Clinical Features, Etiology, and Management Strategies for Canker Sores: A Review study for Causes, Risk Factors, Treatment Options, Research and Innovations

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ABSTRACT

Canker sores, better known in clinical practice as recurrent aphthous stomatitis (RAS), are among the most common conditions of oral mucosa, presenting painful recurrent ulcers. The etiology, hereby proposed as multifactorial will embrace genetic predisposition from nutritional deficiency and lifestyle on one side, and considering clinical presentation, the scope of diagnostic approaches followed by the scope of the treatment that goes from pharmaceutical intervention to more natural choices. It focuses on more preventive practices and novel therapies with elements of immunotherapy, nutrition therapy, and supplementary intake as a source. So, the importance lies in comprehensive management that has an objective of enhancing patient quality. In conclusion, multifaceted management that includes dietary management, topical treatments, good oral hygiene practices, and behavioral changes can be employed effectively to reduce the recurrence among high-risk patients, but with continued research and clinical trials the approach can be well substantiated and therefore these strategies in turn can help develop effective management plans among the affected subjects with RAS. Further research is to be conducted; integrating immunotherapy into nutritional support and systemic treatments may eventually manage canker sores and better quality of life for the afflicted.

Keywords: Canker sores, Recurrent Aphthous Stomatitis, Oral Ulcers, Nutritional Deficiencies, Treatment, Prevention, Immunotherapy.

1. Introduction

Most people in the population will have had at least one episode of canker sores or recurrent aphthous stomatitis. Indeed, RAS is a recurrence of painful ulcers, primarily manifesting as a singularity or multiple lesions on the mucous membrane located in the mouths, which particularly occurs at the area known as the vermilion

border, buccal mucosa, or dorsal side of the anterior tongue segment and/or lips. These ulcers are normally well-defined, round to oval with white to grayish yellow pseudomembrane and with a reddish-colored halo around the whole lesion (Çimen et al., 2003; Probosari, 2023; Ślebioda et al., 2013). Considering clinical variants, there exist three types of RAS namely minor, major, and herpetiform ulcers; and minor RAS is believed to be the most common type (Patil et al., 2014).

Clinically, a diagnosis of canker sores would only be achieved through a keen clinical history and examination. The ulcers are always painful, severely discomforted, especially when they first appear but usually heal after 10 to 14 days without scar formation (Mizrahi et al., 2004). Painful ulcers however may, be complicated with some triggers including stress food and other health condition (Ślebioda et al., 2013). Furthermore, genetic predisposition to RAS has been suggested because familial patterns occur in nearly 40% of cases (Abdullah, 2013). The etiology of canker sores remains not well established. A plethora of factors have, however, been proposed as a reason that leads to the emergence of the disease. Some of the identified elements include dysregulation in the immune system, vitamin deficiencies such as B12 and folic acid deficiency or iron deficiency, and oral trauma localized to the area concerned (Ślebioda et al., 2013). Smoking cessation has also been implicated to be associated with a more common occurrence of RAS, probably due to the lost protective keratinization of the oral mucosa while on tobacco (Rivera et al., 2021). RAS shows an inflammatory nature as can be gathered by systemic diseases, including inflammatory bowel diseases and some autoimmune conditions, which it shares an etiologic relationship with (Ślebioda et al., 2013).

In summary, canker sores are clinically defined by their recurrent nature, painful presentation, and characteristic appearance on the oral mucosa. This may require symptomatic relief and further treatment of potential underlying causes, underlining the need for broad knowledge of not only the clinical features but also of the multifactorial etiology of this relatively common condition. This clinically has the name recurrent aphthous stomatitis (RAS). It is one of the most common conditions in the general population. Lifetime prevalence of RAS ranges between 25% and 50%. This implies that a huge number of people experience this agonizing oral condition at one point in their lifetime (Bilgili et al., 2013; Stoopler, 2024). From many other different research studies, the prevalence of RAS is diverse and depends upon demographic features, age, gender, and also a geographic distribution.

Table 1. Types of Recurrent Aphthous Stomatitis and Characteristics.

Type	Size	Healing Time	Scarring	Key Features	References
Minor RAS	<1 cm	7–14 days	None	Single or multiple small ulcers.	Ślebioda et al., 2013; Zakaria & Hosny, 2018
Major RAS	>1 cm	2–6 weeks	Yes	Deeper, painful ulcers with scarring.	Ślebioda et al., 2013; Probosari, 2023

Herpetiform RAS	1–2 mm (grouped)	7–10 days	Rarely	Clusters mimicking herpes-like lesions.	Probosari, 2023; Shulman, 2004

RAS is an illness related to the occurrence of canker sore primarily depending on age. According to other other research, reports of canker sores are highly prevalent among teenagers and adults aged between 16 years and 25 years (Pangestika & Lubis, 2023; Hollá et al., 2017). However, worth mentioning is that RAS may affect any age range, including children and elderly persons, though in various proportions (Al‐Maweri et al., 2023). Prevalence rates across the age groups show a trend to more susceptibility in the younger populations, possibly due to some physiological change or stressors associated with this life stage (Al‐Maweri et al., 2023).

