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Original Article

Radiology Section

Role of Quantitative Diffusion MRI in Categorisation of Early Changes in Children with Viral Encephalitis

SHAISTA SIDDIQUI, SHAGUFTA WAHAB, RIZWAN AHMAD KHAN

ABSTRACT

Introduction: Viral encephalitis is quite common in this part of world. Magnetic Resonance Imaging (MRI) is the first line investigation modality for the accurate detection and diagnosis of encephalitis. Diffusion-Weighted Imaging (DWI) is increasingly used in diagnosis and characterization of cerebral ischemia and infarcts and its role in other conditions like infections is still being discovered.

Aim: The aim of this study was to determine the role of quantitative ADC values in the assessment of the early, subacute/delayed and post recovery stages of viral encephalitis in paediatric population.

Materials and Methods: Thirty children with encephalitis were studied using both conventional (T2WI and FLAIR) sequences and DWI. These patients were divided into two groups. The Group A patients were those who presented within three days of onset of disease and Group B included those patients who presented after three days of disease onset. The results were compared with the control group for the normal ADC standards. The follow-up of these patients was done three months after the initial onset of symptoms. The ADC values in both the groups were compared to the control group and were statistically analysed.

Results: The ADC values in Group A (early) was low with a mean value of 649.0±52.0 while Group B (subacute/late) showed an increase in ADC with a mean value of 1277.0±138.0. The ADC values of the control group and the Group A patients was found to be statistically significant ($p<0.0002$) indicating the efficacy of DWI in early detection of encephalitis.

Conclusion: MRI and especially FLAIR imaging is the mainstay in the diagnosis of the encephalitic lesions. However, quantitative ADC does help in the early diagnosis of the lesions and in the staging of the lesions. The ADC values were seen to be significantly different in all the 3 groups. Hence, quantitative ADC can be used for staging of the lesions and to predict the resolution of the lesions.

Keywords: Cerebral ischemia, Infarcts, Quantitative ADC

INTRODUCTION

Encephalitis is quite common and often life threatening in the paediatric age group. A wide range of etiologies are implicated with viruses being one of the most common ones [1-3]. Imaging plays important role in confirmation of the diagnosis, in follow-up and in detection of complications [4]. MRI is widely accepted as a sensitive imaging modality for the accurate detection and diagnosis of encephalitis. However, conventional sequences like T1, T2 and Fluid Attenuated Inversion Recovery (FLAIR) may remain unable in demonstrating encephalitic lesions at very early stages [5,6]. DWI is increasingly used in diagnosis and characterisation of various diseases notably, early detection of cerebral ischemia and infarcts and its role in other conditions like infections is still being discovered [7-9]. There is dearth of studies demonstrating utility of DWI in the early detection of viral encephalitis especially in children [1,10,11]. This study was undertaken with the aim to determine the role of addition of quantitative study in DWI and role of ADC values in the assessment of different stages of viral encephalitis in paediatric population.

MATERIALS AND METHODS

This was a retrospective study conducted at the Department of Radiodiagnosis, JN Medical College, AMU, Aligarh, India and included 30 patients diagnosed with viral encephalitis between July 2016 and July 2017 on the basis of clinical, biochemical and conventional radiological features. These patients comprised the case group. The control group included the patients with similar age profile undergoing imaging for some other symptoms and in whom the imaging study was normal.

Both the groups were evaluated with MRI brain performed on Seimens Magnetom Avanto 1.5 T scanner and T2-W spin-echo images and FLAIR images were obtained. DWI was

performed with echo-planar imaging using DRESS sequence. Susceptibility Weighted Imaging (SWI) were also done to check for early haemorrhagic changes in the lesions. The lesions were evaluated on conventional sequences namely T2WI and FLAIR and also on DWI.

The patients within the case group were equally divided into 2 groups on the basis of time of imaging after the onset of symptoms. Group A (early) patients were imaged within three days of the onset of symptoms while Group B (subacute/late) were imaged after three days of onset of symptoms. The imaging in all the cases was done before the institution of treatment. Subsequently, the patients from both the groups were followed up. However, only 18 patients were available for follow-up. Of these, seven patients completely recovered while 11 had some or the other sequelae (six patients had focal neurological deficits, three had seizures while two patients had mental retardation). The ADC values were calculated in each of the groups. These ADC values were compared with control group patients who were imaged for unrelated complaints and showed normal brain imaging and ADC map. The collected data from the case and the control group was statistically analysed using SPSS version 20.

