Value of Magnetic Resonance Spectroscopy MRS in Prolonged Febrile Convulsion in Children

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Abstract

Background: Febrile Convulsion (FC) or Febrile Seizure (FS) is the most common type of seizures that occur in children between the ages of 6 months to 5 years with body temperature over 38ºC and without any infection such as meningitis and encephalitis in the central nervous system. The incidence of FC is 5 cases per 1000 children annually.

Aim of Study: To determine metabolic changes that occur in temporal lobe and hippocampus after prolonged febrile seizures, by using Magnetic Resonance Spectroscopy (MRS).

Patients and Methods: Thirty patients with prolonged febrile seizures more than 15 minutes were included. Control group including thirty child age and gender healthy matched. EEG was done within 72 hour of febrile seizure to all case and control group in the study using Pediatric Neurology Department EEG machine. Also, MRS (Magnetic Resonance Spectroscopy) was done within 48h of febrile seizure to the cases and was done to the control group, by using achieva 1.5t Philips. The spectra were all acquired in conjunction with an MRS study of the brain that included coronal T2, axial & coronal FLAIR images through the temporal lobes, and axial T1 and T2 SE images through the entire brain. To obtain MRS technique, scout imaging of the brain in coronal and sagittal orientations was performed with T1 WI. The MRS was performed using multi-voxel technique (PRESS-CSI sequence with TE/TR=135ms/1690ms, 12 averages, FOV 120 X 120mm^2). The region of interest was placed through whole temporal lobi with the voxel layer position adjusted based on the localization of hippocampi in order to examine the whole hippocampi at long distance (voxel size set to 10 X 10 X 15mm^3). The resonances of major metabolites detected were as follows: The N Acetyl Aspartate (NAA) peak at 2.02ppm, the creatine (Cr) and phosphocreatine peak at 3.02ppm, and the choline (Cho) peak at 3.20ppm.

Results: We found that there was high significant difference between case and control groups regarding MRS. As in the case group there was reduction of NAA and slightly increase in Cho & Cr, which lead to changes in metabolic ratios (NAA/Cr, Cho/NAA & Cho/Cr). While in the control group was normal.

The optimal cut off value of NAA/Cr was less than 2.61, The sensitivity and specificity of NAA/Cr was 96.7% and 93.3% respectively and accuracy was 95%.

While, the optimal cut off value of Cho/NAA more than 0.785, the sensitivity and specificity of Cho/NAA was 96.7% and 80% respectively and accuracy was 88.3%.

While, the optimal cut off value of Cho/Cr less than 2.115, The sensitivity and specificity of Cho/Cr was 93.3% and 93.3% respectively and accuracy was 93.3%.

Conclusion: MR spectroscopy is a very sensitive guiding tool in predicting Temporal Lobe Epilepsy (TLE) and the side of involvement in patients with TLE even in patients with MR negative studies. Also, it helps in detecting abnormal spectra of various brain metabolites at temporal lobe and hippocampus. Further more, it can detect hippocampal injury earlier and with more accurate results than EEG.

Abbreviations:

AUC	: Area Under Curve.
CBC	: Complete Blood Count.
CHESS	: Chemically Selective Saturation.
Cho	: Choline.
cMRI	: Conventional Magnetic Resonance Imaging.
CNS	: Central Nervous System.
Cr	: Creatine.
EEG	: Electroencephalogram.
FC	: Febrile Convulsion.
FLAIR	: Fluid Attenuated Inversion Recovery.
FOV	: Field of View.
FS	: Febrile Seizures.
MRI	: Magnetic Resonance Imaging.
MRS	: Magnetic Resonance Spectroscopy.
MUCH	: Mansoura University Children Hospital.
NAA	: N-Acetyl Aspartate.
PRESS-CSI	: Point Resolved Spectroscopy-chemical Shift Imaging.
SD	: Standard Deviation.
SE	: Spin Echo.
SPSS	: Statistical Package for Social Science.
T	: Tesla.
TE	: Time of Echo.
TLE	: Temporal Lobe Epilepsy.
TR	: Time of Repetition.
ROC	: Reciprocal Operative Curve.

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Introduction

FEBRILE Convulsion (FC) or Febrile Seizure (FS) is the most common type of seizures that occur in children between the ages of 6 months to 5 years with body temperature over 38ºC and without any infection such as meningitis and encephalitis in the central nervous system. The incidence of FC is 5 cases per 1000 children annually [1].

Febrile seizures are classified into two groups including simple and complex seizures. Simple seizures happen with generalized tonic-colonic movements for less than 15 minutes without recurrence in the first of 24 hours. Complex seizures occur more than once in 24 hours for more than 15 minutes and are focal [2].

