Systematic Review

Long-Term Outcomes and Sequelae in Patients with Anti-NMDA Receptor Encephalitis in India: A Systematic Review

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Abstract

Background: Anti-N-methyl-D-aspartate receptor (anti-NMDAR) encephalitis is a potentially reversible autoimmune encephalitis, but cognitive, behavioural, neurological, and functional sequelae may persist despite apparent clinical recovery. Evidence regarding long-term outcomes in Indian patients remains limited. The objective is to systematically review and narratively synthesize the available evidence on long-term outcomes and sequelae of anti-NMDAR encephalitis in India. **Material and Methods:** A systematic review was conducted in accordance with PRISMA 2020. MEDLINE/PubMed, Embase, Scopus, and Web of Science were searched, with supplementary reference and citation searching, through 1 August 2026. Studies conducted in India reporting outcomes at least six months after disease onset, diagnosis, treatment initiation, or hospital discharge were eligible. Data on functional, neurological, cognitive, psychiatric, behavioural, educational, occupational, and social outcomes, as well as relapse, mortality, and prognostic factors, were narratively synthesized because of clinical and methodological heterogeneity. **Results:** Of 388 records identified, 46 full-text reports were assessed and three studies comprising 40 reported patients met the inclusion criteria. The evidence was predominantly paediatric and derived from tertiary-care centres. Substantial neurological and functional improvement was reported; however, persistent sequelae included cognitive and behavioural impairment, speech-language dysfunction, motor deficits, and educational difficulties. Relapse was reported in two studies. Abnormal baseline magnetic resonance imaging was associated with poorer one-year functional outcome and more frequent relapse in one cohort. Interpretation was limited by small samples, heterogeneous follow-up, selected populations, and inconsistent use of standardized multidomain outcome measures. **Conclusion:** Indian evidence suggests that favourable functional recovery after anti-NMDAR encephalitis may coexist with persistent neuropsychiatric and participation-related sequelae. Long-term follow-up should extend beyond global disability measures, and larger prospective multicentre Indian studies using standardized multidomain assessments are needed.

Keywords: anti-NMDA receptor encephalitis; autoimmune encephalitis; long-term outcomes; cognitive sequelae; neuropsychiatric outcomes; relapse; India; systematic review.

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Introduction

Anti-NMDA Receptor Encephalitis: Anti-N-methyl-D-aspartate receptor (anti-NMDAR) encephalitis is an antibody-mediated neurological disorder characterized by a complex combination of psychiatric, cognitive, neurological, and autonomic manifestations. It was initially described in association with ovarian teratoma and subsequently recognized as a distinct autoimmune encephalitis affecting a broader spectrum of patients, including children, adolescents, and adults.[1,2] The disorder is mediated by antibodies directed primarily against the GluN1 subunit of the NMDAR, resulting in receptor internalization and disruption of glutamatergic neurotransmission.[3]

The clinical course typically starts with behavioral changes, psychiatric symptoms, memory impairment, or language impairment, and can then evolve into seizures, movement disorders, altered consciousness, autonomic instability, and central hypoventilation.[4] Children can present with different symptoms than adults, and seizures, movement disorders, behavioural disturbance and speech dysfunction are often prominent.[5] Early recognition can be difficult as the presentation may mimic a primary psychiatric or infectious disorder. Modern diagnostic criteria for autoimmune encephalitis thus focus on clinical diagnosis and appropriate CSF, antibody, electroencephalographic, and neuroimaging evaluation.[6]

Long-Term Recovery and Sequelae: Earlier diagnosis, immunotherapy, tumour removal if appropriate, and intensive supportive care have significantly improved the prognosis of anti-NMDAR encephalitis. In the landmark international cohort reported by Titulaer et al., about four-fifths of patients had a favourable functional outcome at 24 months, and earlier treatment and lower acute disease severity were correlated with

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better outcomes.[7] However, recovery can take months or years after the acute encephalitic phase. Importantly, a good neurological outcome in the world does not mean full recovery. Neuropsychological deficits have been reported even in patients who become functionally independent. Finke et al. showed marked residual impairments, especially in memory and executive functioning.[8] Heine et al. demonstrated that cognitive enhancement can persist for several years, but that clinically significant deficits can remain despite good neurological outcome.[9] A systematic review of cognitive outcomes also found memory, executive, attentional, and processing-speed abnormalities to be important residual sequelae.[10] More recent multidomain studies have confirmed the separation of neurological independence and return to premorbid functioning. Despite improvements in traditional disability measures, persistent cognitive impairment, mood symptoms, fatigue and inability to resume previous work or education have been reported.[11,12] Long-term neuropsychological studies have also shown that children who have recovered from apparent neurological illness continue to have attention problems, fatigue and educational difficulties.[13] Long-term morbidity can thus be more than motor or neurological disability, and may involve psychiatric and behavioural symptoms, speech and language problems, educational or occupational disruption, impaired social functioning and reduced quality of life.[14,15] Another crucial aspect of the disease course is relapse, which can happen following a period of clinical recovery.

Indian Context and Evidence Gap: Anti-NMDAR encephalitis is becoming a common entity in Indian neurological and paediatric practice, but there is limited evidence on long-term outcomes. Long-term neuropsychiatric and functional sequelae have been reported in Indian studies beyond the acute phase. Nair et al. reported speech, memory, behavioural and functional abnormalities that persisted for 6–24 months in children followed up.[16] In the largest eligible Indian cohort, Raja et al. assessed 1- and 2-year outcomes and found associations between baseline MRI abnormalities, functional outcome, and relapse.[17] Gowda et al. reported that children who had a stroke-like presentation had persistent cognitive and behavioural problems and failed to achieve full educational recovery despite significant improvement in the acute neurological syndrome.[18] The observations indicate that apparent functional independence and survival may not be sufficient indicators of long-term recovery in Indian patients. This is especially important as anti-NMDAR encephalitis often occurs in children, adolescents and young adults when they are most active in their education, work and social life. Global disability scales may therefore not adequately reflect the consequences of persistent abnormalities in cognition, behaviour, communication or learning. The Indian context also poses significant issues about access to neuropsychological assessment, psychiatric follow-up, speech and language therapy, educational support, rehabilitation services, and continuity of specialist care. But these aspects of recovery have not been synthesized systematically in the literature available in India.

Rationale for the Systematic Review: While anti-NMDAR encephalitis is now acknowledged as a disorder with prolonged and multi-dimensional recovery in international studies, the evidence in India is fragmented and limited to small cohorts and case series. The results of individual studies are not easily interpretable because of the varying patient populations, length of follow-up, outcome definitions, and assessment methods. A systematic synthesis of Indian evidence is therefore required to describe recovery beyond the acute phase, identify persistent neurological and neuropsychiatric sequelae, explore relapse and mortality, and identify dimensions of long-term recovery that are under-researched. This synthesis could also help to determine if traditional indicators of functional independence are sufficient to reflect the remaining cognitive, behavioral, educational, and social morbidity.

