

Antibiotic Prophylaxis for Implant Surgery in Nigeria: A Web Survey

*Ikimi NU, **Bello SA, ***Agboghoroma GO,
****Obagbemoro KO

Correspondence: Ikimi NU,
Email: ukuoghenenathan@gmail.com

*Dental and Maxillofacial Surgery Department,
State House Medical Centre, State House,
Abuja FCT.

**International Craniofacial Academy,
Gwarinpa, Abuja FCT

***Restorative Unit, National Hospital, Abuja FCT.

****Department of Restorative Dentistry,
Federal Medical Centre, Abeokuta Ogun State.

Key words: Antibiotic Prophylaxis, Dental Implant, Dental Surgeons.

ABSTRACT

Objectives: Bacterial contamination of dental implants during insertion is of serious concern to the Dentist as it poses significant risk to the success of the procedure. Consequently, routine use of antibiotic prophylaxis during dental implant surgery has been recommended. This study was designed to investigate the use of antibiotics prophylaxis for implant surgery among dentists in Nigeria to determine the preferred choice, and the dosage of antibiotics prophylaxis.

Materials and Methods: This was a cross-sectional study on the prescription of antibiotic prophylaxis for implant surgery among dental surgeons in Nigeria. Using Survey Monkey (By Momentive.ai. California, USA), a questionnaire investigating prescription pattern of antibiotic prophylaxis, choice of antibiotics, and dosage was posted electronically on the WhatsApp Group platforms of the Nigeria Dental Association (NDA) for a period of three months. Permission to carry out the survey among dental surgeons on the electronic platform was granted by the NDA. Data was analyzed with SPSS 25.0

statistics program (SPSS® Inc, Chicago, IL, USA) and statistical significance was set for $p \leq 0.05$.

Results: The completed forms were returned by 72 dental surgeons, and, among them, 56 dental surgeons prescribed antibiotic prophylaxis. Among these 56 respondents, 27 favored the administration of antibiotics prophylaxis 24 hours before surgery. Clindamycin was the preferred choice of antibiotics, at a 5-day dose of 150mg 6hourly x 5/7 (p -value=0.044), and Amoxicillin was the second choice of antibiotic prophylaxis at 500mg 8hourly x 5/7.

Conclusion: The result from this study suggests that most of the respondents were using antibiotic prophylaxis in dental implants surgery, and Clindamycin for a 5-day period, beginning 24 hours before surgery, was the preferred choice.

INTRODUCTION

Tooth loss could be distressing for most patients, especially since this leads to a loss of function including occlusal balance, poor masticatory and speech functions, including unsatisfactory esthetics as well as reduced psychosocial wellbeing.¹⁻³ It, therefore, becomes imperative that the missing tooth/teeth is replaced to maintain occlusal and masticatory functions, improve esthetics, and restore confidence.² Removable partial dentures, fixed partial dentures, and complete dentures have been used over the years to replace missing tooth/teeth but none has been more comfortable and acceptable like dental implants, especially when cost is not an issue.² Research has shown improved psychosocial well-being and patient satisfaction following implant therapy.³ Additionally, the use of dental implants has recorded long-term success rates in patients with survival rate of single crown at 94.5% after 5 years,⁴ and reported failures were mainly due to inadequate bone

quality.⁵ Hence, this has led to an increasing number of both dental patients and dental surgeons becoming more interested in dental implants, as well as manufacturers, concomitantly leading to more implant systems being manufactured.⁶ This alludes to the benefit of dental surgeons and their patients having a wide range of implant systems to pick from depending on the cost of implants, design of implants, and the skill of the dental surgeon.^{6,7} However, the use of dental implants is not without challenges, and there are some recorded failures because of complications. Failures of dental implants are either because of early or late complications.²

