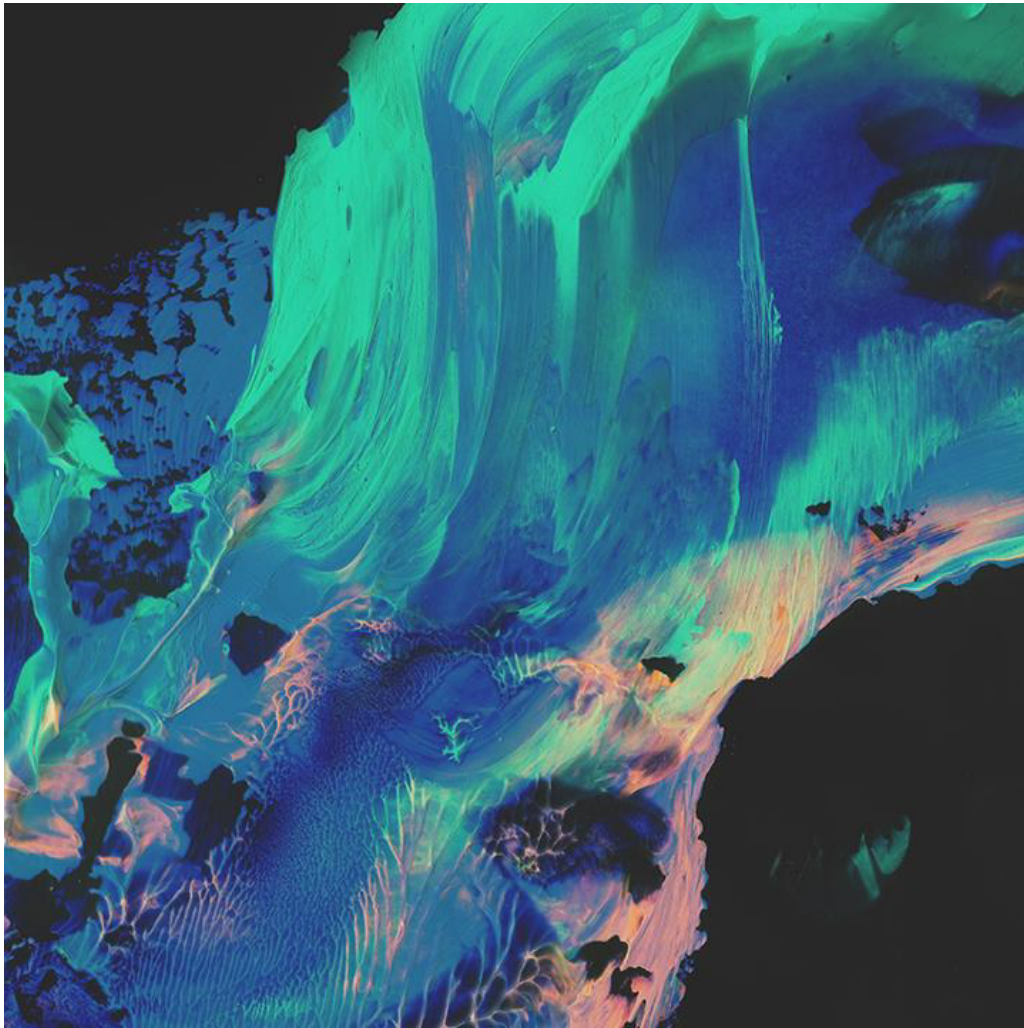




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The Acute Maxillofacial Infection- a retrospective medical journals analysis of patients in inpatient care



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ABSTRACT

Introduction: An absolute majority of dental infections are treated without major complications. In exceptional situations dental infections can spread to surrounding structures such as the airways or even the brain leading to a life-threatening condition that requires hospitalization. According to literature, some qualified risk factors appear to be common in hospitalized patients.

Aim: To outline factors typically seen in patients with acute maxillofacial infections with dental origin at Norrland University Hospital (NUS) and find possible association between these factors and the length of hospital stay.

Methods: A literature review using keywords associated with dental infections and acute throat and head infections was performed. Retrospective structured medical journal reviews of 58 patients suffering from acute maxillofacial infections which required hospitalization at NUS were analyzed. The results were analyzed using IBM SPSS Statistics software and Microsoft Office Excel.

