Original Article

Microbiota of Dental Abscess and their Susceptibility to Empirical Antibiotic Therapy

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Abstract

Context: Resistant pathogens to purulent odontogenic infections have evolved due to misuse of antibiotics. Hence, it is important to use a suitable antibacterial agent. **Aim:** This study aimed to identify the common bacterial species causing odontogenic infections and to determine their antibiotic susceptibility profile to amoxicillin, amoxicillin and clavulanic acid, azithromycin, and linezolid. **Settings and Design:** This was an *in vitro* cross-sectional study. **Material and Methods:** Fifty pus samples from odontogenic abscess were cultured and antibiotic susceptibility tests were performed as per the standard microbiological procedures. **Statistical Analysis Used:** Binomial test and Pearson's Chi-square test were used for statistical analysis. **Results:** Out of the 50 samples cultured, 30 samples showed growth. The distribution of growth among the 30 samples was Gram-positive cocci (n = 23, 67.65%) and Gram-negative bacilli (n = 11, 32.35%). Gram-positive isolates that were grown were *Enterococcus faecalis* (38.24%) followed by *Staphylococcus aureus* (29.41%) and Gram-negative bacilli that were isolated were *Klebsiella pneumoniae* (14.71%), *Pseudomonas aeruginosa* (8.82%), *Escherichia coli* (5.88%), and *Enterobacter* (2.94%). *Enterococcus* isolates were highly susceptible to amoxicillin (76.92%). An increase in the zone of inhibition to amoxicillin–clavulanic acid was appreciated more for *Staphylococcus* (50%) than *Enterococcus* (30.76%). *Enterococcus* and *Staphylococcus* showed high susceptibility of 92.31% and 90% to linezolid, respectively. *E. coli* and *Enterobacter* were 100% susceptible to amoxicillin. All the Gram-negative bacteria except for *P. aeruginosa* were 100% highly susceptible to amoxicillin–clavulanic acid. **Conclusions:** Culture-guided antibiotic prescriptions are necessary to prevent the emergence of antibiotic-resistant bacteria.

Keywords: *Antibiotic sensitivity, culture, dental abscess, disk-diffusion method*

Introduction

Dental abscesses are polymicrobial infections, consisting of aerobes, facultative and obligate anaerobes.[1] In recent times, drug resistance of genetic and acquired nature among the aerobes and facultative anaerobes is increasing due to indiscriminate use of over-the-counter drugs, thereby making treatment difficult.[2] Studies have shown that isolated bacterial pathogens showed resistance to commonly prescribed drugs such as ampicillin, amoxicillin + clavulanic acid.[3] Hence antibiotic therapy with culture-guided prescriptions is necessary. Due to the questionable response of the pathogens to the empirical drugs due to the increase in the incidence of resistance, antibiotic therapy without culture-guided prescriptions may or may not produce good outcomes which might lead to life-threatening situations in certain instances.[4] For a clinician considering antibiotic therapy, data on bacterial etiology and pathogen susceptibility are important. Acquiring such information, though, may take several days or even longer. Recent data on microbiota for purulent odontogenic infections are lacking despite the high frequency of clinical cases. A rational approach to empirical antibiotic selection based on scientifically sound and current experience with the continuously evolving flora of orofacial infections is required.[5] Thus, this study aims to identify the bacterial profile of odontogenic infections (mostly facultative anaerobes and aerobes) and to screen for their respective antibiotic susceptibility profile, as an initiative to avoid the emergence of antibiotic resistance and also to identify the suitable antibiotic for the management of odontogenic infections.