RESULTS

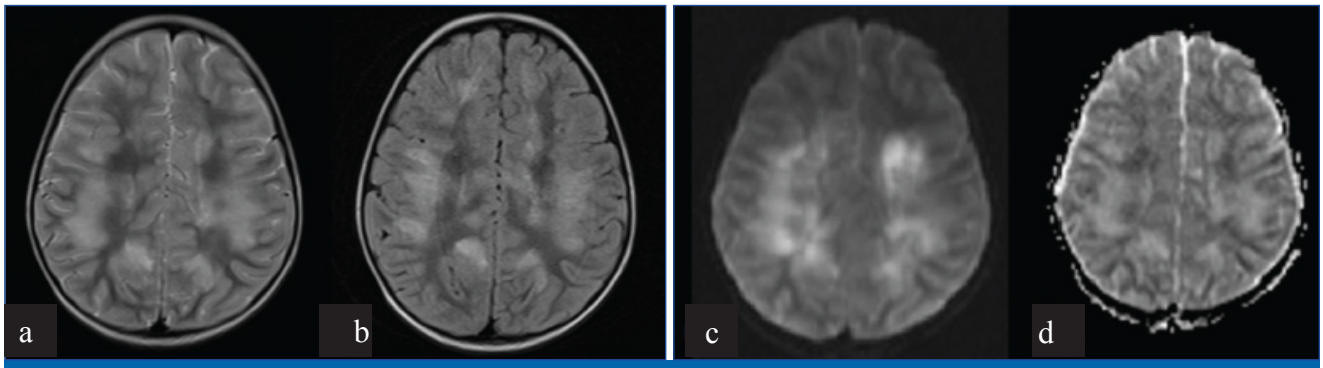
The mean age of the patients in Group A was six years (range: 3-12 years) while the mean age in Group B was eight years (range: 4-12 years). The boys were more commonly affected (ratio was 2:1). However, the distribution among both the groups was similar. The patients of both the groups presented with similar complaints of fever, nausea, vomiting, delirium and unconsciousness. The neurological examination showed upper motor neuron type of weakness in majority (85.0%) of the patients. The ADC of the control group showed a mean value of 803.0±109.0 with values ranging from 627.0 to 1065.0. The Group A patients presenting within 3 days showed a decreased ADC value with a mean range of 649.0±52.0. When compared with the control group using the unpaired 't'-test a statistically significant p-value of 0.0002 was obtained indicating the sensitivity of DWI in the diagnosis of early encephalitis. When compared with the control group using the unpaired 't'-test a statistically significant p-value of 0.0002 was obtained indicating the sensitivity of DWI in the diagnosis of early encephalitis. The ADC values in the Group B patients were seen to be higher than the subjects of control group and Group A. These values were almost double the value of Group A patients with a mean value of 1277.0±138.0. The values were not statistically significant (p>0.005) when compared to both the control group and the Group A, however, a conclusion of a rising trend can be drawn. The values were not statistically significant when compared to both the control group and the Group A yet, a conclusion of a rising trend can be drawn. In the follow-up of patients three months after onset of symptoms, seven patients showed complete resolution of the symptoms with the ADC values reaching almost within normal range with mean value of 836.0±105.0 [Table/Fig-1]. However, 11 patients showed range of complications and sequelae from focal areas of mild gliosis to full blown areas of encephalomalacia. In these patients the ADC values remained increased as expected because of T2 shine through effects [Table/Fig-2-4].

