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Immediate outcome and risk factors determining the outcome of status epilepticus in children attending tertiary care centre

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ABSTRACT

Background: Status epilepticus (SE) is a paediatric and neurological medical emergency, continuous seizure lasting more than 30 min, or two or more seizures without full recovery of consciousness between any of them. Determination of immediate outcome of SE in children in a tertiary care hospital and to identify the risk factors influencing the outcome was the objectives of the present study.

Methods: A study was conducted in Dept of Pediatrics, Tirunelveli Medical College Hospital among the children from 1 month to 12 years of age, who had admitted for SE in hospital's pediatric causality from October 2009 to October 2010 were selected for the study.

Results: Out of 92 patients, total 87 patients completed the study and out of those 74 have recovered and 13 have died. The risk factors significantly affecting the outcome were hypoxia at the time of arrival, decompensated shock, respiratory failure requiring intubation and acidosis.

Conclusions: Proper prehospital therapy, early referral, proper care while transporting, anticipitating risk factors involved, and protocol based approach uniformly at all hospital can reduce the mortality due to status epilepticus in children.

Keywords: Children, Outcome, Risk factors, Status epilepticus

INTRODUCTION

Status epilepticus (SE) is a paediatric and neurological medical emergency associated with significant morbidity and mortality. It represents the reaction of brain to an acute insult or may be an alteration of previously existing epilepsy. The mortality associated with SE in children is considerable without treatment. The incidence of SE has a bimodal distribution with peaks in children aged less than a year and the elderly. SE is defined as a continuous seizure lasting more than 30 min, or two or more seizures without full recovery of consciousness between any of them. However, based on recent understanding of the

pathophysiology, newer definition includes seizures that lasts more than 5 minutes' needs to be treated as SE. If circulation is restored within 3-5 minutes, full recovery may occur, but if hypoxic-ischemia lasts beyond 3-5 minutes some degree of permanent cerebral damage is the rule. Status Epilepticus common in childhood, and the reported current mortality is in the range of 4-6%.⁵ Hypoxia is currently thought to be responsible for most of the complications seen in SE.⁶ SE in children is a lifethreatening condition with serious risk of neurological sequelae. The outcome from an episode of SE is determined primarily by its cause, but the duration of the seizure and prompt, appropriate treatment are still

extremely important contributing factors. Any type of seizure can lead to status epilepticus, but generalized tonic-clonicstatus epilepticus is the most common and most dangerous type.

Though we managed SE in our tertiary care level hospital, we came across poor outcome in SE. Mortality remain high in SE, due to longer duration of travel with prolonged SE, improper prehospital therapy, refractory seizures, etiological factors and risk factors influencing the poor outcome. This study was done to identify these risk factors for both death and neurological sequelae.

The objective of the study was to determine immediate outcome of SE in children in our hospital and to identify the risk factors influencing the outcome of it.

METHODS

A descriptive study was designed and conducted in Dept of Pediatrics, Tirunelveli Medical College Hospital among the children from 1 month to 12 years of age, who had admitted for SE from October 2009 to October 2010 was selected for the study. All children presented with SE non-convulsive SEand generalized), managed with anti convulsant as per protocol in the above age group in emergency room (ER) were included. The cases of seizures controlled before arrival to the hospital or before starting IV therapy, simple partial SE and myoclonic SE, with normal vital signs and without loss of consciousness. Seizures occurred during hospital stay, not at arrival were excluded from the study. All cases presented with SE in hospital's pediatric causality during the study period, included over that period. Totally 92 cases were included. Five cases absconded during hospitalization.

Institutional consent and parental consent were obtained. First the cases were selected as per the inclusion criteria. Each child had been assessed on arrival and a preliminary history was obtained and documented in a preformed profoma. Rapid cardio pulmonary assessment was made, Spo2 on arrival, BP, presence of shock, pupil, were monitored. Before starting IV therapy, blood sample was taken for baseline investigations (sugar, calcium, and electrolytes). Then the cases were managed according to the protocol followed in our ER and admitted in wards/PICU.