Some evidence suggests that the damage caused by Complex Febrile Seizures (CFS) is not limited to the hippocampus but often affects extra-hippocampal structures. CFS in humans is associated with widespread changes in cortical grey matter and subcortical white matter tracts. Electro-encephalogram (EEG) changes as focal EEG slowing or attenuation are present in EEGs obtained within 72 hours of FS attack in a substantial proportion of children that are highly associated with Magnetic Resonance Imaging (MRI) evidence of acute hippocampal injury [3].

Magnetic Resonance Spectroscopy (MRS) is a noninvasive technique capable of providing metabolic information about different tissues. Also, it enables tissue characterization on a biochemical level surpassing that of conventional Magnetic Resonance Imaging (cMRI). It detects abnormalities that are invisible to cMRI because metabolic abnormalities often precede structural changes, but the connection between the severity of metabolic disturbance and structural lesion is not straightforward [4].

Patients and Methods

Study design:

This was a case control study on children with prolonged febrile seizures more than 15 minutes referred to the Emergency Department at Mansoura University Children Hospital "MUCH" from January 2018 to March 2019.

Subjects:

Patient was taken from children attending Emergency Department in MUCH. The study was performed on:

• Thirty patients with prolonged febrile seizures more than 15 minutes.

• Control group including thirty child age and gender healthy matched.

Inclusion criteria:

1- Children with prolonged febrile seizures more than 15 minutes.

Exclusion criteria:

1- Patient with neurodevelopmental delay.

2- History of afebrile seizures.

3- Organic brain lesion.

4- CNS infection or possibility.

5- Evidence of systemic diseases revealed by abnormal CBC.

6- Diabetes.

7- Malnutrition.

Methods:

All participants will be subjected to the following:

1- History taking: In the form of:

    a- Name, age, sex.

    b- History of patient illness.

    c- Duration and previous febrile seizures.

    d- Family history of febrile seizures.

    e- Family history of epilepsy.

    f- History of other medical condition.

2- *Clinical examination:* Physical and neurological examination were performed to exclude associated neurological disease.

3- *Electroencephalogram (EEG):* EEG was done within 72 hour of febrile seizure to all case and control group in the study using Pediatric Neurology Department EEG machine (Nihon Kohden, Japan, Model EEG-1200)). The recording has taken 20-30 minutes using the international 10-20 system scalp electrode placement as shown in Fig. (1).

4- *Neuro imaging:* MRS (Magnetic Resonance Spectroscopy) was done within 48h of febrile seizure to the cases and was done to the control group, by using achieva 1.5t Philips.

Patient preparation:

The patients were asked to remove any ferromagnetic metals (such as coins and pins). Pace-

maker and any ferromagnetic fixating crews or plate were excluded from this examination. All patients and their parents were informed about the MRI magnets, approximate duration and techniques of MRS and were instructed not to move during the examination time.

MRS technique:

• *Patient positioning and preparation for scanning:* Patients were positioned on MRI examination table in the supine position. The MRS examinations were performed in all patients in one session. They were performed at 1.5T super conducting system (Philips Achieve MRI machine, Netherlands). The MR spectroscopy was performed with sedation.

• *Scan setup and scan parameters:* The spectra were all acquired in conjunction with an MRS study of the brain that included 3-mm coronal T2 spin-echo (SE) images, 3-mm axial & coronal FLAIR images through the temporal lobes, and 5-mm axial T 1 and T2 SE images through the entire brain. To obtain MRS technique, scout imaging of the brain in coronal and sagittal orientations was performed with T1 WI (repetition time ms/Echo time ms 500/14, section thickness 3mm) angulation parallel to the long axis of the hippocampus for localization of the transverse plane. The MRS was performed using multivoxel technique (PRESS-CSI sequence with TE/TR=135ms/1690ms, 12 averages, FOV 120 X 120mm^2). The region of interest was placed through whole temporal lobi with the voxel layer position adjusted based on the localization of hippocampi in order to examine the whole hippocampi at long distance (voxel size set to 10 X 10 X 15mm^3).

