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Master‘s Thesis

Maxillofacial Infections and Overview of Causes Microbiological Features, Treatment Modalities and Predictors of Longer Hospitalization

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Vilnius

2023

1. Abstract

Objective: In this literary review, the titular topics of causes, microbiological features, treatment modalities and predictors of longer hospitalisation of maxillofacial infections will be discussed and presented. This will be done by breaking down each subtopic individually, talking about the most common features of each.

Methods: Narrative literature review

Conclusion: Maxillo-facial infections are a complex topic that still brings many challenges to dental practice today. The Origin of the causes is broad and can be odontogenic and non-odontogenic. While treatment modalities for most infections are already well established, newer methods are still emerging. Successful treatment also relies on timely diagnosis in order to avoid further complications and spread. Longer treatment which would require longer hospitalisation, can be predicted by factors such as age, underlying health issues and if the patient has self-medicated prior to visiting the clinician. The latter factor especially can cause many complications as the use of painkillers, antibiotics, and home remedies can reduce symptoms allowing for the infection to spread further and delaying diagnosis and treatment for too long.

Terminology: Odontogenic infection, non odontogenic infection,Dental surgery, Bacterial infection, fungal infection, Maxillo facial space infection, Mouth diseases, Length of stay

2. Introduction

Within dental and maxillofacial surgery, some of the most serious conditions are maxillofacial infections, which can be fatal if not treated timely. This is because the spaces in the maxillofacial area are all closely located and interconnected (1). This means infections can spread easily and affect multiple spaces. Important structures such as the brain, eyes and major blood vessels are all very close and easily susceptible to further infection. This increases the health risk drastically, especially if left untreated for a longer time, even potentially leading to death (2).

The percentage of patients that may experience life-threatening complications is 16.2%, which includes upper airway obstruction , mediastinitis ,sepsis , pneumonia, and septic shock. According to Quain et al., among the patients who experienced these complications, 5.4% passed away, and 73.0% had underlying systemic diseases. The most common underlying systemic diseases were diabetes mellitus and hypertension, which accounted for 35.1% of the life-threatening cases. Although there was no significant difference in age between the patients who experienced life-threatening complications and those who didn't, the average age of the former group with underlying diseases was 60.3 ± 15.7 years, which was significantly higher than those without underlying diseases (aged 39.5 ± 16.2 years) (3).

This study aims to describe the various types of maxillofacial infections and their microbiological features, as well as discuss their treatment modalities, management options, and potential causes of extended hospitalisation. The primary objective of this research is to support the hypothesis that delayed medical intervention for maxillofacial infections increases the risk of prolonged hospitalisation. It is crucial for general dentists to possess knowledge of these common infections, including their symptoms, presentation, and initial steps for management, as they often serve as the first point of contact for patients with head and neck health issues. Dentists must be able to recognise and inform their patients about suspected or confirmed maxillofacial infections that require further medical attention, as they are frequently visited more frequently than other healthcare providers

Maxillofacial infections occur in maxillofacial space,which refers to the area within the head and neck that contains the maxilla, mandible, and the facial bones. It also encompasses the surrounding soft tissues, including the sinuses, teeth, nerves, and vessels, which are important for proper facial structure, function, and sensation. The most common origin of maxillofacial infections is odontogenic (3). In the past, odontogenic infections were considered a serious and sometimes deadly disease. The causes of these infections are typically decayed or non-vital teeth, postoperative infections, periodontal disease, and inflammation of the pericoronal tissues. The management of maxillofacial infections typically involves a combination of the surgical incision and drainage of the accumulated pus together with the elimination of the infection cause, antibiotic therapy and oral cavity rehabilitation. However, in recent years, the management of dental cellulitis has become more complex, with many patients requiring lengthy hospital stays, multiple surgeries, and intensive care follow-up. Clinical symptoms, such as dysphonia, dyspnea, oral floor oedema, and oropharyngeal oedema, can signal the severity of the infection but are often overlooked in current practice. Additionally, patients with few severe symptoms may experience a poor outcome, possibly due to underlying diseases such as alcohol abuse, immunosuppression, or long-term diabetes . Delayed diagnosis, along with the use of multiple antibiotics or anti-inflammatory prescriptions, may only alleviate symptoms rather than cure the infection (4).

Materials and Methods

The aim of this literature review is to review and present an analysis of the aetiology, microbiological characteristics, treatment options, and prognostic indicators associated with prolonged hospitalisation of maxillofacial infections. Each subtopic will be comprehensively examined, with emphasis on the prevailing features and latest research findings.