Bacterial contamination of dental implants during insertion, among other things, can cause implant failures.⁸⁻¹⁰ This contamination could be as a result of accumulation of bacterial biofilms on the surface of the implant during the surgical procedure leading to inflammatory responses of both hard and soft tissues, with the resultant early failure of the implant and failure at long-term follow-ups.^{8,11} Thus, to reduce the failures of dental implants due to early complications, routine use of antibiotic prophylaxis during dental implant surgery has been recommended.^{8,12} Other conditions that may necessitate the dental surgeon's use of antibiotic prophylaxis during implant surgery, but not limited to these conditions, include patients at risk of endocarditis¹³ patients who are severely immunocompromised,¹⁴ and diabetic patients.^{2,15,16} Nevertheless, the success rate or failure of osseointegrated implants in healthy patients with or without the use of antibiotic prophylaxis is still a matter of controversy.^{8,17-20} On the other hand, bacterial resistance is known as the ability of the bacterial to prevent either the bacteriostatic or bactericidal effects of antibiotics.²¹ The abuse of antibiotics through the unnecessary, prolonged, and unplanned usage contributes to the development of bacteria resistance.^{8,21,22} Thus, the objectives of this research were to examine if the use of antibiotic prophylaxis in implant surgery was being practiced among dental surgeons in Nigeria, and to ascertain dentists' preferred choice of antibiotic prophylaxis and dosage.

MATERIALS AND METHODS

This was a transversal study among dental

surgeons practicing implant surgery in Nigeria to investigate their use of antibiotic prophylaxis. The electronic questionnaire used in Turkey²³ was modified with the aid of Survey Monkey (by Momentive.ai. California, USA) and posted electronically from 4th January 2023 to 4th April 2023, to all dentists registered with Nigeria Dental Association (NDA), after obtaining permission from NDA. A total of ten (10) questions were asked with the first two questions seeking to determine place of practice and area of specialization in Dentistry. The next two questions were direct questions such as: "Do you place dental implants", "How long have you been placing dental implants?" Respondents were required to answer "YES, OR NO". The final six questions were designed to investigate at what stage of dental implants placement antibiotics prophylaxis was used, the dose, and the duration of use. A list of antibiotics dental surgeons in Nigeria may use while placing implants were included for questions investigating the choice of antibiotics.

The questionnaires were pretested twice among ten dental surgeons on two different occasions to determine ease of answering the questions. Participants were asked to make comments which were reviewed, and adjustments were made to the question. Estimated time for completion of the questionnaire was two (2) minutes. The questionnaire was posted electronically on two WhatsApp's group platforms of the Nigerian Dental Association platforms (NDA) which had the labels NDA I (Contains 344 registered dentist) and NDA II (which had 392 registered dentist), with a total number of 736 registered dentists. Inclusion criteria for this study were dentists who had placed dental implants, while those who may have placed dental implants previously but were not on any of these platforms were excluded by denying them access to the questionnaire since the questionnaire could not be copied and posted by anybody except the lead author.

The questionnaire was linked only to the lead author, and this was to assure respondents confidentiality. In addition, the process of filling one form closed access to the form the moment respondents clicked the submit button; this prevented the filling of more than one form by any of the respondents. Data collected from the

questionnaire was entered into statistical Package for Social Sciences (SPSS) version 25.0 (SPSS® Inc, Chicago, IL, USA). The percentage response rate was calculated. Descriptive and inferential statistics were calculated, and Pearson’s chi-squared test was used to assess the differences in various time periods of administration of antibiotics. Statistical significance was set at $p \leq 0.05$.

RESULTS

Most respondents in this study, 56 (78%) as indicated from the results above, were making use of antibiotic prophylaxis in dental implant surgery while 16 (22%) were not. (Fig.1)

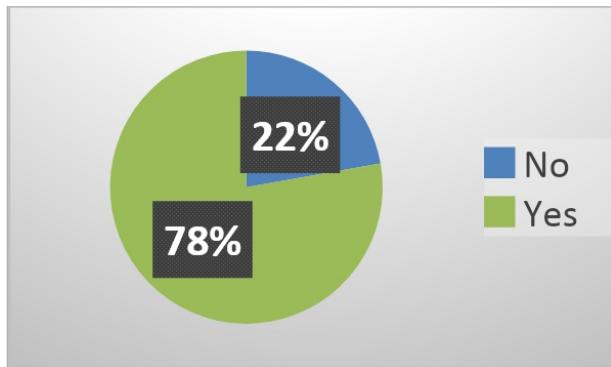


Figure 1: Respondents that use Antibiotic Prophylaxis

Most of the dental surgeons favored 24-hour antibiotic prophylaxis before implant surgery, although this was not statistically significant ($p=0.21$). Interestingly, 16 (22.2%) of the surgeons were administering antibiotic prophylaxis an hour before the implant surgery, while 8.3% administered prophylaxis 12 hours before implant surgery. Table 1

Table 1: Pattern of Antibiotic Prophylaxis.

