Bacterial Isolate and Resistance Patterns of Deep Neck Infections: The Manitoba Experience

by

Kurt Scherle

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Department of Dental Diagnostics and Surgical Sciences

University of Manitoba
Winnipeg, Manitoba, Canada

Abstract

Objective: The purpose of the study is to identify bacteria isolate patterns in deep neck infections managed by Oral & Maxillofacial Surgeons at a tertiary care centre in Manitoba, and analyze resistance profiles of the bacteria to specific antibiotics.

Patients and Methods: A 2-year retrospective chart review on a population treated at a tertiary academic centre with deep neck infections surgically managed by the Oral & Maxillofacial Surgery service. 53 patients underwent surgical incision and drainage, received intravenous antibiotics, and had microbiological testing completed.

Results: There were 25 male (47%) and 28 female (53%) patients treated by incision and drainage in an operating room setting and who had microbiological swabs obtained at the time of surgery. The submandibular space was most commonly involved (64%), followed by buccal space (34%) and lateral pharyngeal space (17%). Twenty five patients had involvement of multiple spaces. The total number of spaces involved was 90. Of the 53 patients treated, 46 grew bacterial cultures. The most commonly isolated bacteria were *Streptococcus viridans, Anaerobic non-spore-forming gram positive bacilli,* and *Prevotella oralis.* On microbiological analysis, anaerobic gram-negative rods grew in 38 cases (72%) and aerobic gram-positive cocci in 33 cases (62%). Resistance to penicillin G was highest (70%).

Conclusions: Patients undergoing surgical incision and drainage by the Oral & Maxillofacial Surgery service tended towards multiple space involvement with submandibular, buccal, and lateral pharyngeal being most common. Cultures more often revealed growth of anaerobes than aerobes. Gram-negative rods and gram-positive cocci were most prevalent. Resistance was highest to the penicillin family of antibiotics, followed by clindamycin.

Introduction

Odontogenic infections are routinely encountered by Oral & Maxillofacial Surgeons, Dentists and other individuals who treat disease of the head, neck, and oral cavity. Most odontogenic infections are readily resolved by removal of the source with or without antibiotic therapy. However, the few that involve deep neck spaces can become life threatening. Prompt airway management, surgical drainage in an operating room (OR) setting, removal of source, and systemic intravenous (IV) antibiotics all play a critical role to these patients[1]. Efficient diagnosis and appropriate treatment can limit regional and distant spread of these infections to cervical fascial planes or beyond.

Early recognition of odontogenic infections is significant as they are a common cause of morbidity and mortality, despite the effective, yet not well used, prevention and control methods[2] . Delayed, inadequate or incorrect treatment can lead to serious and potentially life threatening complications such as spread of infection to the mediastinum[3,4], cavernous sinus[4] and respiratory tract resulting in sepsis, vision loss, meningitis, brain abscess[5],and death.

Deep neck infections of odontogenic origin are polymicrobial in nature[2,3,5,6]. According to the literature, gram-positive cocci (*Streptococcus, Staphylococcus species*) and oral anaerobes (*Bacteroides, Prevotella, Porphyromonas, Peptostreptococcus species*) tend to prevail in these infections[6]. Gram-positive cocci have been found in 57.7% of specimens and gram-negative rods in 33%[7].

Severe odontogenic infections have the ability to spread throughout the fascial planes within the deep neck. These fascial spaces have well defined anatomic

boundaries. Deep neck infections may involve one or more anatomic spaces with an average of 3.3 spaces per patient[6]. As described in comparable studies, in multi-space infections the most commonly involved spaces are the pterygomandibular space at 59%[6] and the submandibular space in 28.2-54%[6,7]. The buccal space was next most commonly involved at 27.5%[7].

Empiric antibiotic therapy upon hospital admission is tailored towards treatment of the most likely etiologic organisms. Commonly prescribed antibiotics include Penicillins, Lincosamides, and Nitroimidazoles[6]. During the surgical incision and drainage process, swabs are taken directly from the infection wound site and submitted for microbiological cultures and sensitivity testing to narrow the spectrum of antibiotics used and identify antibiotic resistance patterns within the bacterial cultures. Comparing Brook and Flynn, the incidence of penicillin resistant strains of bacteria isolated from deep neck infections has risen from 33%[8] in 1991 to 54%[6] in 2006. As resistance rates to penicillins rise, there has been an increasing number of patients treated with other antibiotics. High resistance rates to clindamycin have also been documented. This may necessitate further surgical intervention and a change in antibiotic regime[9].

Certain systemic conditions such as diabetes, acquired immunodeficiency syndrome (AIDS), renal failure, and advanced age are becoming more prevalent. These modify the host response and may be contributing factors to the infectious process[10].

Objective

The objective of this study was twofold; to identify spectra of bacteria present within deep neck infections of odontogenic origin, and to gain understanding of the antibiotic resistance patterns of these bacteria in a Manitoba population. Study results may then be considered when initiating empiric antibiotics for hospital admissions in these patients.

Materials and Methods

This was a retrospective study that identified adult patients who required hospital admission, intravenous antibiotics, and surgical incision & drainage in an operating room setting while under general anesthesia. Records utilized from patient charts included demographics, time related variables and clinical variables.