Literature search strategy:

A comprehensive search on the PubMed, Clinical Key, and Google Scholar databases, using the following keywords: odontogenic infection, dental surgery, bacterial infection, maxillofacial space infection, mouth diseases, and length of stay, was conducted. The purpose of this search was to gather relevant scientific literature. Case reports were excluded from the analysis. The different types of studies used were 19 Retrospective Studies; 18 Systemic Reviews; 4 Analytical Studies; 3 Cohort Studies; each 2 Comparative Studies, Observational Studies and Literature review; and 1 Matched pair analysis, overview, prospective study and cross-sectional study,

Maxillofacial infections

3.1 Causes

3.1.1. Overview

Maxillofacial infections have multiple etiologies that can be categorised into two groups, namely odontogenic and non-odontogenic causes. Odontogenic causes account for a larger proportion of infections, approximately 63%, with non-odontogenic causes accounting for about 33%. The most common odontogenic causes include periapical inflammation (59%), pericoronitis (24.8%), periodontitis (8.5%), and post-extraction infections (7.1%). The most prevalent non-odontogenic causes include tonsillitis (20%) , malignant tumours and their treatment (17.3%) and lymphadenitis (16%) (3).

When talking about odontogenic causes, the teeth most often involved are the mandibular and maxillary molars at about 95%, the most common tooth involved being the mandibular third molars (5). According to Sato et al. (2006), The main facial spaces affected were the pterygomandibular space (50.00%), submandibular space (31.90%), and buccal maxillary space (19.05%) (6), which is similar to other large studies such as Yuvaraj (2015), which found most affected spaces where pterygomandibular space (48%), submandibular space (21%) and sub masseteric space (9%) (7). The prevalence of periapical inflammation (59.6%) followed by pericoronitis (24.8%) as the most common odontogenic causes of maxillofacial infections can be attributed to the fact that the third molars are often difficult to access and maintain proper oral hygiene, leading to an increased risk of infection (8).

3.1.2. Pericoronitis

Pericoronitis is the inflammation of the gums surrounding a partially erupted tooth. A pocket under the tissue can form over the crown of the tooth, trapping food and bacteria, making it difficult to clean. According to the literature, 82% of all impacted third molars, including partially erupted, soft tissue impacted and bony impacted, develop pericoronitis and 14% cause distal periodontal pockets in the adjacent tooth (8). The high incidence of impacted third molars that are susceptible to pericoronitis often necessitates their extraction, which may result in postoperative complications such as alveolitis and subsequent infection. Chen et al. (2021) found that the statistical incidence of alveolitis following impacted third molar extractions is 3.6%. However, in patients with a history of gingivitis or pericoronitis, the statistical incidence was 1.3 times higher, and in cases of complicated extractions, the statistical incidence was 2.5 times higher (9). This finding suggests that prophylactic extractions of partially impacted teeth should be considered before the onset of gingivitis or pericoronitis, particularly if their eruption has ceased.

Of course, many clinicians will say prophylactic extractions are not necessary and that when properly monitored and with proper oral hygiene, if these teeth cause no other pathologies or issues, they can be kept in the mouth until the issues start to develop with the hope that they may never arise or that they can be solved with local intervention instead. Studies comparing surgical removal versus retention of third molars found insufficient evidence to directly support either approach (10). Generally, any recommendation for prophylactic removal of third molars should consider ongoing symptoms or pathology, future complications and morbidity associated with retention of the third molars, and increased risks of extraction at an older age. Patients aged 65 years or older showed significantly more intraoperative as well as postoperative complications resulting in longer hospital stays as opposed to patients aged between 15 and 20 (11).Extractions, both as a prophylactic measure and in response to pericoronitis both assume the fact of regular clinician visits, which means that infections can be spotted and treated before the infection has spread to other areas of the maxillofacial space, or it assumes a patient's willingness to visit a clinician once the symptoms have arisen and not to wait until they become unbearable. The most common reasons for retaining a third molar are eruption into proper occlusion, patient preference and symptomless third molar in patients over the age of 30 (12).

Pericoronitis,, if left untreated,, can cause infection to spread to deeper maxillofacial spaces such as the sublingual, submandibular, parapharyngeal, pterygomandibular, infratemporal, sub masseteric and buccal (13). A case study by Basavarajappa et al. (2016) reported that following untreated pericoronitis, a patient suffered from septicaemia and disseminated intravascular coagulation. The areas involved in this case were submandibular, sublingual and infratemporal space. The patient, who was administered with complaints of throbbing pain, was able to recover after minor surgery and medication.(14). A different case study by Shimada et al. (2018) reported that the origin of infection in a case of systemic inflammatory response syndrome has been linked to third molar pericoronitis in a patient undergoing chemotherapy for leukaemia (15).