Image evaluation, post processing and MRS Metabolite's assessment: Post processing of raw spectroscopic data was performed. In the first step, MRS voxels where hippocampus represented more that 2/3 of the covered tissue were manually selected and those with a spectral error value of greater than 20% were subsequently automatically excluded. By using special software for reporting the calculated MR spectroscopic maps, it is possible to select all voxels within both hippocampi at an overlaid axial flair image. On average, nine voxels were analyzed per right and left hippocampus. The variability in the number of voxels available for analysis was mainly due to exclusion of some voxels because of low quality of spectral data (high error value). Automated techniques from the Philips package were used for global and local shimming and gradient tuning. The amplitude of the Chemical Shift Selective (CHESS) water suppression pulse was adjusted to obtain the maximum water suppression. The resonances of major metabolites detected were as follows: The N Acetyl Aspartate (NAA) peak at 2.02ppm, the creatine (Cr) & phosphocreatine peak at 3.02ppm, and the choline (Cho) peak at 3.20ppm. Spectral post-processing included phase correction to reduce the noise level, baseline correction to eliminate any draft in the baseline, peak calibrations and spectral plotting.
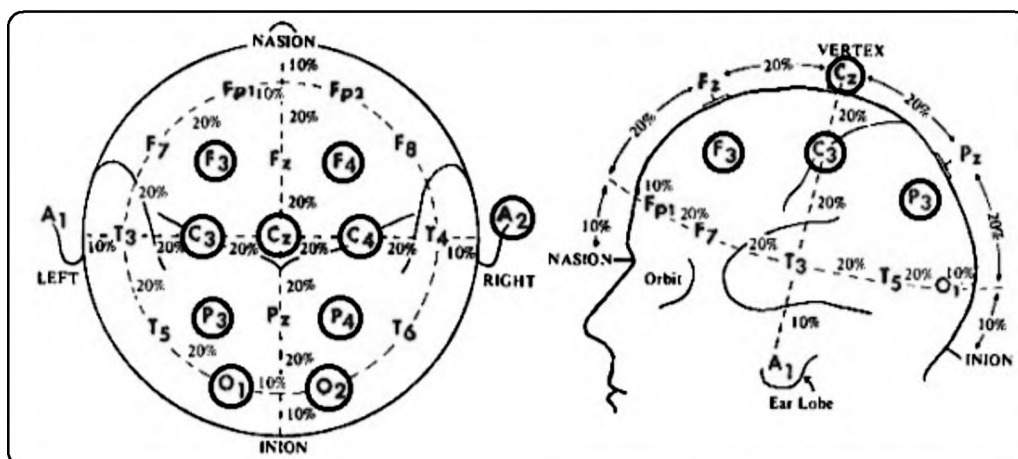

Fig. (1): 10/20 system electrode distances.

Statistical analysis:

Data were tabulated, coded then analyzed using the computer program SPSS (Statistical package for social science) version 23.0 to obtain.

Descriptive data:

Descriptive statistics were calculated in the form of:

1- Mean ± Standard Deviation (SD).

2- Median & range (minimum-maximum).

3- Frequency (number-percent).

Analytical statistics:

In the statistical comparison between the different groups, the significance of difference was tested using one of the following tests:

1- Student's *t*-test (unpaired): Used to compare between mean of two different groups of numerical (parametric) data.

2- Man Whitney: Used to compare between two different groups of numerical (non-parametric) data.

3- Inter-group comparison of categorical data was performed by using chi square test (χ^2-value) or fisher exact when indicated.

Spearman correlation coefficient test was used correlating different parameters.

The sensitivity and specificity of NAA/Cr, Cho/NAA and Cho/Cr to differentiate between FS disease were examined at different cut-off points using Reciprocal Operative Curve (ROC) analysis to determine the best cut-off point as well as the diagnostic power of each test.

A *p*-value <0.05 was considered statistically significant.

Results

After obtaining clinical data as regards febrile seizures of case group and evaluation of case & control group with EEG and neuro-imaging with MRspectroscopy, the following results were obtained.

Table (1): This table shows clinical data in studied groups.

	Case group
Onset of Febrile Seizure (yrs):	
(Median-range)	1.40 (0.50-11.00)
Duration of FS (min):	
(Mean ± SD)	25.50±6.66
Type of Febrile Seizure:	
Focal	1 (3.3%)
Generalized	29 (96.7%)
Family history of FS:	
Negative	26 (86.7%)
Positive	4 (13.3%)
No of previous FS:	
2 times	25 (83.3%)
3 times	5 (16.7%)

Table (2): Comparison between the two groups regarding EEG findings.

EEG findings	Groups				*p*
	Control group		Case group		
	No	%	No	%	
Normal	30	100	19	63.3	<0.001 *
Focal spike	0	0.0	3	10.00	0.23
Generalized spike	0	0.0	3	10.00	0.23
Focal slowing	0	0.0	5	16.7	0.1

This table shows that there was high significant difference between two groups regarding EEG findings as 11 cases out of 30 case group revealed abnormal EEG findings.
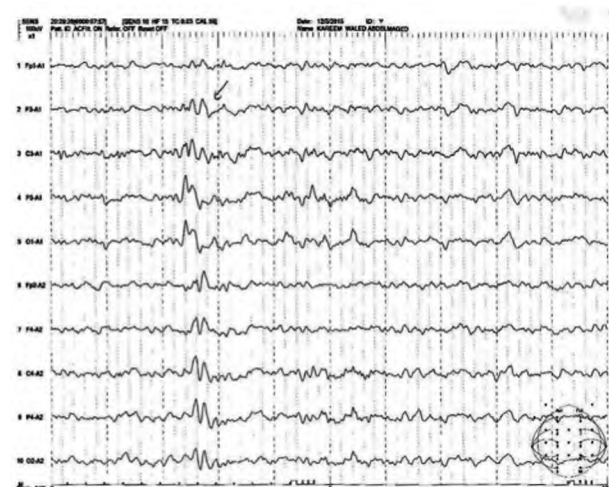

Fig. (2): Generalized spike and slow wave (2Hz) in child with febrile convulsion. EEG suggesting generalized activity.

