

# Effects of Medication on Asthma and the Development of Caries Cavities in Children Aged 3–15 at Luz Hospital in Lisbon, Portugal



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## Abstract

**Background** Asthma and caries cavities affect many children worldwide. Investigating the connection between asthma medication and the development of caries cavities is important for enhancing asthma treatment while reducing oral health risks. Exploring the relationship between asthma medication and caries cavities is compelling due to the limited number of conclusive studies on the subject.

**Aim** To examine the impact of medication on asthma treatment and the occurrence of caries cavities in children aged 3 to 15 years old (Luz Hospital in Lisbon, Portugal). The frequency of caries cavities in 3 different groups was examined. In addition, the possible association of caries cavities with different asthmatic medication was also assessed.

**Material and Methods** A descriptive observational study was conducted on children aged 3 to 15 years old, who attended the immunology-allergology and dentistry services at the Luz Hospital in Lisbon, Portugal, between January 2021 and February 2022. The sample was divided into 3 groups (medicated asthmatics, unmedicated asthmatics, and healthy children without asthma). An intraoral examination was performed to collect the DMFT index (decayed, missing, and filled teeth) to assess the presence of caries cavities. Clinical and dietary data were supplemented with a questionnaire and medical history in all groups. All variables used were qualitative and described using absolute frequencies and percentages.

**Results** The study population consisted of 159 children (52,8% boys and 47,2% girls). Among medicated asthmatic children, 50,3% have at least one tooth affected by caries cavities. The average number of missing, decayed, and filled teeth is significantly higher in the group of children with 'Asthma and medication' (average of 1,34 and standard deviation of 1,686). The mean number of missing, decayed, and filled teeth in the 'Asthma without medication' group (average of 0,87 and standard deviation of 0,921) is slightly higher than that in the 'No Asthma' group (average of 0,74 and standard deviation of 1,163). The caries cavities average probability appearance in the asthma medicated by ANOVA method is  $F(2,156)=3,76$  with the  $p<0,05$  ( $p=0,04$ ).

**Conclusions** These results showed that anti-asthmatic medications may influence the development of caries cavities. The occurrence of caries cavities is more prominent in medicated asthmatic children when compared to unmedicated asthmatic children.

**KEYWORDS** Asthma, Caries cavities, Asthma medication, Children.

## Introduction

Chronic respiratory diseases, such as asthma, chronic obstructive pulmonary disease, and allergic rhinitis, are one of the leading causes of morbidity and mortality worldwide [National asthma education and prevention program, 2007].

Asthma is a problem of public health that affect 100 million of world people. This is a complex disease that affects children and adults, with a high prevalence in children.

As a respiratory disease, asthma diminishes the quality of life of children and their families and contribute to a high social and health costs. Asthma is very common in children and the main characteristics of asthma are variable degree of airflow obstruction, bronchial hyperresponsiveness, and airway inflammation [Worldwide variations in the prevalence of asthma symptoms, 1998; Venkatesan, 2023]. According to the International Study of Asthma and Allergies in Childhood, the prevalence of childhood asthma in the world is greater than 12% and there is enormous variability depending on age and geographical area [Worldwide variations in the prevalence of asthma symptoms, 1998].

In Portugal, there are 175 thousand asthmatic children, and the costs associated with asthma are considerable [Sá-Sousa et al., 2015]. This pathology as a chronic disease involving the airways in the lungs. These airways, or bronchial tubes, allow air to come in and out of the lungs [Papi, 2018]. The treatment of asthma is based on controlling the symptoms with anti-asthma medication. In childhood the medication used are bronchodilators and anti-inflammatory agents [Shipp, 2023]. The current treatment is directed to control the symptoms and prevent exacerbations. The early introduction of anti-inflammatory treatment with inhaled corticosteroids (IC) results in better symptom control, which can preserve lung function in the long term and eventually prevent or attenuate airway remodeling [Mims, 2015]. Some patients with severe asthma may develop irreversible obstruction after many years of disease activity.

Research has investigated how asthma impacts the oral cavity and contributes to the development of caries cavities. Caries, a multifactorial dental disease, affects teeth and leads to various complications [Pitts et al, 2017]. This frequent chronic health children problem has a high prevalence in development countries and could harm patient's life [Mathur, 2018]. Thus, prevention of caries is an important public health issue with the potential of substantial economic gains [Rugg-Gunn, 2013]. The impact of asthma caries cavities goes beyond the individual, affecting the quality of life for both children and their families, along with imposing significant social and health costs.