Detailed history was obtained including duration of seizure, distance from the place where the fits occurred, mode of transport, prehospital therapy, precipitating factors, prior seizures/SE, drug history and compliance development milestone, prior neurological status. Complete clinical examination was made including neurological examination. Relevant investigation was done like CSF analysis CT brain /USG cranium, EEG, etc. during course of illness and therapy were monitored regularly till discharge. Computed tomography of brain was done in all patients with new onset of seizure and

focal seizure. Magnetic resonant imaging of brain was done in selected cases. Final diagnosis of various underlying problems was made based on the clinical history, physical examination and various investigation. The patients were further followed up for any complications acquired during hospital stay, duration of ventilation required length of stay in hospital stay. The neurological status of the child at the time of discharge was noted. Time taken for control of refractory SE, time taken for full recovery of consciousness, requirement for prolonged ventilator support, refractory shock or subsequent shock following midazolam or due to complication like sepsis, maximum dose and duration of ionotropes and midazolam infusions, recurrent of fits, complication were noted. They were followed for one month. Then the neurological status at the end of one month was reassessed. Their neurological status was compared with the previous neurological status.

Outcome was determined by the following variables. Complete recovery with no neurological sequel, and neurological sequele deaths, AMA (discharged against medical advice during the treatment), observations were entered as tables and percentage charts. According to the final outcome the children were divided into two groups. Deaths were taken as poor outcome group and those children recovered completely with or without any new neurological sequel were taken as good outcome. Predictors of poor outcome were analyzed for the following risk factors compared with good outcome groups a considered statistically significant if p value is <0.05.

RESULTS

A total of 92 cases of status epilepticus were included in this study. Table 1 presents demographic characteristics and risk factors at the time of arrival. Out of 92 cases, 54 cases (58.6%) were children <5 years. The mean age of the patients was 4.9 yrs. The youngest age being 2 month. The maximum age being 11 years. Both male and female children were 46 (50%). Prehospital therapy with AED was given to 24 patients and remaining 68 cases were not received prehospital therapy. Out of 23 children who had received prehospital therapy only 16 had proper prehospital therapy. 7 children had received improper medication or drug dosage. 16 children received injection diazepam, 6 children received upto phenytoin and 1 children received phenobarbitone as Prehospital therapy AED.

25 cases of the children with status epilepticus reached hospital from 20-40 km followed by 22 cases from 5-10 kms. 92% (75) of the cases reached ER within 30-60 min and only 18.5% (17) reached with seizure more than 60 min. Mean duration of seizure was 78.12 minutes. Minimum duration was 30 mins and maximum duration was 10 hrs. CSE accounts about 93.5% of the total seizure during arrival. The commonest among them was GTCS - 77 (83.7%). Focal seizure accounts about 8% (7

cases). Out of which 2 cases presented with secondary generalisation. Two cases (2.2%) were multifocal.

Table 1: Demographic characteristics and risk factors at arrival determining outcomes of status epilepticus.

	No of cases (n=92)	%
Age (in years)		
< 1	22	23.9
1- 5	32	34.8
6-10	32	34.8
> 10	6	6.5
Sex		
Male	46	50.0
Female	46	50.0
Prehospital therapy		
Given	24	26.1
Not given	68	73.9
Duration of transport		
<5 km	16	17.4
5-10 km	22	23.9
10-20 km	16	17.4
20-40 km	25	27.2
>40 km	13	14.1
Duration of seizure (in mir	a) at the time of arrival	
30-60 min	75	81.5
>60 min	17	18.5
Type of seizure at arrival		
GTCS	77	83.7
Focal	05	5.4
Focal-S	02	2.2
Multifocal	02	2.2
Nsce	06	6.5
Seizure episode		
First episode of seizure	28	35.0
Previous episode of	C 1	<i>(</i> 5.0
seizure	64	65.0
Febrile or afebrile seizure		
Febrile	65	70.7
Afebrile	27	29.3
Co morbid factors		
Intubation on arrival	9	9.8
Decompensated shock	8	8.7
Hypoglycaemia	9	9.8
Hypocalcaemia	5	5.4
Acidosis	18	19.6
Raised ICT	8	8.7
GGE D A GEGG 11		

CSE: Refers to GTCS either primary or secondary to focal onset, in which whole or part of the body muscles having visible convulsions; NCSE: refers to persistent seizure activity but no visible convulsions. Here they may have subtle signs of seizure activity such as unresponsiveness/ALOC or acute confusion state, apnea, defective DEM, deviation of eyes, nystagmus.

