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Risk Factors of Status Epilepticus in Children Admitted in a Tertiary Care Hospital

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Abstract **Original Research Article**

Background*:** Background: Status epilepticus (SE) is the most common childhood medical neurological emergency. There are many acute illnesses and conditions that might be either the direct cause or the precipitator of status epilepticus. Objective of the study was to assess the risk factors of status epilepticus in children. ***Methods: This cross-sectional study was conducted at the Department of Paediatrics, Institute of Child and Mother Health, from July 2021 to June 2022 following approval from IRB. A total of 115 children admitted with SE were enrolled in this study. After taking informed written consent from legal guardian, a detailed history was taken and thorough clinical examination and necessary investigations were carried out in each case. Data were collected by a semi-structured questionnaire and analyzed by SPSS 24.0. ***Results:*** Mean age of the study children was 4.26±2.90 years, male predominance (53.9%) was found. Family history of febrile seizure and epilepsy was found in 15.7% and 13.9% respectively. Generalized seizure found in 90.4% children. First episode of seizure presenting as status was found in about 68.7% of children. Regarding the causes of status epilepticus, acute symptomatic etiology was seen in 70.4% children, 20% had remote symptomatic (epilepsy) and causes were unidentified in 9.6% respondents. Febrile convulsion was seen in 41.7% and neuro-infection such as meningitis in 22.6% encephalitis in 7%, these were the common acute symptomatic causes. EEG abnormality was observed in 92% of study children, among them leading abnormal finding was focal epileptogenic area in 39.1%. In 31.7% respondents, CSF abnormality was seen. CT/MRI brain findings were abnormal in 55.6% and encephalitis was common abnormal finding in neuroimaging. ***Conclusion:*** Febrile convulsion was the most common risk factors significantly associated with younger age group followed by meningitis and epilepsy which were significantly occurred with older age group.

Keywords: Febrile convulsion, epilepsy, Status Epilepticus, meningitis.

INTRODUCTION

Status epilepticus (SE) is a common neurological emergency that can lead to life-threatening conditions in children, with an incidence of 18-28 cases per 100,000 persons yearly. [1] It affects people of all ages, but is more common in infants. [2] A population-based household survey with Bangladeshi children revealed the prevalence of SE at 8.2% [3], and the mortality rate with SE in children under 10 years is 2.6%. [4] The outcomes of SE are influenced by the underlying etiology, patient's age, the type of SE, and duration of SE. Long-term sequelae after childhood CSE may include neurological, cognitive, and behavioral impairments and impact on quality of life. [5]

There are four types of SE: generalized, focal, non-convulsive, and neonatal. Generalized tonic clonic (GTC) type is the commonest, with the highest morbidity and mortality prevalence among children. [1] The most common causes of SE are due to atypical febrile seizure and meningitis. [2] It may also occur from: stroke, intoxication, infectious or autoimmune encephalitis, metabolic disturbances, abrupt drug or alcohol withdrawal, brain injuries and encephalitis or due to brain neoplasm, dementias. Previously diagnosed

patients with epilepsy are related to triggering factors like sleep deprivation, inappropriate antiseizures medication (ASM) prescription, reduced ASM plasma levels, toxicmetabolic disorders, and lack of adherence to therapy. [6] Seizures usually last for a few minutes, but longer SEs make control difficult and increase the risk of permanent neurological damage. [2] Controlling seizure activity is important, and seizures lasting more than five minutes require pharmacotherapy. [4] Benzodiazepines are considered the best drugs for treating these seizures due to their fast brain absorption. [7] However, recent cases of SE have features such as acute respiratory failure, cardiovascular dysfunction, low systolic blood pressure, and low mean arterial pressure. [8]

Identifying risk factors and preventing acute attacks can reduce morbidity and mortality in children with SE. This study aimed to identify risk factors of SE among children attending a selected tertiary level hospital in Bangladesh.

METHODOLOGY

This This is a Cross-sectional study conducted in Department of Paediatrics, Institute of Child and Mother Health, Dhaka from July 2021 to June 2022 among the children of both sex, age from 1 month to <18 years diagnosed as a case of status epilepticus. Before beginning the study, ethical clearance was obtained from IRB of Institute of Child and Mother Health, Dhaka. Total 115 children admitted with status epilepticus (SE) were enrolled in this study. SE was defined as active seizures of ≥5 minutes' duration or recurrent episodes of seizures without gaining consciousness in between the seizure episodes. A written informed consent was taken from each of the guardians of the participants. The duration of status epilepticus was ascertained from a reliable source like mother, father or who were present at the time of convulsive attacks or medical records and referring physician's note. After securing airway, breathing and circulation all the patients were managed with standard treatment protocol.