Several studies reveal that children with asthma have a higher caries prevalence than healthy children [Ersin et al., 2006; Turkistani, 2010]. Balancing asthma control and oral health is crucial, as certain medications and habits may influence the occurrence of oral diseases [Alavaikko, 2011; Samec 2022]. Patients should carefully manage their medication use, maintain oral hygiene, follow proper eating habits, and use inhalers correctly to minimise oral health risks. Thus, the prevention of caries is an important public health issue, with the potential of substantial economic gains. Children with asthma tend to exhibit a higher incidence of dental caries compared to their healthy peers [Visweswar, 2012]. Indeed, while there is some evidence suggesting that children with asthma may experience higher rates of dental caries compared to non-asthmatic children, the research on this topic is not entirely conclusive [Świątkowska-Bury, 2022].

Various studies [Eloot, 2004; Wierchola, 2006; Jan et al., 2023], indicate potential links due to factors such as medication side effects, including dry mouth from certain asthma medications, which can contribute to an increased risk of cavities. However, more comprehensive and controlled studies are needed to establish a definitive correlation and understand the underlying mechanisms. Therefore, it is of extreme importance to study the relationship between medication, caries, and asthma in childhood. As a matter of fact, there is even some controversy about the relationship between onset of caries and anti-asthma medication.

## Material and methods

### Study Design and Population

This cross-sectional epidemiological study was approved by the Research Ethics Committee of UIC University, Barcelona, Spain (Approval Reference: ODP-ECL-2021-10) and the Research Ethics Committee of the Luz Hospital in Lisbon, Portugal (Approval Reference: CES/32/2020/ME). The study was conducted between both in a time frame that comprises the years of January 2021 and February 2022.

The sample size calculations considered the prevalence of caries cavities in Portuguese children, as well as the number of asthmatic children, by using national epidemiological data. To test the theoretical hypotheses, a sample was created using a purposeful sampling process. A sample of 159 individuals was gathered, divided into 3 independent and balanced groups with 53 cases each (healthy children without asthma, children with asthma and medication, and children with asthma without being medicated).

A random sampling process was used to select the study's sample. The random selection was conducted at the Luz Hospital in Lisbon, Portugal. Each participant required a dental examination. Legal guardians/parents were previously informed about the study and were provided with a written informed consent. All individuals who agreed to participate in the study

met the following inclusion criteria: children aged between 3 to 15 years old, of both sexes, not undergoing orthopedic and/or orthodontic treatment, and parents who were intellectually and physically able to respond to the study questionnaire.

A questionnaire survey was administered, incorporating specific characteristics, and making to the set of variables. The prevalence of untreated caries cavities was defined as the relative frequency of children who had at least one tooth classified as decayed or indicated for extraction due to caries cavities. Clinical examinations were conducted by one Paediatric Dentist. The study use the following inclusion and exclusion criteria.

### Inclusion Criteria

Patients diagnosed with asthma, aged between 3 and 15 years old, who belong to any of the following groups:

- with decayed teeth, where a tooth will be considered decayed if it has a cavity on one or more surfaces.
- whose reason for tooth extraction was due to caries cavities.
- with restoration caused by caries cavities.

### Exclusion Criteria

Patients with unerupted teeth extracted for reasons other than caries cavities. Patients with another pathology.

### Examination

The clinical examination was conducted at the Luz Hospital in Lisbon, Portugal under hospital light and using intraoral mirrors nº5, periodontal probes, and gloves. The children were examined while seated, with their heads in an upright position.

The following variables related to oral health status were evaluated. Caries cavities lesions were assessed following the criteria of WHO, where dental crowns were classified.

The following variables were evaluated using the questionnaire Sociodemographic variables (gender male and female; age, group);

- Eating habits (consumption of sugars: no sugar – 0; 1x per month – 1; 1x per week – 2; 2x per week – 3; more than 3x per week – 4).
- Oral hygiene habits (brushing frequency: does not brush teeth – 0; brushing 1x per day – 1; brushing 2x per day – 2; brushing 3x per day – 3).
- Types of medication (Montelukast – 0; ICS – 1; corticosteroid + bronchodilator – 2; antihistamine – 3).
- Duration of medication (year that began).
- DMFT index (which indicates the sum of teeth Decayed (cavitated), Missing (due to extraction of other reasons), and Filled (restored)).