This patient cohort received treatment between July 2009 and June 2011 by the Oral & Maxillofacial Surgery department at the Health Sciences Centre in Winnipeg, Manitoba, Canada.

The charts selected consisted of 66 adult patients requiring hospital admission and surgical incision and drainage in an OR setting. 10 patients had no swab taken at the time of surgery and were excluded as they provide no information about bacterial patterns or resistance to antibiotics. Patients with deep neck infections not related to an odontogenic source such as osteomyelitis were also excluded (3 patients). Chart review was not performed on patients where hospital admission was not required. Patients who received intravenous antibiotics alone in the emergency department along with those who were treated with local anesthesia in our outpatient clinic were excluded as wound swabs are not routinely obtained.

The 53 patients included in the study were assessed by the Oral & Maxillofacial Surgery team and admitted to the Health Sciences Centre after thorough history and physical examination. Intravenous antibiotics were often initiated in the emergency department. Imaging with a panoramic radiograph or where appropriate an infused computed tomography (CT) scan of the neck, was completed. The offending

odontogenic source was confirmed clinically and radiographically and if a CT scan was completed, the extent and location of the deep neck infection was identified. The incision and drainage process was carried out under general anesthesia. Standard landmarking for incisions for surgical access to the various deep neck spaces were placed on the patients' necks or within their oral cavities. Skin incision and blunt dissection followed to the spaces in question. Wound swabs of any purulent discharge were obtained and sent for testing to the microbiology laboratory for culture, sensitivity, gram stain, aerobes/anaerobes, acid-fast bacilli, and fungi. Once adequate surgical drainage was accomplished, the wounds were irrigated with normal saline. Penrose drains (¼") were then placed into the involved anatomic spaces and sutured to the skin or oral mucosa with 3/0 silk. The odontogenic source was then removed in a standard fashion. A neck dressing of gauze and burn net were applied to the patient. At the completion of the surgical procedure, the patients were assessed by the anesthesia department to determine their post operative destination (ward bed, step down unit, or surgical intensive care unit). The patients then remained in hospital for a minimum of 48 hours, at which point the penrose drains were removed. We do not use drains as a means to deliver irrigation[11]. Intravenous antibiotics were continued for the duration of the hospital stay. Daily vital signs, laboratory values and frequent clinical assessments were completed. If the patient had no improvement in temperature, white blood count (WBC) and swelling, a post-operative CT scan was ordered. If new purulent collections or involvement of additional anatomic spaces were evident on the post-operative CT scan, the operation was repeated with more aggressive dissection of the affected spaces. If the patient showed improvement or resolution of signs and symptoms related

to their infection, and met hospital discharge criteria they were sent home with prescriptions for oral antibiotics, analgesics, and 0.12% chlorhexidine gluconate mouth rinse. Follow-up was scheduled within one week of discharge and microbiological cultures were verified (our institution typically completes culture and sensitivity of wound swabs in 5 days). Antibiotics were only altered if there was evidence of resistance to the prescribed antibiotic.

All data was compiled from charts contained within the medical records department of the Health Sciences Centre in Winnipeg, Manitoba, Canada. The demographic variables recorded were age and sex. Pre-admission variables were: smoking, diabetes, human immunodeficiency virus (HIV) seropositivity, use of immunosuppressive medications (as in the case of organ transplant), and cancer chemotherapy (within one year). Time related variables were the month the patient was admitted and length of stay (LOS). Clinical variables included white blood cell count (WBC), temperature on admission (measured orally at triage within the emergency department), causative teeth, and antibiotic initiated upon hospital admission. For the purpose of statistical analysis, offending teeth were grouped into anterior, posterior (non third molar), and third molar categories for both the maxilla and mandible. The anatomic variables recorded were the deep fascial spaces involved by cellulitis or abscess and number of spaces affected (determined by review of CT scan reports and operative reports).

The microbiological variables were genus and species identification, oxygen requirements (aerobic or anaerobic), antibiotic sensitivity, and number of species isolated per case. In cases where re-operation occurred, multiples cultures were

obtained. Only the culture taken during the first incision and drainage was used in the statistical analysis.

Data was recorded retrospectively and immediately placed in a database using Microsoft Excel (Microsoft, Redmond, WA). Descriptive statistics were calculated for all of the study variables.

Results

A total of 66 patients with deep neck infections of odontogenic origin required admission and were treated by the Oral & Maxillofacial Surgery team at the Health Sciences Centre in Winnipeg, Manitoba between July 2009 to July 2011. The previously mentioned inclusion criteria eliminated 13 of the patients. There were 53 patients (25 male, 28 female) who satisfied the inclusion criteria (Figure 1). The mean ±standard deviation (SD) age of the patients was 36.6±15.2 years with a range of 8 to 70 years.

The number and combination of infected fascial spaces was recorded. A total of 90 infected fascial spaces were identified on 53 patients. The mean±SD of infected spaces per patient was 1.7±0.87 (range, 1 to 4). The most commonly infected space was the submandibular (34 patients, 64%), followed by buccal (18 patients, 34%) and lateral pharyngeal (9 patients, 17%) (Figure 2). Variability existed in the number of infected fascial spaces per patient: one (28 patients, 53%), two (15 patients, 28%), three (8 patients, 15%) and four (2 patients, 4%) respectively (Figure 3).