Table (3): Comparison between the two groups regarding MRS.

	Groups				*p*
	Control group		Case group		
NAA/Cr	3.93	2.43-13.36	1.46	0.87-2.66	<0.001 *
Cho/NAA	0.69	0.06-0.85	1.02	0.67-1.22	<0.001 *
Cho/Cr	2.90	1.92-5.96	1.31	1.08-2.56	<0.001 *

This table shows that there was high significant difference between both groups regarding MRS which shows more reduction in metabolites ratios in case group (NAA/Cr, Cho/NAA, Cho/Cr).
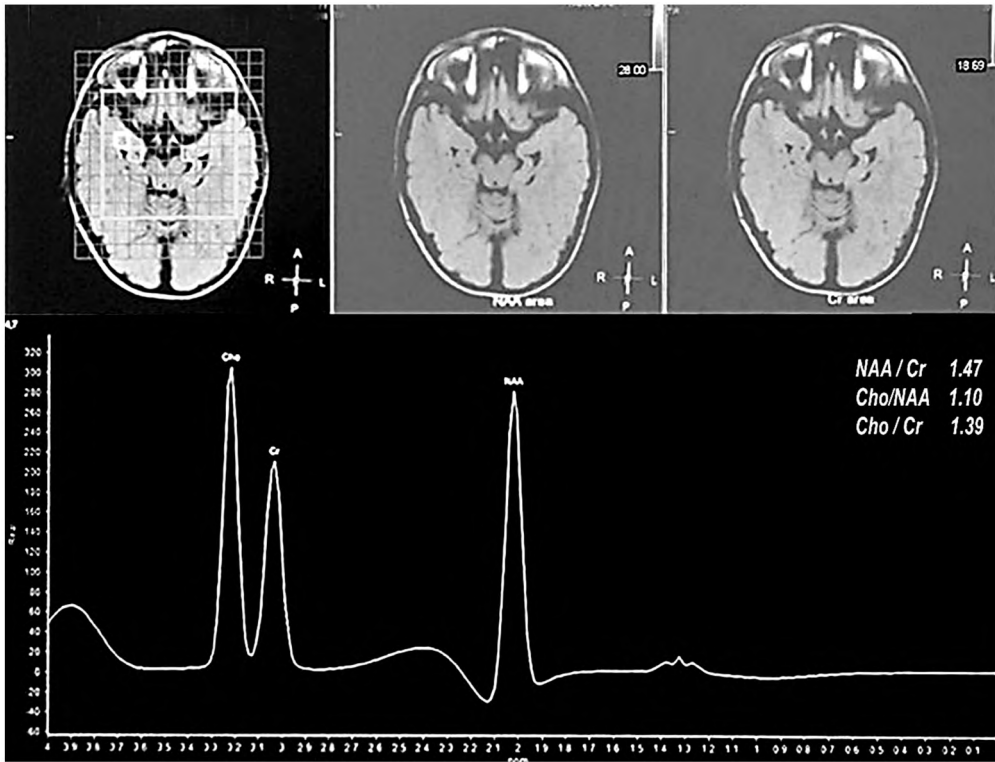
Fig. (3): Multi-voxel MR spectroscopy at right hippocampal region in child presented with febrile convulsions revealed:
• Mildly elevated choline peak.
• Mildly reduced NAA peak.
• Elevated creatine peak.
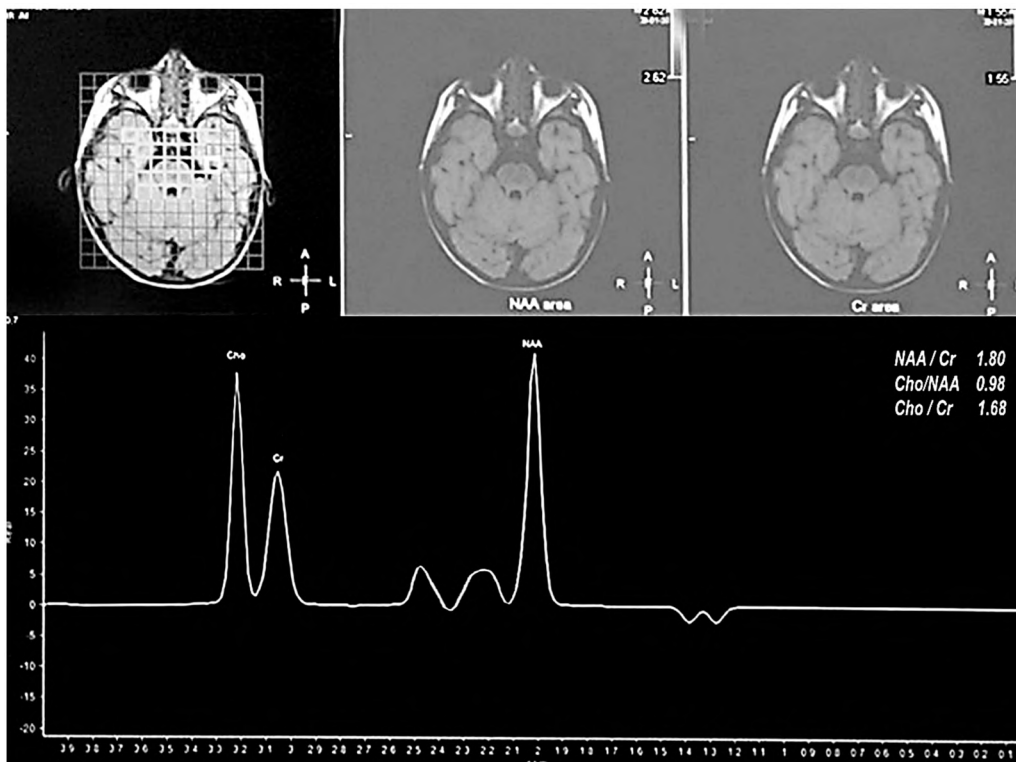• NAA/Cr ratio=1.47.
• Cho/NAA=1.10.
• Cho/Cr=1.39.