Results: The results indicated that overweight/obese people (Body Mass Index ≥ 25) require longer care at the hospital due to their infection. Every other of the hospitalized patients had received dental treatment within 14 days prior to hospitalization.

Conclusions: In situations with acute maxillofacial infections of dental origin requiring hospitalization, BMI ≥ 25 is eventually a risk factor. A group of patients received dental treatment for their infection, but the infection still exacerbated. How come? This requires deeper analysis with further studies.



INTRODUCTION

A dental infection can develop into an acute maxillofacial infection that affects breathing due to swelling resulting in need of emergency hospital interventions and hospitalization.

Few Swedish studies have analyzed this patient group and none have focused on identifying any potential risk factors for acute maxillofacial infections of dental origin for the Swedish population.

A typical dental infection starts with a bacterial infection of the dental pulp and can spread to the surrounding bone and soft tissue manifesting as periapical periodontitis or osteitis (Robertson *et al*, 2015; Erazo, 2021). These infections occur secondary to periodontal or endodontic diseases, dental caries, or pericoronitis (Doll *et al*, 2018; Erazo, 2021). Dental infections can be acute and affect local structures even after dental treatments (Sipavičiūtė & Manelienė, 2014; Erazo 2021). An untreated dental infection can develop into an abscess and spread to other anatomic structures in the jawbone such as bone marrow, sinuses, or even local muscles, fascia and worst scenario the brain as it develops from being a subperiosteal infection to a submucosal one (Almuqamam & Gonzalez, 2021). These acute maxillofacial infections can develop to situations that need acute hospital care (Moghimi *et al*, 2013).

Besides fascial spaces, the route of spreading can be hematogenous or lymphatic (Ogle, 2017), accessing the bloodstream and leading to a bacteremia that can produce distant effects. The spreading of these infections can result in a diffuse spreading in soft tissue, as in the case of phlegmone of the floor of the mouth. According to international literature, 57% of deep neck abscesses caused by infection spreading are due to dental infections (Robertson & Smith, 2009). The spreading of the bacterial infection to the muscle fascia can reach the respiratory tracts and affect breathing which depends on the location of the tooth in the jaw (Almuqamam & Gonzalez, 2021; Moghimi *et al*, 2013; Erazo, 2021). An acute maxillofacial infection is identified by spreading to adjacent structures and includes the five classical inflammatory symptoms; swelling, heat development, redness, pain, and disability.

The treatment of such infections depends on the diagnosis and severity of the infection. If it requires hospitalization, it often consists of surgical drainage and antimicrobial therapy to remove the cause of the infection in combination with symptom relief. Fenoximetylpencillin is the first alternative because of great coverage of the typical oral bacterial flora (Long *et al*,



2008). Clindamycin could be used in case of patients with longer hospitalization period or beta-lactam allergy (Ogle, 2017). Metronidazole is often used as complement.

Several factors can affect the character and the severity of the acute maxillofacial infection. In research these factors have been identified as potential risk factors. Risk factors are factors that increase the risk of an outcome and involve the relationship between causes and their consequences. A predisposing factor is a factor that increases susceptibility to a certain outcome (Svensk mesh. (n.d.). Karolinska institutet). Risk factors associated with the acute maxillofacial infection are among others; diabetes mellitus type I and II, obesity, susceptibility to infection, drug abuse, virulence bacterial species and poor oral hygiene (Al-Zahrani *et al*, 2003; Wood *et al*, 2003; Seppänen *et al*, 2008; Dipesh *et al*, 2010; Juncar, 2014; WHO, 2022; Weise *et al*, 2019; Park J *et al*, 2019; Chigurupati & Shemkus, 2020). Some of these factors are briefly introduced below.

BMI > 30 is associated with lifestyle and scientifically has a strong linkage to several medical conditions. Untreated, these medical conditions can lead to increased morbidity, for example myocardial ischemia and infarction. Obesity is related to increased sugar consumption and often other comorbidities such as diabetes mellitus. Obesity is a predisposing factor for periodontitis in young adults (Al-Zahrani *et al*, 2003; Wood *et al*, 2003). According to Bjørnland (Bjørnland, 2021) BMI >30 and smoking slightly increase the risk of infection.