Review Objective: The aim of this systematic review was to identify, critically appraise and narratively synthesize the available evidence on long-term outcomes and sequelae in anti-NMDAR encephalitis patients in India. The review specifically examined functional outcomes, neurological, cognitive, psychiatric and behavioural sequelae, educational and occupational reintegration, relapse and mortality, and factors associated with long-term outcome.

Materials and Methods

Review Design and Reporting Framework: This systematic review was designed to identify, critically appraise, and synthesize the available evidence on long-term outcomes and sequelae among patients with anti-N-methyl-D-aspartate receptor (anti-NMDAR) encephalitis in India. The review was conducted and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 statement.[19] Owing to anticipated clinical and methodological heterogeneity in study populations, follow-up duration, treatment exposure, and outcome assessment, a narrative synthesis was planned rather than a quantitative meta-analysis.[20]

Review Question: The review addressed the following question: What are the long-term functional, neurological, cognitive, psychiatric, behavioural, educational, occupational, and social outcomes of patients with anti-NMDAR encephalitis reported from India, and what factors have been associated with these outcomes?

Eligibility Criteria:

Population: Studies were eligible if they included children, adolescents, or adults diagnosed with anti-NMDAR encephalitis and reported data from patients evaluated or treated in India. Studies containing mixed populations were considered eligible only when data pertaining specifically to patients with anti-NMDAR encephalitis from India could be separately identified. No restrictions were imposed according to age or sex.

Exposure/Condition: The condition of interest was anti-NMDAR encephalitis diagnosed on the basis of a compatible clinical syndrome supported by anti-NMDAR antibody testing in cerebrospinal fluid and/or serum, or by accepted diagnostic criteria applicable at the time of the study.

Studies of autoimmune encephalitis involving multiple antibody

subtypes were eligible only when outcomes for patients with anti-NMDAR encephalitis could be separately extracted.

Outcomes: The primary outcomes of interest were long-term functional status and persistent neurological, cognitive, psychiatric, or behavioural sequelae.

Additional outcomes included relapse, mortality, educational reintegration, return to employment, social participation, independence in activities of daily living, quality of life, caregiver dependence, and factors associated with long-term outcome.

Functional outcomes included those measured using validated instruments, such as the modified Rankin Scale or Liverpool Outcome Score, as well as clearly defined author-reported categories including complete recovery, partial recovery, persistent disability, or dependency.

Neurological sequelae included persistent seizures or epilepsy, movement disorders, motor deficits, speech or language impairment, sleep disturbances, autonomic dysfunction, and other residual neurological abnormalities.

Cognitive outcomes included persistent deficits involving memory, attention, executive function, language, learning, processing speed, or overall cognitive performance. Psychiatric and behavioural outcomes included depression, anxiety, psychosis, aggression, irritability, emotional dysregulation, hyperactivity, apathy, and other persistent behavioural disturbances.

Minimum Follow-up Duration: For inclusion in the primary long-term outcome synthesis, studies were required to report outcome assessment at least six months after disease onset, diagnosis, initiation of treatment, or hospital discharge.

When several follow-up assessments were available, the longest adequately reported follow-up was preferentially extracted, while clinically relevant outcomes at earlier eligible time points were also recorded.

Eligible Study Designs: Observational cohort studies, longitudinal studies, cross-sectional studies containing eligible long-term outcome data, and case series were considered for the primary synthesis.

Individual case reports were not incorporated into estimates or descriptive summaries of outcome frequency. However, case reports describing unusual long-term complications, exceptionally delayed relapse, or other clinically important sequelae were considered separately as supplementary evidence.

Reviews, systematic reviews, editorials, commentaries, conference abstracts without adequate patient-level information, guidelines, and consensus statements were not eligible for the primary synthesis but were used, where appropriate, for citation searching and contextual interpretation.

Exclusion Criteria: Studies were excluded from the primary synthesis if they met one or more of the following criteria: (1) the study population was not from India; (2) India-specific data could not be separately extracted; (3) anti-NMDAR encephalitis outcomes could not be distinguished from other forms of autoimmune encephalitis; (4) the reported outcome assessment occurred before six months; (5) the duration of follow-up could not be established as meeting the prespecified minimum threshold; (6) no relevant long-term outcome was reported; or (7) the publication represented a duplicate or substantially overlapping patient cohort without providing unique long-term outcome information.

Information Sources: A comprehensive literature search was undertaken to identify studies reporting anti-NMDAR encephalitis in India. The search framework included MEDLINE/PubMed, Embase, Scopus, Web of Science, and Google Scholar, supplemented by searches of India-focused sources and citation databases where applicable.

Reference lists of eligible studies and relevant reviews were examined to identify additional publications. Forward citation searching of key Indian anti-NMDAR encephalitis studies was also undertaken to identify subsequent reports containing longer follow-up or additional outcome information.

The search covered the available literature from database inception to the final search date.

Search Strategy: The search strategy combined controlled vocabulary, where available, with free-text terms relating to anti-NMDAR encephalitis, long-term outcome, sequelae, follow-up, recovery, disability, relapse, cognition, psychiatric outcomes, and India.

The principal concepts were combined using Boolean operators and included terms such as “anti-NMDA receptor encephalitis,” “anti-NMDAR encephalitis,” “N-methyl-D-aspartate receptor encephalitis,” “autoimmune encephalitis,” “long-term outcome,” “follow-up,” “sequelae,” “recovery,” “disability,” “cognitive outcome,” “neuropsychiatric outcome,” “psychiatric outcome,” “relapse,” and “India.”

Search syntax was adapted to the requirements of individual databases. No restrictions according to age or sex were applied. Reference-list screening and citation tracking were used to supplement electronic database searching. The complete database-specific search strategies are provided in the supplementary material.

Study Selection: Records retrieved through the electronic database searches and supplementary citation and reference searching were collated before screening. Duplicate records were identified and removed prior to title and abstract screening. No automation tools were used for record exclusion.

