



Original Research

Neurological Manifestations in Patients Presenting with Uremic Encephalopathy at a Tertiary Care Hospital

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ABSTRACT

Objective: To assess the neurological presentation in patients with uremic encephalopathy and its correlation with the severity of the disease at a tertiary care centre and to find out its prevalence.

Materials & Methods: This is an observational cross-sectional study that was carried out at Lady Reading Hospital, Peshawar. The patients were sampled consecutively, giving a total of 230 patients with uremic encephalopathy. Neurological evaluation was carried out using clinical examination, laboratory, and selected neurophysiology tests. The associations were tested by chi-square and t-tests.

Results: The most frequent neurological manifestations were altered consciousness (77.4 percent), followed by confusion (67 percent) and asterixis (38.2 percent). Of all cases, 26.9 per cent had seizures. Renal failure (stage 4 and above) was highly correlated with severe neurological dysfunction (p-value < 0.001). The most common EEG abnormalities were diffuse slowing and triphasic waves. Of the patients, 45.2 per cent had a complete recovery after dialysis, with 6.9 per cent dying.**

Conclusion: Neurological signs and symptoms in uremic encephalopathy were common and were closely associated with the degree of renal failure. Early diagnosis and prompt dialysis were correlated with a better neurological outcome.

Keywords: Uremic Encephalopathy, Altered Consciousness, Neurological Manifestations, Renal Failure, Dialysis And Tertiary Care Hospital.

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INTRODUCTION

Neurological involvement in uremic encephalopathy is more commonly observed in patients with uremic encephalopathy in clinical nephrology and neurology. The condition can be seen in late renal failure when the accumulation of uremic toxins causes changes in the central nervous system and results in changes in the state of the CNS. It is called a complex metabolic brain disorder occurring in chronic kidney disease and

acute kidney injury. The pathophysiology is associated with the accumulation of nitrogenous waste products and impairment of the pathways of neuronal signaling. The clinical spectrum is wide, comprising cognitive decline, alteration of consciousness, seizures, and neuromuscular irritability. The disease burden is formidable in tertiary care centers where delayed presentation occurs often, and challenges are faced in management because of multisystem involvement.

There have been several studies on the neurological effects of uremia; however, there is a concern for variability in clinical presentation. Untreated uremic encephalopathy has been correlated with early milder cognitive disturbances and later development of coma. This difference in symptoms has been attributed to differences in the rate of accumulation of toxins and individual susceptibility of the central nervous system.² The ability to identify early neurological signs is underutilized in healthcare systems in developing countries and is frequently made at later stages of the disease process. This delay contributes to increased morbidity and longer hospital stay.

EEG abnormalities have been described in patients with uremic encephalopathy, and the abnormalities have been related to the severity of the clinical symptoms. In these patients, the typical electrocardiographic pattern is diffuse slowing and triphasic waves. All of these results confirm the metabolic nature of cerebral dysfunction and help in the diagnosis in unclear clinical situations. Although the diagnostic modalities are present in tertiary care hospitals, there is still a lack of standardization of screening protocols and awareness among primary care providers, which creates the challenge of underutilization.

Neurological dysfunction in the uremic state is polyetiological and related to osmotic imbalance, inflammatory mediators, and neurotransmitter metabolism. Guanidino compounds have been suggested to be connected to changes in neuronal excitability and seizures.⁴ Oxidative stress and endothelial dysfunction also play a role in cerebral

oedema and disturbed cerebral perfusion. All of these processes combine to lead to gradual loss of function and neurological function.

Symptoms range from headache, confusion, disorientation, agitation, myoclonus, and seizures. In severe cases, stupor and coma occur and require intensive care management. Asterix has also been reported in advanced stages of disease. Diagnostic confusion is a frequent issue with the presentation of the disorder; often it is misdiagnosed as a primary neurological disorder in emergencies. This is a factor in the delay of starting renal replacement therapy.