Diabetes mellitus is a disease that increases susceptibility to infection and can be an immunosuppressive disease if not controlled. Uncontrolled diabetes can also lead to spreading of severe dental infections due to its immunosuppressive effect (Robertson *et al*, 2015). Diabetes mellitus can be either congenital (type I) or lifestyle-related (type II). In type I diabetes, the body stops producing insulin, as the body's immune system attacks and destroys the insulin-producing cells in the pancreas, which in the long run leads to a total lack of insulin. Type II diabetes is more complex as the body still produces insulin but with occurrence of insulin resistance. Either because the body cannot produce enough insulin or because the body cells lose their insulin sensitivity (Dipesh *et al*, 2010; WHO, 2022).

Immunosuppression caused by medical conditions/diseases, treatments, or a combination of both can increase susceptibility to infection. Under this category fall even diabetes, malnutrition and drug abuse (Chow, 2014; Robertson *et al*, 2015). The progression of bacteremia into septicemia with more serious symptoms has been found to be more common in immunocompromised patients (Ogle, 2017) and association with systemic



complications is more common in these patients as reflected in a retrospective study from Finland (Seppänen *et al*, 2008). Interesting to note that according to Ogle (2017) diabetes is the most common immunocompromising situation that the dentist meets in patients (Ogle, 2017).

Substance abuse includes many substances such as alcohol, tobacco/nicotine (Smoking, moist tobacco), addictive stimulant drugs such as amphetamines and opioids. Chronic drug abusers can also suffer from chronic malnutrition and thus be immunocompromised. Smoking and alcohol abuse are causes for arrested healing in fractures and some drugs (ex. Crystal meth) can cause osteonecrosis. (Bonanthaya *et al*, 2021)

Dental infections initially manifest as an aerobic bacterial-assisted infection which changes to an infection consisting of anaerobic bacteria. These bacteria release toxins causing tissue degradation, an immunological reaction with abscess formation and pus increasing the spreading risk. These infections can be limited to the area of infection or spread to other structures depending on the host defense mechanism (Robertson & Smith, 2009). Typically, a polymicrobial aerobic and anaerobic spectrum of oral bacteria, for example *Streptococcus viridans* have been shown by intraoperative swab specimens from infections (Bahl *et al*, 2014). According to a journal review conducted by Bertossi *et al* (Bertossi *et al*, 2017), of hospitalized patients due to several acute dental abscesses, 7 % of the patients contained exclusively aerobic bacteria, 20% of the samples anaerobic and 68% of the patients had a combined aerobic/anaerobic bacteria flora.

Notable aerobic bacteria are gram-positive aerobic cocci such as the group *Streptococcus milleri*, which are often responsible for dental abscesses and seen to account for the majority of the early parts of infections in the head and neck region. The anaerobic proportion includes both anaerobic gram-positive cocci and anaerobic gram-negative rods, namely *Bacteroids* and *Fusobacterium*. Aerobic/anaerobic combinations of bacteria with *Streptococcus milleri* and *Fusobacterium* have been related to more severe lateral and retropharyngeal infections (Peterson, 2010).

For the individual patient, a severe maxillofacial infection can be a life-threatening situation. And there is a need to increase the knowledge about risk factors linked to maxillofacial infections with dental origin.



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The aim of this study was (a) to describe patients hospitalized due to acute maxillofacial infections at Norrlands University Hospital (NUS) and (b) to evaluate if there is an association between the length of hospitalization and the predisposing factors of acute

maxillofacial infection. The null hypothesis was that no predisposing risk factors for the exacerbation of dental infections into acute maxillofacial infections affect the length of stay for hospitalized patients.

METHODS

Access and literature review

A literature review (figure.1) was done using PubMed and books with help of filters (abstract and full text human studies, peer review articles, Swedish or English) Mesh terms, inclusion and exclusion criteria (table. 1). An additive literature search with the same filter and Mesh terms was carried out in September 2022 to strengthen the background and incubate new research published in the field between June and August 2022. The literature review identified potential risk factors that were repeatedly discussed in literature.