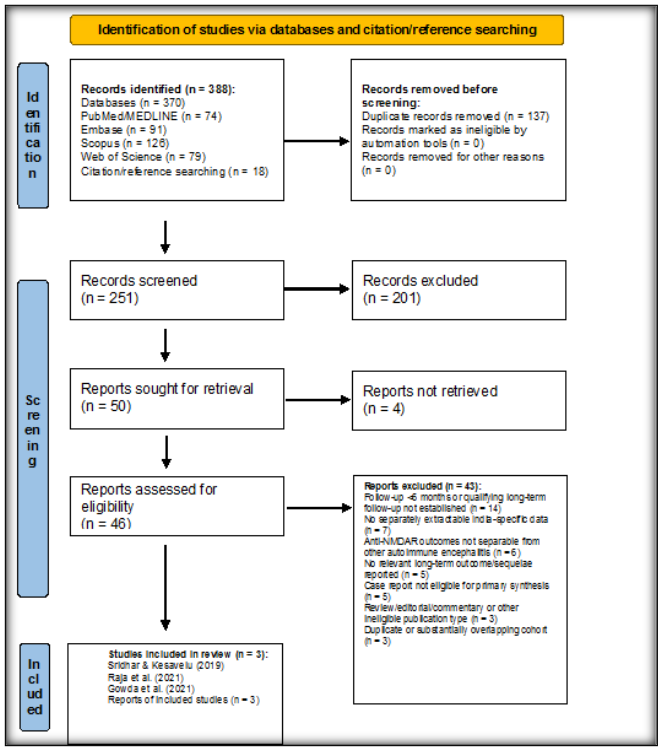
Titles and abstracts of the remaining records were screened against the prespecified eligibility criteria. Reports considered potentially eligible were retrieved in full text and assessed for inclusion. Full-text eligibility was determined according to geographic setting, diagnostic ascertainment of anti-NMDAR encephalitis, availability of separately extractable India-specific data, study design, duration of follow-up, and reporting of relevant long-term outcomes.

Studies were required to provide an outcome assessment at least six months after disease onset, diagnosis, treatment initiation, or hospital discharge for inclusion in the primary long-term synthesis. Studies involving multiple autoimmune encephalitis subtypes were included only when anti-NMDAR-specific outcome data could be separately extracted.

Reasons for exclusion at the full-text stage were documented using predefined categories, including follow-up of less than six months or inability to establish qualifying long-term follow-up,

absence of separately extractable India-specific data, inability to distinguish anti-NMDAR outcomes from other autoimmune encephalitis subtypes, absence of relevant long-term outcomes or sequelae, ineligible publication type, case-report design for the primary synthesis, and duplicate or substantially overlapping patient cohorts.

The study-selection process and reasons for exclusion at the full-text stage were documented using a PRISMA 2020 flow diagram [Figure 1]



*Database-specific counts are shown; citation/reference searching identified an additional 18 records. Search completed 1 August 2026.

Data Extraction: A standardized data-extraction framework was developed before evidence synthesis. For each eligible study, information was extracted on bibliographic characteristics, study design, study setting, recruitment period, sample size, age distribution, sex distribution, diagnostic methods, antibody testing, clinical presentation, treatment, duration of follow-up, outcome assessment methods, and long-term outcomes.

Outcome data were extracted separately across predefined functional, neurological, cognitive, psychiatric/behavioural, educational/occupational, relapse, and mortality domains.

Whenever available, numerical outcome data were extracted using the original numerator and denominator rather than percentages alone. For studies reporting outcomes at multiple time points, outcome timing was recorded explicitly.

Reported prognostic factors were extracted together with the outcome examined, direction of association, statistical analysis, and whether the reported association was adjusted for potential confounding.

Outcomes and Outcome Domains: Long-term outcomes were organized into predefined domains to facilitate comparison across clinically heterogeneous studies.

The functional outcome domain included complete recovery, good functional outcome, partial recovery, persistent disability, dependency, and validated global disability scores.

Neurological sequelae included persistent seizures or epilepsy, movement disorders, motor deficits, speech and language dysfunction, sleep disturbances, autonomic symptoms, and other residual neurological abnormalities.

Cognitive sequelae included memory impairment, attention deficits, executive dysfunction, learning difficulties, language dysfunction, impaired academic performance, and abnormalities detected on formal neuropsychological assessment.

Psychiatric and behavioural sequelae included persistent psychosis, depression, anxiety, aggression, irritability, hyperactivity, emotional dysregulation, apathy, and other behavioural disturbances.

Participation-related outcomes included return to school or college, academic functioning, return to employment, independent living, social participation, quality of life, and caregiver dependence or burden.

Relapse and mortality were considered separately. Where reported, the timing and clinical manifestations of relapse and subsequent treatment were extracted.

Assessment of Risk of Bias: Methodological quality and risk of bias were evaluated using Joanna Briggs Institute critical appraisal principles appropriate to the design of each included study.[21]

Assessment considered clarity of eligibility criteria, participant selection, reliability of anti-NMDAR encephalitis diagnosis, completeness and duration of follow-up, validity and consistency of outcome measurement, identification and management of potential confounding, appropriateness of statistical analysis, and completeness of outcome reporting.

Risk-of-bias judgments were made at the domain level rather than by calculating an aggregate numerical quality score. Particular attention was given to selection bias in small or phenotype-specific case series, attrition during long-term follow-up, reliance on retrospective clinical records, and the use of non-standardized outcome assessments.

Data Synthesis: Because substantial heterogeneity was expected in study populations, clinical severity, treatment strategies, duration of follow-up, and methods of outcome assessment, quantitative meta-analysis was not undertaken.

Findings were synthesized narratively and organized according to predefined outcome domains. These comprised functional outcomes, neurological sequelae, cognitive sequelae, psychiatric and behavioural sequelae, educational and occupational reintegration, relapse, mortality, and factors associated with long-term outcome.

Study-specific denominators were retained throughout the synthesis. Outcome proportions from clinically or methodologically heterogeneous studies were not statistically pooled.

Particular emphasis was placed on distinguishing global functional independence from complete neuropsychiatric recovery. Findings derived from validated outcome instruments were considered separately from descriptive clinician- or

caregiver-reported outcomes where appropriate.

Management of Overlapping Cohorts: Potential overlap between publications originating from the same institution or research group was assessed using recruitment periods, clinical setting, patient characteristics, sample size, age distribution, and other available cohort characteristics.

Where substantial overlap was identified or suspected, publications were not automatically treated as independent patient cohorts. The report providing the longest follow-up or most comprehensive long-term outcome information was preferentially used as the principal source. Companion publications were used only when they contributed unique outcome information, and potentially duplicated participants were not added independently to descriptive sample totals.

Assessment of Certainty and Limitations of the Evidence: The overall strength of the evidence for each outcome domain was interpreted qualitatively according to the consistency of findings, methodological limitations of the contributing studies, sample size, directness of the evidence, completeness of follow-up, and reliability of outcome measurement.

Particular caution was applied to conclusions based on single-centre case series, very small samples, selected clinical phenotypes, non-standardized outcome definitions, or findings derived from a single study. Associations between clinical characteristics and subsequent outcomes were interpreted as observational associations and not as evidence of causality.

Results

Search Results and Study Selection: The literature search was last updated on 1 August 2026. A total of 388 records were identified, of which 370 were retrieved through electronic database searching and 18 through supplementary reference-list and citation searching. The database search yielded 74 records from MEDLINE/PubMed, 91 from Embase, 126 from Scopus, and 79 from Web of Science.