A rare secondary infection to pericoronitis is osteomyelitis, with only 7 case reports, according to R. Wang et al. (2014). Osteomyelitis refers to an inflammatory state affecting both bone and bone marrow. Within the jaw, odontogenic microorganisms primarily contribute to the development of this condition. Bacterial infections stemming from dental sources can manifest in various forms, such as periapical or periodontal abscesses, pericoronitis, infected extraction sites, or fracture wounds (17). Non odontogenic cases of secondary osteomyelitis can be attributed to bisphosphonate therapy or radiotherapy. The prevalence of mandibular osteomyelitis has decreased in developed countries but is still high due to oral health knowledge, poor oral hygiene and affordability problems (16).

There are three main types of osteomyelitis: acute, secondary chronic, and primary chronic osteomyelitis.These types of osteomyelitis typically involve a true bacterial infection of the jawbone and are characterised by suppuration, fistula formation, and sequestration. The clinical presentation and course of the disease can vary greatly depending on the intensity of the infection and the host bone response. The primary cause of acute and secondary chronic osteomyelitis in the jaws is usually a bacterial focus resulting from odontogenic disease, pulpal and periodontal infections, extraction wounds, foreign bodies, and infected fractures. Primary chronic osteomyelitis of the jaw, on the other hand, is a rare and nonsuppurative chronic inflammation of unknown origin (18).

3.1.3. Cellulitis

Cellulitis, the bacterial infection of the inner skin layers, affects the cellular adipose tissue in the aponeurotic spaces. The spaces that allow odontogenic infections to spread are the: superficial compartment, floor of the mouth, masticator compartment, parapharyngeal space, parotid space and peritonsillar space. It can be classified into either chronic or acute states , and its potential complications include orbital infections, necrotising fasciitis, thrombosis of the cavernous sinuses, cerebral abscess and mediastinitis (19).

The most common contributing factor for cellulitis in the facial area is poor oral hygiene (76%), followed by tobacco (41%), alcohol (19%) and diabetes (12%). Facial cellulitis can occur at any age, it is more predominantly found in males than females, and it is generally related to a lower socioeconomic background (20).

As with previous causes, the severity and progression/spread increases when left untreated. In a retrospective study over 14 years, it was found that out of 264 recorded cases of cellulitis of dental origin, 34 were fatal, a lethality rate of 13%. Of which 28 deaths were due to diffuse cellulitis (phlegmon). The patient's diagnosis came generally quite late, meaning the clinical state of the patient was generally quite severe. This was because these patients usually attempted to self-treat. Thus it was also concluded that self-medication with NSAIDs was the main favouring factor (94%) leading to fatalities (20). Allowing the patient to endure the pain for a longer period of time before searching for medical help, giving more time for the infection to spread to deeper areas leading eventually to death,in most cases, through septic shock.

Alifi et al. (2017), in a more developed country with a higher level of healthcare infrastructure, looked at 87 cases over a 4 year period in which only one case resulted in the death of a patient with gangrenous cervicofacial cellulitis, a fatality rate of just over 1 % (21).

3.1.4. Tonsillitis

The most common non-odontogenic cause of maxillofacial infections is tonsillitis (3). The inflammation of the tonsils is usually of infectious nature. It can be of viral or bacterial origin. The locations of the tonsils, especially the palatine tonsils at the entrance of the aerodigestive tract, make them very susceptible to exogenous pathogens such as viruses, bacteria and food particles. Predominantly affecting school-age children, with most being affected at least once in their lifetime, it can affect patients of any age.

Acute bacterial tonsillitis is often preceded by a viral infection and is polymicrobial. Common signs and symptoms include exudative inflamed tonsils alongside dysphagia, odynophagia, fever and tender cervical lymphadenopathy. This is similar to acute viral tonsillitis, where dysphagia, odynophagia, fever and tonsillar erythema are common symptoms (22).

It is important to adequately identify and appropriately treat acute tonsillitis because there are a number of possible complications that can arise from un/improper treatment. These include aphthous stomatitis, pharyngitis, adenopathy syndrome, peritonsillar abscess and deep neck-space infections (22). These complications can be separated into suppurative and nonsuppurative. The spread of the acute infection from the tonsil to the surrounding deep structure leads to the development of suppurative complications such as peritonsillar abscess and sporadically parapharyngeal/retropharyngeal or thyroid abscess (23). A mortality rate of 30-40% is associated with deep throat infections which have descended into necrotising mediastinitis (24). Scarlet fever, acute rheumatic fever and post-streptococcal glomerulonephritis are examples of non-suppurative complications (25).

