly associated with

favorable outcomes. This reinforces the importance of clinical vigilance and rapid initiation of immunotherapy, even before antibody results are confirmed.

Importantly, 7.7% of patients had a relapse within three months, which is within the range previously reported. Most of these relapses were managed with reinitiation of immunotherapy without increased mortality or irreversible damage, further illustrating the need for follow-up of greater than a few years, as well as caregiver education regarding early signs of recurrence.

Limitations of this study include single center design and small sample, and thus possible lack of generalizability. Furthermore, both long term outcomes beyond three months were not recorded, and neurocognitive recovery, an important domain in pediatric populations, was not systematically evaluated. In addition, there was limited availability of access to antibody tests based on financial and logistical constraints, and this may have resulted in underdiagnosis of some subtypes.

However, it shows limitations of this study, but also the crucial aspects of pediatric autoimmune encephalitis that are relevant for clinicians in low-resource settings. Increased awareness, along with standardized diagnostic protocols and development of national guidelines for optimal time and complete treatment, are advocated as a result of the findings. More multicenter, longitudinal studies are needed to fully understand the fetal and long-term neurodevelopmental impact as well as to optimize treatment strategies suited for the pediatric population.

CONCLUSION

The concept that pediatric autoimmune encephalitis is a heterogeneous disease with important clinical heterogeneity is underscored in this study and emphasizes the importance of early recognition. The most common features were behavioral changes, seizures, and altered consciousness; anti-NMDAR was the predominant subtype. Most patients received timely diagnosis supported by EEG, MRI, and CSF findings, and early immunotherapy, resulting in favorable outcomes. Early treatment has the important association with improved recovery, underlining the need for greater clinical vigilance and early intervention. The study is limited in its single center design; however, it provides clinically relevant insights in these resource limited settings. Longer term cognitive and functional outcomes for children affected should be the focus of future multicenter research so as to optimize their care.

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