

MMED (ORL) RESEARCH REPORT:

Title:

Microbiology of Submandibular Space Infections at the
University of the Witwatersrand

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University of the Witwatersrand, Johannesburg, in part fulfillment of the
requirements for the degree of Master of Medicine in the specialty of
Otorhinolaryngology (MMC022).

I, Shivesh Harichander Maharaj, declare that this thesis is my own work. It is being submitted for the degree of Master of Medicine in the University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination at this or any other University.

Shivesh Harichander Maharaj

10th of December 2009

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

Division of the Deputy Registrar (Research)

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)
R14/49 Maharaj

CLEARANCE CERTIFICATE

PROTOCOL NUMBER M070621

PROJECT

Microbiology of Submandibular Space
Infections at the University of the
Witwatersrand

INVESTIGATORS

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Ortorhinolaryngology Dept

DATE CONSIDERED

07.06.29

DECISION OF THE COMMITTEE*

APPROVED UNCONDITIONALLY

Unless otherwise specified this ethical clearance is valid for 5 years and may be renewed upon application.

DATE

07.08.16

CHAIRPERSON


(Professors PE Cleaton-Jones, A Dhali, M Vorster,
C Feldman, A Woodiwiss)

*Guidelines for written 'informed consent' attached where applicable

cc: Supervisor : Prof PC Modi

DECLARATION OF INVESTIGATOR(S)

To be completed in duplicate and ONE COPY returned to the Secretary at Room 10005, 10th Floor, Senate House, University.

I/We fully understand the conditions under which I am/we are authorized to carry out the abovementioned research and I/we guarantee to ensure compliance with these conditions. Should any departure to be contemplated from the research procedure as approved I/we undertake to resubmit the protocol to the Committee. I agree to a completion of a yearly progress report.

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES

Dedicated to my wife and family

Abstract:

The submandibular space is part of the deep neck fascial spaces.

Infection within these spaces can cause significant mortality and morbidity.

The infections are usually opportunistic, being commensal micro-organisms from the oral cavity and oro-pharynx.

The study is a review of the microbiology of the submandibular space infections seen at the tertiary academic referral hospitals, University of the Witwatersrand. The period of the study is from the 1st January 2006 to 31st December 2006.

93 patients were reviewed of which 52 had aspirates taken.

The predominant micro-organisms were the Gram positive anaerobic cocci.

Their resistance and sensitivity pattern was also studied.

A literature search for this category of infection was also conducted.

The most commonly isolated micro-organisms were the gram positive cocci.

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List of Abbreviations:

- 1)CT : computer-assisted tomography**
- 2)MRI : Magnetic Resonance Imaging**
- 3)MRSA : Methicillin resistant Staph Aureus**
- 4)Aids: Acquired Immune deficiency Syndrome**
- 5)Mmed: Masters in medicine**
- 6)Freq : frequency**
- 7)Cum: cumulative**
- 8)HIV : Human Immunodeficiency Virus**

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Microbiology of Submandibular Space

Infections

Definitions:

Microbiology: The study of microorganisms.

Submandibular space: A space located inferior to the mylohyoid muscle and superior to the hyoid bone, in the neck. Bounded by the body of the mandible, the lower surface of the mylohyoid muscle above and the superficial layer of deep cervical fascia below.

It contains the superficial part of the submandibular salivary gland, anterior belly of digastric muscle, and the submandibular and submental lymph nodes.
(Proops DW, Scott- Brown's Otolaryngology, 1997)

Introduction:

The structures within the neck are surrounded by a fibrous connective tissue called the cervical fascia. This tissue envelops the muscles, neurovascular bundles and aerodigestive organs.

The fascia is divided into a deep and superficial layer. These layers of fascia create potential spaces. These spaces are divided into superficial and deep spaces.

The submandibular space is part of the deep neck spaces.

The submandibular space can be affected by many disease processes including acute and chronic infections. These infections can lead to a suppurative process occurring within the submandibular space.