List of investigated factors:

- Sex
- Age
- Ethological dental treatments (up to 14 days before the exacerbation)
- Overweight/Obesity (BMI ≥ 25)
- Diabetes (type I and II)
- Wisdom teeth involvement
- Susceptibility to infection (by either medicines or diseases or both)
- Penicillin allergy- beta lactam allergy
- Substance abuse (current)
- Underweight (BMI $< 18,5$)
- Bacteria (what bacteria is dominantly present in the infection in each case)
- Length of hospital stay in days

Review of medical records

A structured retrospective journal analysis was performed after identification of the patient cohort using ICD-10 codes associated with spread infection. Only patients that required hospitalization in NUS between 2007-2020 were included. All patients had infections with dental origin and were diagnosed with at least one of the conditions mentioned in table.1. The exact diagnosis was extracted from medical records and chosen together with our supervisor.



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Patients hospitalized due to reasons that were irrelevant to this study such as osteoradionecrosis, jawbone necrosis, squamous cell carcinoma and pronounced dental fear were excluded.

Medical records in paper were reviewed retrospectively and divided between the authors and discussed between them after the first journal review. In cases where information about the factors was missing or difficult to access, both authors went through the journals and came to joint decisions together with the supervisor regarding inclusion, exclusion or the need for a more external search. Information was missing for length and weight, results from bacterial tests and type of previous dental treatment (14 days before hospitalization). The information here was obtained by the supervisor via access to the dental journal system T4, and the program ROS for bacterial- test results. The primary outcome variable was length of hospitalization.

Statistics

The data was collected in Microsoft Excel primarily and then analyzed using IBM SPSS Statistics. For the descriptive statistics, information about each factor was extracted from the medical records and transferred to the excel file under the correct factor and the correct patient code number. Some factors were divided into two different groups and others more than two. For each factor, percentages, median and mean were calculated.

The obesity factor is based on a BMI equal to or greater than 30 according to the World health organization (WHO 2022). However, since many of the included patients were on the borderline between overweight (BMI ≥ 25) and obesity, we decided that these groups would be combined to simplify the presentation of the data.

To identify if the data was normally distributed, histograms were analyzed. Since the distribution of the included variables was skewed, all statistical comparisons were performed using Mann–Whitney U test. The chosen level of significance was $\alpha=0.05$. All p- values were calculated using independent Mann-Whitney U test.

Non-parametric tests are carried out by medians for two groups and then Mann-Whitney is used and these tests can thus be based on fewer assumptions. No power-test of the included factors was performed.

Ethical reflection

The patient's integrity is at risk as personal data information may be disseminated in the analysis of medical records. To avoid this risk, all patient data has been handled



pseudo-anonymously after our supervisor (MS) coded the records of all included patients. The code key was locked by our supervisor and will be destroyed as soon as the study is completed. A report on ethical review of the study via Etikforum - Department of Odontology,

has been made and a statement from the board has approved the study with the condition that a consent and approval from the operations manager for the Head, Neck and Throat department at NUS and the head of maxillofacial surgery clinic must be given for the supervisor to extract and anonymize the medical records requested, which has been done and approved to begin data collection and to have the medical records reviewed based on the study's questions.

As for the structured literature search around published literature we see no ethical problem as we will work with reviewed references and the benefit of searching exceeds the risk. The benefit of literature search is answering one of the primary questions, education about acute maxillofacial infections with dental origin for the authors and readers, but also knowledge increase in the field and hopefully scientific findings that help dental clinics to prevent such acute infections.

The result from this structured retrospective journal analysis increases the knowledge about severe acute maxillofacial infections.

RESULTS

In total, 58 out of 65 patients diagnosed with at least one of the aforementioned diagnoses were included. Table.2 presents descriptive statistics for the included patients.

There was a male dominance in the patient cohort. The mean age was 45.5 years (range 8 – 71 years). The longest hospital stays belonged to men. The mean age for the patient cohort was 45.5 years, the median age was 47. The mean hospitalization was 3.7 days (range 1 – 17), with no statistical difference between younger (≤ 47 year) and older (> 47 year) patients ($p=0.82$) or sex ($p=0.72$).

48 % of the patient cohort had undergone a dental treatment up to 14 days before admission (figure.2). Extraction and endodontic treatment were most frequent. Our results do not show a statistical significance between received dental treatment and length of hospitalization, ($p=0.22$).

The factor overweight/obese ($BMI \geq 25$) showed significant association ($p=0.003$) (figure.3). Information about BMI was available on 45% of the included patients.



