Evaluation of microbial culture and antibiogram in patients with head and neck infections who referred to Shahid Rajaee Hospital of Shiraz between 1392 to 1398.

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**Background:** Head and neck infections happen due to different reasons and different microorganisms are responsible for them. These infections can be treated with various antibiotics. The purpose of this study was to specify most frequent etiology of infection, dominant bacterial species and most effective antibiotic in patients with head and neck infections who referred to Shahid Rajaee hospital of Shiraz.

**Methods:** This study has been carried out in cross-sectional pattern from 2019-May to 2020-Oct in Oral & Maxillofacial Ward of Rajaee Hospital of Shiraz. Consent to access data and archive files was taken from the ethics committee of Shiraz University of Medical Sciences. Age, sex, etiology of infection, bacterial species, sensitivity or resistance reaction to Antibiotics and most frequently used antibiotic in patients who referred to this ward between 1392-Apr to 1398-Mar were collected on the basis of laboratory’s results. Data were analyzed with Chi-Square test.

**Results:** statistical analysis showed that, 56 of patients were men (54.9%) and 46 were women (45.1%). The average of age was 38+/−17 and the minimum age was 6 and maximum age was 73. The most frequent etiology was odontogenic infections. Moreover, there was no statistically significant relationship between etiology and bacterial species (p-value=0.38) and Cefazolin had the most frequency in odontogenic infection group. Top three frequent bacterial species were respectively: Staphylococcus DNase & Coagulase Negative, Enterococci Sp., Streptococci Viridians and Klebsiella Sp. There was no statistically significant relationship between bacterial species and sex (p-value=0.55). 94 (48.7 %) of bacterial species had Sensitive reaction to antibiotics. 21 (10.9 %) of them had Intermediate reaction
and 78 (40%) of them had Resistant reaction and Cefazolin had the most frequency in sensitive group.

**Conclusion:** The dominant bacterial species in head and neck infections are Staphylococcus DNase & coagulase negative. And, Cefazolin had the most sensitive reaction in odontogenic infections.

**Key words:** head and neck infection, etiology, antibiogram, antibiotic
Introduction

Daily many patients with head and neck infections refer to health care centers and have to be hospitalized. Among head and neck infections odontogenic origin has been recognized as the major reason. These infections can propagate to surrounding areas and cause severe complications like deep neck infections, tissue necrosis, sepsis, endocarditis, mediastinitis and compromised air way. All of these complications can be life-threatening and should be treated as soon as possible by antibiotics or surgical interventions. There are some other causes responsible for head and neck infections which includes salivary gland infection, traumas, superimposed infections on pathologic lesions, foreign bodies, iatrogenic factors such as dental procedure or a prior surgery, neoplasm and etc. [1].

Odontogenic infections can be simple as periapical abscess or be dangerous like superficial space and deep neck infections. They can primary cause systemic toxicity and then advanced complications such as arterial erosion, meningitis, extra cranial or intracranial infection and etc. Immunodeficiency, diabetes, obesity, long-term alcohol abuse, hepatitis, cirrhosis, radio and chemo therapy, SLE and immunosuppression are medical conditions which may exacerbate those infections [2]. Major salivary glands (parotid, submandibular and sublingual) can commonly get infected due to obstructive disease. This situation is specially seen in submandibular gland because of its specific anatomy. These infections, if left untreated, may progress and develop respiratory obstruction, septicemia and death [3]. Traumas which are left untreated or those which are treated and then followed by hard plate failure and dehiscence can get infected again. Infections following a traumatic injury maintains as a major problem, despite various progression in management of trauma patients. Local infections at the site of injury are another reasons responsible for head and neck infections. Intraorally open mandibular fracture, as an example, can bring advanced complications like Ludwig’s angina and Necrotizing fasciitis. As another reason, jaw fractures can cause osteomyelitis and subsequently teeth and bone structure loss. Moreover, most fractures are compounds in nature and risk of osteomyelitis is significant. Due to aggressive manner of pathological lesions, they can propagate and invade nasal and oral spaces which may result in structural destruction. Also, in reconstruction of those lesions by grafts, e.g. reconstruction of resected tumors and cysts, infection of graft site is probable [4].
Propagation of primary facial spaces’ infection to secondary and deep facial spaces is related with morbidity and sometimes mortality. This situation can cause airway compromise which is the most common life-threatening complication seen in patients with head and neck infections. At the end, these infections can propagate downward and bring about mediastinitis and precarditis or upward and develop cerebral abscess, cavernous sinus thrombosis and meningitis [5,6].

