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NEUROLOGICAL MANIFESTATIONS OF SCRUB TYPHUS: CLINICAL SPECTRUM, NEUROIMAGING FINDINGS, AND PREDICTORS OF ADVERSE NEUROLOGICAL OUTCOMES IN HOSPITALIZED PATIENTS

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ABSTRACT

Background. Scrub Typhus is an increasing zoonotic disease caused by the mite-borne organism Orientiam tsutsugamushi, which is prevalent in both India and other countries in Asia and affects the central nervous system in many cases. However, the relationship between the clinical characteristics, neuroimaging findings and neurological outcomes in hospitalized patients is not yet well defined. This study aims to see the neurological involvement in scrub typhus patients who were hospitalized concerning their clinical presentation, imaging findings and adverse outcomes.

Methods. Over a two-year period, an observational prospective study was conducted in the Department of General Medicine at Sudha Medical College and Bharat Vikas Institute of Medical Sciences, Kota. A total of 50 patients with laboratory-confirmed scrub typhus were recruited using non-probability consecutive sampling. The demographic, clinical, neurological as well as laboratory data were acquired from a patient interview, clinical observations as well as hospital documents, and MRI findings, when clinically required and available, were documented. Discharge status was complete recovery, residual disabilities or death. All the data were descriptively analyzed with the statistical software Microsoft Excel using frequencies and percentages.

Results. Neurological symptoms were revealed in 30 of 50 patients (60%). The most common neurologic symptom was unconsciousness (10 patients, 20%), followed by meningitis (7, 14%), seizure (6, 12%), cerebellar disorders (4, 8%) and peripheral neuropathy (3, 6%). Of those 30 patients, 21 (70%) had MRI abnormalities, the majority being meningeal enhancement (9 patients), followed by brain edema (5), white matter pathology (4) and brain stem/cerebellar pathology (3), with nine patients having a normal MRI scan. At the moment of discharge, 38 patients (76%) have completely recovered, 8 (16%) were left with some neurological deficits, and 4 (8%) died.

Conclusion. Scrub typhus can lead to serious neurological diseases, and clinical evaluation and MRI imaging yield useful information although a normal MRI does not rule out a neurological problem. Assessment of neurological status early, MRI when relevant and conducting a full assessment of neurological function prior to discharge is recommended. Restrictions related to the small sample size do not permit generalization of results and larger multicenter studies with more prolonged follow-ups are required to establish independent predictors of neurological morbidity and mortality.

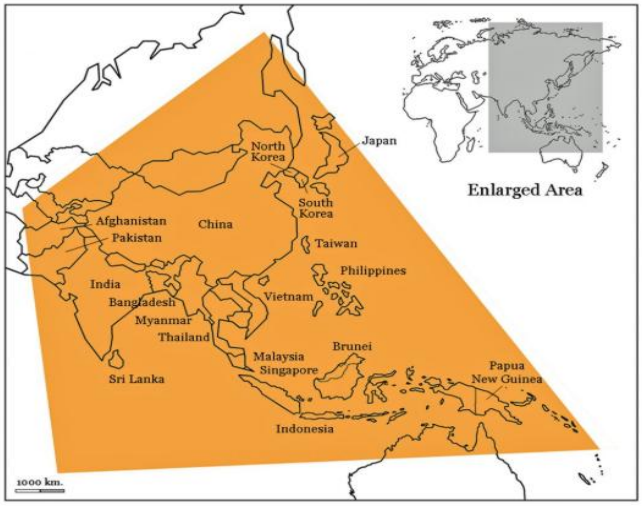
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INTRODUCTION

Background and Context

Scrub Typhus is an emerging, mite-borne zoonotic infectious disease caused by *Orientia tsutsugamushi* with a global presence. However, predominantly, the disease affects the population of India, China, Thailand, Malaysia, Korea and other Asian nations [1]. In these regions, the disease has been characterised as endemic and presents significant public health concerns to the local authorities. The geographical spread of the disease spans a region of around 13,000,000 square kilometres in the Asia-Pacific,

