PREVALENCE AND ASSOCIATED FACTORS OF PHENYTOIN INDUCED GINGIVAL OVERGROWTH (PIGO) AMONG CHILDREN RECEIVING PHENYTOIN TREATMENT IN SELECTED ADDIS ABABA GOVERNMENTAL HOSPITALS, ETHIOPIA, CROSS-SECTIONAL STUDY.

A RESEARCH THESIS SUBMITTED TO ADDIS ABABA UNIVERSITY, COLLEGE OF HEALTH SCIENCES, PEDIATRICS AND CHILD HEALTH DEPARTMENT, FOR THE PARTIAL FULFILMENT OF THE REQUIREMENT FOR THE SPECIALTY CERTIFICATE PROGRAM IN PEDIATRICS AND CHILD HEALTH.

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DECLARATION

ADDIS ABABA UNIVERSITY COLLEGE OF HEALTH SCIENCES SCHOOL OF MEDICINE DEPARTMENT OF PEDIATRICS AND CHILD HEALTH

I, the undersigned Pediatrics and Child Health Resident declare that this thesis done is my original work in partial fulfillment for the certificate of Pediatrics and Child Health.

Title- prevalence and associated factors of phenytoin-induced gingival overgrowth (PIGO) among children who took phenytoin in selected Addis Ababa Governmental Hospitals, Ethiopia, Cross-Sectional study.

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ACRONYMS AND ABBREVIATIONS

AED …….. Antiepileptic drugs
CCB ……..... Calcium Channel Blocker
DIGH …….. Drug -induced gingival hyperplasia
GO …….. Gingival overgrowth
PHE ……. Phenytoin
PIGO ……. phenytoin-induced gingival overgrowth
QOL ……. Quality of life
SPSS ……. Statistical Package for Social Sciences version 25
TASH ……. Tikur Anbessa Specialized Hospital
YK12 HMC ……. Yekatit 12 Hospital Medical College

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ABSTRACT

Background

Gingival overgrowth (GO) is a frequent complication associated with various medications, including anticonvulsants such as phenytoin, which is a medication commonly prescribed to treat epilepsy. Other drugs, such as immunosuppressant and calcium channel blockers can also cause GO. Phenytoin is a particularly concerning medication, as it is estimated that 30–50% of patients taking it experience significant gum enlargement. This side effect, known as phenytoin-induced gingival overgrowth (PIGO), can cause considerable cosmetic and functional problems, especially for children, because phenytoin remains widely used, particularly in developing countries. This is reflected in research conducted at Tikur Anbessa Hospital in Addis Ababa, Ethiopia. Among children with epilepsy who were on monotherapy, phenytoin was the most commonly used medication, accounting for 33.6% of the cases. This study investigated the prevalence of PIGO and associated factors among children in Addis Ababa-selected governmental hospitals, which is highly relevant.

Objectives

This study aims to address the prevalence and associated factors of phenytoin-induced gingival overgrowth (PIGO) among children receiving phenytoin treatment in selected Addis Ababa governmental hospitals, in Ethiopia.

Methodology

This study was conducted using a hospital-based cross-sectional study design from August 2024 to January 2025 GC at Tikur Anbessa Specialized Hospital and Yekatit 12 Hospital pediatric neurology follow-up clinics. Using a single population proportion formula with 95% confidence and 5% precision, the required sample size was 328. The data were entered into the Statistical Package for Social Sciences version 27 (SPSS) for subsequent descriptive and analytical statistical analysis where applicable. Descriptive statistics were employed to summarize the data, and the results were presented using tables and figures. All variables were included in the bivariate logistic regression analysis. Variables with a p-value of less than 0.2 were further considered for multivariate logistic regression to identify potential predictors of PIGO. A statistically significant association was defined as a p-value of <0.05.

Result

Among 328 enrolled patients, 171 (52.1%) developed PIGO, resulting in a prevalence of 52.1%. Children aged 4–5 years had a 4.9-fold increased risk (AOR = 4.9, 95% CI = 1.892–12.632), while those aged 6–12 years had a 5.96-fold increased risk (AOR = 5.962, 95% CI = 2.659–13.368) compared to the 1–3-year age group .Longer phenytoin use was a significant factor; children on phenytoin for 13–24 months had a 5.5-fold higher risk than those on it for 3–6 months ($p = 0.004$, AOR = 5.548, 95% CI = 1.742–17.675). Higher doses also increased risk; children taking 5–10 mg/kg/day had a 5.7-fold greater likelihood of developing PIGO compared to those on <5 mg/kg/day ($p < 0.000$, AOR = 5.704, 95% CI = 3.060–10.633). Additionally, children using other AEDs had a 3.26-fold higher risk than those on phenytoin alone ($p < 0.000$, AOR = 3.259).

Conclusion

In this study, the prevalence of PIGO was 52%, slightly above half .Age, duration of phenytoin use, dosage, and the use of additional antiepileptic drugs (AEDs) were identified as significant predictors of PIGO.

1, INTRODUCTION

1.1. Background

Epilepsy is the most common chronic neurological complaint in humans [1]. The frequence of epilepsy in developed countries reaches roughly 1%, rising to 2% in lower advanced nations [2]. Epilepsy treatment is grounded on medicine curatives that aim to help cases achieve seizure freedom without adverse goods.

One of the ant seizure drug used for seizure control is phenytoin. Phenytoin is one of the most common prescribed medications to treat epilepsy and it may also be used in cases of neuralgias and cardiac arrhythmias [3].

In a study conducted at Tikur Anbessa Specialized Hospital (TASH) on the use of multipleanti-seizure drugs and patterns of seizure control in children with epilepsy at the neurology follow-up clinic, data from 226 out of 355 actors on monotherapy were analyzed. Among these actors, 76(33.6%) were using phenytoin, 71(31.4%) were using phenobarbitone, 58(25.6%) were using sodium valproate, and 20(8.8%) were using carbamazepine [4].

The first report of GO associated with the habitual use of phenytoin was published in 1939[5]. It's estimated that roughly 30 to 50 % of cases taking phenytoin develop significant gingival differences [6].

PIGO can do beforehand within 3 months of medicine use and may reach a state of equilibrium frequently within the first year of the beginning of treatment [7]. PIGO seems to be more prevalent in children and teenagers, but there's no difference in its incidence with respect to sex or ethnical group [8].

The mechanisms involved in the development of PIGO are multiple and complex including differences at the cellular and molecular situations involving fibroblasts, cytokines, growth factors, and inheritable vulnerability [9].

PIGOs have several important cosmetic and medical implications. Because of adding mindfulness and concern about appearance and tone- image, especially among adolescents, phenytoin- convinced gingival overgrowth (PIGO) may produce compliance issues with the failure of else effective remedy [10].

Gingival overgrowth also leads to the conformation of pockets within the gingivo- dental sulcus with implicit accumulation of debris, leading to poor dental hygiene, halitosis, and gingival bleeding [10].

The problem of PIGOs is very relevant to developing countries because phenytoin is a veritably generally specified drug because of cost and familiarity and is generally not substituted by other antiepileptic medicines (AEDs), indeed where it's doable [10].