Structural causes of neurological decline are excluded by imaging studies such as computed tomography and magnetic resonance imaging. Findings may be non-specific, but in advanced cases, cerebral oedema and changes in the white matter have been reported. The following radiological features are suggestive of metabolic encephalopathy but are not diagnostic. So, clinical correlation is still necessary for the diagnosis of uremic encephalopathy.

Chronic kidney disease is still on the rise in developing nations' tertiary care hospitals where diabetes, hypertension, and glomerular diseases are on the rise. This has resulted in more uremic complications such as neurological involvement.⁷ The difficulty of obtaining early nephrology services and the time taken to start dialysis also add to the risk of encephalopathy. Important contributing factors are health system constraints and patient-related delays.

Local population studies of neurologic effects of uremic encephalopathy are quite sparse and scattered. The majority of studies that are currently available are small, retrospective, and non-standardized neurological assessments.⁸ Not much information is available on the frequency distribution of individual neurological signs and their association with biochemical parameters. Moreover, there is a scarcity of data from tertiary care hospitals in Pakistan about systematic evaluation of these manifestations.

Although there has been some research on biochemical abnormalities, neurological profiling has been underutilized in the literature so far. This leaves much work to be accomplished in the realm of understanding the entire clinical picture of uremic encephalopathy in hospitalized patients. Early identification of neurological markers can help to provide timely intervention and enhance clinical outcomes. The use of standardised neurological assessment is also not widely used in clinical settings, reducing the availability of data.

Another significant deficiency is the prognostic significance of neurological symptoms in uremic encephalopathy. The degree of neurological dysfunction and the mortality outcome are not well defined.¹⁰ This relationship should help in risk stratification and clinical decision-making in the intensive care unit. Additionally, there is limited evidence on recovery patterns following initiation of dialysis and supportive therapy.

A systematic evaluation of the neurological manifestations of patients presenting with uremic encephalopathy is needed in tertiary care hospitals of Pakistan. Reliable documentation of clinical features can help enhance the accuracy of diagnosis and treatment. The early identification of neurological signs could help to initiate dialysis in time, thereby preventing the morbidity of delayed dialysis.

This study aims to assess neurological presentation in patients with uremic encephalopathy in a tertiary care hospital and to find out the frequency and pattern of these neurological presentations and their correlation with clinical severity to provide a better approach to diagnosis and treatment.

MATERIALS AND METHODS

Study Design and Setting

This study was of descriptive, observational, and cross-sectional type, which was carried out in a major tertiary care teaching hospital (LHPS) of Peshawar city (Lady Reading Hospital) with a huge

number of nephrology and neurology referrals from Khyber Pakhtunkhwa and its adjoining areas. The study took place from 23 February 2025 until 23 December 2025. For the total sample size, the number of patients chosen in the study was 230, obtained by a consecutive non-probability sampling technique. The patients who met the diagnostic criteria for uremic encephalopathy were selected in the medical wards of the emergency department and in the dialysis unit. The study was designed to systematically assess neurological features with the use of standardized clinical tools and confirmation of renal dysfunction by laboratory analysis.

Ethical Consideration

The study was conducted after obtaining ethical approval from the **Institutional Review Board (IRB), Lady Reading Hospital Medical Teaching Institution (LRH-MTI), Peshawar**, prior to data collection, under **Reference No. 523/LRH/MTI, dated 02/12/2025**. All patients provided informed consent; where a patient was unable to provide consent due to altered mental status, consent was obtained from the legal guardian. Patient information was kept strictly confidential throughout the study. All procedures were performed in accordance with the principles of the Declaration of Helsinki. No additional invasive procedures were performed solely for research purposes, and routine patient management was not modified for study participation.

Study Population and Sampling Technique

Patients were eligible for inclusion if they were of either gender and all age groups of adults, presenting with clinical features suggestive of uremic encephalopathy. Consecutive sampling was used to minimize selection bias and to make sure that the hospital population was represented. Consultant nephrologists and neurologists were consulted in all patients to confirm the diagnosis.

The diagnosis of uremic encephalopathy was made on the clinical neurological basis and advanced renal failure with elevated blood urea and serum creatinine levels and the absence of other structural or infectious causes of altered mental status.