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Material and Methods

This is a prospective, cross-sectional *in vitro* study performed on fifty pus samples collected from 50 patients with odontogenic abscess (26 males [52%] and 24 females [48%]) aged between 5 and 75 years. Through a literature survey and pilot study, it was observed that nearly 3% of patients had purulent discharge from odontogenic infections. Assuming the margin of error as 5%, with an α level of 0.05, the sample size was calculated using the formula:

$n = p \times q \times (1.96 \div d)^2$ where $P = 0.03$, $q = 1 - P = 0.97$; $d = 0.05$ and $Z_\alpha = 1.96$

(Z_α is standard normal value with 95% confidence interval for $\alpha = 0.05$)

Thus, the minimum sample size required was 45. Considering 10% attrition rate, 50 samples were selected using a systematic random sampling method over a period of 4 months. In this prospective study, patients with pus discharge from various odontogenic infections such as periapical abscess ($n = 26$), periodontal abscess ($n = 20$), and pericoronal abscess ($n = 4$) were enrolled from the outpatient department of oral medicine and radiology with appropriate consent. Patients who were on antibiotic therapy either at the time of the study (or) in the recent past were excluded from the study. The study protocol was approved by the Institutional Ethics Committee (SBDCH/IEC/04/2019/4, dt. 05/06/2019). The study followed all principles of the Helsinki Declaration 2013. Written informed consent was obtained from all the study subjects before sample collection. Sample collection was done intraorally by isolating the area of the swelling in relation to the offending tooth by cotton rolls and suction for periapical and periodontal abscess. For pericoronal infections, the plaque was removed from the partially erupted tooth by cotton swabs and it was isolated accordingly. In periapical abscess, the corresponding X-rays showed ill-defined radiolucency in the apex of the offending tooth. For periodontal abscess, there was bone loss found with radiolucency around the tooth root in the corresponding X-rays. Then, the pus was aspirated using a sterile syringe/collected using two sterile cotton swabs from the pyogenic orifice. It was transported immediately to the microbiology laboratory in a sealed sterile container and was processed as per the standard microbiological procedures.

One cotton swab was used for Gram staining and the other swab was used for bacterial culture. Pus samples were inoculated on sterile blood agar (5% sheep blood) and MacConkey agar plates. The inoculated blood agar plates were incubated in a candle jar and the MacConkey agar plates were incubated aerobically at 37°C overnight in the bacteriological incubator and examined for bacterial growth. Then, the bacteria were identified to the genus level. After identification, antibiotic susceptibility testing was performed using the Kirby–Bauer Disk diffusion method as per the Clinical and Laboratory Standards Institute (CLSI) guidelines, 2019. Briefly, lawn culture of the test organism was made on separate Muller–Hinton agar plate using ethylene oxide-sterilized cotton swabs (HiMedia Laboratories Pvt Ltd., Mumbai, India). Then, the antibiotic disks, amoxicillin (20 μg), amoxicillin–clavulanic acid (20/10 μg), linezolid (30 μg), and azithromycin (15 μg) were placed and the plates were incubated aerobically at 37°C overnight. The diameter of the zones of inhibition around the antibiotic disks was measured and recorded. *Staphylococcus aureus* ATCC 25923, *Escherichia coli* ATCC 25922, and *Enterococcus faecalis* ATCC 29212 were used as Quality control strains.

Statistical analysis

A Microsoft Excel spreadsheet was used for data entry such as sample number, age, gender, presence of growth, species, and antibiotic sensitivity to amoxicillin, amoxicillin plus clavulanic acid, azithromycin, and linezolid. Statistical calculation was performed on IBM SPSS software (Version 24) (Armonk, NY: IBM Corp, Released 2016). Bacterial profile in each type of abscess, sensitivity of Gram-positive Cocci, and Gram-negative bacilli to empirical antibiotic therapy were evaluated using the binomial test and Pearson's Chi-square test.

