

## Risk Factors for Epilepsy in Pediatric Patients Undergoing Follow-Up at Yekatit 12 Hospital Medical College, Addis Ababa, Ethiopia: A Case-Control Study

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### Abstract

**Background:** Epilepsy stands as a persistent and significant neurological disorder, ranking among the primary contributors to disability in Ethiopia.

**Objective:** To evaluate the risk factors for epilepsy among children undergoing follow-up at Yekatit 12 Hospital Medical College, Addis Ababa Ethiopia 2023.

**Methods:** An unmatched case-control study design was implemented to investigate epilepsy risk factors among patients attending the neurology clinic at Yekatit 12 Hospital Medical College, a teaching hospital in Addis Ababa, Ethiopia, in 2023. The study included 87 cases selected from individuals with epilepsy and 174 controls chosen from non-epileptic patients attending the general paediatrics clinic at the same hospital during the same timeframe. Data on the identified risk factors were gathered through personal interviews using a structured questionnaire and by reviewing medical records. Subsequently, the collected data were coded, checked for accuracy, and entered into Epi-Info-7. The information was then exported to SPSS Version 26 for analysis. Bivariate and multivariate logistic regression analyses were conducted, and both crude and adjusted odds ratios with 95% confidence intervals were calculated. A significance level of  $p < 0.05$  was employed to indicate statistical significance.

**Results:** Of the cases, 58 (66.7%) and among the controls, 95 (57.9%) had a mean age of  $5.8 \pm 4.0$  and  $5.8 \pm 3.6$  years, respectively. The probability of experiencing epilepsy was higher in children with a family history of epilepsy (AOR: 5.69, 95% CI (2.051, 15.84)), an Apgar score  $<6$  (AOR: 7.51, 95% CI (1.55, 36.26)), a history of CNS infection (AOR: 14.26, 95% CI (3.28, 62.08)), and current neurological impairment (AOR: 8.07, 95% CI (1.10, 59.07)).

**Conclusion:** This study identified an increased likelihood of epilepsy in individuals with a family history of the condition, an Apgar score  $<6$ , a history of CNS infection, and current neurological impairment.

**Keywords:** Epilepsy; Addis Ababa; Ethiopia; Child health; Y12HMC

**Abbreviations:** AOR: Adjusted Odd Ratio, APGAR: Appearance, pulse, grimace, activity, and respiration, CI: Confidence Interval, COR: Crude Odds Ratio; OR: Odd Ratio; SPSS: Statistical Package for Social Science Software; SSA: Sub-Saharan Africa; Y12HMC: Yekatit 12 Hospital Medical College.

### Background

Epilepsy is a neurological disorder defined by the occurrence of two or more unprovoked seizures unrelated to acute metabolic disorders. It may result in loss of consciousness, disruptions in movement, and disturbances in sensation (including vision, hearing, and taste), autonomic function, mood, and mental processes [1]. Epilepsy stands as the most prevalent neurological disorder globally, affecting 50 million individuals, with roughly 80% residing in resource-limited developing countries. The highest incidence of epilepsy occurs during childhood [2].

The overall lifetime occurrence of epilepsy is 3%, with over half of the cases initiating in childhood. The annual prevalence is estimated at 0.5–1.0% [3]. Worldwide, epilepsy impacts over 50 million individuals, and around 85% of those affected reside in developing countries, including Ethiopia [4].

The elevated incidence of epilepsy in developing countries is attributed to a higher risk of acute and chronic brain infections, along with pre- and post-natal obstetric complications that may result in brain damage [5]. While there is published data on the incidence of epilepsy

in sub-Saharan Africa, the comprehensive information indicates a notably higher annual incidence in less developed countries at 81.7 per 100,000 compared to 45.0 per 100,000 in more developed countries [6]. The prevalence of epilepsy stood at 5.2 per 1000 individuals at risk, with rates of 5.8 for males and 4.6 for females. The peak age-specific prevalence was observed in the 10-19 years age group [7].

The impact of epilepsy in children extends across social, emotional, and overall family functioning. Particularly in Africa, epilepsy remains stigmatized, largely due to traditional beliefs associating it with spirituality [8].