Infections within the submandibular space can spread along fascial planes into the neck and into the mediastinum. It can also involve the neurovascular structures within the neck. Surgery is often necessary to establish drainage; and for the culture diagnosis of micro-organisms.

Antibiotics are vital in treatment. These antibiotics need to adequately cover the micro-organisms that cause infection within the submandibular space. The choice of antibiotic is best determined by culture and sensitivity reports.

Literature review:

Sources of Infection:

According to Harrison et al (2005), antibiotics have reduced the prevalence, and improved the outcome of deep neck space infections; however deep neck infections do continue to be associated with severe illness and death.

The submandibular space abscess was the most common area of infection (67%), followed by the Lateral pharyngeal space (17%), Ludwig's angina (12%) and the Retropharyngeal space (4%) as reported in a paper by Jankowska (2003) , involving 24 patients with deep neck infections.

Prior to the introduction of antibiotics, upper airway infections including tonsillitis, sinusitis and otitis media were the principal causes of deep neck space infections. While these are still common sources in the pediatric population, after antibiotics were introduced, the principal source of infection in adults became odontogenic infections. This is still one of the most common sources of infection today, affecting primarily the submandibular space.

Occasionally, infections of the parotid or submandibular gland can be complicated by involvement of the deep spaces. Bodner et al(1982) in a study of submandibular sialolithiasis in children pointed out that the main complaint in acute sialadenitis is a submandibular swelling. This swelling however is often confined to the gland, but may go on to involve the submandibular space.

Upper aerodigestive tract trauma, both penetrating and iatrogenic including intubation and instrumentation, was, and still is a fairly common source of infections involving the neck spaces.

Not only of historical interest, but also with the current resurgence of TB, infections of the prevertebral space as a result of tuberculosis of the cervical spine must be considered.

A relatively new etiology is intra-venous(IV) drug abuse involving the neck veins as a source of IV access. Finally, in a large percentage of neck infections the initial source is never identified.

Clinical presentation:

The signs and symptoms of submandibular space infections have changed since the introduction of antibiotics. Localizing symptoms such as fluctuance and pointing have become less common. Fever is still very common and can be seen with infections of any neck space. Pain and swelling are commonly present.

Dysphagia is more common when the parapharyngeal and retropharyngeal spaces are involved. Trismus is seen with involvement of the submandibular space or anterior aspect of the parapharyngeal space. Other symptoms may include respiratory distress if the abscess partially compromises the airway and dental complaints if this is the source of infection.

Microbiology:

In terms of the microbiology of deep neck space infections, important changes have occurred. Today nearly 40% of infections are caused by mixed flora (oral and oropharyngeal).

Stalfars et al(2004) , stated that submandibular space infections (originating from oral mucosal infections, dental infections, submandibular salivary gland infection, blunt or penetrating trauma to the region, and spread from adjacent spaces) commonly cultured anaerobic bacteria : Bacteroides species and Peptostreptococcus. Staphylococcus aureus and Streptococcus species dominate among the aerobic bacteria. Other changes include the emergence of gram-negative organisms, primarily Klebsiella as important pathogens. Bubbico et al(2004) reported an unusual presentation of Actinomycosis of the submandibular gland.

In a study done by Brook et al(1991), on the microbiology of suppurative parotitis in 23 aspirates it was found that the predominant bacteria were Bacteriodes (6 isolates) and Staph Aureus (6 isolates).

In another study done by Brook (2002) ,aspirates from all three pairs of major salivary glands ,the predominant aerobes were Staph Aureus and Haemophilus Influenzae.

The predominant anaerobes were gram negative bacilli (including Prevotella and Fusobacterium spp.)

Changing patterns of infection:

Due to the widespread use of antibiotics certain patterns of resistance have emerged. Currently, Methicillin Resistant Staph Aureus (MRSA) is responsible for a number of serious infections. Abscess secondary to intravenous drug abuse is likely to harbor these organisms. The frequency of beta-lactamase production by oral anaerobes has also increased.

Intravenous drug abuse and the AIDS epidemic have given rise to certain differences between these groups and the general population in terms of presentation and of the organisms responsible for infection. There is a large amount of submandibular space swellings that are non-infectious, as De Vries et al (1988), points out, that the histology of salivary gland masses, in particular the submandibular gland, can include lymphoma.