Once the child was stabilized, data which included age, sex, duration of seizures before and after admission, type and number of antiepileptic drugs (AEDs) used for control of status epilepticus (SE), history of previous seizure, seizure type (focal or generalized), duration of the seizure (over 60 minutes and less than 60 minutes), amily history of febrile convulsion (FC), family history of epilepsy, history of previous SE, length of hospital stay, etiology (febrile status epilepticus, acute symptomatic, remote symptomatic, congenital brain abnormalities, unknown), about drug compliance in case of known epilepsy cases were taken, General physical examination and detailed neurological examination were performed. Other regular investigations like complete blood count, blood chemistries including serum calcium, random blood sugar, serum sodium level were performed as required to ascertain etiology and to guide management. Cerebrospinal fluid (CSF) study results (normal or abnormal), brain imaging (CT scan and MRI) and electroencephalography (EEG) were done. Neuroimaging was performed in a corporate hospital as this facility was unavailable in our centre. CSF and EEG were performed in ICMH. With all aseptic precautions Lumber puncture (LP) was done in suspected cases and CSF was sent for study. With all necessary precaution. EEG was done in both awake & sleep state and reported by peadiatric neurologist. Any abnormality in CT scan or MRI, including congenital or acquired, was recorded. Case of SE was classified as refractory, nonrefractory and super refractory status epilepticus (RSE) and recorded accordingly.

After collection of all the required data, these were checked, verified for consistency and tabulated using the SPSS version 24. Continuous data were expressed as mean and standard deviation and categorical data were expressed as frequency and percentage. To determine the association between categorical variables, chi square test and unpaired t test were done. Statistical significance was set as 95% confidence level at 5% acceptable error level ($p<0.05$).

RESULT

This cross-sectional study was conducted in the Department of Paediatrics, Institute of Child and Mother Health, Dhaka. Total 115 children admitted with status epilepticus were included in this study. The main aim of the study was to find out the risk factor of status epilepticus among children admitted in a tertiary care hospital.

Table I: Age group of the study children (n=115)

Age (years)	Frequency	Percentage
<1	14	12.2
1-3	36	31.3
4-6	41	35.7
7-9	19	16.5
10-12	5	4.3
Mean±SD	4.26± 2.90	
Range (min-max)	0.5- 12.0	

Table I shows that the mean age was 4.26±2.90 years with 41(35.7%) children belonged to age 4-6 years of group.

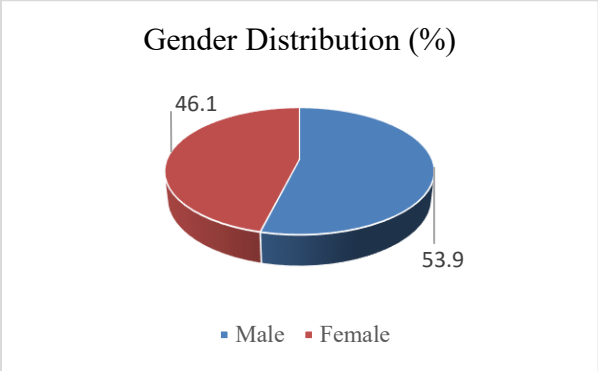

Figure 1: Pie chart showing gender of the children (n=115)

Figure 1 shows that 62(53.9%) children were male and 53(46.1%) were female. Male female ratio was 1.16:1.

Table II: Family history of study children (n=115)

	Frequency	Percentage
Family history of febrile seizure		
Yes	18	15.7
No	97	84.3
Family history of epilepsy		
Yes	16	13.9
No	99	86.1

Table III shows the clinical presentation of the respondents; most of them had fever 75(65.2%) followed by frothing 13(11.3%), unconsciousness 9(7.8%), neck rigidity7(6.1%), cyanosis 7(6.1%) and tongue bite 3(2.6%).