Table 1 also revealed that 35% of the patients were presented with first episode of seizure and 65% with previous history. 70.7% (65) cases presented with fever. The risk factors included intubation on arrival,

decompensated shock, hypoglycaemia, hypocalcaemia acidosis and raised ICT significantly affected the outcome of SE in children. Among them acidosis was the most common risk factor-18 (19.6%).

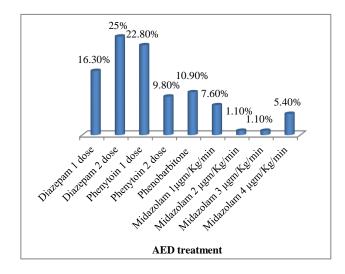


Figure 1: AED treatment response.

Out of 92 cases, 23 cases (25%) responded to 2^{nd} doses of IV diazepam followed by 22.8% responded 1st dose of phenytoin (Figure 1). In 48 cases (41.3%) seizure terminated with 2 doses of diazepam. 30 cases responded to IV Phenytoin. 15% (14 out of 92) cases had refractory SE and out of them, 7 survived and 5 died. In the 7 cases survived with RSE, seizure controlled with minimum of midazolam infusion 1 µgm/Kg/min to maximum of 4 µgm/Kg/min.

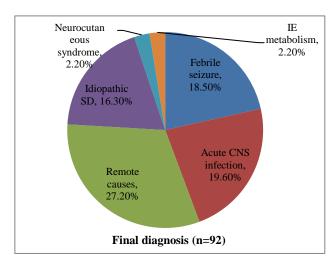


Figure 2: Etiology.

The most common etiology associated with status epilepticus in 92 children was remote causes 27.2% (25 cases), next being acute CNS infection 19.6% (18 cases), febrile seizure 18.5% (17 cases) and cryptogenic/idiopathic SD 16.3% (15 cases) (Figure 2). CSF Analysis: CSF analysis was done for 21 children, 6 cases had normal CSF finding.

Table 2: Final outcome.

Outcome	No of cases (n=92)	%
Recovered without sequele	69	75.0
Recovered with sequel	05	5.5
Death	13	14.0
AMA	5	5.5
Total	92	100

15 cases had abnormal values. CT brain done for 44 cases.30 cases had abnormal findings. MRI done for 9 cases, all showed abnormal findings.

In this study out of 92 cases, 74 cases (75.0%) recovered. Among those recovered, 5 cases (5.5%) recovered with new neurological sequele; 13 cases (14%) died and 5 cases (5.5%) discharged against medical advice.

Table 3: Analysis of risk factors determining the outcome of status epilepticus.

	Recovered (n=74)	Death (n=13)	Total (n=87)	P value
Age				
<1 yr	19 (86.4%)	3 (13.6%)	22 (100%)	
1-5 yrs	27 (87.1%)	4 (12.9%)	31 (100%)	Chi ² : 0.519; df: 3;
6-10 yrs	25 (83.3%)	5 (16.7%)	30 (100%)	p- Value: 0.915
>10 yrs	3 (75.0%)	1 (25.0%)	4 (100%)	
Distance KM				
<5	15 (93.8%)	1 (6.3%)	16 (100%)	
5-10	18 (100%)	0 (0%)	18 (100%)	Ch. 2, 16,070, 16, 4,
11-20	13 (81.3%)	3 (18.8%)	16 (100%)	Chi ² : 16.070; df: 4;
21-40	22 (88%)	3 (12%)	25 (100%)	p- Value: 0.003
>40	6 (50 %)	6 (50%)	12 (100%)	
Prehospital therapy				
Yes	17 (73.9%)	6 (26.1 %)	23 (100%)	Chi ² : 3.055; df: 1;
No	57 (89.1%)	7 (10.9 %)	64 (100%)	p- Value: 0.08
Duration of seizure (minutes)				
30-60	66 (93.0%)	5 (7.0 %)	71 (100%)	Chi ² : 18.959; df: 1;
>60	8 (50.0 %)	8 (50.0 %)	16 (100%)	p- Value: 0.000
Fit type				
GTCS	64 (86.5%)	10 (13.5%)	74 (100%)	
NCSE	3 (50%)	3 (50%)	6 (100%)	Chi ² : 7.151; df: 3; p- Value: 0.067
FOCAL	0 (0%)	5 (100%)	5 (100%)	
FOCAL-S	0 (0%)	2 (100%)	2 (100%)	
Fever H/O				
Febrile	54 (84.4%)	10 (15.6%)	64 (100%)	Chi ² : 0.089; df: 1; p-
Afebrile	20 (87%)	3 (13%)	23 (100%)	Value: 0.766
Neurological status				
Normal	48 (90.6%)	5 (9.4%)	53 (100%)	Chi ² : 3.238; df: 1; p-
Abnormal	26 (76.5%)	8 (23.5%)	34 (100%)	Value: 0.072
Comorbid factors				
Shock	6 (8.11%)	2 (15.38%)	8 (9.2%)	0.000
Fever	54 (72.97%)	10 (76.92%)	64 (73.56%)	0.766
Raised ICT	6 (8.10%)	0 (0%)	6 (6.897%)	0.287
Intubation	11 (14.86%)	8 (69.54%)	19 (21.84%)	0.000
SaO2 on arrival (low)	30 (40.54%)	9 (69.23%)	39 (44.83%)	0.004
Hypoglycaemia	5 (6.76%)	4 (30.76%)	9 (10.34%)	0.015
Hypocalcaemia	8 (10.81%)	8 (69.54%)	16 (18.39%)	1.000
Acidosis	8 (10.81%)	8 (69.54%)	16 (18.39%)	0.000
Delay in regain consciousness after seizure	22 (29.73%)	2 (15.38%)	24 (27.58%)	0.942