There are also gender differences in the prevalence of canker sore. Evidence shows that RAS was reported more among women than among men. Studies are said to report a higher incidence of ulceration in women compared to the men counterpart (Afridi et al., 2014; Sajewicz-Radtke et al., 2023). Some reasons that may explain these differences have been attributed to hormonal fluctuation, stress-related psychological events, and gender-associated differences in lifestyles (Ślebioda et al., 2013). Geographically, the prevalence of RAS may differ significantly. For example, it has been reported that the prevalence rates may also vary by racial and ethnic demographics, and some reports indicate greater prevalence rates in certain populations (Taher, 2024). In some environments, it has even been reported with prevalence rates as high as 44.5% for recurrent oral ulcers; hence, local factors that may comprise dietary habits as well as environmental influences may likely explain the variability between the prevalence rates (Ghosal et al., 2020).

In summary, canker sores are among the most common oral conditions, widely prevalent in the general population and with a wide range of lifetime prevalence rates. Age, gender, and geographic location are among the factors largely determining the prevalence rates for RAS. Such demographic variation needs to be well-understood to plan targeted approaches toward prevention and treatment of the affected populations. Knowledge about etiology, therapy, and prevention of recurrent aphthous stomatitis or canker sores is fundamental practice knowledge in the field of healthcare for many reasons. Canker sores are the most common diseases involving oral mucosa, presenting as painful ulcerations that strongly interfere with the quality of a patient's life in eating, speaking, and oral hygiene practices (Rivera, 2019). This implies that proper management strategies are needed in preventing and controlling RAS, especially among populations like dental students (Rahmadhany et al., 2022).

The etiology of the canker sores is also multifactorial involving genetic and immunological factors as well as environmental factors. Psychological stress has been explained as an important predisposing condition in the disease, arguing then that the mental health determinants would feature in both the study and treatment management of this disease also, according to Syifa, (2023). Systemic disorders and nutritional deficiencies can enhance frequency and severity of outbreaks of outbreak and thus require holistic assessment of the patient regarding the need for treatment, from the perspective of Rivera, 2019. The mode of treatment has included

pharmacological intervention and alternative therapies as explored. For example, topical agents like triamcinolone acetonide can also be used for symptomatic relief (Dhopte & Bagde, 2022). Even recently tetrahydrocurcuminoids have come into attention that they not only ameliorate but also curb the disease progression symptomatically, without any adverse effect (Majeed et al., 2020). Other herbal remedies studied for potential anti-inflammatory activities were Calendula officinalis, indicating the possibility that natural products might participate in healing canker sores (Khairnar et al., 2013).

Preventive measures also play a very important role in the management of canker sores. The treatment of causes such as stress, nutritional deficiency, and other hygiene measures improves oral health preventively for the development of an attack (Rahmadhany et al., 2022). Moreover, knowledge about disease-causing pathogens like Helicobacter pylori related to oral diseases has been important for preventive measures as well as for guidance about the treatment procedure (Moradi et al., 2023). This then leads to such in-depth knowledge regarding the cause, treatments received, and precautions involved in managing canker sores. With this aspect of information, medical doctors gain knowledge for better case management through an establishment basis. Beyond such bases in case management, generally, this information contributes to a good patient health status as well as an amalgamation between the physical and psychosocial factors while considering patients for management purposes.

2. Causes and Risk Factors

Canker sores, clinically recurrent aphthous stomatitis, are among the most common conditions presenting with pain and recurrent ulcers in the oral cavity. The etiology for canker sores is complex and multifactorial with several primary causes proposed in the literature. Nutritional deficiency is one of the major factors related to the development of canker sores. Through research, it has been seen those deficiencies in vitamins B12, folic acid, and iron are some of the causes that trigger RAS. For example, it has been proven that patients with recurrent aphthous ulcers recover with nutritional supplementation, especially vitamin B12 (Sharma et al., 2022). It postulates that nutritional status could be implicated in the development of these ulcers; deficiencies compromise both mucosal integrity and immune function (Hazeem, 2024).

Psychological stress, especially associated with trauma, has been implicated as another possible causality for canker sores. Stress is said to have played an incremental factor with RAS; most report recurring attacks coincide with stressful events (Hazeem, 2024; Sabbagh & Felemban, 2016). Traumatizing the oral mucosa through dental procedures or even biting into oneself causes ulcers (Chavan et al., 2012). This indicates that both physical as well as psychological stressors contribute to interference with normal healing of the oral mucosa, causing ulceration. Immunodeficiency is another very strong cause for canker sores. There is evidence to

indicate that RAS relates to an autoimmune response and T lymphocytes play an important role in the inflammatory reaction involved in the process of ulcer formation (Hazeem, 2024; Sabbagh & Felemban, 2016). In addition to this immune-mediated component, evidence that suggests a greater level of angiogenic factors, including VEGF, within the tissue surrounding aphthous ulcers may be reflective of some deficiency in epithelialization and healing (Arbiser et al., 2003).

Recently, of interest has been the involvement of the microbiome in RAS with reports pointing that certain bacterial colonization may initiate ulcers. For example, certain bacteria, such as Escherichia coli, are thought to be related to the formation of aphthous ulcers. However, mechanisms are not clear (Yang et al., 2020). This would indicate a possibility of microbial factors acting as contributing factors to the ulcerative process with host immune responses. Regarding lifestyle factors believed to cause canker sores, smoking cessation is included. Those who quit tend to have a rising onset of RAS, merely due to the change in the mucosal environment of the mouth, or changes in the process by which keratinization has post-stop smoking (Rivera et al., 2021). Thus, it can be concluded that mostly external conditions, such as habitual and lifestyle change, trigger a disease.