Table III: Clinical presentation of the study children during admission (n=115)

Clinical presentation*	Frequency	Percentage
Fever	75	65.2
Frothing	13	11.3
Unconsciousness	9	7.8
Neck rigidity	7	6.1
Cyanosis	7	6.1
Tongue bite	3	2.6

Table III shows the clinical presentation of the respondents; most of them had fever 75(65.2%) followed by frothing 13(11.3%), unconsciousness 9(7.8%), neck rigidity7(6.1%), cyanosis 7(6.1%) and tongue bite 3(2.6%).

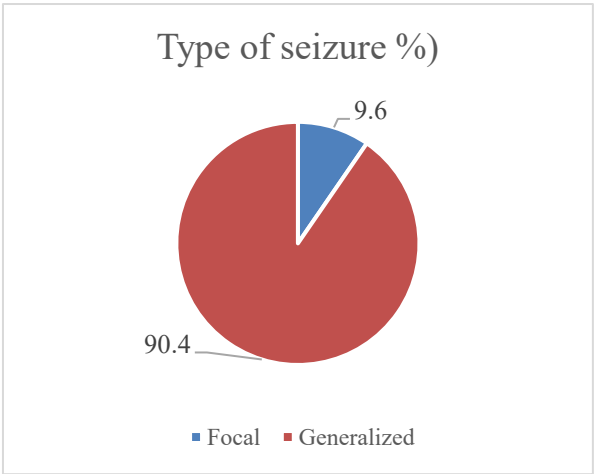

Figure 2: Pie chart showing type of seizure of the children (n=115)

Figure 2 shows that majority of the respondents had generalized seizure 104(90.4%), while only 11(9.6%) had focal seizure.

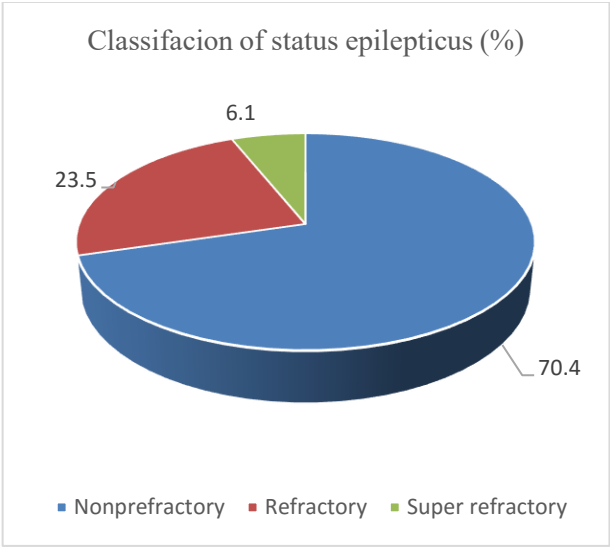

Figure 3: Pie chart showing classification of status epilepticus (n=115)

Figure 3 shows that about 81(70.4%) respondents had non-refractory status epilepticus, while 27(23.5%) had refractory and 7(6.1%) had super refractory status epilepticus.

Table IV: History of convulsive attack among study children (n=115)

	Frequency	Percentage
Age of onset of 1st attack		
<1 year	34	29.5
1-3 years	27	23.5
4-6 years	32	27.8
7-9 years	18	15.7
10-12 years	4	3.5
Number of episodes		
1st episode	79	68.7
2 or more	36	31.3
Treatment history for previous attack of seizure (n=36)		
Not on treatment	7	19.4
Discontinuation of AED	13	36.1
On oral medication	16	44.4

Table IV shows that age of onset of convulsion among respondents were <1 year 34(29.5%) and 79(68.7%) respondents had 1st episode of convulsion. Thirty-six (31.3%) respondents had 2 or more episode of convulsion, among them 16(44.4%) was on oral medication, 13(36.1%) had history of discontinuation of AED and 7(19.4%) was not on treatment.

Table V: Biochemical parameters of the study children (n=115)

Parameters	Frequency	Percentage
Serum electrolyte		
Normal	111	96.5
Imbalance (hyponatremia)	4	3.5
S. Calcium		
Normal	112	97.4
Abnormal (hypocalcemia)	3	2.6
Capilary blood glucose		
Normal	109	94.8

Abnormal (hypoglycemia)	6	5.2

Table V shows that about 3.5% respondents had hyponatremia 2.6% had hypocalcemia and 5.2% had hypoglycemia.