With a resurgence of tuberculosis among the immunocompromised population as well as the population in general, one has to be aware of Pott's diseases of the cervical spine as a source of prevertebral space infections with the potential for spread to the other deep spaces of the neck. Stanley et al (1983) concluded that cervicofacial mycobacterial infections might present as parotid and submandibular space masses.

They added that successful treatment would require medication as well as excision of the submandibular and/or parotid gland with the accompanying lymph nodes. Important differences in presentation that can lead to early diagnosis include initial complaints consisting mainly of neck pain and stiffness as well as neurological findings including paraplegia.

Investigation:

CT and MRI imaging has truly revolutionized the diagnosis and management of submandibular space infections. The CT scan allows identification of the clinical stage of the infection and thus differentiates cellulitis from abscess. Misa Sumi et al (1999) discuss the benefits of CT and MRI scanning.

Management:

Treatment of deep neck space infections can be divided into nonsurgical and surgical therapy. Nonsurgical treatment consists of intravenous antibiotics that are either empirical, covering gram positive and anaerobic organisms, or based on cultures obtained from needle aspiration if the particular abscess is amenable to needle drainage.

Surgical drainage can be divided into internal or external drainage. Internal or intraoral drainage is appropriate for isolated, peritonsillar abscess and sublingual abscess clearly limited to the floor of mouth.

Nahlieli et al (2000), described endoscopic treatment of salivary gland inflammatory diseases to great effect.

When the infection involves the retropharyngeal space and is complicated by airway compromise or extension to other spaces, then external drainage is appropriate. The external approach is also used for drainage of the submandibular space because of the important structures found in this space. Irrigation of the space can also be done in this approach. Several factors determine the course of treatment with which a particular patient is treated. In the past, most patients were treated with surgical drainage at an early stage. In those that were treated conservatively their response to antibiotic therapy and any signs of impending complications were used to gauge which patient required formal surgical drainage.

Complications:

Complications, although rare nowadays, are important to keep in mind because of their potential for severe morbidity and even death, as well as the fact that their early recognition is important to further management.

Aspiration is most commonly seen as a result of spontaneous intraoral drainage, with its resultant airway compromise or pneumonia. Airway compromise can also be a result of intraoral swelling. In the past this was most commonly seen with Ludwig's angina. Due to the anatomic relationships of the submandibular space and other deep neck spaces, extension into the mediastinum is possible. This can cause a mediastinitis as well as resulting pericarditis or empyema.

Due to the close proximity of the parapharyngeal space, through which infections can spread from one space to another, to the vascular structures of the neck, septic thrombophlebitis of the internal jugular vein is a fairly common complication that can lead to septic thromboemboli with proximal extension leading to lateral sinus thrombosis and distal embolization resulting in pneumonia. An extremely rare but catastrophic complication is vascular erosion of the great vessels of the neck. This is usually heralded by sentinel bleeds from the mouth or nose.

MATERIALS AND METHOD:

Aim of the study: To determine the Microbiology of Submandibular Space Infections. in patients admitted to the tertiary referral hospitals, at the University of the Witwatersrand as recorded in the ward admissions book.

Application made for Ethics Approved: M 0702621

Study design: A retrospective review.

Study Location: The tertiary referral hospitals at the University of the Witwatersrand.

Study Period: The period to be reviewed was from the 1st January 2006 to the 31st December 2006.

Study Population: Patients admitted to the referral hospitals with submandibular space infections.

An essential part of the management of these patients includes a routine aspiration of the abscess. The pus is sent off to the National Health Laboratory Service for routine microscopy and culture.

The characteristics of these aspirates was reviewed. These characteristics include:

- whether an organism/s were identified
- what organisms were identified
- the culture result
- the antibiotic sensitivities

Data Collection: The admissions books in the casualty were studied for patients admitted for submandibular space infections.

These patients were then followed to the ward admission book and the files were reviewed.

