



ST. PAUL HOSPITAL MILLENNIUM MEDICAL COLLEGE

GRADUATE STUDY PROGRAM

Prevalence of malnutrition and associated factors among epileptic children having follow up at neurology clinic of St Paul Hospital Millennium Medical College, Ethiopia, 2023.

Investigator: Yihalem Abebe (MD, Pediatrics Resident)

Addis Ababa, Ethiopia

February, 2024 G.C.



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Investigator: Yihalem Abebe (MD, Pediatrics Resident)

Advisor: Dr. Tigist Bacha (MD, Pediatrics Emergency and Critical Care Specialist, Pediatrics Cardiac Intensivist, MPH)

Co-advisor: Dr Endayen Deginet (MD, Pediatrics Neurologist)

A Research Thesis to be submitted to the Department of Pediatrics for the Partial Fulfillment of the Requirements for Postgraduate Diploma in Pediatrics and Child Health

Addis Ababa, Ethiopia

February, 2024 G.C.

DECLARATION

I hereby declare that; this thesis report is my original work and has not presented for a degree by another person in this or any other university and all source material used for this thesis have been acknowledged.

Name: _____

Signature _____

Date _____

Name of Advisor: _____

Signature _____

Date _____

Name of Co-advisor: _____

Signature _____

Date _____

Abstract

Background: The presence of malnutrition on top of seizure load in children with epilepsy results in poor control and untoward neurologic outcome. There are different factors that affect the interaction between the presence of epilepsy and malnutrition.

Objective: To determine the prevalence of malnutrition and its associated factors among children with epilepsy who have follow up at SPHMMC neurology clinic from August 01/2023 to October 30/2023.

Method: Hospital based cross sectional study was conducted. Data was collected prospectively by using a pretested and structured questionnaire containing sociodemographic, clinical and anthropometry parameters. Each epileptic child was taken until the final sample size is reached during follow up dates. The collected data was coded and checked for completeness and entered to epi-info version 7.0 and exported to SPSS version 26.0 for analysis. Descriptive statistics, Bi-variate and multivariate binary logistic regression was performed.

Result: From 422 children screened for malnutrition, the overall prevalence of malnutrition was 38.6%. From all children included in the study, 56 (13.3%), 71 (16.8%) and 41 (9.7%) had severe wasting, underweight and stunting, respectively. While 60 (14.2%), 62 (14.7%) and 57 (13.5%) had moderate wasting, underweight and stunting, respectively. About 45 (10.7%) children had microcephaly(<-3 SD). Children for whom vitamin D level determined during their routine follow up (n= 268), 49 (18.3%) were deficient for vitamin D, 97 (36.2%) children had vitamin D insufficiency. From the revised available CBC results (n= 401), 40 (10.0%) had anemia with low MCV for age. The risk of malnutrition in children with out neurologic comorbidities other than epilepsy was lower than those with comorbidities (AOR= 0.517(95% CI: 0.296-0.902, p-value= 0.02). Feeding difficulties (AOR= 2.033 (95% CI: 1.612-10.567, p-value= 0.000) and poor adherence to followup (AOR= 2.033 (95% CI: 1.612-10.567, p-value= 0.008) were significantly associated with malnutrition.

Conclusion: Nutritional screening and intervention should be part of routine epileptic care. Children with epilepsy and associated severe neurologic impairment like cerebral palsy may need the greatest nutritional support.

Key words: Malnutrition, Epilepsy, Children, Ethiopia

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Acronyms and Abbreviations

ASDs	Anti-seizure drugs
BMI	Body mass Index
CI	Confidence Interval
CP	Cerebral Palsy
Dr	Doctor
PEU	Pediatric Emergency Unit
ETB	Ethiopian Birr
G.C	Gregorian Calendar
GERD	Gastroesophageal Reflux Disease
GI	Gastrointestinal
HC	Head circumference
Ht	Height
ILAE	International League Against Epilepsy
MCV	Mean Corpuscular Volume
MD	Medical Doctor
MUAC	Mid-Upper Arm Circumference
SPHMMC	Saint Paul Hospital Millennium Medical College
SPSS	Statistical Package for Social Sciences
WHO	World Health Organization
Wt	Weight

1. Introduction

1.1. Background

Malnutrition is broad which includes both under and over nutrition. Under nutrition is an imbalance between the supply of nutrients and body's demand for them to ensure growth, maintenance, and specific functions. The prevalence of malnourished people in the world population reached 10.9 percent in 2017, which is higher among low and middle income countries. The prevalence of malnutrition in Ethiopia is high that stunting, underweight, and wasting were 37%, 21%, and 7%, respectively. (1, 2)

According to the 2016 Global Burden of Disease Collaborators epilepsy represents a relevant fraction of the worldwide disease burden. WHO's 2010 Global Burden of Disease study ranks epilepsy as the second most burdensome neurologic disorder worldwide in terms of disability-adjusted life years and it was higher in low/middle-income countries than in high-income countries. (3)

Epilepsy is the most common chronic neurologic disorder in children with variable clinical manifestations. Children with epilepsy have an enduring propensity to generate epileptic seizures. According to the International League Against Epilepsy (ILAE), epilepsy is defined as having at least two unprovoked or reflex seizures occurring >24 h apart. About 10.5 million children worldwide are affected by epilepsy. Prevalence increases with age and peaks at 5–9 years of age in children. Eighty percent of children with epilepsy live in low and middle income countries. Epilepsy, therefore, appears to have a root in poverty. About 80–90% of epileptics receive no treatment in low and middle income countries (4, 28).

Both epilepsy and malnutrition are important public health problems in sub-Saharan Africa with major medical, sociocultural, and economic implications. The annual incidence of epilepsy in Ethiopia was 64 in 100,000 and age-specific incidence was highest in the group aged 0-9 years. Ten percent had seizures every day, 14% had seizures every week, and 33% had seizures every month. (5, 6)

Malnutrition and neurodisability are both major public health problems in Africa. This happens throughout life and starts with maternal malnutrition affecting fetal neurodevelopment with both immediate and lifelong implications. Macro- and micro-nutrient deficiency can both cause and be caused by neurodisability. (7, 8)

A relationship between epilepsy and malnutrition in low and middle income countries has been suspected for many years. Malnutrition may contribute to the high prevalence of epilepsy in such countries via several mechanisms. However, because of attitudes toward epilepsy and food taboos in sub-Saharan Africa, epilepsy may also contribute to malnutrition. (9)

Malnutrition in epileptic children is due to multiple factors including; inadequate intake as consequence of vomiting, chewing and swallowing difficulty, cognitive impairment and severity and type of underlying neurologic disorder and epileptic drug use. (5, 6) In particular, some drugs affect the regulation of energy balance and appetite with consequent loss (topiramate) or gain (carbamazepine, valporate) of body weight. Phenytoin, phenobarbital, and carbamazepine can interfere with vitamin D metabolism and increase the risk of osteopenia and osteoporosis. (10,11)

1.2. Statement of the Problem

Malnutrition leads to poor quality of life and increased mortality. Even though primary malnutrition is an important problem to be addressed by our society, in some cases the malnutrition could be secondary to some medical disease or these diseases may be a contributing factor, epileptic disorder could be one of the commonest conditions. (12)

