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Emotional intelligence in children with epilepsy



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ABSTRACT

Objective: Epilepsy is a prevalent neurological disorder in the pediatric population, often accompanied by comorbidities, drug-related burdens, and psychosocial issues. Emotional intelligence (EI) is a crucial aspect of neurocognitive functioning that may be impaired in various clinical conditions. This study aimed to assess EI and its associated risk factors in children with epilepsy.

Methods: In a case-control design, we recruited 47 children with epilepsy (37 males, mean age 10.5 ± 3.1 years) and age- and gender-matched controls. Participants were evaluated using the Emotional Quotient Inventory: Youth Version (EQ-I:YV). We included risk factors, including comorbidities, perinatal complications, epilepsy characteristics, and magnetic resonance imaging results to predict EI.

Results: Results indicate that children with epilepsy demonstrated significantly lower EI scores compared to controls (Total EQ score: p = 0.031, intrapersonal: p < 0.001, adaptability: p = 0.03, and general mood: p < 0.001, adaptability: p = 0.03, and general mood: p < 0.001, adaptability: p = 0.03, and general mood: p < 0.001, adaptability: p = 0.03, and general mood: p < 0.001, adaptability: p = 0.03, and general mood: p < 0.001, adaptability: p = 0.03, and general mood: p < 0.001, adaptability: p = 0.03, and general mood: p < 0.001, adaptability: p = 0.03, and general mood: p < 0.001, 0.001). Multiple linear regression analysis indicated that lower total EQ scores were associated with the number of anti-epileptic drugs, age, seizure frequency, MRI abnormalities, aura, and early onset of seizures.

Conclusions: The study provides evidence that children with epilepsy exhibit lower EQ scores than control group, with notable differences in intrapersonal skills, adaptability, and general mood. Additionally, age, and some seizure-related factors predicted decreased total EO scores. These findings emphasize the need to consider EI in the context of pediatric epilepsy, as impaired EI may contribute to further psychosocial challenges faced by affected children.

1. Introduction

Epilepsy is a chronic neurological condition, marked by unprovoked and recurrent seizures (Adamczyk et al. 2021), and affects over 50 million people worldwide, with higher in low-income countries (Neligan et al., 2012). It is one of the most common chronic neurological disorders in children, affecting approximately 1% of the pediatric population (Aaberg et al., 2017). Childhood epilepsy is not only associated with underlying medical conditions but is also accompanied by psychiatric comorbidities and social difficulties (Fastenau et al., 2008; Reilly et al., 2014a, 2014b). In addition, psychiatric comorbidities, such as attention

deficit hyperactivity disorder (ADHD), anxiety, intellectual disability, and autism spectrum disorders, are common in children with epilepsy (Alfstad et al., 2016; Reilly et al., 2014a, 2014b).

Emotional intelligence (EI) is the ability to understand, manage, and express emotions effectively (Salovey and Mayer, 1990). It is a complex construct that encompasses a range of skills, including self-awareness, self-regulation, social awareness, relationship skills, and empathy.

There is growing evidence that EI may be impaired in children with epilepsy (Malhi et al. 2022). Studies have shown that children with epilepsy are more likely to have difficulties with emotion recognition, empathy, and social skills (Austin et al. 2011). These difficulties can lead

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to problems with peer relationships, academic performance, and overall well-being (Gul and Hussain, 2016).

While studies have explored EI in various populations, including Mongolian children with ADHD (Bayarsaikhan, Avirmed et al. 2023), research on EI in children with epilepsy remains limited. Although the Mongolian population exhibited a low quality of life and susceptibility to mental distress, it should be noted that the assessments were limited to adults and did not include data on children (Bat-Erdene et al., 2023; Lkhagvasuren et al., 2023).

This study aimed to investigate EI in children with epilepsy and identify potential risk factors in Mongolia. By understanding the EI profile of children with epilepsy, we can develop targeted interventions to enhance their emotional competencies, thereby promoting their social integration, academic success, and quality of life.