A search was conducted of all the patients with aspirates documented in the progress notes.

The following information of the aspirates was then be obtained from the National Health Laboratory service. The parameters included:

- A code (patients names was not used)
- Age
- Gender
- Microbiology of infection
- Sensitivities to antibiotics

Data analysis : Data Analysis and Presentation

Analysis of data was carried out by the MMed candidate (Dr SH Maharaj) at the Department of Otorhinolaryngology Head and Neck Surgery. A probability (p) value of less than (or equal to) 0.05 is regarded as significant.

The following software applications were used for data management, statistical analysis and presentation:

- Microsoft Access 2003 Database for data storage, retrieval and selection
- Microsoft Excel 2003 Spreadsheet for descriptive data analysis, summary statistics and comparison of sample means
- Microsoft Word 2003 Word Processor for final documentation and presentation

Evaluation of data from identified microorganisms with respect to prevalence, age and gender of patients, and antibiotic sensitivity-resistance patterns was done. Special attention is given to comparative analysis of:

- The bacterial profile in male patients as compared to female patients.
- The bacterial profile in the various hospitals.
- The antibiotic sensitivities recorded.

RESULTS:

The period of the study resulted in 95 patients presenting with submandibular space infections. An aspirate was taken and submitted for further investigation in 55 of the subjects). 40 patients have no recorded aspirate.

The 55 aspirates provided a yield of 36 identified organisms on microscopy and culture.

Growth	Frequency	Percentage	Cumulative
No bacterial growth	1 9	3 4 . 5 5	3 4 . 5 5
Bacterial growth	3 6	6 5 . 4 5	1 0 0 . 0 0
Total	5 5	1 0 0 . 0 0	

Table 1: showing frequency in identifying organisms in the aspirates taken.

The table shows that in the 55 aspirates taken 36 resulted in an organism being identified which is a percentage of 65.45 percent, thus showing that there is a significant yield in doing the aspirate, as an organism is identified 65.45 percent of the time.

A further extrapolation of the data reveals that this percentage stays the same for hospital, age and gender.

Thus there is no association between the following variables and growth of an organism. The p values for the following associations are:

Between positive isolation and Gender = 0.29;

Between positive isolation and age = 0.482;

Between positive isolation and the hospital = 0.429

Characteristics of the patients:

Age:

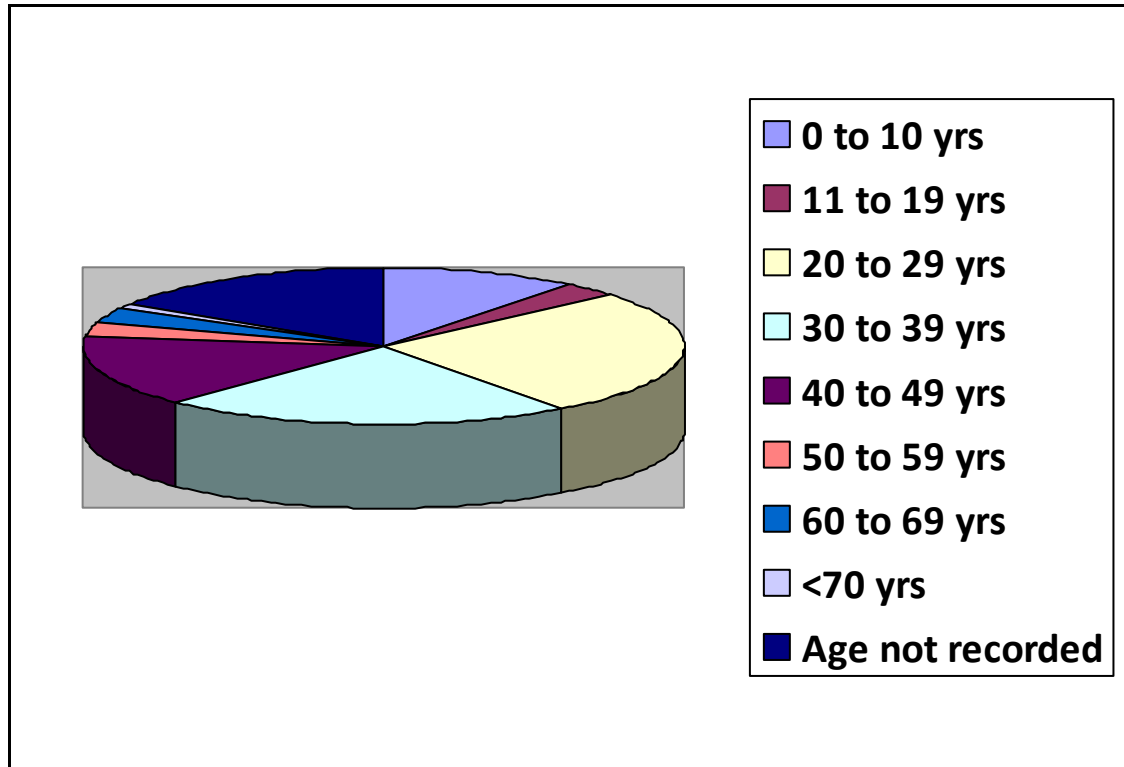
The age ranged from 5 months to 66 years & 3 were not stated. The average age of the study group was 36.5 years.