Analysis of outcome

Out of 92 cases, 5 went on AMA and didn't complete the study to know the outcome. So, the outcome of remaining 87 cases are analysed here.

Analysis of risk factors determining the outcome of status epilepticus is presented in Table 3. The table explains the outcome across the various age groups. Out of the total 87 patients 74 (85.1%) have recovered and 13 (14.9%) have died. Almost the same proportion is maintained across the all age groups. So, the age is not having significant association with the outcome (p >0.05). Outcome is good among cases travelled less than 10 km and mortality is very low among children travelled less than 10 km. Mortality is very high among 12 children travelled more than 40 km. Out of 12 cases, 6 cases (50%) recovered and 6 cases (50%) died. It shows that lower the distance better the outcome and higher the distance higher bad outcome (death). The association is also statistically significant (p <0.05).

The cases had prehospital therapy had poor outcome (26.1%) than the case who didn't receive (7%) prehospital therapy (p > 0.05). Prolonged duration of the seizure before arrival to ER had poor outcome. This is also statistically significant (p < 0.05). Among the seizure type, death occurred in cases with GTCS and NCSE. Out of 74 cases with GTCS 10 cases died and in NCSE 3 cases (50%) died out of 6 cases (100%).

Among the previously neurological abnormal children of 34 cases, 23.5% (8) cases had poor outcome. Only 9.4% (5) of the neurologically normal children (n=53) had poor outcome. But this different is not statistically significant (p >0.05). The risk factors significantly affecting the outcome were hypoxia at the time of arrival, decompensated shock, respiratory failure requiring intubation and acidosis (p <0.05).

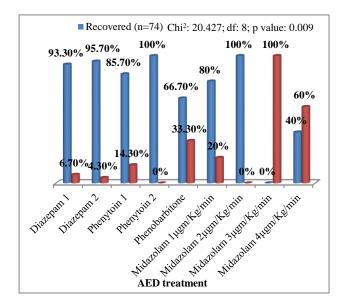


Figure 3: AED treatment response and outcome.

Figure 3 reveals the response and outcome of AED treatment. If the seizure control is poor with initial first line AED, mortality is very high. In children receiving Midazolam infusion (3-4 μ gm/Kg/min) had poor outcome. This is also statistically significant p <0.05.

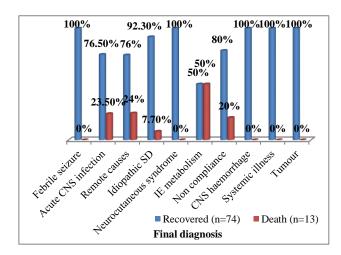


Figure 4: Etiology and outcome.