Results

Among the 50 samples, 30 samples belonging to 18 males and 12 females showed growth. Among the 30 samples, 17 (56.67%) were periapical abscess, 10 (33.33%) were periodontal abscess, and 3 (10%) were pericoronal abscess. Thirty-four isolates of bacterial pathogens were obtained from the 30 samples. Twenty-six had monoculture (1 isolate per sample) and 4 had mixed bacterial growth (2 isolates per sample). Among the 34 bacterial isolates, Gram-positive cocci (67.65%) were the most frequently isolated organism than Gram-negative bacilli (32.35%) [Figure 1]. The growth observed was predominantly of Gram-positive cocci such as *E. faecalis* (38.24%) followed by *S. aureus* (29.41%) and Gram-negative bacilli such as *Klebsiella pneumoniae* (14.71%), *Pseudomonas aeruginosa* (8.82%), *E. coli* (5.88%), and *Enterobacter* (2.94%) [Figure 1]. Among the 17 samples from periapical abscess, 7 (35%) *E. faecalis*, 7 (35%) *S. aureus*, 2 (10%) *K. pneumoniae*, 2 (10%) *P. aeruginosa*, 1 (5%) *E. coli* and 1 (5%) *Enterobacter* were isolated. Aerobes and facultative anaerobes were more frequently isolated in periapical abscess than any other dental abscesses. Among the 10 samples from periodontal abscess, 6 (54.55%) *E. faecalis*, 2 (18.18%) *S. aureus*, 2 (18.8%) *K. pneumoniae*, and 1 (9.09%) *P. aeruginosa* were isolated. Among the three samples from pericoronal abscess,

1 (33.33%) *S. aureus*, 1 (33.33%) *K. pneumoniae*, and 1 (33.33%) *E. coli* were isolated. *S. aureus* and *Klebsiella Pneumonia* were the most frequent facultative anaerobes found among all types of abscess [Figure 2]. The predominant isolates from various samples were tested for antibiotic susceptibility. The same type of species isolated from various samples yielded different antibiotic susceptibility results. Among the 13 *E. faecalis* isolates, majority of the isolates 12/13 (92.31%) were susceptible to linezolid (P = 0.003) compared to amoxicillin 10/13 (76.92%) (P = 0.092) and azithromycin 6/13 (46.2%). According to this study, linezolid would be an effective antibiotic in the treatment of dental abscess caused by *Enterococci* [Table 1]. Among the 10 *S. aureus* isolates, one isolate was found to be resistant to all the antibiotics tested. Majority of the *Staphylococcus* isolates 9/10 (90%) (P = 0.021) were susceptible to linezolid compared to amoxicillin 8/10 (80%) (P = 0.109) and azithromycin 5/10 (50%) [Table 2]. Since no interpretation criteria by CLSI and European Committee on Antimicrobial Susceptibility Testing (EUCAST) guidelines are available for amoxicillin–clavulanic acid for *Staphylococcus* and *Enterococcus* by disk-diffusion method, no interpretations were recorded. However, on the addition of clavulanic acid to amoxicillin, increased zone of inhibition was seen in 4/13 (30.76%) of the *Enterococci* isolates and 5/10 (50%) of the *Staphylococcus* isolates. Antibiotic sensitivities for *E. faecalis* and *S. aureus* to empirical antibiotic therapy are tabulated in Tables 1 and 2. Among the Gram-negative bacilli isolates (Enterobacteriaceae), all the *K. pneumoniae* isolates were 100% resistant to amoxicillin compared to *E. coli* and *Enterobacter* which were 100% susceptible to amoxicillin [Table 3]. All the *K. pneumoniae* isolates were β-lactamase producers, which were judged by the increment in the zone of inhibition when clavulanate was combined with amoxicillin. Therefore, amoxicillin–clavulanic acid would be effective against β-lactamase producing *Klebsiella* species according to this study. Since no zone of inhibition was observed in all *P. aeruginosa* isolates to amoxicillin, it was considered to be 100% resistant. 1/3 (33.33%) isolate showed intermediate sensitivity to amoxicillin and clavulanic acid and 2/3 (66.67%) were resistant to amoxicillin and clavulanic acid (P = 1.000) [Table 4]. Antibiotic susceptibility patterns of the *K. pneumoniae, E. coli*, *Enterobacter,* and *P. aeruginosa* to empirical antibiotic therapy are tabulated in Tables 3 and 4.