agegrp	Freq.	Percent	Cum.
1	10	10.53	10.53
2	3	3.16	13.68
3	25	26.32	40.00
4	21	22.11	62.11
5	14	14.74	76.84
6	3	3.16	80.00
7	3	3.16	83.16
8	1	1.05	84.21
.	15	15.79	100.00
Total	95	100.00	

Table 2: showing the age distribution of the patients included in the study.

Key Age group :	1 less than 10 years of age
	2 between 11 to 19 years of age
	3 between 20 to 29 years of age
	4 between 30 to 39 years of age
	5 between 40 to 49 years of age
	6 between 50 to 59 years of age
	7 between 60 to 69 years of age
	8 greater than 70 years of age

Graph 1:



Age distribution graph

Most of the patients ranged between the 3rd to the 5th age group, the trend is such that the greatest number of samples fall between the ages of 20 to 40 years of age.

Gender:

Table 4

gender	Freq.	Percent	Cum.
Male	46	48.42	73.68
Female	24	25.26	98.95
No gender recorded	25	26.31	125.26
Total	95	100.00	

Gender distribution

Table 3: showing the gender distribution of the study group.

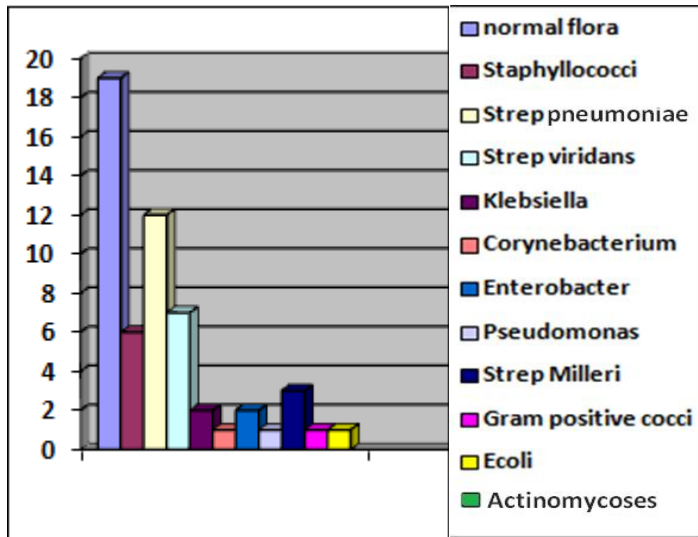
In the study sample, there were more male than female patients recorded, however, there were 25 patients with no recorded gender, and this may bias the result. Thus, no further comments can be made about the gender of the sample size.

