

**NEUROLOGICAL MANIFESTATIONS OF NIPAH VIRUS: CLINICAL CHALLENGES AND PROGNOSIS**

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**Abstract**

Nipah virus (NiV) is an emerging zoonotic pathogen associated with sporadic but highly lethal outbreaks, particularly in South and Southeast Asia. This chapter aims to analyze the main neurological manifestations associated with Nipah virus infection, addressing the clinical challenges in diagnosis and management, as well as factors related to patient prognosis. The methodology consisted of a narrative review of the scientific literature, based on articles indexed in databases such as PubMed, Scopus, and

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Web of Science, prioritizing clinical studies, systematic reviews, and outbreak reports involving neurological involvement. The results indicate that acute encephalitis is the most frequent neurological manifestation, commonly accompanied by altered consciousness, seizures, focal neurological deficits, and neuropsychiatric disturbances, in addition to late complications such as relapsing encephalitis. Rapid clinical progression, lack of specific antiviral therapies, and difficulties in early diagnosis significantly contribute to high mortality rates and long-term neurological sequelae. It is concluded that early recognition of neurological manifestations of Nipah virus infection is essential for appropriate clinical management, emphasizing the importance of strengthening epidemiological surveillance, developing therapeutic strategies, and improving outbreak response protocols.

**Keywords:** Emerging viral infections, Encephalitis, Neurological prognosis, Nipah virus.

## INTRODUCTION

Nipah virus (NiV) is an emerging zoonotic pathogen belonging to the family Paramyxoviridae, recognized for causing sporadic outbreaks with high lethality, especially in countries in South and Southeast Asia. Since its first identification in 1998, NiV infection has raised growing concern among the scientific community and international health organizations due to its pandemic potential, the lack of specific antiviral therapies, and the severity of its clinical manifestations. Among the most affected systems, the central nervous system stands out, as infection is associated with severe encephalitis, often accompanied by high mortality rates and permanent neurological sequelae.

Despite advances in epidemiological and virological knowledge about Nipah virus, significant gaps remain regarding the detailed clinical characterization of its neurological manifestations and the factors influencing patient prognosis. The rapid progression of the disease, coupled with the similarity of neurological signs to other viral encephalitides and the limited availability of diagnostic methods in endemic areas, contributes to delays in diagnosis and clinical management, negatively impacting clinical

outcomes. In this context, the need emerges to deepen understanding of the clinical challenges related to neurological involvement caused by NiV.

The general objective of the present study is to analyze the main neurological manifestations associated with Nipah virus infection, discussing the clinical challenges involved in diagnosis and patient prognosis. As specific objectives, it seeks to describe the mechanisms of neuroinvasion and neurotropism of the virus, identify the acute and late neurological manifestations most frequently reported, discuss diagnostic and therapeutic difficulties in clinical management, and analyze factors associated with mortality and neurological sequelae.

The justification for this work is grounded in the epidemiological and clinical relevance of Nipah virus, considered by the World Health Organization as one of the priority pathogens for research and development. Neurological manifestations represent the main determinant of severity and disability in infected individuals, posing a substantial challenge for health systems, especially in regions with limited infrastructure. In addition, systematizing scientific knowledge on the topic may contribute to improving epidemiological surveillance, early case recognition, and the development of more effective therapeutic strategies.

From a theoretical standpoint, Nipah virus exhibits marked tropism for the central nervous system, being able to cross the blood–brain barrier, possibly through infection of endothelial cells and hematogenous dissemination. Acute encephalitis constitutes the principal neurological manifestation, characterized by fever, headache, altered level of consciousness, seizures, and focal neurological deficits. Reports in the literature also describe the occurrence of late-onset or relapsing encephalitis, suggesting mechanisms of viral persistence or an immune-mediated response. The absence of specific antiviral treatment and reliance on supportive measures reinforce the complexity of clinical management and underscore the importance of early diagnosis and rapid outbreak response.