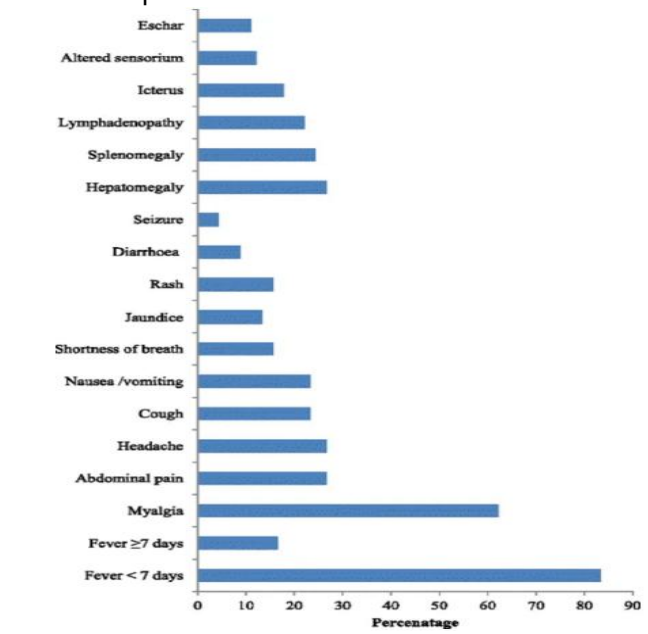
with isolated cases in Latin American nations like Peru and Chile [2].



(Source: The Ohio State University [2])

Figure 01: Geographical spread of Scrub Typhus

The key symptoms of the disease range from high fever and chills to multi-organ failure. It has been found that the Central Nervous System (CNS) of the human body is affected by the disease, which leads to severe neurological dysfunction in 20% of the patients [3]. Other common symptoms of the disease include fever, headache, rash and eschar, along with complications in the cardiovascular and renal systems. A review study by Kore and Mahajan [4] found that, in India, the most common symptom of Scrub typhus is persistent fever for less than 7 days (>80%), followed by myalgia (>60%) and hepatomegaly (30%) in states such as Kerala, Tamil Nadu, Jammu & Kashmir, Himachal Pradesh and West Bengal. Therefore, urgent measures to ensure early diagnosis and treatment of such patients at local hospitals are crucial to ensure a significant reduction in prevalence.



(Source: Kore and Mahajan [4])

Figure 02: Clinical symptoms of scrub Typhus among hospitalised patients in India

The technology of neuroimaging, particularly MRI (Magnetic Resonance Imaging), provides important diagnostic information regarding neurological complications related to Scrub Typhus. According to Yadav and Yadav [5], an increase in the cortical and subcortical T2/FLAIR hyperintensities, consistent T2 hyperintensity in the spinal cord and patchy lesions in the white matter of the brain are key identifiers of the disease. Despite this, the relationship between clinical characteristics, abnormalities identified through neuroimaging and subsequent outcomes regarding the disease remains insufficiently established. Therefore, further investigation of the neurological manifestations of the disease needs to be conducted in real-life conditions (hospitalised patients).

AIM AND OBJECTIVES

The aim of the research is to examine the neurological manifestation of Scrub Typhus patients in hospitalised conditions in relation to clinical symptoms, neuroimaging characteristics and predictors of adverse neurological outcomes.

Objectives

- To identify the clinical spectrum and frequency of neurological manifestations of hospitalised Scrub Typhus patients in India.
- To evaluate neuroimaging abnormalities and its association with neurological complications among Scrub Typhus patients.
- To examine the clinical, biochemical and radiological factors associated with adverse neurological outcomes.
- To understand neurological recovery, mortality and disability of patients at the time of hospital discharge in India.

Research Question

- Is the clinical spectrum and frequency of neurological manifestations of hospitalised Scrub Typhus patients in India significantly large to estimate the disease extent?
- How are neuroimaging abnormalities used for the identification of Scrub Typhus patients before hospitalisation?
- What are the clinical, biochemical and radiological factors associated with adverse neurological outcomes for Scrub Typhus patients?
- What is the ratio of mortality, disability and recovery among hospitalised Scrub Typhus patients in India?