After removal of 137 duplicate records, 251 unique records underwent title and abstract screening. Of these, 201 were excluded because they did not meet the prespecified eligibility criteria. Full-text retrieval was sought for 50 potentially relevant reports; four reports could not be retrieved, leaving 46 full-text reports for eligibility assessment.

Of the 46 full-text reports assessed, 43 were excluded. The most frequent reason for exclusion was a follow-up duration of less than six months or inability to establish a qualifying long-term follow-up interval (n=14). Other reasons were absence of separately extractable India-specific data (n=7), inability to separate anti-NMDAR outcomes from those of other autoimmune encephalitis subtypes (n=6), absence of relevant long-term outcomes or sequelae (n=5), case-report design not eligible for the primary synthesis (n=5), ineligible publication type such as a review, editorial, or commentary (n=3), and duplicate or substantially overlapping patient cohorts (n=3).

Three studies fulfilled all prespecified eligibility criteria and were included in the primary narrative synthesis. The complete study-selection process and reasons for full-text exclusion are presented in the PRISMA 2020 flow diagram [Figure 1].

Characteristics of Included Studies: Three Indian studies comprising 40 reported patients with anti-NMDAR encephalitis met the prespecified eligibility criteria and were included in the primary narrative synthesis. The studies were published between 2019 and 2021 and were conducted at tertiary-care centres in Chennai and Bengaluru. Two studies included exclusively paediatric populations, whereas one included both paediatric and adult patients. Study characteristics are summarized in [Table 1].

Table 1: Characteristics of studies included in the systematic review

Study	Setting	Study design	Population	Sample size	Follow-up	Principal long-term outcomes assessed
Nair et al,[16] 2019	Tertiary-care centre, Kerala, India	Paediatric case series	Children with anti-NMDAR encephalitis	6	6–24 months	Functional and neuropsychiatric outcome, speech/language deficits, memory and behavioural sequelae, relapse
Raja et al,[17] 2021	NIMHANS, Bengaluru, India	Retrospective chart review	Paediatric and adult patients with anti-NMDAR encephalitis	28	Functional outcome at 1 and 2 years; relapse assessed within 2 years	Functional outcome, relapse, MRI and EEG associations with outcome
Gowda et al,[18] 2021	Indira Gandhi Institute of Child Health, Bengaluru, India	Retrospective phenotype-selected paediatric case series	Children with CSF-positive anti-NMDAR encephalitis presenting with stroke-like manifestations	6	Extended longitudinal follow-up	Neurological recovery, cognitive and behavioural sequelae, educational reintegration, relapse

Abbreviations: anti-NMDAR, anti-N-methyl-D-aspartate receptor; CSF, cerebrospinal fluid; EEG, electroencephalography; MRI, magnetic resonance imaging; NIMHANS, National Institute of Mental Health and Neuro Sciences.

Nair et al,[16] reported a paediatric case series of six children with anti-NMDAR encephalitis who were followed for 6–24 months. The study evaluated clinical and neuropsychiatric recovery and documented residual abnormalities involving speech, memory, behaviour, motor function, and writing ability during follow-up.

Raja et al,[17] reported the largest included study, comprising 28 patients with anti-NMDAR encephalitis treated at the National Institute of Mental Health and Neuro Sciences (NIMHANS), Bengaluru. The cohort included 18 paediatric and 10 adult patients. Functional outcomes were evaluated at one and two years, and clinical relapse was assessed

during two years of follow-up. The study additionally examined associations between initial magnetic resonance imaging (MRI) and electroencephalographic (EEG) abnormalities and subsequent functional outcome and relapse.

Gowda et al,[18] reported six children selected from a source population of 24 children with cerebrospinal fluid (CSF) anti-NMDAR antibody-positive encephalitis treated at the Indira Gandhi Institute of Child Health, Bengaluru. The reported subgroup comprised children presenting with hemiparesis or other stroke-like manifestations. Follow-up included assessment of neurological recovery, cognitive and behavioural difficulties, educational reintegration, and relapse.

Follow-up duration and outcome assessment differed across the included studies. Nair et al. reported outcomes over 6–24 months, Raja et al. assessed functional outcome at one and two years, and Gowda et al. provided extended longitudinal follow-up of their selected paediatric subgroup. Outcome measures ranged from structured functional assessment to descriptive clinical, neuropsychiatric, cognitive, behavioural, and educational outcomes. Detailed study-level data extraction, including long-term outcome domains and prognostic variables, is provided in Supplementary Table S2.

Characteristics of Study Populations: The three included studies described 40 patients with anti-NMDAR encephalitis. The populations differed with respect to age distribution, sex distribution, and clinical phenotype. Two studies were restricted to paediatric patients, whereas Raja et al. included both children and adults. Consequently, the available long-term Indian evidence was weighted toward paediatric disease.

Nair et al,[16] included six children aged approximately 2–11 years, five of whom were female. Neuropsychiatric manifestations were prominent during the illness, and the cohort demonstrated a range of behavioural, speech and language, cognitive, seizure-related, and movement manifestations. All six children underwent follow-up extending for at least six months.

Raja et al,[17] included 28 patients, comprising 18 children and 10 adults. Seventeen of the 18 paediatric patients and five of the 10 adult patients were female. The study represented the largest and most age-diverse cohort among the included studies. Baseline MRI and EEG findings were recorded and subsequently evaluated in relation to long-term functional outcome and relapse.

Gowda et al,[18] reported a selected subgroup of six children drawn from a source population of 24 children with CSF-confirmed anti-NMDAR encephalitis. Selection of the reported subgroup was based on the presence of hemiparesis or other stroke-like manifestations. Behavioural change and regression of speech were present in all six children. Seizures and movement abnormalities were also observed in several patients.

Of the 40 reported participants across the three studies, at least 30 were children or adolescents. All included studies originated from tertiary-care settings, and no population-based Indian cohort reporting eligible long-term outcomes was identified.

Diagnostic assessment varied between studies. CSF anti-NMDAR antibody positivity was explicitly documented in the Gowda et al. cohort, while anti-NMDAR encephalitis was established according to the diagnostic and antibody-testing procedures reported by the individual studies. MRI and EEG formed part of the clinical evaluation in the larger cohort reported by Raja et al., in which these investigations were additionally examined for their association with subsequent outcome.