The first sign of blowup is observed in the interdental papilla region. Gradationally, gingival lobulations extend along the labial, lingual, and coronal aspects to cover entire anatomic crowns of teeth.
The gum appears thick, flexible, and freckled. The goods are most apparent in the anterior part of the mouth [11].

Colorful grading systems are used for quantifying the inflexibility of PIGO, which is important for remedial decision timber and exploration purposes. This study utilizes the Angelopoulos and Goaz bracket system, an extensively honored system for assessing the extent of gingival overgrowth.

1.2. Statement of the problem

Certain drugs might cause gum adverse effects known as drug-induced gingival hyperplasia (DIGH). This causes swelling, bleeding, and problems with chewing, speaking, and aesthetics. In severe situations, DIGH can cause loose and perhaps lost teeth due to jawbone collapse (alveolar bone absorption). All of these concerns have a major impact on a patient's quality of life (QOL) [12]. Phenytoin is a frequent anti-epileptic medicine in impoverished countries, and it has a GO adverse effect. A study conducted at Tikur Anbessa Specialized Hospital looked at the usage of several anti-seizure drugs as well as seizure control patterns in children with epilepsy at the neurology follow-up clinic. The study looked at individuals on monotherapy, and 76 of them (33.6%) were taking phenytoin [4].

1.3. Significance of the study

To our knowledge, no studies have been conducted on the prevalence of PIGO in Ethiopia or its associated variables.
This study is the first of its kind conducted at TASH and will provide valuable insight into the prevalence and associated factors of phenytoin-induced gingival overgrowth in patients taking the medication.

Understanding these factors will contribute to a better overall comprehension of the condition and help improve patient care. Additionally, the findings of this study can serve as baseline data, offering a useful reference for future research and guiding other investigators in related studies.

2. LITERATURE REVIEW

A comprehensive research by São Paulo State University (UNESP) examined the prevalence of gingival hyperplasia caused by anticonvulsant drugs. The authors searched the PubMed and Embase databases for relevant papers published between January 1984 and March 2020. Their systematic search yielded 4,471 references, and after careful review, nine studies were included, totaling 632 participants. Notably, all of the included studies had a minimal risk of bias.

This review looked at how carbamazepine, ethosuximide, phenytoin, primidone, phenobarbital, and sodium valproate were used to treat seizures. The investigations found a substantial association between different types of anticonvulsants and the occurrence of GO, with rates ranging from 0% to 73%.

Phenytoin, in particular, emerged as the medication with the highest incidence of GO, ranging from 15.61% to 73% in patients.

In conclusion, this review highlights phenytoin (PHE) as the anticonvulsant with the strongest association with GO, with a reported incidence ranging from 15.61% to 73% [13].

Another cross-sectional study, conducted in 2020 by the Department of Neuroscience at the University of Padova, Italy, also investigated the prevalence of gingival overgrowth induced by anticonvulsant drugs in epileptic patients. This research included 213 participants, ranging from 5--80 years old and encompassing both genders. Among these patients, 162 met the inclusion criteria and were required to have been on the same anticonvulsant medication for at least one year.

The experimenters employed the modified Harris and Ewalt bracket system and O'Leary's shrine control record (OLR) to assess the inflexibility of gingival overgrowth. Phenytoin is associated with gingival overgrowth in 50% of cases [14].

Experimenters have conducted a community- based cross-sectional study in Ferrara, Northern Italy, to probe the frequence of gingival blowup in habitual druggies of phenytoin (PHE) and identify implicit threat factors.

The study revealed that approximately 40% of chronic PHE users experienced gingival enlargement.

Interestingly, factors such as sex, age, age at treatment initiation, treatment duration, and oral hygiene practices did not significantly influence the risk of developing GO. However, a direct

correlation was observed between daily PHE dosage and GO risk, suggesting a dose-dependent effect.

Additionally, a study indicated that younger age and poor oral hygiene might predispose individuals to more severe forms of gingival involvement [15].

Another study performed by Universitat Auto`noma de Barcelona, Barcelona, Spain investigated the prevalence and risk factors associated with gingival enlargement (increased gum tissue) in patients with epilepsy taking antiepileptic medications.

The study employed a cross-sectional design, comparing data from 59 patients on these medications with a control group of 98 individuals. To assess gingival enlargement, researchers have utilized two scoring methods: the gingival overgrowth index (GOI) for measuring vertical overgrowth and the Miranda-Brunet index (MBI) for measuring horizontal overgrowth. Additionally, they evaluated gingival inflammation (gingival index), plaque buildup (plaque index), and probing depth [16].

The study revealed significant findings. The prevalence of gingival enlargement, measured by both the GOI and MBI indices, was considerably greater ($p < 0.0001$) in the anticonvulsant group than in the control group. Notably, the phenytoin group displayed a significantly greater prevalence of gingival enlargement for both indices than did the group taking other anticonvulsant medications.

Interestingly, among the potential risk factors investigated, only the level of gingival inflammation (gingival index) was significantly associated with the development of gingival enlargement.

The risk of developing gingival enlargement (odds ratio) was substantially greater for phenytoin therapy (52.6) than for other anticonvulsant medications (6.6) on the basis of the MBI score.However, after adjusting for preexisting gingival inflammation, these odds ratios decreased to 5.7 and 18.1, respectively [16].

Another study investigated the factors influencing the enlargement of gum tissue (gingival enlargement) caused by phenytoin. Researchers recruited outpatients attending the epilepsy clinic at Prince Mshiyeni Memorial Hospital in Durban, South Africa, who were currently taking phenytoin. Among the 134 patients studied, 62% had a moderate or severe degree of gingival enlargement (PIGE score > 1), whereas 8% had no enlargement (PIGE score of 0). Interestingly, while plaque buildup showed a moderate association with gingival enlargement (correlation coefficient of 0.4), no other single factor had a statistically significant individual impact.

However, when researchers used a more complex analysis (multiple linear regression), factors that initially seemed unimportant became more relevant. This analysis revealed that bacterial plaque ($p < 0.0001$), younger age ($p < 0.01$), and higher levels of free phenytoin in the bloodstream ($p < 0.03$) were associated with an increased risk of gingival enlargement [17].

3. OBJECTIVE

3.1. General objective

- To determine the prevalence and associated factors of PIGO among children receiving phenytoin treatment in selected Addis Ababa Governmental Hospitals.

3.2. Specific objectives

- To Determine the Prevalence of PIGO and
- To identify factors associated with PIGO development include the following:
    - Demographic factors (age, sex and others)
    - Phenytoin treatment characteristics (dosage, duration, and concomitant use of other antiseizures)
    - Oral hygiene practices

4. METHOD AND MATERIALS

4.1. Study setting

The research was carried out in the pediatric neurology follow-up clinics of Tikur Anbessa Specialized Hospital and Yekatit 12 Hospital Medical College.

TASH is the largest tertiary hospital in Addis Ababa, Ethiopia. It was created in 1974, is run by Addis Abeba University, and is Ethiopia's largest teaching hospital, educating hundreds of medical students and residents each year. The hospital treats roughly 400,000 people each year.