Inclusion Criteria

Patients were eligible for inclusion if they had clinical evidence of seizures, confusion or altered mental status, disorientation, or other neurologic abnormalities associated with renal failure. Laboratory parameters were elevation of serum urea and creatinine consistent with advanced renal dysfunction in need of, or eligible for, dialysis. This included newly diagnosed renal failure patients as well as patients with known chronic kidney disease (CKD) stages four and five. Patients who provided consent or had attendants were able to do so; in the case of impaired consciousness were the only patients who were enrolled in the study.

Exclusion Criteria

Patients were excluded if the neurological symptoms had been caused by any other identifiable etiology, such as intracranial hemorrhage, ischemic stroke, brain tumor, central nervous system infections, hepatic failure, or severe electrolyte imbalance not caused by uremia. Patients with known psychiatric illness resulting in altered behavior without metabolic derangement were also excluded. People who suffered a head injury or fell into a drug-induced coma were excluded. Patients who did not have a completed medical record, or who left outpatient care prior to completion of diagnostic evaluation, were also excluded from this study.

Data Collection Procedure

The data were collected through a structured proforma, which was created for the purpose of this study. A detailed history was obtained of the

duration of renal disease, comorbid conditions, and presenting neurological complaints. A clinical examination of level of consciousness, cognitive status, cranial nerve involvement, motor function, reflex changes, and seizures or movement disorders was carried out. Laboratory studies included a complete blood count (CBC), blood urea nitrogen (BUN), serum creatinine (SCr), electrolytes, and arterial blood gas (ABG) analysis. Surgical exploration of the brain was indicated when appropriate, and computed tomography was performed. In selected cases, electroencephalography was carried out to record cerebral dysfunction patterns.

Neurological Assessment

Standardized bedside neurological examination techniques were performed. Glasgow Coma Scale was used for the assessment of level of consciousness. Patients responded co-operatively, and cognitive function was assessed by orientation, attention, and response to commands. Examination of the motor system included the evaluation of tone, power, reflexes, and presence of asterix and/or myoclonus. Seizure activity was noted from clinical observation and patient history. All findings were noted at the time of admission and in the hospital during the patient's treatment to monitor any progression or improvement once dialysis began.

Treatment Protocol Documentation

Although treatment was not a variable intervention of the study, all patients received standard care according to hospital protocols. Patients with definite indications for renal replacement therapy were started on hemodialysis. Supportive management comprised correction of electrolyte imbalance, control of blood pressure, and management of underlying causes of renal failure. Neurological symptoms were documented, if applicable, to assess trends in clinical improvement in response to dialysis.

Statistical Analysis

SPSS version 25 was used to analyse the data. Demographic and clinical data were summarized by descriptive statistics. The quantitative variable data – age, serum urea, serum creatinine – were analyzed for mean and standard deviation. Categorical variables such as gender, neurological manifestations, and clinical features were analyzed for frequencies and percentages. To assess association between categorical variables, e.g., severity of renal failure and presence of specific neurological symptoms, the Chi-square test was used. Where appropriate, independent sample t test was used to compare means. P-value < 0.05 was regarded as statistically significant.

Ethical Consideration

The study was conducted after receiving ethical approval from the institutional ethical review board of Lady Reading Hospital, Peshawar, before data collection. All patients or legal guardians were provided with informed consent if the patient was unable to provide it due to altered mental status. Patient information was kept confidential throughout the study. All procedures were performed following the principles of the Declaration of Helsinki. No other invasive procedures were used for research, and patient management was not modified for study entry.

Data Collection

The data were validated and quality-controlled. To ensure the validity of data collection, all assessments were performed by trained clinicians under the supervision of senior consultants. Data was monitored regularly to prevent errors and missing data. Pre-final analysis was conducted after double-checking laboratory results and clinical findings. To ensure accuracy and reliability in the study outcomes, discrepancies in data were handled through discussion with the main investigators.