Thirty eight (72%) cases cultured anaerobic gram-negative rods with *Prevotella oralis* most prevalent (12 cases, 23%). Other members of the *Prevotella* genus (*P. intermedia, diseans* and *buccae*) were also cultured (12 cases, 23%). Thirty three (62%) cases cultured aerobic gram-positive cocci with *Streptococcus viridans* most prevalent (11 cases, 21%). *Staphylococcus sp.* was identified in 12 cases (22%). The next most prevalent organisms were anaerobic gram-positive rods (12 cases, 23%) which included anaerobic non-spore-forming gram-positive bacilli (11 cases, 21%).

Nine cases (17%) showed no culture after 5 days and thirteen cases (25%) cultured normal respiratory flora. Yeast organisms were cultured within three cases (6%). These are outlined in Table 1.

Sensitivity data was present in 10 patients and showed penicillin resistance in seven cases (70%), clindamycin (4 cases, 40%), two cases (20%) for each ampicillin, oxacillin and erythromycin (Figure 4). The total culture rather than individual bacteria strains were identified as being sensitive or resistant, as per our laboratory standard protocol.

The most commonly prescribed antibiotics upon admission to our centre were clindamycin (36 cases, 67.9%) followed by a combination of ampicillin and metronidazole (8 cases, 15.1%).

Clinical variables analyzed showed a WBC mean±SD of 12.9±5.6, with a range of 3.7 to 40.8 X $10^3/\mu$L. The initial core temperature as measured orally at the emergency department triage desk ranged from 36.4ºC to 39.4ºC with a mean± SD of 37.3ºC± 0.67ºC. Length of stay was 4.8± 3.3 days with a range of 2 to 15 days.

The most frequently involved tooth was the mandibular third molar (27 cases, 50.9%) followed by mandibular posterior tooth (24 cases, 45.3%) and maxillary third molar (7 cases, 13.2%) (Figure 5). The overall number for this category adds up to over 100% as cases often had more than one offending tooth. Deep neck infections were most prevalent during January (9 cases) and October (6 cases) (Figure 6).

There were 17 patients (32.1%) who were smokers in this study. Diabetes (insulin and non-insulin dependent) was a comorbidity in 4 patients (7.5%). Three patients (5.7%) had previous cancer. None of the patients were taking

immunosuppression medications and none were HIV seropositive. One patient had idiopathic thrombocytopenic purpura as diagnosed by the hematology service while admitted for his odontogenic infection. One patient suffered from alcohol dependance.

Discussion

Odontogenic infections are routinely treated as an outpatient office procedure. Misdiagnosed, untreated, or rapidly spreading infections have potential to be life threatening by spreading into deep neck spaces. In this study we retrospectively analyzed 53 patients diagnosed with a deep neck infection of odontogenic origin. All patients within the study were admitted to the hospital and treated in an OR setting for incision and drainage. The specific aim was to identify bacteria isolated from the deep neck spaces and resistance patterns of microorganisms in a Manitoba population.

There was no statistical difference between male and female patients, with a mean age of 36.6±15.2 years. This data was similar to other deep neck infection of odontogenic origin publications[6,7,9,12,13]. Multiple space infections are more commonly seen than single space infections of odontogenic origin[6,7]. The current literature shows some variability in the most commonly affected space. The pterygomandibular, submandibular, and buccal spaces were most commonly infected in one study[6]. Other studies describe the submandibular, submental and lateral pharyngeal spaces as the most common[7,13]. Our data found the submandibular space (64.2%) was affected nearly two fold more often than the buccal space (34%) followed by the lateral pharyngeal space (17%). This was likely due to the odontogenic source being most often a mandibular third molar (50.9%) or a mandibular posterior tooth (45.3%). Our institution had similar results to Flynn et al where maxillary teeth were infrequently the source of the deep neck infection[6].

Bacteria cultured from our patient population demonstrated a mixture of aerobes and anaerobes. Infections due to gram-negative and anaerobic organisms is rising

when compared with historical literature. This may be related to improvements in isolating and culturing methods of anaerobic organisms[14]. Our study showed predominance of anaerobic species, specifically anaerobic gram-negative rods (71.7%), over aerobic gram-positive cocci (62.3%). The most common isolates were *Prevotella oralis* (22.6%) followed by *Streptococcus viridans* (20.8%). *Prevotella* species were cultured in 46% of cases. We employed a swab method for bacterial culture in our institution which usually produces a higher aerobic yield when compared to aspiration collection[15]. Our result, of a higher proportion of anaerobic gram-negative rods followed by aerobic gram-positive cocci, are consistent with multiple other studies[6,8,15].

Our study had an average of 2.5 isolates per patient, slightly fewer than comparable studies[6,7]. As mentioned earlier, we utilize a swab method and this may account for the lower number of isolates per patients in our study. Studies which obtained specimens from aspirating averaged from 3 to 3.3 isolates per sample[16,17].