The pediatric neurology follow-up clinic has 2 rooms that are open throughout the working days with pediatric neurologists and pediatric residents. It experiences a high volume of patients, with an average of 650 to 750 cases seen per month. Among these cases, seizure disorders are a prevalent concern, accounting for approximately 450 to 500 patients monthly.

Yekatit 12 Hospital, originally established in 1923 E.C. (1930/1931 G.C.) under the name Bethsaida, meaning "house of sick people", .Founded with a capacity of only 25 beds, the hospital has grown significantly over time.

In recognition of its expanding educational and training programs, Yekatit 12 Hospital was designated a hospital medical college by the Addis Ababa city government in 2011 G.C.

Pediatric neurology clinics, which are held twice a week on Tuesday and Wednesday afternoon with pediatric neurologist and pediatric residents, the pediatric neurology clinic experiences a high volume of patients, with an average of 400 to 550 cases seen per month. Provide vital services for children in Addis Ababa facing neurological challenges.

I selected Tikur Anbessa Specialized Hospital (TASH) and Yekatit 12 Hospital for this research because of several factors. First, both hospitals possess pediatric neurology clinics staffed by pediatric neurologists. This ensured access to the specific patient population required for my study. Second, the chosen hospitals facilitated easier data collection. Finally, the locations of these facilities allowed me to recruit a diverse group of patients from various regions of the country.

4.2. Study design

Two-center institution-based cross-sectional study.

4.3. Study Period

The study was conducted from August 2024 to January 2025Gc.

4.4. Population

Source Population: All the children took phenytoin and were followed up at Tikur Anbessa Specialized Hospital or Yekatit 12 Hospital Medical College pediatrics neurology clinic.

Study population: includes children on phenytoin treatment, followed at the Pediatric Neurology Clinics of Tikur Anbessa or Yekatit 12 Hospitals, accompanied by caregivers, meeting inclusion criteria, and willing to participate during the study period.

4.5. Sample size and sampling technique

The single population proportion formula for a cross-sectional study used to calculate sample size

$$n = (z\alpha/ 2) 2 p(1- p)/ D2$$

n is the minimum needed sample size,

Zα/ 2 is the value under the standard normal table for a given confidence interval (1.96 for 95 CI),

p is the stylish estimate of frequence since we don't have a preliminarily performed study in our country, we took 50% to increase the strength of the study, and

d is the margin of error(0.05).

n = (1.96) 2(0.5(0.5)/ (0.05) 2 = 384

Since the sample frame is lower than 10,000, we use the adaptation formula,

nadj. = n/((1(n/ N)). where nadj. = Acclimated sample size, n = advised sample size, n = 384 and N = source population, N = 2214

Nadj. = 384/(1384/2214) ≈ 328.

The sampling procedure employed a non-probability total enumerative sampling method. As a result, all patients who attended their neurology follow-up appointments, were on phenytoin drug and met the addition criteria were included in the study until the asked sample size was reached.

The final advised sample size for the study was proportionally allocated to each selected hospital. Using the proportional allocation formula, 186 cases were from TASH, and 142 cases were from Yekatit 12 Hospital.

4.6 Inclusion and exclusion criteria

4.6.1 Inclusion criteria – All children included in this study received follow-up care at the pediatric neurology clinic of either Tikur Anbessa Specialized Hospital (TASH) or Yekatit 12 Hospital. They were treated with phenytoin for a minimum of three months and are currently taking phenytoin.

4.6.2 Exclusion criteria - This study excluded participants who met any of the following criteria:

- A history of gingival overgrowth prior to phenytoin treatment.(diagnosed by a physician)
- Age-inappropriate dentition (fewer than 6 teeth for their age).
- The duration of phenytoin treatment was less than 3 months.
- Individuals who declined to participate in the research.

4.7 Study Variables

4.7.1 Dependent variables- :

Phenytoin-induced Gingival Overgrowth (PIGO)

4.7.2 Independent variables-

Demographic data (age, sex, address, economic status, family educational level), tooth brushing practice, dose of phenytoin, duration of treatment, other concomitant drug usage (anticonvelsant,ccb,imunosupressant,folic acid).

4.8 Data collection and measurement

Data was collected from three sources: the iCare system, interviews with family members, and evaluations of children using standardized questionnaires. These assessments were conducted by residents and trained nurses during regular pediatric neurology follow-up appointments at Tikur Anbessa Specialized Hospital and Yekatit 12 Hospital. The questionnaire consisted of four sections: Part I Sociodemographic data, Part II Drug Information, Part III Oral Health Habits and Dental History, Part IV Assessment of Gingival Overgrowth.

To ensure accuracy, data collectors were trained in the PIGO classification system, with a reference image included in the questionnaire for consistency. In addition to reviewing the iCare system, they also personally examined the children and collected further information using a structured questionnaire.

The questionnaire was carefully designed by reviewing relevant literature, pretested before use, and adapted to ensure clarity and reliability. It was prepared in English and uploaded to the KoboToolbox platform to facilitate efficient data collection.

4.8.1 Data Quality Assurance

The principal investigator carefully reviewed the data to ensure it was accurate, complete, and collected using the right methodologies. Trained nurses and residents were responsible for gathering the data. To confirm the questionnaire's dependability, it was pretested with 5% of the sample in a different context. However, these findings were not used in the final study. The study followed stringent ethical norms.

4.9 Data analysis

The completed data was coded, put into Excel, and then exported to SPSS version 27 for further analysis by the lead investigator. The data was meticulously cleansed to assure its accuracy and authenticity.

Descriptive statistics and logistic regression were applied. To account for confounding factors, variables with p-values ≤ 0.2 were included in a multivariate logistic regression model. The crude odds ratio (COR) and adjusted odds ratio (AOR) were calculated using a 95% confidence interval (CI), with a p-value of less than 0.05 indicating statistical significance.

4.10 Ethical considerations

Data was collected anonymously, without participants' names or other identifying identifiers. Prior to data collection, caregivers provided verbal consent.

The Pediatrics and Child Health Department's, Research and Publications Committee of TASH, Yekatit 12 Hospital Medical College, and the Addis Abeba Health Bureau all provided formal letters of ethical clearance. Furthermore, confidentiality was preserved by eliminating patient identification and assigning code numbers.

4.11. Plan for dissemination of results

The study's findings will be presented at the research defense day, and an official report, both soft and hard copies, will be submitted to the Department of Pediatrics and Child Health at Addis Abeba University, Yekatit 12 Hospital, and the Addis Abeba Health Bureau. The research findings will also be published in local and international scientific journals.

4.12 Operational Definition

GO is defined as the formation of extracellular matrix in gingival connective tissues, notably collagenous components, with various degrees of inflammation [18].