In addition to this social rejection, seizure occurrence can be responsible for anxiety, decreased food intake and long-term malnutrition. In most patients with epilepsy, if they had poor control and poor quality of life, it is better to screen for malnutrition especially in low and middle income countries because it has a negative effect on seizure control. The possible mechanisms are like the reduction of the seizure threshold due to biochemical alterations by malnutrition or an immunological vulnerability that result from malnutrition reduces resistance to infection.(12, 13)

The magnitude and factors associated with undernutrition in children with epilepsy are believed to vary by socioeconomic and demographic factors status including age and sex, comorbid condition, clinical presentation, and treatment related factors. Moreover, epilepsy in low and middle income countries is considered as an evil spirit, and children with epilepsy are usually socially isolated and neglected. Some food items are excluded from the diet of children with epilepsy because they are thought to provoke seizure attacks. Thus, the knowledge, attitude, and practice of guardians towards feeding children with epilepsy can also affect the nutritional status in such population. (11, 14)

In patients with poorly controlled epilepsy and disturbed quality of life for patients and guardians, it is worth to screen for and managing under-nutrition, especially in low and middle income countries. (15, 16, 17)

1.3. Rationale of the Study

Comorbid conditions like malnutrition are associated with increased mortality and morbidity in epileptic children with prolonged hospital stay, poor seizure control and poor quality of life. Therefore, identification and timely management of malnutrition and controlling seizure is most important for normal neurocognitive and physical development of the child.

There is a need for regular anthropometric monitoring of children with drug-naive epilepsy with targeted interventions to correct malnutrition in them during the course of epilepsy management. Such anthropometric measurements should commence at the time of starting patients on anti-epileptic drugs or earlier. This will help the managing physician to also manage the underlying malnutrition and investigate and explore the underlying cause.

There are few researches done on epileptic disorder in children and as to our knowledge there is only one study in Ethiopia which assesses magnitude of malnutrition among epileptic children. Having a specific figure of malnutrition and factors associated with increased risk has to be addressed to design interventional policy. This study will be conducted to assess determinant factors affecting magnitude of malnutrition among children with epilepsy and to set recommendations and public health intervention for nutritional screening and nutritional supplementation among children with epileptic disorder.

Given our current state of understanding of malnutrition in epileptic children, a pragmatic and comprehensive approach may be the most reasonable:

- (1) Active screening of patients with epilepsy for malnutrition
- (2) Identifying associated factor of malnutrition in those children with epilepsy
- (3) Individualized dietary interventions to ensure that they are consuming sufficient calories to meet their energy needs, to optimize cellular function and neurodevelopment.

2. Literature Review

A study was conducted in India from September 2017 to August 2018 among children with generalized epilepsy and healthy controls to investigate their anthropometric profile and nutritional status. The result showed significantly higher malnutrition in cases than in controls. But there was insignificant difference in the socioeconomic status and educational levels between the parents of cases and controls. (18)

In a population-based study conducted by medical university of South Carolina, United States to assess comorbidities of epilepsy beyond seizure, nutritional deficiency were the prevalent somatic comorbidity overall and strongly associated with epilepsy. (19)

In a study done on children with refractory epilepsy treated at the Child Neuropsychiatry Department, Casimiro Mondino Foundation (Pavia, Italy) (from 1995 to 2000), based on anthropometric measurements; 40% of children were malnourished and 24% has wasting. The degree of neurological impairment and the presence of feeding problems were correlated with body weight. The nutritional status was worse in the more disabled children. Many children with refractory epilepsy would benefit from individual nutritional assessment and management as part of their overall care. (20)

An Italian case series assessed nutritional problems in children with neuromotor disabilities affected by cerebral palsy, epileptic encephalopathy, and severe psychomotor developmental delay. More than 44% individuals of the study population were at risk of malnutrition, with associated feeding difficulties, progressive depletion of weight and reduced daily calorie intake. (21)

A cross-sectional prospective study done in Turkey aimed to determine the prevalence and severity of malnutrition with respect to underlying diagnosis and co-morbid nutrition and feeding related problems in pediatric neurology outpatients. The prevalence of acute malnutrition was 17.7%. Acute (mild in majority of cases) malnutrition rate was 13.8% in patients with epilepsy. (23)

A Case-control study was conducted in Iran during 2013-2014 in patients with refractory epilepsy. BMI for age was less in epileptic patients. There was no significant difference between sex groups regarding anthropometric indices. There was significant difference between height and predominant time of epilepsy, results showed no significant relation between types of epilepsy and frequency of epilepsy with anthropometric indices. (24)

Nationwide registry-based study in Norway from both outpatient consultations and hospitalized children done from 2008 to 2013 to assess comorbidity and childhood epilepsy, the prevalence of malnutrition and feeding difficulty were high. Malnutrition and eating difficulty were 1 out of 6 in the children with epilepsy overall. (25)

A Population-based study was done to assess association between childhood disability and malnutrition among children aged <18 years living in Bangladesh from 2017 to 2018. The result showed that the prevalence of underweight and stunting was highest among children with epilepsy, it was 75.9% and 79.4% respectively. In addition it showed the high prevalence of malnutrition among these children was associated with educational level and socioeconomic status of the parents.(26)

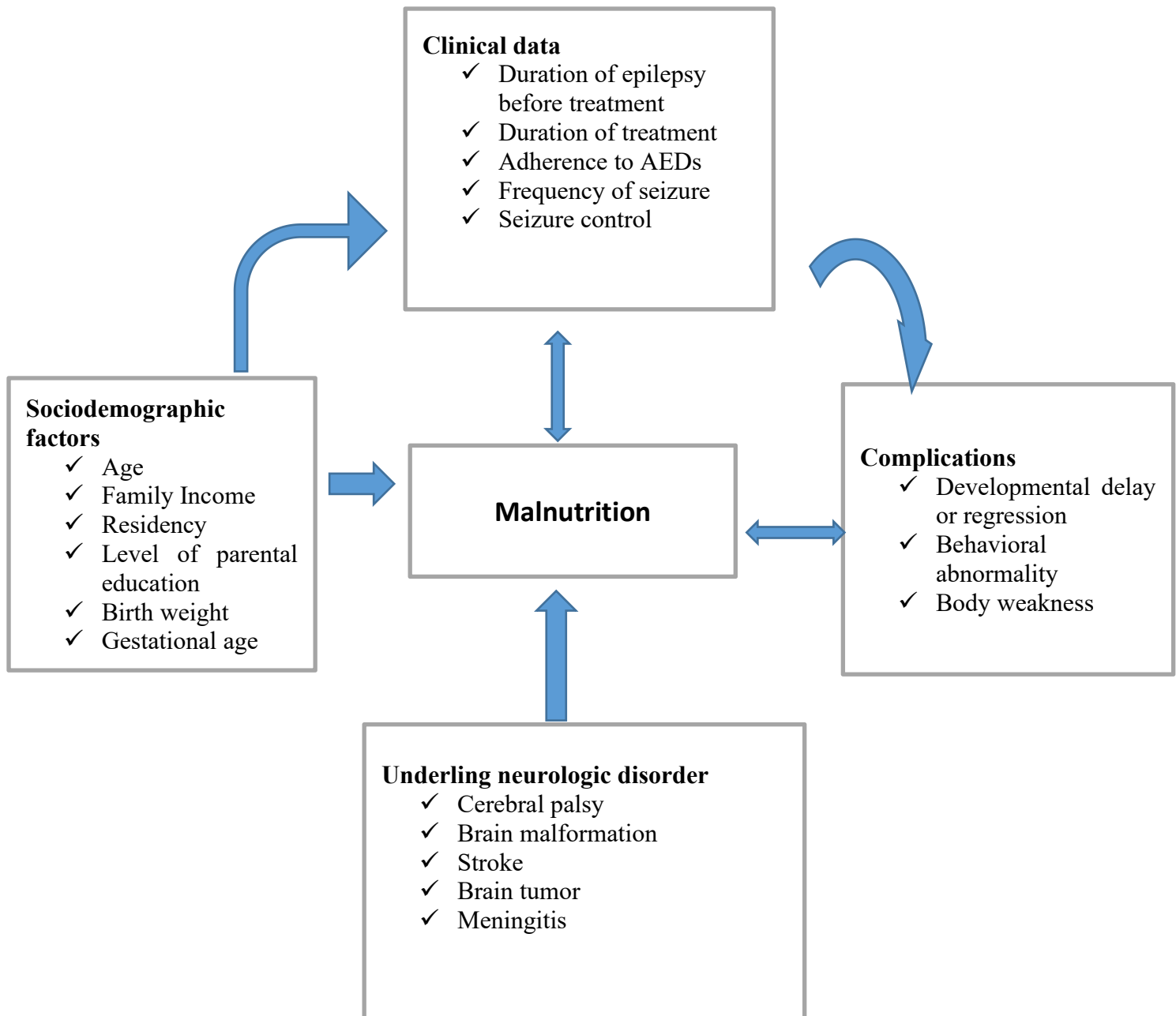
A cross-sectional prospective study conducted in a Turkey tertiary pediatric outpatient neurology clinic among children with neurological disabilities in 2015 showed 13.8% epileptic children were found to have malnutrition with different severity mild acute malnutrition, moderate acute malnutrition and sever acute malnutrition (10.6%, 2.9% and 0.2%) respectively. Prolonged meal time(> 30 min), stressful meal time to child or parent, lack of weight gain not just weight loss and cough during feeding were associated with increased risk of malnutrition.(27)