Table VI: EEG profile of the study children with history of epilepsy (n=25)

EEG findings	N=25	%
Normal	02	8.0
Abnormal	23	92.0
Focal epileptogenic area	9	39.1
Asymmetric/Polymorhic slow wave	6	26.1
Non-specific asymmetric finding	4	17.4
Focal cerebral dysfunction	3	13
Complex partial seizure	1	8.3

Table VI shows that about EEG done in 25(21.74%) of the respondents among them abnormal findings was seen in 23(92%).

Table VII: CSF profile of the study children in whom LP was done (n=82)

CSF profile	Frequency	Percentage
Normal	56	68.3
Abnormal	26	31.7
TC of WBC (/cmmu)	50.8 ±6.3	
Nutrophil (%)	86.2 ±11.4	
Lymphocyte (%)	35.8 ±6.3	
Protein (mg/dl)	113.8 ±9.7	
Glucose (mg/dl)	31.0 ±6.0	

Table VII shows that CSF study was done in 82(71.3%) of the respondents and among them abnormal finding was seen in 26(31.7%) suggestive mostly of neuro-infection. None of the culture was positive.

Table VIII: Neuro-imaging profile of study children (n=9)

MRI/ CT-scan	Frequency	Percentage
Normal	4	44.4
Abnormal	5	55.6
Suggestive of encephalitis	3	60.0
Generalized cerebral atropy	2	40.0

Table VIII shows that CT & MRI was done 9(7.8%) of the respondents and among them abnormal finding was seen in 5(55.6%). Encephalitis was most common findings 60%.

Table-IX: Etiologies of Status Epilepticus in study children (n=115)

Etiology	No. of cases (%)
Acute symptomatic	**81(70.4%)**
Febrile convulsion	48
Meningitis	26
Encephalitis	8
Hypoglycemia	6
Hyponatremia	4
Hypocalcemia	3
Remote symptomatic	**23(20%)**
Epilepsy	23
Unknown	**11(9.6%)**

Table IX shows that acute symptomatic etiology was 70.4%, remote symptomatic was 20% and 9.6% had unknown causes.

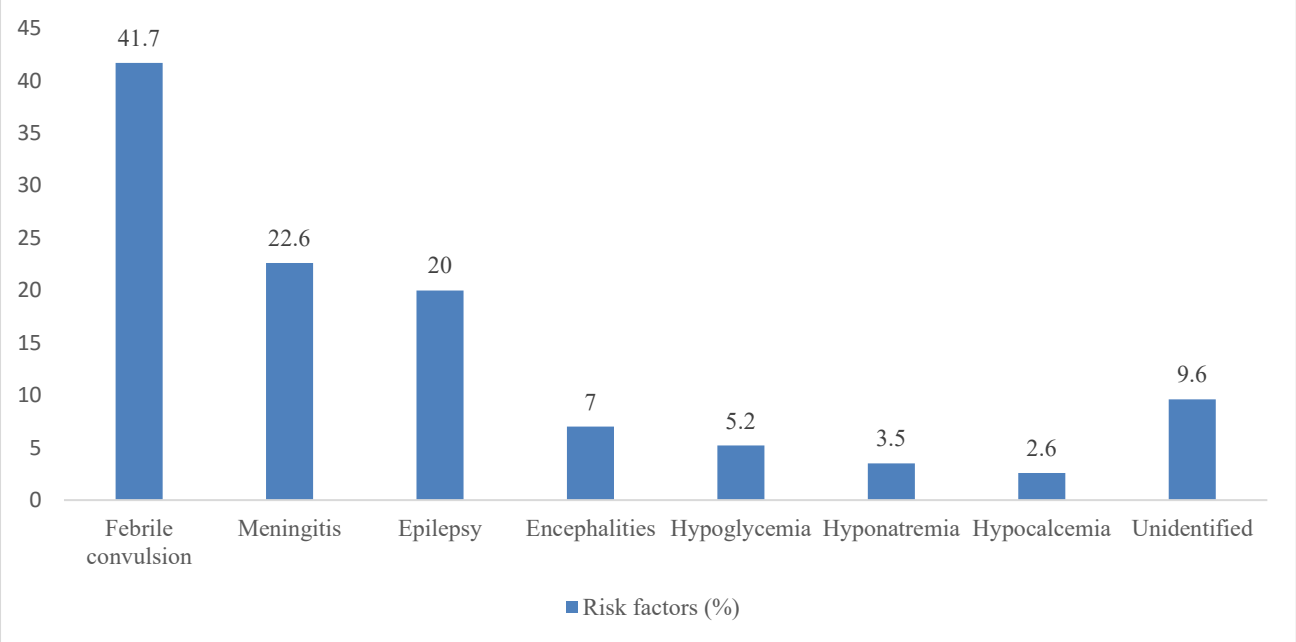

Figure 4: Bar diagram showing risk factors of status epilepticus among respondents

