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Role of MRI in Detection of Neurological complications in Patients with Chronic Kidney Disease

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Abstract:
Background and objectives: *Patients with chronic kidney disease (CKD), a critical and rapidly growing global health problem, suffer from a number of complex neurological complications potentially affecting all levels of the nervous system including vascular damage and cognitive dysfunction. Neurological complications in hemodialysis patients are often underdiagnosed and undertreated. It is of great significance to detect the neurological complications and improve the prognosis of CKD patients. Neurological examination alone is usually not sufficient to distinguish the underlying pathologies. Many new noninvasive Magnetic Resonance Imaging (MRI) techniques have been steadily used for the diagnosis of occult central nervous system complications in CKD patients. This gives an opportunity to understand the pathophysiological mechanisms of these neurological disorders. This article illustrates the range of MRI findings of neurological complications in chronic kidney disease patients and outlines the applications of advanced MRI techniques.*
Methodology: *The aim of the study is to study the distribution and nature of cranial MRI findings in chronic kidney disease and to correlate the MRI findings with Stage of CKD and state of dialysis. This study was conducted in the Department of Radio-Diagnosis at NRI General Hospital, Chinakakani, Guntur Dt. in 60 patients who were referred to the department of Radiology with chronic kidney disease from October 2013 to September 2015.*
Results: *Out of 60 patients, who were examined, 40 showed abnormal findings on MRI and 20 were normal. Out of the 40 abnormal cases, 12 showed atrophy making it the dominant finding. Out of the 40 cases showing abnormal findings, 26 patients were on dialysis and 14 were non-dialysis cases. Out of the 40 abnormal cases, 34 belonged to CKD stage V.*
Conclusion: *Out of the 40 patients who showed abnormal findings, 34 belonged to CKD stage V making it the highest incidence. CKD stage III showed no abnormal findings on MRI.*
Keywords: *chronic kidney disease, MRI, neurological complications*

I. Introduction

10% of the population worldwide is affected by chronic kidney disease (CKD), and millions die each year because they do not have access to affordable treatment [1]. According to the 2010 Global Burden of Disease study, chronic kidney disease was ranked 27th in the list of causes of total number of deaths worldwide in 1990, but rose to 18th in 2010 [2]. KDOQI (Kidney Disease Outcomes Quality Initiative) defines CKD as kidney damage or glomerular filtration rate (GFR) <60 mL/min/1.73 m^2 for 3 months or more, irrespective of cause. eGFR can be estimated from calibrated serum creatinine and estimating equations, such as the Modification of Diet in Renal Disease (MDRD) study equation or the Cockcroft-Gault formula. But according to National Kidney Foundation, the preferred method is by using CKD-EPI Creatinine 2009 Equation. Disease severity is classified into five stages according to the level of GFR [3](Table 1).

Patients with renal failure often have signs and symptoms related to fluid and electrolyte disturbances, anaemia, malnutrition, bone disease and gastrointestinal problems. Vascular and neurologic impairment, in particular remain an important source of morbidity and mortality in this vulnerable patient population. In this paper, disease related and treatment related neurological complications in renal failure will be reviewed. With the introduction of dialysis and renal transplantation, the spectrum of neurological complications changed [4]. The incidence and severity of uremic encephalopathy, atherosclerosis, neuropathy and myopathy have declined but many patients fail to fully respond to dialytic therapy. Moreover, dialytic therapy or kidney transplantation may even induce neurological complications. Dialysis dementia, dialysis dysequilibrium syndrome, hypertensive encephalopathy and cerebrovascular accident due to ultrafiltration-related arterial hypotension can occur as a direct consequence of dialysis. Furthermore, dialysis is associated with aggravation of atherosclerosis and can contribute to the development of Wernicke's encephalopathy, haemorrhagic stroke,

subdural hematoma, osmotic myelinolysis, opportunistic infections, intracranial hypertension and neuropathy. Use of immunosuppressive drugs can cause encephalopathy, movement disorders, opportunistic infections, neoplasms, myopathy and progression of atherosclerosis.

