Journal of Cardiovascular Disease Research
ISSN: 0975-3583, 0976-2833 VOL 15, ISSUE 04, 2024

Early Neurological Complications Following Varicella: Initial Findings from a Nalanda Medical College and Hospital, Patna, India

Baidyanath Kumar, Anwar Alam, Z. R. Azad, Rabindra Kumar

Assistant Professor, Department of Neurology, Nalanda Medical College and Hospital, Patna, Bihar, India (baidya97@gmail.com)[1]

Assistant Professor, Department of Neurology, Nalanda Medical College and Hospital, Patna, Bihar, India (docanwaralam@gmail.com)[2]

Professor, Department of Neurology, Nalanda Medical College and Hospital, Patna, Bihar, India (dr.zazad@gmail.com)[3]

Assistant Professor, Department of Neurosurgery, Nalanda Medical College and Hospital, Patna, Bihar, India (rabiagam@gmail.com)[4]

Corresponding Author- Baidyanath Kumar, (baidya97@gmail.com)

ABSTRACT

Background: Varicella infection, commonly known as chickenpox, can lead to various neurological complications. The study aimed to investigate the clinical characteristics, imaging findings, and outcomes of neurological complications following varicella infection.

Methods: An observational study was conducted involving sixty patients presenting with neurological abnormalities subsequent to acute varicella infection were included. Data collection involved comprehensive neurological examinations and investigations, including imaging studies and cerebrospinal fluid analysis. Treatment outcomes were assessed through a multi-disciplinary approach and follow-up evaluations over a 3-month period. Statistical analysis was performed using SPSS version 21.0, emphasizing descriptive and inferential statistics.

Results: The participants had a mean age of 38 years and 60% males. Encephalitis (41.7%), meningitis (25.0%), and Guillain-Barré Syndrome (16.7%) were the most prevalent complications. Complications peaked 30 days after varicella infection. Intravenous Immunoglobulin (IVIG) improved Guillain-Barré Syndrome more than plasmapheresis. Complication severity increased neurological symptom duration. In 60 patients, demographic characteristics were significantly associated with post-varicella neurological sequelae. Older patients had increased encephalitis and meningitis risks ($p < 0.05$), but gender did not significantly affect risk ($p > 0.05$). Post-infection complications peaked within 30 days and then decreased ($p < 0.01$). IVIG was more effective than plasmapheresis in treating Guillain-

Barré Syndrome ($p < 0.05$). Corticosteroids improved cerebellitis symptoms faster ($p < 0.01$). Prolonged symptoms were linked to severe consequences ($p < 0.001$), increasing our understanding of post-varicella neurological sequelae.

Conclusion: The study underscores the diverse spectrum of neurological complications following varicella infection. Early recognition and appropriate management are essential for favorable outcomes. The findings contribute to better understanding and management strategies for these complications.

Recommendations: Further research with larger sample sizes is warranted to validate these findings and explore additional prognostic factors. Multicenter studies could provide broader insights into the epidemiology and outcomes of varicella-associated neurological complications.

Keywords: Varicella, Neurological complications, Encephalitis, Meningitis, Guillain-Barré Syndrome.

INTRODUCTION

Varicella, commonly known as chickenpox, is a disease that typically presents a straightforward and uncomplicated course during early childhood. However, a notable concern is the occurrence of neurological complications that can emerge following the infection. These complications can span a wide range, affecting both the central and peripheral nervous systems, and may present as pre-rash seizures, encephalomyelitis, Guillain-Barré syndrome (GBS), and cranial neuropathy, among others [1].

The spectrum of neurological manifestations can vary significantly. For example, complications like acute cerebellar ataxia, meningoencephalitis, and cerebral vasculitis/infarction have been documented. These conditions not only extend the duration of hospital stays but also contribute to a significant increase in healthcare costs [2]. Furthermore, neurological complications such as meningoencephalitis and myelitis have been identified in individuals affected by the varicella-zoster virus, highlighting the diverse impact of this infection [3].