Serial Number	ADC Values in Controls	ADC Values in Patients (<3 days) Gp A	ADC Values in Patients (>3 days) Gp B	ADC Values in Follow-up Patients with Complete Resolution (After 3 Months)
1	783	654	1124	958
2	782	602	1079	876
3	739	669	1116	992
4	750	671	1259	784
5	767	702	1346	732
6	672	605	1180	748
7	627	609	1406	764
8	766	701	1589	-
9	828	732	1392	-
10	901	661	1303	-
11	779	698	1402	-
12	853	552	1248	-
13	953	598	1301	-
14	1065	588	1139	-
15	786	692	1276	-
Mean	803	649	1277	836
Standard Deviation	109	52	138	105

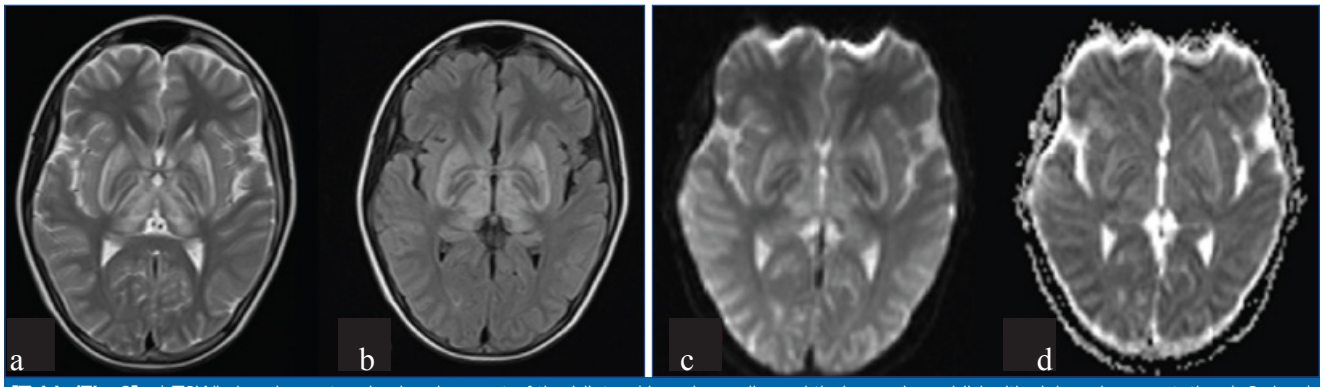
[Table/Fig-1]: Shows the ADC values in the various groups.

DISCUSSION

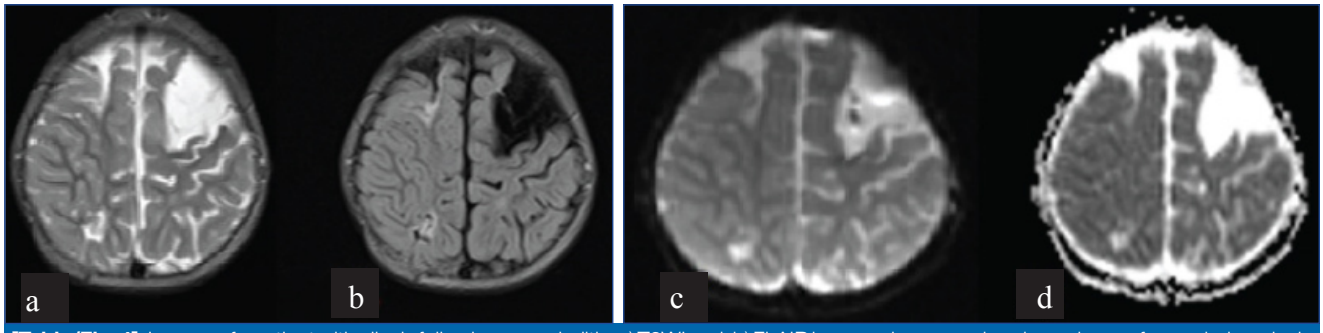
Viral encephalitis is one of the commonest infections affecting children these days. It is broadly divided into acute and chronic stage. In the acute stage of viral encephalitis, there is congestion, perivascular cell infiltration or perivascular cuffing with thrombus formation [1,14]. The postulated mechanism regarding increased signal on DWI is due to the presence of cytotoxic oedema in the affected grey matter [15,16]. In the early subacute and later stages, vasculitis and perivascular cell infiltration decrease as also the severity of diffusion restriction leading to increase in ADC values [11]. These stages are associated with vasogenic oedema and hence the lesions in the later stages of the disease become more apparent on T2 and FLAIR imaging. In the chronic stages where there is partial recovery, residual necrosis and demyelination are present which are responsible for increased signal on T2 and FLAIR sequences along with higher ADC values [1,10]. This was the possible mechanism depicted in our study as well where, in the initial stage there was a fall in the ADC values with a subsequent rising trend. Similar findings were also



[Table/Fig-2]: a) T2WI showing multiple altered signal intensity areas in the bilateral temporal lobes in a child of early (<3 days) encephalitis; b) The lesions appear to be more on FLAIR images; c) DW imaging of the same lesions; d) The lesions showing low ADC values on the ADC map indicating acute nature of the lesion.