Culture and sensitivity patterns were reviewed for all patients in the study. Our institution provides sensitivity and resistance analysis to the cultures as a single entity. There is no individualized data per specific bacteria cultured. A study by Sakamoto reported beta lactamase from *Prevotella* and *Porphyromonas* is penicillinase[18]. Approximately one third of *Prevotella* and *Porphyromonas* are beta lactamase producers, whereas other groups of anaerobic bacteria have remained substantially stable in their susceptibility patterns[19]. In some of our cases found to be penicillin G resistant, beta lactamase production by *Prevotella* species (found in 46% of cases) may have provided some protection for other bacteria against penicillin.

Our data revealed a penicillin resistance in 70% of all cases which reported sensitivity data. In a 1991 study, 33%[8] showed penicillin resistant strains, while Flynn et al demonstrated a 54%[6] finding in 2006, suggesting an overall increase in penicillin resistance in odontogenic infections. This was a limitation of our study as sensitivity data was only returned for 10 cases. During the incision and drainage procedure, the microbiological requisition is completed requesting cultures and sensitivities.

All cases which showed penicillin resistance also cultured anaerobic gram-negative bacteria. Penicillin resistance occurs mainly because of synthesis of beta-lactamase by the offending bacteria[20]. Beta-lactamase producing strains are usually found in the gram-negative spectrum[20]. Anaerobic gram-negative rods such as *Prevotella* and *Fusobacterium*, are able to split beta-lactamase antibiotics[20]. Conversely, almost all beta-lactamases of the clinically relevant bacteria in deep neck infections of odontogenic origin can be neutralized by clavulanic acid, a widely used inhibitor of beta-lactamases[21].

Clindamycin (67.9%) was used more often than any other antibiotic at our institution. These numbers are dramatically different from other studies where clindamycin was only used in 8%[6] and 18%[9] of cases. Resistance to clindamycin was found in 40% of our cases with sensitivity data. This statistic is worrisome as a recent study found resistance rates to be 17%[6], corroborating our observation of a rise in clindamycin resistant organisms in odontogenic infections.

Ampicillin combined with metronidazole was used in 15.1% of cases. Other institutions often used penicillin[6] or ampicillin/sulbactam(Unasyn™)[9] as a first-line therapy, the latter of which is not available in Canada. In our institution, patients often

delay presention or present after failing a course of penicillin family antibiotics. In penicillin failures, the source of the infection was rarely removed which likely contributed to the antibiotic failure. Our emergency department and surgical infectious disease service often initiate or suggest clindamycin for deep neck infections of odontogenic origin as first line therapy followed by third generation cephalosporin (ceftriaxone) combined with metronidazole as a second line treatment.

The mean core temperature of our patients at triage and WBC was comparatively lower than other studies[6]. Our patients often presented normothermic (37.3ºC± 0.67ºC) with only slight elevation of WBC (12.9±5.6) confirming that normal prediction variables of systemic infection are not always seen in deep neck infections of odontogenic origin.

Early recognition and treatment of odontogenic infections can provide a reduction in costs to the healthcare system and to society as a whole(missed work or school days). The average LOS of our patients was 4.8± 3.3 days which is not statistically significant when compared to one other study (5.1±3.0)[6]. The admission cost to our institution is $1,680.00 (CAN) per day. The average patient in our study utilizes $8,064.00 in public resources not including operating room time or accounting for stays in the intensive care unit. There were a total of 253 patient admission days within the time frame of our study. This resulted in an estimated $425,040.00 in provincial resources for our patient population. These results stress the importance of early diagnosis and treatment of odontogenic infections under local anesthesia in an office setting to prevent not only the burdens on both the healthcare system and society but the potential threat to the patients' lives.

Conclusion

The results of this study suggest that resistance rates to antibiotics are rising for this group of patients. As resistance increases, alternative antibiotics combinations such as second or third generation cephalosporins with metronidazole, fluoroquinolones or introduction of a medication such as ampicillin/sulbactam into Canada may play a role in future treatment of deep neck infections. Given the significant rise in resistance, we suggest utilizing clindamycin only for patients who are penicillin allergic and not routinely as a primary medication to treat these infections. Strong consideration should be given to avoid clindamycin in non penicillin allergic patients and instead using an alternate regimen such as a fluoroquinolone or a second generation cephalosporin combined with metronidazole. We also advocate for early recognition and treatment of odontogenic infections to prevent the progression into the spaces within the deep neck.