Figure 1; Degree of gingival enlargement

Degree of gingival hyperplasia according to modified index by **Angelopoulos & Goaz 1972**

Grade	Hyperplasia	Size	Tooth coverage
0	No	Normal	No
1	Minimal	<2 mm	Cervical 3rd or less
2	Moderate	2-4 mm	Middle 3rd
3	Severe	>4 mm	More than 2/3rd

Figure 2; Angielopoulos & Goaz classification

5. RESULT

5.1. Socio demographic characteristics of the respondents

From August 2024 to January 2025 Gc, a total of 328 study participants were enrolled in this study from two public hospitals in Addis Ababa, Ethiopia. Of these, 186 participants (56%) were from Tikur Anbessa Specialized Hospital, while 142 participants (44%) were from Yekatit 12 Hospital Medical College.

All 328 participants were successfully interviewed, resulting in a 100% response rate. Regarding age distribution, 48.8% of the participants were school-age children (6–12 years old), while 18% were preschoolers, and 17.7% were toddlers.

In terms of gender, 226 participants (68.9%) were male, while 102 (31%) were female. The majority of children, 284 (86.6%), resided in urban areas.

When looking at caregivers, 250 participants (76.2%) were cared for by both parents (mother and father), while 56 (17.1%) were under the care of their mother only.

Regarding caregiver education levels, 54 caregivers (16.4%) had no formal education, 167 (50.9%) had completed secondary school, and 107 (32.6%) had attained a tertiary level of education.

5.2 Drug Information and Medical Characteristics of Study Participants

Out of the participants, 215 (65.5%) had been taking phenytoin for >= 24 months, followed by 72 participants (22.0%) who had been on the medication for 3 to 6 months.

Regarding dosage, 183 participants (55.8%) were receiving 5–10 mg/kg/day, while 142 participants (43.3%) were taking less than 5 mg/kg/day.

In terms of other antiepileptic medications used alongside phenytoin, 167 participants (50.9%) were on additional therapy. Among them, sodium valproate was the most commonly used medication (88 participants, 46.8%), followed by phenobarbital (35.1%), clonazepam (7.4%), and carbamazepine (6.4%).

Variables	Category	Frequency(N=328)	Percent
Age	**1–3 years**	58	17.7%
	4–5 years	59	18.0%
	6–12 years	160	48.8%
	13–18 years	51	15.5%
Gender	**Male**	226	68.9%
	Female	102	31.1%
Residency	**Urban**	284	86.6%
	Rural	44	13.4%
Care Giver	**Mother & Father**	250	76.2%
	Mother only	56	17.1%
	Father only	7	2.1%
	Grandparents	9	2.7%
	Orphaned	6	1.8%
Income	**< =7500**	102	31.1%
	7500 – 35000	223	68.0%
	> =35000	3	.9%
Educational Status	**Master's degree**	7	2.1%
	Bachelor's degree	47	14.3%
	Certificate or diploma	53	16.2%
	10+2	35	10.7%
	1 to 10	132	40.2%
	Illiterate	49	14.9%
	Other	5	1.5%

Table 1; Sociodemographic characteristics

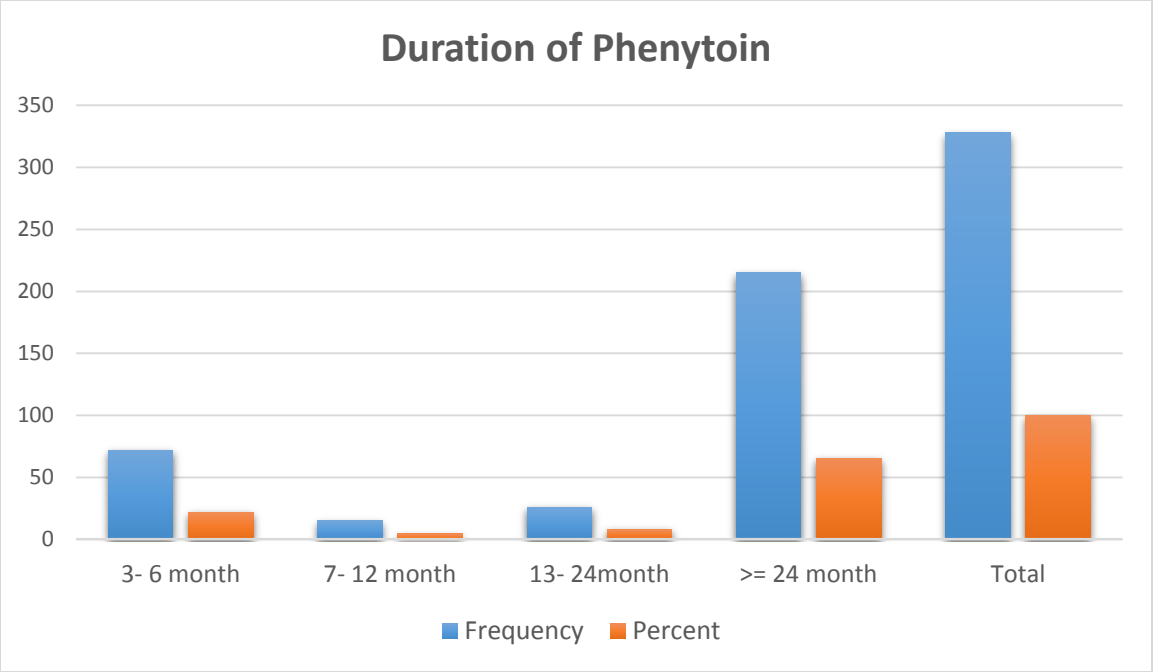
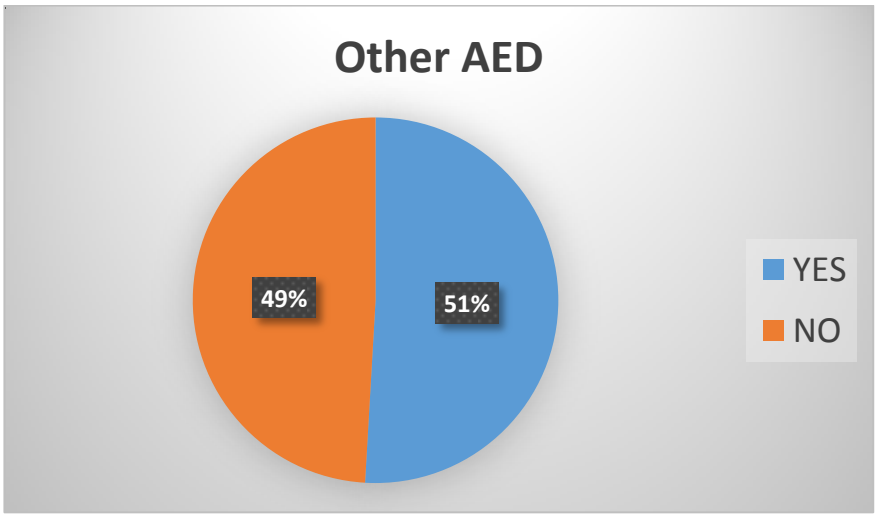


Figure 3; Duration of phenytoin usage

Variable		Frequency	Percent
How many mg of phenytoin take per day	< 5mg/kg/day	142	43.3%
	5-10mg/kg/day	183	55.8%
	>=10mg/kg/day	3	.9%
	Total	328	100.0%

Table 2; Phenytoin dosage mg/kg/day

Figure 4; usage of AED other than phenytoin



Variables		Frequency	Percent
How often brush your teeth	Never	137	41.8%
	Once	116	35.4%
	Twice	75	22.9%
Mouthwash usage	Yes	131	39.9%
	No	197	60.1%
folic acid usage	Yes	16	4.9%
	No	312	95.1%

Variable	Responses		
		Number	Percent
Others AED	Phenobarbital	66	35.1%
	Sodium valproate	88	46.8%
	Lamotrigine	5	2.7%
	Carbamazepine	12	6.4%
	Clonazepam	14	7.4%
	Other	3	1.6%
	Total	188	100.0%

Table 3; Other AED usage

5.3 Oral Health Habits and Dental History characteristics of the respondents

Out of the participants, 137 (41.8%) never brush their teeth, whether using commercial or local toothbrushes. Meanwhile, 116 participants (35.4%) brush once a day, and 75 (22.9%) brush twice daily.

