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### **Original research**

# Characterization of recurrent aphthous stomatitis in a young population



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#### ABSTRACT

**Aim:** To characterize recurrent aphthous stomatitis in a young population and investigate the association between these lesions and predisposing factors, as well as potential modifications in children's daily routines.

**Methods:** The data was collected by delivering a questionnaire to students attending S. Miguel Primary School, in Vizela, as well as to their parents/guardians. A literature review was conducted, using scientific databases such as PubMed, Cochrane and the Virtual Library of the University of Porto.

**Results:** A common prevalence of aphthous ulcers was found in 53.0% of the sample. Most participants reported a number of lesions between 1 and 5, located in the jugal/labial mucosa, healing within 4 to 7 days. About 46.4% of the participants had a family history of this disease, mainly on the mother's side. About 29.6% of the students associated aphthae with traumatic events in the oral mucosa, while 9.8% associated them with stress. A significant association was found only between the frequency of aphthae and gastrointestinal disorders, and not with other factors. A significant use of topical medications was detected, and the pharmacist was the most consulted healthcare professional.

**Conclusion:** This study's findings were in line with previous data on the clinical characteristics of aphthae and confirm the negative impacts of this disease on children's quality of life, reporting its association with gastrointestinal disorders. (Rev Port Estomatol Med Dent Cir Maxilofac. 2018;59(1):10-17)

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#### 11

# Caracterização da estomatite aftosa recorrente numa população infantojuvenil

RESUMO

**Objetivo:** Caracterizar a estomatite aftosa recorrente numa população infantojuvenil, averiguando a sua relação com fatores predisponentes e possíveis modificações nas rotinas diárias das crianças.

**Métodos:** Os alunos da Escola Básica de S. Miguel, Vizela, e respetivos encarregados de educação foram submetidos a um questionário. Foi também realizada uma revisão da literatura nas bases de dados PubMed, Cochrane e Biblioteca Virtual da Universidade do Porto.

**Resultados:** Foi determinada uma prevalência de aftas em 53,0% dos participantes, sendo que a maioria referiu um número de lesões entre 1 e 5, com localização na mucosa jugal/ labial e com período de cicatrização de 4 a 7 dias. Cerca de 46,4% da amostra apresentou história familiar, tendo sido a mãe o progenitor mais indicado. Cerca de 29,6% dos inquiridos associaram a presença de aftas com eventos traumáticos na mucosa oral, enquanto 9,8% associaram com o stress. Foi apenas encontrada uma associação significativa entre a frequência de aftas e alterações gastrointestinais, não se verificando o mesmo com outros fatores. Verificou-se ainda uma utilização acentuada de medicamentos tópicos, sendo o farmacêutico o profissional de saúde mais consultado.

**Conclusões:** Os resultados deste estudo estão de acordo com a literatura quanto às características clínicas das aftas e quanto ao impacto negativo desta doença na qualidade de vida das crianças, verificando-se a relação com alterações gastrointestinais. (Rev Port Estomatol Med Dent Cir Maxilofac. 2018;59(1):10-17)

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#### Introduction

Palavras-chave:

Medicina oral

Infantojuvenil

Recorrente

Estomatite

Aftas

Aftosa

The recurrent aphthous stomatitis (RAS) is the most common ulcerous disease of the oral mucosa.<sup>1,2</sup> It usually onsets in childhood and affects about 25% of the world population.<sup>3-6</sup> Its typical lesions are well-circumscribed rounded ulcers surrounded by a peripheral halo of erythema, with a white/yellowish fibromembranous center. It has three main presentations: minor, major and herpetiform, of which the minor is the most common. In the minor presentation, the aphthae generally heal in 4 to 7 days without leaving a scar, while in the major presentation aphthae need a larger period and might leave a scar.<sup>3-6</sup>

The etiopathogeny of RAS is still unknown and is often multifactorial. Several factors have been suggested as triggering agents, including local factors, such as local trauma, which is considered an etiological agent of RAS in susceptible patients.<sup>1,7,8</sup>