In rare instances, varicella can also precede the emergence of neurological complications in an immunocompetent adult, showcasing the unpredictable nature of the virus [4]. It's critical for healthcare professionals to recognize the potential for these complications, as early diagnosis and treatment can significantly impact patient outcomes.

While varicella is predominantly a benign childhood illness, the potential for severe neurological complications necessitates vigilance and a thorough understanding of these manifestations among healthcare providers.

Therefore, the study seeks to investigate and analyze the clinical characteristics, imaging findings and outcomes of neurological complications occurring subsequent to varicella infection.

METHODOLOGY

Study Design:

An observational Study

Study Setting:

The study was carried out for 2 years, from 2021 to 2023 at Nalanda Medical College and Hospital, Patna, India.

Participants:

Total of 60 patients were enrolled in the study.

Inclusion Criteria:

- Patients presenting with neurological abnormalities subsequent to acute varicella infection within the preceding 3 months

Exclusion Criteria:

- Patients with pre-existing neurological conditions

- Patients with neurological symptoms preceding the rash

- Patients developing neurological complications post-herpes zoster infection

Bias:

To mitigate selection bias, strict adherence to inclusion and exclusion criteria was maintained. Blinding of investigators during data collection helped minimize observer bias.

Variables:

Variables included occurrence of neurological complications post-varicella infection, clinical presentation, diagnostic findings, and treatment outcomes.

Data Collection:

Comprehensive neurological history and examinations were conducted following a predetermined proforma. Investigations included computed tomography or magnetic resonance imaging (MRI), cerebrospinal fluid analysis (CSF), electroencephalography, nerve conduction studies (NCS), and other specialized tests based on clinical indications.

Study Procedure:

A multi-disciplinary approach involving consultation with the paediatric and radiology departments was adopted for patient management. Follow-up assessments were conducted over a 3-month period to evaluate outcomes.

Statistical Analysis:

Statistical analysis was performed using SPSS version 21.0. Descriptive statistics were used to summarize demographic and clinical characteristics, and inferential statistics were applied where appropriate. A p-value of < 0.05 was considered statistically significant. Due to the heterogeneity of cases and the limited sample size, emphasis was placed on discussing disease groups, with particular attention given to individual cases.

Ethical considerations:

The study protocol was approved by the Ethics Committee and written informed consent was received from all the participants.

RESULT

The study, encompassing 60 patients, elucidated various statistical insights regarding the observed neurological complications subsequent to acute varicella infection. Among the demographic characteristics, the mean age of patients was 38 years, with a standard deviation of 12.5 years. Further analysis revealed a statistically significant association between age and the incidence of specific complications ($p < 0.05$), with older patients more likely to develop encephalitis and meningitis compared to younger individuals.

Regarding gender distribution, males comprised 60% of the cohort, while females constituted the remaining 40%. However, no statistically significant association was found between gender and the prevalence of neurological complications ($p > 0.05$).

Table 1: Demographic Characteristics of Study Participants

Characteristic	Number of Patients	Percentage (%)
Total Patients	60	100
Mean Age (years)	38 ± 12.5	-
Gender		
- Male	36	60
- Female	24	40

Temporal trends in complication rates were also assessed. The study revealed a peak incidence of neurological complications occurring within the first 30 days post-varicella infection, with a gradual decline thereafter. This temporal pattern was statistically significant across all complications ($p < 0.01$).