RESULTS

Demographic Characteristics and Baseline Profile of Patients

A total of 230 patients diagnosed with uremic encephalopathy were included in the study. The demographic evaluation showed a predominance of male patients with a slightly higher frequency compared to female patients. The mean age of the study population reflected middle- to elderly age groups, with significant representation of patients having chronic kidney disease stage five. Most patients presented with advanced biochemical derangement at admission, with markedly elevated serum urea and creatinine levels. Altered mental status was the most frequent presenting feature, followed by seizures and motor dysfunction.

Table 1: Demographic and Baseline Clinical Characteristics of Patients.

Variable	Value
Total patients	230
Mean age (years)	56.8 ± 14.3
Male	138 (60%)
Female	92 (40%)
Known CKD	162 (70.4%)
New-onset renal failure	68 (29.6%)
Mean serum urea (mg/dL)	176.5 ± 42.7
Mean serum creatinine (mg/dL)	6.9 ± 2.1

The table demonstrates that most patients were known cases of chronic kidney disease with significantly deranged renal function parameters at presentation, indicating late-stage disease burden.

Frequency of Neurological Manifestations in Uremic Encephalopathy Patients

Neurological assessment revealed that altered level of consciousness was the most common manifestation observed in the majority of patients.

Confusion and disorientation were also frequently recorded. Seizure activity was noted in a significant subset of patients, while movement disorders such as asterixis and myoclonus were present in moderate frequency. Cognitive impairment was more prominent in patients with prolonged disease duration and delayed dialysis initiation.

The findings indicate that the encephalopathy spectrum ranged from mild cognitive dysfunction to severe coma with multiple overlapping neurological features.

Association Between Renal Function Severity and Neurological Presentation

A statistically significant association was observed between severity of renal dysfunction and the presence of severe neurological manifestations.

Patients with higher serum creatinine and urea levels were more likely to present with seizures, coma, and severe cognitive impairment. The chi-square test demonstrated a significant correlation between advanced renal failure and neurological deterioration.

The statistical analysis confirms that progression of renal failure is strongly associated with worsening neurological status in uremic encephalopathy patients.

Electroencephalographic Findings in Patients with Uremic Encephalopathy

Electroencephalography was performed in 112 selected patients with moderate to severe neurological impairment. The most common abnormality was diffuse slowing of background activity, followed by triphasic waves. These findings apply only to the subgroup that underwent EEG and should not be generalized to all 230 participants.

The EEG findings support a metabolic encephalopathy pattern consistent with uremic toxin accumulation affecting cerebral function.

Table 2: Frequency of Neurological Manifestations in Study Population.

Neurological Manifestation	Number of Patients (n)	Percentage
Altered consciousness	178	77.4%
Confusion & disorientation	154	67.0%
Seizures	62	26.9%
Asterixis	88	38.2%
Myoclonus	74	32.1%
Cognitive impairment	96	41.7%
Coma state	48	20.9%

Table 3: Association of Renal Function Severity with Neurological Severity.

Severity of Renal Dysfunction	Mild Neurological Symptoms	Severe Neurological Symptoms	p-value
Moderate (n=72)	54	18	<0.001
Severe (n=158)	46	112	<0.001
Total	100	130	<0.001

Table 4: EEG Findings in Patients with Neurological Impairment.

EEG Pattern	Number of Patients (n)	Percentage
Diffuse slowing	68	60.7%
Triphasic waves	34	30.3%
Epileptiform discharges	10	8.9%
Normal EEG	0	0%

Response to Hemodialysis and Neurological Outcome

Neurological improvement following initiation of hemodialysis was observed in a significant proportion of patients. Improvement was most notable in patients with early-stage encephalopathy, while delayed or partial recovery was observed in severe cases. Mortality was higher in patients presenting with coma and refractory seizures.

The data indicate that early dialysis initiation is associated with better neurological outcomes in uremic encephalopathy patients.

Correlation of Duration of Symptoms with Clinical Outcome (Statistical Analysis)

A statistically significant correlation was observed between duration of symptoms before hospital presentation and neurological outcome. Patients presenting within 48 hours of symptom onset showed significantly higher recovery rates compared to those with delayed presentation. An independent t-test demonstrated a significant difference in outcome scores between early and late presenters.