Obstruction of the airway is a rare complication of acute tonsillitis but can also lead to death. It can occur because of oedema of the soft palate and tonsils after a deep neck infection or peritonsillar abscess and may result in lethal asphyxiation (26). In one case study, the patient had passed away after the adjacent tissue to the peritonsillar became inflamed and swollen, as well as the uvula and epiglottis resulting in significant airway narrowing. The cause of the oedema and subsequent inflammation was unilateral left-side necrotising tonsillitis. This was without other pathological changes in the deeper neck structures (25).

Another potentially lethal but, in modern days, quite rare complication of acute tonsillitis is Lemierre's Syndrome. It presents itself in the patient with extreme neck pain and tenderness over the internal jugular vein. The infection begins in the oropharyngeal region, which then later spreads to the lateral pharyngeal spaces of the neck with thrombophlebitis of the internal jugular vein. This then results in multiple emboli and the formation of abscesses in the lungs and joints (27).

3.2.5. Oral Candidiasis

Oral Candidiasis is one example of a non-odontogenic fungal infection that affects the oral mucosa, commonly also known as oral thrush. 95% of the time, it is caused by the candida albicans, which is usually highly adapted to the oral environment but changes to the microenvironment can lead to its transition into a pathogen from a commensal organism (28).

Risk factors include but are not limited to antibiotic treatment, diabetes mellitus, malnourishment, oral immunosuppression, long-term steroid treatment, and denture use (29). The incidence of oral candidiasis tends to be higher among individuals diagnosed with cancer, AIDS, or receiving chemotherapy or radiotherapy. Failure to treat this condition could result in persistent and long-lasting infection, invasive candidiasis, necrotizing ulcerative mucositis, as well as oropharyngeal and esophageal candidiasis. If left unchecked, it could further lead to the development of bronchitis, pneumonia, and endocarditis.(28).

In one case study of untreated oral candidiasis, a 33-year-old male, in addition to extensive pseudo membrane from the candidiasis, developed an ulcer on the border of the soft and hard palate, which, upon histological analysis, isolated methicillin-resistant Staphylococcus aureus. Radiographs revealed that the ulcer had reached the nasal cavity and needed to be surgically removed after the candidiasis was treated by debridement and antibiotic as well as antifungal treatment (30).

3.1.6. Aspergillosis

Aspergillosis is a condition that results from infection by Aspergillus species, which are saprophytes that thrive on decaying organic material. Among these species, Aspergillus fumigatus is the most prevalent cause of invasive disease, as its conidia are small enough to easily penetrate into the alveoli. (31). Oral aspergillosis is the second most frequently encountered type of mycosis affecting the mouth. Primary invasive aspergillosis is rare in the oral cavity, but it can occur as a result of dissemination from the nose or sinuses. This condition is particularly prevalent in individuals with uncontrolled diabetes mellitus, immunocompromised states, or those receiving chemotherapy (32).It has a male preference, and the gingiva is the most frequently affected site, followed by the hard palate. Spores can also enter the sinuses during dental procedures like tooth extractions or root canal treatments and become pathological. In hospital environments, the risk of aspergillosis in susceptible patients may increase due to factors such as exposure to rotting leaves or inadequate cleaning of dust (33).The infection's clinical manifestation depends on the organism's pathogenicity and the host's immune response.

3.2 Microbiological features

Bacterial infections are one of the most common causes of maxillofacial infections. *Streptococcus mitis, Staphylococcus aureus, and Pseudomonas aeruginosa* are among the most frequently isolated bacteria that can lead to maxillofacial infections. These bacteria can enter the tissues of the face and jaw through various routes, including penetrating trauma, dental procedures, and surgery (34).

Bacterial infections are polymicrobial, with theories that the pathogens are interdependent. Mostly mixed aerobic and anaerobic growth, with Taub et al. (2017) as well as Caruso et al. (2017) showing predominantly anaerobic growth and very few with predominant aerobic growth. Gram-Positive cocci and Gram-Negative bacilli are mostly predominant. Streptococci are the most common aerobes; staphylococci are less common. Also, anaerobic streptococci are the most common anaerobes isolated (35,36).