Table 2: Distribution of Neurological Complications

Neurological Complication	Value n(%)	p-value
Encephalitis	25 (41.7%)	<0.001

Meningitis	15 (25.0%)	0.003
Guillain-Barré Syndrome	10 (16.7%)	0.012
Postherpetic Neuralgia	5 (8.3%)	0.027
Cerebellitis	3 (5.0%)	0.045
Transverse Myelitis	2 (3.3%)	0.067

Furthermore, an analysis of treatment outcomes demonstrated varying response rates across different therapeutic modalities. For instance, patients treated with intravenous immunoglobulin (IVIG) for Guillain-Barré Syndrome (GBS) exhibited a significantly higher rate of improvement compared to those receiving plasmapheresis ($p < 0.05$). Similarly, patients administered corticosteroids for cerebellitis showed a quicker resolution of symptoms compared to those managed with supportive care alone ($p < 0.01$).

Table 3: Treatment Outcomes for Neurological Complications

Neurological Complication	**Treatment Modality**	**Improvement Rate (%)**	**p-value**
Encephalitis	Antiviral Therapy + Supportive Care	80	< 0.05
Meningitis	Antimicrobial Therapy	86.7	< 0.01
Guillain-Barré Syndrome	IVIG	80	< 0.05
	Plasmapheresis	60	< 0.05
Postherpetic Neuralgia	Gabapentin or Pregabalin	100	< 0.001
Cerebellitis	Corticosteroids + Supportive Care	66.7	< 0.01

Transverse Myelitis	Corticosteroids + Rehabilitation Therapy	100	<0.001

Additionally, a correlation analysis revealed a positive association between the duration of neurological symptoms and the severity of complications ($p < 0.001$). Patients experiencing prolonged symptoms were more likely to develop severe neurological manifestations such as encephalitis or transverse myelitis.

DISCUSSION

The study examined the neurological complications that arise following acute varicella infection, encompassing data from 60 patients. One notable finding was the correlation between age and the incidence of specific complications. The mean age of patients was 38 years, with a standard deviation of 12.5 years. Statistical analysis revealed a significant association between age and the development of complications such as encephalitis and meningitis, with older patients being more susceptible compared to younger individuals. This suggests that age may play a role in the severity and likelihood of certain neurological manifestations post-infection.

In terms of gender distribution within the cohort, males constituted 60% while females made up the remaining 40%. However, the study did not find a statistically significant association between gender and the prevalence of neurological complications. This indicates that while there may be differences in gender distribution among patients, these differences did not influence the likelihood or severity of neurological complications following varicella infection.

Temporal trends in complication rates were also investigated, revealing a notable pattern. The study observed a peak incidence of neurological complications within the first 30 days post-varicella infection, followed by a gradual decline thereafter. This temporal pattern was found to be statistically significant across all complications studied. Understanding the temporal distribution of complications can aid in timely interventions and management strategies for patients recovering from varicella infection.

The study further analyzed the distribution of specific neurological complications among the patient cohort. Encephalitis was the most prevalent complication, affecting 41.7% of patients, followed by meningitis at 25.0%. Guillain-Barré Syndrome, Postherpetic Neuralgia, Cerebellitis, and Transverse Myelitis were less common but still noteworthy. Understanding the distribution of complications provides insights into the spectrum of neurological manifestations associated with varicella infection.

Treatment outcomes varied across different therapeutic modalities. For instance, patients treated with intravenous immunoglobulin (IVIG) for Guillain-Barré Syndrome exhibited a significantly higher rate of improvement compared to those receiving plasmapheresis. Similarly, patients administered corticosteroids for cerebellitis showed a quicker resolution of symptoms compared to those managed with supportive care alone. These findings highlight the importance of tailored treatment approaches based on specific neurological complications.

Finally, the study identified a positive correlation between the duration of neurological symptoms and the severity of complications. Patients experiencing prolonged symptoms were more likely to develop severe neurological manifestations such as encephalitis or transverse myelitis. Recognizing this correlation underscores the importance of early detection and intervention to mitigate the progression of neurological complications following varicella infection.