Regarding systemic factors, the infection by *H. pylori* has been reported as an etiological factor of RAS.<sup>9</sup> The ulcerous colitis and the Crohn's disease have also been associated with the appearance of oral ulcers similar to the ones of RAS.<sup>1</sup> Some authors state that patients with RAS have a higher prevalence of celiac disease and that RAS may be their first complaint.<sup>10-13</sup>

The role of genetic factors is also important in the etiology of RAS, as it is thought that at least 40% of patients with RAS have a family history of that condition. These patients tend to develop RAS at an earlier age, with more-severe symptoms and frequent episodes.  $^{4\text{-}6,14,15}$ 

It is thought that some allergies can cause RAS. Hypersensitivity to some food components and oral microbial agents are considered potential etiological factors.<sup>1,16,17</sup>

The association between RAS and some nutritional and blood deficits has been studied, and patients with RAS have been proved to present iron, B12 vitamin, folic acid and hemoglobin deficits more frequently.<sup>18</sup> The fact that 5-10% of patients with RAS present low blood levels of folate, zinc, iron, and B1, B2, B6 and B12 vitamins may suggest these nutritional deficits as potential causes.<sup>1,19,20</sup>

Stress-causing events were also subjectively found to be strongly associated with RAS episodes, but not with these episodes' duration. Furthermore, it was demonstrated that experiencing a stress-inducing situation raises almost three times the odds of RAS occurring.<sup>21</sup>

Lastly, RAS treatment acts mainly on symptoms' relief, and a topical approach is effective in most patients. Nevertheless, systemic treatment should be considered in patients with multiple episodes of minor RAS or patients with major RAS.<sup>1</sup>

The present work aims to characterize RAS in a young population, according to its frequency, location, painful symptomatology, applied therapies and time of healing. It also aims to study these lesions' association with predisposing factors and potential changes in children's daily routines.

#### Materials and methods

Information was obtained using a questionnaire that was completed by children from 3 to 11 years old who attended the S. Miguel Primary School (Escola Básica de S. Miguel), in Vizela, and another questionnaire that was completed by the corresponding parents/guardians for validation of the answers. To create the data extraction form and write the paper, the authors conducted a comprehensive literature review using the PubMed and Cochrane databases, as well as the Virtual Library of the University of Porto, introducing and combining the following keywords "recurrent aphthous stomatitis", "gastrointestinal", "trauma", "questionnaire", "inquiry" and "questions". The following inclusion criteria were defined for the selection of the articles: full text available, publication in the last 5 years, and article written in English, Portuguese or Spanish. Subsequently, studies essential for a better understanding of the subject were found in the references of the articles obtained in the first selection, and were included due to their relevance and extreme importance for the correlation between the results obtained and the existing knowledge in the literature

A meeting was held with the Board of the Schools Group of Infias (which includes the S. Miguel Primary School), in which the whole study was explained, and the authors were authorized to conduct it. Then, the questionnaires were delivered to the students, under the researcher's guidance. Considering that the children's answers could be difficult to assess, certain instruments were included in the questionnaire elaboration to simplify the understanding of the questions, such as cards with illustrative images (including examples of aphthae in the oral cavity and foods such as green vegetables and legumes) and an adapted pain scale<sup>22</sup> to aid its interpretation. Later, with the teachers' help, the questionnaires were handed to the parents or guardians of each participating child, who were asked to complete them at home and then deliver them at the school. After every questionnaire had been delivered to the school, they were all handed to the researcher.

This research was approved by the Ethics Committee of the Faculty of Dental Medicine of the University of Porto. Every data were collected after obtaining written consent for participation in the study, as established by the Declaration of Helsinki.