Cerebrovascular disease is a predominant cause of morbidity and mortality in patients with chronic renal failure. Haemorrhagic stroke may include intracerebral, subarachnoid or subdural hemorrhage. Osmotic myelinolysis in patients with renal failure mainly occurs within the central basis pontis, but extrapontine regions including the midbrain, thalamus, basal nuclei and cerebellum can be affected as well. Neurological infections in patients with renal failure mainly present as acute, subacute or chronic meningitis, encephalitis, myelitis or brain abscess. Although development of neoplasms in the neurologic system is rare, malignant meningioma and primary central nervous system lymphoma have been described in end stage renal failure.

This study is an effort to study the distribution and nature of cranial MRI findings in chronic kidney disease and to correlate the MRI findings with stage of CKD and state of dialysis.

II. Materials And Methods

This cross-sectional study was conducted on 60 patients clinically diagnosed to have chronic kidney disease who were referred to the Department of Radio-Diagnosis at NRI General Hospital, Chinakakani, Guntur from October 2013 to September 2015.

Inclusion Criteria: All patients who were diagnosed to have stage 3 to stage 5 chronic kidney disease and presented with neurological symptoms were imaged.

Exclusion Criteria: Patients with cardiovascular disease, pacemakers, aneurysmal clips, claustrophobia, previous known cerebrovascular disease and patients who underwent renal transplant.

Examination Technique: MR imaging was performed with a clinical 1.5T Signa Excite system (General electrical medical systems, Milwaukee, USA). A dedicated eight channel high resolution head coil was used. T1 FLAIR axials, T2 axials, T2 FLAIR axials, DWaxials, GRE axials sequences of brain were done. MR angiography sequences were also done in few patients. Contrast was not given in any of the cases. The study parameters monitored were the stage of CKD and whether the patient was on hemodialysis or not.

III. Results And Observations

The present study sample included 60 patients diagnosed with stage 3 to stage 5 chronic kidney disease including patients with and without dialysis.

Regarding age and gender distribution of abnormal MRI findings in our study: maximum percentage of patients was in the age of 40-59 years (32%), with male preponderance (60%), when compared to females who accounted for (40%) of cases (Tables 2 & 3). The incidence of CKD stage 5 was more compared to CKD 3 and 4 (Table 4). Patients of stage 1 and 2 were not included in the study. In this study of 60 patients, 32 patients were on dialysis while 28 were not on dialysis (Table 5). Out of 60 patients who were examined, 40 showed abnormal findings on MRI and 20 were normal (Table 6).

Out of the 40 abnormal cases (Table 7), 12 showed atrophy (Fig 1) making it the dominant finding, 8 patients showed abnormal white matter signal intensities (Fig 2), acute infarcts (Fig 3) were seen in 5, haemorrhage (Fig 4,5) in 2, demyelination (Fig 6,7) in 5, microbleeds (Fig 8) in 2, calcified granulomas in 2, posterior reversible encelopathy syndrome (PRES) (Fig 9,10) was seen in 4 patients.

Out the 40 cases showing abnormal findings, 26 patients were on dialysis and 14 patients were non-dialysis cases (Table 8).

Out of the 40 abnormal cases, 34 belonged to CKD stage 5, making it the highest incidence. CKD 3 showed no abnormal findings on MRI (Table 9).

Highest percentage of abnormal findings was seen in 60-79 age group, 12 abnormal and 14 normal (Table 10).

IV. Tables And Figures

Table 1 - Stages of Kidney Disease according to GFR

Stage	Description	GFR
At increased risk	Risk factors like diabetes, high blood pressure, family history, older age	More than 90
1	Kidney damage with normal kidney function	90 or above
2	Kidney damage with mild loss of kidney function	89 to 60
3a	Mild to moderate loss of kidney function	59 to 44
3b	Moderate to severe loss of kidney function	44 to 30
4	Severe loss of kidney function	29 to 15
5	Kidney failure	Less than 15

Table 2 - Age distribution of patients studied

Age (in years)	Cases	Percentage (%)
< 20	6	10
20 - 39	13	22
40 - 59	19	32
60 - 79	14	23
80 and above	8	13
Total	60	100