Table 2: Clinical and treatment characteristics of the included studies

Study	Population characteristics	Prominent clinical features	First-line immunotherapy	Escalation/second-line therapy	Relevant treatment observations
Nair et al., 201916	Six children; five female; approximately 2–11 years	Neuropsychiatric manifestations, speech/language dysfunction, seizures and movement abnormalities	Corticosteroids and IVIG	Additional immunotherapy used in selected patients	Recovery continued over prolonged follow-up in several children
Raja et al., 202117	28 patients: 18 paediatric and 10 adult	Broad clinical spectrum of anti-NMDAR encephalitis; MRI and EEG abnormalities evaluated	First-line immunotherapy according to clinical severity	Second-line immunotherapy used in selected patients	Treatment exposure varied according to disease severity and response
Gowda et al., 202118	Six phenotype-selected children from 24 CSF-positive cases	Hemiparesis/stroke-like presentation; behavioural change and speech regression in all; seizures and movement abnormalities in several	Corticosteroids; three children additionally required IVIG	Rituximab administered to one child following relapse	Initial neurological improvement occurred despite later cognitive/behavioural morbidity in some children

Abbreviations: anti-NMDAR, anti-N-methyl-D-aspartate receptor; CSF, cerebrospinal fluid; EEG, electroencephalography; IVIG, intravenous immunoglobulin; MRI, magnetic resonance imaging.

Treatment Characteristics: Immunotherapeutic management varied across the included studies according to disease severity, clinical response, and local treatment practice. First-line treatment consisted predominantly of high-dose corticosteroids, intravenous immunoglobulin (IVIG), plasma exchange, or combinations of these therapies. Escalation to second-line immunotherapy was reported in patients with inadequate response to initial treatment, severe disease, or subsequent relapse.

In the paediatric series reported by Nair et al,[16]

immunotherapy included corticosteroids and IVIG, with escalation of treatment in selected children according to clinical response. Additional immunotherapeutic agents were used in patients requiring further treatment. Recovery occurred over a prolonged period in several children, and neurological and neuropsychiatric improvement continued during follow-up.

Raja et al,[17] reported the use of first- and second-line immunotherapeutic strategies in their mixed paediatric and adult cohort. Treatment varied according to clinical severity and response to initial therapy. The observational design did not involve randomized allocation to individual treatment regimens.

In the Gowda et al,[17] series, three of six children demonstrated rapid clinical improvement following corticosteroid treatment, whereas the remaining three required additional IVIG before substantial improvement was observed. One child subsequently experienced a relapse and was treated with rituximab, followed by clinical improvement.

Supportive and symptomatic therapies were administered according to clinical requirements across the studies. These included antiseizure treatment and management of behavioural, movement, autonomic, and other complications of the acute encephalitic syndrome where indicated.

Treatment protocols, timing of initiation, sequencing of first- and second-line therapies, and criteria for escalation were not uniform across studies. None of the included studies was designed as a comparative trial of long-term treatment effectiveness. Treatment exposures are therefore presented descriptively.

Long-Term Functional Outcomes: Long-term functional recovery was reported in all three included studies, although outcome definitions and assessment methods varied substantially. The available evidence generally demonstrated improvement following the acute phase of anti-NMDAR encephalitis, but residual neurological, cognitive, behavioural, and communication difficulties persisted in a subset of patients.

Raja et al,[17] provided the most systematic assessment of long-term functional outcome. Among 28 patients, functional status was evaluated at one and two years after illness. Initial magnetic resonance imaging (MRI) abnormalities were associated with poorer functional outcome at one year. Of 15 patients with an abnormal initial MRI, approximately 53% had a poor functional outcome at one year, compared with approximately 8% of 12 patients with a normal initial MRI. Electroencephalographic abnormalities were also evaluated in relation to outcome; among patients with an abnormal initial EEG, approximately 40% had a poor outcome at one year and 15% at two years. The association between initial EEG abnormality and outcome at two years was not statistically significant.

Nair et al,[16] followed six children for 6–24 months and assessed outcome using the Liverpool Outcome Score together with clinical neuropsychiatric assessment. Recovery was incomplete in several children at the reported follow-up assessments, with residual deficits involving speech, memory, behaviour, motor function, and writing ability. The reported Liverpool Outcome Scores ranged from 2 to 4, indicating varying degrees of residual disability rather than uniformly complete recovery.

Gowda et al,[18] described substantial early neurological improvement in their six phenotype-selected children. Three children achieved full clinical recovery within approximately seven days following corticosteroid therapy, whereas three demonstrated improvement after approximately 20 days following additional intravenous immunoglobulin. Despite this early clinical improvement, four of the six children were subsequently reported to have cognitive decline and behavioural problems. Thus, early improvement in the acute neurological syndrome did not necessarily correspond to complete longer-term neuropsychiatric recovery.

Taken together, the studies demonstrated that substantial functional improvement was common, but the definition of recovery differed considerably. Global or clinician-defined functional improvement could coexist with persistent deficits in cognition, behaviour, communication, and educational functioning.

Neurological Sequelae: Persistent neurological abnormalities were reported across the paediatric studies, although individual sequelae were not assessed systematically using uniform outcome measures.

Speech and language dysfunction represented a prominent residual manifestation. In the series by Nair et al,[16] persistent abnormalities included mutism, speech regression, speech delay, and dysgraphia. Expressive aphasia was reported to be the last major symptom to regress during recovery. One child had residual hemiparesis in association with mutism, demonstrating that focal motor deficits could persist beyond the acute phase.

Gowda et al,[18] specifically investigated children presenting with hemiparesis or stroke-like episodes. All six children had hemiparesis at presentation, accompanied by behavioural change and regression of speech. Three experienced seizures, including one child with epilepsiapartialiscontinua, while two had dystonia and choreoathetosis. Although neurological improvement occurred following immunotherapy, residual neurocognitive and behavioural abnormalities remained in several children during follow-up.

Seizure recurrence was reported in association with relapse in the available evidence. Gowda et al. documented a later relapse in one child, who subsequently improved following treatment with rituximab. Raja et al. also documented clinical relapse during longer-term follow-up. However, the included studies did not consistently distinguish acute symptomatic seizures, seizures occurring as part of clinical relapse, and chronic post-encephalitic epilepsy. Consequently, the long-term incidence of epilepsy following anti-NMDAR encephalitis could not be determined.

Persistent movement disorders, autonomic dysfunction, and sleep-related sequelae were not systematically assessed at long-term follow-up. The available evidence therefore

suggests that residual neurological morbidity may involve speech and language dysfunction, focal motor impairment, and recurrent seizure-related disease, but its frequency and duration remain uncertain.

Cognitive Sequelae: Cognitive outcome was incompletely and inconsistently assessed despite evidence of persistent cognitive morbidity in the included studies. Formal comprehensive neuropsychological testing was not uniformly employed, and cognitive sequelae were generally identified through clinical assessment, caregiver observations, or functional and scholastic performance.

In the paediatric series by Nair et al,[16] residual neuropsychiatric abnormalities included memory impairment, speech and language dysfunction, and dysgraphia. These deficits persisted for months after the acute illness in some children. The prolonged recovery of expressive language was particularly notable, with expressive aphasia described as the last major manifestation to regress.