A descriptive cross-sectional study was done to determine the prevalence of malnutrition among children aged 6 months to 18 years with epilepsy, attending the Neurology Clinic of the University of Nigeria Teaching Hospital. The overall prevalence of malnutrition was 22.5%. Wasting, stunting, overweight, and obesity accounted for 5.8%, 9.2%, 10.8%, and 5.8% of malnutrition rates, respectively. Some participants had more than one form of malnutrition. There were no statistically significant differences between various forms of malnutrition and the gender, age group, and socio-economic status of study participants. (28)

A matched population-based cross-sectional survey was performed in rural areas of Benin among patients with epilepsy and controls. The prevalence of malnutrition was higher in cases than in controls (22.1% vs. 9.2%). Social factors were significantly different between cases and controls. Feeding difficulties were more frequent and health status was worse in cases. (29)

A single-center cross-sectional study was conducted at the pediatric neurology clinic of the University of Gondar Comprehensive Specialized Hospital, Ethiopia. Anthropometric measurements taken and undernutrition defined based on the world health organization criteria. The overall magnitude of undernutrition was 141(59%) of which 89(63.1%) had moderate to severe stunting, 91(64.5%) moderate to severe wasting, and 39(27.7%) had both. Being male, low paternal level of education, presence of delay in motor development, and gum hyperplasia, were significantly associated with undernutrition. (30)

Conceptual frame work



3. Objectives

3.1. General Objective

- ✓ To Assess the prevalence of malnutrition and associated factors among epileptic children having follow up at neurology clinic of St Paul Hospital Millennium Medical College, Ethiopia, 2023

3.2. Specific Objectives

- ✓ To determine the prevalence of Malnutrition among Epileptic Children having Follow up at neurology clinic of St Paul Hospital Millennium Medical College, Ethiopia, 2023.
- ✓ To identify Factors associated with malnutrition in Epileptic Children Having Follow up at neurology clinic of St Paul Hospital Millennium Medical College, Ethiopia, 2023.

4. Methodology

4.1. Study design and period

Hospital based cross sectional study was conducted prospectively among epileptic children aged 3 months to 18 years, having follow up at pediatrics neurology clinic of St Paul millennium medical college from August 01/2023 to October 30/2023 G.C.

4.2. Study area

The study was conducted at St Paul millennium medical college (SPHMMC). SPHMMC is one of the most ancient teaching hospitals in Ethiopia. It is the second largest tertiary hospitals in the capital Addis Ababa with a catchment population of more than 5 million. In addition to an inpatient capacity of more than 700 beds, on average 1200 emergency and outpatient clients are seen daily in the hospital. The pediatrics department has 50, 40, 41 and 6 beds at NICU, emergency, ward and pediatric ICU, respectively. The team is composed of sub-specialists and general pediatricians. Pediatrics neurology patients are being seen at PEU, general wards and follow up clinics. On average 250 to 300 neurologic cases are being seen each month with a half a day schedule three times per week base. The team is composed of two pediatric neurologist, residents, medical interns and nurses.

4.3. Source and Study population

4.3.1. Source population

The source population were all patients visiting SPHMMC pediatric follow up clinic.

4.3.1. Study population

Those children age 3 months to 18 years, with follow up for epileptic disorder and visiting SPHMMC from August 01/2023 to October 30/2023 G.C.

4.4. Eligibility Criteria

4.4.1. Inclusion criteria

All patients 3 months to 18 years of age diagnosed with epilepsy and having follow up at SPHMMC neurology clinic during the study period were included.

4.4.2. Exclusion criteria

Those children with concomitant non-neurologic medical problems.

4.5. Sample size and sampling technique

4.5.1. Sample size Determination

The required minimum sample size was calculated using a single population proportion formula. Taking the population proportion as 50% the sample size is determined as follows:

$$n = (Z_{\alpha/2})^2 \times P (1 - P) / d^2$$

$$n = (1.96)^2 \times 0.5(1-0.5) / (0.05)^2 = 384.$$

After adding 10% for non-respondents the final sample size was 422 epileptic patients.

$$N_f = 422$$

Where:

N_f = final sample size

P = was the proportion of children with epilepsy and malnutrition taken as 50%

$Z_{\alpha/2}$ = Critical value at 95% confidence level of certainty (1.96)

d = the margin of error between the sample and the population = 5%

4.5.2. Sampling technique

Every epileptic child was included until the sample size is reached.

4.6. Study variables

4.6.1. Dependent variable

- ✓ Malnutrition

4.6.2. Independent variables

- ✓ Socio-demographic factors
- ✓ Neurologic comorbidities other than epilepsy (Cerebral palsy, developmental delay, psychiatric illness)
- ✓ Duration of illness before treatment,
- ✓ Duration of treatment
- ✓ Adherence to follow up and anti-seizure medications
- ✓ Seizure control
- ✓ Frequency of follow up, number of medications
- ✓ Complementary feeding, feeding problems, sunlight exposure

4.7. Operational definitions

- ✧ **Epilepsy:** The presence of two or more seizure 24hr apart or single seizure with possibility of recurrence or the diagnosis of a certain epileptic syndrome.
- ✧ **Malnutrition:** children who fulfill the WHO diagnostic criteria of malnutrition.
- ✧ **Good adherence:** patient is taking > 85% of monthly prescribed ASDs.
- ✧ **Poor adherence:** patient is taking < 85% of monthly prescribed ASDs. (2)
- ✧ **Neurologic Comorbidities:** neurologic diseases other than epilepsy
- ✧ **Good seizure control :** Maximum of three seizure episodes in the last 3 months after treatment initiation.
- ✧ **Poorly controlled epilepsy:** more than four seizure episodes in the last three months after treatment initiation and needed treatment escalation/change.
- ✧ **Feeding difficulties:** the presence of difficulties with chewing or swallowing of food and/or regurgitation after feeding.
- ✧ **Low vitamin D level:** A serum vitamin D less than 30ng/ml (<20ng/ml is deficient , 20-30ng/ml is insufficient).