Statistical analysis was conducted using the IBM SPSS 23.0 and the Microsoft Office Excel 2013 software. After applying the Cronbach's alpha test, seven questions used in both questionnaires were validated for reliability ( $\alpha > 0.8$ ). The chi-square test was used to analyze the association between certain variables (association between aphthae and predisposing factors such as gastrointestinal disorders, allergies, daily toothbrushing frequency, use of orthodontic appliance, placement of pens/pencils in the oral cavity and consumption of some foods). A significance level of 5% was used in every test.

#### Results

This study included 183 children (91 male and 92 female) aged between 3 and 11 years (Figure 1).



The children's responses were found to be in agreement with their parents' responses, since the Cronbach's alpha test gave alpha values higher than 80% for the seven questions that allowed this validation.

A prevalence of aphthae was found in 53.0% of the participants (Table 1), showing an odds ratio of 1.33 (0.743;2.378). Girls had aphthae more often than boys, with most of them

Table 1. Distribution of aphthae occurrence by sex							
		Do you have aj	Total				
		No	Yes				
Sex	Male	46	45	91			
	Female	40	52	92			
Total		86	97	183			

Table 2. Pain classification								
	How would you classify the pain caused by aphthae (1 to 5)?							
		1	2	3	4	5	Total	
	1	17	1	3	1	0	22	
How is the pain	2	5	25	6	0	0	36	
you feel when you have aphthae,	3	0	5	45	5	0	55	
from 1 to 5?	4	0	3	5	21	0	29	
	5	0	1	2	5	13	21	
Total		22	35	61	32	13	163	
Chi-Square Test							р	
Pearson Chi-Square						0.00		



reporting 1 to 5 lesions (95.8%), located in the jugal/labial mucosa (67.3%) (Figure 2) and taking 4 to 7 days to heal (92.8%).

The most frequent answer (33.7% of children; 37.4% of parents) to the pain scale used in the questionnaire was number 3 – moderate pain (Table 2). The chi-square test was used to analyze the association between the children's and parents' answers, which were in agreement (p-value <0.01%). Approximately 46.4% of participants had a family history of RAS (Figure 3), mainly on the mother's side. Around 29.6% of the students associated the presence of aphthae with traumatic events on the oral mucosa (Table 3), showing an odds ratio of 36.0 (13.010;99.617), i.e., the likelihood of parents perceiving aphthae as occurring in children after an injury to the oral cavity was 36 times higher when their children also considered it compared to when they did not. On the other hand,

Table 3. Aphthae occurrence after trauma in the oral cavity / stress episodes									
					Do you think a	phthae occur mainl	у		
		After your child injures one area of the oral cavity?					When y any	your child tious/nerv	is more ous?
		No	Yes	Total	•		No	Yes	Total
Do you have aphthae after hurting an area of your mouth?	No/Expected Count	108/87,3	6/26,7	114/114,0	Do you have	No/Expected Count	145/134,4	2/12,6	147/147,0
	Yes/Expected Count	16/36,7	32/11,3	48/48,0	when you are more	Yes/Expected Count	4/14,6	12/1,4	16/16,0
	Total/Expected Count	124/124,0	38/38,0	162/162,0	anxious or nervous?	Total/Expected Count	149/149,0	14/14,0	163/163,0

Table 4. Application of the Chi-Square test for analysis of the association between aphthae and predisposing factors									
		Does your child have any gastrointestinal disorders?	Does your child have any allergies?	How many times a day does your child brush their teeth?	Is your child currently wearing an orthodontic appliance?	Does he/she often put pens/pencils in the oral cavity?	How often does your child ingest green vegetables?	How often does your child ingest legumes?	
How often do aphthae appear in your child's oral cavity?	t	9.506	3.441	3.667	4.043	1.510	14.628	10.489	
	df	3	3	6	3	3	9	12	
	р	0.023	0.328	0.722	0.257	0.680	0.102	0.573	

t – value; df – degrees of freedom; p – value.