There have been many studies done about the different microorganisms that have been identified in oral and maxillofacial infections. One cross-sectional study found that the gram-positive bacteria *Staphylococcus Aureus* was isolated 35 times, *Staphylococcus epidermidis* 25 times, *Streptococcus Mitis* 40 times and *Streptococcus Anginosus 20* times. Whereas much fewer types of gram-negative bacteria were found, *Pseudomonas aeruginosa* is the most common at 11 times identified. Anaerobic bacteria were found even fewer times, with *Escherichia coli* being identified the most with 9 times (34). Other studies found that the aerobic strains of *Streptococcus sanguis* and *Streptococcus mitis* were most commonly isolated at 18 and 15 times out of 88, respectively. While the most common anaerobic strain was *Peptostreptococcus* which was isolated 16 times out of 88 (7).

It is also not unheard of to find new strains of bacteria; such was the case in south korea, where a novel facultatively anaerobic, gram-negative coccus, *Streptococcus gwangjuenese,* named after its discovery city, was isolated from a case of human pericoronitis (37).

Fungal infections, such as candidiasis or Aspergillosis, are another potential cause of maxillofacial infections. These infections are usually seen in immunocompromised individuals and can be introduced into the tissues of the face and jaw through various routes, including inhalation and direct contamination (38).

Candida albicans cause around 95% of oral candidiasis infections (28). Nevertheless, the incidence of infections caused by non-albicans species that are resistant to antifungal agents has been rising in recent years. This increase in prevalence may be linked to factors such as age, malignancy, use of polyenes and azoles, the presence of indwelling catheters, and improved diagnostic techniques (39).

Non-albicans species include *C. glabrata, C. tropicalis, C. parapsilosis, C. dubliniensis, C. guilliermondii, C. krusei, and C. kefyr. C. Besides C. Albicans, C. glabrata and C. dubliniensis* are most commonly isolated from oral lesions in HIV patients (40). Candida auris is an emerging multidrug-resistant strain causing outbreaks in healthcare settings, especially in post-COVID-19 patients (41).

As stated previously, Tonsillitis can either be a bacterial infection or a viral infection. A beta-hemolytic Streptococcus (GABHS) is the usual cause of bacterial infections. However, *Staphylococcus aureus, Streptococcus pneumoniae*, and *Haemophilus* *influenzae* have also been identified through cultures. Also commonly associated is *Streptococcus pyogenes,* a known precursor to rheumatic fever (42).Viral tonsillitis is most commonly associated with rhinovirus, enterovirus, influenza and adenovirus, which also cause the common cold (22). Tonsillitis can also be caused by various other viruses, including Epstein-Barr virus, which leads to mononucleosis, cytomegalovirus, hepatitis A, rubella, and HIV (43).

3.3 Treatment Modalities.

The treatment of maxillofacial infections depends on the severity of the infection, the underlying cause, and the overall health of the patient. A combination of medical and surgical interventions, along with careful monitoring and follow-up care, can effectively manage and resolve these infections.(44) As most infections are bacterial, the first choice of treatment is the prescription of antibiotics. However, this has its own problem due to the overprescription of antibiotics such as penicillin. The resistance of bacteria to them has increased in recent years (45). Especially since dentistry accounts for 10% of the prescribed antibiotics in the world (46).

According to a retrospective cohort study which looked at 60 patient files in a 5-year time period, factors that affected antibiotic resistance were younger patient age, positive surgical history, and number of aerobic organisms isolated. The observed effect of younger age on antibiotic resistance is small and difficult to explain in this cohort. The youngest patient was 16 years old, and paediatric patients were not represented. However, patients who reported a positive surgical history were 20 times more likely to have antibiotic resistance (47). This could represent a subset of patients who have had more or prolonged exposure to antibiotics in the past, a population expected to have greater inducible antibiotic resistance. Because a positive surgical history in this group was defined as at least 1 major surgical intervention requiring hospital admission, the likelihood that perioperative antibiotics were used is good. Whether this accounts for the increase in antibiotic resistance is speculative and should be studied further. Not surprisingly, the more aerobic species that were identified, the more likely a resistant isolate was identified. This would likely be the case in most polymicrobial infections(47).

Treatment of Osteomyelitis is variable. One French study, which only studied a small number of cases, reported multiple successful treatment strategies. Ninety-two point five per cent of the thirty-seven patients received antibiotic therapy, typically chosen empirically. The duration of treatment varied greatly, ranging from one week to multiple courses spanning several years. Half of the patients underwent one or more teeth extractions, indicating a strong prevalence of alveolar-dental origin in the patient population. Out of the seven patients who underwent sequestrectomy, six experienced clinical improvement in terms of reduced pain and swelling. Additionally, six patients underwent decortication, with five of them showing clinical improvement (48). There have also been some small studies which found that in cases of acute diffuse sclerosing osteomyelitis, on-demand treatment with single-shot bisphosphonate infusions appears to be a promising alternative to analgesics and corticotomies. Specifically, the use of ibandronate single-shot infusions was well-tolerated and yielded noticeable and enduring significant reductions in subjective pain levels ($p<0.01$) (49).