4.8. Data Collection Instrument

The data source for the study was patients medical records and from the care giver or guardian. A structured and pretested questionnaire was used to collect data. The Questionnaire includes: sociodemographic factors, clinical parameters, investigation results.

4.9. Data collection Procedure

Selection and training of data collectors was made, with training conducted for 3 data collectors (residents) for 1 day on the objectives of the study and other 2 days how to collect the data.

Questioner was collected by trained residents working at the area. Demographic data, clinical history, physical finding including anthropometric evaluation was assessed and filled in the questionnaire. Clinical pallor and gross signs of rickets were checked with values of Complete blood count (CBC) and serum vitamin D level determined during routine follow up within 3 months prior or during the study period were taken.

4.10. Data quality control

Pretest was done among 5% of the total sample size. Principal investigator was also supervising the data collection process throughout the collection period.

4.11. Data analysis

The data was cleaned and refined by principal investigator among randomly selected patients during data collection. The collected data was coded and checked for completeness and entered to Epi-Info version 7.0 and exported to SPSS version 26.0 for analysis. Descriptive statistics like frequency and mean were used. Binary and multivariate logistic regression model were fitted to identify factors associated with malnutrition among patients on epilepsy follow up.

Odds ratio with 95 % confidence interval was estimated to determine the strength of association. Variables with odds ratio having a P-value of < 0.05 in multivariate analysis were considered as an independent predictor of malnutrition.

4.12. Ethical Consideration

The ethical clearance was obtained from SPHMMC ethical review committee, written consent obtained from hospital administration, and confidentiality of the information ensured using codes rather than names during registering data. During data collection, the data collector clearly explained the purpose of the research to the participants and informed consent was obtained from each participant. Participants were also informed that participation was on voluntary basis and name was not disclosed. Children with malnutrition were linked to nutritional rehabilitation center.

4.13. Dissemination and utilization of the result

After being completed the research paper will be submitted and presented in the department of Pediatrics and child health, SPHMMC. After incorporation of comments and suggestions, if possible, the findings will be presented in different seminars, meetings and workshops and will also be published in peer reviewed international and national journals.

5. Result

5.2. Socio-demographic characteristics

We studied 422 children with epilepsy who visited the pediatric neurology clinic during the study period with a response rate of 100%. The mean ($\pm$ SD) age was 7.32 ± 0.43 years, with a male to female ratio of 1.5: 1. From a total of 422 study participants, 184 (43.6%) were from five year to ten years (Table 1). About 254 (60.2%) were males.

The Gestational age at birth was mainly term, 389 (92.2%) (Table 1), and 60.4% of the respondents had normal birth weight. About 71.6% of mothers were educated up to primary and above. The paternal educational status parallels that of mother's. From the respondents most of them were urban residents (80.1%). Only 14.5% of the families had an average monthly income of less than five-thousand ETB. In about 63.5% of the cases the family size was between four and seven.

Table 1: Sociodemographic characteristics of children with epilepsy at St Paul hospital millennium medical college, August 01-October 30/2023 (n=422)

Variables	Category	Frequency	Percent
Age	< 1year	18	4.3
	1-5 years	155	36.7
	5-10 years	184	43.6
	10-18 years	65	15.4
Sex	Male	254	39.8
	Female	168	60.2
GA at birth	Preterm	29	6.9
	Term	389	92.2
	Unknown	4	0.9
Residence	Urban	338	80.1
	Rural	84	19.9
Maternal education	Unable to write and read	44	10.4
	Able to read and write	76	18.0
	Primary and above	302	71.6
Paternal education	Unable to write and read	33	7.9
	Able to read and write	89	21.1
	Primary and above	300	71.0
Family size	<4	63	15.1
	5-7	271	63.5
	>7	88	21.2

5.2. Clinical and treatment-related characteristics

The duration of illness before treatment initiation was assessed, in 225 (53.3%) children anti-seizure drug was initiated after six to two years of seizure onset (Table 2). During the study period, 288 (68.2%) took anti-seizure treatment for more than one year.

The average frequency of follow up was variable where 346 (82%) children came every two to three months. The seizure control was good in 298 (70.6%) of epileptic children on follow up while the rest had poor control. About 386 (91.5%) children had good adherence to follow up and drugs. Neurologic comorbid illnesses other than epilepsy were also assessed, 78 (18%) and 105 (24.8%) children had cerebral palsy and developmental delay, respectively. Two-hundred-twenty-nine (54.3%) of them were taking single medication while 175 (41.4%) and 18 (4.3%) were taking two and three medications, respectively.

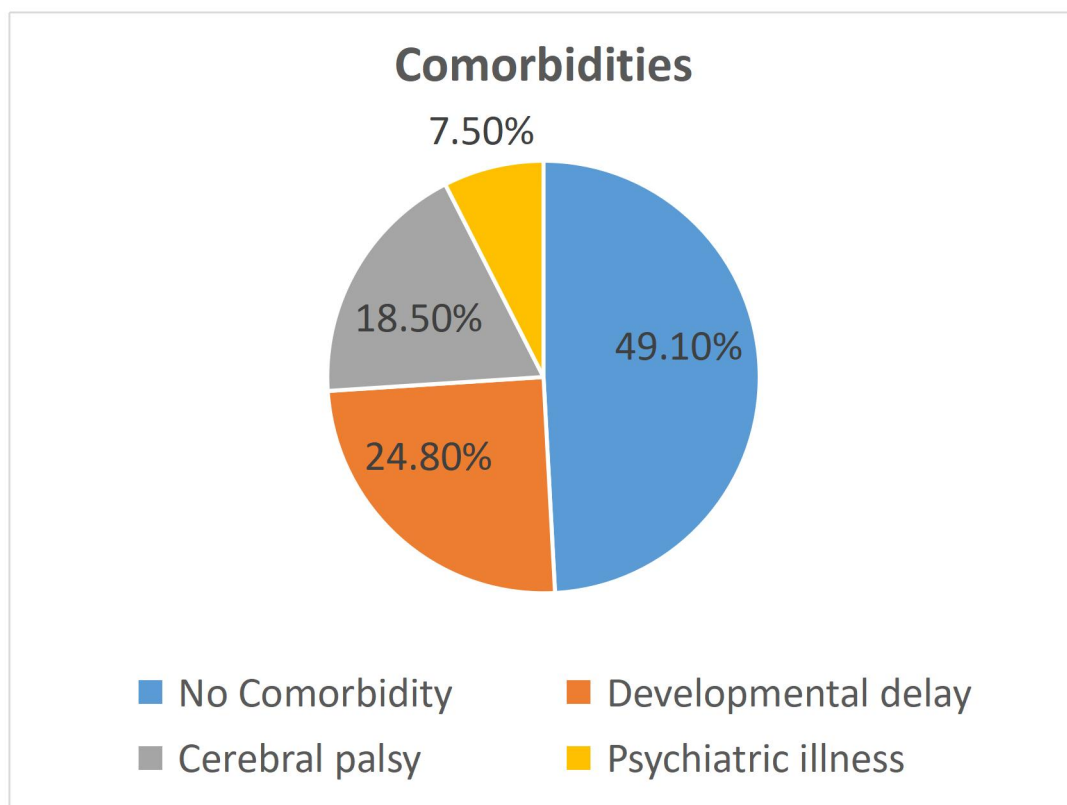


Figure 1 Neurologic comorbidities other than epilepsy among epileptic children having follow up at SPHMMC neurology clinic, from August 1-October 30/2023 GC, Ethiopia.