Gowda et al,[18] provided more explicit evidence of persistent cognitive morbidity. Four of the six children were reported to have cognitive decline together with behavioural problems despite improvement in their acute neurological manifestations. Because these six children represented a selected subgroup with stroke-like or hemiparetic presentation, the proportion cannot be extrapolated to unselected children with anti-NMDAR encephalitis; nevertheless, the findings demonstrate that persistent cognitive impairment may remain after apparent neurological improvement.

Raja et al,[17] primarily evaluated global functional outcome and clinical relapse rather than providing a detailed multidomain analysis of long-term cognition. Consequently, the extent to which patients classified as having favourable functional outcomes experienced persistent deficits in memory, attention, executive function, processing speed, or social cognition could not be determined from the reported outcome measures.

Across the included evidence, standardized longitudinal assessment of memory, executive functioning, attention, processing speed, language, and social cognition was limited. No study provided sufficiently uniform quantitative neuropsychological data to estimate the prevalence of individual cognitive sequelae. The available evidence nevertheless demonstrated that cognitive recovery could remain incomplete even when substantial neurological or global functional improvement had occurred.

Psychiatric and Behavioural Sequelae: Psychiatric and behavioural abnormalities were prominent components of the clinical course of anti-NMDAR encephalitis and persisted beyond the acute phase in a subset of patients. However, long-term psychiatric outcomes were not evaluated using uniform standardized instruments across the included studies.

Nair et al,[16] documented persistent neuropsychiatric manifestations during follow-up in their six paediatric patients. Residual abnormalities included behavioural disturbances such as aggression, in addition to memory and communication difficulties. Recovery of neuropsychiatric function occurred gradually and was not uniform across patients.

Persistent behavioural morbidity was also reported by Gowda et al,[18] Four of the six children in their phenotype-selected series had cognitive decline accompanied by behavioural problems during follow-up despite improvement in the acute neurological syndrome. Because this cohort specifically comprised children with stroke-like or hemiparetic presentations, the proportion affected cannot be interpreted as an estimate of the prevalence of behavioural sequelae among unselected children with anti-NMDAR encephalitis.

Raja et al,[17] primarily assessed global functional outcome and relapse rather than standardized long-term psychiatric outcomes. Consequently, the frequency of persistent depression, anxiety, psychotic symptoms, emotional dysregulation, or other specific psychiatric disorders could not be determined from the available data.

Overall, the included studies demonstrated persistence of behavioural and neuropsychiatric abnormalities after the acute illness in some patients. However, standardized psychiatric interviews, symptom-specific rating scales, and longitudinal assessments of emotional and behavioural functioning were not consistently reported.

Educational, Occupational, and Social Reintegration: Educational and social reintegration were infrequently assessed as formal long-term outcomes. The available evidence was almost exclusively paediatric, and none of the included studies provided a systematic evaluation of return to employment or occupational functioning in adults.

Nair et al,[16] reported return-to-school information during follow-up. Two of the six children were reported to have returned to school, while residual speech, memory, behavioural, motor, and writing difficulties affected recovery in other patients. These observations indicate that neurological improvement did not uniformly correspond to restoration of premorbid educational functioning.

Gowda et al,[18] also documented school reintegration during longitudinal follow-up. Four of the six children returned to school, while persistent cognitive decline and behavioural problems were reported in four children. Return to school therefore did not necessarily indicate complete cognitive or behavioural recovery.

Raja et al,[17] did not provide sufficiently detailed educational, occupational, or social participation outcomes to permit systematic assessment of reintegration in the mixed-age cohort.

No included study systematically evaluated return to employment, independent living, social participation, quality of life, caregiver burden, or family functioning using validated measures. Consequently, the longer-term impact of anti-NMDAR encephalitis on participation and societal functioning in Indian patients remains incompletely characterized.

Long-term functional, neurological, cognitive, behavioural, and participation-related outcomes across the included studies are summarized in [Table 3].

Table 3: Long-term outcomes and sequelae

Study	Follow-up	Functional outcome	Neurological sequelae	Cognitive sequelae	Psychiatric/ behavioural sequelae	Educational/social outcome
Nair et al., 201916	6–24 months	Variable residual disability; Liverpool Outcome Score used	Persistent speech/language dysfunction; mutism, speech regression/delay, hemiparesis and dysgraphia reported	Memory impairment and language-related deficits reported	Persistent behavioural abnormalities, including aggression, reported in individual patients	2/6 children reported to have returned to school
Raja et al., 202117	Functional outcome at 1 and 2 years	Poor 1-year functional outcome in ~53% of patients with abnormal initial MRI vs ~8% with normal MRI	Detailed individual long-term neurological sequelae not systematically characterized	Detailed standardized cognitive outcomes not reported	Detailed standardized long-term psychiatric outcomes not reported	Educational, occupational and social reintegration not systematically reported
Gowda et al., 202118	Extended longitudinal follow-up	Initial neurological improvement following immunotherapy; residual morbidity persisted in some children	Stroke-like/hemiparetic deficits; seizures and movement abnormalities formed part of the clinical phenotype	Cognitive decline reported in 4/6 children during follow-up	Behavioural problems reported in association with cognitive decline	4/6 children returned to school; residual cognitive/behavioural difficulties persisted in some

Abbreviations: MRI, magnetic resonance imaging.

Table note: Outcome definitions and follow-up assessments were heterogeneous across studies. Gowda et al. comprised a phenotype-selected subgroup of six children with stroke-like manifestations drawn from a source cohort of 24 CSF anti-NMDAR-antibody-positive children; its proportions should therefore not be interpreted as prevalence estimates for an unselected anti-NMDAR encephalitis population.

Relapse: Relapse was reported in the included Indian literature, although definitions, follow-up duration, and methods of ascertainment differed between studies.

Raja et al,[17] provided the most detailed assessment of relapse over a two-year period. Relapse was more frequent among patients with abnormal initial MRI findings than among those with normal initial MRI findings. Approximately 53% of patients with an abnormal initial MRI experienced at least one relapse within two years, compared with approximately 15% of patients with a normal initial MRI. The MRI-stratified analysis included 15 patients with abnormal MRI findings and 12 with normal findings rather than the entire cohort of 28 patients.

Gowda et al. documented relapse in one of six children during longitudinal follow-up. The relapsing patient received rituximab and subsequently demonstrated clinical improvement.

No relapse was reported among the six children in the series by Nair et al. during the available follow-up of 6–24 months.

Because of the small study populations, differences in follow-up duration, selected nature of the Gowda et al. cohort, and heterogeneity in relapse ascertainment, an overall relapse proportion was not calculated. The available studies nevertheless demonstrate that recurrent disease can occur after initial clinical improvement.

Mortality: Mortality was not a prominent long-term outcome in the three included studies. The available reports primarily described survivors who underwent longitudinal assessment, and no sufficiently uniform mortality data were available to estimate an India-specific long-term case-fatality proportion.