Canker sores are clinically known as recurrent aphthous stomatitis (RAS). These are painful lesions that affect the mucosa of the oral cavity and have a multifactorial etiology associated with dietary, environmental, and lifestyle factors said to provoke their onset. Dietary factor accounts for one of the biggest contributors of canker sores. These are certain foods, particularly acidic and spicy, such as citrus fruits, tomatoes, and nuts. These are the types of foods that usually cause RAS (Bandari, 2024; "Prevalence and Age-Related Risk of Three Clinical Variants of Aphthous Stomatitis: a Retrospective Study", 2020). There is also the aspect of nutritional deficiency with some people lacking vitamins B12, folate, and iron. This means that proper nutrition is essential to keep healthy oral conditions ("Prevalence and Age Related Risk of Three Clinical Variants of Aphthous Stomatitis: a Retrospective Study", 2020; Rivera, 2019). In addition, overconsumption of processed foods and sugars may accelerate inflammation and increase the chances of having these ulcers (Rivera et al., 2021).

Some environmental factors that have been proven to affect the incidence and severity of the canker sores, include stress. Stress contributes hormonal effect that can weaken the immunes system of a human to oral lesions (Natto et al., 2021; Priambodo et al., 2021). In addition, lifestyle factors, including irregular sleep patterns and lower levels of physical activity, which are mainly contributed by the stressful phase of the COVID-19 pandemic, have been identified to be associated with the development of canker sores (Wahyuni et al., 2022). The psychological impact of stress, that is, anxiety and depression, has also been identified as a risk factor in the presentation of RAS (Priambodo et al., 2021; Probosari, 2023).

Lifestyle habits is a major prevention of canker sore, mostly of the habit of smoking and habits related to oral hygiene, where the smoker changes the oral keratinization of the mucosa so that the ulcers will not be formed but within weeks after quitting, RAS becomes elevated (Rivera et al., 2021). Poor oral hygiene, such as poor brushing and flossing, will cause inflammation and pose a risk of canker sores

(Suharja, 2022). Moreover, any type of traumatic injury to the oral mucosa from dental devices or injuries from accidental bites may precipitate painful canker sores (Suharja, 2022). Summary Canker sores are influenced by an interplay of multifactors that include dietary, environmental, and lifestyle factors. These etiologic factors can provide much insight into the management as well as prevention of recurrent aphthous stomatitis.

Nutritional deficiencies particularly iron, zinc, and vitamin B12, have been implicated in the pathogenesis of canker sore. Some of the possible ways in which this may be related are compromising integrity of the oral mucosa or affecting immune function because of which the susceptibility for forming these painful lesions may go up. The condition of Vitamin B12 deficiency has been very pertinent in this case. Vitamin B12 plays a significant role in cellular metabolism, majorly in DNA synthesis and in the formation of red blood cells. Deficiency in the vitamin caused mucosal changes within the mouth like glossitis and stomatitis in the form of ulcers, which are popularly termed as canker sores Kozlak et al. (2010). There is ample research proving that patients with RAS also demonstrate very low serum levels of vitamin B12, and some studies claim as much as 26.2% of patients with RAS demonstrating significant deficiencies in vitamin B12, iron, and folic acid (Pişkin et al., 2002). This may be due to dietary inadequacy, particularly in individuals with very strict vegetarian or vegan diets, during which animal products are completely absent; these are the primary sources of vitamin B12 (Bondu et al., 2019).

Another very important factor that comes along with the occurrence of canker sores is iron deficiency. Iron is necessary for many physiological processes, such as oxygen transport and immune function. Iron deficiency can thus impair healing of oral mucosa thereby increasing susceptibility to ulcers. In fact, there exists evidence showing that most RAS patients have iron deficiency; some research even reported that 5% of all patients diagnosed with RAS had deficiency of iron (Pişkin et al., 2002). This condition can further be complicated by gastrointestinal diseases that cause an impairment in iron absorption that exposes the patient to the occurrence of canker sores (Oviedo et al., 2017). The second cause of canker sores is zinc deficiency. Zinc is important in providing immunity, wound healing, and integrity to the mucosal barrier. The above amount of zinc deficiency could further weaken the immunity and may result in delayed healing of ulcers which appear on the mouth and render an individual prone to recurrent ulcers.

For example, inflammatory bowel disease patients, having lesser amounts of vitamin B12 in the bloodstream, indicate it can facilitate a mechanism of action in these trace elements so they might mutually modulate one another positively towards alteration of oral status (Oviedo et al., 2017; Mousavi & Moradzadegan, 2022). Lacking iron, zinc, and vitamin B12 contributed substantially to the development of canker sores caused by impairment of immune functions, compromise of mucosa integrity, and interference with healing. Dietary modification or supplementation would help reduce the incidence as well as the severity of RAS.

3. Types and Characteristics

Canker sores, or recurrent aphthous stomatitis (RAS), can be categorized into minor, major, and herpetiform forms. Each type is different in terms of size; the number of these lesions at a given time and the healing rate, which really helps in diagnosis and its management. Minor Canker Sores are the most common RAS variant and make up about 75-85% of all cases "Prevalence of aphthous stomatitis reported in a private dental institution - a retrospective study" (2021) Mustafa & Alzubaidee, 2020). Such ulcers usually have less than 1 cm in diameter and without clear out-lining features, as defined by the pseudo membrane which could be whitish or gray, it surrounds an erythematous halo. Ślebioda et al., 2013; Zakaria & Hosny, 2018. Minor canker sores take 7 to 14 days to heal without leaving scars; they are usually solitary lesions, although several may be present at one time (Shulman, 2004; Zakaria & Hosny, 2018). Patients are quite painful, but the ulcers do not scar on healing (Misra et al., 2013).