While there is compelling evidence indicating specific etiological factors for epilepsy, the cause remains unknown in approximately 70% of cases. Risk factors for epilepsy vary between childhood and later stages of life and encompass conditions linked to an elevated occurrence

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of epilepsy. These factors include head injury, perinatal insults, central nervous system (CNS) infections, and febrile convulsions [9].

Advancements in comprehending this debilitating disease have been made through data derived from the aetiology, epidemiology, and historical aspects of epilepsy. However, investigations from various countries indicate that the causes of epilepsy remain incompletely understood [10]. For example in paediatric research, approximately 60-70% of children diagnosed with epilepsy are identified to have either idiopathic or cryptogenic epilepsy [11]. However, the study area lacks adequate research on the scope of the problem and its underlying factors, hindering the formulation of informed policies. Therefore, precise identification of the risk factors for epilepsy could potentially empower us to formulate strategies for its prevention.

## Method and Materials

The research was conducted at Yekatit 12 Hospital Medical College, a teaching hospital located in Addis Ababa, Ethiopia. The study spanned from March 2023 to August 2023 and employed an unmatched case-control design. The cases included children diagnosed with epilepsy, while the controls encompassed children without epilepsy, all receiving care at the Medical College Hospital. Informed consent was obtained from the guardians of the participating children. The study focused on children aged 3 months to 14 years clinically diagnosed with epilepsy, characterized by the occurrence of two or more unprovoked seizures consecutively within the preceding period. Exclusions comprised children with only febrile seizures and those with significant comorbidities, such as notable mental sub-normality or systemic diseases. Controls were children aged 3 months to 14 years without epilepsy attending the same hospital.

Structured questionnaires were administered to parents or guardians of the children, adapting the questionnaire through a comprehensive review of existing literature and similar previous studies. Following a pre-test and subsequent adjustments, clinical information for the children was retrieved from their medical records. Each respondent underwent an individual interview, where they were seated and given a detailed overview of the study's objectives, the assurance of confidentiality, and clear explanations of key terms.

After conducting data completeness checks, the information was entered into Epi Info version 7, and subsequently exported to SPSS version 26 for further data cleaning and analysis. Continuous variables were summarized using mean and standard deviation, while categorical

variables were expressed as relative frequencies or proportions. To investigate the association between independent variables and the dependent variable, binary logistic regression analysis was utilized.

During the bivariate analysis, independent variables with a p-value of  $< 0.2$  were considered for inclusion in the multivariable analysis model. Ultimately, independent variables with a p-value  $< 0.05$  were considered statistically significant.

## Results

### Socio-demographic characteristics of the participants

In this study, a total of 251 participants were included, consisting of 87 previously diagnosed epilepsy patients (cases) and 164 controls, yielding a response rate of 96.2%. Among the cases, 58 (66.7%) had a mean age of  $5.8 \pm 4.0$  years, while in the control group, 95 (57.9%) had a mean age of  $5.8 \pm 3.6$  years. The majority of both cases (88.5%) and controls (82.3%) were born to mothers under the age of 35. In terms of maternal education, 15 (17.2%) of the cases and 21 (12.8%) of the controls had no formal education. Notably, 28.7% of cases had a family history of epilepsy compared to 6.7% among the controls (Table 1).

### Maternal factors

Regarding maternal factors, a considerable 17.9% of cases had a history of hypertension, whereas only 9.9% among the controls had a maternal history of hypertension. Additionally, a small percentage, 3.8% of cases and 1.3% of controls, reported a maternal history of gestational diabetes. However, maternal infection during pregnancy was notably higher among cases, with 20.9%, compared to 3.1% among controls. History of drug intake during pregnancy was reported by 10.3% of mothers with epileptic children, while a smaller proportion (5.5%) of mothers without epileptic children had a history of drug intake. Furthermore, a substantial 18.4% of mothers with epileptic children had a history of spontaneous abortion, whereas 13.6% of mothers without epileptic children reported a similar history (Table 2).