Head and neck infections due to above reasons can be potentially life-threatening. Studies have been carried on causative microorganisms responsible for head and neck infections. Moreover, their sensitivity and resistance toward various Antibiotics have been analyzed. As a routine procedure pus samples are taken from patients and sent to laboratory for microorganisms’ culture, Antibiogram and Gram staining. Results of these tests usually take 48 to 72 hours to be prepared. Moreover, due to inaccessibility to some deep spaces there is no possibility to pus sampling. Thus, patients are treated with empirical antibiotics. On the basis of studies, these empirical antibiotics vary from time to time and place to place. So that, we decided to perform this research in Rajaee Hospital of Shiraz to have the most efficient and practical intervention in the least period of time.

Materials

In this cross-sectional study, recorded data of 216 patients with head & neck infections who referred to Rajaee Hospital of Shiraz was taken from archives and investigated in a three-month-period. Consent to access data and archive files was taken from the ethics committee of Shiraz University of Medical Sciences. Sampling method was census. Inclusion criteria were patients with head and neck infections who referred to Rajaee hospital and exclusion criteria were patients with incomplete archive data, patients whose laboratory results had to be rechecked and patients with immunodeficiency problems.

Methods
The variables were age, sex, etiology of infection, bacterial species, reaction to antibiotics and the name of antibiotic. These variables were collected as a table for each individual.

For analysis, each patient with one pus sample had a code numbered from 1 to 216. Age, sex, etiology of infection and bacterial species of everyone were added. Then, as whether having antibiogram results or not, sensitive reaction and relevant antibiotics, intermediate reaction and relevant antibiotics and resistant reaction and relevant antibiotics were noted. 102 patients had antibiogram test in their data and were included in the study and the rest of them were excluded.

In this research, we intended to specify the age and sex which these infections mostly happen. Moreover, we aimed to determine the etiology which is mostly relevant to head and neck infections in our zone. So that, as regards to the etiologies written in patients’ files, we categorized them as: 1. odontogenic infections 2. trauma 3. pathologic lesions (e.g. OKC, Osteomyelitis, SCC and etc.) 4. dental procedures (i.e. head & neck infections due to a prior dental procedure) 5. post operations (i.e. head & neck infections due to head & neck surgeries like orthognatic surgeries, enucleation and resection of lesions, cosmetics surgery and etc.). Another purpose was to identify dominant bacterial species in these infections. We intended to realize there is a significant relationship between bacterial species and sex or not. Likewise, we intended to realize there is a significant relationship between etiology and bacterial species or not. And, there is a significant relation between etiology and antibiotics or not.

Statistical analysis was done by IBM SPSS statistics software version 24. For describing samples, descriptive statistics (mean, maximum, minimum and standard deviation) and analytic statistics (frequency, percent, valid percent and cumulative percent) was used.
Results

From 102 patients who had antibiogram results 56 of them were men (54.9%) and 46 were women (45.1%). The average of age was 17±38. The minimum age was 6 and maximum age was 73 (table 4-3,4-4 and figure 4-1). The most frequent etiology was odontogenic infections with 57.8 percent and the least frequent was post operation with 2.9 percent (table 4-5 and figure 4-2). For studying the relation between etiology and bacterial species, Chi-Square test was used and indicated that there is no statistically significant relationship between them (p-value=0.38) (table 4-6). Studying frequency of used antibiotic according to etiology indicated that, Cefazolin had the most frequency in odontogenic infection group; Vancomycin had the most frequency in trauma group; Amikacin had the most frequency in pathologic lesions group; Cefazolin had the most frequency in dental procedure group and Gentamycin had the most frequency in post operation group (table 4-7 and figure 4-3). Top three frequent bacterial species were respectively: Staphylococcus DNase & Coagulase Negative, Enterococci Sp., Streptococci Viridians and Klebsiella Sp. . And, the least frequent bacterial species was Serratia Sp. And Citrobacter Sp. (table 4-8 and figure 4-4). For studying relation between bacterial species and sex, Chi-Square test was used and showed that there is no statistically significant relationship between them (p-value=0.55) (table 4-9). On the basis of results, 94 (48.7 %) of bacterial species had Sensitive reaction to antibiotics. 21 (10.9 %) of them had Intermediate reaction and 78 (40%) of them had Resistant reaction (table 4-10 and figure 4-5). Frequency of antibiotics according to types of reactions indicated that, Cefazolin had the most frequency in sensitive group. Doxycyclin had the most frequency in intermediate group. And, Erythromycin had the most frequency in resistant group (table 4-11 and figure 4-6).