Interpretation of mortality is additionally limited by the small samples, tertiary-care setting, and requirement for long-term follow-up, which may preferentially select patients surviving the acute phase. Mortality was therefore retained as an outcome of interest but was not quantitatively summarized.

Factors Associated With Long-Term Outcome: Potential prognostic factors were evaluated most systematically by Raja et al. The principal investigated factors included abnormalities on initial MRI and EEG and their relationships with subsequent functional outcome and relapse.

Initial MRI abnormality was associated with poorer functional outcome at one year. Among 15 patients with an abnormal initial MRI, approximately 53% had a poor functional outcome at one year, compared with approximately 8% of 12 patients with a normal initial MRI. Abnormal initial MRI findings were also associated with a greater frequency of relapse during two years of follow-up, with relapse occurring in approximately 53% of patients with abnormal MRI findings compared with approximately 15% of those with normal MRI findings.

Initial EEG abnormalities were also examined in relation to subsequent functional status. Among patients with an abnormal initial EEG, approximately 40% had a poor outcome at one year and approximately 15% had a poor outcome at two years. The association between initial EEG abnormality and functional outcome at two years was not statistically significant.

The smaller paediatric studies were not sufficiently powered to identify independent prognostic factors. Although treatment response, severity of neurological manifestations, relapse, and persistence of cognitive or behavioural abnormalities were described, these studies did not provide adequately adjusted analyses to determine independent

predictors of long-term outcome.

Overall, the Indian evidence concerning prognostic factors was derived predominantly from a single retrospective cohort. MRI and EEG abnormalities may identify patients at risk of less favourable recovery, but the available observational evidence does not establish these findings as independently validated prognostic markers.

Study-specific findings regarding relapse, mortality, and factors associated with long-term outcome are summarized in [Table 4].

Table 4: Relapse, mortality and factors associated with long-term outcome

Study	Relapse	Mortality	Factors evaluated for association with outcome	Main reported association
Nair et al., 201916	No relapse reported among 6 children during available follow-up	No long-term mortality signal reported in the followed cohort	No adequately powered prognostic analysis	No independent prognostic factors established
Raja et al., 202117	Relapse assessed within 2 years; ~53% with abnormal initial MRI vs ~15% with normal MRI experienced ≥1 relapse	Long-term mortality not sufficiently characterized for comparative analysis	Initial MRI and EEG abnormalities	Abnormal initial MRI was associated with poorer functional outcome at 1 year and greater frequency of relapse within 2 years; longer-term association of EEG abnormality with functional outcome was less consistent
Gowda et al., 202118	1/6 children experienced a later relapse; treated with rituximab with subsequent clinical improvement	No death reported among the selected 6 children	No formal prognostic analysis	Sample size and phenotype selection precluded identification of independent prognostic factors

Risk of Bias: The methodological quality of the three included studies was assessed using Joanna Briggs Institute critical appraisal principles appropriate to the respective observational study designs. Overall, the evidence base was characterized by moderate to high risk of bias, principally related to small sample sizes, retrospective or descriptive study designs, participant selection, heterogeneous outcome assessment, and limited control of potential confounding. Detailed item-level critical appraisal of the included studies is provided in Supplementary [Table S3].

The study by Nair et al. was judged to have moderate-to-high overall risk of bias. The study provided longitudinal follow-up extending from 6 to 24 months and reported functional and neuropsychiatric outcomes in all six children. However, the very small sample size, case-series design, absence of a comparator group, and limited adjustment for potential determinants of outcome restricted the strength of the evidence. Although the Liverpool Outcome Score provided a structured measure of functional status, several cognitive, psychiatric, and behavioural outcomes were based predominantly on clinical assessment rather than standardized domain-specific instruments.

Raja et al. was rated as having moderate overall risk of bias and provided the strongest prognostic evidence among the included studies. The study had the largest sample size and measured outcomes at pre-specified one and two year intervals. However, its retrospective nature may have resulted in some limitations in participant selection, clinical record completeness, and outcome ascertainment. The analyses exploring the relationship between baseline MRI and EEG abnormalities and subsequent outcome were informative, but limited by the small sample size and limited adjustment for potential confounders, which limited the certainty of the prognostic conclusions. Furthermore, not all patients were included in every imaging-stratified analyses.

Gowda et al. was judged to have high overall risk of bias for estimating long-term outcomes in the general anti-NMDAR encephalitis population. The six reported children were deliberately selected from a larger source cohort of 24 CSF-antibody-positive patients on the basis of hemiparesis or stroke-like presentation. This phenotype-based selection substantially limited representativeness and generalizability. Although extended follow-up provided useful information regarding persistent cognitive, behavioural, educational, and neurological morbidity, formal standardized cognitive and disability assessments were not consistently employed.

Across the three studies, outcome measurement was heterogeneous. Global functional assessments were more frequently reported than detailed neuropsychological, psychiatric, educational, or quality-of-life outcomes. Potential confounding by disease severity, treatment timing, intensive-care requirements, and escalation to second-line immunotherapy was incompletely addressed. No included study was a prospective multicentre cohort specifically designed to evaluate standardized long-term outcomes.

The domain-level risk-of-bias judgments are summarized in [Table 5].

Table 5: Summary of risk-of-bias assessment for included studies

Domain	Nair et al., 2019	Raja et al., 2021	Gowda et al., 2021
Participant selection	Moderate concern	Moderate concern	High concern
Diagnostic ascertainment	Low concern	Low–moderate concern	Low concern
Adequacy of follow-up	Low–moderate concern	Low concern	Low–moderate concern
Outcome measurement	Moderate concern	Moderate concern	High concern
Control of confounding	High concern	Moderate–high concern	High concern
Completeness of reporting	Moderate concern	Low–moderate concern	Moderate concern
Generalizability	Moderate–high concern	Moderate concern	High concern
Overall risk of bias	Moderate–high	Moderate	High

Overall Summary of the Evidence: Three Indian studies comprising 40 reported patients provided eligible evidence regarding outcomes at least six months after anti-NMDAR encephalitis. The evidence was predominantly paediatric and originated exclusively from tertiary-care settings. Considerable heterogeneity was present in study design, clinical phenotype, duration of follow-up, treatment exposure, and methods of outcome assessment.

Substantial neurological and functional improvement was reported across the included studies. However, residual morbidity was documented in multiple domains, including speech and language, cognition, behaviour, motor function, and educational performance. In the paediatric studies, persistent neuropsychiatric abnormalities were reported despite improvement in the acute neurological syndrome, and return to school did not invariably indicate complete cognitive or behavioural recovery.

Relapse occurred in the larger mixed-age cohort and in the phenotype-selected paediatric series, whereas no relapse was reported in the six-child series by Nair et al. Differences in follow-up duration and study populations precluded calculation of a combined relapse proportion.