2. Materials and methods

2.1. Study design and participants

This cross-sectional descriptive study was conducted at Mongol-Japan hospital, the first university hospital in Mongolia, aiming to evaluate emotional intelligence in children with epilepsy. From a total of 256 children with epilepsy were examined in the pediatric neurology clinic in the Mongolia-Japan hospital, from January 2020 to January 2022, 110 children were participated in the study. Out of fifty children who matched the inclusion criteria assessed for eligibility, 3 children were excluded due to incomplete data. (Fig. 1) The inclusion criteria for the epilepsy group were (1) age between 7 and 17 years; (2) epilepsy was diagnosed according to International League Against Epilepsy (ILAE) 2014 criteria (Fisher et al., 2017a, 2017b); (3) active epilepsy (on 1 or more Antiepileptic drugs (AEDs) and/or had a seizure in last year) (4) the ability to read and write letters and numbers (5) the caregiver of the child was willing to participate in this study. The exclusion criteria were (1) the history of epilepsy surgery or head injury; (2) the presence of psychiatric illness and autistic spectrum disorder; (3) other relevant medical conditions (endocrine, metabolic, hepatic, cardiac or renal disorder). Controls included age/ sex-matched children with epilepsy group, admitting the general pediatric outpatient department for non-neurological illnesses. The controls recruited from the outpatient clinic for acute upper respiratory tract infection during the data collection period. The inclusion criteria for the control group were: (1) matching age and gender as the epilepsy group, (2) absence of neurological disorders, including epilepsy, (3) no history of psychiatric disorders, including autistic spectrum disorder. All participants and their parents were provided to a clear and detailed explanation about the purposes of the study and the procedures involved. All parents provided their informed consent in written form. The procedure was approved by the local ethics committee, according to the rules of good clinical practice, in keeping with the Declaration of Helsinki.

2.2. Data collection

Questionnaire and anamnesis were collected from children and their parents between April 2022, and September 2022 at outpatient department of pediatrics. The researcher explained every question of the survey to the participants selected for the study. Perinatal history, including gestational age at birth, labor complication, newborn resuscitation, neonatal disease, and comorbidities, was taken from their parents and caregivers by a pediatrician or pediatric neurologist. Seizure-related factors that are possibly associated with EI were taken from only children with epilepsy. While, EQ-I:YV was assessed by a psychologist. Clinical assessment, electroencephalography, and neuroimaging data were reviewed by 2 pediatric neurologists who manage patients with epilepsy in their clinical practice. They classified seizures and epilepsy syndromes proposed by the task force of ILAE in 2017 (Fisher et al., 2017a, 2017b).



Fig. 1. Flow diagram of the study. Out of total of 256 children with epilepsy, 110 children were selected in the study. Of these children, 60 children excluded according to exclusion criteria. Of 50 children were eligible for the study, whereas 3 children were removed due to incomplete data. The study included 47 children with epilepsy and the same size of control group.

B. Enkhtuya et al.

2.2.1. The Bar-On Emotional Quotient Inventory

A questionnaire interview was conducted using EQ-I:YV (Bar-On and Parker, 2000; Bar-On, 2006). Long form of EQ-I:YV consisted of 60 items that are distributed across the following 7 scales.

It has a 4-point Likert scale; 1-never, 2-occasionally, 3-often, and 4always. A standard score of 90 to 110 indicates effective emotional and social functioning. A score above 110 suggests the high emotional and social skills, while a score below 90 indicates low competence and the need to increase skills in that area. During analysis, total EQ scores were grouped into low (EQ score below 90), normal (EQ scores between 90–110), and high (total EQ scores above 110) (Bar-On, 2006).

2.3. Statistical analysis

All data were statistically analyzed using SPSS Statistics for Windows, Version 26. Differences between groups were calculated using the Independent-Samples-*t*-test when the dependent variables were grouped, and the independent variables continued. Kolmogorov-Smirnov as well as Shapiro-Wilk Tests were used to analyze data distribution. In case of not normally distributed data, non-parametric Mann–Whitney–U test was calculated. Effect sizes were calculated by Cohen's d test for independent *T-test* or by r for Mann-Whitney test, as well as Cramer's *V* as appropriate. *P*-value less than 0.05 in all analysis was considered statistically significant in all tests. Multiple linear regression analyses were done to identify the predictors correlated to the total EQ scores.