Major aphthous ulcers, also known as Sutton's ulcers, occur less frequently and account for about 10-15% of all cases with RAS ("Prevalence of aphthous stomatitis reported in a private dental institution - a retrospective study", 2021; Ślebioda et al., 2013). These ulcers are larger than 1 cm and thus penetrate much deeper in the tissue. They cause worse pain for a longer time, and heal relatively slowly, normally between 2 to 6 weeks (Ślebioda et al., 2013; Shulman, 2004). Main canker sores often lead to scarring when healing and a few of these are related to systemic conditions or other systemic diseases (Misra et al., 2013; Probosari, 2023). These are more sensitive and, therefore, would require stronger therapies other than the superficial ulcers (Tanacan et al., 2022).

Herpetiform canker sores

Herpetiform Canher Sores are the least amongst RAS. Cases compose only about 1-5% of all cases made diagnoses (Prevalence of aphthous stomatitis reported in a private dental institution - a retrospective study", 2021; Ślebioda et al., 2013). The lesions from such ulcers are smaller, having diameters up to 1-2mm and are normally coherent into bigger sites for ulcerations (Shulman, 2004; Zakaria & Hosny, 2018). Herpetiform ulcers occur in groups, are more painful than minor ulcers, and heal in about 7 to 10 days (Probosari, 2023; Zakaria & Hosny, 2018). Like others, recurrent herpetiform canker sores very often are frequent and almost appear like herpes simplex viruses because of their way and congregation (Ślebioda et al., 2013; Misra et al., 2013). Summary Major and minor and herpetiform vary greatly with each other; minor is very small and tend to heal fast, will not scar, while major are quite large, quite deep, and may cause scarring in some cases. Herpetiform canker sores usually occur multiform, extremely painful and can recur frequently. Therefore, appreciation of these variations is crucial in the achievement of effective diagnosis and management of recurrent aphthous stomatitis.

The most common mucosal lesion of the mouth is technically known as recurrent aphthous stomatitis (RAS). Canker sores cause painful ulcers in the oral mucosa. There are various types of canker sores, which heal up at different times and tend to

scar; however, in most cases, they are self-limiting and heal with negligible scarring. Average healing time for canker sores is 7 to 14 days. Mizrahi et al. noted that even though canker sores may cause the most agonizing pain in general for the first 3 to 4 days, this pain subsides, leaving sores to heal in a period of 10-14 days without scarring (Mizrahi et al., 2004). Similarly, Sabbagh and Felemban observed that RAS ulcers also heal spontaneously within the same period, further supporting the theory that these lesions are self-limiting and rarely scar (Sabbagh & Felemban, 2016). The explanation for this fast healing is that the non-keratinized oral mucosa regenerates, which is essentially focused on RAS (Rivera, 2019).

The literature is always stating that RAS does not cause deep scars after healing. In the context of scarring, canker sores are unique compared to other oral lesions such as traumatic ulcers or herpes simplex lesions that could cause more pronounced scarring. For example, Majeed et al. observed that the healing abilities of the oral mucosa are such that canker sores heal without scarring (Majeed et al., 2020). Such a characteristic is very important to patients because, as far as aesthetic and functional implications are concerned, scarring can be very important in oral health.

In addition, the care of canker sores often involves topical treatments which are used to reduce pain as well as to promote healing and will further reduce the opportunity for scarring. Treatments like topical corticosteroids and mucoadhesive films have been demonstrated in practice to reduce symptoms and increase healing (Dhopte & Bagde, 2022; Fernandes et al., 2018). This will help to regulate the inflammatory response that encourages healing, while the risk of complications, such as scarring, will also be reduced. Conclusion The average healing time for canker sores is 7 to 14 days without leaving deep scars, hence making it different from all other oral ulcers. This rapid healing can be attributed to the regenerative capabilities of the oral mucosa. This is further supported by appropriate therapeutic interventions.

4. Symptoms and Clinical Presentation

The clinical term for this condition is recurrent aphthous stomatitis (RAS), which is characterized by painful ulcerations that usually involve the non-keratinized mucosa of the mouth. Symptoms can be divided into the prodromal and the acute phase of ulceration that occur before and at the onset of the lesion. Some patients may experience prodromal symptoms prior to the development of the actual canker sores. Patients typically present with focal burning or paresthesia’s within the oral cavity. Typically, this lasts for a few hours to several days before the emergence of the ulcers (Dhopte & Bagde, 2022; Ślebioda et al., 2013). There is discomfort or tenderness in the localized area, which may precede the actual ulcer formation (Rivera, 2019).

During the acute phase, typical presentations for canker sores consist of painful round or oval ulcers with well-defined borders, frequently having erythematous halos. These ulcers usually have a yellow or grayish floor and may vary in size

(Jurge et al., 2005; Sabbagh & Felemban, 2016). These lesions are very painful, and their pain becomes even more pronounced by such minor things as eating, drinking or even speaking, meaning quality of life is significantly hampered for those affected (Mizrahi et al., 2004). Ulcers resolve on their own in 7 to 14 days; however, a lot of repeated RAS happens to cause frequent recurrence per year (Rivera, 2019; Parra-Moreno et al., 2023).

Apart from these, other predisposing factors for increased frequency and severity are nutritional deficiency, stress, hormonal change, and some systemic disease conditions. For example, in smoking cessation, the recent quitters have a higher incidence of canker sore because their oral mucosa has changes in this condition (Rivera et al., 2021). Other comorbid conditions also encompass inflammatory bowel disease, which is an illness known to be associated with a higher prevalence of oral lesions, including canker sores, such as those found by Valentini et al. (2023). The characteristic symptoms of the prodromal phase, as usually reported before and at the onset of canker sore development, are tingling and burning sensations. Painful ulceration is the symptom that presents itself with some clinical characteristics peculiar to this acute phase. All of these symptoms can thus aid in the early detection and intervention for RAS.