Table 2: Clinical characteristics of children with epilepsy at St Paul hospital millennium medical college, August 01-October 30/2023(n=422)

Variables	Category	Frequency	Percent
Duration of illness before diagnosis	< 6 months	103	24.4
	6-12 months	111	26.3
	12-24 months	114	27.0
	> 2 years	94	22.3
Duration after treatment initiation	< 6 months	65	15.4
	6-12 months	69	16.4
	12-24 months	122	28.9
	> 2 years	166	39.3
Seizure control	Good	298	70.6
	Poor	124	29.4
Average frequency of follow up	Monthly	40	9.5
	Every 2 months	125	29.6
	Every 3 months	221	52.4
	Every >3 months	36	8.5
Adherence to follow up and drugs	Good	386	91.5
	Poor	36	8.5
Number of anti-seizure medications	One	229	54.3
	Two	175	41.4
	Three and above	18	4.3
Comorbid illnesses	Cerebral palsy	78	18.5
	Developmental delay	105	24.8
	Psychiatric illness	32	7.5
	No comorbid illness	207	49.1

5.3. Nutrition related responses/findings

From 422 children screened for malnutrition, the overall prevalence of malnutrition was 38.6%. From all children included in the study, 56 (13.3%), 71 (16.8%) and 41 (9.7%) had severe wasting, underweight and stunting, respectively. While 60 (14.2%), 62 (14.7%) and 57 (13.5%) had moderate wasting, underweight and stunting, respectively. About 30 (7.1%) children had stunting alone, 68 (16.1%) had both wasting and stunting. And 45 (10.7%) children had microcephaly(<-3 SD). From children for whom vitamin D level determined during their routine follow up (n= 268), 49 (18.3%) were deficient for vitamin D, 97 (36.2%) children had vitamin D insufficiency. But only one third of patients had clinical evidence of rickets. From the revised available CBC results (n= 401), 40 (10.0%) had anemia with low MCV for age.

From the total of 422 participants, feeding difficulties (like problems with chewing food, swallowing and regurgitation) were reported in 55 (13%) children.

Table 3: Nutritional assessment of children with epilepsy at St Paul hospital millennium medical college, August 01-October 30/2023 (n=422)

Variables	Category	Frequency	Percent
Feeding difficulties	Yes	55	13.0
	No	367	87.0
MUAC/BMI/WFH	<-3 SD	56	13.3
	-3 to -2 SD	60	14.2
	>+3 SD	4	0.9
	Normal	302	71.6
WFA	Severe under weight	71	16.8
	Moderate under weight	62	14.7
	Normal	299	68.5
HFA	Severe stunting	41	9.7
	Moderate stunting	57	13.5
	Normal	324	76.8
HC/Age	<-3 SD	45	10.7
	-3 to -2 SD	22	5.2
	>+3 SD	2	0.5
	Normal	353	83.6
Vitamin D level (n= 268)	Insufficient	97	36.2
	Deficient	49	18.3
	Normal	122	45.5
Hematocrit (n= 401)	Normal	361	90.0
	Anemia (low MCV)	40	10.0

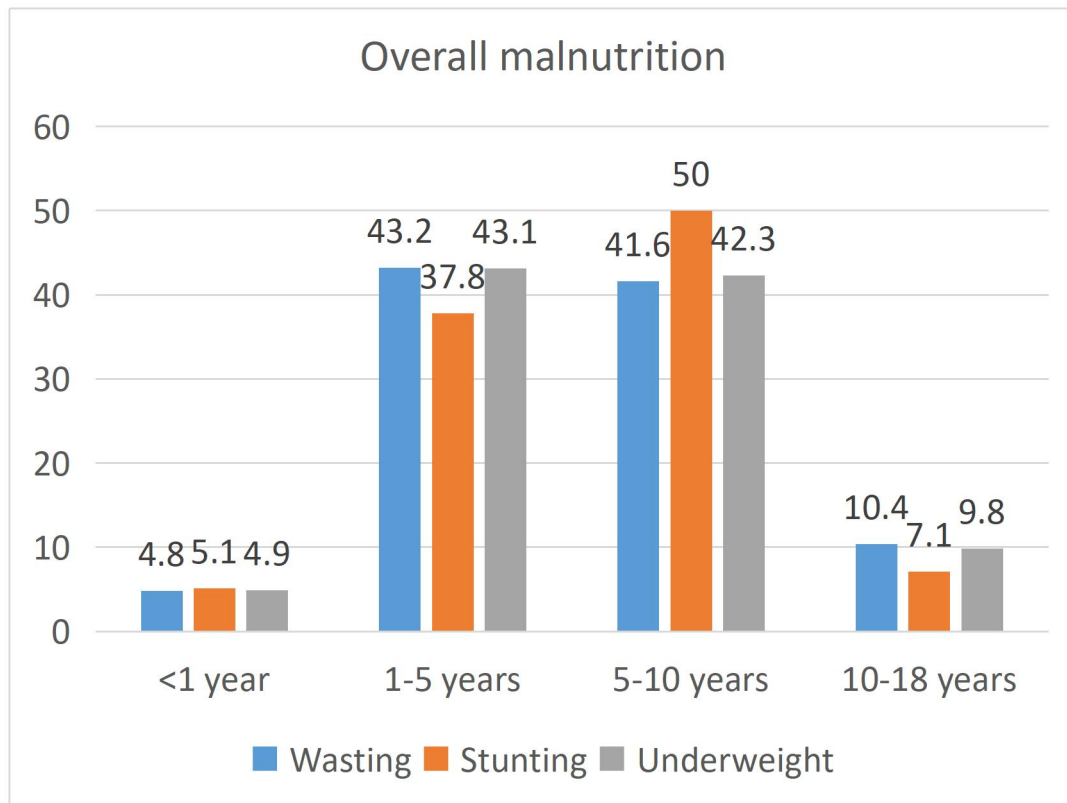


Figure 2: Overall prevalence of malnutrition among epileptic children on follow up at SPHMMC neurology clinic, from August 1-October 30/2023 GC, Ethiopia.