Fig. (4): Multi-voxel MR spectroscopy at left hippocampal region in child presented with febrile convulsions revealed:
• Mildly elevated Cho peak.
• Mildly elevated Cr peak.
• NAA/Cr=1.80.
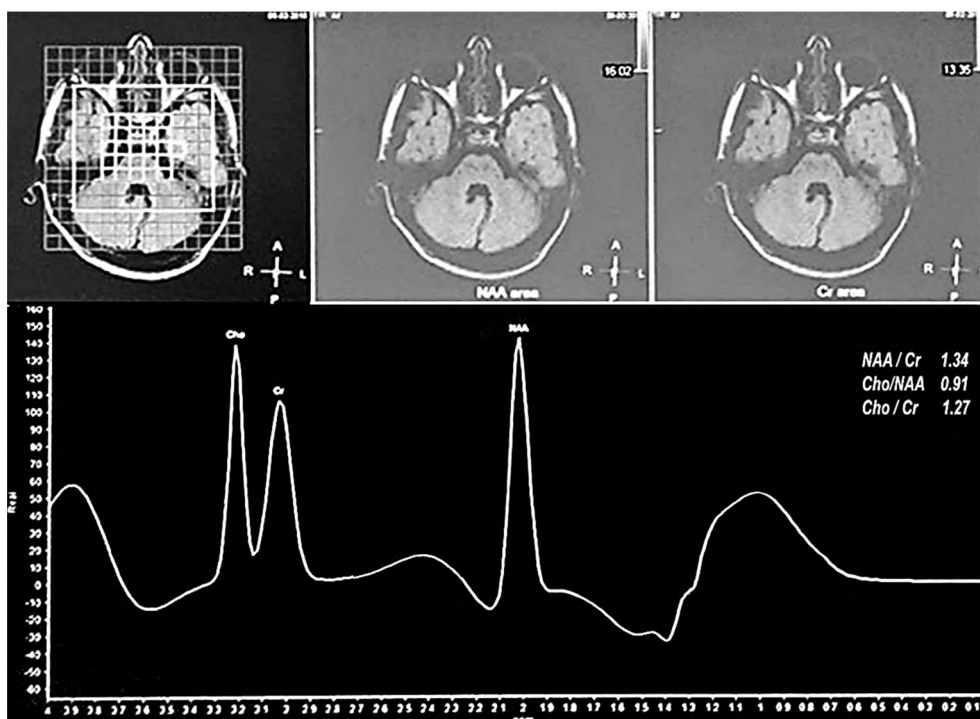• Cho/NAA=0.98.
• Cho/Cr=1.68.

Fig. (5): Multi-voxel MR spectroscopy at left hippocampal region in child presented with febrile convulsions revealed:
• Mildly elevated Cho peak.
• Elevated Cr peak.   • Cho/NAA=0.91.
• NAA/Cr=1.34.   • Cho/Cr=1.27.

Table (4): Comparison between patients with normal and abnormal EEG group regarding MRS.

	EEG				p
	Normal		Abnormal		
NAA/Cr	1.56	1.15-2.23	1.21	0.87-2.66	0.12
Cho/NAA	1.03	0.81-1.22	0.89	0.67-1.13	0.1
Cho/Cr	1.45	1.08-2.56	1.29	1.13-1.54	0.18

This table shows that there was no significant difference between patients with normal and abnormal EEG regarding MRS.

The ROC curve was plotted to identify MRS changes (NAA/Cr --- Cho/NAA --- Cho/Cr) in patients with prolonged febrile seizures.