This phenomenon or state known as Recurrent Aphthous Stomatitis (RAS), informally called 'severe canker sores,' may result in severe disablement of the quality of life that a person can and presumably likes to lead because such ulcers are painful, meaning there is considerable psychological strain apart from their clinical concern. RAS is the recurrent painful ulceration of oral mucosa that creates hurdles in food intake, speaking, and oral hygiene practices. These ulcers may also have a form of physical pain, which cripples the patients and negatively affects their productivity (Dhopte & Bagde, 2022; Rivera, 2019). The individual with RAS reports a reduced capacity for oral functioning due to recurrent ulcers, thereby reducing their welfare at both the body and mental levels (Alvarez-Azaustre et al., 2021).

Psychological manifestation cannot be ruled out for these recurrent canker sores. Chronic pain and aching with RAS can heighten stress and anxiety; that in turn could worsen the condition as well as the canker sores themselves (Syifa, 2023. This vicious cycle of psychological stress and self-manifestation, owing to canker sores, leads to a vicious situation where patients get entangled by continuous cycles of pain as well as emotional suffering. Psychological factors predispose to developing RAS, which proves that mental health is an integral element in the management of the illness (Syifa, 2023). Other than direct effects on the physical and psychological structures, major canker sores also have social effects. One may experience shyness or social loneliness because of the visible sores and pain that accompany them to hinder social activities and relationships (Alvarez-Azaustre et al., 2021). This inability to carry out activities fully may then add up to feelings of isolation and depression, making the general effect on quality of life worse.

Moreover, recurrent canker sores have economic costs which cannot be ignored. Such frequent visits to doctors and hospitals, their treatments, and the possibility of losing the opportunity to work due to the disabling nature of the disease pose added

economic burdens on the affected individuals and their families. This being the case, physical, emotional, and economic, can then be used to indicate how severe canker sores affect the quality of life in so many different dimensions.

Table 2. Risk Factors and Preventive Measures for RAS.

Risk Factor	Mechanism	Preventive Measures	References
Nutritional Deficiencies	Impaired mucosal integrity and immunity	Balanced diet, supplementation (B12, Iron)	Rivera, 2019
Stress	Immune suppression and hormonal changes	Mindfulness, meditation	Syifa, 2023
Poor Oral Hygiene	Increased irritation and infection risk	Regular brushing, flossing, antiseptic mouthwash	Suharja, 2022
Smoking Cessation	Altered keratinization post-cessation	Gradual cessation plans	Rivera et al., 2021

5. Diagnosis

The most common oral mucosal lesion is canker sores, or recurrent aphthous stomatitis (RAS), which presents painful ulcers that affect primarily the non-keratinized mucosa. Diagnosis usually is made by history and examination, as there are no specific laboratory tests for RAS. The clinical features include single or multiple painful ulcers varying in size and number that usually heal spontaneously within 7 to 14 days without scarring (Sabbagh & Felemban, 2016; Rivera, 2019; Mizrahi et al., 2004). Healthcare providers rely on certain criteria to establish a diagnosis. For example, International Study Group for Behçet's Disease proposed that recurrent oral ulcers should be recurrent at least three times a year in addition to other clinical features, such as recurrent genital ulcers or ocular involvement (\"undefined\", 2021). This requires that one eliminates other diseases which, just like RAS, are known to present oral lesions, such as Behçet's disease and Crohn's disease which, according to Guareschi (2024), is associated with oral ulcers manifestation (Parra-Moreno et al., 2023).

The history taken forms the basis for RAS diagnosis. They usually present in with a history of recurrences and are always painful at the onset of ulcers before the burning sensations take over over visible ulcers (Rivera, 2019; Mizrahi et al., 2004). Any other condition, for differential diagnosis, would also entail systemic symptom or another concomitant disorder such as gastrointestinal disorders or autoimmune diseases; the clinician is necessitated to consider it in diagnosing them (Huppert et al., 2006). In addition to this clinical examination, there has been an added notion supported by several studies that use real-time polymerase chain reaction, qPCR to aid in the search for suspected underlying infections such as Helicobacter pylori especially for unusual clinical presentations or even cases when suspecting systemic presence of this condition (Valdez-Gonzalez et al., 2014). These methods, while not quite used in conventional diagnosis of this condition in most clinics. Summary In general, the clinical diagnosis of canker sores relies mainly on a full history and

physical examination. While other systemic conditions need to be ruled out based on the varying medical guidelines that have specific criteria, the perspective in terms of diagnosis and management needs to be quite broad.

6. Treatment Options

Painful, open lesions which affect quality of life are included in the diagnosis for the term canker sores or aphthous ulcers. Mainly treated with OTC drugs for pain attenuation and stimulation of healing, various topical agents and natural remedies, in conjunction with nutritional supplements, constitute feasible options as outlined in the literature. Topical corticosteroids, including triamcinolone acetonide, are the most frequently used drugs for canker sores due to their anti-inflammatory effect. They cause less inflammation and pain at the site of application and, therefore, enable ulcers to heal faster (Liu et al., 2012). Mucoadhesive buccal films with corticosteroids have also been investigated because they provide extended contact with the ulcer, which may improve the therapeutic index (Fernandes et al., 2018). Topical analgesics also have the advantage of immediacy in pain relief and, hence, are preferred by patients who seek symptomatic relief (Virajitha, 2024).