Motivation and Rationale

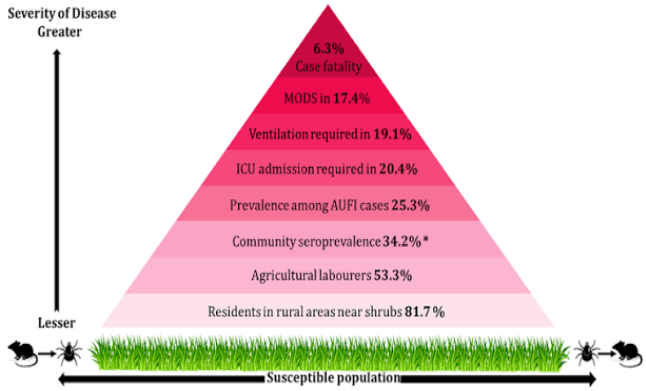
The motivation behind this research is mainly related to the large clinical burden of Scrub Typhus patients experienced by the healthcare workers across India. Moreover, despite advances in diagnostic imaging through MRI and clinical management, identifying patients at risk of adverse neurological outcomes remains challenging in rural areas. In this context, understanding the relationship between neuroimaging findings and clinical symptoms of the disease among the patients is crucial to address healthcare needs. Therefore, evidence from hospitalised patients in India could address existing gaps in clinical knowledge. As a result, it may contribute to the development of contextual understanding among healthcare policymakers and healthcare staff to reduce mortality and ensure patient-centred care.

LITERATURE REVIEW

The clinical spectrum and frequency of neurological manifestations of hospitalised Scrub Typhus patients in India

Basu and Chakravarty [6] explain that neurological involvement may result from direct infection, vascular inflammation and immune-mediated mechanisms. Nevertheless, the clinical manifestations are different, and it is hard to diagnose it at the initial stages.

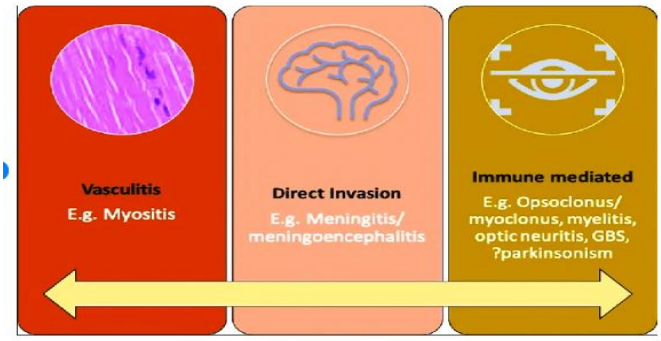
In a systematic review and meta-analysis, Alam et al. [3] studied the neurological manifestations and case fatality of scrub typhus. Their results show that neurological complications contribute to the disease burden. Nevertheless, the differences in the study populations and diagnostic criteria do not allow the direct comparison of the prevalence across regions. In the same vein, Rehani et al. [7] found a wide range of neurological manifestations in patients with the condition. Their results confirm the significance of neurological examination at the time of hospital admission and not just fever, rash and eschar.



(Source: Devasagayam et al. [8])

Figure 03: Burden of scrub typhus in India

Even recent evidence suggests that other systemic complications may be accompanied by neurological involvement. Reba and Gunasekaran [9] note encephalitis and meningitis as other complications that need to be identified clinically on time. However, a lot of the Indian evidence available is based on retrospective research, as well as, on select cases of neurology. Thus, the current study explores the clinical prevalence and range in 50 patients in the hospital in Kota.