3. Results

A total of 94 children participated in this study, ranging in age from 7 to 17 years. The study consisted of 2 groups: children with epilepsy (n = 47) with a mean age of 10.6 years, SD = 3.1, 54% male; and control

Table 1

Emotional of	quotient	competencies	and	skills	assessed	
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EQ subscales	Abilities
Intrapersonal	Self-awareness and self-expression:
Self-regard	Accurately perceive, understand, and accept oneself
Emotional self-	Be aware of and understand one's emotion
awareness	
Assertiveness	Effectively and constructively express one's emotion and oneself
Independence	Be self-reliant and free of emotional dependency on others
Self-actualization	Strive to achieve personal goals and actualize one's potential
Interpersonal	Social awareness and interpersonal relationships:
Empathy	Be aware of and understand how-others feel
Social responsibility	Identify with one's social group and cooperate with others
Interpersonal	Establish mutually satisfying relationships and relate
relationship	well with others
Stress management	Emotional management and regulation:
Stress tolerance	Effectively and constructively manage emotions
Impulse control	Effectively and constructively control emotion
Adaptability	Change management:
Reality-testing	Objectively validate one's feelings and think with external
Flexibility	Adapt and adjust one's feelings and think with external reality
Problem-solving	Effectively solve problems of a personal and
	interpersonal nature
General mood	Self-motivation:
Optimism	Be positive and look at the brighter side of life
Happiness	Feel content with oneself, others, and life in general
Total EQ (describes	comprises the following four factorial components:
overall emotional-	Intrapersonal, Interpersonal, Stress Management, and
social intelligence)	Adaptability.
Positive Impression	correction factor that is used to adjust scores in order to
	correct for social response bias and designed to identify
	individuals who may be attempting to create an
	exaggerated positive impression of themselves.

group (n = 47) matched by age and sex (t = 0.33, p = 0.73). A summary of the patient findings is provided in Table 2.

Gestational age at birth was significantly same for both groups. Labor complications, newborn resuscitations, and neonatal diseases and comorbidities were statically high among children with epilepsy.

Table 3 shows clinical characteristics of children with epilepsy.

The mean age at onset of seizures was 4.4 ± 2.9 years, while the median was 3 years (interquartile range: 2–7 years). One third children experienced first seizure at less than 2 years of age, of whom more than half had experienced seizure at the first year of life. In terms of seizure frequency, monthly seizures (74.7%) were reported high in those children. Focal seizure (51%) was dominant over generalized (34%) and unknown (15) seizures. Therefore, 21 (44.7%) children had taken 2 or more AEDs, and MRI showed abnormality in 11 (23.4%) children.

Using EQ-I:YV, Intrapersonal scale, adaptability scale, total EQ scores, and general mood scale were statistically lower compared to the control group. On the other hand, there were no differences in the positive impression scale, stress management and interpersonal scale between the two groups (p = 0.6, p = 0.53, p = 0.2), (Table 4).

Details on correlations between EQ scores and factors are described in Appendix 2. Table 5 shows the results of multiple linear regression with the enter method. They indicate that the predictive factors accounted for 87% of the variance of the Total EQ score (p < 0.001, F=12.08). There were no outliers (Cook's distance < 1), and the independence assumption was satisfied (1.5 < Durbin Watson). The distribution of the residuals satisfied normality assumptions.

This demonstrates that the total EQ scores was predicted by the number of AEDs (p < 0.001), frequency of seizure (p = 0.009), age (p = 0.01), MRI abnormality (p = 0.019), aura (p = 0.027), and age of seizure onset (p = 0.043). The number of medications showed the highest correlation to total EQ scores. Increasing the number of medications by one, total EQ scores decreases by 6.992 point. In continuous variables, the age, also, contributed negatively lower total EQ scores. Moreover, having daily seizure, abnormal MRI, aura, and the first seizure onset before 24 months of life showed negative correlation to total EQ scores compared to reference group.

4. Discussion

Our findings showed that children with epilepsy had significantly lower EI scores compared to non-epilepsy group. This result was consistent with other similar studies where children with newly diagnosed early-onset epilepsy reported that children with epilepsy had more than twice as neurobehavioral difficulties as a control group (Hunter et al., 2019). In meta-analysis included 19 studies, children and adolescents with epilepsy exhibited a deficit in social cognition and facial emotion recognition. These support evidence that while epilepsy primarily alter brain function, it can also impact various aspects of individual's cognitive and emotional process (Sun et al., 2022). In our analysis, subscales of EI, including intrapersonal scale, adaptability, general mood, positive thoughts, and total EQ scores were statistically lower than the control group. It shows similar results to the study conducted on 134 participants with epilepsy in 2017, which aimed to investigate the relationship between coping strategies and EI in patients with epilepsy. Using the EQ-I:YV, this study demonstrated that the highest score obtained in EI components was related to empathy, and the lowest score belonged to the component self-control or impulse control (Hajisabbagh et al., 2019). Comparably to the present result, a numerous study indicated the high self-stigma, and low self-esteem in children and adolescent (Ghanean et al., 2013; Scatolini et al., 2017). Furthermore, the study composed of 87 children with epilepsy showed the deficit in adaptive skills, but could not reveal the differences between subtypes of focal seizures and seizure-related factors (Villarreal et al., 2014). A deterioration of particular emotional scale may result of underlying disease, psychosocial burden, effect of medication, and poor health program.