### Statistical Analysis

Statistical analysis was conducted by using the Statistical Package for Social Sciences (SPSS, version 19.0). Initially, descriptive analyses were conducted to obtain central tendency measures (mean/median) and dispersion (standard deviation SD, and quartiles) for numerical variables, as well as absolute and relative frequencies for categorical variables.

In addition to descriptive analysis, utilising measures of central tendency (mean), dispersion (SD), and association (correlation coefficients), the following methods were also used:

- One-way Analysis of Variance (ANOVA), which allowed the identification of significant differences among the analysed groups concerning a specific characteristic.
- Exploratory Factor Analysis (EFA), with factor extraction using the principal component method. This allowed for

the representation of the original variables in a reduced number of factors or components (dimensions). The retained factors were those with an eigenvalue greater than 1, in accordance with the scree plot and the percentage of retained variance. The KMO criterion was employed to assess the validity of the EFA.

- The internal consistency of each dimension was measured using Cronbach's  $\alpha$ .
- Simple and multiple linear regressions were employed to find the factors that explain (or predict) the variation of a specific variable.

Results with a statistically significant probability (p-value) less than or equal to 0.05 were considered. All analyses were conducted using IBM SPSS Statistics software version 27.

## Results

This study's sample is composed by 159 patients, from the obtained sample 52.8% were males and 47.2% females. The patient divided into 3 independent and balanced groups with 53 cases each: Children without asthma, Children with asthma and medicated, Children with asthma without medication. In this study the number of decayed teeth in children with asthma is higher than in healthy children (figure 1). It should also be noted that the number of decayed teeth in children with asthma and medicated, is the highest, among the three groups with the average value of 1,34 and standard deviation of 1,686. The caries cavities average probability appearance in the asthma medicated by ANOVA method is  $F(2,156)=3,76$  with the  $p<0,05$  ( $p=0,04$ ). Given the difference of incidence of caries cavities in the asthma medicated group it is important understand which key factors are contributing to this variance, for this reason, it was introduced a set of variables to evaluate the correlation with caries cavities appearance (Table 1), the results reveal particular relevant correlations regarding:

- Sugar intake, which the higher the frequency of sugar intake, the greater the probability of caries cavities, with the significant correlation coefficient at 0,244 with a significance level of  $p<0,01$ .
- The beginning age of medication shows the later the asthma medication is started, the greater the likelihood of caries cavities, with the significant correlation coefficient at 0,225 with a significance level of  $p<0,01$ .
- The number of medication intake reveals that, the more medication, the greater the chances of having decayed/ filled teeth with the moderate correlation coefficient at 0,163 with a significance level of  $p<0,05$ .

In addition, when analysing the set of correlations of the variables oral hygiene habits, age and sugar intake in the three groups, the intake of sugars shows a positive and significant correlation also in the group of children without asthma that have a significative correlation coefficient of 0,418 with a significance level of  $p<0,05$ .

Regarding the intaking of isolated medication, in the asthma and medicated group, there was no significant correlation with the appearance of caries cavities, the significance level of - 0,099 (ICS), 0,237 (corticosteroid + bronchodilator), 0,409 (antihistamine) and 0,781 (Montelukaste) is not statistically significant. This conclusion derives from the application of the simple linear regression method summarised in the predictive model in Table 2.

Considering the previous results, the intaking of medication together was analysed, and two components were extracted,

the first one joined the variable of the frequency of inhaled corticosteroids (0,896) and the frequency of Montelukast (0,711), with a greater weight of the frequency of inhaled corticosteroids. The second component is mainly dominated by the frequency of corticosteroids + bronchodilator (0,909) and the frequency of antihistamines (0,617), but the latter with a lower weight. The effect of the second component (frequency of corticosteroid + bronchodilator and frequency of antihistamine) is positive and significant ( $\beta=0,262$ ;  $p<0.05$ ). For this reason, another analysis was conducted to examine the effect of the second component in the presence of other explanatory factors (table 3). The two factors with a positive and significant effect are the higher frequency of the combination of ICS and antihistamine ( $\beta=0,220$ ;  $p<0.05$ ) and sugar intake ( $\beta=0.229$ ;  $p<0.05$ ). The latter factor gained prominence in the presence of other factors in this model, but no other factor showed an effect in explaining the presence of caries cavities/filling.