Regarding the use of mouthwash or toothpaste, 131 participants (39.9%) reported using it, while 197 participants (60.1%) did not.

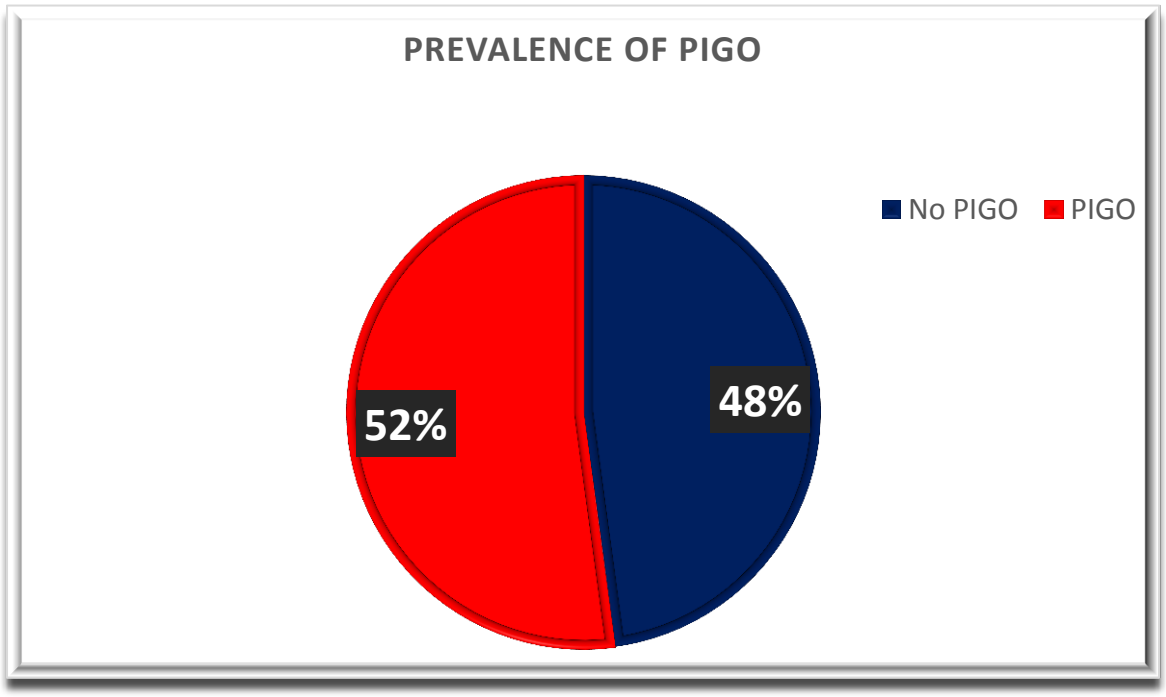
In terms of folic acid usage, 312 participants (95.1%) did not use it, while 16 participants (4.9%) did.

Table 4; Oral health habit

5.4 The prevalence of phenytoin induced gingival overgrowth (PIGO)

In this study, out of 328 participants, 171(52.1%) of them developed phenytoin induced gingival overgrowth.

Figure 5; Prevalence of PIGO



5.5 The determinate variable for the occurrence of PIGO

All study variables were tested by binary logistic regression analysis and variable those had less than 0.2 P- values were candidate for the multivariate logistic regression to control confounding variable and to determine potential predictors of PIGO.

The results of this study showed that children aged **4–5 years** have a **4.9-fold increased risk** of developing PIGO compared to those in the **1–3-year** age group (**AOR = 4.9, 95% CI = 1.892–12.632**). Similarly, children aged **6–12 years** are at an even higher risk, with a **5.96-fold**

increase in the likelihood of developing PIGO compared to those aged **1–3 years** (**AOR = 5.962, 95% CI = 2.659–13.368**).

Gender also plays a significant role, as **females are nearly twice as likely** to develop PIGO compared to males (**AOR = 1.955, 95% CI = 1.037–3.685**).

The **duration of phenytoin use** is another key factor. Children who had been taking phenytoin for **13–24 months** had a **5.5-fold increased risk** of developing PIGO compared to those who had been on phenytoin for only **3–6 months** (**p = 0.004, AOR = 5.548, 95% CI = 1.742–17.675**).

Additionally, the **dosage of phenytoin** significantly impacts the risk. Children receiving a dose of **5–10 mg/kg/day** were found to have a **5.7-fold increased risk** of developing PIGO compared to those taking less than **5 mg/kg/day** (**p < 0.000, AOR = 5.704, 95% CI = 3.060–10.633**).

Moreover, the use of **other anti-epileptic drugs (AEDs)** was identified as a significant predictor. Children taking additional AEDs had a **3.26-fold higher risk** of developing PIGO compared to those who were not using any other AEDs (**p < 0.000, AOR = 3.259**).

Table 5; Multivariate logistic regression analysis of factors affecting PIGO

Independent Variables					95% C.I.	
		COR	P- value	AOR	Lower	Upper
Age	1–3 years		**.000**			
	4–5 years	2.821	**.001**	4.888	1.892	12.632
	6–12 years	3.422	**.000**	5.962	2.659	13.368
	13–18 years	1.825	**.008**	3.952	1.435	10.888
Gender	Male	1.664	**.038**	1.955	1.037	3.685
Duration of Phenytoin Use	3- 6 months		**.014**			
	7- 12 months	.933	.589	.674	.160	2.828
	13- 24months	2.644	**.004**	5.548	1.742	17.675
	>= 24 month	1.703	.064	1.912	.964	3.794
Phenytoin Dose	< 5mg/kg/day		**.000**			
	5-10mg/kg/day	2.997	**.000**	5.704	3.060	10.633
	>=10mg/kg/day	2.796	.969	1.593	1.900	15.87
Other AED Use	Yes	2.847	**.000**	3.259	1.798	5.905
Mouth wash or tooth paste	Yes	1.878	.194	1.472	.822	2.638

6. DISCUSSION

This study examines the prevalence and associated factors of phenytoin-induced gingival overgrowth (PIGO) among children taking phenytoin at two public hospitals in Addis Ababa, Ethiopia. Among the 328 participants, 171 (52.1%) developed PIGO, resulting in a prevalence rate of 52%.