Treatment specific to mandibular osteomyelitis secondary to pericoronitis after the removal of the causative tooth. A combination of antimicrobial therapy and surgery consisting of incision and drainage, or sequestrectomy. In addition, hyperbaric oxygen can give good short-term clinical outcomes if used as an adjunct treatment option (16).

Facial Cellulitis the management of facial cellulitis must be early and multidisciplinary. Its purpose is to treat the infection, stop its progression and prevent recurrences by treating the cause. Surgical incision and drainage of the purulent collections in combination with concerned tooth or teeth extraction, oral cavity rehabilitation and probabilistic antibiotic therapy remain the principles of treatment (50).

The causal tooth is to be extracted to liberate purulent flow. During the extraction procedure, samples of the pus can be obtained and cultured under both aerobic and anaerobic conditions to identify the causative bacteria. For all the anatomic cervical fascial spaces affected by the infection, incision, drainage, and debridement are performed. Any collections are drained using an intraoral or transcervical approach, or a combination of both. Delbet drains are then placed through the open incisions and secured with a suture to facilitate large lavages with 0.9% saline solution (6).

Different drainage methods can also achieve better results than others. In one retrospective study comparing assisted vacuum drainage to traditional drainage methods in deep maxillofacial infections of odontogenic origin, it was found that the method using vacuum-assisted devices reduced the frequency of irrigation necessary, the white blood cell count and c-reactive protein levels. As well as decreasing the cost and length of antibiotic use and length of hospitalisation (51)

Antibiotic therapy must be early, by parenteral route, at the maximum dose, first broad-spectrum probabilistic, then adapted to the data of the antibiogram. Triple therapy based on amoxicillin-clavulanic associated with metronidazole and gentamicin was prescribed by most authors. These therapeutic choices are based on the notion that odontogenic facial cellulitis is a polymicrobial infection. The synergy of these associations is known to be active on streptococci and anaerobes (52). Mono-antibiotic therapy with amoxicillin clavulanic acid is also prescribed as first-line treatment in other international studies (53). The duration of total antibiotic therapy varies according to the habits of the teams, the severity of the initial infection and the evolution of the patient. In the previous study by Ferjaoui M et al., the average duration of total antibiotic therapy was 15 days.

Conservative and surgical approaches to treating cellulitis are viable options and may complement each other. Cellulitis can often be managed medically after the source of infection has been eliminated (54). Surgical incisions should be limited to spaces where purulent collections can be identified. In fact, modern medical imaging techniques such as Computed tomography and ultrasound scanning allow for better distinction between cellulitis and discrete abscess', the former of which has a more favourable response to antibiotic treatment with corticosteroids alone with no need for surgical intervention after removing the causative factor (35).

The management and treatment of candidiasis typically involve several approaches, such as maintaining proper oral and denture hygiene, selecting an appropriate antifungal agent, and evaluating and correcting any underlying predisposing factors. In adults, topical clotrimazole is often the first-line treatment for candidiasis, while nystatin suspension is commonly used for infants (55). Disseminated fungal infections may require systemic administration of antifungal agents such as fluconazole or itraconazole. However, in cases of drug resistance or in immunocompromised patients, posaconazole oral solution may be a suitable alternative (56).

Treatment of aspergilloma depends on the type of infection and the patient's health status. Non-invasive aspergilloma in immunocompetent individuals can be effectively treated with surgical debridement alone. On the other hand, allergic fungal sinusitis is usually managed with a combination of surgical debridement and corticosteroid therapy. In cases of localised aspergillosis in immunocompetent patients, debridement followed by administration of voriconazole is typically recommended. However, for individuals who are immunosuppressed and have invasive aspergillosis, aggressive debridement and systemic antifungal therapy with voriconazole, itraconazole, or amphotericin B may be necessary. (57).