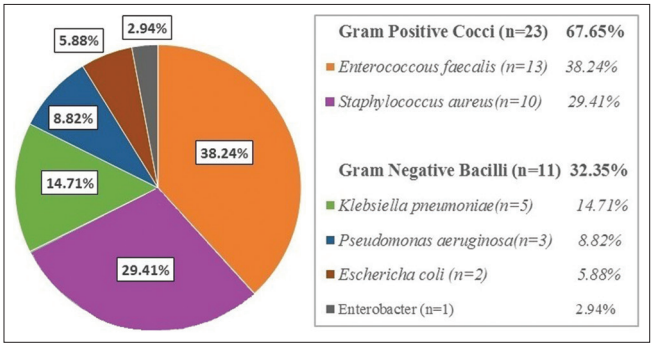

Figure 1: Distribution of the isolated bacteria

Discussion

Despite the increased incidence of odontogenic infections, there is a paucity of data on the bacteriological profile and the antimicrobial resistance pattern of the isolates. Such data are a prerequisite for the development of clinical recommendations and guidelines on the antibiotic prescribing practices to be adopted by dentists for the therapeutic management of odontogenic infections. In this study, the specimens were analyzed for facultative anaerobes and aerobes. This was done to elicit if there was any variation from the species reported in the previous studies. Among the isolated pathogens, Gram-positive bacteria dominate the Gram-negative bacteria in the present study [Figure 1] which is consistent with the previous report by Brescó-Salinas *et al*.[6] in 2006. In this study, *E. faecalis* was the most predominant organism isolated

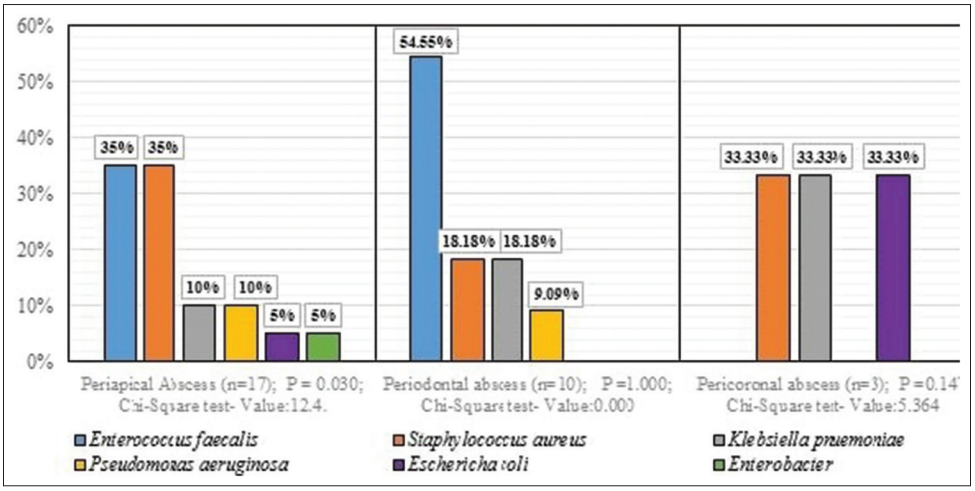

Figure 2:Distribution of bacteria according to the type of abscess

Table 1: Sensitivity of Gram-positive bacteria - *Enterococcus faecalis* - to empirical antibiotic therapy

Antibiotics	Susceptibility pattern	Species	One-sample binomial test
		Enterococcus faecalis (*n*=13), *n* (%)	*P*
Amoxicillin	Sensitive	10 (76.92)	0.092
	Resistant	3 (23.08)	
Azithromycin	Sensitive	6 (46.15)	Sensitive versus intermediate: 0.125
	Intermediate	1 (7.69)	Sensitive versus resistant: 1.000
	Resistant	6 (46.15)	Intermediate versus resistant: 0.125
Linezolid	Sensitive	12 (92.31)	0.003
	Resistant	1 (7.69)	

Table 2: Sensitivity of Gram-positive bacteria-*Staphylococcus aureus* to empirical antibiotic therapy

Antibiotics	Susceptibility pattern	Species	One-sample binomial test
		Staphylococcus aureus (*n*=10), *n* (%)	*P*
Amoxicillin	Sensitive	2 (20.00)	0.109
	Resistant	8 (80.00)	
Azithromycin	Sensitive	5 (50.00)	Sensitive versus intermediate: 0.453
	Intermediate	2 (20.00)	Sensitive versus resistant: 0.727
	Resistant	3 (30.00)	Intermediate versus. resistant: 1.000
Linezolid	Sensitive	9 (90.00)	0.021
	Resistant	1 (10.00)	