Table 3 - Gender distribution of patients studied

Gender	Cases	Percentage (%)
Male	36	60
Female	24	40
Total	60	100

Table 4 - CKD staging of patients studied

CKD stage	Cases	Percentage (%)
Stage 3	5	8.3
Stage 4	14	23.4
Stage 5	41	68.3
Total	60	100

Table 5 - Patients on dialysis v/s non-dialysis

	Cases	Percentage (%)
On hemodialysis	32	53
Not on hemodialysis	28	47
Total	60	100

Table 6 - Incidence of abnormal findings on MRI

	Cases	Percentage (%)
Abnormal	40	67
Normal	20	33
Total	60	100

Table 7 - Abnormal findings on MRI

Finding	Cases	Percentage (%)
Atrophy	12	30
White matter hyperintensities	8	20
Acute infarcts	5	12.5
Hemorrhage	2	5
Osmotic demyelination syndrome	5	12.5
PRES	4	10
Microbleeds	2	5
Calcified granulomas	2	5
Total	40	100

Table 8 - Abnormal MRI findings correlation with hemodialysis status

	Abnormal Cases	Percentage (%)
On hemodialysis	26	65
Not on hemodialysis	14	35
Total	40	100

Table 9 - Abnormal MRI findings correlation with CKD stage

CKD stage	Abnormal cases	Percentage (%)
Stage 3	0	0
Stage 4	6	15
Stage 5	34	85
Total	40	100

Table 10 - Abnormal MRI findings correlation with age

Age (in years)	Total casesN=60	Abnormal casesN=40	Percentage (%)
< 20	6	3	50
20 - 39	13	7	54
40 - 59	19	10	53
60 - 79	14	12	86
80 and above	8	8	100

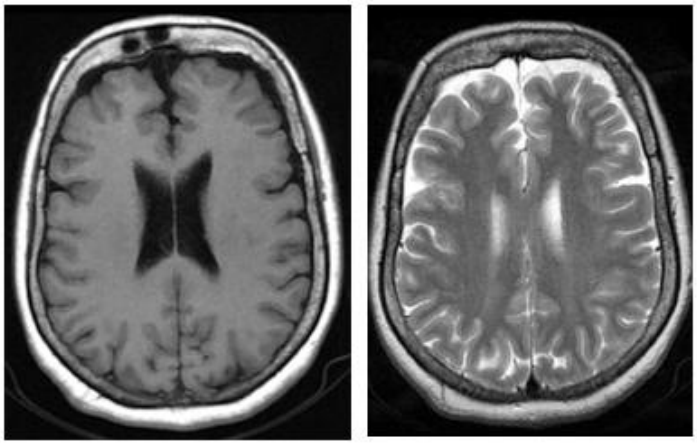

Fig 1 – T1, T2 axials: cerebral atrophy significantly in bilateral frontal regions

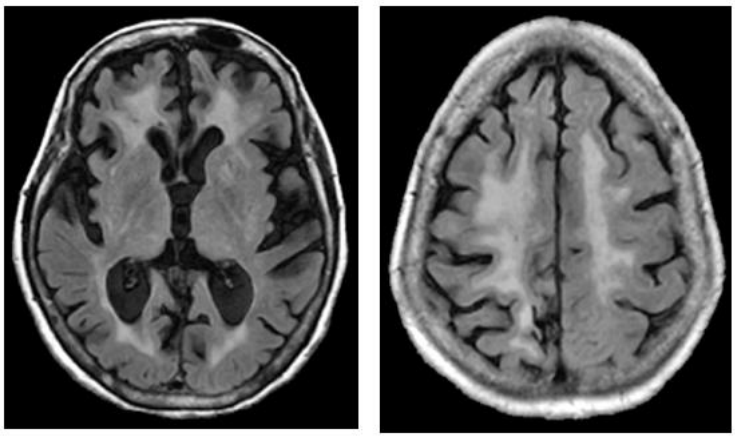

Fig 2 – FLAIR axials: white matter hyperintensities in bilateral periventircular regions and centrum semiovale