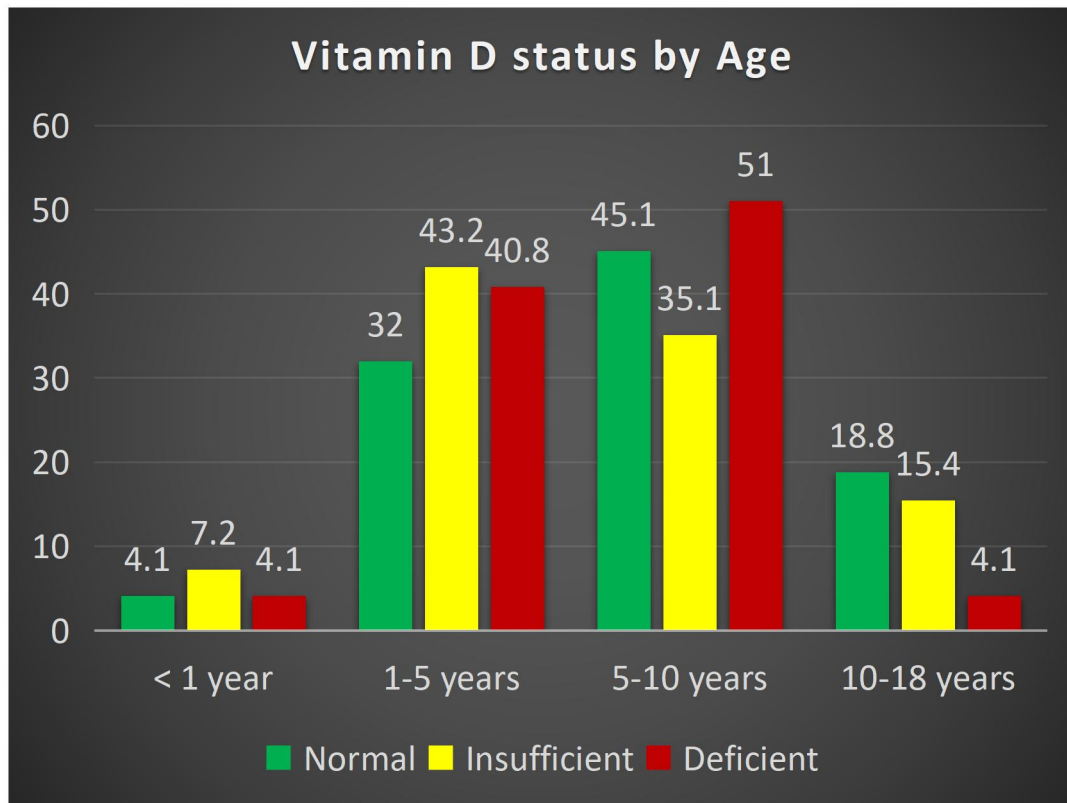


Figure 3: Vitamin D status of epileptic children on follow up at SPHMMC neurology clinic, from August 1-October 30/2023 GC, Ethiopia

Table 4: Binary logistic analysis of selected factors associated with malnutrition among epileptic children at SPHMMC pediatric neurology follow-up clinic, 2023(n= 422)

Variable	Category	Undernutrition		COR(95%CI)	P-value
		Yes	No		
No of medications	Two or more	72	123	1.922(1.259-2.934)	0.002
	Single	53	174	1	
Seizure control	Poor	56	68	2.733 (1.752-4.263)	0.000
	Good	69	229	1	
Adherence	Poor	16	20	2.033 (1.016-4.068)	0.045
	Good	109	277	1	
Comorbidities	Yes	83	92	4.403(2.821-6.873)	0.000
	No	42	205	1	
Residence	Rural	27	57	1.160(0.693-1.941)	0.572
	Urban	98	240	1	
Maternal education	Unable to write and read	11	33	0.667 (0.385-1.157)	0.150
	Able to read and write	25	51		
Paternal education	Primary and above	89	213	1	0.611
	Unable to write and read	9	24	0.857 (0.473-1.552)	
	Able to read and write	17	72		
	Primary and above	99	201	1	
Family size	<5	25	38	1	0.060
	> 5	100	259	0.587 (0.337-1.022)	
Feeding difficulties	Yes	42	13	11.055 (5.666-21.569)	0.000
	No	83	284	1	

Table 5: Multivariate logistic analysis of factors associated with malnutrition among epileptic children at SPHMMC pediatric neurology follow-up clinic, 2023(n= 422)

Variable	Category	Undernutrition		AOR (95% CI)	P-value
		Yes	No		
Adherence	Poor	16	20	2.033 (1.612-10.567)	0.008
	Good	109	277	1	
Comorbidities	Yes	83	92	2.517(1.296-6.902)	0.020
	No	42	205	1	
Number of medications	Two or more	72	123	1.280 (1.011-15.286)	0.215
	Single	53	174	1	
Seizure control	Poor	56	68	1.457 (0.843-2.518)	0.177
	Good	69	229	1	
Feeding difficulties	Yes	42	13	5.176 (2.441-10.976)	0.000
	No	83	284	1	

6. Discussion

6.1. Prevalence of malnutrition among epileptic children

In this study, the overall prevalence of undernutrition in children with epilepsy was 38.6%. The finding in our study is higher than the findings in similar studies done in Turkey (13.8%), Norway (16.6%), at Neurology Clinic of the University of Nigeria Teaching Hospital (22.5%), Benin (22.1%) (22, 24, 26, 28, 29). This difference can be attributed to the socio-economic and cultural differences between the study populations. Children with epilepsy in low and middle income countries are usually outcast from society, and some food items are excluded from the diets of epileptic patients. Moreover, prevention, screening and treatment of nutritional disorders in children with epilepsy and overall epileptic care in high income country settings is better than the care in low and middle income countries.

The finding in our study is also higher than the finding in a database consolidating the result of 13 epidemiological studies of epileptic children done in sub-Saharan African countries (25.4%) which included a larger sample size that might cause a significant difference in the magnitude of malnutrition between the two studies.

However, our finding was lower than the findings of a similar study done at the University of Gondar comprehensive specialized hospital (59%) (30) where almost half of the participants were rural residents in whom early treatment and follow up is unlikely. And also lower than a similar study done in Bangladesh where the prevalence of underweight and stunting was 75.9% and 79.4% respectively. (25). This could be due to difference in the anthropometric parameter used in the study (they used weight for age as an indicator of wasting). We employed BMI/age, WFH and/or MUAC/ age.

From children for whom vitamin D level determined during their routine follow (n=268) vitamin D was found low in 54.5% children (of them one third had vitamin D deficiency). This finding is lower than the report from USA (n=78), Saudi(n=159) and Australian(n=111) children where 75%, 73.5% and 63 % of epileptic children had low vitamin D level, respectively. The low vitamin D level was associated with poly-therapy in the above studies where most children were taking but not in our study. But higher than the result in Malaysian children, 42.2% (n=244). (31,32,33,34).

6.2. Factors associated with malnutrition

After a multivariate logistic analysis factors like parental educational status, number of anti-seizure medications, gender, age and family size were not found to have significant association with malnutrition in epileptic children. The same finding was reported in a similar study done at the Neurology Clinic of the University of Nigeria Teaching Hospital where no statistically significant differences was seen between various forms of malnutrition and the gender, age group, and socio-economic status of study participants (28).

Epileptic Children with poor adherence to their follow up and anti-seizure medications were two times at risk for malnutrition than those with good adherence to follow up and medications (AOR= 2.033 (95% CI: 1.612-10.567, p-value= 0.008). This is due to the lack of timely nutritional screening and early interventions for imminent undernutrition. And the severe forms of acute malnutrition can be reduced in part with appropriate adherence to medical follow up.

The risk of malnutrition in children with out neurologic comorbidities other than epilepsy was lower than those with other comorbidities (AOR= 0.517(95% CI: 0.296-0.902, p-value= 0.02). This was also seen in a similar study conducted at the pediatric neurology clinic of the University of Gondar Comprehensive Specialized Hospital, where the presence of comorbidities like delay in motor development was associated with increased prevalence of malnutrition (30). The same study in Italy showed higher odds of malnutrition in those with neurologic impairments on top of epilepsy (20).