Isolated bacteria

Culture code	Freq.	Percent	Cum.
1	19	20.00	20.00
2	6	6.32	26.32
3	12	12.63	38.95
4	7	7.37	46.32
5	2	2.11	48.42
6	1	1.05	49.47
7	2	2.11	51.58
8	1	1.05	52.63
9	3	3.16	55.79
10	1	1.05	56.84
11	1	1.05	57.89
.	40	42.11	100.00
Total	95	100.00	

Table 4: showing the statistical distribution of the isolated bacteria.

Culture code: 1-normal flora, 2-staphylococci, 3-streptococci pneumoniae, 4-strep viridians, 4-klebsiella, 5-corynebacterium, 6-Enterobacter, 7-Pseudomonas, 8-strep milleri, 9-gram positive, 10-Ecoli, 11-Actinomycoses
40 patients with no aspirate recorded



Graph 2: Distribution of isolates

There were 9 different types of bacteria that were isolated on the samples. There were also samples that yielded a result on the gram stain but no identification on culture. A large number of samples also came back with the result of normal flora of the oral cavity, or no pathogen isolated.

Antibiotic Sensitivities

Seven of the aspirates were tested for antibiotic sensitivities and resistance. Four of the organisms were Staph Aureus, from these aspirates were sensitive to Cloxacillin and three of these four were resistant to Penicillin and Ampicillin. Two of the samples were Strep Pyogenes, sensitive to penicillin and erythromycin. One of the samples with a mixed infection - Strep Viridans & Klebsiella of which the Klebsiella was sensitive to cefazolin, cefuroxin, co-amoxiclav but resistant to ampicillin.

Age	Sex	Gram Stain	Organism Isolated	Antibiotic Sensitivity
10 months	M	Gram Positive cocci	Staph Aureus	Sensitive Cloxacillin, resistant to penicillin/ampicillin
3yrs 8mths	M	Gram Positive cocci	Staph Aureus	Sensitive Cloxacillin, resistant to penicillin/ampicillin
38	M	Gram Positive cocci	Staph Aureus	Sensitive Cloxacillin, resistant to penicillin/ampicillin
42	F	Gram Positive cocci	Staph Aureus	Sensitive Cloxacillin
23	F	Gram Positive cocci	Strep Pyogenes	Sensitive to penicillin & ampicillin & erythromycin
Not stated	M	Gram Positive cocci	Strep Pyogenes	Sensitive to penicillin & erythromycin & clindamycin
33	M	Gram Positive cocci	Strep Viridans & Klebsiella	Sensitive to cefazolin,cefuroxin,co-amoxiclav.Resistant to ampicillin

Table 5 – Antibiotic Sensitivities

DISCUSSION:

The study illustrates the importance of aspiration of the submandibular abscess for culture and sensitivity. This routine investigation is often omitted in our study population. However it is clearly evident that the yield of getting a result in terms of gram staining and culture is good.

The gram stain and the culture of the micro-organisms is not only a vital tool but can also determine further management of the patient.

The microbiology of the aspirates in the study population was in keeping with studies done in other centers such as those done by Janowski(2003) . The most commonly isolated micro-organism being the gram positive cocci, in particular, Streptococci and Staph Aureus.

This was in keeping with the results found by Selfars et al (2004), who attributed the microbiology to the primary source of the infection, that is the oral cavity mucosa and odontogenic infection.

The incidence of tuberculosis in our study population was low and this is primarily due to the lack of request for investigation for tuberculosis. In the study only one of the aspirates was sent for Acid fast bacilli and TB culture. This microscopy and culture was negative; however more samples are required to assess the incidence of TB in the patient population. Thus there is not enough material to make an accurate assessment of the role of TB in our study population.

The sample population ranged from children, (the youngest aspirate being from a five month old), to adults (the oldest sample being taken from a 66 year patient). However, the vast majority of patients were adults. This is in keeping with Salfers et al (2004) who also found predominance in adults. Brook (2002) in a study of 47 aspirates found 7 patients below the age of 18.

A possible explanation for the findings in our population is that needle aspiration is more challenging and risky in children and the parent may not always consent to the procedure.

It is also possible that most of the cases in children present with a submandibular space which often resolves on antibiotic therapy.