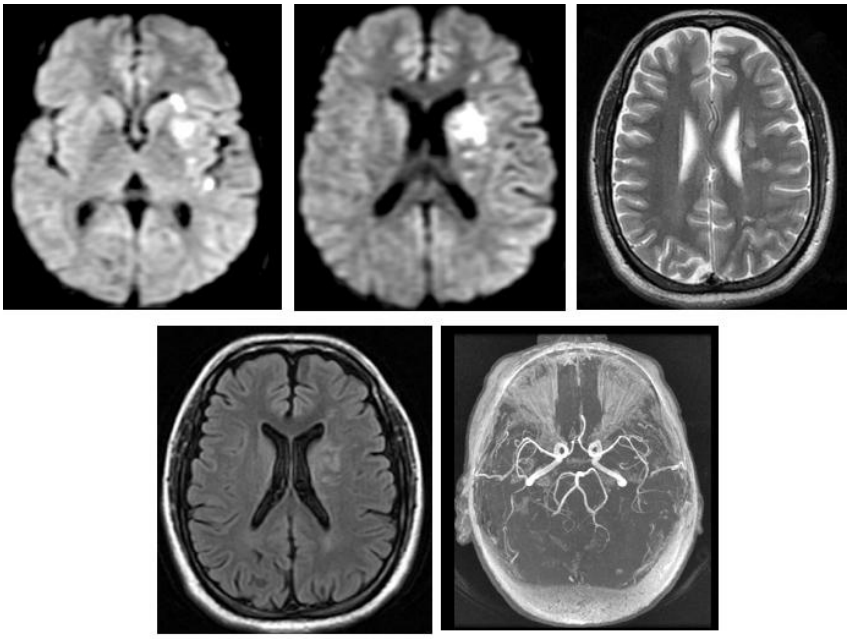

Fig 3 – T2 & FLAIR hyperintensities in left basal ganglia and parietal region – s/o acute infarct. MRA normal.

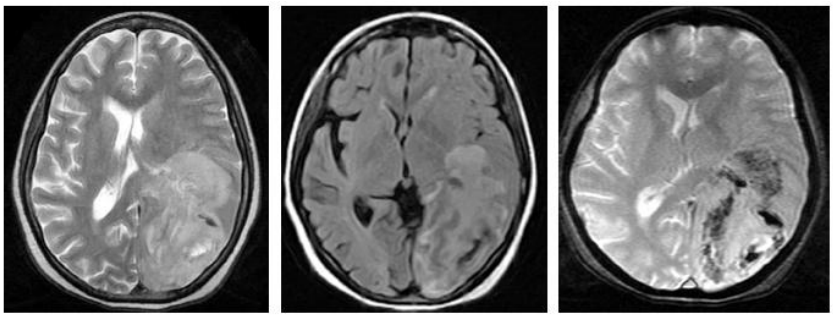

Fig 4 – T2 & FLAIR hyperintensity with GRE blooming in left parieto-occipital region – s/o of haemorrhage