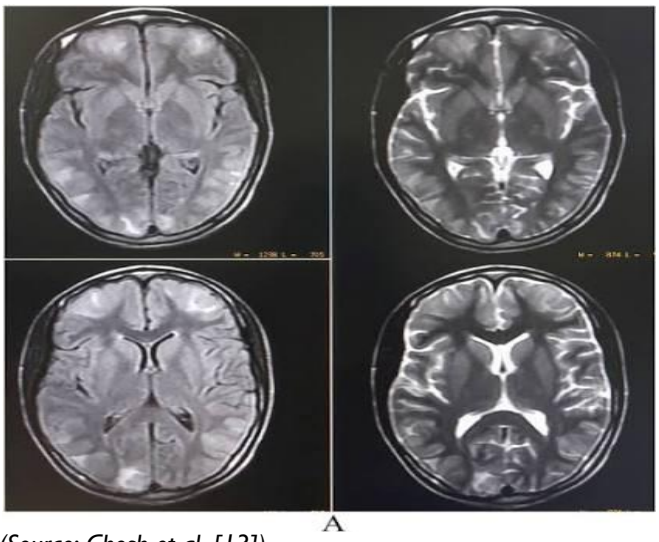
(Source: Garg and Manesh [10])

Figure 04: Neurological factors of Scrub typhus

NEUROIMAGING ABNORMALITIES AND THEIR ASSOCIATION WITH NEUROLOGICAL COMPLICATIONS AMONG SCRUB TYPHUS PATIENTS

Shalini et al. [11] studied 55 patients with neurological scrub typhus who underwent MRI in the 2026 South Indian cohort study. Abnormalities were detected in 46 patients (83.6%), and the most common one was leptomeningeal enhancement (49.1%). The paper offers valuable clinical-radiological data. Its retrospective nature and choice of patients having MRI, though, could restrict the generalisation of the results to all hospitalised patients.

Other neurological and radiological manifestations such as meningeal enhancement, infarctions and brainstem abnormalities were also found to vary, as reported by Mohammed Ansari et al. [12]. These results indicate that MRI is capable of aiding clinical diagnosis, but an abnormal scan alone is not enough to make the diagnosis. The results of MRI should be analysed in conjunction with the neurological examination, serological confirmation and lab tests.



(Source: Ghosh et al. [13])

Figure 05: Neurological and neuropsychiatric manifestations of Scrub typhus

THE CLINICAL, BIOCHEMICAL AND RADIOLOGICAL FACTORS ASSOCIATED WITH ADVERSE NEUROLOGICAL OUTCOMES

Modi et al. [14] showed that scrub typhus can result in both central and peripheral neurological complications at the same time. Their case report demonstrates the need to be aware of atypical neurological presentations. But case reports cannot determine distinct predictors of mortality or disability.

Reba and Gunasekaran [9] emphasise the relationship between severe neurological complications and increased clinical risk. However, the predictive ability of single laboratory and radiological variables needs to be explored further with bigger samples of patients. Thus, the current study will involve a comparison of clinical severity, biochemical deviations and MRI results with poor discharge outcomes.

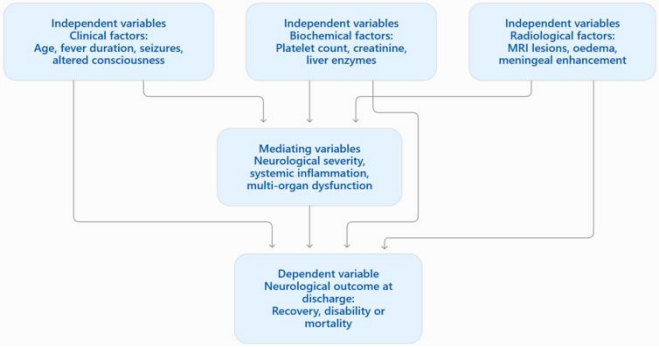
NEUROLOGICAL RECOVERY, MORTALITY AND DISABILITY OF PATIENTS AT THE TIME OF HOSPITAL DISCHARGE IN INDIA

Alam et al. [3] emphasise that neurological complications are crucial in the assessment of mortality caused by scrub typhus. Modi et al. [14] also show that neurological involvement can be severe and may lead to the necessity of further treatment and a longer period of clinical observation. Further evidence is given in the 2026 imaging cohort by Shalini et al. [11] which suggests that radiological

abnormalities can be resolved, but there are patients who can acquire residual structural alterations.