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Figure 1

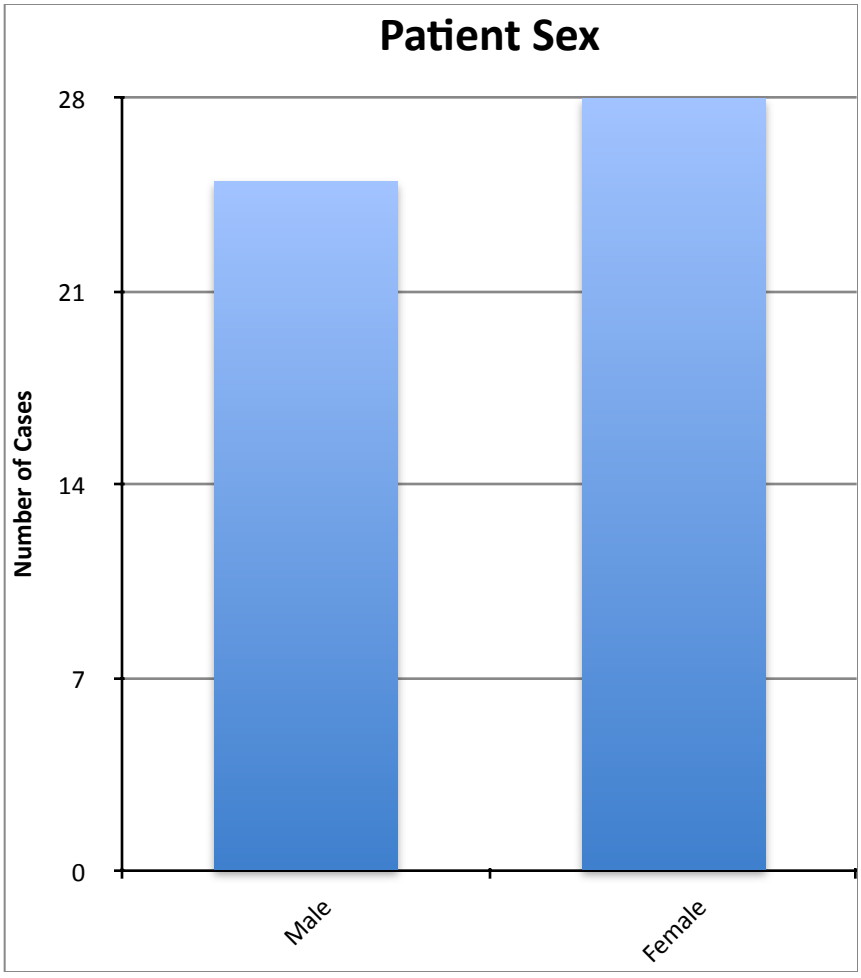

Figure 2

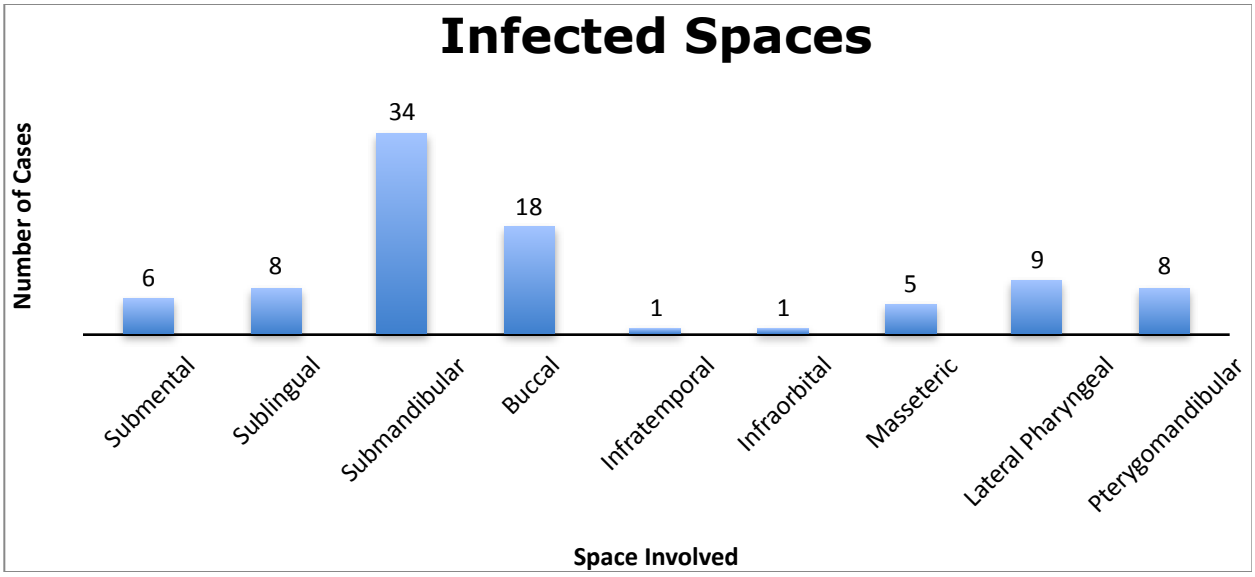
Infected Spaces
Number of Cases
6
8
34
18
1
1
5
9
8
Submental
Sublingual
Submandibular
Buccal
Infratemporal
Infraorbital
Masseteric
Lateral Pharyngeal
Pterygomandibular
Space Involved