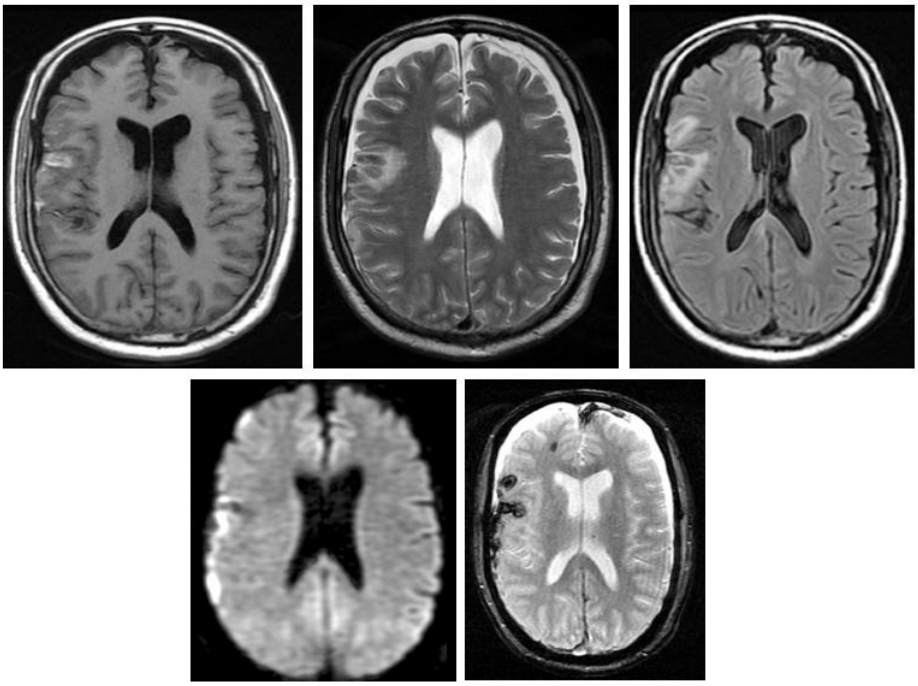

Fig 5 – T1, T2 & FLAIR hyperintensities with DWI restriction and GRE blooming in right parietal sulcal spaces – s/o subarachnoid haemorrhage

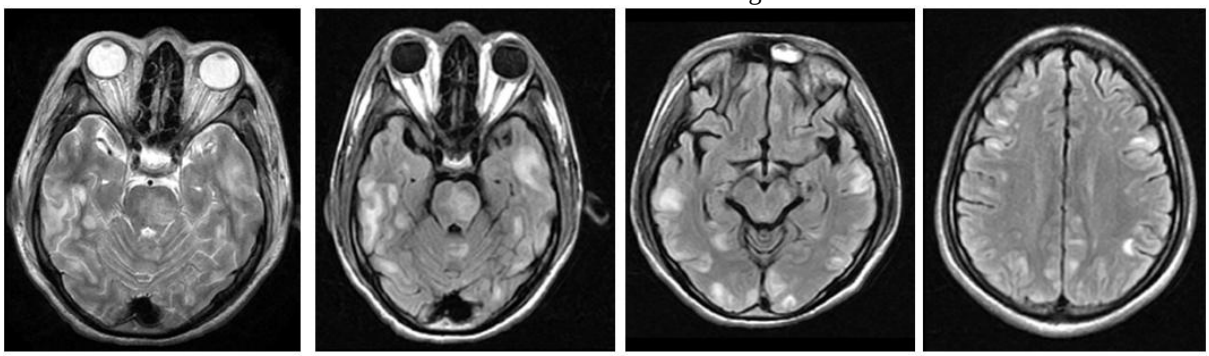

Fig 6 – T2 & FLAIR hyperintenisties in pons, bilateral frontal, temporal, parietal and occipital regions – s/o demyelination

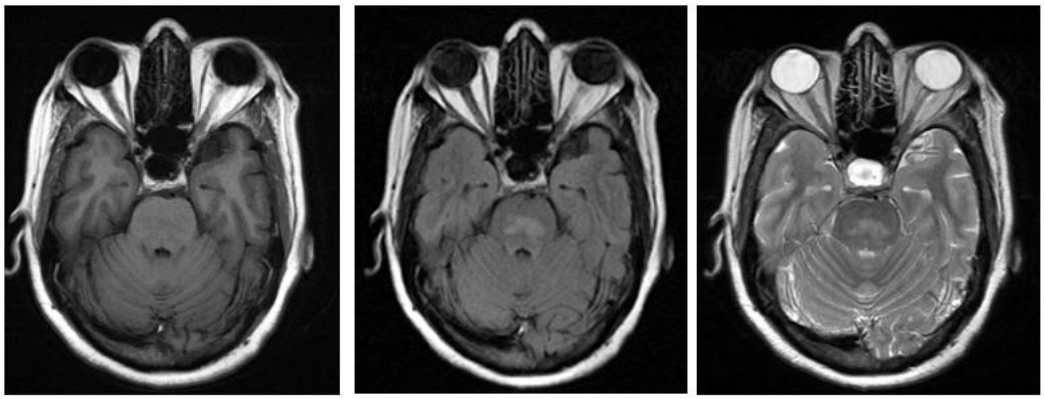

Fig 7 – T1 hypo, T2 & FLAIR hyperintenisty in pons – s/o central pontine myelinolysis