### Perinatal factors

A notable proportion (10.3%) of children diagnosed with the disease and 6.1% among the control group were delivered at home. Concerning the mode of delivery, 70.1% of children with the disease and 75.0% of controls underwent spontaneous vaginal delivery (SVD). Among these deliveries, nearly one-third of children with epilepsy and 26 (15.9%) of controls experienced prolonged labour. Moreover,

**Table 1:** Socio-demographic characteristics among cases and controls in among children on follow-up at Yekatit 12 Hospital Medical College, Addis Ababa, Ethiopia, 2023.

Variables	Cases (n=87)		Controls (n=164)	
	Frequency(n)	Percent (%)	Frequency(n)	Percent (%)
<b>Age in years</b>				
< 6 years	47	54.0	90	54.9
6 years & above	40	46.0	74	45.1
<b>Maternal age at the time of delivery</b>				
< 35 years	77	88.5	135	82.3
35 years & above	10	11.5	29	17.7
<b>Mother' Educational status</b>				
No formal education	15	17.2	21	12.8
Primary education	26	29.9	52	31.7
Secondary education	25	28.7	46	28.0
College/university	21	24.1	45	27.4
<b>Family history of Epilepsy</b>				
Yes	25	28.7	11	6.7
No	62	71.3	152	92.7

**Table 2:** Proportion of maternal factors for epilepsy between cases and controls among children on follow-up at Yekatit 12 Hospital Medical College, Addis Ababa, Ethiopia, 2023.

Variable	Cases		Controls	
	Frequency (n=87)	Percent (%)	Frequency (n=164)	Percent (%)
<b>Maternal hypertension history</b>				
Yes	15	17.9	15	9.9
No	69	82.1	136	90.1
<b>Maternal gestational diabetes history</b>				
Yes	3	3.8	2	1.3
No	76	96.2	150	98.7
<b>Maternal infection</b>				
Yes	18	20.9	5	3.1
No	68	79.1	155	96.9
<b>Maternal history of drug intake</b>				
Yes	9	10.3	9	5.5
No	78	89.7	154	94.5
<b>Maternal history of spontaneous abortion</b>				
Yes	16	18.4	22	13.6
No	71	81.6	140	86.4

**Table 3:** Proportion of perinatal risk factors for epilepsy among cases and controls among children on follow-up at Yekatit 12 Hospital Medical College, Addis Ababa, Ethiopia, 2023.

Variables	Cases		Controls	
	Frequency (n=87)	Percent (%)	Frequency (n=164)	Percent (%)
<b>Place of Delivery</b>				
Home	9	10.3	10	6.1
Health facility	78	89.7	154	93.9
<b>Mode of delivery</b>				
Cesarean section	26	29.9	41	25.0
SVD	61	70.1	123	75.0
<b>Prolonged labor</b>				
Yes	26	34.2	26	17.4
No	50	65.8	123	82.6
<b>APGAR &lt;6 /didn't cry</b>				
Yes	28	32.9	10	6.2
No	57	67.1	150	93.8
<b>Pre or post term delivery</b>				
Yes	9	11.5	11	7.4
No	69	88.5	138	92.6

11 (12.6%) of children with epilepsy and 15 (9.1%) of controls were uncertain about whether they had prolonged labour during birth. During the delivery process, almost a quarter of children with epilepsy and 10 (6.2%) of controls either had an APGAR score <6 or did not cry (Table 3).

### Postnatal factors

The data suggests a notable disparity in the prevalence of febrile convulsions and neurologic impairment between children with epileptic disease and the control group. Additionally, the incidences of head injury, CNS infection, and CNS malformation appear to be more pronounced among those diagnosed with epilepsy.

Among the entire pool of study participants, 13 (14.9%) of children

diagnosed with epileptic disease and 9 (5.5%) of the control group had a history of febrile convulsions. Similarly, 24 (27.6%) of children with epileptic disease and 4 (2.4%) of the controls exhibited neurologic impairment. The occurrences of head injury, central nervous system (CNS) infection, and CNS malformation were 1 (1.1%), 19 (21.8%), and 11 (12.6%) among cases, respectively (Figure 1).

