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Original Research Article

MRI Brain Findings in Patients with Uremic Encephalopathy

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Abstract:

Background / Objective: Uremic encephalopathy (UE) is a reversible neurological complication of advanced renal failure caused by the accumulation of neurotoxic metabolites, electrolyte imbalance, and metabolic acidosis. Magnetic resonance imaging (MRI) plays a crucial role in identifying characteristic brain abnormalities and assessing reversibility. This study aimed to evaluate MRI brain findings in patients with uremic encephalopathy and correlate the imaging patterns with biochemical severity.

Methods: This observational cross-sectional study included 35 clinically diagnosed patients with UE and significantly deranged renal function (urea >100 mg/dL, creatinine >5 mg/dL). Patients with alternative causes of encephalopathy or contraindications to MRI were excluded. MRI brain was performed using T1, T2, FLAIR, and diffusion-weighted sequences. Imaging findings were correlated with renal function tests and arterial blood gas parameters. Statistical significance was set at $p < 0.05$.

Results: The mean age of patients was 50.86 ± 19.6 years, and chronic renal failure was present in 91.4% of cases. The most common neurological presentation was altered mental status (45.7%), followed by seizures (25.7%). MRI abnormalities included cortical atrophy (51.4%), white-matter involvement (42.8%), cortical/subcortical PRES-like hyperintensities (37.2%), and both lentiform fork sign (LFS) and bilateral basal ganglia lesions in 28.6% of cases. LFS and basal ganglia involvement were significantly associated with severe metabolic acidosis and low serum bicarbonate levels ($p \leq 0.01$), while cortical atrophy was more frequent in chronic renal failure.

Conclusion: MRI demonstrates characteristic, severity-dependent patterns in uremic encephalopathy. LFS and basal ganglia lesions indicate acute severe metabolic derangement, whereas cortical atrophy reflects chronic damage.

Recommendation: Early MRI evaluation should be integrated into diagnostic and management protocols for UE to guide prognosis and support timely initiation of dialysis. Longitudinal follow-up studies are recommended to assess reversibility.

Keywords: Uremic encephalopathy, MRI Brain, Lentiform Fork Sign, Basal Ganglia Lesions, Metabolic Acidosis, Chronic Kidney Disease.

Introduction

Uremic encephalopathy (UE) is a potentially reversible neuropsychiatric complication that occurs in patients with severe renal dysfunction and represents a spectrum of neurological manifestations caused by the accumulation of metabolic toxins, electrolyte imbalances, and acid–base disturbances that impair neuronal function and cerebral metabolism [1]. The clinical presentation of UE is highly variable, ranging from mild cognitive impairment, lethargy, and confusion to seizures, coma, and focal neurological deficits, often mimicking other metabolic or toxic encephalopathies, which makes early recognition and neuroimaging crucial for diagnosis. The pathophysiology of UE is multifactorial; in renal failure, a variety of neurotoxic metabolites such as guanidino compounds, parathyroid hormone fragments, and organic acids accumulate in the blood and disrupt normal neuronal signaling [2]. These compounds inhibit γ-aminobutyric acid