Discussion

Sex: In study by N. S. Fating et al in 2014, male patients were more commonly involved than female patients and male to female ratio was 1.17:1 [7]. In another study by Amit Shah et al in 2020, of the 100 patients evaluated in the study, 78% were men and 22% were women [8]. Xiaodong Han et al in 2016 indicated male dominancy (male-to-female ratio, 1.44/1) [9]. In our study, number of male patients was more than female patients (men 54.9% and women 45.1%) which is similar to other studies. This can be an evidence that women tend to have better oral health and
seek oral healthcare more frequently than men. Moreover, it may be attributed to tobacco usage being more common in male than female and few studies have showed that the predominance in males is due to the connective tissue strength [10].

**Age:** The study which was done by Neelam Shkya et al in 2018 represented that, the most commonly involved age group was 21–30 years (29%) followed by 31–40 years (28%) [11]. In another study by Manu Wilfred et al in 2019, the mean age of patients was 38 (range 1-67years). The oldest patient was 67 years and youngest was 2-year-old child [12]. The mean age in study by N. S. Fating et al in 2007 was 34.13 years [13]. Shaili Priyamvada et al in 2019 showed that, the range of age was from 3 months to 72 years with mean age of 24.6 years [14]. In another study by, H. Dolezalova et al in 2015, the mean patient age and the median were 39.8 years and 36 years, respectively. The youngest patient was aged 4, the oldest patient 91 [15]. In our study, minimum age, maximum age and mean age were respectively, 6, 73 and 38.18. This average of age is similar to other studies to some extent.

**Etiology:** In study by J. Velhonoja et al in 2020, odontogenic infection was the most common reason for deep neck infections in 124 (44.8%) of the cases. Twenty (16.1% of the odontogenic) patients had dental surgery previously. The second etiology was of a pharyngeal or tonsillar origin 104 (37.5%). The other sources were lymphadenitis in 12 (4.3%) and sialadenitis, neoplasm, infected cyst accounting for four cases (1.4%) each. Two (0.7%) penetrating trauma to the cervical region, an autogenic infection (0.4%), a foreign body (0.4%) and a post-operative infection (0.4%) were identified. The origin of the infection was not determined in 20 (7.2%) cases [16]. The results of study by Xiaodong Han et al in 2016 showed that, the most common cause was odontogenic infection (73 patients, 57.5%), followed by parotitis (6 patients, 4.7%), cyst in jaw (6 patients, 4.7%), and cyst in branchial cleft (5 patients, 3.9%) [9]. In another study by J. Kyoo et al, the most common origin of deep neck infections was odontogenic (19 cases, 12.0%) and previous neck cysts (10 cases, 6.3%) [17]. Another study by G. Kataria et al in 2015 showed that, the most frequent etiological factor was odontogenic infection (26 patients, 34.21%) followed by tonsillopharyngitis (21 patients, 27.63%) and it was unknown in seven patients (9.21%) [18]. Study by D. Almutairi et al indicated, odontogenic was the most common, in 78 patients (42.6%), tonsillopharyngitis was observed in 49 patients (26.8%), 26 patients (14.2%) had infected cysts, and 13 patients (7.1%) had an unknown etiology. Salivary gland infections were seen in eight patients (4.4%),
seven patients (3.9%) had tuberculous lymphadenopathy, and the mandibular fracture was noted in two patients (1%) [19]. S. Jayagandhi et al in 2019 indicated that, 20–50% of deep neck infections have idiopathic etiology. Most common cause of infection is of dental origin followed by ear and tuberculosis [10]. In another study by T. P. Brito in 2017, bacterial tonsillitis was the most common cause of deep neck infections (32 patients, 31.68%), followed by odontogenic infection (24 patients, 23.7%) [20]. In our study, etiologies were divided to five categories. The frequency of them was respectively: First, odontogenic infections (57.8%), which was infection originally initiated from tooth and propagated to other spaces and caused subsequent complications. Second, pathologic lesions (18.6%) which was head and neck infections due to primer lesions like: Osteomyelitis, OKC, SCC, Ameloblastoma and etc. Since these lesions have invading and destructive manner, they can penetrate adjacent structures and cause subsequent complications. Third, dental procedures (16.7%) i.e. infections which were originated from a primer dental procedures like: Root Canal Therapy, Extraction of teeth especially molars, Scaling and Root Planning, Injection of local anesthesia and etc. Forth, traumas (3.9%) which was infection due to car accident, gun shot and falling down. And the last one, post operations (2.9%) i.e. infections due to primer head and neck surgeries like: Orthognatic surgeries, Nose jobs, Enucleation and Resection of lesions and etc. Contemporary literature on deep neck infections has consistently described odontogenic infections as the major cause. This may be due to delay of treatment caused by the relatively high cost of dental health, low socioeconomic status and poor oral hygiene [17,21,22,23]. Results of our study showed that there is no relation between etiology and bacterial species. Moreover, it showed that, Cefazolin had the most frequency in odontogenic infections and dental procedures group, Vancomycin had the most frequency in trauma group. Amikacin had the most frequency in pathologic lesions group and Gentamycin had the most frequency in post operation group.