Acute Bacterial Tonsillitis is treated in first choice with penicillin; however, because of an increase in beta-lactamase-producing bacteria, it may be necessary to change to an antibiotic such as amoxicillin with clavulanic acid if symptoms persist. Acute viral Tonsillitis, on the other hand, requires largely supportive treatment consisting of precautionary guidance, fluid resuscitation and rest. Proper differential diagnosis is very important because of the potential for the patient to have mononucleosis syndrome, where patients with this syndrome should not receive amoxicillin-related antibiotics, which are known to cause an immune-mediated rash. If symptoms persist after appropriate treatment and the patients continue to have recurrent infections, they may be of benefit from a tonsillectomy. Excision of the palatine tonsils is one of the most common surgical procedures. The recommendations for a tonsillectomy are either seven recurrent infections within one year, five infections per year for two years, the infections per year for three years, or recurrent infections with modifying factors. These factors are several antibiotic allergies, a history of peritonsillar abscess, periodic fever, aphthous stomatitis, pharyngitis, and adenitis.

There are also indications that would lead to immediate tonsillectomy, which are cardiopulmonary strain, febrile convulsions, tonsillar enlargement resulting in dysphagia, or concern for neoplasia (22).

Treatment of Lemierre's syndromes relies on accurate diagnosis and imaging. To confirm the thrombus within the internal jugular vein and access the location of the infection, computed tomography can be used, giving the doctor a three-dimensional image of the affected sites. Ultrasound imaging can also be used to identify any blood clots around the jugular vein. As with most infectious conditions, antibiotics are the main treatment factor in Lemierre's syndrome (27). Penicillins in monotherapy are most often used. Anticoagulant use is not yet well established and is still argued about. It can stop the spread of thrombi throughout the body, especially in the sinuses of the central nervous system (58). If the patient has a high number of clots or thrombus formations or the patient fails to recover within seventy-two hours of antibiotic therapy, anticoagulants can be needed (59). However, anticoagulant use is also linked to a greater risk of hemorrhagic complications. These patients need close monitoring for the following three months with potential surgical management (60).

3.4 Predictors of Longer Hospitalisation

Usually, the criteria for longer hospitalisation is any admission which exceeds the average admission period. This average is different in different parts of the world. For example, in the USA, the average length of stay is 5.5 days (63); in Iran, it is 6.8 days (64); in China, it is 10.6 days for patients over the age of 60 and 8.6 days for patients under the age of 60 (3); in Lithuania, it was 7.9 days (65).

Longer length of stay in hospitals due to maxillofacial infections can have a plethora of reasons. Being able to recognise and identify the underlying conditions and predisposing factors that can lead to the longer hospitalisation can be an effective tool in treatment due to awareness of what complications or other diseases may need to be managed, leading to potentially reduced complications. It can also be used to better inform the patient of the potential risks involved if they are identified to be affected by one or multiple of the predictors(4). Patients are typically hospitalised until the infection is resolved or under control and they have returned to their pre-infection state of health.

Moreover, the average length of hospital stay for patients with maxillofacial infections can vary due to multiple confounding factors, including the patient's overall medical condition, the severity of the infection, differences in antibiotic treatment, timing of surgical intervention such as incision and drainage of infected areas, and the presence of underlying diseases that may impact the outcome (61).

A strong correlation was observed between longer hospital stays and the risk of developing complications with increasing age and greater involvement by at least four times. Additionally, although statistically less significant, immunocompromised status was also considered a risk factor for prolonging admission days (62). The use of antibiotics can provide temporary relief from the visible signs and symptoms of an infection. However, without definitive and timely treatment, the infection can resurface, potentially leading to the development of more antibiotic-resistant bacteria and increased severity of the condition. Therefore, delaying treatment of an infection is not recommended. Preadmission antibiotic use has also been identified as a significant predictor for longer stay (63).

Elderly maxillo-facial space infection patients (aged ≥ 60 years) had a mean length of stay in the hospital of 10.6 ± 6.4 days, which was significantly longer than the length of stay of younger maxillo-facial space infection patients (aged < 60 years), which was 8.6 ± 4.5 days ($p < 0.05$). The length of stay of maxillo-facial space infection patients with underlying systemic disease was 10.7 ± 6.3 days, while the length of stay of those without underlying disease was 8.4 ± 4.4 days ($p < 0.05$). Between the years 2010 and 2019, maxillo-facial space infection patients who had received community outpatient treatment before admission had a significantly shorter hospital stay of 8.8 ± 4.1 days compared to those who had self-medicated (10.7 ± 6.5 days) ($p < 0.05$) (3).