Diabetes (type I and II) were 10% in this patient cohort. Diabetes showed non-significant relation to length of hospitalization in days, ($p=0.37$), (figure.4).

Majority of the patients had the infection in the mandible, 29% were wisdom teeth and 71% other molars. The rest were other molars where the 1:st molar was more frequent, predominantly in the right side of the mandible.

General health based on susceptibility to infection was affected in 24.1% of those admitted to NUS and showed no statistical significance in relation to length of hospitalization in days ($p=0.45$).

DISCUSSION

From our literature review, several factors described as risk factors were identified. We defined the primary outcome variable as length of hospitalization. The results in this study agree with the literature (Moghimi *et al*, 2013; Doll *et al*, 2018; Park *et al*, 2019; Rautaporras *et al*, 2022) where the mandible was most frequently affected in acute maxillofacial infection. A Finnish study also found that the most common severe infection site was the mandible (85%), where the most affected teeth were first and second molars (45%) and wisdom teeth (40%) (Rautaporras *et al*, 2022). The structured retrospective journal analysis identified more men but no significant difference was seen regarding the length of stay between the sexes. A similar study published in 2022 in Finland demonstrated even sex distribution and median age of 43 years old which agrees with our results (Rautaporras *et al*, 2022). A factor that showed an interesting outcome in our data was dental treatment, the difference was, however, non-significant between patients who did and did not receive a dental treatment.

The results suggesting that although some of these patients have received a dental treatment for their infection before admission, the infection can still exacerbate, might be misleading. It is important to reflect upon certain questions like how many successful extractions and endodontic treatments the dentist implement on the public dental care every day? i.e., how many infection treatments are successful compared to how many get hospitalized? Maybe some of the patients who were not treated in early stages might have avoided the complications that required hospitalization if they actually did receive a treatment. The patients who received treatment may have other host relevant factors that increase their need for more care, such as immunosuppression, medication or illness.



The only factor that was found to have a significant association with length of hospital stay was the patient's Body Mass Index (BMI). The data regarding BMI was not complete, but the factor could still be considered to be relevant. On the other hand, conclusions must be drawn with caution since missing values makes it less reliable to draw conclusions regarding this factor.

Every other person (52%) in Sweden is today diagnosed with overweight or obesity. Both diagnoses have increased especially among younger people, but also in the age group 45–64 years. The increase happened between 2006–2020 in all age groups (Folkhälsomyndigheten 2022). Based on the percentage of being either overweight or obese people in Sweden (52%) we can predict that 14 of our patients are obese or overweight. This number agrees to a certain extent with the number of patients with available information which was 16. This consequently means that the data obtained in the category can be considered representative for the Swedish population.

However, the percentage obtained in this study is higher than population percentage of overweight and obese people in Sweden. That suggests that overweight/obesity can eventually be a risk factor for acute maxillofacial infections. Obesity can be connected to several factors of interest, starting with oral infectious diseases such as periodontitis and caries (Al-Zahrani *et al*, 2003; Wood *et al*, 2003; Willershausen, 2004).

Positive correlation between BMI and TNF α concentration in gingival crevicular fluid in young adults has been shown by an experimental study (Lundin *et al*, 2004). Chronic disease affects the immune system and the ability to heal in addition to obesity's direct effect on the immune system, through a variety of immune mediators (Adiponectin, Leptin induction, etc) which leads to increased susceptibility to infections (Andersen *et al*, 2016). However, the evidence of particularly life-threatening infections in obese people has so far been limited. Data suggest that overweight people are more likely to develop infections of various types including postoperative infections and other nosocomial infections, and they tend to suffer from more severe complications of common infections (Falagas & Kompoti, 2006).

When comparing the means of hospital stay, patients with diabetes had one day longer than non-diabetics. However, the difference in hospital stay between the two groups is statistically



non-significant. Looking at it in a different way, around 5% of the Swedish population has diabetes (Svenska Diabetesförbundet, 2022). In this study about 10% (similar to prevalence globally 9,8% (IDF Diabetes Atlas 2021)) of the patients were diabetics, suggesting that

diabetes is eventually a risk factor for Swedes and even a challenge as the incidence was shown to be increasing and according to (WHO, 2022), type II diabetes has quadrupled during 1980–2015 globally.