Figure 3

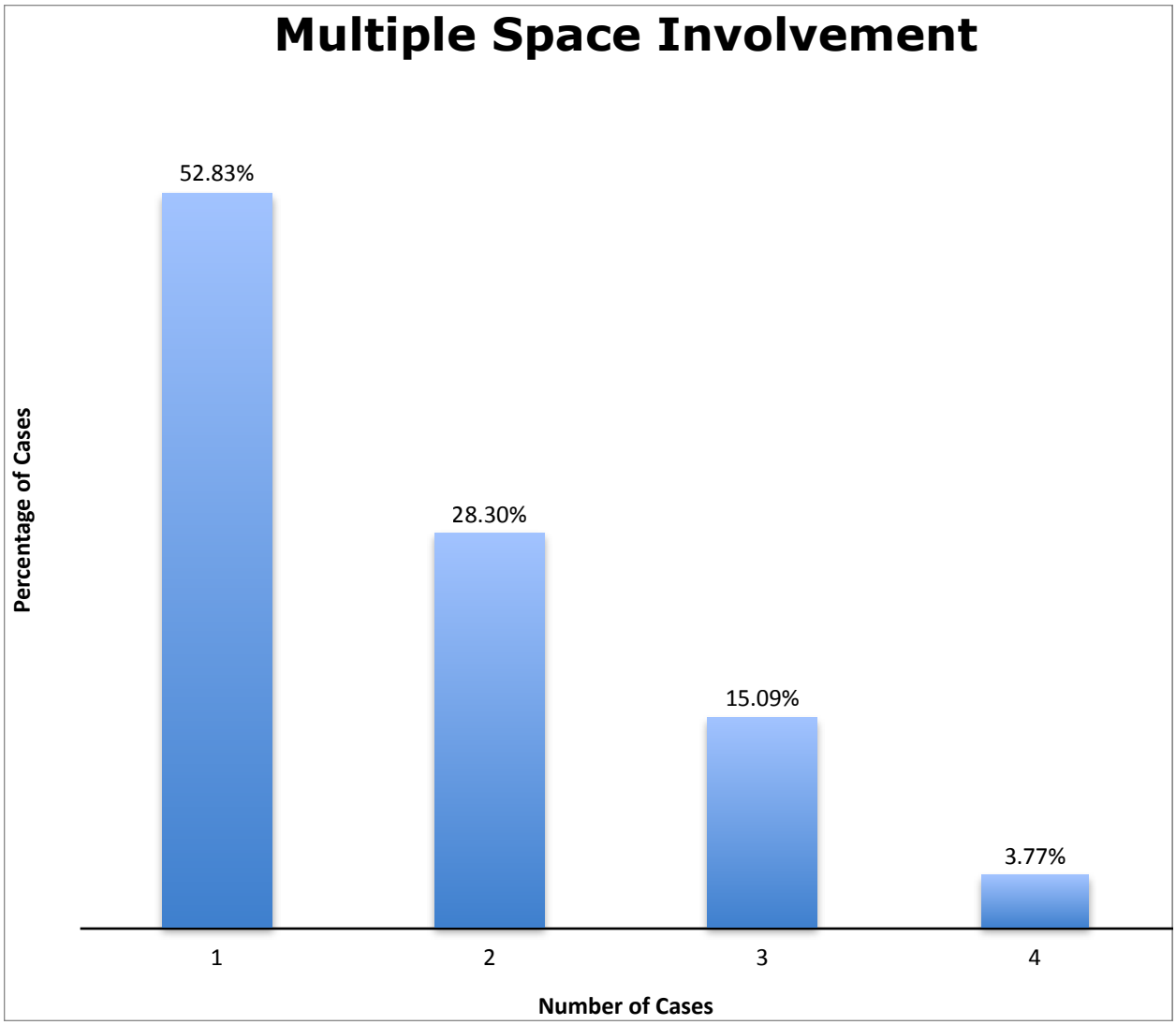
Multiple Space Involvement
52.83%
28.30%
15.09%
3.77%
Percentage of Cases
1
2
3
4
Number of Cases

Figure 4

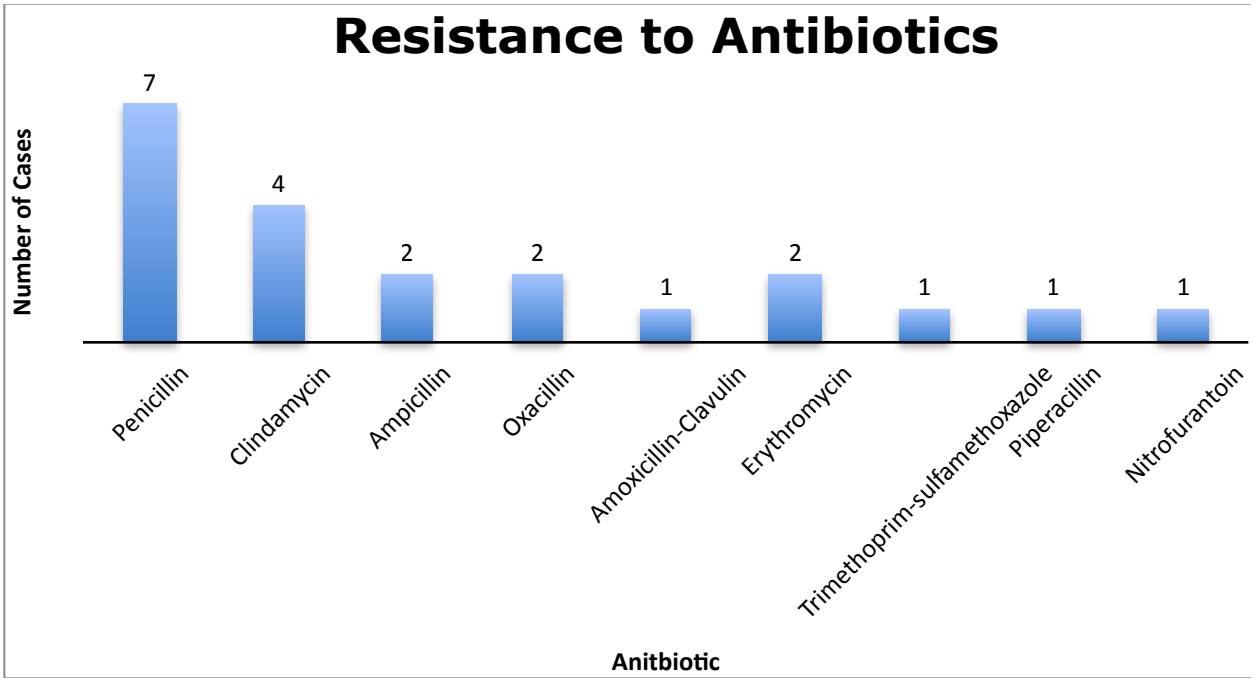
Resistance to Antibiotics
Number of Cases
7
4
2
2
1
2
1
1
1
Penicillin
Clindamycin
Ampicillin
Oxacillin
Amoxicillin-Clavulin
Erythromycin
Trimethoprim-sulfamethoxazole
Piperacillin
Nitrofurantoin
Anitbiotic