In this study, 87 children out of 92 cases who completed the study, 74 cases recovered and 13 cases died due to varied etiology (Figure 4). All the febrile seizure cases presented as SE had good outcome. Acute CNS infections, remote causes, non-compliance of AED, IEM, were the etiological factors influence the poor outcome.

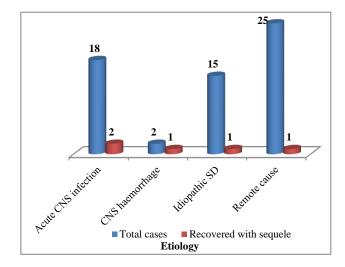


Figure 5: Number of cases recovered with sequele and outcome.

Among 87 cases, 5 cases developed neurological sequele. The most common etiological agents associated with sequele are acute CNS infection, CNS haemorrhage, Idiopathic SD, remote cause (Figure 5).

DISCUSSION

In this study, a total of 92 cases of SE within the study period were selected. The mean age of the patient in the

present study was 4.9 years. The youngest age being 2 months and the eldest being 11 years. Children <1-year account for 22 cases and 54 cases were children <5 years. Almost 60% of them were in the group <5 years. Out of 92 children, male children were 46 (50%) and female children were 46 (50%). Maytal et al reported mean age was 5 years and weak evidence of difference of sex.⁷

Out of the 92 children, 16 cases (17.4%) of the children with SE reached to the hospital in less than 5 km; 22 cases from 5-10 km; 16 cases from 10-20 km; 25 cases from 20-40 km and 13 cases from more than 40 km. Mean duration being 19 km. Minimum duration travelled was 0.5 km and maximum duration was 60 km.

Prehospital therapy with AED given to 24 patients (26.1%), remaining 68 (73.9%) didn't receive any prehospital therapy with AED, though some of them had been referred. Out of 23 children 16 received injection diazepam, 6 children received up to phenytoin and 1 child received phenobarbitone as prehospital therapy AED.

92% (75) of the cases reached ER within 30-60 min and 18.5% (17) reached with seizure more than 60 min. K. Eriksson reported similar results. 8

CSE accounts about 93.5% of the total seizure during arrival. The commonest among them was GTCS - 77 (83.7%). Focal seizure accounts about 8 % (7 cases). Out of which 2 cases presented with secondary generalisation. Two cases (2.2%) were multifocal. Six cases (7 %) were NCSE, of which 4 cases were of initial GTCS and 2 cases were of initial focal seizure.

35% presented with first episode of seizure and 65% with previous history of seizure. Out of 92 cases, 70.7% (65) cases presented with fever and 29.3% (27) cases were afebrile. Garzon et al study showed 40.6% with no prior history of seizure. Mah JK et al reported 43% with first episode of seizure. Out of seizure.

In this study, risk factors associated with SE are intubation on arrival, decompensated shock, hypoglycaemia, acidosis, raised ICT. The above risk factors significantly affect the outcome of SE in children. Among them acidosis is the most common risk factor 18 (19.6%).

Out of 92 cases, in 15 cases (16.3%) seizure stopped with $1^{\rm st}$ dose of IV diazepam and 23 cases (25%) responded to $2^{\rm nd}$ doses of IV diazepam. In 48 cases (41.3%) seizure terminated with 2 doses of diazepam. 30 cases responded to IV Phenytoin.

15% (14 out of 92) had refractory SE and out of them, 7 survived and 5 died. In the 7 cases survived with RSE, seizure controlled with minimum of Midazolam infusion 1 μ gm/Kg/min to maximum of 4 μ gm/Kg/min. Garzon et al informed 11.3% incidence of RSE.⁹ In this study cases gone for RSE had poor outcome.

The most common etiology associated with SE in 92 children was remote causes 27.2% (25 cases), next being acute CNS infection 19.6% (18 cases), febrile seizure 18.5% (17 cases) and cryptogenic/idiopathic SD 16.3% (15 cases). Hui Ac et al, study shows that acute CNS infection was a predictor of poor outcome. Murthy JM et al reported CNS infection accounts for significant number of cases.¹¹

74 cases (75.0%) out of 92 were recovered among which 5 cases (5.5%) recovered with new neurological sequel, 13 cases (14%) died and 5 cases (5.5%) discharged against medical advice.