An interesting balance and imbalance relationship between blood sugar levels, immune system and dental infections is discussed in literature. Uncontrolled diabetes can be a predisposing factor for more severe infections as an inflammatory response occurs due to the immune response to high blood sugar levels and the presence of inflammatory mediators, leading to insufficient insulin production. Hyperglycemia in uncontrolled diabetes patients is thought to cause dysfunction of the immune response and failure to control the spread and invasion of pathogens. Therefore, diabetics are more susceptible to infection (Juncar *et al*, 2014; Berbudi *et al*, 2020) However, in this patient cohort, no data was available if diabetes was uncontrolled and therefore we cannot make any conclusions for this patient category.

Several factors were thought to be analyzed, but information about a number of them was missing in the medical records. This resulted in exclusion of factors due to lack of information and representative data. The specimen collection was not conducted for the majority of the patients therefore both factors; type of bacteria and Penicillin allergy were removed from this report as well as malnutrition and substance abuse. Smoking was a factor of interest that couldn't be analyzed in this study. However, Rautaporräs, 2022 (Rautaporräs *et al*, 2022) showed that smoking was significantly associated with acute teeth removal in patients hospitalized postoperatively due to an acute maxillofacial infection.

Multiple questions arose after we conducted our study that are worth reflecting upon. For instance, Does the number of days in hospital stay always reflect the severity of the infection? Why was specimen collection not conducted on all patients that required hospitalization even though it is part of the treatment protocol in Sweden? Are the reports missing? Wasn't the analysis conducted in the first place? The answers won't be provided in this report, but these questions are thought to stimulate the interest in this area of research. One can speculate about the timespan between the arrival of the patient to the ward and the surgical debridement and effect for the infection.



Finally, whether it is representative on a national and international level has been discussed above for several factors and it can be said that for this time and this particular population, the study is found to be representative.

CONCLUSION

Due to the retrospective nature of our study, we were unable to draw greater conclusions about risk factors for acute maxillofacial infections with a dental origin, as this requires a longitudinal prospective study. Therefore, the null hypothesis could only be partially rejected. We could however identify one possible predisposing factor for prolonging hospital stay due to a severe maxillofacial infection. Body mass Index (BMI) ≥ 25 is a potential risk factor for the population living in the geographical area that is supported by Norrland University Hospital. A group of patients received dental treatment prior to their infection, but the infection still exacerbated, highlighting that complications can occur independent of treatment.

Strength and limitations:

Several relevant factors were included, which is a strength of this study. The study can be used as a ground for future comparisons at the NUS to research possible changing characteristics of acute maxillofacial infection.

Several limitations of this study were identified: limited number of patients, missing information about factors makes it difficult to draw concrete conclusions. Also limited research in the study area in Sweden made it difficult to compare our results with other areas in Sweden.

The result from the study rise however several topics for recommendations and research:

1. Should specimen collection and BMI registration be implemented in the Swedish routine protocol for treatment of acute maxillofacial infections?
2. What are the economic consequences of the acutization of maxillofacial infections in need of hospitalization?
3. Do the acute maxillofacial infection differ over time (past and present) in terms of frequency, pathogenesis, predisposing factors, and treatment options?

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Table.1 Inclusion and exclusions criteria, medical records and literature review

Inclusions criteria	Exclusion criteria
Medical records	
<ul style="list-style-type: none"> Required hospitalization in NUS Diagnosed with at least 1 of the conditions listed: K045 (Chronic periradicular osteitis) K046/K047 (Periradicular abscess with and without fistula) K052 (Acute periodontitis) K102 (Inflammatory conditions of the jaws) K122 (Inflammation and abscess in the oral region) Infections with dental origin 	<ul style="list-style-type: none"> The main reason of hospitalization is not a dental origin infection
Literature review	
<ul style="list-style-type: none"> Articles in Swedish or English Books in Swedish or English Human studies with at least 20 cases/ patients The study should be as varied in patient cases as possible (gender, age) Articles about deep throat infections but dental origins that involved hospitalization Peer review articles Articles with established or suspected potential risk factors for acute maxillofacial infections 	<ul style="list-style-type: none"> Acute maxillofacial infections with no dental origin Occasional cases No hospitalization Non peer review articles
<p>Used Mesh terms when searching via database Pubmed and Google.com</p> <p><u>Used search terms in Pubmed:</u> <i>Acute dental abscess, Acute maxillofacial infections, Acute oromaxillofacial infections, Infections of the Oral Cavity, Neck, and Head, Odontogenic Abscess Hospital, Odontogenic Abscess Hospital length, Local odontogenic infection, Systemic odontogenic infection, Odontogenic infection and diabetes, Odontogenic infection and Obesity, Odontogenic infection and oral hygiene, Odontogenic infection and bacteria, Odontogenic infection treatment,</i></p>	