Figure 5

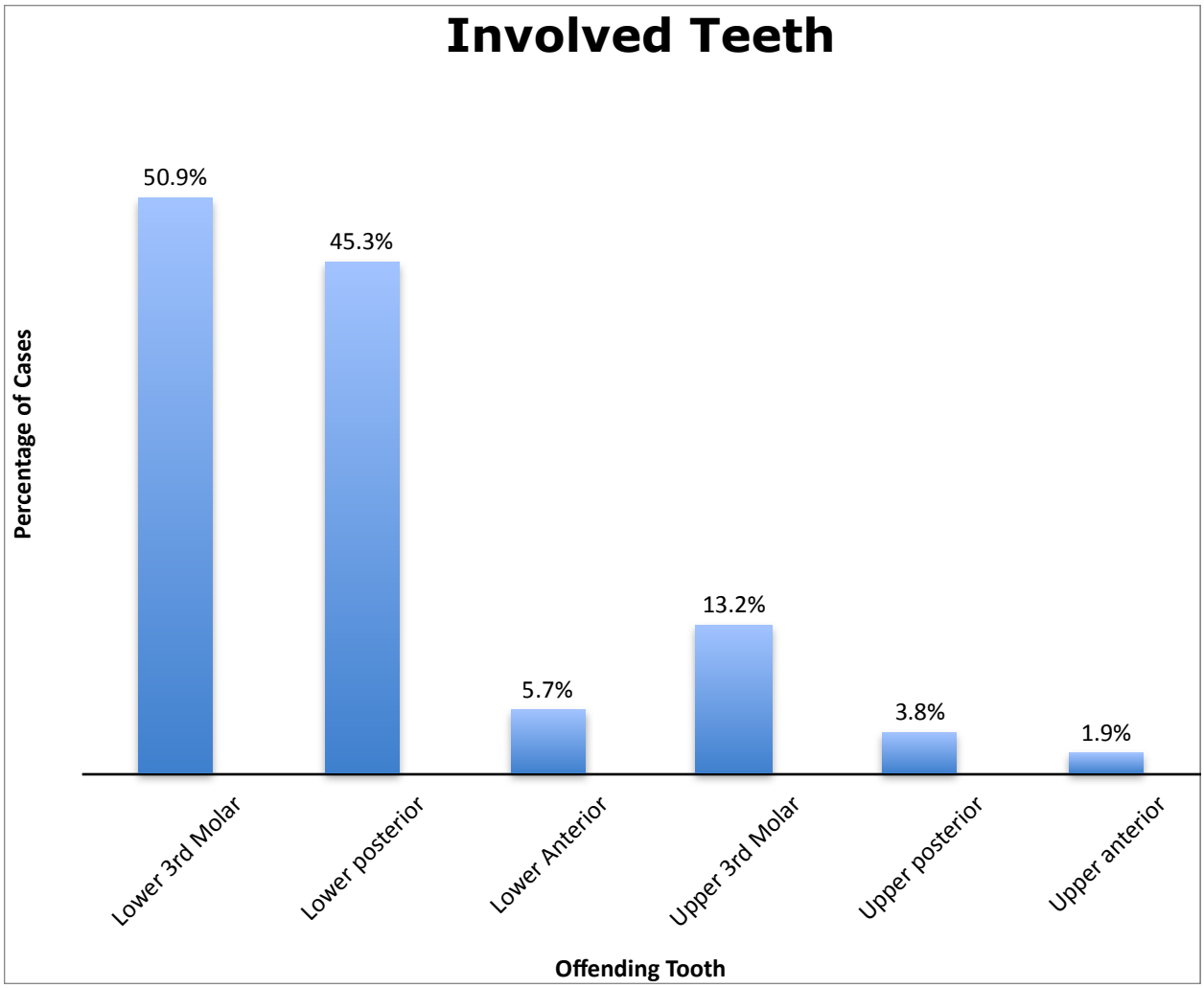
Involved Teeth
Percentage of Cases
50.9%
45.3%
5.7%
13.2%
3.8%
1.9%
Lower 3rd Molar
Lower posterior
Lower Anterior
Upper 3rd Molar
Upper posterior
Upper anterior
Offending Tooth