### Factors associated with epilepsy

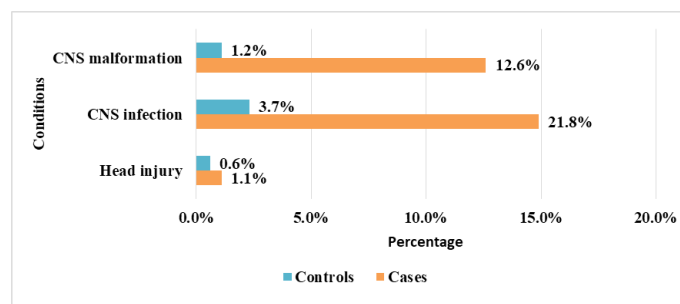
Both bivariate and multivariable logistic regression analyses were employed to ascertain the factors linked with epilepsy. During the bivariate analysis, factors such as the age of the child, maternal age at the time of delivery, family history of epilepsy, maternal history of hypertension, maternal infection, maternal history of drug intake, APGAR score <6 or absence of crying, prolonged labor, febrile convulsions, Central Nervous System (CNS) infection, and existing neurological impairment displayed a p-value of less than 0.25, prompting their inclusion in the subsequent multivariable analysis. This process aimed to identify and confirm factors independently associated with epilepsy in the studied population.

Following the adjustment for potential confounding variables through multivariate logistic regression analysis, four variables-Family history of epilepsy, APGAR score <6 or absence of crying during birth, history of Central Nervous System (CNS) infection, and current neurologic impairment-emerged as independent factors associated with epileptic disease, exhibiting a statistically significant p-value of less than 0.05. This indicates that even after accounting for other variables, these four factors retained their individual significance in influencing the occurrence of epileptic disease in the studied population.

In the analysis incorporating multiple variables, it was revealed that the likelihood of being diagnosed with epilepsy was notably elevated among certain groups of children. Specifically, those with a family history of epilepsy (Adjusted Odds Ratio [AOR]: 5.69, 95% Confidence Interval [CI]: 2.05, 15.84), those who scored an APGAR <6 or did not cry during birth (AOR: 7.51, 95% CI: 1.55, 36.26), individuals with a history of central nervous system (CNS) infection (AOR: 14.26, 95% CI: 3.28, 6.08), and those currently experiencing neurological impairment (AOR: 8.07, 95% CI: 1.10, 9.07) demonstrated statistically significant associations with epilepsy in the study setting (Table 4).

### Discussion

In the bivariate analysis of this study, various factors exhibited a noteworthy association with epilepsy. However, upon conducting multivariate logistic regression analysis, only a family history of epilepsy, an APGAR score <6 or absence of crying during birth, a history of Central Nervous System (CNS) infection, and current neurologic impairment demonstrated statistically significant associations with epilepsy. This suggests that, when considering multiple factors



**Figure 1:** Prevalence of common postnatal risk factors for epilepsy among children on follow-up at Yekatit 12 Hospital Medical College, Addis Ababa, Ethiopia, 2023.

**Table 4:** Variables linked to epilepsy in children undergoing follow-up at Yekatit 12 Hospital Medical College in Addis Ababa, Ethiopia, in the year 2023.

Variables	Epilepsy		COR (95%CI)	AOR (95%CI)	p-value
	Cases (%)	Controls (%)			
<b>Maternal age at the time of delivery</b>					
< 35 years	77(88.5)	135(82.3)	1.65(0.76,3.58)	1.75(0.56,5.47)	0.33
35 years and above	10(11.5)	29(17.7)	1	1	
<b>Family history of Epilepsy</b>					
Yes	25(28.7)	11(6.7)	5.57(2.58,12.01)	5.69(2.05,15.84)	0.001*
No	62(71.3)	152(93.3)	1	1	
<b>Maternal hypertension history</b>					
Yes	15(17.9)	15(9.9)	1.97(0.91,4.26)	1.09(0.29,4.05)	0.9
No	69(82.1)	136(90.1)	1	1	
<b>Maternal infection</b>					
Yes	18(20.9)	5(3.1)	8.21(2.93,23.01)	3.86(0.78,19.22)	0.099
No	68(79.1)	155(96.9)	1	1	
<b>Maternal history of drug intake</b>					
Yes	9(10.3)	9(5.5)	1.97(0.75,5.17)	0.21(0.03,1.60)	0.133
No	78(89.7)	154(94.5)	1	1	
<b>APGAR &lt;6 /didn't cry at birth</b>					
Yes	28(32.9)	10(6.3)	7.37(3.36,16.13)	7.51(1.55,36.26)	0.012*
No	57(67.1)	150(93.8)	1	1	
<b>Prolonged labor</b>					
Yes	26(34.2)	26(17.4)	2.46(1.30,4.64)	0.87(0.30,2.55)	0.8
No	50(65.8)	133(82.6)	1	1	
<b>Febrile convulsions</b>					
Yes	13(14.9)	9(5.5)	3.03(1.24,7.40)	2.49(0.72,8.63)	0.151
No	74(85.1)	155(94.5)	1	1	
<b>CNS infection</b>					
Yes	19(22.1)	6(3.7)	7.45(2.47,19.53)	14.26(3.28,6.08)	0.001*
No	67(77.9)	158(96.3)	1	1	
<b>Neurological impairment</b>					
Yes	24(27.6)	4(2.4)	15.24(5.08,45.68)	8.07(1.10,9.07)	0.040*
No	63(72.4)	160(97.6)	1	1	