Evidence concerning predictors of long-term outcome was limited primarily to the study by Raja et al. Abnormal initial MRI findings were associated with poorer functional outcome at one year and a greater frequency of relapse within two years. EEG abnormalities were also examined in relation to functional outcome, although the longer-term association was less consistent.

Long-term mortality, chronic epilepsy, standardized neuropsychological performance, psychiatric diagnoses, quality of life, occupational reintegration, independent living, social participation, and caregiver burden were either inconsistently assessed or not reported in sufficient detail for systematic comparison.

Overall, the available Indian literature demonstrated clinically important long-term morbidity following anti-NMDAR encephalitis but was limited by small samples, heterogeneous outcome definitions, selected patient populations, retrospective or descriptive designs, and limited use of standardized multidomain follow-up assessments. Accordingly, the findings were synthesized narratively, and no quantitative pooling was undertaken.

Discussion

Principal Findings: Three Indian studies with 40 reported patients of anti-NMDAR encephalitis with long-term follow-up of at least 6 months were identified in this systematic review.[16–18] Although the studies varied in design, population, and outcome measures, a common theme was that a significant number of patients had ongoing cognitive, behavioural, speech-language, motor, and educational challenges, with some patients having a significant recovery.[16–18] Longer follow-up also showed relapse.[17,18] The principal finding is that good global functional outcome does not necessarily mean full recovery. This is particularly important in children and young adults, where deficits in memory, executive function, language, behaviour and learning can have a significant impact on education, independence and social participation, despite apparent neurological improvement.[8–10,13]

Functional Recovery and Persistent Neuropsychological Morbidity: The Indian findings are broadly consistent with international evidence. In the landmark observational cohort reported by Titulaer et al., approximately four-fifths of patients achieved a favourable functional outcome by 24 months, demonstrating the substantial recovery potential of anti-NMDAR encephalitis.[7] However, detailed neuropsychological studies indicate that cognitive recovery may lag behind gross neurological recovery.

Finke et al. demonstrated persistent deficits particularly involving memory and executive functioning.[8], while Heine et al. showed that cognitive improvement may continue for several years despite residual impairment in some patients.[9] More recent multidomain studies have similarly demonstrated persistent cognitive and mood-related morbidity and incomplete return to premorbid functioning despite improvement in conventional disability measures.[11,12]

This pattern is reflected in the Indian paediatric literature. Nair et al. documented prolonged speech-language, memory, and behavioural abnormalities.[16], while Gowda et al. reported persistent cognitive and behavioural problems despite improvement in acute neurological manifestations.[18] These findings support multidomain follow-up rather than reliance on global disability scales alone.

Cognitive, Behavioural, and Educational Outcomes: Cognitive and behavioural sequelae were among the most important residual abnormalities identified in the Indian studies, although standardized neuropsychological and psychiatric assessments were infrequently used.[16–18] Reported problems included memory impairment, behavioural disturbance, speech and language dysfunction, cognitive decline, and scholastic difficulties.[16,18]

International paediatric evidence reinforces these concerns. De Bruijn et al. demonstrated persistent neuropsychological difficulties, fatigue, and problems with educational reintegration despite generally favourable neurological outcomes.[13] Other paediatric outcome studies have similarly demonstrated that conventional functional recovery may underestimate persistent cognitive and adaptive difficulties.[22,23]

Educational or occupational reintegration should therefore be assessed separately from neurological independence. Long-term psychosocial and quality-of-life studies have shown that residual difficulties may continue after apparent functional recovery.[14,15] In the Indian setting, this is particularly relevant because access to neuropsychological assessment, speech therapy, educational support, and structured rehabilitation may vary considerably.

Relapse and Prognostic Factors: Relapse occurred in two of the three included Indian studies. Raja et al. reported recurrent disease during two years of follow-up.[17], while Gowda et al. described a later relapse requiring rituximab.[18] These observations are consistent with the established relapsing potential of anti-NMDAR encephalitis.

International studies demonstrate that recurrence may occur months or years after the initial episode. Gabilondo et al. showed that relapses may occur after prolonged intervals and

can present with a more restricted symptom spectrum than the initial illness.[24] In children, Nosadini et al. similarly demonstrated that relapse may occur after substantial periods of apparent recovery.[25] Large longitudinal cohorts have also confirmed relapse as a clinically relevant component of the long-term disease course.[26]

Raja et al. additionally reported an association between abnormal initial MRI findings and poorer one-year functional outcome and more frequent relapse, while the relationship between EEG abnormalities and longer-term outcome was less consistent.[17] International prognostic studies have identified additional factors associated with outcome, including treatment delay and acute disease severity.[7,27] However, the prognostic findings from the Indian cohort should be interpreted cautiously because of its small retrospective sample. Larger prospective studies are required before MRI or EEG abnormalities can be regarded as validated prognostic markers in Indian patients.

Clinical Implications and Research Gaps in India: Long-term follow-up should not be limited to seizure control and gross neurological recovery, but should also include cognitive, language, behavioural, mood, educational/occupational, and relapse monitoring. Structured return to school assessment, neuropsychological evaluation and speech or behavioural rehabilitation may be especially needed for paediatric patients. There is also published rehabilitation experience that suggests that multidisciplinary rehabilitation is important in the recovery from anti-NMDAR encephalitis.[28,29] The evidence base in India is still small and heterogeneous, with most of the studies being tertiary centre studies with a paediatric population.[16–18] There is limited standardized information on adult outcomes, quality of life, caregiver burden, chronic epilepsy, fatigue, sleep disturbance and rehabilitation. Future studies should focus on prospective multicentre cohorts with uniform follow-up periods and multidomain outcome measures.

Strengths and Limitations of This Review: This review focused on long-term outcomes in Indian patients with a minimum follow-up period of 6 months and included cognitive, behavioural, educational, and relapse-related sequelae as well as conventional functional disability. The main drawbacks of its use were the small number of eligible studies, the small total sample size, the lack of uniformity in follow-up, the predominance of paediatric tertiary-centre populations, and the lack of uniformity in the use of standardized outcome measures.[16–18] The evidence included was mostly retrospective or descriptive, and one study included a phenotype-selected subgroup.[18] which reduced generalizability. However, the overall results are in line with the international evidence that recovery from anti-NMDAR encephalitis is long and complex, and that good functional outcome can be accompanied by ongoing cognitive, neuropsychiatric and participation impairments.[8,9,11–15]

Conclusion

Indian evidence suggests that substantial functional recovery after anti-NMDAR encephalitis may coexist with persistent cognitive, behavioural, speech-language, and educational sequelae, while relapse remains an important long-term concern. Follow-up should therefore extend beyond global disability measures to include neuropsychiatric and participation-related outcomes. Larger prospective multicentre Indian studies using standardized long-term assessments are needed to better define recovery and guide rehabilitation.

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