Figure 4 shows that risk factors among respondents showed most of them had suffered from febrile convulsion 48(41.7%) followed by meningitis 26(22.6%), epilepsy 23(20.0%), encephalitis 8(7.0%), hypoglycaemia 6(5.2%), hyponatremia 4(3.5%), hypocalcemia 3(2.6%) and unidentified 11(9.6%).

Table X: Association between risk factors with age (n=115)

Risk factors	Age (years)				
	n	Mean ±SD	n	Mean ±SD	P-value
Febrile convulsion	48	2.5±1.8	67	5.6± 2.9	0.001^{s}
Meningitis	26	5.9±2.9	89	3.7± 2.7	0.001^{s}
Epilepsy	23	5.3±2.7	92	4.0± 2.9	0.049^{s}
Encephalities	8	5.8±2.4	107	4.2± 2.9	0.135^{ns}
Hypoglycemia	6	5.3±2.2	109	4.2± 2.9	0.359^{ns}
Hyponatremia	4	4.5±3.7	111	4.3± 2.9	0.872^{ns}
Hypocalcemia	3	4.2±3.0	112	4.3± 2.9	0.983^{ns}
Unidentified	11	5.1±3.6	104	4.2± 2.8	0.299^{ns}

s= significant, ns= not significant, P value reached from unpaired t-test

Table X shows that febrile convulsion significantly associated with younger age group while meningitis and epilepsy significantly occurred with older age group.

Table XI:

	Duration of convulsion at presentation						P-value
	5-30 Min (n=61)		30-60 Min (n=21)		>60 Min (n=33)		
	n	%	n	%	n	%	
BDZ	36	59.0	5	23.8	2	6.1	
BDZ+PHT	20	32.8	9	42.9	9	27.3	0.001^{s}
BDZ+PHT+PB	5	8.2	7	33.3	15	45.5	
BDZ+PHT+PB+MZ	0	0.0	0	0.0	7	21.2	

s= significant, P value reached from chi square test

Table XI shows that majority (59.0%) of the respondents who presented with shortest duration of convulsion (<30 min) needed mostly single AED. Added was needed in those cases who presented with (30-60 min) maximum (42.9%) needed 2AED, followed by 3AED, respondents who presented with (>60 min) majority (45.5%) of them needed 3rd or 2nd AED

followed by 4thAED. Which were statistically significant.

Table XII: Association between etiological classification with refractory and nonrefractory SE (n=115)

Classification	Refractory SE (n=34)		Non-Refractory SE (n=34)		
	n	%	n	%	
Acute symptomatic	22	64.7	59	72.8	
Remote symptomatic	4	11.8	19	23.5	0.003[s]
Unknown	8	23.5	3	3.7	

Table XII shows that acute symptomatic and remote symptomatic caused simple non-refractory status. Whereas unknown etiology caused prolong refractory status epilepticus.

Table XIII: Association between risk factors with refractory and non-refractory SE (n=115)

	n	%	n	%	
Febrile convulsion	0	0.0	48	59.3	0.001[s]
Meningitis	14	41.2	12	14.8	0.003[s]
Epilepsy	4	11.8	19	23.5	0.118[ns]
Encephalities	8	23.5	0	0.0	0.001[s]
Hypoglycemia	2	5.9	4	4.9	0.575[ns]
Hyponatremia	0	0.0	4	4.9	0.241[ns]
Hypocalcemia	2	5.9	1	1.2	0.208[ns]
Unidentified	8	23.5	3	3.7	0.002[s]

Table XIII shows that febrile convulsion 59.3% is associated significantly with non-refractory status epilepticus and neuro-infection such as meningitis 41.2%, encephalitis in 23.5% and unidentified 23.5% risk factor significantly associated with refractory status epilepticus.