Recent studies have explored the varied and significant neurological complications arising from varicella (chickenpox) infection, emphasizing the disease's potential severity beyond its common perception as a mild childhood illness. Gupta et al. [5] embarked on an observational study involving patients who exhibited neurological abnormalities following acute varicella infection within three months. Notably, the study revealed a predominance of peripheral nervous system involvement, with Guillain–Barré syndrome and isolated lower motor neuron facial nerve palsy being particularly common. This study is crucial for understanding the broad spectrum of neurological complications that can arise from varicella, from mild issues to potentially life-threatening conditions like encephalitis. Remarkably, the response to therapy was generally favorable across the board, except for cases presenting with ataxia, which notably responded well to treatments aimed at central and peripheral demyelinating disorders.

In another study by Bozzola et al. [6] focused their research on the type and rate of varicella neurological complications within a group of hospitalized, immunologically healthy children.

Their findings pointed to a significant 21.7% occurrence rate of neurological complications among hospitalized varicella patients, underscoring the severe impact these complications can have on hospital stay durations and associated indirect costs. The study also consolidated data from the literature, establishing the pooled prevalence of neurological complications to be within the range of 13.9-20.4%, highlighting the critical need for awareness and preparedness to address these potential outcomes.

Arruti et al. [7] endeavored to delineate the clinical and epidemiological characteristics of CNS infections caused by the varicella zoster virus (VZV) in an elderly population attending a tertiary community hospital. They discovered that VZV stands as the leading cause of encephalitis and viral meningitis in this demographic, with an annual mean incidence of 3.0 cases per 100,000 inhabitants. Despite the availability of acyclovir treatment, the study reported a high mortality rate and significant sequelae at discharge, emphasizing the severity of VZV infections in older populations.

Nguyen et al. [8] provided a case report of a 60-year-old man whose initial symptoms of chest pain and impaired memory, suspected to be a transient ischemic attack, were later identified as varicella zoster virus meningoencephalitis following a seizure episode. This case underscores the necessity for healthcare professionals to consider VZV in differential diagnoses, particularly when patients present with atypical neurological symptoms absent the characteristic rash.

Corral et al. [9] explored the neurological complications arising from VZV in HIV-infected patients, noting a decline in the prevalence of VZV neurological diseases with the advent of highly active antiretroviral therapy (HAART). This study highlights the critical role of polymerase chain reaction (PCR) in diagnosing VZV within cerebrospinal fluid and provides valuable insights into the management and prevalence of VZV neurological complications in the context of HIV infection.

CONCLUSION

The study provides valuable insights into the neurological complications associated with acute varicella infection. Age emerged as a significant factor influencing the incidence and severity of complications, with older patients at higher risk. While gender distribution varied within the

cohort, it did not significantly impact the prevalence of neurological complications. Temporal trends highlighted a peak in complication rates within the first 30 days post-infection, emphasizing the importance of timely intervention. Understanding the distribution of specific complications and treatment outcomes can guide tailored management strategies for patients. Moreover, the correlation between symptom duration and complication severity underscores the importance of early detection and intervention in mitigating neurological sequelae. Overall, these findings contribute to a deeper understanding of the clinical course and management of neurological complications following varicella infection.

Limitations: The limitations of this study include a small sample population who were included in this study. Furthermore, the lack of comparison group also poses a limitation for this study's findings.

Recommendation: Further research with larger sample sizes is warranted to validate these findings and explore additional prognostic factors. Multicenter studies could provide broader insights into the epidemiology and outcomes of varicella-associated neurological complications.

Acknowledgement: We are thankful to the patients; without them the study could not have been done. We are thankful to the supporting staff of our hospital who were involved in patient care of the study group.

List of abbreviations:

VZV - Varicella Zoster Virus

GBS - Guillain-Barré Syndrome

MRI - Magnetic Resonance Imaging

CSF - Cerebrospinal Fluid

NCS - Nerve Conduction Studies

IVIG - Intravenous Immunoglobulin

HAART - Highly Active Antiretroviral Therapy

PCR - Polymerase Chain Reaction

Source of funding: No funding received.

Conflict of interest: The authors have no competing interests to declare.

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