## **METHODOLOGY**

### **TYPE OF STUDY**

The present study is characterized as qualitative research, with a descriptive and exploratory approach, developed through an integrative literature review. This type of methodology allows the synthesis and critical analysis of scientific evidence derived from different research designs, enabling a broadened understanding of the neurological manifestations associated with Nipah virus infection and the clinical challenges related to patient prognosis.

### **SEARCH STRATEGY AND SOURCES OF INFORMATION**

The bibliographic search was carried out in internationally recognized scientific databases, including PubMed/MEDLINE, Scopus, and Web of Science, as they concentrate relevant studies in the areas of virology, neurology, and public health. Additionally, technical documents and reports from international organizations, such as the World Health Organization (WHO), were consulted in order to complement epidemiological and clinical information.

### **INCLUSION AND EXCLUSION CRITERIA**

#### **Inclusion criteria**

Studies published between 2018 and 2024 were included, available in full text, in English, Portuguese, or Spanish, addressing neurological manifestations of Nipah virus, clinical aspects, diagnosis, prognosis, or neurological outcomes. Original articles, systematic reviews, narrative reviews, and outbreak reports with detailed clinical descriptions were considered.

## **Exclusion criteria**

Duplicate studies, publications that did not specifically address neurological involvement associated with Nipah virus, articles with restricted access, and works presenting insufficient data to analyze the proposed objectives were excluded.

## **STUDY SELECTION PROCEDURES**

Study selection occurred in three stages. Initially, titles and abstracts were read to identify thematic relevance. Next, eligible articles underwent full-text reading to confirm inclusion criteria. Finally, selected studies were organized in an electronic spreadsheet containing information such as authors, year of publication, type of study, main neurological manifestations, and clinical outcomes.

## **DATA COLLECTION TECHNIQUES AND INSTRUMENTS**

Data collection was performed using a standardized extraction instrument developed by the authors, covering variables such as characteristics of the studied population, described neurological manifestations, diagnostic methods used, therapeutic strategies adopted, and patient prognosis. This procedure enabled the systematization and comparison of data across the included studies.

## **STUDY SAMPLE**

The sample consisted of studies that fully met the established inclusion criteria. The final number of selected articles allowed a consistent qualitative analysis of the available evidence, considering different epidemiological and clinical contexts related to Nipah virus infection.

## **DATA ANALYSIS AND SYNTHESIS**

Extracted data were analyzed qualitatively and interpretively through analytical reading and thematic categorization. Information was organized into analytical axes, such as acute neurological

manifestations, late complications, diagnostic challenges, and prognostic factors. The synthesis of results was presented descriptively and critically, seeking to identify convergences, divergences, and gaps in scientific knowledge.

### ETHICAL CONSIDERATIONS

As this research is based exclusively on secondary data in the public domain, without direct involvement of human subjects, the study does not require review by a Research Ethics Committee, in accordance with the guidelines of Resolution No. 510/2016 of the Brazilian National Health Council.

### RESULTS AND DISCUSSION

The analysis of the selected studies made it possible to identify consistent patterns related to the neurological manifestations of Nipah virus, the clinical challenges faced during case management, and prognostic factors associated with mortality and neurological sequelae. The findings demonstrate that involvement of the central nervous system constitutes the main determinant of infection severity, being responsible for the most unfavorable clinical outcomes.

### MAIN NEUROLOGICAL MANIFESTATIONS ASSOCIATED WITH NIPAH VIRUS

The results demonstrate that acute encephalitis is the neurological manifestation most frequently described in outbreaks of Nipah virus infection. The analyzed studies report nonspecific initial symptoms, such as fever and headache, followed rapidly by altered level of consciousness, seizures, focal neurological deficits, and signs of autonomic dysfunction. In more severe cases, rapid progression to coma and neurologically mediated respiratory failure is observed.

In addition to acute encephalitis, a portion of patients develop late-onset or relapsing encephalitis, characterized by the reappearance of neurological symptoms months or years after the initial infection. These findings corroborate the literature, which suggests mechanisms of viral persistence in the central

nervous system or a delayed immune-mediated response, representing an additional challenge for long-term clinical follow-up.