Nevertheless, there is a paucity of similar information in the literature on neurological disability, particularly at hospital discharge. This leads to the necessity to study discharge outcomes in a systematic manner. The current research will categorise the results as full neurological recovery, neurological disability and mortality.

Conceptual framework

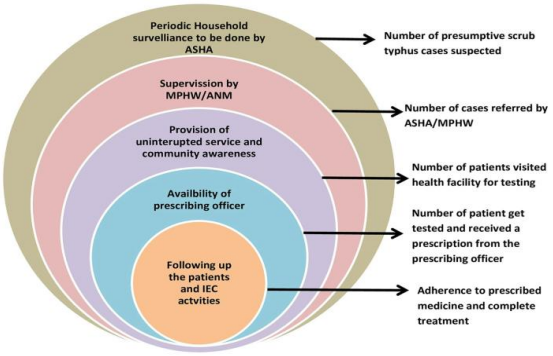


(Source: Self-created)

Figure 06: Conceptual framework

Theoretical framework

The clinical disease-severity and prognostic framework is used to guide the research. This modality presupposes that the interplay of clinical manifestations based on infection, systemic organ pathology, and neurological damage affects the outcome of patients. Neurological complications may be due to direct infection, vascular damage and immune-mediated reactions [6]. Hence, the clinical evaluation and the MRI results cannot be viewed separately but in conjunction with each other. This model facilitates the study of potential correlations among patient factors, disease severity and neurological recovery.



(Source: Jain et al. [15])

Figure 07: Development of early diagnosis strategy of Scrub typhus in India

LITERATURE GAP

Alam et al. [3] defined the neurological burden of scrub typhus via a systematic review, but lacked hospital-based data from Kota. Modi et al. [14] also emphasised the severity of neurological complications but were not able to determine their overall prevalence and predictors. Mohammed Ansari et al. [12] characterised significant neurological and MRI changes in 17 patients, but the small, selective sample did not allow broader clinical comparisons. Likewise, Shalini et al. [11] placed primary emphasis on neuroimaging results, instead of combining clinical with biochemical and radiological predictors and discharge outcomes. Consequently, the current research considers these factors in a combination of 50 patients hospitalised in Kota, where neurological recovery, disability and mortality are given special focus.

RESEARCH METHOD

Research design

An observational prospective study has been carried out in a hospital over a period of two years in the Department of General Medicine, Sudha Medical College and Bharat Vikas Institute of Medical Sciences, Kota. The paper has looked at the clinical presentation, neuroimaging features and discharge outcomes of inpatients diagnosed with scrub typhus. No experimental intervention is presented. The patients were treated based on the decision of the clinical team and the hospital protocol.

Data collection method

The information has been gathered through patient interviews, clinical observation, laboratory reports and hospital medical records. Data will comprise demographic data, fever span, neurological data, platelet count, liver and renal data tests and other pertinent inflammatory data. Where there is a clinical indication for imaging, and the imaging is available, MRI findings have been documented. Confirmation of scrub typhus was done according to the recommended diagnostic criteria of the hospital, which is usually the IgM ELISA or PCR where possible. Standardised categories have been used to record neurological status and final outcomes at discharge.

Sampling and sample size

The study has recruited 50 eligible hospitalised patients through a non-probability consecutive sampling technique in the study period. Inclusion criteria included patients with laboratory-confirmed scrub typhus and clinical information. Patients with other known causes of neurological disease or inadequate clinical history were excluded. All potential respondents were approached until the necessary number of respondents was reached.

Data analysis method

Data entry, coding and quantitative analysis were done in Microsoft Excel. The patient characteristics and clinical findings will be described in terms of frequencies, percentages, means, and standard deviations. Cross-tabulation might be used to compare neurological presentation and MRI changes to discharge outcomes. The main findings were represented using bar charts and pie charts. Descriptive differences between patients with favourable and adverse outcomes have also been analysed using Excel. Results were interpreted with great caution due to the small sample size.