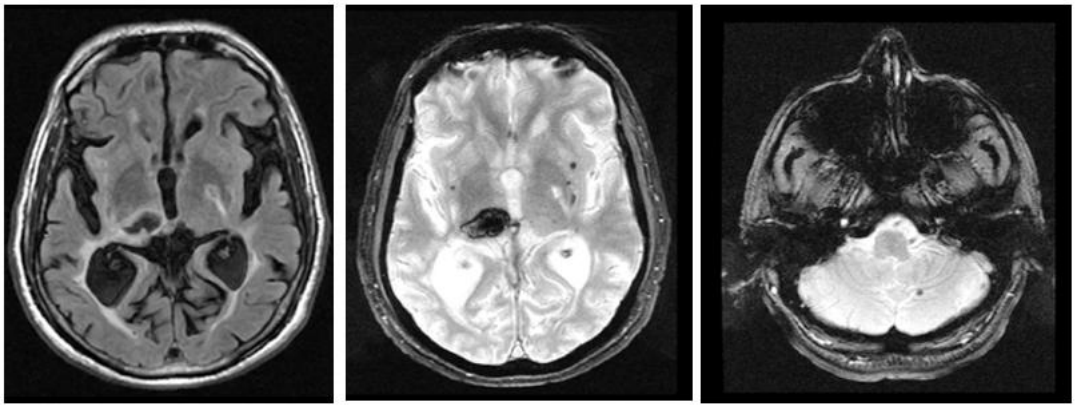

Fig 8 – Small foci of GRE blooming in bilateral capsuloganglionic regions, cerebellum – s/o microbleeds and right thalamus s/o hematoma

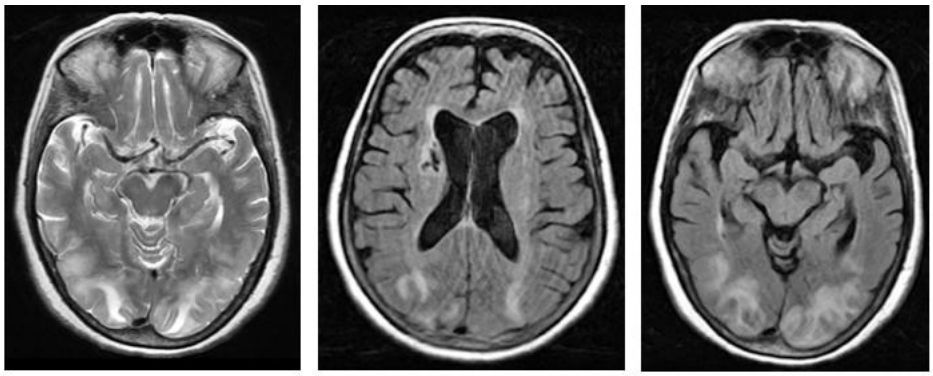

Fig 9 – T2 & FLAIR hyperintensities in bilateral parieto-occipital regions – s/o PRES