Table 3: Sensitivity of Gram-negative bacteria - *Klebsiella pneumoniae, Escherichia coli*, and *Enterobacter* - to empirical antibiotic therapy

Antibiotics	Susceptibility pattern	Species		
		Klebsiella pneumoniae (*n*=5), *n* (%)	*Escherichia coli* (*n*=2), *n* (%)	*Enterobacter spp.* (*n*=1), *n* (%)
Amoxicillin	Sensitive	0	2 (100.00)	1 (100.00)
	Resistant	5 (100.00)	0	0
Amoxicillin+clavulanic	Sensitive	5 (100.00)	2 (100.00)	1 (100.00)
	Intermediate	0	0	0
	Resistant	0	0	0
Azithromycin	Sensitive	3 (60.00)	2 (100.00)	1 (100.00)
	Intermediate	0	0	0
	Resistant	2 (40.00)	0	0

Table 4: Sensitivity of Gram-negative bacteria - *Pseudomonas aeruginosa* - to empirical antibiotic therapy

Antibiotics	Susceptibility pattern	Species	One-sample binomial test
		Pseudomonas aeruginosa (*n*=3), *n* (%)	*P*
Amoxicillin	Sensitive	0	-
	Resistant	3 (100.00)	
Amoxicillin+clavulanic	Sensitive	0	1.000
	Intermediate	1 (33.33)	
	Resistant	2 (66.67)	

which is similar to the study by Brescó-Salinas *et al*.[6] in 2006 where *E. faecalis* and *Streptococcus species* were the predominant facultative anaerobes isolated. In the present study, the species differed slightly among all the type of abscesses and also aerobes and facultative aerobes were more frequently isolated in periapical abscesses. These results were similar to the study by Kuriyama *et al*.[7] in 2000. Periapical abscess was the most common abscess in this study. This is similar to the study done by Kuriyama *et al*.[7] in 2000 where the periapical abscess was 78%, then periodontal abscess 15% and pericoronal abscess 11%. In the present study, the predominant

organisms isolated from periapical abscess were both *E. faecalis* (35%) and *S. aureus* (35%) [Figure 2]. This is in accordance to the study done by Brescó-Salinas *et al*.[6] in 2006 where *E. faecalis* (19.2%) was the most predominant organism isolated from periapical infections among the facultative anaerobes.