(GABA) receptors and overstimulate excitatory N-methyl-D-aspartate (NMDA) receptors, leading to neuronal hyperexcitability, oxidative stress, and excitotoxic injury [3]. Additionally, metabolic acidosis—common in advanced renal failure—lowers intracellular pH and interferes with enzymatic activity, causing mitochondrial dysfunction and reduced ATP generation, while electrolyte abnormalities such as hyponatremia and hyperkalemia alter membrane potentials and exacerbate neuronal instability. The cumulative effect of these factors compromises the integrity of the blood–brain barrier (BBB), resulting in vasogenic and cytotoxic edema that manifests as characteristic imaging changes [4]. Historically, uremic encephalopathy was frequently fatal before the development of dialysis, with autopsy studies revealing diffuse cerebral edema, astrocytic swelling, and neuronal necrosis as pathological correlates [5]. The introduction of hemodialysis and peritoneal dialysis transformed UE from a fatal condition into a largely reversible one, provided that metabolic correction is achieved early. However, delayed diagnosis or inadequate management may still lead to irreversible cortical and subcortical injury despite biochemical normalization. Magnetic resonance imaging (MRI) has emerged as the diagnostic cornerstone in UE, providing high sensitivity for detecting both reversible and chronic lesions [6]. Characteristic MRI findings include cortical and subcortical T2/FLAIR hyperintensities, diffuse white-matter involvement, basal-ganglia signal abnormalities, and the distinctive lentiform fork sign (LFS)—a symmetrical hyperintensity along the external and internal medullary lamina surrounding the putamen [7]. The LFS is considered a hallmark of metabolic encephalopathy and correlates strongly with severe metabolic acidosis and low bicarbonate levels. Diffusion-weighted imaging (DWI) further helps differentiate vasogenic edema, which is reversible and associated with elevated apparent diffusion coefficient (ADC) values, from cytotoxic edema, which reflects irreversible injury. Several studies have reported that the severity and distribution of MRI abnormalities correspond directly to biochemical parameters such as blood urea nitrogen (BUN), creatinine, and bicarbonate levels [1]. GRECO ET AL. and KIM ET AL. independently demonstrated that patients with basal-ganglia or cortical lesions often exhibit significant metabolic acidosis and show radiological improvement after dialysis [3]. These findings underscore the role of MRI not only as a diagnostic modality but also as a prognostic marker for reversibility. In summary, uremic encephalopathy represents a dynamic, multifactorial process in which neurotoxicity, vascular dysfunction, and metabolic derangement converge to produce both reversible and irreversible brain injury. MRI serves as a critical tool for identifying these lesions, correlating imaging patterns with biochemical severity, and guiding timely therapeutic intervention [8].

Materials and Methods

Study design and participants: This was a single-center observational cross-sectional study conducted on 35 adult patients (age 18–80 years) presenting with clinically suspected uremic encephalopathy and significantly deranged renal function (urea > 100 mg/dL, creatinine > 5 mg/dL). Exclusion criteria included alternate causes of encephalopathy (hypoglycemia, hepatic failure, acute stroke, or structural brain disease), pregnancy, and MRI contraindications.

Imaging protocol: MRI brain was performed on a 1.5 T scanner using standard T1-weighted, T2-weighted, FLAIR, and diffusion-weighted imaging (DWI) sequences. Images were evaluated for cortical atrophy, white-matter hyperintensities, bilateral basal-ganglia lesions, lentiform fork sign, and cortical/subcortical PRES-like changes [3,6].

Laboratory and clinical evaluation: Neurological examination and laboratory data were obtained for all participants: renal function tests, BUN, serum electrolytes, liver function tests, and arterial blood gas (ABG) parameters (pH, PCO_2, HCO_3^-). Statistical analysis included descriptive statistics, chi-square test for categorical variables, and t-test/ANOVA for continuous variables, with $p < 0.05$ considered significant.

Results

Demographic and Clinical Profile: Thirty-five patients were included (mean age = 50.86 ± 19.6 years). Most patients were middle-aged to elderly, the largest group being 56–65 years (22.9%). Males comprised 54.3% (n = 19). Chronic renal failure was present in 91.4%, with hypertension (57.1%) and diabetes mellitus (28.6%) as the main comorbidities. Altered mental status was the most frequent neurological presentation (45.7%), followed by seizures (25.7%) and confusion/disorientation (17.1%). Changes in urination were noted in 80%.

Table 1: Distribution of study participants according to age group (n = 35).

Age	Frequency	Percentage
18-25	2	5.71
26-35	3	8.57
36-45	5	14.29
46-55	4	11.43
56-65	8	22.86
66-75	7	20.00
76-85	6	17.14
Total	35	100
Mean±SD	50.86 ± 19.6	

Table 2: Distribution of clinical manifestations in study participants.