Table 2

Demographic and perinatal characteristics for both groups, n = 97.

Frequency (n) Percent (%) Frequency (n) Percent (%)	0.8	
٨σ٩	0.8	
	0.8	
Pre-puberty (7-11 years) 26 55.3 21 44.7		0.021
Puberty (11-17 years) 25 53.2 22 46.8		
Sex		
Male 54 57.4 54 57.4	1	0.020
Female 40 42.6 40 42.6		
Gestational age at birth		
Preterm 8 17.0 3 6.3		
Term 38 80.8 44 93.6	0.1	0.173
Postterm 1 2.1 0 0		
Labor complication		
Yes 10 21.2 2 4.2	0.001	0.358
No 37 78.8 38 80.8		
Unknown 7 14.8		
Newborn resuscitation		
Yes 5 10.6 1 2.1	0.001	0.335
No 42 89.4 38 80.8		
Unknown 8 17.1		
Neonatal disease		0.372
Yes 6 12.8 1 2.1		
No 41 87.2 39 82.9	0.001	
Unknown 5 10.6		
Comorbidities		
Yes 5 10.6 1 2.1	0.02	0.240
No 42 89.4 46 97.9		

The *P*-values were calculated using the χ^2 test. The effect sizes were determined by Cramer's *V*.

Table 3

Clinical characteristics of children with epilepsy.

Seizure characteristics	Frequency (n)	Present (%)	
Age at first seizure			
Before age 24 months	11	23.4	
After age 24 months	36	76.6	
Frequency of seizure			
At least one a month	35	74.7	
Irregular	11	25.3	
Type of seizure*			
Focal	24	51	
Generalized	16	34	
Unknown	7	15	
Duration of seizure			
< 5 min	38	80.8	
5 < minutes	9	19.2	
Occurrence time of seizure			
Only day / only night	28	59.5	
At anytime	19	40.5	
The longest duration of seizure remission			
< 6 months	38	80.8	
6 < months	9	19.2	
Aura			
With aura	16	34	
Without aura	22	66	
Number of AEDs			
Monotherapy	26	55.3	
$2 \leq AEDs$	21	44.7	
MRI abnormality			
Yes	11	23.4	
No	23	48.9	
Unknown	13	27.6	

* according to ILAE 2017 classification of seizure types (Fisher et al., 2017a, 2017b); AEDs: Anti-Epileptic drugs; MRI: Magnetic Resonance Imaging

In our study, almost all subscales of EQ scores were lower than the standard score (100) of the Bar-On test for both groups. It was consistent with the case control study compared EI on chronic diseases, such as obstructive sleep apnea syndrome. This study noticed that interpersonal scales, adaptability stress management and total EQ were significantly different between case and a control groups (Parisi et al., 2017). It may

indicate that emotional points could be under the borderline, regardless of whether the disease is chronic or acute.