Acute odontogenic infection treatment, Untreated dental infection. Oral and Maxillofacial Surgery, Maxillofacial Surgery, Acute odontogenic infection, Acute dental infection, Acute oro-maxillofacial infection, Oral Surgical Procedures, Obesity/complications, Obesity/pathology, Obesity/physiopathology, Odontogenic, Orofacial infections and Retrospective analysis.

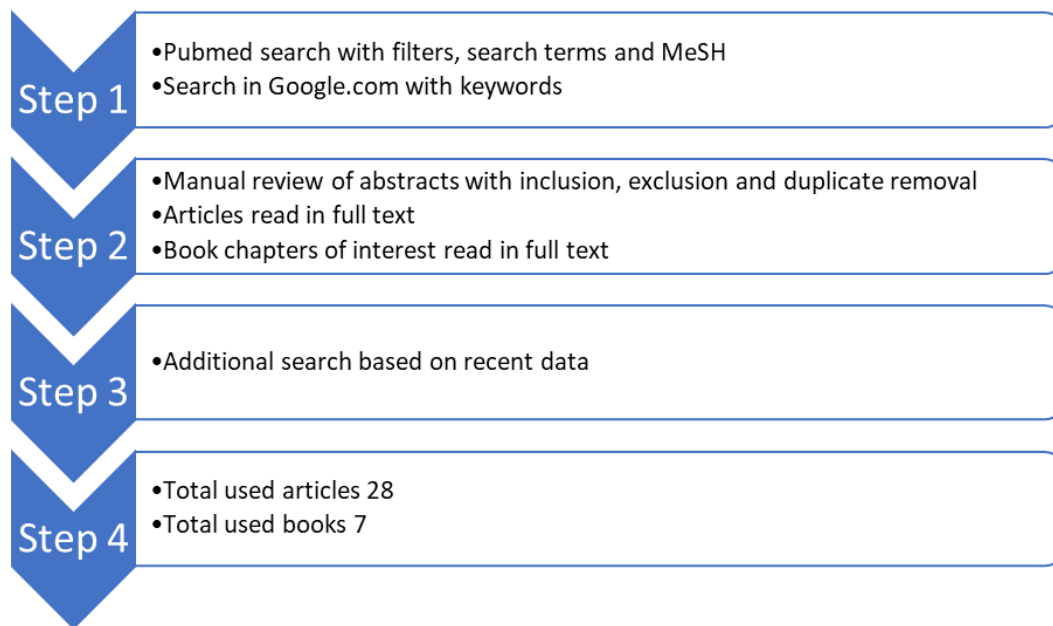
Used search terms in Google.com: *Acute maxillofacial infections, Acute oromaxillofacial infections, Infections of the Oral Cavity, Neck, and Head, Diabetes in Sweden, Diabetes globally, Obesity BMI, Obesity in Sweden, Obesity globally.*

Table.2 Descriptive statistics for 58 included patients

Factors	Subgroups		Nr of patients (out of 58)	Percent
Sex	<u>Male</u>		34	58.6%
	<u>Female</u>		24	41.4%
Age	≤ 47		29	50.0%
	>47		29	50.0%
Dental treatment- no earlier than 14 days before hospitalization	<u>Yes</u>	<u>Extraction</u>	15	25.9%
		<u>Endodontics</u>	10	17.2%
		<u>Other (restorations and scaling)</u>	3	5.2%
	<u>No treatment earlier than 14 days before hospitalization</u>		30	51.7%
Overweight/obesity (BMI (≥ 25))	<u>Info available</u>	<u>Overweight/Obese</u>	16	44.8%
		<u>Non-obese</u>	10	
	<u>Info missing</u>		32	55.2%
Diabetes	<u>Diabetics</u>		6	10.3%
	<u>Non-diabetics</u>		52	89.7%
Wisdom tooth involvement	<u>Wisdom tooth</u>	<u>Maxilla</u>	1	1.7%
		<u>Mandible</u>	16	27.6%
	<u>Other molars in the mandible</u>		41	70.7%
Susceptibility to infection	<u>Affected either by medicine, disease or both</u>		14	24.1%
	<u>Unaffected</u>		44	75.9%
	Mean	Median	Max	Min
Age	45.5	47	75	8
Hospitalization (days)	3.7	3	17	1