## Discussion

Asthma is a prevalent chronic respiratory disease affecting millions worldwide, especially children. This study, conducted during pandemic, aimed to investigate the potential connection between asthma medication and the occurrence of caries cavities in children aged 3 to 15 years old.

Multiple mechanisms have been suggested in the existing literature to elucidate the potential effects of prolonged corticosteroid (CS) use on the prevalence of caries cavities [Sag, 2007]. Patients receiving anti-asthma treatment should receive guidance on adequately using their prescribed inhalers. This is particularly important due to the frequent and direct contact between the inhaler formulations and the oral cavity, which heightens the risk of oral tissue damage and, consequently, the onset of pathologies. Notably, certain dry powder inhalers are recognised to contain sugar, aimed at enhancing the drug's taste tolerability upon administration [Jan et al., 2023; Scribante et al., 2024]. Stensson et al. [2018] allude the rationale provided for this correlation, claiming that it could be attributed to the inclusion of fermentable carbohydrates, such as lactose monohydrate, in anti-asthmatic medications. According to Alavaikko [2011], asthmatic children double the likelihood of experiencing caries cavities in both primary and permanent dentition. A systematic review that analysed 1026 articles between January 2001 and January 2023 found that 14 studies reported an increase in caries cavities with the use of CS [Wu, 2019]. Lastly, Nørrisgaard et al. [2023] argued that the use of ICS,  $\beta_2$ -agonists, or the occurrence of asthma symptoms within the initial six years of life did not show any correlation with the onset of caries cavities or enamel defects. Nørrisgaard et al. [2023] focus on just the first six years of a child's life, and its smaller sample size compared to more extensive studies previously discussed could be the reasons for differing results.

To further explore the factors contributing to the development of caries cavities, the study examined correlations between various variables and the existence of caries cavities. Three key context variables showed a significant positive correlation with caries cavities occurrence: sugar intake, the age at which medication is started, and the number of drugs taken. This highlights the importance of these factors in caries cavities formation, considering the potential impact of pandemic-related changes in lifestyle and healthcare practices.

In the group without asthma, the frequency of sugar intake was significantly associated with caries cavities occurrence, emphasising the role of dietary habits in oral health. However,

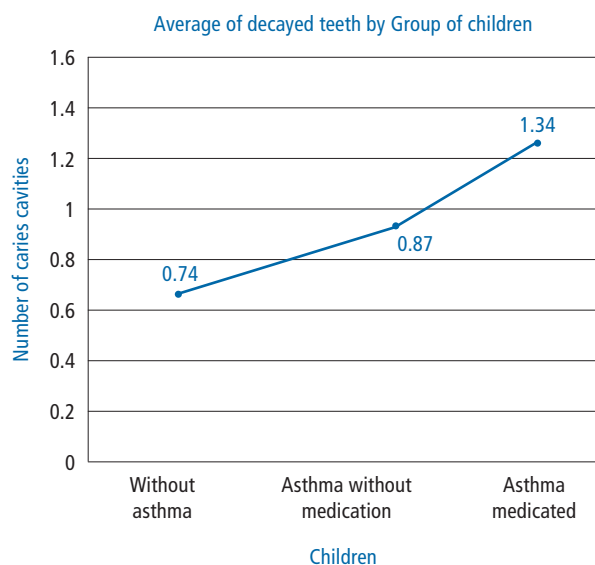


**FIG.1** Graphic of the average number of caries cavities per group of children.

this correlation was not significant in asthmatic groups, suggesting that other factors, such as medication, may override the impact of sugar intake in these cases, potentially influenced by the altered lifestyle patterns during the pandemic period of this study analysis.

As this study, some research [Tootla,2005; Ersin et al.,2006] has examined the connection between specific asthma medications and the incidence of dental decay. Among the four medications analysed, corticosteroids combined with bronchodilators showed the strongest association with caries cavities occurrence. This finding underscores the need for awareness and monitoring of dental health in children using this type of medication, especially considering the additional challenges posed by the pandemic.