Table (5): The cut off value of MRS (NAA/Cr --- Cho/NAA --- Cho/Cr) in patients with prolonged febrile seizures by Reciprocal Operative Curve (ROC).

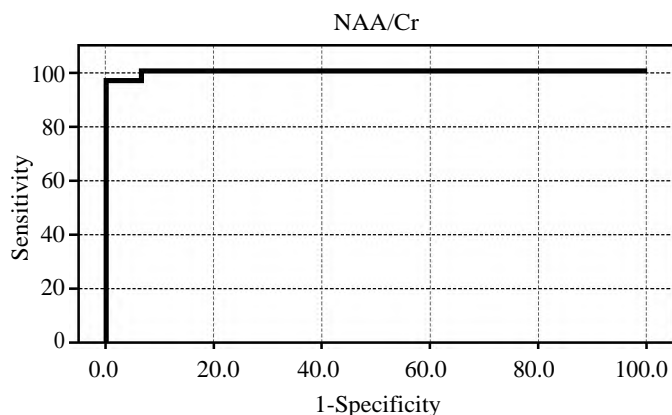|	AUC (95%CI)	Cutoff	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
NAA/Cr	0.99 (0.99-1.00)	<2.61	96.7	93.3	93.5	96.6	95.0
Cho/NAA	0.97 (0.93-1.00)	>0.785	96.7	80.0	82.9	96.0	88.3
Cho/Cr	0.98 (0.95-1.00)	<2.115	93.3	93.3	93.3	93.3	93.3

Fig. (6): ROC curve to determine the cut off value of NAA/Cr in patients with prolonged febrile seizures.

AUC (Area Under the Curve) was 0.99 (0.99-1), the optimal cut off value was less than 2.61, the sensitivity and specificity of NAA/Cr was 96.7% and 93.3% respectively, the positive predictive value was 93.5%, the negative predictive value was 96.6% and accuracy was 95%.
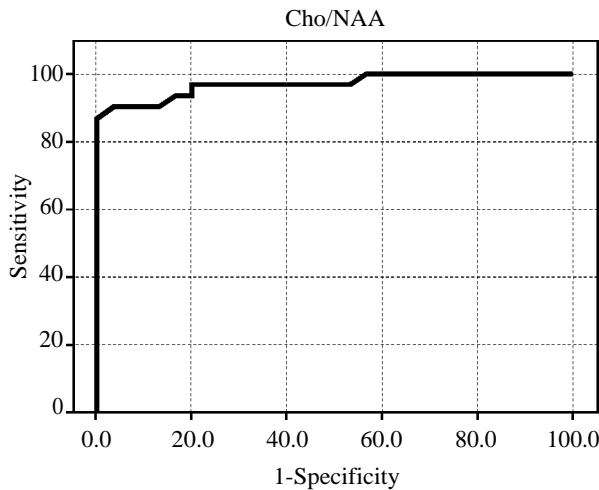

Fig. (7): ROC curve to determine the cut off value of Cho/NAA in patients with prolonged febrile seizures.

AUC (Area Under the Curve) was 0.97 (0.93-1), the optimal cut off value was more than 0.785, the sensitivity and specificity of Cho/NAA was 96.7% and 80% respectively, the positive predictive value was 82.9%, the negative predictive value was 96% and accuracy was 88.3%.
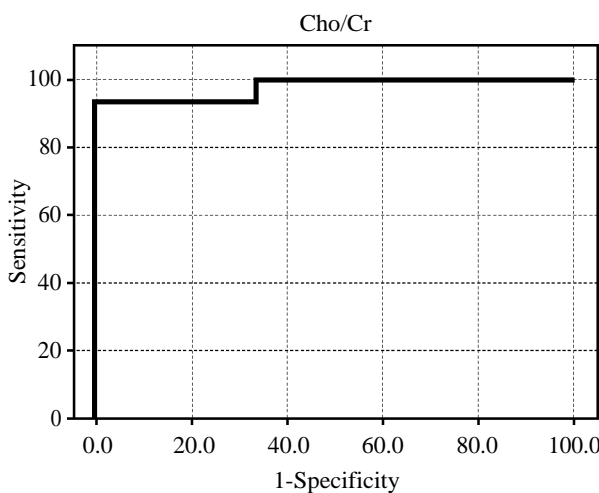

Fig. (8): ROC curve to determine the cut off value of Cho/NAA in patients with prolonged febrile seizures.

AUC (Area Under the Curve) was 0.98 (0.95-1), the optimal cut off value was less than 2.115, the sensitivity and specificity of Cho/Cr was 93.3% and 93.3% respectively, the positive predictive value was 93.3%, the negative predictive value was 93.3% and accuracy was 93.3%.

Discussion

Febrile Convulsion (FC) or Febrile Seizure (FS) is the most common type of seizures it occur in children between the ages of 6 months to 5 years with body temperature over 38ºC and without any infection such as meningitis and encephalitis in the central nervous system. The incidence of FC is 5 cases per 1000 children annually [1].