Figure.1 Overview of literature search



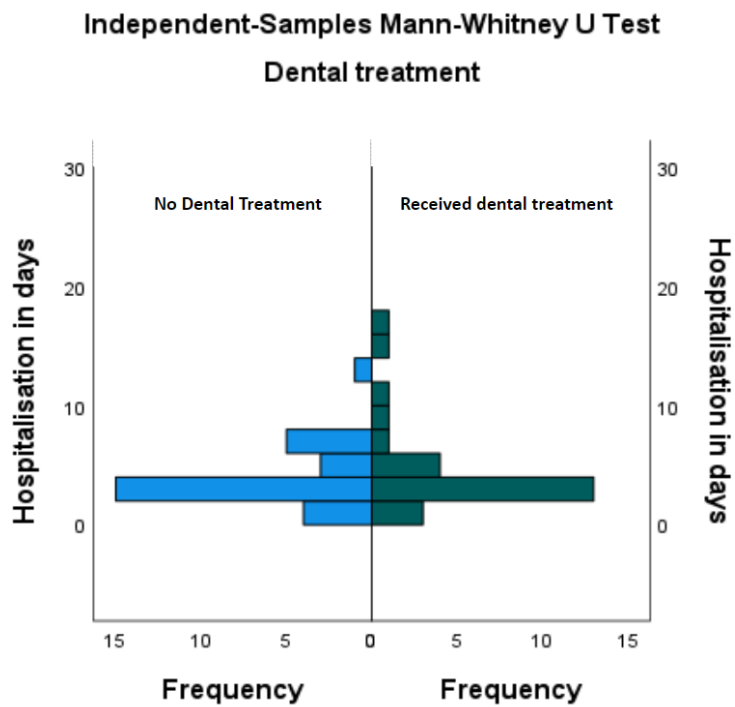


Figure.2 Histogram from SPSS of Hospitalisation vs Dental treatment. No significant difference was found between the group that received dental treatment (no earlier than 14 days before hospitalization) and the one that did not ($p=0.22$).



Figure.3 Histogram from SPSS of Hospitalisation vs Overweight/obesity. A significant difference ($p=0.003$) was found between overweight/obese patients compared the non-overweighed/obese patients.

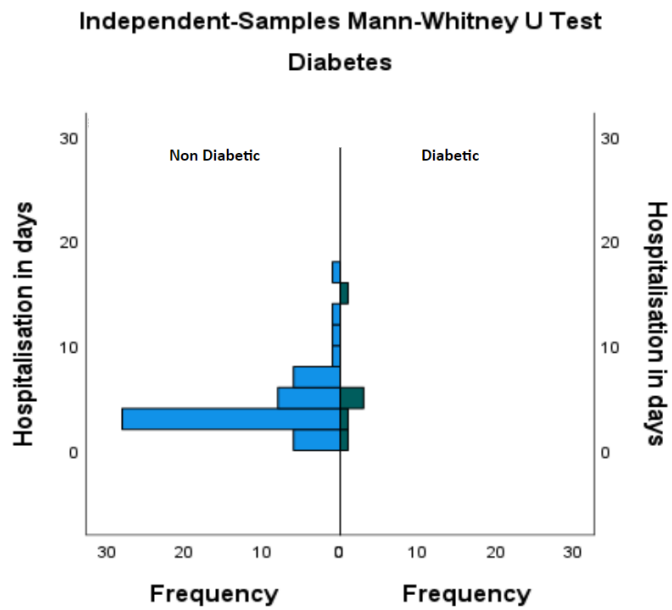


Figure.4 Histogram of Hospitalisation vs Diabetes. A non-significant difference was found between diabetic and non-diabetic patients ($p=0.37$).