An aspirate is thus not always possible in children and is usually only done when the cellulitis does not respond to antibiotic therapy and progresses to an abscess.

It is important to note that the vast majority of submandibular space infections result from odontogenic infection. However, in our study the source of the infection was not always stated and thus, further comments cannot be made.

The culture results in our population reflect a single organism in the majority of patients and a mixed infection was only seen in one patient. This finding was different to other studies such as Brook (2002) who reported a combination of anaerobic gram-negative bacilli and *Peptostreptococcus* in eight specimens.

The resistance and sensitivity patterns of the micro-organisms in the study were conducted in seven samples. The two dominant organisms were *Staph Aureus* & *Streptococcus*.

The Staph Aureus was sensitive to Cloxacillin and resistant to Penicillin and Ampicillin.

The Streptococcus species was sensitive to Penicillin, Ampicillin & Erythromycin.

Klebsiella was isolated in one of the samples and was sensitive to Cefazolin, Cefuroxin and Co-amoxiclav but resistant to Ampicillin.

In the study population there was one aspirate that demonstrated Methicillin Resistant Staph Aureus(MRSA)

The clinical implication of the above findings are important, in that all patients presenting with submandibular space infections are treated with intravenous antibiotics. This can be as the sole treatment or as an adjunct to surgery. In the study population, the first line drug of choice for a patient upon first presentation is Co-amoxiclav. Our study however indicates that most of the samples have Streptococcus and Staph Aureus isolated.

It is worth noting that the Staph Aureus is sensitive to Cloxacillin but resistant to Penicillin and Ampicillin. Thus first line antibiotic treatment should include Staph Aureus cover, as the Co-amoxiclav may not be adequate.

The study done by Bubbico reported a case of Actinomycosis of the submandibular gland. In this study none of the samples demonstrated this finding.

However, two samples yielded Enterobacter and Enterococci which has not been previously reported in the literature. These two types of bacteria are commensals within the gastro-intestinal tract, especially the lower gut and means of spread could be a feecal oral spread and poor hand hygiene.

A single aspirate cultured Kleibsiella, this was reflected in a study done by Brook et al (1991) who reported gram-negative organisms to be seen in aspirates from hospitalized patients.

The effect of the AIDS and HIV has not changed the pattern of disease as seen in the study, and there were no opportunistic micro-organisms isolated. However a larger sample population should be studied over a longer period to make a comment on the effect of Immunosuppression and opportunistic infections.

CONCLUSIONS

The submandibular space infection continues to be source of morbidity in the study population and is often treated with broad-spectrum antibiotics with resolution and recovery.

A needle aspiration of the abscess should be a recommended investigation and as seen in the study, when an aspirate is done a micro-organism may be identified.

It is also a relatively simple procedure done in the hands of a medical doctor and should be done on a more regular basis.

The limits of the study include the size of the sample study , a larger sample will provide better statistical analysis. In particular a larger sample of aspirates, in this study only 53 of the 93 patients had aspirates. With more aspirates a better representation of the bacteria may be identified.

A one year interval provides a basic trend of the organisms but a 5 or 10 year study will provide more information.

As with all retrospective study designs there are limits in terms of the variables studied, and the bias involved. These events have already happened and thus cannot be modified, as seen in this study by the low number of aspirates done on children. Thus a comment can not be made on the trends seen in children

The micro-organisms seen are in keeping with the commensal bacteria of the oral cavity, and the antibiotic treatment of these infections should be directed towards these micro-organisms, however due to the changing spectrum of diseases and patients, regular surveillance of the micro-organisms need to be done.

The pattern of infection and micro-organisms causing submandibular space and deep neck space infections needs to be constantly reviewed to avoid complacency and ensure better patient care.

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Appendix 1 : Data Sheet

Microbiology of Submandibular Space Infections. in patients admitted to the tertiary referral hospitals, at the University of the Witwatersrand as recorded in the ward admissions book.

Ethics Approved: M 0702621

Study design: A retrospective review.

Patient hospital number

Code

Gender

Age

Aspirate

- organisms were identified
- the culture result
- the antibiotic sensitivities