When compared to previous studies, this prevalence appears to be within a similar range. A systematic review conducted by São Paulo State University (UNESP) investigated the prevalence of gingival overgrowth induced by anticonvulsant medications. Phenytoin, in particular, was found to have the highest incidence, with prevalence rates ranging from 15.61% to 73% in patients [13].

These substantial variations in the prevalence of PIGO can be due to differences in definition(s), detection method(s), study methodology, sample size, age of the study population, and concurrent administration of other medicines, dose, and duration of phenytoin treatment [10].

A cross-sectional study undertaken in 2020 by the Department of Neuroscience at the University of Padova, Italy, looked into the prevalence of gingival overgrowth caused by anticonvulsant medicines in epileptic patients. The study discovered that phenytoin was associated with gingival overgrowth in 50% of cases, which is quite similar to the results of this study [14].

Another study conducted at Prince Mshiyeni Memorial Hospital in Durban, South Africa, investigated the factors influencing gingival enlargement caused by phenytoin. The study found that 62% of patients had a moderate or severe degree of gingival enlargement (PIGE score >1). This prevalence is slightly higher compared to the findings of the present study [17].

The results of this study indicate that children aged 4–5 years have a 4.9-fold increased risk of developing phenytoin-induced gingival overgrowth (PIGO) compared to those in the 1–3-year age group (AOR = 4.9, 95% CI = 1.892–12.632). Similarly, children aged 6–12 years have a 5.96-fold increased risk (AOR = 5.962, 95% CI = 2.659–13.368).

When comparing these findings with other studies, there is limited research conducted solely on children. Although several studies have investigated PIGO, there is no study that specifically examines the association between PIGO and different age groups in children.

However, available evidence suggests that younger individuals are, to some extent, more susceptible to severe drug-induced gingival overgrowth (DGO) than adults [15] [19]. Several studies have reported that younger patients tend to develop more severe lesions.

Epidemiological studies conducted by various researchers have demonstrated that the likelihood of developing PIGO in epileptic children and adolescents is higher than in adults [20].

The duration of phenytoin use is a key factor in the development of phenytoin-induced gingival overgrowth (PIGO). In this study, children who had been taking phenytoin for 13–24 months had a 5.5-fold increased risk of developing PIGO compared to those who had been on phenytoin for only 3–6 months ($p = 0.004$, AOR = 5.548, 95% CI = 1.742–17.675).

Several investigations have also found a substantial relationship between gingival enlargement and both phenytoin treatment duration and plasma phenytoin levels (Panuska et al., 1961; Little et al., 1975) [21]. However, other investigations have demonstrated no statistically significant connection between total plasma phenytoin levels, treatment duration, and gingival expansion (Hassell et al., 1984; Da).

Although this study did not assess serum phenytoin levels, the findings support a significant association between PIGO and the duration of treatment, consistent with previous research.

In this study, the dosage of phenytoin was found to significantly impact the risk of developing phenytoin-induced gingival overgrowth (PIGO). Children receiving a dose of 5–10 mg/kg/day had a 5.7-fold increased risk of developing PIGO compared to those taking less than 5 mg/kg/day ($p < 0.000$, AOR = 5.704, 95% CI = 3.060–10.633).

Similarly, a community-based cross-sectional study conducted in Ferrara, Northern Italy, reported comparable findings. The researchers observed that as the daily dose of phenytoin increased, the likelihood of developing drug-induced gingival overgrowth (DGO) also rose. Their results align with experimental studies, suggesting that DGO is a dose-dependent side effect, with its severity potentially influenced by local factors. A direct correlation between daily phenytoin dosage and gingival overgrowth risk further supports the notion of a dose-dependent effect [15].

In this study, the use of additional antiepileptic drugs (AEDs) was identified as a significant risk factor for phenytoin-induced gingival overgrowth (PIGO). Children taking other AEDs alongside phenytoin had a 3.26-fold higher risk of developing PIGO compared to those who were not using any additional AEDs ($p < 0.000$, AOR = 3.259).

When comparing these findings with other studies, the association between concomitant AED use and gingival overgrowth appears inconsistent. For instance, cross-sectional studies conducted in both South Africa and Italy found no significant link between gingival enlargement and the use of additional anticonvulsants such as phenobarbitone and carbamazepine[15][17].

Greenwood et al. (1986) found a higher prevalence of PIGO among patients taking numerous anticonvulsants. In contrast, Maguire et al. discovered that individuals treated with phenytoin alone or in combination with valproic acid had a lower frequency of drug-induced gingival overgrowth (DGO) than those treated with other co-administered antiepileptic drugs. These disagreements underscore the heterogeneity in study results and imply that other factors may influence the connection between AED use and gingival overgrowth [22].

Furthermore, our study identified no statistically significant link between the existence of PIGO

and oral hygiene levels. This finding is similar with prior research [15], which found no obvious link between oral cleanliness and the development of PIGO.

6.2 Strength and limitation of the study

6.2.1 Strengths of the Study

- This is the first study conducted in our setting.
- It is a multi-center study conducted in two public hospitals.
- The response rate was 100%, allowing us to assume that the target population is accurately represented.

6.2.2 Limitations of the Study

- Since this study is cross-sectional, it does not establish a cause-and-effect relationship between dependent and independent variables.
- Previous studies have found a significant association between phenytoin drug serum levels, dental plaque degree, and PIGO. However, in this study, serum levels and dental plaque scores were not included.

7. Conclusion

This study provides valuable insights into the prevalence and risk factors associated with phenytoin-induced gingival overgrowth (PIGO) among children receiving phenytoin treatment at two public hospitals in Addis Ababa, Ethiopia.

The findings indicate a prevalence rate of 52.1%, which is comparable to previous studies conducted in different settings.

Age, duration of phenytoin use, dosage, and the use of additional antiepileptic drugs (AEDs) were identified as significant predictors of PIGO.

Interestingly, this study found no statistically significant relationship between PIGO and oral hygiene status. While this aligns with some previous research, it contradicts other studies suggesting that poor oral hygiene may exacerbate the condition.

Further research, particularly prospective studies evaluating serum phenytoin levels and genetic predispositions, is needed to better understand the underlying mechanisms of PIGO and develop more effective preventive strategies.

8. RECOMMENDATION

Based on the major results acquired from the research presented in the previous sections, the following recommendations were made.

1. This study serves as a starting point to raise awareness among healthcare professionals about the prevalence of PIGO and its associated risk factors, ultimately improving patient care.
2. Children taking phenytoin should have regular dental check-ups to detect early signs of gingival overgrowth and prevent severe cases.
3. Parents and caregivers should be educated on proper oral hygiene and the importance of early dental care to reduce the risk of PIGO.
4. Future research should include serum phenytoin levels and dental plaque scores to better assess their correlation with PIGO severity, as previous studies have suggested a potential link.
5. This study will be a clue to make further qualitative study.