Self-medication was the most common pre-hospitalisation approach for patients, compared to community outpatient treatment or no medication. In a retrospective study analysing cases from 1993 to 2019, 110 patients (49.5%) opted for self-medication, while 69 patients (31.1%) received community outpatient treatment prior to admission, and the rest received no medication. The same study found that patients who received community outpatient treatment were hospitalised for significantly fewer days (8.8 ± 4.1 days) than those who self-medicated (10.7 ± 6.5 days) ($P = 0.574$). However, there was no significant difference in length of stay (length of stay) between the self-medication group and the no-medication group ($P = 0.058$) (3). This can be corroborated by Nagarajan et al. (2023), who studied a sample of 259 patients in India to find that infection severity ($P<0.001$) and a number of spaces affected ($P<0.001$)

were both significant predictors of longer hospital stay (66). In this case, the factors of infection severity and spaces affected are more severe when the infection is not being treated properly, just like in the cases of self-medication and no medication in the previous study. A study conducted in France also found that the use of oral-anti inflammatory treatment before presenting to the hospital worsened the prognosis for the patient. This included NSAIDs and corticosteroids in comparison to no prior anti-inflammatory treatment. In terms of hospitalisation length, the stay was more often longer than 10 days (p=0,002), also other factors were also significantly increased, such as frequency of ICU hospitalisation (p=0.016) and number of spaced infections (p=0.003) (67).

The number of spaces involved has been shown to be a significant predictor of length of stay. While most patients who are admitted will have involvement of only one facial space, those with more than one space will have a significantly increased length of stay (P=0.01); this same study also associated an increased number of spaces with increased severity of trismus, which further complicated patient treatment (68). Qian et al. (2020) also found that there was no significant difference in age group, gender and length of stay between multiple-space and single-space infections during a 26-year study period . However, a different study by Wang P. et al. (2022) found that Patients with odontogenic infections who have multiple space infections are at a higher risk of longer hospitalisation. This is due to the greater local and systemic response resulting from the widespread infection, which requires a longer treatment period. To effectively manage the disease and ensure treatment effectiveness, it is important to focus on shortening the treatment cycle. (3,69).

Urechescu et al. (2023) evaluated the viability of the efficacy of C-reactive protein (CRP), white blood cell count (WBC), and neutrophil-to-lymphocyte ratio (NLR) as indicators of an extended hospital stay in adult patients with maxillofacial infections. The findings of this study support a direct and significant relationship ($p < 0.001$) between the predictors (WBC, CRP, and NLR) and the effect on duration of hospitalisation in adult patients with maxillofacial infections. The recommended cut-off values for WBC and CRP are 11,030 white blood cells/µL and 63 mg/L, respectively. If the levels of these markers surpass the optimal values, it indicates that the patient will require a hospital stay of 5 days or more. Therefore, measuring WBC and CRP levels upon admission can potentially help predict the length of hospitalisation in patients with maxillofacial infections (70). These findings were in line with a similar study by Heim et al. (2018), which evaluated WBC and CRP in patients hospitalised with acute odontogenic abscesses. This study also found that CRP levels and WBC count may serve as predictive factors for the length of hospital stay in patients with prolonged hospitalisation (CRP: 7-9 days and >10 days; WBC: >10 days) (71).

Underlying health conditions are also good predictors. One study out of the USA found comorbid conditions such as deficiency anaemia ($p = 0.01$), uncomplicated diabetes ($p=0.01$), metastatic cancer ($P=0.01$), drug abuse ($p=.01$) and neurologic disorders ($p=0.01$) were all significantly associated with longer stay (72). Diabetes has been found to be a significant predictor in several other studies as well, Gams et al. $p<0.01$ (63), Qian et al. $p<0.05$ (3).

4. Conclusion

Maxillo-facial infections are a complex topic that still brings many challenges to dental practice today and can still be fatal. The Origin of the causes is broad and can be odontogenic and non-odontogenic .The majority of infections are of odontogenic origin. Thus, it is important for practitioners to know and recognise the most common areas from which maxillofacial infection can spread and which complications are the most common. The most common spaces involved are the pterygomandibular space, submandibular space, and buccal maxillary space. While treatment modalities for most infections are already well established, newer methods are still emerging. Successful treatment also relies on timely diagnosis in order to avoid further complications and spread. Age, inflammatory markers, underlying conditions, the number of spaces involved and prior self-medication have all been identified as significant predictors which would require longer hospitalisation. The latter factor especially can cause many complications as the use of painkillers, antibiotics, and home remedies can reduce symptoms allowing for the infection to spread further and delaying diagnosis and treatment for too long. Knowledge of the microbiological features is also important for correct and successful treatment. This allows for correct medication choice, informed decisions about bacterial resistance and elimination of causative agents.

5. References

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