[Table/Fig-3]: a) T2WI showing extensive involvement of the bilateral basal ganglia and thalamus in a child with delayed presentation (>3 days) of viral encephalitis; b) These lesions appear more extensive and better delineated in FLAIR images; c) The increased ADC values on DWI; d) The increased ADC values on the ADC map as well.



[Table/Fig-4]: Images of a patient with gliosis following encephalitis: a) T2WI and; b) FLAIR images show a wedge shaped area of encephalomalacia in the left parietal lobe along with few small focal areas of gliosis in the right parietal lobe; c) T2 shine through is evident in the DWI in the same patient; d) The ADC map of the same patient.

reported by Kiroglu Y et al., [9]. He reiterated the conclusion that DWI is more sensitive in the early stages of encephalitis as compared to conventional sequences [9]. This was the possible mechanism depicted in our study as well where, in the initial stage there was a fall in the ADC values with a subsequent rising trend.

For the follow-up of the cases and the identification and the quantification of the sequelae of encephalitis, T2WI and FLAIR turned out to be as good as or better than DWI. We found that DWI was better in early stages due to cytotoxic oedema in majority of the patients, while FLAIR images were better in late stage because by now there is lot of vasogenic oedema. Prakash M et al., found in his study that conventional imaging like T2WI and FLAIR sequences are superior or at par with DWI when evaluating chronic stages of encephalitis [10]. This feature of DWI being the superlative imaging modality in early stages while FLAIR for the late stages was seconded by Katirag A et al., and Renard D et al., [16,17]. These studies compared the DWI and FLAIR imaging in early stages and chronic stages of encephalitis using topographical scoring system and both of them independently concluded that DWI should be the sequence of choice in acute stages white FLAIR fares better in chronic stages.

Another important feature which was observed in our study was that the involvement of the basal ganglia and thalami or the appearance of haemorrhage within the encephalitic lesions was associated with a poor prognosis. This finding was also agreed upon by Renard D et al. He even proved using topographical analysis that early thalamic involvement was better appreciated on FLAIR sequence rather than DWI [17]. Hence, prognostic factors were listed to be extensive lesions early in the disease, low ADC values, thalamic involvement and presence of haemorrhage if any. We corroborated the clinical finding of poor clinical outcome in patients with involvement of brain deep grey matter by demonstrating the association of ADC values with extensive involvement of parenchyma. One of our patients who presented late and developed haemorrhagic changes in the lesion progressed to full fledged encephalomalacia. Hence, early detection is of paramount importance.

LIMITATION

The major limitation of the study was the small sample size. Secondly, documentation of less number of sequelae in post recovery stage. This was attributed to the loss of 12 patients in follow-up period. The follow-up should have been more frequent for a better understanding of ADC value map. However, monetary constraints precluded more frequent imaging. A larger study on this subject may answer these queries.

CONCLUSION

This study signifies the definite role of DWI in the early detection of encephalitic lesions thereby ensuring early initiation of therapy and therefore fewer complications and sequelae. This study also reiterates superiority of MRI for the diagnosis of encephalitis. Another clinical significance that can be drawn from this study is that the complete recovery of encephalitis patients without sequelae was associated with normalisation of ADC values.

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AUTHOR(S):

1. Dr. Shaista Siddiqui
2. Dr. Shagufta Wahab
3. Dr. Rizwan Ahmad Khan

PARTICULARS OF CONTRIBUTORS:

1. Assistant Professor, Department of Radiodiagnosis, JN Medical College, AMU, Aligarh, UP, India.
2. Associate Professor, Department of Radiodiagnosis, JN Medical College, AMU, Aligarh, UP, India.
3. Associate Professor, Department of Paediatric Surgery, JN Medical College, AMU, Aligarh, UP, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:

Dr. Shagufta Wahab,
Kashan-e-Wahab, Street No. 4, Iqra Colony,
Aligarh-202001, Uttar Pradesh, India.
E-mail: drshaguftawahab@rediffmail.com

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