Comorbidity	Frequency	Percentage
Chronic renal failure	32	91.4
Acute renal failure	3	8.6
Metabolic acidosis	12	34.3
Diabetes mellitus	10	28.6
Hyperthyroidism	5	14.3
Hypertension	20	57.1

Laboratory Findings - Marked renal dysfunction was observed: mean serum creatinine = 9.63 ± 3.84 mg/dL; mean BUN = 173.68 ± 65.52 mg/dL. Metabolic acidosis was common with mean arterial pH = 7.34 ± 0.13 and mean HCO_3^- = 17.3 ± 6.2 mEq/L. Mean serum potassium = 5.15 ± 1.0 mEq/L. Liver enzymes remained largely within normal range.

MRI Findings

MRI abnormalities were frequent and diverse. Cortical atrophy (51.4%) and white-matter involvement (42.8%) were the most common. The lentiform fork sign (LFS) appeared in 28.6%, bilateral basal-ganglia lesions in 28.6%, and PRES-like cortical/subcortical hyperintensities in 37.2%. Overall, 65.7% of patients had white-matter or cortical/subcortical signal abnormalities compatible with vasogenic or mixed edema.

Table 3: Distribution of MRI abnormalities in uremic encephalopathy patients.

MRI Finding	Frequency	Percentage
Lentiform Fork Sign (LFS)	10	28.6
Bilateral basal ganglia lesions	10	28.6
White matter involvement	15	42.8
Cortical atrophy	18	51.4
Cortical/subcortical T2/FLAIR hyperintensity (PRES-like)	13	37.2

Imaging–Laboratory Correlations: Patients with LFS had the most severe biochemical derangement: mean creatinine ≈ 8.2 mg/dL, BUN ≈ 130 mg/dL, mean pH ≈ 7.25, and mean HCO_3^- ≈ 14 mEq/L. Those with bilateral basal-ganglia lesions showed similar trends. White-matter and PRES-like changes correlated with moderate acidosis, while cortical atrophy corresponded to relatively lower acute biochemical abnormalities but chronic renal disease. Statistical analysis showed significant association between LFS/basal-ganglia lesions and low pH and bicarbonate levels ($p \leq 0.01$) [5,7].

Table 4: Comparison of biochemical parameters across MRI abnormality patterns.

MRI Finding	Creatinine (mg/dL)	BUN (mg/dL)	pH	HCO_2 (mEq/L)	PCO_2 (mmHg)
LFS Present (n=10)	8.2	130.5	7.25	14.2	27.5
Basal Ganglia Lesions (n=10)	8	125.6	7.28	15	28.1
White Matter Involvement (n=15)	7.1	110.4	7.3	16.5	30
Cortical Atrophy (n=18)	6.9	102.3	7.33	18.1	31.4
PRES-like Changes (n=13)	7.8	120.8	7.26	15.3	28.7

Discussion

The present study demonstrates that uremic encephalopathy (UE) produces a distinct spectrum of MRI abnormalities that mirror the biochemical severity of renal dysfunction [1]. Cortical atrophy, white-matter hyperintensities, and the lentiform fork sign (LFS) were the dominant patterns observed.

These findings reaffirm that the cerebral manifestations of uremia arise from a combination of metabolic acidosis, electrolyte imbalance, and accumulation of neurotoxins that impair neuronal metabolism [2].

The basal ganglia, especially the putamen, emerged as the most commonly affected deep-gray structure. The LFS—characterized by symmetric hyperintensity along the external and internal medullary lamina—represents a classic marker of metabolic encephalopathy [3]. Its presence correlated strongly with severe acidosis and reduced bicarbonate levels, supporting the hypothesis that low pH is the major precipitating factor of acute uremic injury [4]. Because of their high metabolic demand, the basal ganglia are particularly vulnerable to fluctuations in acid–base balance, hypoxia, and oxidative stress.