The presence of feeding difficulties (problems of chewing food, swallowing and vomiting after feeding) were significantly associated with increased prevalence of malnutrition in epileptic children (AOR= 5.176 (95% CI: 2.441-10.976, p-value= 0.000). This is in line with a similar study done in Benin (29), Turkey tertiary pediatric outpatient neurology clinic (22) and Italy (20) where feeding difficulties were associated with increased risk of malnutrition in epileptic children (26). Those difficulties are more common in those with cerebral palsy and developmental delay where nutritional intake is likely to be inadequate resulting in malnutrition.

7. Strength and Limitation of study

7.1. Strength

The study sample size is fair and at least vitamin D status was assessed which is likely the first in looking at micro-nutrient deficiency in epileptic children in our setup.

7.2. Limitation

This study has some limitations.

It would have been better if it was done in case-control design to compare the magnitude of malnutrition with the non-epileptic children.

The baseline nutritional status of epileptic children before the onset of the illness and treatment initiation is unknown and it is difficult to exactly see the cause and effect relation between epilepsy and malnutrition.

8. Conclusion and recommendation

8.1. Conclusion

The study result showed that the overall magnitude of malnutrition among epileptic children at SPHMMC pediatric neurology follow-up clinic was 36.7%, where 29.6% had moderate to severe wasting. The prevalence of malnutrition was significantly associated with the presence of comorbidities other than epilepsy, problems with feeding, feeding by self and poor adherence to followup and anti-seizure medications.

8.2. Recommendation

Individualized dietary interventions to ensure that they are consuming sufficient calories to meet their energy needs, to optimize cellular function and neurodevelopment.

Our routine follow ups at neurology clinic must be holistic and beyond drug refill.

The importance of proper counseling on good adherence to follow up and anti-seizure medications can not be overlooked.

Children with epilepsy and associated severe neurologic impairment like cerebral palsy may need the greatest nutritional support to the extent of alternative feeding routes like gastrostomy tubes.

References

1. Tekile, A.K., Woya, A.A. and Basha, G.W., 2019. Prevalence of malnutrition and associated factors among under-five children in Ethiopia: evidence from the 2016 Ethiopia Demographic and Health Survey. *BMC research notes*, 12(1), pp.1-6.
2. Ethiopian Mini Demographic and Health Survey (mEDHS), 2019, Addis Ababa
3. Newton, C.R. and Garcia, H.H., 2012. Epilepsy in poor regions of the world. *The Lancet*, 380(9848), pp.1193-1201.
4. Carpio, A. and Hauser, W.A., 2009. Epilepsy in the developing world. *Current neurology and neuroscience reports*, 9(4), p.319.
5. Kassie, G.M., Kebede, T.M. and Duguma, B.K., 2014. Knowledge, attitude, and practice of epileptic patients towards their illness and treatment in Jimma University specialized hospital, Southwest Ethiopia. *North American journal of medical sciences*, 6(8), p.383.
6. Beyene, A., Ayalew, A.F., Mulat, G., Simachew Kassa, A. and Birhan, T., 2020. The treatment outcomes of epilepsy and its root causes in children attending at the University of Gondar teaching hospital: A retrospective cohort study, 2018. *PloS one*, 15(3), p.e0230187.
7. Muhigwa, A., Preux, P.M., Gerard, D., Marin, B., Boumediene, F., Ntamwira, C. and Tsai, C.H., 2020. Comorbidities of epilepsy in low and middle-income countries: systematic review and meta-analysis. *Scientific reports*, 10(1), p.9015.
8. Kerac, M., Postels, D.G., Mallewa, M., Jalloh, A.A., Voskuil, W.P., Groce, N., Gladstone, M. and Molyneux, E., 2014, March. The interaction of malnutrition and neurologic disability in Africa. In *Seminars in pediatric neurology* (Vol. 21, No. 1, pp. 42-49). WB Saunders.
9. Crepin, S., Houinato, D., Nawana, B., Avode, G.D., Preux, P.M. and Desport, J.C., 2007. Link between epilepsy and malnutrition in a rural area of Benin. *Epilepsia*, 48(10), pp.1926-1933.
10. da Silva, D.C.G., da Cunha, M.D.S.B., de Oliveira Santana, A., dos Santos Alves, A.M. and Santos, M.P., 2022. Malnutrition and nutritional deficiencies in children with cerebral palsy: a systematic review and meta-analysis. *Public Health*, 205, pp.192-201.

11. Wasterlain, C.G., 1976. Developmental effects of seizures: role of malnutrition. *Pediatrics*, 57(2), pp.197-200.
12. Baskind, R. and Birbeck, G.L., 2005. Epilepsy-associated stigma in sub-Saharan Africa: the social landscape of a disease. *Epilepsy & Behavior*, 7(1), pp.68-73.
13. Aydin, K., Akbas, Y., Unay, B., Arslan, M., Cansu, A., Sahin, S., Dilber, C., Gungor, O., Aksoy, A., Yuksel, D. and Gurkas, E., 2018. A multicenter cross-sectional study to evaluate the clinical characteristics and nutritional status of children with cerebral palsy. *Clinical nutrition ESPEN*, 26, pp.27-34.
14. Tekile, A.K., Woya, A.A. and Basha, G.W., 2019. Prevalence of malnutrition and associated factors among under-five children in Ethiopia: evidence from the 2016 Ethiopia Demographic and Health Survey. *BMC research notes*, 12(1), pp.1-6.
15. Hackett, R. and Iype, T., 2001. Malnutrition and childhood epilepsy in developing countries. *Seizure*, 10(8), pp.554-558.
16. Babikir, H.E. and Singh, P., 2020. Neurology of Nutritional Disorders. *Clinical Child Neurology*, pp.483-527.
17. Crepin, S., Godet, B., Chassain, B., Preux, P.M. and Desport, J.C., 2009. Malnutrition and epilepsy: a two-way relationship. *Clinical Nutrition*, 28(3), pp.219-225.
18. Fong CY, Kong AN, Poh BK, Mohamed AR, Khoo TB, Ng RL, Noordin M, Nadarajaw T, Ong LC. Vitamin D deficiency and its risk factors in Malaysian children with epilepsy. 2016 Aug;57(8):1271-9
19. Ahmed, M. E., Tiwari, S., Verma, D. K., Bajpai, M., Koonwar, S., & Kumar, N. (2019). Anthropometric profile and nutritional status in children with generalized epilepsy. *Int J Contemp Med Res [IJCMR]*, 6(5), 4-7.
20. Selassie, A.W., Wilson, D.A., Martz, G.U., Smith, G.G., Wagner, J.L. and Wannamaker, B.B., 2014. Epilepsy beyond seizure: a population-based study of comorbidities. *Epilepsy research*, 108(2), pp.305-315.
21. Bertoli, S., Cardinali, S., Veggiotti, P., Trentani, C., Testolin, G. and Tagliabue, A., 2006. Evaluation of nutritional status in children with refractory epilepsy. *Nutrition journal*, 5(1), pp.1-9
22. Sangermano, M., D'Aniello, R., Massa, G., Albano, R., Pisano, P., Budetta, M., Scuccimarra, G., Papa, E., Coppola, G. and Vajro, P., 2014. Nutritional problems in children with neuromotor disabilities: an Italian case series. *Italian journal of pediatrics*, 40(1), pp.1-5.