Reliability and validity

There was a standardised data collection sheet that enhanced consistency. Both clinical and lab data have been verified with original hospital records. Duplicates and missing values have been checked and reviewed prior to analysis. Findings from MRI were measured using consistent radiological categories. Validity was enhanced by the use of the established diagnostic criteria. Nevertheless, bias may be introduced due to differences in imaging availability, incomplete records and interpretation by observers.

Ethical consideration

Recruitment was done with ethical approval from the concerned Institutional Ethics Committee. Participants or authorised representatives who have appropriate understanding have given informed consent. Coded records

were used to ensure patient confidentiality. There was no impact of participation on treatment decisions. Only academic and research purposes have been used for the data.

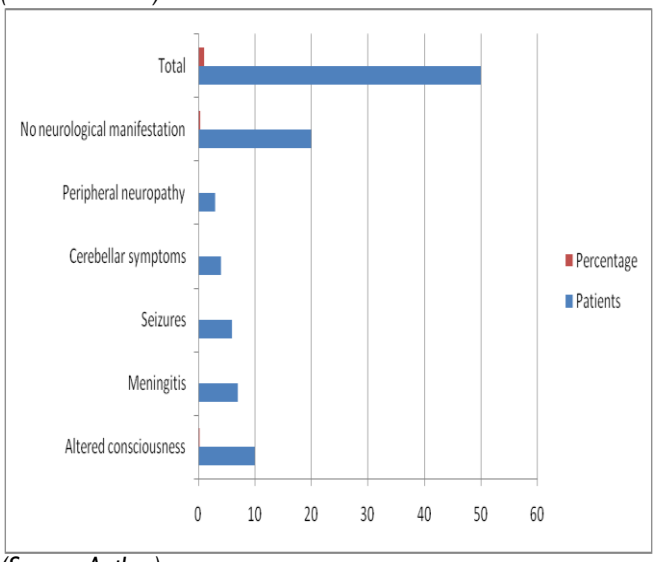
RESULTS AND DISCUSSION

There were 50 hospitalised patients in the sample. Neurological manifestations were demonstrated in 30 patients (60%), and 20 patients (40%) did not show neurological manifestations.

Table 01: Clinical spectrum

Neurological manifestation	Patients	Percentage
Altered consciousness	10	20%
Meningitis	7	14%
Seizures	6	12%
Cerebellar symptoms	4	8%
Peripheral neuropathy	3	6%
No neurological manifestation	20	40%
Total	50	100%

(Source: Author)



(Source: Author)

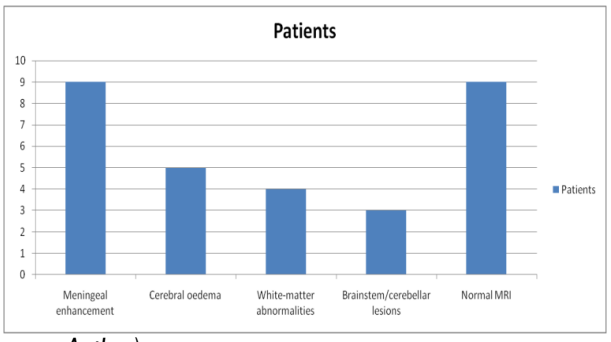
Figure 08: Clinical spectrum of neurological manifestations

The most common phenomenon in this sample is altered consciousness. This implies that special consideration should be paid to neurological evaluation at the time of admission. But the distribution cannot determine the actual prevalence in Kota.