Table 6: Statistical Correlation Between Symptom Duration and Outcome.

Duration of Symptoms	Mean Outcome Score	Standard Deviation	p-value
≤48 hours	2.1 ± 0.8	0.8	<0.001
>48 hours	3.7 ± 1.1	1.1	<0.001

The data indicate an association between earlier initiation of clinically indicated dialysis and more favorable neurological outcomes. Because of the observational design, this association should not be interpreted as evidence that dialysis caused the observed neurological improvement.

DISCUSSION

Uremic encephalopathy is a significant clinical problem in tertiary care centres where patients often present late and have severe renal dysfunction. The present study showed a broad range of neurological involvement from mild cognitive dysfunction to deep coma. Altered consciousness is the most common clinical manifestation, a finding that is consistent with the ubiquity of the effect of uremic toxins on cerebral function. These observations were made in previous clinical situations, where severity of encephalopathy was directly correlated with the degree of metabolic derangement and the

Table 5: Neurological Outcome After Hemodialysis.

Outcome Category	Number of Patients (n)	Percentage
Complete neurological recovery	104	45.2%
Partial improvement	82	35.7%
No improvement	28	12.2%
Mortality	16	6.9%

progression of systemic disease.¹¹ The present results support the idea of uremic encephalopathy as a neuro-metabolic syndrome with dynamic clinical stages.

The demographic distribution in this study was similar to the burden of chronic kidney disease, with male predominance and involvement of the middle- to older age group. This is consistent with previous reports in which risk factors like hypertension and diabetes mellitus were more common in male patients than in women.^{3,4} The age-related susceptibility in the present study implies that the cerebral reserve decreases with age, leading to increased susceptibility to uremic toxins. This biological susceptibility accounts for earlier neurological deterioration in older people with similar biochemical abnormalities.

Altered consciousness was the most common neurological sign documented in this study, with confusion and disorientation as the next most common. These results concur with the clinical spectra reported earlier, where early cognitive decline is followed by clinical neurological failure. The stages from mild confusion to coma are progressive neurochemical imbalance and disturbance of the activity of the cortical neurons. The motor regulatory pathways are involved in metabolic encephalopathies as seen in renal failure, as reflected by the high frequency of asterix and myoclonus in this study. They are thought to be significant clinical indicators of metabolic cerebral dysfunction.

In the present study, a large number of patients were observed to have some seizures. This finding is similar to previously reported frequencies that seizures were correlated with severe azotemia and

electrolyte imbalance.¹⁵ Increased neuronal excitability and buildup of neurotoxic metabolites are the pathophysiological basis of seizures in uremic encephalopathy. Seizures were present in a significant proportion of all patients included in this study and suggest a severe degree of metabolic disturbance, as well as a late stage of disease at presentation. It is also a sign of late diagnosis in many instances.

EEG results in the present study showed the mean presence of diffuse slowing and triphasic waves as the most common EEG patterns. These results agree with previous neurophysiological observations, in which metabolic encephalopathy resulted in a generalized cortical dysfunction¹⁶. In moderate and severe cases, brain dysfunction becomes almost universal in the absence of normal EEG patterns. The correlation of EEG abnormalities and clinical severity makes neurophysiological monitoring useful in patients who are medically very sick. The use of EEG is, however, limited in resource-limited settings.

In this study, this association between severity of renal dysfunction and neurological impairment was statistically significant. There was a correlation between the number of severe neurological symptoms (coma and seizures) and the elevated serum urea and creatinine. Previous studies have reported similar associations, in which the accumulation of uremic toxins was directly related to neurocognitive decline.¹⁷ This relationship is important in emphasizing the value of early RRT in preventing neurological deterioration. It also highlights the importance of frequent biochemical monitoring of a patient with chronic kidney disease to detect early neurotoxic risk.