23. Tekin, H., Tekgül, H., Yılmaz, S., Arslangiray, D., Reyhan, H., Serdaroğlu, G. and Gökben, S., 2018. Prevalence and severity of malnutrition in pediatric neurology outpatients with respect to underlying diagnosis and co-morbid nutrition and feeding related problems. *The Turkish Journal of Pediatrics*, 60(6), pp.709-717.
24. Aminzadeh, V., Dalili, S., Ashoorian, Y., Kohmanae, S. and Rad, A.H., 2016. Anthropometric indices in children with refractory epilepsy. *Iranian Journal of Child Neurology*, 10(1), p.47
25. Aaberg, K.M., Bakken, I.J., Lossius, M.I., Lund Søråas, C., Håberg, S.E., Stoltenberg, C., Surén, P. and Chin, R., 2016. Comorbidity and childhood epilepsy: a nationwide registry study. *Pediatrics*, 138(3).
26. Jahan, I., Karim, T., Al Imam, M.H., Das, M.C., Ali, K.M., Muhit, M. and Khandaker, G., 2019. Childhood disability and nutrition: Findings from a population-based case control study in Rural Bangladesh. *Nutrients*, 11(11), p.2728.
27. Léonard, M., Dain, E., Pelc, K., Dan, B. and De Laet, C., 2020. Nutritional status of neurologically impaired children: Impact on comorbidity. *Archives De Pédiatrie*, 27(2), pp.95-103.
28. Aronu, A., Uwaezuoke, N., Bisi-Onyemaechi, A., Ubesie, A. and Ojinnaka, N., 2022. Nutritional status of children with epilepsy, attending the Pediatric Neurology Clinic of University of Nigeria Teaching Hospital, Enugu. *International Journal of Medicine and Health Development*, 27(1), pp.63-63.
29. Crepin, S., Houinato, D., Nawana, B., Avode, G.D., Preux, P.M. and Desport, J.C., 2007. Link between epilepsy and malnutrition in a rural area of Benin. *Epilepsia*, 48(10), pp.1926-1933.
30. Genet, G.B., Teshager, N.W. and Toni, A.T., 2022. Six in ten children with epilepsy visiting the University of Gondar comprehensive specialized hospital were undernourished: a cross-sectional study. *BMC nutrition*, 8(1), p.112.
31. Al Khalifah R, Hamad MH, Hudairi A, Al-Sulimani LK, Al Homyani D, Al Saqabi D, Bashiri FA. Prevalence and Related Risk Factors of Vitamin D Deficiency in Saudi Children with Epilepsy. *Children (Basel)*. 2022 Nov 5;9(11):1696.
32. Fong CY, Riney CJ. Vitamin D deficiency among children with epilepsy in South Queensland. *J Child Neurology*. 2014 Mar;29(3):368-73.
33. Shellhaas RA, Barks AK, Joshi SM. Prevalence and risk factors for vitamin D insufficiency among children with epilepsy in USA. *Pediatric Neurology*. 2010 Jun;42(6):422-6.

Annex

Consent form

A questionnaire prepared to assess the prevalence of malnutrition and associated factors among epileptic children having follow up at neurology clinic of St Paul Hospital Millennium Medical College, Ethiopia, 2023.

Hello, how are you?

My name is Dr Yihalem Abebe, a postgraduate student from SPHMMC, department of pediatrics and child health. Now I am collecting data from children with epilepsy coming to SPHMMC, pediatric neurology follow up clinic.

The purpose of this questionnaire is to gather information about the prevalence of malnutrition and associated factors among children with epilepsy. The research will be beneficial for the participants for the future better nutritional assessment during clinic follow up visits among patient with epilepsy and improve the quality of life. The results of the study will be used as a base line to improve health related quality of life. We will ask you a series of questions which will take about 15 minutes and then there will be measurements on your weight, height, head and upper arm circumferences. Your willingness to answer all of the questions would be appreciated. Your genuine response to these questions will help for the correct findings of the study. Your answers will be kept confidential and we will not write your name in the questionnaire. You have the right not to respond to any of the questions and you can interrupt at any point during interview. If you have any question, don't hesitate to ask the interviewer.

Would you agree to participate in the study?

Yes _____ No _____

If yes, continue to the next. If no, skip to the other participant

Respondent code ----- Date of interview-----

Interviewer name-----Signature-----

Supervisor name ----- Signature -----

Thank you for your cooperation!

Questionnaire

Part 1: Sociodemographic data

S.No	Questions	Coding Categories	Code
100	sex	Female	1
		Male	2
101	Age	_____ years -----in months (if < 2yrs)	
102	Gestational age at birth	Term/Preterm	
103	Birth weight (if known)	_____ k.g (if known)	
104	Residence	Urban	1
		Rural	2
105	Maternal occupation?	Employed (Gov. or Private)	1
		House wife/ Merchant/ Farmer/daily laborer	2
		Other specify-----	3
106	Maternal educational Status	Unable to read and write	1
		Literate (read & write)	2
		Primary education (1-8)	3
		Secondary education (9-12)	4
		Tertiary (above 12)	5
107	Paternal Educational status	Unable to read and write	1
		Literate (read & write)	2
		Primary education (1-8)	3
		Secondary education (9-12)	4
		Tertiary (above 12)	5
108	Household estimated income per month	_____ birr/month or estimation	
109	Number of Family members?	_____	
110	Nutritional history	✓ Duration of exclusive breast feeding (for those	

		who are <5yrs) ✓ Frequency of feeding/day _____ ✓ Problem with chewing/swallowing or any vomiting/regurgitation after feeding : yes/no ✓ Complementary feeding: adequate/inadequate ✓ Sun light exposure: adequate/inadequate ✓ History of cow's milk exposure: yes/no ✓ Who is feeding the child? Self/Parent/Other	
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Part II: Clinical questionnaires

No	QUESTIONS	Responses	Code
200	Age at diagnosis	-----Months -----Years (if >2yrs)	
201	Symptom duration before diagnosis	-----Months -----Years (if >2yrs)	
202	Duration after diagnosis of epilepsy?	-----Months -----Years (if >2yrs)	
205	Seizure control	1. Good control 2. Poorly controlled	
206	Average frequency of follow up	Monthly	1
		Every 2months	2
		Every 3months	3
		>3months	4
207	Any comorbid illness other than Epilepsy	CP, Developmental delay, Known genetic syndrome	
208	Adherence to follow up and drugs	1. Good 2. Poor	

Part III: Physical examination during follow up

300	General appearance	1. looks malnourished: Yes/No	
		3. Conjunctival/palmar pallor: Yes/No	
		4. Gross peripheral signs of Rickets	
		5. Other specify -----	
301	Anthropometric assessment.	1. Weight kg Hight..... cm	
		3. Head circumference.....cm	
		4. MUAC----cm	
		1. Wt/Ht or Wt/L-----Z score	
		2. BMI/A-----Z score	
		3. Ht/A----- Z score	
302	Any Investigation now/in the past six month (Only if done)	4. Hc/A.....z score	
		5. Wt/age.....z score	
		1. Hematocrit.....MCV.....	
		2. Vitamin D level.....	

Part IV: Management

400	Number of medication	1. One 2. Two 3. Three 4. More than Three	
401	List any side effect of medication if any		