AOR= Adjusted Odds Ratio, COR=Crude Odds Ratio, 1= Reference category

simultaneously, these specific variables retained their significance in relation to the occurrence of epilepsy.

In the findings of this research, a strong relationship was identified between epilepsy and a familial history of the condition (Adjusted Odds Ratio: 5.69, 95% Confidence Interval (2.05, 15.84)). This discovery aligns with results from previous studies conducted in Kenya, Tanzania, and India. The consistency of these findings across diverse geographical locations supports the notion that a family history of epilepsy may be a significant factor influencing the occurrence of the condition [12-14].

The findings indicated a noteworthy connection between individuals with an APGAR score <6 or those who did not cry during birth (Adjusted Odds Ratio: 7.51, 95% Confidence Interval (1.55, 36.26)) and the likelihood of developing epilepsy. This observation is consistent with comparable outcomes identified in research conducted in Sub-Saharan African (SSA) countries, such as Kenya and Tanzania. This underscores the consistency of the association across diverse populations in the SSA region and India [12-15].

Within this study, children with a prior history of Central Nervous System (CNS) infection exhibited a 14-fold higher likelihood of experiencing epilepsy compared to those without such a history. These findings are consistent with a community-based study conducted in Tanzania, reinforcing the association between CNS infections and the increased risk of epilepsy in children [15], and a study done in Turkey [16]. In contrast, a study conducted in Jordan revealed that although there were more patients with a history of Central Nervous

System (CNS) infection compared to controls, this difference did not reach statistical significance. This suggests that, unlike the findings in the current study, the association between a history of CNS infection and the occurrence of epilepsy was not statistically significant in the Jordanian study [17].

Lastly, there was a strong likelihood of an association between current neurologic impairment and epilepsy, with individuals experiencing an 8-fold increase in the odds (Adjusted Odds Ratio: 8.07, 95% Confidence Interval (1.10, 9.07)). Similar findings have been reported in other studies involving children from Tanzania, reinforcing the connection between present neurologic impairment and the heightened risk of epilepsy [15]. It is probable that this relationship is not causative but rather stems from a shared aetiology influencing both epilepsy and cognitive impairment. Support for this hypothesis is evident in studies indicating that cognitive impairment occurred before the onset of seizures. This suggests a common underlying factor contributing to both conditions rather than one directly causing the other [18].

It is crucial to recognize the limitations inherent in this study. While it contributes to the limited body of research on predictors of epilepsy, it is important to note certain drawbacks, including its retrospective design and the relatively smaller sample size. These limitations imply that the findings should be interpreted with caution, and future studies with larger sample sizes and prospective designs may provide a more comprehensive understanding of the predictors of epilepsy.

## Conclusion

In summary, this study identified an elevated risk of epilepsy within the examined population. Notably, factors such as a family history of epilepsy, an Apgar score <6 or the absence of crying at birth, a history of Central Nervous System (CNS) infection, and existing neurological impairment exhibited statistically significant associations with epilepsy among patients attending Yekatit 12 Hospital Medical College in Addis Ababa, Ethiopia.

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