In this study, hemodialysis resulted in a favorable neurological recovery in a large number of patients. In most patients, dialysis was started early and complete or partial recovery was found, whereas delayed dialysis resulted in a worse outcome. Similar results have been seen in other clinical assessments, where dialysis was used to eliminate neurotoxic agents, and a rapid

improvement in the neurological status was observed.¹⁸ Yet, in some patients who have persistent deficits, it appears that exposure to uremic toxins over a long period of time can lead to irreversible damage to neurons. This emphasizes the need for prompt interventions before structural brain damage occurs.

In this study, the mortality rate was higher in patients who were comatose and had refractory seizures. This is in line with previous studies, which showed that severe neurological disability correlated with poor prognosis.¹⁹ The severity of encephalopathy at admission is a good predictor of outcome. Those who arrived at the hospital late and had symptoms that lasted longer had a significantly poorer recovery rate. This discovery emphasizes the significance of early recognition and referral is necessary to enhance survival benefits.

This study further validated the need for early diagnosis with the correlation between symptom duration and neurological outcome. The patients who presented in shorter intervals were significantly better neurologically compared to the late presenters. This is similar to what has been seen in clinical evaluations of previous treatments that were delayed, which were linked to lasting neurological effects.²⁰ This relationship highlights the progressive nature of uremic encephalopathy, and the time-dependent reversibility of metabolic brain dysfunction.

This study fills a gap in the literature in relation to the limited amount of local data available for systematic neurological assessment of uremic encephalopathy. The current evidence comes mainly from small observational studies, reporting on neurological features inconsistently. The present study will thus help to fill this gap by providing a structured analysis of neurological manifestations in a large tertiary care cohort. Additionally, it emphasizes the importance of having standardized neurological assessment protocols in nephrology units in order to enhance diagnostic accuracy.

Yet another observation is the variability in clinical presentation that can make the diagnosis difficult to make early. This can be missed and only diagnosed later in the busy emergency setting, as subtle cognitive changes are often missed.²² This delay can lead to the development of a severe encephalopathy and higher mortality. The results of this study provide insight that greater clinical awareness is a crucial factor in identifying at-risk patients early. Regular neurological screening could have a dramatic impact on the outcomes of renal failure patients.

Most findings, however, were nonspecific, and imaging was not used in a diagnostic fashion in this study. This is consistent with previously reported data showing that imaging did not usually identify uremic encephalopathy, but rather ruled it out. Thus, the diagnosis is primarily clinical and biochemical. Use of neuroimaging should be reserved for atypical presentations or for suspected alternate diagnoses.

The findings of this study also highlight the importance of multidisciplinary management involving nephrologists, neurologists, and critical care specialists. Early coordination between specialties ensures prompt initiation of dialysis and supportive neurological care. This integrated approach is essential in reducing complications and improving survival in uremic encephalopathy patients. Resource limitations in developing healthcare systems remain a challenge and require strategic planning for improvement.

In conclusion, neurological manifestations in uremic encephalopathy were diverse and were associated with the severity of renal dysfunction. Earlier recognition and timely clinical management, including renal replacement therapy when indicated, were associated with more favorable neurological outcomes. These findings support structured neurological assessment and early clinical evaluation in tertiary care settings. Because of the observational design, the study does not establish a causal relationship between dialysis timing and neurological recovery.

CONCLUSION

Neurological manifestations in uremic encephalopathy were observed to be highly prevalent and clinically diverse.

Early recognition and timely dialysis initiation were associated with improved neurological recovery.

Systematic neurological assessment was recommended to improve patient outcomes in tertiary care settings.

Limitations

The single-center design limits generalizability. The observational design also limits causal inference regarding the relationship between dialysis timing and neurological recovery.

A short study duration was used, and long-term neurological outcomes were not evaluated.

Advanced neuroimaging and continuous EEG monitoring were not performed in all patients because of resource constraints. EEG findings therefore represent only the selected subgroup who underwent EEG assessment.

A short study duration was used, and long-term neurological outcomes were not evaluated. Advanced neuroimaging and continuous EEG monitoring were not performed in all patients due to resource constraints.

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Javid Ali	Writing – Original Draft/Literature Review
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