Another adjunct that has been stressed in the treatment of canker sores is nutritional supplementing. Studies indicate that vitamin and mineral supplementations have also been effective in reducing the number and severity of such lesions, mostly those that are prone to conditions such as inflammatory bowel disease (Valentini et al., 2023). THC added has been hopeful in clinical methods where symptoms of canker sores and gingivitis decline in several weeks since starting treatment (Majeed et al., 2020). This would mean that nutritional therapy and topical therapy both can be applied in the treatment of canker sores. Some of the advantages of natural remedies, such as propolis, when applied in the treatment of oral lesions, have been presented. Propolis has anti-inflammatory and healing properties that might help minimize pain caused by canker sores, Son (2024). Other plants, such as those in the Garcinia genus, also have been utilized in the treatment of oral ulcers and are providing an alternative remedy to conventional treatments (Rosyidah et al., 2020).

The most effective and often prescribed over-the-counter treatment and widely used for canker sores include topical corticosteroids, analgesics, nutritional supplements, and natural remedies. All these treatments help improve symptoms or remove them to heal canker sores and thereby improve the outcome of such treatments. Topical corticosteroids and antimicrobial mouthwashes are usually the first lines of management in the case of recurrent aphthous stomatitis, or canker sores. Even though the two are symptomatic treatment measures, they are achieved through different mechanisms and, therefore, have different profiles regarding efficacy.

The most common topical corticosteroid agents are triamcinolone acetonide and dexamethasone because of their high anti-inflammatory potential. These agents are beneficial in managing pain and inflammation characterizing the canker sore, hence healing. Corticosteroids have proven effective in achieving marked symptoms improvement in patients with RAS, particularly when administered early during the ulcerative phase (Cao, 2024; M, 2022). However, the fear of systemic side effects

when used for a long time makes it necessary to use them judiciously (Duarte et al., 2011; Lee et al., 2013).

Conversely, the main reason for using antimicrobial mouthwashes is for their antiseptic properties in formulations such as chlorhexidine, povidone-iodine, and benzydamine hydrochloride. Antimicrobial mouthwashes may contribute to the secondary infections within ulcerated tissues by reducing the microbial load in the oral cavity (M, 2022; Fernandes et al., 2018). Antimicrobial mouthwashes provide symptomatic relief, and help in oral hygiene, but the recurrence of canker sores has been said to be much less prevented by them rather than by corticosteroids (M, 2022). In addition, antimicrobial drug abuse may result in additional complications like oral candidiasis, especially in immunocompromised patients with altered flora of the oral cavity (Tan & Suryana, 2021; Patil et al., 2015).

In a clinical set-up, the choice between application of topical corticosteroid and antimicrobial mouthwashes would be determined mainly by the severity of the pre-existing symptoms and the general health of the patient. For example, if there is severe and inflamed symptomatology, the anti-inflammatory mouthwashes using corticosteroids would typically be prescribed as a method of immediate relief to control the symptoms (Cao, 2024; M, 2022). Alternatively, antimicrobial mouthwashes can be considered for patients seeking prevention-type treatment or those experiencing recurrent ulcers but not aggressive type anti-inflammatory treatment (M, 2022; Fernandes et al., 2018).

Table 3. Treatment Options for RAS.

Category	Examples	Mechanism of Action	References
Pharmacological Agents	Triamcinolone acetonide, THC	Anti-inflammatory, accelerates healing	Dhopte & Bagde, 2022; Majeed et al., 2020
Nutritional Supplements	Vitamin B12, folate, zinc	Supports immune and mucosal health	Valentini et al., 2023
Natural Remedies	Propolis, Calendula officinalis	Anti-inflammatory and wound healing	Son, 2024; Khairnar et al., 2013
Preventive Care	Antimicrobial mouthwashes	Reduces microbial load, prevents infection	Fernandes et al., 2018

7. Prevention Strategies

Canker sores, also known as recurrent aphthous stomatitis (RAS), are painful ulcers within the mouth and can seriously impair quality of life. Still, there is no clear etiology for this condition; however, it has been possible to establish some lifestyle and dietary modifications helpful in preventing an episode of canker sore. These include dietary supplementation, stress management, and oral hygiene. Dietary supplementation is one of the primary preventive measures against this condition. Nutritional deficiencies, especially vitamins and minerals like vitamin B12, folate, and iron, are associated with the development of RAS according to Rivera (2019). A

systematic review shows that supplementing with β-1,3;1-6 glucans would strengthen the immune responses and heal the ulcers as the severity would be minimized in case of canker sores patients (Ramberg et al., 2010). Intake of anti-inflammatory compounds, including tetrahydro curcuminoids, has also been shown to provide promise for symptom relief and preventing disease progression, as cited by Majeed et al. (2020). A balanced diet rich in fruits, vegetables, and whole grains can provide essential nutrients that support oral health and immune function, thereby potentially reducing the incidence of canker sores.

Another important determinant in the prevention of canker sores is stress management. Psychological stress has been identified as one of the major predisposing factors for RAS (Syifa, 2023). Stress causes many physiological changes, including immune suppression, which could make the occurrence and severity of canker sores worse (Sharma, 2024). Mindfulness, meditation, and regular exercise reduce levels of stress and may prevent the occurrence of canker sores. One essential thing is proper oral hygiene, for the prevention of canker sores. Oral hygiene mainly causes inflammation or irritation in the oral mucosa and may lead the formation of the ulcers (Suharja, 2022). There should be oral hygiene consisting of regular brushing and cleaning with a floss coupled by rinsing using antiseptic mouthwash, which helps prevent dental infection or diseases, eventually reducing infection risks that will cause the canker sore formation. The well-known irritants like spicy food and acidic drinks would also be avoided to minimize mucosal irritation to its barest minimum (Sabbagh & Felemban, 2016).