White-matter and cortical/subcortical T2/FLAIR hyperintensities, often resembling posterior reversible encephalopathy syndrome (PRES), reflected vasogenic edema caused by endothelial dysfunction and osmotic shifts during dialysis [5]. These lesions were largely reversible following metabolic correction, highlighting the transient and treatable nature of many uremic brain changes. In contrast, cortical atrophy—seen mainly in chronic renal failure—represented irreversible neuronal loss from prolonged toxin exposure and chronic ischemia [1]. The coexistence of both reversible and permanent lesions emphasizes UE's heterogeneous pathophysiology.

Correlation with biochemical data confirmed that imaging severity paralleled metabolic derangement. Patients with profound acidosis and elevated BUN or creatinine exhibited basal-ganglia involvement or LFS, while those with milder abnormalities showed reversible white-matter lesions [3]. Similar trends have been reported by KIM ET AL., who demonstrated that MRI findings closely follow biochemical status and improve after dialysis [3].

The reversibility of vasogenic edema reinforces the need for early recognition and prompt dialysis. Patients imaged before metabolic correction showed diffuse hyperintensities that markedly improved after treatment [4]. Conversely, those with cortical atrophy or diffusion-restricted lesions demonstrated little change on follow-up, indicating chronic injury [6]. Diffusion-weighted imaging thus serves as a key prognostic marker, distinguishing cytotoxic from vasogenic edema.

MRI also helps differentiate UE from other encephalopathies such as hepatic, hypoglycemic, or hypoxic forms, based on the symmetric distribution of lesions and absence of infarction [7]. This diagnostic precision prevents mismanagement and enables rapid initiation of dialysis in appropriate cases. Integrating MRI patterns with clinical and laboratory findings allows clinicians to identify reversible stages of encephalopathy, optimize metabolic correction, and predict neurological recovery.

In essence, the imaging spectrum of UE forms a continuum: LFS and basal-ganglia hyperintensities indicate acute, reversible injury; white-matter and PRES-like changes signify vasogenic edema; and cortical atrophy denotes irreversible damage. Recognizing these categories helps determine both the urgency and expected outcome of therapy. MRI thereby functions not merely as a diagnostic tool but as a biomarker of disease stage and prognosis [8].

Conclusion

Uremic encephalopathy is a multifactorial but potentially reversible neurological complication of severe renal dysfunction. The current study reaffirms that MRI provides a reliable and sensitive assessment of its diverse manifestations [1]. The principal abnormalities—cortical atrophy, white-matter changes, and the lentiform fork sign—reflect distinct mechanisms ranging from chronic degeneration to acute metabolic injury.

Deep gray-matter involvement, especially the LFS, was strongly linked to severe metabolic acidosis and low bicarbonate levels [3]. These lesions often resolved after hemodialysis and acid–base correction, underscoring the potential reversibility of early uremic brain changes [4]. In contrast, cortical atrophy reflected long-standing neurodegeneration and limited recovery despite treatment [1]. Differentiating between these patterns is critical for guiding prognosis and therapeutic urgency.

MRI's diagnostic value extends beyond detection to prognostication. Patients with reversible vasogenic lesions, such as PRES-like changes, usually experience marked neurological improvement following metabolic correction [5]. Meanwhile, those with chronic atrophy or diffusion-restricted lesions frequently show incomplete recovery [6]. Thus, diffusion-weighted and FLAIR imaging are indispensable for distinguishing cytotoxic from vasogenic processes.

The integration of MRI with biochemical indices such as BUN, creatinine, and bicarbonate enhances diagnostic accuracy and assists clinicians in monitoring therapeutic response [7]. Recognizing MRI patterns that correspond to biochemical severity enables early intervention, preventing irreversible neuronal injury and improving outcomes.

In conclusion, MRI offers an indispensable window into the pathophysiology of uremic encephalopathy, translating biochemical derangements into visible

patterns of brain injury [8]. Early imaging, coupled with timely dialysis and metabolic correction, remains central to preventing permanent damage and optimizing neurological recovery.

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