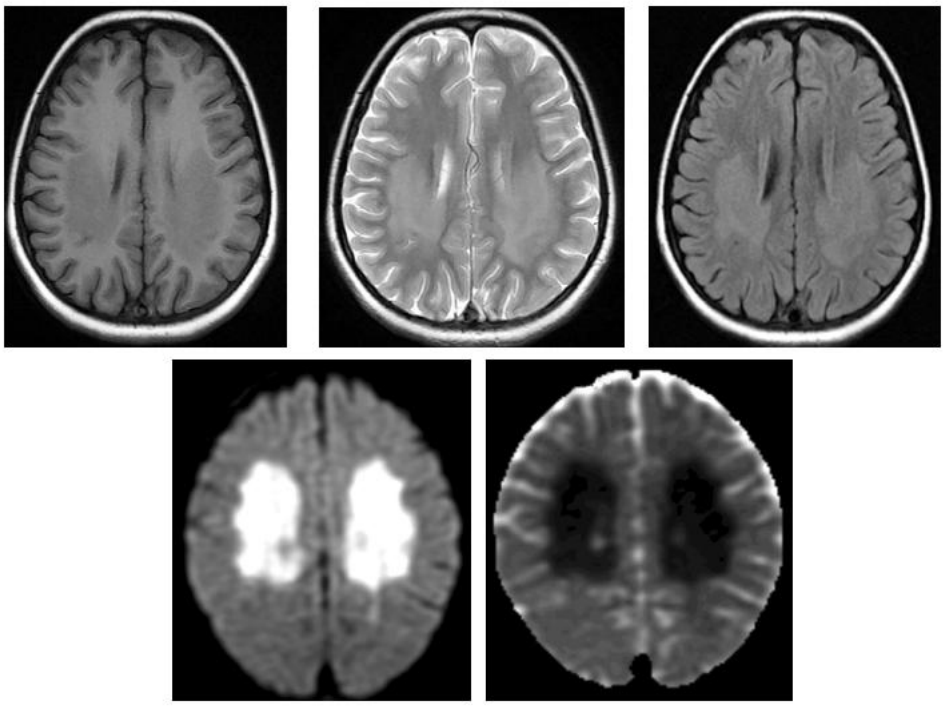

Fig 10 – T1 hypo, T2 & FLAIR hyperintensities with DWI restrictions in bilateral parietal regions – s/o PRES with cytotoxic edema

V. Discussion

Neuroimaging helps in understanding the effect of CKD on brain structure, function, and associated behaviours. Early diagnosis of the abnormality and rectifying it with medical means will improve patient's condition and reduce mortality. Kidney function may affect brain function on many levels, ranging from developmental alterations and vascular injury to disorders of metabolism. Neurological complications due to altered kidney function include uremic encephalopathy, atherosclerosis, neuropathy and myopathy.

MRI [5] is more sensitive than CT for detection of neurological complications associated with CKD. The wide range of neurological complications show varied T1, T2, FLAIR and DWI findings such as:

Cerebral infarction: Intensity increase in the territory of the arterial supply, T2-weighted and FLAIR sequences; low signal in ADC, high signal in DWI.

Intracerebral hemorrhage

Intraparenchymal: Isointense on T1-weighted sequences; low central and high peripheral signals on T2-weighted sequences, blooming on gradient sequences.

Subdural: Crescent-shaped, iso/hypointense on T1-weighted sequences; low signal on T2-weighted sequences.

Epidural: Biconvex, isointense on T1-weighted sequences; high signal on T2-weighted sequences.

Subarachnoid: Subarachnoid space hyperintensity on FLAIR images.

Posterior reversible encephalopathy syndrome: Bilateral parieto-occipital region (most common) hypointense on T1-weighted sequences and hyperintense on T2-weighted and FLAIR sequences; high ADC, and low DWI signal.

Osmotic demyelination syndrome: Pontine and/or extrapontine areas have symmetric increased signals on T2-weighted and FLAIR sequences.

Cerebral infections: Hypointense on T1-weighted sequences; hyperintense on T2-weighted sequences; contrast enhancement following intravenous contrast administration.

Sinus vein thrombosis: Increased dural sinus signal_on T1-weighted and T2-weighted sequences.

Dialysis disequilibrium syndrome: Cerebral edema (hypointense on T1-weighted sequences; hyperintense on T2-weighted sequences), particularly in posterior parietooccipital regions.

In this study 60 cases of CKD were included and MRI of brain was done. It was a prospective study for a period of 2 years. Patients came with complaints of headache, focal neurological deficits, altered sensorium and loss of consciousness. Since neuroimaging in CKD patients is relatively a new concept, not many studies were there reporting the incidence of different findings in CKD patients. However, few studies were done to look for the incidence of a particular finding.