Previous reports suggest that unnecessary antibiotic prescriptions significantly contribute to the development of antibiotic resistance. Furthermore, antibiotic prophylaxis (potential overuse of antibiotics) is hardly ever addressed in dentistry. Hence, periodic surveillance for antibiotic resistance, education on antibiotic stewardship, routine audit, and feedback could be an intervention in hospital dental care and outpatient dental settings.[8] Brescó-Salinas *et al*.[6] in 2006 had 91.4%, 34.2%, 91.4% of susceptibility of *E. faecalis* for amoxicillin, azithromycin, and linezolid, respectively, which is in accordance with this study [Table 1]. *S. aureus* was 37% sensitive to amoxicillin, according to Mahalle *et al*.[9] in 2014, 76.95% were sensitive to Azithromycin, according to Jagadish Chandra *et al*.[10] in 2017 and 60% sensitivity for linezolid, according to Jindal *et al*.[11] 2019 respectively. These studies are in accordance to this study [Table 2]. *K. pneumoniae* was 36.4% sensitive to amoxicillin according to Shah *et al*.[12] in 2016 and 31.25% sensitive to azithromycin according to Al-Mehedi *et al*.[13] in 2015 which was contrary to the present study. It was 100% sensitive to amoxicillin clavulanate in the study conducted by Mahalle *et al*.[9] in 2014 which is similar to the present study [Table 3]. For *E. coli*, according to Jagadish Chandra *et al*.[10] in 2017, it is 100% sensitive to amoxicillin and according to Mahalle *et al*.[9] in 2014, it is 100% sensitive to amoxicillin clavulanate. These studies are similar to this study. According to Al-Mehedi *et al*.[13] in 2015, it is 0% sensitive to azithromycin. This study is contrary to the present study [Table 3]. For Enterobacter species, according to Abdulla *et al*.[14] in 2009, it is 0% sensitive to amoxicillin, according to Prakash *et al*.[15] in 2016, it is 0% sensitive to amoxicillin clavulanate. These studies are similar to this study. According to Jagadish Chandra *et al*.[10] in 2017, it is 100% sensitive to azithromycin. This study is contrary to the present study [Table 3]. According to Shah *et al*.[12] in 2016, the aerobe *P. aeruginosa* was 0% sensitive to amoxicillin which is similar to the present study and amoxicillin clavulanate was 0% sensitive which was contrary to the present study [Table 4]. Amoxicillin and amoxicillin–clavulanic acid are the empirical drugs used for facultative anaerobes and aerobes. Erythromycin or azithromycin are used when patients are allergic to the penicillin group of antibiotics.[16-18] Metronidazole is excellent for acute infections and obligate anaerobes developing resistance against it are rare.[19] Hence in the present study, only the facultative anaerobes and aerobes are isolated and screened for sensitivity to amoxicillin, amoxicillin–clavulanic acid, and azithromycin. Linezolid, an oxazolidinone, a recent reserve drug, is used against multidrug-resistant Gram-positive organisms. Hence, linezolid was also tested along with the commonly prescribed drugs.[20] Linezolid is not recommended for Gram-negative bacteria and no interpretation criteria were provided by both CLSI and EUCAST guidelines. In case of *E. coli* and *Enterobacter* which were 100% susceptible to amoxicillin, prescribing amoxicillin and clavulanic acid is not required as they would result in the emergence of drug-resistant strains. Since piperacillin–tazobactam is a suitable drug for *Pseudomonas* species,[21] culture and antibiotic susceptibility tests for piperacillin–tazobactam are required before prescribing the same. Recent reports showed that there is an emergence of beta-lactamase-producing *K. pneumoniae*[22] which were similar to this study results. Teoh *et al*.[23] in 2021 concluded in their systematic review of eight studies that there are no ideal antibiotic regimens for treating orofacial infections. They also stated that broad-spectrum antibiotics ought not to be prescribed as narrow-spectrum antibiotics also offer effective results for otherwise healthy people. Thus in concurrence with Teoh *et al*.,[23] the results of our study suggest that the antibiotic resistance pattern of the patient's dental microbiota needs to be evaluated for effective antibiotic therapy and to reduce the development of resistance. Antibiotic-resistant bacterial strains that are associated with dental and oral-maxillofacial infections are a significant cause of mortality and morbidity worldwide and are a cause of severe health concern.[24-26] Hence, patient education and awareness about the proper use of antibiotics should be made known to the general public to avoid misuse of antibiotics such as over-the-counter drugs and self-medications.

Limitations

Of the 50 samples, only 30 samples showed growth. This could be because of patients who did not reveal the intake of over-the-counter antibiotics before sample collection. Nonbeta-lactamase-producing *Enterococci* susceptible to ampicillin were predictively assumed to be susceptible to amoxicillin-clavulanate as CLSI does not give interpretative criteria for the same.

Future research directions

Continued research pertaining to orofacial infection of odontogenic origin with larger sample size is needed periodically as different bacterial strains emerge and the bacterial resistance to various antibiotics may vary from time to time. Advanced, rapid, feasible, cost-effective, less tedious, and less technique sensitive laboratory procedures to process and to identity the bacterial strains and their sensitivity to antibiotics are required to combat emerging resistant strains.

Conclusions

This study reveals that culture-guided antibiotic prescriptions are necessary to prevent the emergence of

microbial resistance to antibiotics, thus preventing the spread of antibiotic-resistant bacterial species.

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Conflicts of interest

There are no conflicts of interest.

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