#### Table 5. Types of therapy and access to therapies

Table 5. Types of thera	py and access to merapie	5		
		Frequency	Percentage	Valid percentage
Valid	Topical	77	42.1	95.1
	Systemic	1	0.5	1.2
	Topical home medicine	3	1.6	3.7
	Total	81	44.3	100.0
Missing	System	102	55.7	
Total		183	100.0	
Valid	Own initiative	17	9.3	21.0
	Pharmacist	37	20.2	45.7
	Dentist	6	3.3	7.4
	Family doctor	13	7.1	16.0
	Pediatrician	8	4.4	9.9
	Total	81	44.3	100.0
Missing	System	102	55.7	
Total		183	100.0	



Figure 4. Therapies applied

9.8% associated aphthae with stress-causing events (Table 3), showing an odds ratio of 217.55 (36.076;1311.309), i.e., the likelihood of parents considering that aphthae appeared in their children when they were anxious/nervous was manifestly superior when their children also considered it comparing to those who did not.

A significant association was found between the frequency of aphthae and gastrointestinal disorders (p = 0.023). However, the aphthae's association with allergies or other factors such as daily toothbrushing frequency, use of orthodontic appliance, placement of pens/pencils in the oral cavity and consumption of some foods (vegetables, legumes) was not statistically significant (Table 4).

Although most of the respondents referred not applying any treatment (Figure 4), a marked use of topical drugs was found, with the pharmacist being the most consulted healthcare professional (Table 5).

#### Discussion

In this study, 97 children (53.0% of the study population) stated having aphthae regularly. Although this is not a real prevalence, the obtained percentage for aphthae occurrence is similar to the one described by Rogers,<sup>23</sup> who indicates that the prevalence of RAS may vary between 5% and 50%, depending on the studied population. According to the same author, females are more affected by this condition.<sup>23</sup> Nevertheless, no association was found between aphthae occurrence and gender in the present study.

Most of this research's participants stated that the number of lesions in each RAS episode was between 1 and 5. Moreover, most of them also indicated a time of healing of 4 to 7 days. These results suggest that the majority of the participants probably had a minor manifestation of RAS, which, according to Rogers,<sup>24</sup> is the most common one and is characterized by a number of lesions between 1 and 5. The corresponding time of healing is also consistent with the literature.<sup>25</sup> Regarding the lesions' localization, this study revealed that RAS appeared in any area of the oral cavity and that the most frequent localization was the jugal and labial mucosa, which is consistent with other studies published by several authors.<sup>3-5,26</sup>

In the study by Gavic et al.,<sup>27</sup> a pain scale of 0 to 10 (with 0 corresponding to slight pain/burn and 10 corresponding to extreme pain) was applied, with 7 being the most indicated number, which is close to extreme pain. In the young population of this study, using a simplified pain scale (from 1 to 5, with 1 corresponding to no pain and 5 to intense pain), the most indicated response by the children was number 3 (Table 2). These results suggest that in younger age groups the pain felt in the presence of these lesions is considered moderate.

Krisdapong et al.<sup>28</sup> concluded that RAS has an impact on oral hygiene and dietary habits. The same was verified in this study, as approximately 60 of the parents/guardians claimed that their children avoided brushing the areas affected by aphthae. This finding suggests that children do not brush their teeth effectively in the areas near the lesions, so as to avoid the pain. Furthermore, 60.9% of the parents/guardians stated that their children had difficulty chewing food. These findings are consistent with the literature, where RAS is described as painful and capable of creating difficulties in daily activities such as talking, laughing and chewing.<sup>4,28,29</sup>

In this research, 46.4% of the students had a family history of RAS. This percentage is higher than the one presented by Gürkan et al.,<sup>15</sup> where 35.8% of the patients had a family history of RAS. This difference might be explained by the fact that the studied age groups were more limited in the present research (3-11 years) in comparison with the ones studied by Gürkan et al.<sup>15</sup> (2-17 years). The present study also revealed that, of both parents, the mother seemed to contribute more to the family history of this condition.