In present study, 12 patients out of 60 (20%) showed atrophy, with 10 showing diffuse cerebral atrophy and 2 showing frontal atrophy. Atrophy was dominantly seen in older age group i.e. >80 years (4/8 patients). In

a study conducted by Yusuke Yakushiji et al. [6] on 610 Japanese adults with CKD; 302 men and 308 women; mean age, 56.4 yr. Atrophy was found in 25 cases (4.1%). In present study it was 20%. High percentage of atrophy in present study may be due to less sample size. According to this study low GFR is significantly associated with cerebral atrophy. In present study, 8 out of 12 atrophy cases are in stage 5 disease and 4 out of 12 are from stage 4 disease. This is correlating with the study compared.

White matter hyperintensities (WMH) are often incidentally discovered on T2-weighted MRI. WMH may carry an increased risk of stroke, cognitive decline and dementia [7]. In present study 8 out of 60 cases showed T2 and FLAIR hyperintensities with DWI hypointense and ADC hyperintense in bilateral periventricular white matter and centrum semiovale corresponding to small vessel disease. In a study conducted by Martinez-Veaet al. [8] in 52 patients with CKD stages 3 and 4 (38 men and 14 women); mean age, 49 yr. WML were 33%. In this study they came to 14%.

CKD is associated with high risk of stroke. It is found to be higher in patients on dialysis. 5 out of 60 cases showed acute infarcts. 2 out of 60 cases showed hemorrhage. One of the cases showed large hematoma in left parietal, occipital and temporal regions and other case showed SAH in right parietal region. In a study done by Kunitoshi Iseki et al [9] on 1609 patients of CKD, 41 patients showed findings - 8 cerebral infarction (0.8%), 31 cerebral hemorrhage (3.1%), and 2 subarachnoid hemorrhage (0.2%). In present study, cerebral infarction is 8.5%, cerebral hemorrhage is 1.5% and SAH is 1.5%.

Gradient-echo T2-weighted sequence is highly sensitive for detecting cerebral microbleeds which have been reported to be a risk factor for future cerebrovascular events and a marker of cerebral small vessel disease in the general. In haemodialysis patients, there is a significantly higher prevalence of cerebral microbleeds compared with normal subjects. In our study, 2 cases showed microbleeds in basal ganglia, thalami and cerebellum. In a study by Watanabe [10] in 80 hemodialysis patients; 34 men and 46 women; mean age, 62.9 yr, microbleeds were seen in 35%. In our study it is 7.7 % (28 hemodialysis patients).

Osmotic demyelination syndrome has been reported in patients with endstage renal disease, but the specific MRI findings in this patient group have not been documented in detail. Osmotic demyelination syndrome is a well-known clinicopathologic entity characterized by edema and demyelination in the pons and extrapontine areas. In present study 5 out of 60 (8%) cases showed T1 hypo to isointense and FLAIR hyperintensity in central pons with no diffusion restriction on DWI. This is in favour of osmotic demyelination syndrome with demyelination or transient edema in pons.

The posterior reversible encephalopathy syndrome (PRES) is characterized by headache, seizures, altered mental status and visual disturbances. It is a clinical and radiological entity and typically causes the reversible changes in the posterior circulation system of the brain. In present study 4 cases showed hyperintensities on T2W and FLAIR sequences. 3 out of 4 showed bilateral parietal and occipital region involvement, one case involved bilateral frontal, parietal, occipital, cerebellar, midbrain and pontine involvement.

Presently there are no studies for the incidence of central pontine myelinolysis [11,12,13] and PRES [14,15,16,17] in CKD patients. However few case reports were published indicating these findings in CKD patients. 2 out of 60 cases showed small foci of blooming on GRE sequences, suggestive of non-specific calcified granulomas.

VI. Conclusion

During the period of 2 years of study, 60 cases of chronic kidney disease were evaluated with MRI brain. 40 cases showed abnormal MRI findings. The maximum numbers of cases were of CKD stage V. Incidence of males is more than females. The youngest patient was 17 years and the eldest was 85 years. Maximum numbers of abnormal cases were in the age group of 40-59 years, patients on dialysis and CKD stage5. The commonest finding was cerebral atrophy. Not many studies are there for the incidence of different neurological findings in CKD. This is a relatively new study and maybe limited by the small sample size (n=60).

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