DISCUSSION

Total 115 children admitted with status epilepticus were included in this study. Most of them were below 6 years of age and male predominance (53.9%) was found. Family history of febrile seizure and epilepsy was found in 15.7% and 13.9% respectively. 90.4% children had generalized seizure. First episode of seizure presenting as status was found in about 68.7% of children. Acute symptomatic etiology was significant risk factor for non_RSE. Regarding the causes of SE acute symptomatic etiology was seen in 81(70.4%) children, 20% had remote symptomatic (epilepsy) and causes were unidentified in 9.6% respondents. Febrile convulsion was seen in 41.7% and neuro-infection such as meningitis in 22.6% encephalitis in 7%, these were the common acute symptomatic cause followed by hypoglycemia 5.2%, hyponatremia 3.5% and hypocalcemia 2.6%. Among the risk factor febrile convulsion significantly associated with younger age group while meningitis and epilepsy significantly occurred with older age group.

The mean age of children was 4.26±2.90 years while majority belonged to 4-6 years of age group. In two previous studies, reported mean age 4.5±3.7 years and another study found mean age 5.74±4.75 years respectively which corresponded with the current study population. [9, 10]

In this study it is observed that 53.9% children were male and 46.1% were female. Male female ratio was 1.16:1. In some previous studies Alyoubi *et al.,* Absar *et al.,* and Arun *et al.,* also reported slight male predominance (58%), (56%) and (54%) respectively. [9-11]

In this study family history of febrile seizure was present in 18 respondents and family history of epilepsy was present in 16 respondents. Family history of febrile seizure was also observed by Arun *et al.,* in this study in 13 (26%) children, by Absar *et al.,* in 23% children, Beegum *et al.,* found 47(77%) cases and Dasgupta *et al.,* (2019) in 7(14.0%) of children respectively. [11, 12] Also, Shinnar *et al.,* found in their study that 11% had a family history of epilepsy while 15% had a family history of febrile seizures. These findings are comparable to current study. [13]

Our study showed that most of the respondents were presented with fever, frothing, neck unconsciousness, rigidity, cyanosis and tongue bite. Fever and seizure were seen in 100% cases along with nonspecific systemic symptoms in the study of Absar *et al.,* [11] Dasgupta *et al.,* reported, fever with seizures (72.0%) was significantly more prevalent among the chief complaints followed by unprovoked seizures (14.0%). [14] Doumbia, *et al.,* observed fever was present in 86% of patients. [15] These findings are consistent with current study with slight variations.

In this study we found that cases of generalized seizure were 90.4%, while 9.6% had focal segmental seizure. In similar type of previous studies reported by Alyoubi *et al.,* generalized seizure was 56 (91.8%) and focal seizure was 5(8.2%), Absar *et al.,* generalized seizure was 95% and focal seizure was 5% and Dasgupta *et al.,* GTCS was (74.0%) followed by focal seizure (18.0%) respectively. [9, 10, 14] Findings of all these studies correspond with present study.

Current study showed that about 81 respondents had non-refractory status epilepticus, while 27 had refractory and 7 had super refractory status epilepticus. Beegum *et al.,* (2021) reported 81(72.9%) cases were refractory and 5(4.5%) cases were super refractory SE in her study. Kantanen *et al.,* observed 75 respondents with RSE in their study, among them 21% were SRSE. Barzegar *et al.,* reported RSE was present in 40.15% of respondents with CSE. [16] Hussain *et al.,* found 36% the cases were RSE. These findings vary with our findings. [12]

We found age of onset of convulsion among respondents were between <1 years of age group 29.5%. About 79 respondents had 1st episode of convulsion and 36 respondents had 2 or more episode of convulsion. Absar *et al.,* (2020) reported age of onset of convulsion were more in 1-2 years of age group (47%). Arun *et al.,* observed about 36 (72%) of children had first episode of seizure presenting as status epilepticus. These findings correspond with present study with slight variations. [10]

Biochemical parameters of the study showed that about 3.5% respondents developed electrolyte imbalance, 2.6% had hypocalcemia and 5.2% had hypoglycemia. In similar studies Selvan *et al.,* found hypoglycemia 6%, hypocalcemia 1.5% and hyponatremia in 7.5% cases and Alyoubi *et al.,* observed electrolyte imbalance in (11.9%). So metabolic/biochemical imbalance can be considered as a risk factors of CSE, other studies suggested that. [2, 9]