2-4 % percent of children experiences FC during the first 6 years of life and almost one third of them have been experienced recurrent episodes. Therefore, identification of these risk factors appear to be necessary to prevent recurring attacks. Febrile seizures are classified into two groups including simple and complex seizures. Simple seizures happen with generalized tonic-colonic movements for less than 15 minutes without recurrence in the first of 24 hours. Complex seizures occur more than once in 24 hours for more than 15 minutes and are focal [2].

Children with multiple risk factors have the highest risk of recurrence. A child with two or more of the risk factors as listed in has a recurrence rate greater than 30% at 2 years; a child with three or more risk factors has a recurrence rate greater than 60% [5].

Risk factors for recurrent febrile seizures:

• Younger than 18 months at onset.

• Duration of fever (i.e., shorter duration of fever before seizure equals higher risk of recurrence).

• Family history of epilepsy (possible).

• Family history of febrile seizures.

• Degree of fever (i.e., the lower the peak fever, the higher the rate of recurrence).

Some evidence suggests that the damage caused by CFS is not limited to the hippocampus but often affects extra-hippocampal structures. CFS in humans is associated with widespread changes in cortical grey matter and subcortical white matter tracts. It seems likely therefore that any deleterious effects of childhood PFS may also affect extra-hippocampal structures, which may be important in other subsequent epileptic disorders [6].

MRS is a noninvasive technique capable of providing metabolic information about different tissues; also it enables tissue characterization on a biochemical level surpassing that of conventional Magnetic Resonance Imaging (cMRI). It detects abnormalities that are invisible to cMRI because metabolic abnormalities often precede structural

changes. Proton MRS has the potential to identify metabolic abnormalities before structural changes exist, it was shown that MRS detects abnormalities in patients who had normal MRI examination, i.e. patients with negative MRI. Metabolic abnormality may precede the development of structural lesion, but the connection between the severity of metabolic disturbance and structural lesion is not straightforward [4].

The current study aimed to determine changes that occur in temporal lobe and hippocampus after prolonged febrile seizures, by using MRS (Magnetic Resonance Spectroscopy).

The present study included 30 children with febrile seizures 30 age and gender matched healthy controls.

The diagnostic value of EEG is limited in children with FC. It is normal in 60% of simple FCs. However, EEG abnormality is reported at a level of 2-86% [7]. In the present study according to EEG findings in case group; 16.7% had focal slowing, 10% had focal spikes and 10% had generalized spikes while 63.3% had normal EEG.

In a study conducted by Canpolat and his colleagues, EEG was performed post seizure in 22.5% of all cases, 10.7% of those with simple FC and 75% of cases of complex FC. 65% of first EEGs were pathological, while 98.1% of final EEGs were normal [8]. This supports the idea that routine control EEGs are not useful guides in monitoring and treatment.

In the present study there was no significant difference between normal and pathological EEG regarding MRS in the case group.

In the present study we found that there was high significant difference between both groups regarding MRS. As in the case group there was reduction of NAA and slightly increase in Cho & Cr, which lead to changes in metabolic ratios (NAA/Cr, Cho/NAA & Cho/Cr). While in the control group was normal.

However, Aun and his colleagues found that the side of maximum NAA reduction often coincides with the side of EEG abnormality. A major clinical challenge pertains to patients classified as having non lesional epilepsy [9]. MRS may be helpful in the identification of the seizure focus in refractory focal epilepsy patients without obvious MR imaging abnormalities. These abnormalities consisted of decreased NAA and increased Cho,

lateralized to the seizure focus, similar to the patients with hippocampal sclerosis [10].

In the present study we found that regarding the optimal cut off value of NAA/Cr was less than 2.61 (considered pathognomonic if below 2.61), the sensitivity and specificity of NAA/Cr was 96.7% and 93.3% respectively, the positive predictive value was 93.5%, the negative predictive value was 96.6% and accuracy was 95%.

While, the optimal cut off value of Cho/NAA more than 0.785 (considered pathognomonic if more than 0.785), the sensitivity and specificity of Cho/NAA was 96.7% and 80% respectively, the positive predictive value was 82.9%, the negative predictive value was 96% and accuracy was 88.3%.

While, the optimal cut off value of Cho/Cr less than 2.115 (considered pathognomonic if below than 2.115), the sensitivity and specificity of Cho/Cr was 93.3% and 93.3% respectively, the positive predictive value was 93.3%, the negative predictive value was 93.3% and accuracy was 93.3%.

NAA is believed to be located primarily within neurons, and the loss of NAA signals is consistent with neuronal loss or damage. While the basis for the increase in the Cho and Cr signals remains unclear, one possible explanation is provided by the study of neuronal cells, which showed that the concentrations of Cho and Cr are much higher in astrocyte and oligodendrocyte preparations than in cerebellar granule neurons. It may be that the changes in Cho and Cr reflect reactive astrocytosis. Thus, the decrease in NAA: (Cho + Cr) ratios in ipsilateral MTLs may reflect the neuronal loss and reactive gliosis as observed in mesial temporal sclerosis in TLE [4].