In a nutshell, a multi-dimensional approach involving dietary supplements, stress management, and oral hygiene practices could help avoid recurrent episodes of canker sores. Thus, factors that affect lifestyle can lower their possibilities of experiencing recurrent attacks of the painful condition. Painful oral ulcers, clincher described as recurrent aphthous stomatitis (RAS), have the potential for poor quality of life in risky subjects. These often recur for most individuals due to genetic vulnerability combined with nutritional deficiency and possibly other environmental stimuli. Can't help but suggest a more long-term preventive measure rather than managing the recurrence of canker sores.

Dietary modification and nutritional supplementation may be a practical avenue. Rivera et al have also identified that the following nutrient deficiencies are strong, independent predictors of increased susceptibility to RAS: vitamin B12, folate, and iron. (2021) and Sabbagh & Felemban (2016). Supplemental intakes of these nutrients reduced frequencies of recurrent episodes of canker sores. As can be seen, a meta-analysis highlighted that there was a better prevention of the recurrences of RAS which resulted from the treatments for nutritional deficiencies; therefore, patients categorized to high risk should be often evaluated for their intake of diet and supplemented correspondingly (Sabbagh & Felemban, 2016; Parra-Moreno et al., 2023).

Topical treatments and supplementary drugs could be administered in addition to those discussed above. The newest curcuminoids derivations from turmeric identified as tetrahydrocurcuminoids (THC), orally administered for 21 days, significantly alleviated the manifestation and even reversed the further development

of canker sores, according to a review by Majeed et al., (2020). Recently, even low-level laser therapy has evolved, and its effectiveness has been established, which has come out in relief from pain and healing time for RAS lesions, say Dhopte & Bagde (2022). Such treatments not only render symptomatic relief but also partake in disease management thus reducing recurrences.

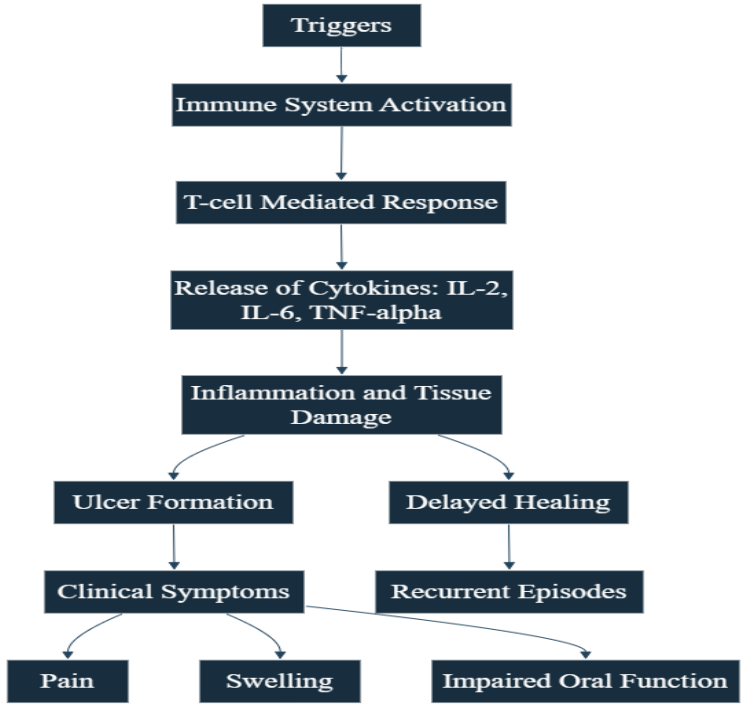

Fig 1. Pathophysiology of Recurrent Aphthous Stomatitis (RAS). This diagram illustrates the progression of RAS from triggering factors (nutritional deficiencies, stress, trauma, or microbial dysbiosis) to immune system activation, cytokine release, inflammation, and ulcer formation, leading to clinical symptoms like pain, swelling, and impaired oral function. Delayed healing often results in recurrent episodes.

Or else, poor oral hygiene also promotes the canker sores too. As a result, this poor oral hygiene aggravates the condition, thus increasing the recurrence of cases (Suharja, 2022). The frequency of recurrent infections that can trigger RAS can be minimized by conducting regular dental check-ups and using antiseptic mouthwashes (Fernandes et al., 2018). Besides, anti-inflammatory and analgesic natural remedies, such as clove oil used in treatment, have been of great assistance in helping patients manage symptoms and avoid relapse in some patients (Silva et al., 2023). Lastly, behavioral changes like stress management and smoking cessation will prevent the recurrence of the canker sores. Stress is one of the triggers for RAS;

however, mindfulness and relaxing exercises may also be effective (Rivera, 2019). Moreover, the prevalence of canker sores increases right after smoking cessation for some subjects because of mucosal changes in keratinization, and the incidence decreases among those who have had long time since smoking cessation (Rivera et al., 2021).

8. When to Seek Medical Attention

Canker sores, or recurrent aphthous stomatitis (RAS) in medical jargon, are very common oral mucosal lesions characterized by painful ulcerations that can significantly affect the quality of life of the patient. Most cases resolve spontaneously within one to two weeks; however, some clinical signs would dictate the assessment of the practitioner. These consist of frequency and severity of episodes, onset of systemic symptoms, and characteristics of the lesions.