In the young population of this study, 48 participants (29.6% of the sample) reported episodes of RAS associated with a previous trauma in the oral cavity. The percentage obtained in this regard was lower than the one detected by Wray et al.<sup>8</sup> (43.3%). On the other hand, only 9.8% of the participants reported episodes of stress associated with the occurrence of aphthae. This result reflects an association between stress and RAS less frequent than the one presented by Bratel and Hakeberg,<sup>30</sup> in whose study 15.8% of the patients indicated stress as a potential etiological factor for aphthae development. These results may be explained by the fact that the studies found in the literature included samples that were essentially composed of adults, whereas the present study focuses on a markedly younger population.

In the present study, a significant association was found between the frequency of aphthae and gastrointestinal disorders. However, the aphthae's association with allergies, daily toothbrushing frequency, use of orthodontic appliance, placement of pens/pencils in the oral cavity and consumption of some foods (green vegetables and legumes) were not statistically significant. Only 6.0% of the studied sample presented some gastrointestinal disorders. This percentage is inferior to the one reported in the study by Diaz et al.,<sup>31</sup> where 35.8% of the studied cases showed gastrointestinal disorders (namely, gastroenteritis, malabsorption syndrome, ulcerous colitis and giardiasis). However, it is important to note that the study by Diaz et al.<sup>31</sup> included adult patients, whereas the present research focused on a much younger population.

Regarding the therapies used, most of the parents/guardians indicated that they did not apply any type of treatment and waited for the lesions to heal spontaneously. These actions may result from the fact that there is not yet a definitive treatment protocol for RAS.<sup>32</sup> According to Ranganath and Pai,<sup>32</sup> this situation is explained by the lack of clinical trials and the differences in response between different patients. Nevertheless, it may also be explained by the fact that the exact etiology of RAS is still unknown.<sup>23</sup>

Of the group who stated applying some therapy, most used topical drugs (namely, drugs including hyaluronic acid), which is consistent with the existing literature, where topical drugs are described as the therapy of choice for most patients with RAS.<sup>3,33</sup> Regarding the access to these drugs, many of the respondents had consulted a pharmacist. Only 7.4% of the participants reported having consulted the dentist, which is a lower percentage than what was expected, considering that the dentist is the healthcare professional with the most adequate knowledge for the diagnosis and treatment of this type of lesions.

One of this study's limitations was the fact that the information was obtained only using a questionnaire, without any complementary clinical observation. Furthermore, it was not possible to distinguish between aphthae (clinical situations of RAS) and traumatic ulcers. There is a need for more studies that include evaluating the influence of the predisposing factors in the development of RAS. More studies about how this condition affects the daily routines and the quality of life, as well as the therapies usually used, are also required to allow a more effective action to understand this condition.

#### Conclusions

This study's results are consistent with the literature regarding aphthae's clinical features. The previously referred association between aphthae and gastrointestinal disorders was shown in this study.

An association between traumatic events in the oral mucosa or stress episodes and the development of aphthae was also found, although in a less frequent proportion than in other previous studies.

A marked percentage of family history was detected, mainly on the mother's side, thus reinforcing the pertinence of further exploring this line of research. This research also allowed to reinforce the information in the literature about the negative impact of this condition on the quality of life, as well as the preference for topical therapies.

#### **Ethical disclosures**

**Protection of human and animal subjects.** The authors declare that no experiments were performed on humans or animals for this study.

**Confidentiality of data.** The authors declare that they have followed the protocols of their work center on the publication of patient data.

**Right to privacy and informed consent.** The authors have obtained the written informed consent of the patients or subjects mentioned in the article. The corresponding author is in possession of this document.

#### **Conflict of interest**

The authors have no conflicts of interest to declare.

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#### **Appendices**

Supplementary content associated with this article can be found, in the online version, at http://doi.org/10.24873/j. rpemd.2018.06.222.

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