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9. REFERENCE

[1] Commission on Epidemiology and Prognosis, International League Against Epilepsy. Guidelines for epidemiologic studies on epilepsy. Epilepsia. 1993;34:592-6.

[2] Sander JW, Shorvon SD. Epidemiology of the epilepsies. J Neurol Neurosurg Psychiatry. 1996;61(5):433-43.

[3] Guncu GN, Cxaglayan F, Dincxel A, Bozkurt A, Sayg S, Karabulut E. Plasma and gingival crevicular fluid phenytoin concentrations as risk factors for gingival overgrowth. J Periodontol. 2006;77:2005-10.

[4] Deginet E, Ayalew M, Getahun M. Multiple anti-seizure medications use and pattern of seizure control in children with epilepsy at neurology follow up clinic, Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia. Afr Health Sci. 2023 Jun;23(2):732-42. doi: 10.4314/ahs.v23i2.84.

[5] Kimball OP. The treatment of epilepsy with sodium diphenyl hydantoinate. JAMA. 1939;112:1244-5.

[6] Modeer T, Domeij H, Andurén I, Mustafa M, Brunius G. Effect of phenytoin on the production of interleukin-6 and interleukin-8 in human gingival fibroblasts. J Oral Pathol Med. 2000;29(10):491-9.

[7] Seymour RA, Ellis JS, Thomason JM. Risk factors for drug-induced gingival overgrowth. J Clin Periodontol. 2000;27(4):217-23.

[8] Lin K, Guilhoto LM, Yacubian EM. Drug-induced gingival enlargement—part II. Antiepileptic drugs: not only phenytoin is involved. J Epilepsy Clin Neurophysiol. 2007;13(2):83-8.

[9] Kanno CM, Oliveira JA, Garcia JF, Castro AL, Crivelini MM. Effects of cyclosporin, phenytoin, and nifedipine on the synthesis and degradation of gingival collagen in tufted capuchin monkeys (Cebus apella): histochemical and MMP-1 and -2 and collagen I gene expression analyses. J Periodontol. 2008;79(1):114-22.

[10] Arya R, Gulati S. Phenytoin-induced gingival overgrowth. Acta Neurol Scand. 2012;125(3):149-55. doi: 10.1111/j.1600-0404.2011.01535.x.

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[11] Seymour RA, Ellis JS, Thomason JM. Drug-induced gingival overgrowth and its management. J R Coll Surg Edinb. 1993;38:328-32.

[12] Dongari-Bagtzoglou A. Informational paper: drug-associated gingival enlargement. J Periodontol. 2004;75:1424-31.

[13] Cláudio MM, Rodrigues JVS, Garcia VG, Theodoro LH. Prevalence of gingival hyperplasia induced by anticonvulsants: A systematic review. Braz Dent Sci. 2021;24(1):1-9. doi: 10.14295/bds.2021.v24i1.2112.

[14] Gallo C, Bonvento G, Zagotto G, Mucignat-Caretta C. Gingival overgrowth induced by anticonvulsant drugs: A cross-sectional study on epileptic patients. J Periodont Res. 2021;56(2):363-9. doi: 10.1111/jre.12828.

[15] Granieri E, Desideráa M, Cinzia V, Maria M, Tola R, Paolino E, Govoni V, Calinaa G. Phenytoin-induced gingival overgrowth: A community-based cross-sectional study in Ferrara, Italy. Neuroepidemiology. 1997;16.

[16] Brunet L, Miranda J, Roset P, Berini L, Farre Â, Mendieta C. Prevalence and risk of gingival enlargement in patients treated with anticonvulsant drugs. Eur J Clin Invest. 2001;31

[17] Majola MP, Mcfadyen ML, Connolly C, Nair YP, Govender M, Laher MHE. Factors influencing phenytoin-induced gingival enlargement. J Clin Periodontol. 2000;27:506-12.

[18] Corrêa JD, Queiroz-Junior CM, Costa JE, Teixeira AL, Silva TA. Phenytoin-induced gingival overgrowth: A review of the molecular, immune, and inflammatory features. Biol Psych. 2011;2011:497850. doi: 10.5402/2011/497850.

[19] Addy V, McElnay JC, Campbell N, D'Arcy PF. Risk factors in phenytoin-induced gingival hyperplasia. J Periodontol. 1983;54(6):373-7.

[20] Thomason JM, Seymour RA, Ellis JS, Kelly PJ, Parry G, Dark J. Iatrogenic gingival overgrowth in patients medicated with nifedipine and immunosuppressants. J Clin Periodontol. 1992;19(5):281-5

[21] Panuska HJ, Gorlin RJ, Bearman JE, Peterson WC. The effect of anticonvulsant drugs upon the gingiva: a series of analyses of 1048 patients. J Periodontol. 1961;32(1):15-28.

[22] **Maguire JH, Greenwood RS, Lewis DV, Hassell TM.** Phenytoin-induced gingival overgrowth incidence is dependent upon co-medication. *J Dent Res.* 1986;65(2):249.

10. ANNEXE 1

Information and consent form.

Dear Participant,

My name is Dr.G/Egziabher Kassa and I am a pediatric and child health final year resident at TASH. I am currently doing my research on the prevalence and associated factors of phenytoin-induced gingival overgrowth (PIGO) among children receiving phenytoin treatment in selected Addis Ababa Governmental Hospitals.

The purpose of this study is to address the prevalence and associated factors of phenytoin-induced gingival overgrowth (PIGO) among children receiving phenytoin treatment in selected Addis Ababa governmental hospitals.

The data gathered will be used solely for the purposes of this study. Your responses will be kept totally confidential, and none of them will have any effect on you. Your involvement will greatly contribute to the corpus of knowledge in this field and is critical to the success of this study, but it is entirely voluntary. If you prefer not to participate in the study, you may do so at any time. I'd want to thank you in advance for your participation. If you have any questions or need to contact the researcher, please use the contact information provided below.

Respectfully,

Dr. G/Egziabher Kassa

+251-926470248

E-mail; ethio274@gmail.com

Consent form

I declare that the purpose, procedure as well as, the risks and benefits of the study have been explained to me and that I understand. I hereby agree to take part in the study.

11, Annex 2
Questionnaire

Part 1: Sociodemographic Data

1. **Id No**: ……
2. **Age**: …… (Years)
3. **Weight**: ……. (KG)
4. **Gender**: A, Male B, Female
5. **MRN**: ……
6. **Place of Residency**: A, Urban B, Rural
7. **Care Giver of the Child**:
    - A. Mother & Father
    - B. Mother only
    - C. Father only
    - D. Grandparents
    - E. Orphaned

Family History

8. **Income of the Family**: per month
    - A. <1,000 birr
    - B. 1,000-4,999 birr
    - C. 5,000-9,999 birr
    - D. 10,000-14,999 birr
    - E. >15,000 birr
9. **Educational Status of Parents**:
    - A. Master's degree
    - B. Bachelor's degree
    - C. Certificate or diploma
    - D. 10+2
    - E. 1 to 10
    - F. Illiterate
    - G. Other (please specify)….