Seizure-related factors can differently affect cognition in individuals with epilepsy, including the etiology of seizure, age at onset of the seizure, the frequency and type of seizure, prolonged seizure, hereditary factors, the number of AEDs, and epilepsy surgery (Meador, 2002; Motamedi and Meador, 2003; Loring et al., 2007). In our study, there were a significant correlation to decreased EQ scores and some factors; the number of AEDs, MRI abnormality, having aura, and early onset seizure. The cognitive impairments are not only associated with seizure, AEDs can adversely affect cognitive function by suppressing neuronal excitability or enhancing inhibitory neurotransmission (Park and Kwon, 2008). In our study, the number of AEDs was negative correlation to total EQ scores compared to children on monotherapy. As the number of medication increased, total EQ score decreased. Similarly, a several studies found that polytherapy was associated with worse overall cognitive performance and quality of life in children with epilepsy compared to monotherapy (Quon et al., 2020; Giménez DeGeorge et al., 2021). Addition to the number of medications, type of AEDs had different effect on emotional regulation, such as effect on language of topiramate and zonisamide (Eddy et al., 2011; Quon et al., 2020). This highlights the importance of carefully considering medication regiment and their potential impacts on overall psychological function. Moreover, the relationship between early-onset seizures and poor cognitive outcomes had previously been noted in a number of population-based studies (Høie et al., 2005; Berg et al., 2008; Rantanen et al., 2011). The study indicated that children who experienced seizures at a young age (<24 months) were at a higher risk for intellectual disability compared to the age of seizure onset at 24-60 months and after 60 months (Hunter et al., 2019). A similar result showed in our findings that children who experienced first seizure in the first 24 months of life showed lower total EQ scores than those who had late onset seizure. This may be due to the impact of seizures on the developing brain, as well as the long-term potential side effects of AEDs. The study indicated that prolonged seizures or frequent recurrent seizures were at particular risk for brain injuries that can result in cognitive impairment (Holmes, 2015). Seizure can lead to a range of cellular and metabolic changes in the brain, including neuronal loss in the hippocampus, change in

Table 4

Subscales of emotional quotient in the epilepsy group and the non-epilepsy group, n = 97.

Emotional Quotient	Epilepsy group		Non-epilepsy group			t/z	P-value	Effect size	
	Mean	SD	Median	Mean	SD	Median			
Interpersonal scale	98.8	8.8	99	98.7	8.9	98	0.48	0.9 *	0.001
Intrapersonal scale	89.6	11.3	91	97.6	10.9	100	0.70	0.001 *	0.720
Stress management scale	84.0	9.4	83	83.1	7.1	82	0.05	0.6 *	0.108
Adaptability criteria	95.6	12.8	95	101.4	12.7	101	0.87	0.03 *	0.454
General mood scale	82.0	12.9	80	92.0	12.2	96	-3.461	$0.001^{\#}$	0.260
Total EQ	90.1	9.8	90	94.1	7.9	94	0.09	0.03 *	0.449
Positive Impression scale	97.7	9.7	98	100.7	12.7	102	-1.991	$0.2^{\#}$	0.086

The *P*-values were calculated using independent *T*-test* and Mann-Whitney test[#], as appropriate. The effect sizes were determined by Cohen's *d* for independent *T*-test, or *r* for Mann-Whitney test.

Table 5

Multiple linear regression on the total EQ scores by age, gender, and seizure-related factors, n = 47.

Independent variables	r	В	Beta	t	P- value	95.0% Confidence Interval for B	
						Lower Bound	Upper Bound
Constant		116.148		28.000	0.000	107.676	124.620
Age	-0.061	-0.731	-0.223	-2.733	0.010	-1.278	-0.185
Gender (ref: male)	0.075	1.134	0.058	0.662	0.513	-2.366	4.633
Number of AEDs	-0.764	-6.992	-0.585	-6.748	< 0.001	-9.109	-4.876
Having daily seizure (ref: irregular seizure frequency)	-0.297	-7.675	-0.297	-2.789	0.009	-13.295	-2.055
MRI abnormality (ref: no abnormality)	0.009	-4.355	-0.190	-2.470	0.019	-7.955	-0.754
Aura (ref: without aura)	-0.170	-3.763	-0.184	-2.321	0.027	-7.075	-0.451
Age of seizure onset (ref: onset before 24 months of life)	-0.545	-4.519	-0.197	-1.858	0.043	-9.484	0.447
Seizure duration (ref: longer than 5 min)	-0.172	-2.638	-0.107	-1.252	0.220	-6.943	1.666
Trigger (ref: without trigger)	-0.280	0.673	0.032	0.338	0.738	-3.396	4.741
Having monthly seizure (ref: irregular seizure frequency)	-0.217	-3.830	-0.195	-1.849	0.074	-8.060	0.400
Seizure occurs only in the daytime (ref: at any time of the day)	0.457	4.334	0.159	1.361	0.184	-2.171	10.839
Seizure occurs only at night (ref: at any time of the day)	0.016	1.863	0.095	0.966	0.342	-2.077	5.803
Postictal: sleep (ref: having a postictal headache, dizziness, etc)	0.325	2.367	0.103	1.118	0.272	-1.957	6.691
Postictal: as usual (ref: having a postictal headache, dizziness, etc)	-0.16	-2.436	-0.099	-1.150	0.259	-6.762	1.891
Generalized seizure (ref: focal seizure)	-0.116	-1.906	-0.098	-1.117	0.273	-5.390	1.578
Unknown seizure (focal seizure)	0.082	-0.183	-0.007	-0.082	0.935	-4.753	4.386
Model summary		R	R square	F value	Durbin-Watson	Cook's distance	P value
		0.930	0.866	12.083	1.575	0.030	< 0.0001

ref: a reference group for categorical variables.