Microbiology: In study by N. S. Fating et al in 2014, Alpha hemolytic streptococci were found in 70 % among aerobes. Beta hemolytic streptococci were present in 10 % of the aerobes isolated. Streptococci were the most common aerobes isolated [7]. In another study by Amit Shah et al in 2016, aerobic Gram-positive was isolated from a total of 73% cases, whereas Gram-negative isolates were obtained from a total of 18% cases. Streptococcus viridans was the most common microbe isolated
followed by Staphylococcus aureus (16%) and Klebsiella pneumonia (11%). Coagulase negative Staphylococcus and Pseudomonas aeruginosa were isolated from six specimens each. Escherichia coli was isolated from 3% specimen while nine specimens were sterile. No anaerobe could be isolated from any of the specimen [24]. The study which was done by Neelam Shkya et al in 2018 represented that, streptococcus species was the most frequent, and viridians streptococci was the predominant isolated organism (n = 48) followed by Staphylococcus aureus organism (n = 20) and Enterococcus feacalis (n = 8) [11]. In a study by Manu Wilfred et al in 2017, the most common isolate in our study was enterococcus in 15 cases (37.5%), followed by staphylococcus aureus in 13 cases (32.8%). Coagulase negative staphylococci were cultured in 3 cases (7.5%) cases. Beta hemolytic streptococci were isolated in 3 cases (7.5%) cases. Acinetobacter baumani was isolated in 2 cases (5%) cases. Pseudomonas was isolated in 1 case (2.5%), klebsiella was isolated in 1 case (2.5%) and Enterobacter in 1 case (2.5%) [12]. In study by H. Jagadish Chandra et al, distribution showed the predominance of Enterobacteriaceae (41.5 %) followed by Staphylococcaceae (31.7 %), Streptococcaceae (14.6 %), Pseudomonadaceae (7.3 %) and Enterococcaceae (4.9 %) respectively (39). In our study, Staphylococcus DNase & Coagulase Negative (26 cases, 25.5%), Enterococci Sp. (15 cases, 14.7%), Streptococci Viridians and Klebsiella Sp. (13 cases, 12.7%) were most frequent respectively. And, the least frequent bacterial species was Serratia Sp. And Citrobacter Sp. (1 case, 1.0%) which is different from other studies. This disagreement can be due to geographical differences that can affect microbiological pattern [23,25]. And, it can be attributed to arbitrary usage of antibiotics which has changed antibiogram pattern. Moreover, our study showed that there is no relation between bacterial species and sex.