Burtscher and Holtas found that, the ratio of reduction of NAA: (Cr + Cho) was more important than the absolute decreased intensity value of NAA alone. The critical level of ratio reduction of N-acetyl aspartate in relation to Creatine + Choline was considered pathognomonic if below 0.71 in unilateral cases of temporal lobe epilepsy as compared to the contra-lateral normal side [11].

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إستخدام الرنين الطيفى المغناطيسى لتحديد التغيرات داخل آنسجة المخ عند الأطفال الذين يعانون من التشنجات الحرارية

التشنجات الحرارية هى الأكثر شيوعاً فى مرحلة الطفولة، حيث تصل نسبة حدوثها بين الأطفال إلى واحد بين كل عشرة أطفال. وهى سبب رئيسى لزيارة قسم الطوارئ فى مستشفى الأطفال وتعتبر مصدراً لقلق الأسرة وتوترها. التشنجات الحرارية هى التشنجات الناجمة عن الحمى (أكثر من ٣٨ درجة سيليزيه). وعادة ما تحدث التشنجات الحرارية عند الأطفال الصغار الذين تتراوح أعمارهم بين ٦ أشهر وه سنوات. تصنف التشنجات الحرارية إلى ثلاثة أنواع: بسيطة ومعقدة، والتشنجات الصرعية الوضعية. التشنجات الحرارية البسيطة هى تشنجات عامة وتستمر لأقل من ١٥ دقيقة، ولا تتكرر فى غضون ٢٤ ساعة. التشنجات الحرارية المعقدة تدوم لفترات طويلة (أكثر من ١٥ دقيقة) وهى تشنجات جزئية وتتكرر فى غضون ٢٤ ساعة. التشنجات الصرعية الوضعية وتستمر آكثر من ٣٠ دقيقة.

لذلك يتم الآن إستخدام بعض الوسائل والطرق التشخيصية لتحديد التغيرات داخل آنسجة المخ ومنها إستخدام الرنين الطيفى المغناطيسى وهو عبارة عن وسيلة تشخيصية غير تداخلية والتى تستخدم لتحديد التغيرات الكيميائية التى تحدث داخل آنسجة المخ بعد حدوث تشنجات حرارية والتى تظهر مبكراً عن نتائج رسم المخ وبدون إنتظار التغيرات التركيبية التى تحدث فى المخ ثم تظهرها آشعة الرنين المغناطيسى.

ومن خلال نتائج الدراسة توصلنا إلى الآتى:

- متوسط العمر لمجموعة الحالات كان ٣١ شهر.
- يمثل التاريخ الإيجابى للتشنجات الحرارية ١٣.٣٪ من مجموعة الحالات.
- تمثل التشنجات العامة ٩٦.٧٪ من الحالات.
- يتراوح الوقت الزمنى للتشنجات بين ٢٥.٥±٦.٦٦ دقيقة.
- فيما يتعلق بتكرار التشنجات فقد لوحظت مرتين فى ٨٣.٣٪ من الحالات وثلاث مرات فى ١٦.٧٪ من الحالات.
- يمثل رسم المخ الغير طبيعى ٣٦.٤٪ من الحالات.
- تم رصد إختلاف وضع بين مجموعتى الدراسة فيما يتعلق بالرنين الطيفى.
- بالنسبة ل ن آسيتيل آسبرتات/كرياتين:
  - قيمة القطع المثلى كانت آقل من ٢.٦١.
  - قيمة الحساسية ٩٦.٧٪.
  - قيمة الخصوصية ٩٣.٣٪.
  - القيمة التنبؤية الإيجابية ٩٣.٥٪.
  - القيمة التنبؤية السلبية ٩٦.٦٪.
  - الدقة ٩٥.٦٪.
- بالنسبة ل كولين/ن آسيتيل آسبرتات:
  - قيمة القطع المثلى كانت آكثر من ٠.٧٨٥.
  - قيمة الحساسية ٩٦.٧٪.
  - قيمة الخصوصية ٨٠٪.
  - القيمة التنبؤية الإيجابية ٨٢.٩٪.
  - القيمة التنبؤية السلبية ٩٦٪.
  - الدقة ٨٨.٣٪.
- بالنسبة ل كولين/كرياتين:
  - قيمة القطع المثلى كانت آقل ٢.١١٥.
  - قيمة الحساسية ٩٣.٣٪.
  - قيمة الخصوصية ٩٣.٣٪.
  - القيمة التنبؤية الإيجابية ٩٣.٣٪.
  - القيمة التنبؤية السلبية ٩٣.٣٪.
  - الدقة ٩٣.٣٪.