neurogenesis, and synaptic reorganization. These changes can contribute to behavioral and cognitive impairment, which may worsen over time with repeated seizures (Lukoyanov et al., 2004). A case-control study conducted in Africa highlighted that individuals with epilepsy had decreased executive functions and verbal fluency compared to controls. Additionally, this study found a significant relationship between high seizure frequency and poor cognitive performance (Celik et al., 2015). This was consistent with our findings that children with daily seizure had a decrease in the total EQ score compared to children with irregular seizure. Unlikely to common seizure-related factors, having aura, and abnormal MRI correlated to lower total EQ scores in our study. On the contrary, our findings did not show strong and significant relationship between EI and some seizure-related factors, including seizure type, having trigger, seizure occurrence time, as well as seizure duration in children with epilepsy. Therefore, a single factor cannot account for cognitive decline in epilepsy, it might be explained by a multiple mechanism, such as signaling pathways and neuronal network function (Holmes, 2015). Epilepsy can affect cognition, but cognitive decline can in turn affect epilepsy (Helmstaedter and Witt, 2017). In addition to the seizure-related factors, aging adversely affected quality of life and cognition in individuals with epilepsy (Devinsky et al. 1999). Our study presents comparable findings, whereby a one-year increase in age led to a decrease in total EQ of 0.731.

Our study had a several limitations. Firstly, we did not examine the relationship between AEDs type, etiology of epilepsy, electroencephalography and EI. Secondly, the study was relatively small sample size, and single center trial. Lastly, intelligence test and some seizure-related factors were not taken into account in this study.

Significant strengths of this study included that study participants were screened for EI by using long form of EQ-I:YV, and this assessment can give us the more information about different subscales of EI in children with epilepsy. Furthermore, the factors that can affect total EQ scores were detected in group with epilepsy.

As a high-risk group, children with epilepsy should be noted to pay attention to their emotional conditions. There is a lack of emotional and social training for children with epilepsy in Mongolia. Our study suggests that there is a need for additional programs in schools to develop intrapersonal and adaptability skills of children with epilepsy. It might help to prompt necessary interventions and prevent the development of more severe psychological problems in those children. Moreover, the study revealed some seizure-related factors that could have impact on child's emotional health. Therefore, it is essential for parents, teachers, and social workers to collaborate and pay more attention to children with early onset seizures, frequent seizures, and on polytherapy.

5. Conclusion

The study found that children with epilepsy had lower EQ scores in intrapersonal skills, adaptability, general mood, positive thoughts, and total EQ. Moreover, the study identified age and seizure-related factors, including medication count, daily seizures, MRI abnormalities, having an aura, and early onset of seizures as predictors of decreased total EQ. These findings highlight the importance of considering emotional intelligence in the context of pediatric epilepsy, as impaired EQ may contribute to further psychosocial challenges faced by affected children.

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CRediT authorship contribution statement

Battamir Enkhtuya: Conceptualization, Formal analysis, Investigation, Methodology, Resources, Writing – original draft. Battuvshin Lkhagvasuren: Validation, Formal analysis, Editing - Original Draft, Visualization. Uranbileg Sainbat: Investigation, Resources, Data Curation. Binderiya Bayanmunkh: Investigation, Resources, Data Curation Tovuudorj Avirmed: Validation, Visualization, Bayarmaa Tsend: Conceptualization, Methodology, Formal analysis, Writing -Original Draft, Funding acquisition. Amgalan Bayarsaikhan: Conceptualization, Methodology, Visualization, Supervision.

Declaration of Competing Interest

The authors declare that they have no competing interests.

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Compliance with ethical standards

The study was approved by the local ethics committee, according to the rules of good clinical practice, in keeping with the Declaration of Helsinki.

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B. Enkhtuya et al.

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