In the group with asthma without medication, oral hygiene habits significantly influenced the occurrence of caries cavities, with more frequent brushing associated with a higher number of decayed and filled teeth. This intriguing result hints that other unconsidered variables may play a significant role in this group's oral health, warranting further investigation, particularly in the context of the pandemic. In their scoping review, Dickson-Swift et al. [2022] have indicated that the pandemic has influenced oral health outcomes.

In the group with asthma with medication, it is confirmed that children with asthma, especially those on medication, are at a higher risk of developing caries cavities. Factors such as sugar intake, the age of medication initiation, and the number of drugs taken also play essential roles in caries cavities formation.

Mazzoleni et al. [2008] found that these children tended to have a higher risk of developing caries cavities compared to non-asthmatic controls. Gani et al. [2020] propose that asthma influences the onset of oral diseases directly and indirectly through the impact of the medications used to treat it. The two authors [Mazzoleni et al., 2008; Gani et al.,2020] come to the same conclusion.

The cross-sectional epidemiological study outlined in the provided text delves into the oral health status of children with and without asthma in Portugal. It is noteworthy for its meticulous approach, including the approval from two reputable Research Ethics Committees, ensuring compliance with ethical standards

| Variables <sup>a</sup>            | Correlation coefficient | Sig.        |
|-----------------------------------|-------------------------|-------------|
| Age                               | 0,043                   | $p>0,05$    |
| Sugar intake                      | 0,244**                 | $p<0,01$ ** |
| Oral hygiene habits               | 0,022                   | $p>0,05$    |
| Number of years of medication     | 0,109                   | $p>0,05$    |
| Age of onset of medication intake | 0,225**                 | $p<0,01$ ** |
| Number of medications taken       | 0,163*                  | $p<0,05$ *  |
| Number of daily medication doses  | 0,149                   | $p>0,05$    |

<sup>a</sup> Group 'Asthma and medication'

\* a correlation is significant at the 0,05 level (2-tailed).

\*\* a correlation is significant at the 0,01 level (2-tailed).

Note: Pearson correlation.

**TABLE 1** Correlations between the number of decayed teeth and contextual variable.

in research. The study spanned from January 2021 to February 2022, providing a snapshot of oral health within that period. One of the key elements discussed was the process of selecting participants. Purposeful sampling was strategically used to establish balanced groups among healthy children, children with medicated asthma, and those who are not medicated. The study's reliance on random sampling further strengthens its validity, mitigating selection bias. Moreover, the inclusion criteria, such as age range and parental capacity to respond to questionnaires, contribute to the study's rigor. The evaluation of oral health status encompassed various variables, including caries cavities assessed by a Paediatric Dentist following WHO criteria. Additionally, the questionnaire examined socio-demographic factors, eating and oral hygiene habits, types, and duration of medication, and the DMFT index. Overall, this study presents a comprehensive analysis of oral health in children with asthma, shedding light on potential factors contributing to caries cavities prevalence. Its meticulous methodology and thorough statistical analysis make it a valuable contribution to the field of paediatric dentistry and respiratory medicine.

Dental care, especially for children with asthma, is crucial in preventing and managing caries cavities [Harrington, 2016]. This research contributes to our understanding of the complex interplay between oral health and chronic respiratory conditions, highlighting the need for a comprehensive approach to healthcare in children with asthma, particularly during extraordinary circumstances like a global pandemic. According to Homaira et al. [2022] COVID-19 pandemic has altered health care for chronic conditions. Further studies are needed to explore additional factors that may influence dental health in these populations and to develop effective preventive strategies, considering the dynamic nature of public health challenges.

Understanding the relationship between asthma, medication, and oral health is crucial for providing comprehensive healthcare to children. However, this study conducted at Luz Hospital in Lisbon, Portugal sheds light on limitations that must be acknowledged and interpreting its findings. This text delves into these limitations, emphasising the need for further research to enhance our understanding of this complex relationship. The study utilised a sample size of 159 children, which, while

| Coefficients <sup>a,b</sup>     |                             |            |                           |        |        |
|---------------------------------|-----------------------------|------------|---------------------------|--------|--------|
| Variables                       | Unstandardized Coefficients |            | Standardized Coefficients | t      | Sig.   |
|                                 | B                           | Std. Error | Beta                      |        |        |
| (Constant)                      | 1,570                       | 1.026      | -                         | 1,529  | 0,133  |
| Montelukaste                    | 0,226                       | 0,810      | 0,400                     | 0,279  | 0,781  |
| ICS                             | -0,792                      | 0,470      | -0,236                    | -1,684 | -0,099 |
| Corticosteroid + Bronchodilator | 0,566                       | 0,473      | 0,167                     | 1,197  | 0,237  |
| Antihistamine                   | -0,434                      | 0,521      | -0,117                    | -0,834 | 0,409  |

*a* Group 'Asthma and medication'.