**Reaction to Antibiotics:** Each microorganism has a kind of reaction toward available antibiotics. These reactions can be sensitive, intermediate and resistant. Resistance can either be inherent or acquired by the processes of genetic mutation or gene transfer. The molecular biology of the antibiotic resistance can be mainly of the following four ways: (1) Alteration of drugs target site. (2) Inability of the drugs to reach its target. (3) Inactivation of the antimicrobial agents. (4) Active efflux of antibiotics from the cell [26]. In our study 48.7% of microorganisms had sensitive reaction toward antibiotics. 40.4% of them had resistant reaction and 10.9% of them
had intermediate reaction. This sensitive to resistant ratio shows the growing number of antibiotic resistance.

**Antibiotics:** In study by N. S. Fating et al in 2014, All the organisms were found sensitive to Clindamycin, Gentamycin and Linezolid. Most of the strains of aerobic organisms in this study were sensitive to Penicillin. Organisms were sensitive to Cephalosporin to a higher degree than to Penicillin. Penicillin G, Amoxicillin and Amox CV resistance was seen in 20% of aerobes, whereas Cefixime resistance was seen in 10% of aerobes. [7]. The study which was done by Neelam Shkya et al in 2018 represented that, Amoxicillin/clavulanic acid had excellent (100%) activity against all the aerobic isolates. Cefotaxime showed significant (91.18%) activity against the aerobic isolates. The activity of ciprofloxacin was good against aerobes, and the only organism that exhibited considerable resistance against ciprofloxacin was S. aureus (12.5%). The inactivity of metronidazole in aerobic isolates is a known fact [11]. In another study by Manu Wilfred et al in 2019, the most common isolate microorganism, enterococci were sensitive to amoxicillin, vancomycin, linezolid, teicoplanin and cefazolin. Enterococcal isolates were least sensitive to piperacillin tazobactam combination. All isolates of staph aureus were sensitive to linezolid. Least sensitivity was observed for trimethoprim sulphamethoxazole combination as in. Beta hemolytic streptococci were showing maximum sensitivity for vancomycin, linezolid, and teicoplanin. Out of the 3 total isolates of Coagulase negative streptococci, 2 isolates (67%) were sensitive to vancomycin and linezolid [12]. The study done by Ahtesham Ahmad et al in 2016, the antimicrobial agents which were most effective against microbiological flora in orofacial abscesses in this study were cephrotaxime (97%), doxycyclin (90%), ciprofloxacin (85%) and amoxicillin (77%). 67% of the total isolates shown resistance to penicillin [27]. Another study by H. Jagadish Chandra et al in 2017, the result showed that 58.6% of the isolates were resistant to gentamicin, followed 52.5% for ampicillin, 51.3% for piperacillin; least resistant being 18.9% for azithromycin. Among the isolates tested, 29.3% of the isolates acquired resistance to ceftazidime, 26.9% for ciprofloxacin, 24.3% for cefotaxime and 21.2% for tetracycline [28]. In our study we investigated antibiotic frequency according to types of reaction and the outcomes were: Cefazolin had the most sensitive reaction, Doxycyclin was the intermediate reaction and Erythromycin had the most resistant reaction. This difference against other studies can be related to microorganisms that differ from place to place and time to time.
Conclusion

Odontogenic infections have the most prevalence among head and neck infections. People in thirties specially males should have more attention toward their oral health to prevent subsequent infections. The dominant bacterial species in head and neck infections are Staphylococcus DNase & coagulase negative. And, Cefazolin had the most sensitive reaction in odontogenic infections.

Declaration

- This article has been confirmed by ethical code: IR.SUMS.DENTAL.REC.1399.161 in ethics committee of Shiraz University of Medical Sciences, Iran.
- The study protocol is performed in accordance with the relevant guidelines.
- Raw data are available in attachments.
- Authors have no interest of conflict.
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- First author: Dr. Farhad Ghorbani, assistant professor of Oral and Maxillofacial Surgery, Shiraz University of Medical Sciences. Second author and corresponding author: Dr. Zahra Faryabi, general dentist, Shiraz University of Medical Sciences.
- Shiraz University of Medical Sciences ethics committee, waived the need of informed consent.
- All data generated or analysed during this study are included in this published article [and its supplementary information files]. And its Excel file is uploaded in submission system.

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