Table 02: MRI findings among 30 neurological patients

MRI finding	Patients
Meningeal enhancement	9
Cerebral oedema	5
White-matter abnormalities	4
Brainstem/cerebellar lesions	3
Normal MRI	9

(Source: Author)



(Source: Author)

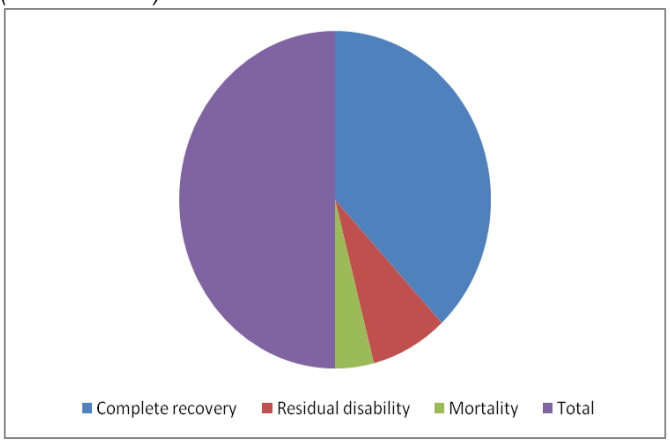
Figure 09: MRI findings of neurological patients

The observed MRI abnormalities are found in 21 out of 30 patients (70%). The most common abnormality is meningeal enhancement. There are, however, nine patients with normal MRI findings with neurological symptoms. This reinforces the fact that MRI should not be used to substitute clinical assessment.

Table 03: Neurological outcomes of hospital discharge

Outcome	Patients	Percentage
Complete recovery	38	76%
Residual disability	8	16%
Mortality	4	8%
Total	50	100%

(Source: Author)



(Source: Author)

Figure 10: Discharge outcomes of the patients

The results suggest that the majority of patients achieve full recovery, and 24% of the patients are disabled or dead. This emphasises the significance of early diagnosis, proper treatment and follow-up. Nonetheless, the small samples may not allow making any conclusions about the highly generalisable clinical outcomes.

In general, the review illustrates the possibility of comparing clinical, biochemical and radiological data with discharge outcomes. This would require a bigger sample and a longer follow-up in order to come up with predictable predictors of neurological disability and mortality.

CONCLUSION AND RECOMMENDATIONS

Scrub typhus may result in serious neurological effects, such as altered consciousness, meningitis, seizures and peripheral neurological disorders. MRI and clinical assessment give complementary data to detect neurological involvement. These manifestations and their correlation with biochemical abnormalities and discharge outcomes are investigated in the current clinical research study in Kota in relation to 50 hospitalised patients.

It is proposed to make the following recommendations:

1. Hospitals are advised to enhance early neurological evaluation of confirmed scrub typhus patients.
2. MRI is recommended in cases of suspected neurological complications, when imaging is clinically necessary.
3. There should be monitoring of clinical and biochemical indicators to identify patients who are at risk of deterioration.
4. Prior to discharge from the hospital, standardised neurological assessment should be done.
5. Independent predictors of adverse outcomes should be studied using further multicentre studies involving more participants and extended follow-up.

The research can provide potential local clinical evidence and help improve the treatment of neurological complications with scrub typhus.

FUNDING

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

INFORMED CONSENT

Written informed consent was obtained from all participants before enrolment. For patients with altered consciousness or who were otherwise unable to give consent, consent was obtained from a legally authorised representative. No identifiable patient information is included in this manuscript.

ETHICAL STATEMENT

Formal ethical approval was not required for this study, as it was a non-interventional observational study in which all patients received standard care according to the decision of the treating clinical team and hospital protocol. The study was conducted in accordance with the principles of the Declaration of Helsinki (2013 revision). Patient confidentiality was maintained through coded records, and participation had no bearing on treatment decisions.

CONFLICT OF INTEREST

The authors declare that they have no conflicts of interest relevant to this work.

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AUTHOR CONTRIBUTIONS

Dr Anwar Ul Haq Ansari: Conceptualisation, study design, supervision, interpretation of results, and drafting of the original manuscript.

Dr Rameshwar P Gupta: Methodology, patient recruitment, data collection, and critical revision of the manuscript for important intellectual content.

Dr Anil Mangal: Data collection and curation, data analysis, literature review, and review and editing of the manuscript. All authors read and approved the final manuscript and agree to be accountable for all aspects of the work.

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