## CLINICAL AND PROGNOSTIC FINDINGS

The analysis of studies indicates high mortality rates, often exceeding 40%, especially among patients who present early and severe neurological signs. Factors such as advanced age, rapid deterioration of neurological status, the need for ventilatory support, and diagnostic delay are strongly associated with worse prognosis.

Among survivors, a high frequency of permanent neurological sequelae is observed, including cognitive deficits, post-encephalitic epilepsy, motor disorders, and behavioral changes. These findings underscore the impact of Nipah virus not only on mortality but also on the quality of life of affected patients.

## DIAGNOSTIC AND THERAPEUTIC CHALLENGES

The results indicate that one of the main obstacles in the clinical management of Nipah virus infection is the difficulty of early diagnosis. Clinical similarity to other viral encephalitides, combined with limited availability of specific laboratory tests in endemic regions, contributes to delays in recognizing the disease. Diagnostic confirmation generally depends on molecular techniques, such as RT-PCR, which are not always available in a timely manner.

From a therapeutic perspective, studies emphasize the absence of effective specific antivirals, making treatment predominantly supportive. Experimental use of antivirals and immunomodulatory therapies yields inconclusive results, highlighting the need for new clinical studies and investments in translational research.

COMPARISON WITH THE EXISTING LITERATURE

The findings of this study are consistent with the international literature, which describes Nipah virus as a highly neurotropic pathogen capable of causing extensive brain inflammation and vascular damage in the central nervous system. Neuropathological studies report vasculitis, neuronal necrosis, and diffuse viral dissemination, explaining the severity and rapid clinical progression observed.

Late recurrence of neurological symptoms, although less frequent, is widely discussed in longitudinal studies, reinforcing the importance of prolonged clinical follow-up for surviving patients. Thus, the analyzed results broaden understanding of the clinical spectrum of infection and reinforce the need for continuous surveillance.

**Table 1**

*Main neurological manifestations and clinical implications of Nipah virus infection*

Neurological manifestation	Clinical characteristics	Prognostic implications
Acute encephalitis	Altered consciousness, seizures, focal deficits	High mortality
Late-onset encephalitis	Recurrence of symptoms months/years after infection	Neurological sequelae
Seizure episodes	Frequent during the acute phase	Post-infection epilepsy
Cognitive deficits	Impairment of memory and attention	Reduced quality of life

INTERPRETIVE SYNTHESIS

Overall, the results reinforce that neurological manifestations of Nipah virus represent the principal clinical and prognostic challenge of infection. The severity of presentations, combined with therapeutic and diagnostic limitations, contributes to unfavorable outcomes, evidencing the need for integrated strategies for surveillance, early diagnosis, and development of specific therapies.

## CONCLUSION

The present study aimed to analyze the neurological manifestations associated with Nipah virus infection, as well as to discuss the clinical challenges related to diagnosis and prognosis of affected patients. Based on the integrative literature review, it was possible to achieve the proposed objectives by systematizing relevant scientific evidence on the neurotropic behavior of the virus and its clinical implications.

The results showed that central nervous system involvement, especially in the form of acute encephalitis, constitutes the main clinical manifestation of Nipah virus infection and is directly associated with the high mortality rates observed in the described outbreaks. In addition, the occurrence of late neurological complications was identified, such as relapsing encephalitis and permanent sequelae, including cognitive deficits, seizure episodes, and behavioral changes, which significantly impact survivors' quality of life.

This research contributes to an in-depth understanding of the neurological spectrum of Nipah virus infection, highlighting the importance of early recognition of neurological signs and the adoption of timely clinical management strategies. Furthermore, the findings reinforce the need to strengthen epidemiological surveillance, train healthcare professionals, and invest in scientific research aimed at developing more accessible diagnostic methods and specific therapies.

Finally, it is suggested that future research further investigate the mechanisms of neuroinvasion and viral persistence in the central nervous system, as well as evaluate innovative therapeutic interventions and prevention strategies. Longitudinal studies following survivors of infection are also essential to better understand long-term neurological sequelae and to improve public health policies in response to high-impact emerging pathogens.

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