Part 2: Drug Information

10. **How long have you been taking phenytoin medication?**
    - A. 3 months to 6 months
    - B. 6 months to 1 year
    - C. 1 year to 2 years
    - D. > 2years

11. **How many milligrams of phenytoin do you take each day?** …… (Mg/dose)
12. **Are you currently taking any other medications besides phenytoin? (You can choose more than one)**
    - A. Phenobarbital
    - B. Sodium valproate
    - C. Levetiracetam
    - D. Lamotrigine
    - E. Carbamazepine
    - F. Clonazepam
    - G. Other (please specify) ……

Part 3: Oral Health Habits and Dental History

13. **How often do you brush your teeth each day (either commercial or local toothbrushes)?**
    - A. Never
    - B. Once
    - C. Twice
    - D. More than Twice
14. **Do you use any mouthwash or toothpaste?**
    - A. Yes
    - B. No
15. **Did you take folic acid while you were taking phenytoin?**
    - A. Yes
    - B. No
    - C. Don't know

Part 4: Assessment of Gingival Overgrowth (To be completed by an investigator, pediatric resident, or trained data collector)

16. **Assessment of Gingival Overgrowth based on Angelopoulos & Goaz classification**

ውድ ተሳታፊ፣

እኔ ዶ/ር ገብረ እግዚአብሔር ካሳ እባላለሁ። በጥቁር አንበሳ ስፔሻላይዝድ ሆስፒታል የመጨረሻ አመት የህፃናት ህክምና እና የህፃናት ጤና ሐኪም ነኝ።

በተመረጡ የአዲስ አበባ መንግሥታዊ ሆስፒታሎች ውስጥ፣ የፌኒቶይን ሕክምና የሚወስዱ ሕፃናት ላይ በፌኒቶይን ምክንያት የሚፈጠር የድድ መጠን መጨመር (PIGO) ስርጭትን እና የሚያስከትሉ ምክንያቶችን ለማጥናት ምርምሬን እያደረግሁ ነው።

የጥናቱ ዓላማ

የዚህ ምርምር ዓላማ፣ በተመረጡ የአዲስ አበባ መንግሥታዊ ሆስፒታሎች ውስጥ፣ የፌኒቶይን ሕክምና የሚወስዱ ሕፃናት ላይ የPIGO ስርጭትን እና የሚያስከትሉ ምክንያቶችን ማወቅ እና ማጥናት ነው።

የመረጃ መጠበቅና እሴቶች

- የተሰበሰበው መረጃ በዚህ ጥናት ላይ ብቻ ይጠቀማል።
- ምስጢራዊነት በጥብቅ ይጠበቃል።
- የእርስዎ ተሳትፎ በጥናቱ ላይ ትልቅ አስተዋጾ ያለው ሲሆን፣ ለህፃናት ጤና ሥነ ሥርዓት ማሻሻል ይረዳል።

የተሳትፎ ነፃነት

- በዚህ ጥናት የሚሳተፉት በፈቃደኝነት ብቻ ነው።
- በማንኛውም ጊዜ ከጥናቱ መውጣት ይችላሉ።

የጥያቄ እና እውቂያ መረጃ

ማንኛውም ጥያቄ ካለዎት፣ ወይም በተጨማሪ መረጃ ማግኘት ከፈለጉ፣ እባኮትን እኔን ያነጋግሩ።

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የፍቃድ ቅፅ

እኔ የጥናቱ ዓላማ፣ አሰራሩ እና የሚገኙ ጥቅሞች እንደተገለፀልኝ እና እንደተረዳሁት አውጃለሁ። በፈቃደኝነት በዚህ ጥናት ለመሳተፍ ተስማምቻለሁ።

ስም: _____
ፊርማ: _____
ቀን: _____

- መጠይቅ

ክፍል 1: ሶሺዮዲሞግራፊ

1. መታወቂያ ቁጥር፡……

2. ዕድሜ፡ ……

3. ክብደት፡…….

4. ጾታ፡- ሀ፣ ወንድ ለ፣ ሴት

5. ኤምአርኤን: …….

6. የመኖሪያ ቦታ: A, ከተማ B, ገጠር

7. የሕፃን እንክብካቤ ሰጪ፡-

- o A. እናት እና አባት o B. እናት ብቻ o C. አባት ብቻ o D. አያቶች o E. ወላጅ አልባ
- የቤተሰብ ታሪክ

8. የቤተሰቡ ገቢ: በወር

- o A. <1,000 ብር
- o B. 1,000-4,999 ብር
- o C. 5,000-9,999 ብር
- o D 10,000-14,999 ብር
- o E>15,000 ብር

9. የወላጆች የትምህርት ሁኔታ፡-

- o A. ማስተርስ ዲግሪ
- o B. የባችለር ዲግሪ
- o c. የምስክር ወረቀት ወይም ዲፕሎማ
- o D. 10+2
- o E. 1 እስከ 10
- o F. ያልተማረ
- o G. ሌላ (እባክዎ ይግለጹ)….

ክፍል 2: የመድሃኒት መረጃ

10. የፌኒቶይን መድሃኒት ምን ያህል ጊዜ እየወሰዱ ነው?

- o A. ከ3 ወር እስከ 6 ወር
- o B. ከ6 ወር እስከ 1 አመት
- o C. ከ1 ዓመት እስከ 2 አመት
- o D. >ከ 2 አመት በላይ……

11. በየቀኑ ስንት ሚሊግራም ፌኒቶይን ትወስዳለህ? …… (Mg/dose)

12. በአሁኑ ጊዜ ከፋኒቶይን በተጨማሪ ሌሎች መድሃኒቶችን እየወሰዱ ነው? (ከአንድ በላይ መምረጥ ይችላሉ)

- o A. phenobarbiton
- o B. sodium valporate
- o C. Levetiracetam
- o D. Lamotrigine
- o E,Carbamazepine
- o F. Clonazepam
- o G. ሌላ (እባክዎ ይግለጹ) ……

ክፍል 3፡ የአፍ ጤና ልማዶች እና የጥርስ ታሪክ

13. በየቀኑ ምን ያህል ጊዜ ጥርስዎን ይቦርሹታል (የንግድ ወይም የአካባቢ የጥርስ ብሩሽዎች)?

- o A. በጭራሽ
- o B. አንዴ
- o C. ሁለት ጊዜ
- o D. ከሁለት ጊዜ በላይ

14. ማንኛውንም የአፍ ማጠቢያ ወይም የጥርስ ሳሙና ትጠቀማለህ?

- o A. አዎ
- o B. አይ

15. ፌኒቶይንን በሚወስዱበት ጊዜ ፎሊክ አሲድ ወስደዋል?

- o A. አዎ

- o B. አይ
- o C. አላውቅም
- ክፍል 4፡ የድድ እድገት ግምገማ (በመርማሪ፣ በህፃናት ሐኪም ወይም በሰለጠነ መረጃ ሰብሳቢ የሚጠናቀቅ)

16. በአንጀሎፖሎስ እና ጎአዝ ምደባ ላይ የተመሰረተ የድድ በላይ እድገት ግምገማ