*b* Dependent variable: number of lost, decayed, and filled teeth.

Note: Reference variable – Does not take = 0.

**TABLE 2** Coefficients of medication.

| Coefficients <sup>a</sup>                       |                             |            |                           |        |         |
|-------------------------------------------------|-----------------------------|------------|---------------------------|--------|---------|
| Variables                                       | Unstandardized Coefficients |            | Standardized Coefficients | t      | Sig.    |
|                                                 | B                           | Std. Error | Beta                      |        |         |
| (Constant)                                      | 0,388                       | 0,591      | -                         | 0,656  | 0,513   |
| Corticosteroid + Bronchodilator + Antihistamine | 0,289                       | 0,138      | 0,220                     | 2,085  | 0,039 * |
| ICS & Montelukast                               | -0,084                      | 0,139      | -0,064                    | -0,607 | 0,545   |
| Gender                                          | 0,050                       | 0,202      | 0,019                     | 0,248  | 0,804   |
| Age                                             | 0,024                       | 0,031      | 0,062                     | 0,775  | 0,440   |
| Dietary habits/Sugar intake                     | 0,269                       | 0,094      | 0,229                     | 2,874  | 0,005 * |
| Oral hygiene habits                             | -0,145                      | 0,223      | -0,051                    | -0,651 | 0,516   |
| Years of medication                             | 0,018                       | 0,057      | 0,041                     | 0,319  | 0,750   |

*a* Dependent variable: number of lost, decayed, and filled teeth.

**TABLE 3** Coefficients of all combined variables.

considerable, may need to provide more statistical power for robust conclusions. The relatively small number of participants in each group could compromise the precision of the results. Moreover, conducting the study in a specific hospital setting might limit the generalisability of the findings to a broader population. Results observed in Lisbon, Portugal may not accurately reflect outcomes in different geographic locations or healthcare settings. Another potential issue is the recall bias, as participants may inaccurately remember or report relevant information such as their habits, medication use, or other relevant information. Such biases can impact the validity of the study's conclusions. Understanding how these conditions interact with asthma and medication is essential for comprehensive healthcare planning.

The cross-sectional design of the study, capturing data at a single point in time, restricts the ability to establish causation or assess changes over time. Additionally, while the study evaluates the impact of medication on oral health, it lacks depth in exploring specific dosage, duration of medication use, and adherence patterns. These factors are crucial for understanding the true effects of medication on oral health outcomes. The study explains only a small proportion of the variability in outcomes, suggesting that other unexplored factors may contribute to the observed patterns. Further research is necessary

to elucidate these factors and their impact on the relationship between asthma, medication, and oral health.

It is essential to acknowledge the impact of the pandemic on the study and data collection. Restrictions on movement and access to healthcare facilities may have hindered data collection efforts. Participants' willingness to engage with researchers may have been affected due to concerns about virus transmission. Furthermore, disruptions to routine healthcare services, including dental examinations, may have influenced the accuracy of oral health assessments.

Although the study offers important insights into how asthma and its treatment affect children's oral health, it is crucial to carefully consider these results in light of the previously mentioned limitations. Further research with larger and more diverse samples, longitudinal designs, and comprehensive exploration of relevant factors is necessary to advance our understanding in this field. Only through rigorous investigation it will be possible to develop effective strategies for addressing the complex interplay between asthma, medication, and oral health in children.

## Conclusions

- Children diagnosed with asthma with undergoing medication, exhibit a higher susceptibility to caries cavities

- in comparison to their healthy counterparts.
- Each of the medication alone had no significant effect on the appearance of caries cavities.
- Specific asthma medications, notably corticosteroids + bronchodilator+ antihistamines, showed a strong association with caries cavities occurrence.
- Strong and meaningful associations were observed between the presence of caries cavities and three variables: the intake of sugar, the commencement age of medication, and the quantity of drugs administered.

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