5 cases out of 92, went on AMA and didn't complete the study to know the outcome. Only 87 cases were analysed. Out of 87 patients 74 (85.1%) have recovered and 13 (14.9%) have died. Almost the same proportion is maintained across the all age groups. So, the age is not having significant association with the outcome (p >0.05).

Outcome was good among cases travelled less than 10 kms and mortality is very low among children travelled less than 10 kms. Mortality is very high among 12 children travelled more than 40 kms. Out of 12 cases, 6 cases (50%) recovered and 6 cases (50%) died. The results showed that lower the distance better the outcome and higher the distance higher bad outcome (death). The association was also statistically significant (p <0.05). K. Eriksson concluded that the association between treatment delay and response became significant after 30 minutes when this was analyzed as a single variable (p = 0.003). §

Those cases had prehospital therapy had poor outcome 6 cases, (26.1%) than the case who didn't receive prehospital therapy 7 cases (10.9%). But this difference is not statistically significant (p >0.05). Those cases who received prehospital therapy had poor outcome (26.1%). This may be due the improper drug dosage at lower level hospitals and delayed referral. Alldredge et al suggested that prehospital administration of diazepam may shorten the duration of SE in children and simplify the subsequent management of these patients in the emergency department.¹²

Prolonged duration of the seizure before arrival to ER had poor outcome (p <0.05). Gulati et al found that seizure duration more than 45 minutes is significantly associated with higher mortality. Study of Kwong et al also supported that seizure duration more than 60 minutes had adverse outcome. ¹⁴

From the result, it was observed that all the proportions of outcome are maintained almost equally in both the febrile and afebrile group. Among the seizure type, death occurred in children with GTCS and NCSE. Out of 74 cases with GTCS 10 cases died and in NCSE 3 cases (50%) died out of 6 cases (100%). This shows that

number of death among children with GTCS is common but in NCSE 3 cases (50%) died out of 6 cases (100%).

If the seizure control was poor with initial first line AED, mortality was very high. In children receiving Midazolam infusion (3-4 $\mu gm/Kg/min)$ had poor outcome. Among the previously neurological abnormal children of 34 cases, 23.5% (8) cases had poor outcome. Only 9.4% (5) of the neurologically normal children (n=53) had poor outcome. Kwong et al observed that paediatric patients with SE who had normal neurodevelopmental status before the onset of an attack and who did not sustain an acute insult to the central nervous system or have progressive encephalopathy had good prognosis. 14

The risk factors significantly affecting the outcome were hypoxia at the time of arrival, decompensated shock, respiratory failure requiring intubation and acidosis (p <0.05). Gulati et al showed presence of septic shock (p-0.001) were associated with significant mortality.¹³

Out of 92 case, 87 cases who completed the study, 74 cases recovered and 13 cases died due to varied etiology. All the febrile seizure cases presented as SE had good outcome. Acute CNS infection, remote causes, noncompliance of AED, IEM, were the etiological factors influence the poor outcome. Reports of Kwong et al supported the influence of etiological agents like symptomatic etiology, remote cause, refractory SE on the poor outcome. ¹⁴

CONCLUSION

Children with status epilepticus who had normal neurodevelopment status before the onset of an attack and who did not sustain an acute insult to the central nervous system had favorable outcomes. Seizures therefore last longer before medical care is reached, and are thus more refractory to treatment. This factor might be more important. Duration and distance travelled to seek medical advice are also important risk factors that influencing the poor outcome. Hence early institution of proper time framed therapy even by the nearest hospital will improve the outcome. Atleast proper prehospital therapy like the use of IM/IV midazolam or IV/PR diazepam will have good outcome. Airway stabilization with supplementary oxygen while transporting the child from periphery could result in better outcome in SE.

Although the outcome is dependent on etiology, appropriate early management along with specific AED therapy as per protocol may reduce some of the morbidity associated with CSE. Acute CNS infection is one of the independent risk factor for poor outcome. Individual risk factors and complication to be anticipated and early intervention for complication like shock respiratory failure, aspiration, hypoglycaemia or hyperglycaemia, dyselectrolytemias to achieve good outcome.

Proper prehospital therapy, early referral, proper care while transporting, anticipitating risk factors involved, and protocol based approach uniformly at all hospital can reduce the mortality due to status epilepticus in children.

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Ethical approval: The study was approved by the

Institutional Ethics Committee

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