Figure 6

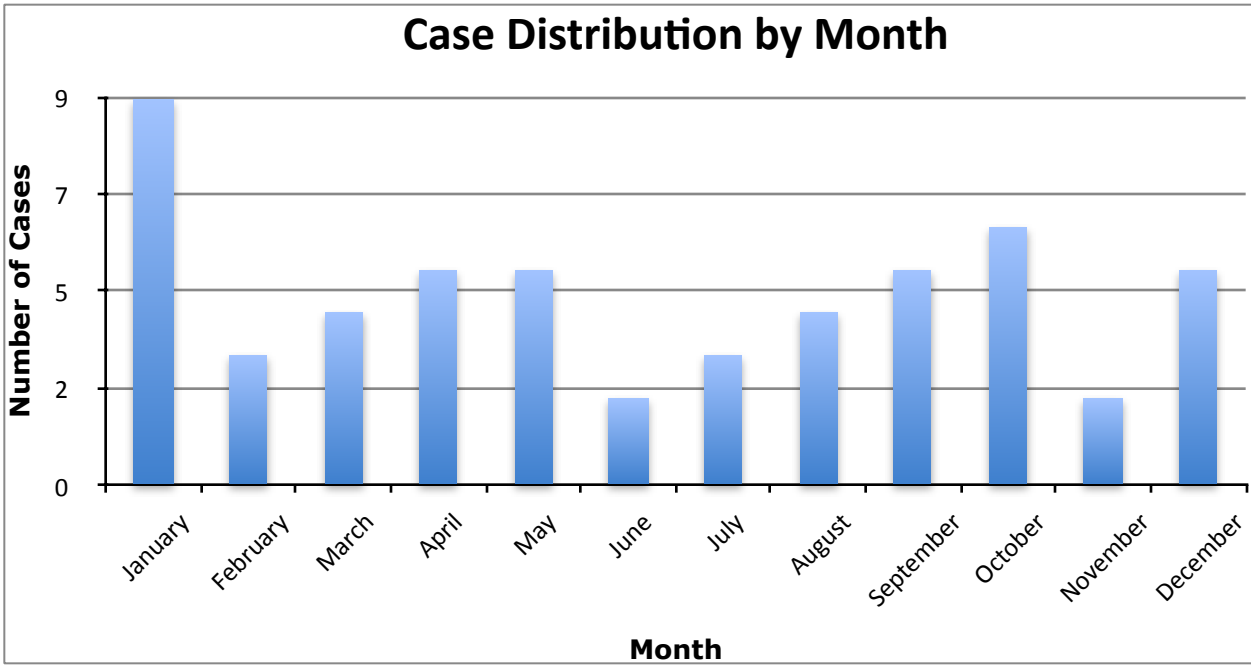
Case Distribution by Month
Number of Cases
9
7
5
2
0
January
February
March
April
May
June
July
August
September
October
November
December
Month

Table 1

Detailed Microbiological Data (n=53)

	Number of Cases	% Cases
Normal Respiratory Flora	13	24.5%
No Culture after 5 Days	9	17.0%
Aerobic Gram Positive Cocci	33	62.3%
Streptococcus sp.	5	9.4%
Streptococcus milleri	2	3.8%
Streptococcus Viridans	11	20.8%
Beta Hemolytic Streptococcus B	1	1.9%
Streptococcus Anginosus	2	3.8%
Staphylococcus sp.	5	9.4%
Coagulase Negative Staphylococci	6	11.3%
Beta Hemolytic Staphylococcus Aureus	1	1.9%
Aerobic Gram Positive Rod	7	13.2%
Diphtheroids	7	13.2%
Aerobic Gram Negative Cocci	3	5.7%
Neisseria	2	3.8%
Moraxella Caterrhalis	1	1.9%
Aerobic Gram Negative Rod	2	3.8%
Hemophilus sp.	2	3.8%
Anaerobic Gram Positive Cocci	11	20.8%
Peptpstreptococcus	1	1.9%
Anaerobic Gram Positive Cocci	8	15.1%
Eggerthella lenta	1	1.9%
Peptoniphilus asaccharolyticus	1	1.9%
Anaerobic Gram Positive Rod	12	22.6%
Bacillus sp.	1	1.9%

Anaerobic Non Spore Forming Gram Positive Bacilli	11	20.8%
Anaerobic Gram Negative Cocci	3	5.7%
Anaerobic gram negative cocci	1	1.9%
Veillonella sp.	2	3.8%
Anaerobic Gram Negative Rod	38	71.7%
Prevotella Intermedia	9	17.0%
Prevotella diseans	1	1.9%
Prevotella buccae	2	3.8%
Prevotella Oralis	12	22.6%
Anaerobic Gram Negative Rods	9	17.0%
Bacteroides Fragalis	3	5.7%
Fusobacterium	2	3.8%
Yeast	3	5.7%
Yeast Like	2	3.8%
Candida Glabrata	1	1.9%