The first sign that one needs professional assistance is the frequency and the severity of the occurrence. Patients whose episodes are recurrent, where an event occurs more than once a year, may indicate underlying conditions that need to be further investigated. According to Rivera et al., RAS is the most common oral mucosal disease, and recurrence implies that its etiology could be more complex than single events, possibly related to systemic diseases or nutritional deficiencies (Rivera, 2019). Other reasons why a person would visit a doctor are if the ulcers are in many places or very large, as those usually have management issues and typically do not heal with treatments that can be bought in a store (Ślebioda et al., 2013).

Red flag-the lesions of oral ulcers occur in association with systemic signs and symptoms. Such signs and symptoms as fever, malaise, or gastrointestinal complaints raise suspicion for an underlying systemic condition, such as IBD or celiac disease, which may present in the oral cavity (Valentini et al., 2023). Valentini et al. reported that oral manifestations in patients with IBD often call for customized treatment strategies focused on both the oral lesions and intestinal disease (Valentini et al., 2023). This, therefore, becomes a sign to the patient that he must consult a healthcare provider since this combination of oral ulcers with systemic symptoms warrants it.

Sometimes, lesions themselves will be of value for diagnostic information. Canker sores appear as shallow ulcers that are painful with a gray or whitish base and red halo. But atypical presentation that includes deep ulcers with a very unusual and greater than two-week duration, and especially in individuals with marked swelling or hemorrhage could suggest grave underlying pathologies like viral infections or malignancies (Sabbagh & Felemban, 2016). Sabbagh and Felemban are adamant that most canker sores are self-limiting; however, in case they do not respond to conventional treatments or have some peculiar features, a healthcare provider should evaluate them to rule out other pathologies (Sabbagh & Felemban, 2016).

9. Research and Innovations

Recent developments in immunotherapy increasingly contribute to their application in sores known as recurrent aphthous stomatitis, which is defined as painful ulcers on

oral mucosa and is often described as an immune-mediated response or nutritional deficiency as well as several systemic diseases ("Prevalence and Age Related Risk of Three Clinical Variants of Aphthous Stomatitis: a Retrospective Study", 2020). The most recent studies pointed to immunotherapy as a good tool in managing conditions underlying the pathologies of canker sore, which is bad enough in exacerbating clinical signs and symptoms.

This list may include oral mucosal immunotherapy, thereby allowing direct delivery routes of allergens into the oral mucosa. According to Turkalj (2024), oral mucosal immunotherapy with its mechanism of enhancing immune responses at the site of lesions offers an ideal possibility for lessening the severity and recurrence of canker sores. This can be achieved through findings by Shi et al. (2021) such as modulation of local immune responses that aids in enhancing the oral health's clinical condition by, among others, managing mouth ulcers. The tetrahydrocurcuminoids (THC) also proved effective in the management of the manifestations of canker sores. A clinical trial has shown that oral supplementation with THC led to the alleviation of symptoms within three weeks and arrested the progression of the disease without any adverse effects (Majeed et al., 2020). This, therefore, indicates that immunomodulatory drugs might prove useful in the management of canker sores as they lead to a decrease in inflammation and healing.

Nutritional support, furthermore, is a management for canker sores, especially for those diagnosed with underlying conditions like inflammatory bowel disease, and celiac disease; the diseases cause oral manifestation that responds well to systemic therapies that are targeted to control the primary disease (Valentini et al., 2023). Nutritional assistance support combined with immunotherapy improves the treatment outcomes of suffering patients with recurrent canker sores. Not excluded, however, is the immune system involvement in pathogenesis. Research has proven that immunotherapy, which also includes the use of immune checkpoint inhibitors, can be used in treating oral lesions through acting via immune modulation (Shi et al., 2021). This is because immune dysregulation could be involved in canker sores and new avenues of therapy are obtained through targeting these pathways. Thus, overall, advancement in immunotherapy, especially by OMIT methods or the use of immunomodulatory agents like THC, is a promising strategy for canker sores treatment. The therapeutic approach to symptoms and the deep-set immune mechanism causes the condition.

Abbreviations

RAS: Recurrent aphthous stomatitis

THC: Tetrahydrocurcuminoids

OTC: Over-the-counter

IBD: Inflammatory bowel disease

qPCR: Quantitative polymerase chain reaction

10. Conclusion

The very common oral disease of canker sores seriously impacts quality of life in patients with their pain and recurrence. The etiology is multifactorial: nutritional, environmental, and genetic. As such, understanding has progressed sufficiently to allow for more specific management. Pharmacological management and the addition of natural remedies, coupled with preventive care, all provide relief and reduction of recurrence. Newer therapies like immunotherapy, nutritional supplementation, and so many more represent some promising avenues for further management. Therefore, full, individualized approaches are vital for good outcomes and place significant emphasis on early detection with holistic care. In summary, the management of canker sores somewhat relies on topical corticosteroids and antimicrobial mouthwashes; both have advantages and disadvantages regarding the interventions. Topical corticosteroids are more helpful as short-term treatments with symptom relief and inflammation control. Antimicrobial mouthwashes promote oral hygiene and prevent infections. Treatment should be individualized for the patient, depending on the needs and his or her response to the treatment.

Conflict of Interest

The authors declare they don't have any conflict of interest in the form of finance or other things.

Author contributions

All authors participated in data collection, manuscript review, editing, table creating and given the final approval for manuscript submission to journal.

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Ethical Approval

Not Applicable

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