CSF study was done in 82(71.3%) of the respondents and among them abnormal findings was in 26(31.7%). None of the culture had positive growth. In studies conducted by Arun *et al.,* they found abnormal CSF in 3(15.8%); two cases were culture positive and Dasgupta *et al.,* (2019) observed abnormal CSF in 5(10.0%). These findings were not compatible with current study. [10]

EEG was done in about 25(21.74%) of the respondents among them abnormal findings was 23(92%), most of them were known case of epilepsy. Focal epileptogenic area and asymmetric/polymorphic slow wave were common abnormal finding. The study conducted by Dasgupta *et al.,* they found abnormal EEG in 32% cases, among them most common abnormal findings were epileptiform discharges followed by diffuse slowing and Beegum *et al.,* (2021) observed abnormal EEG in 35(83.3%). These findings are comparable to present study. [12, 14]

Our study showed that CT & MRI was done in 9(7.8%) of the respondents and among them abnormal findings was in 5(55.6%). Encephalitis (60%) was common abnormal findings. In previous studies conducted by Dasgupta *et al.,* reported abnormal findings was 42%; Encephalitis followed by Periventricular leucomalacia were common abnormal findings and Arun *et al.,* found abnormal in 34% cases. [10, 14] These findings are corresponding with present study with slight variation.

Risk factors in this study among respondents showed that most of them suffered from febrile convulsion followed by meningitis, epilepsy. Risk factors was reported by Alyoubi *et al.,* in his study as febrile seizure 30.5%, electrolyte imbalance 11.9% and CNS infections 6.8% showed Arun *et al.,* found risk factors were epilepsy 58% and febrile seizure 24%, Beegum *et al.,* [9, 12] showed febrile status 45.9% and meningoencephalitis 21.6% in their study respondents. Majority of their findings were consistent with present study.

In this study we found significant association between duration of convulsion at presentation with use of number of medications. Majority of the respondents who presented with shortest duration of convulsion (<30 min) needed mostly single AED. Added was needed in those cases who presented with (30-60 min) maximum 9(42.9%) needed 2AED, followed by 3AED, respondents who presented with (>60 min) majority of them 15(45.5%) needed 3rd or 2nd AED followed by 4thAED which were statistically significant. Slight variation was found by study conducted by Parvin *et al.,* (2019) observed < 1 hour of convulsion diazepam was effective in 76.92%, PHT in 15.4% and PB in 7.7% cases and 1-6 hours of convulsion diazepam was effective in 43.4% cases, both PHT and PB were effective in 16.9% and MZ in 18.8% cases. Arun *et al.,* observed, 72 % cases needed 2 AED,20% cases needed 3AED and 8% required >3AED for seizure control. [10]

Present study showed that acute symptomatic etiology was the leading casues of CSE than remote and unidentified causes and it was significantly associated risk factor for non-RSE in 59(72.8%). Barzegar *et al.,* (2015) reported acute symptomatic cases found in RSE about 41.15% and 15.19% in non-RSE, it was statistically significant risk factor associated with RSE. [18] These findings are consistent with current study with slight variation.

This study showed that febrile convulsion occurred more in younger children, while meningitis,

epilepsy(remote) were associated with older children. Similar findings with slight variation was found by Beegum *et al.,* they observed younger children are more prone for febrile status and acute symptomatic etiology while older children are more likely to have remote or cryptogenic causes. [12]

The current study observed febrile convulsions was most common risk factor and significantly associated with non-refractory SE. Meningitis, encephalitis and unidentified risk factors were found significantly associated with refractory SE (41.2%), (23.5%) and (23.5%) of study children respectively. Studies conducted by Beegum *et al.,* observed febrile status and meningoencephalitis commonly associated with RSE and Barzegar *et al.,* reported febrile seizures were significantly associated with non RSE. These findings were not consistent with current study. [12, 18]

CONCLUSION

Febrile convulsion was the most common risk factors, significantly associated with younger age group while meningitis and epilepsy significantly occur in older age group. Because of the single-center non-randomized design, study sample small, the study findings could not be generalized. So, further multicenter studies with larger sample size are recommended.

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