Before Implant Surgery	Distribution (%)	X ²	p-value
48 hours before surgery	3(4.2)		
24 hours before surgery	27(37.5)	0.170	0.210
12 hours before surgery	6(8.3)		
1 hour before surgery	16(22.2)		
30Minutes before surgery	4(5.6)		
Total	56(77.8)		

A 5-day regular dose pre- and post-surgery was preferred by 58.3% of respondents among the 56 dentists that used antibiotic prophylaxis in implant surgery. Although this

was a simple majority among the dental surgeons placing implants in this present study, this was found to be statistically significant ($p=0.044$). Table 2

Table 2: Pattern of Antibiotic Prophylaxis.

No of Days Antibiotics is Given	Frequency (%)	X ²	p-value
Single Dose	4(5.6)		
5 Days Dose	42(58.3)	0.270	0.044
7 Days Dose	7(9.7)		
2 Weeks Dose	3(4.2)		
Total	56(77.8)		

More dental surgeons in this study (30.6%) preferred Clindamycin (150mg 6hrly x 5/7) as their first choice for antibiotic prophylaxis. ($p=0.18$) The use of Cephalosporins and Erythromycin was not common among dentists in this study. Table 3

Table 3: Choice of Antibiotic Prophylaxis

Preferred Choice of Antibiotics	Frequency N (%)	X ²	p-value
Amoxicillin (500mg 8hrly x 5/7)	20(27.8)		
Metronidazole (400mg 8hrly x 5/7)	2(2.8)		
Clindamycin (150mg 6hrly x 5/7)	22(30.6)	.184	.182
Aminopenicillin + Beta-lactamase Inhibitors (125mg 12hrly x 5/7)	8(11.1)		
Cephalosporins (250mg 6hrly x 5/7)	0(0)		
Erythromycin (500mg 12hrly x 5/7)	0(0)		
Azithromycin (500mg daily x 5/7)	2(2.8)		
Total	54(75.0)		

DISCUSSION

The study was based on a convenience sample collected from the number of dentists registered with Nigerian Dental Association (NDA) who responded to the questionnaires sent electronically. Regrettably, it may not be possible to calculate the exact number of Nigerian dentists who are placing dental implants in Nigeria, because a government registered association of dental implantologists is yet to exist in Nigeria which may have served as a pool for this study. A word of caution here is that because of the low response rate, the result may not be a generalization of the practice of implant dentistry in Nigeria.

The study reported that 78% of the 72 dental surgeons that returned the completed questionnaire used antibiotic prophylaxis while placing dental implants, while 22% did not. This indicates the need to establish guidelines for the practice of implant dentistry in Nigeria. Antibiotic

prophylaxis may reduce the risk of infection caused by Streptococci, gram-anaerobic and gram-anaerobic bacilli in implant surgery¹⁹ because because the guidelines would recommend acceptable regimens of antibiotic prophylaxis use in Nigeria. However, the use of systemic antibiotic prophylaxis in dental implant surgery, and their degree of success or failure in healthy subjects have scarcely been documented in the literatures to the best of our knowledge.^{19,24}

This study reported that 78% of the respondents use antibiotic prophylaxis. This result is close to the report of a study conducted in the United Kingdom (UK),¹ where 72% of dental surgeons among 109 who completed a questionnaire claimed that they practice the use of antibiotic prophylaxis in implant surgery. The present result is, however, higher than the 39.1% of dentists who always use antibiotic prophylaxis, as reported by a Turkish survey.²³ It is also higher than the report from a Spanish study,¹⁹ where 55.6% out of 200 implantologists claimed they use antibiotic prophylaxis during implant surgery. The reason for the present study's result could be that the dentists may feel the implant patient might not follow good oral hygiene instructions after placing the implants.

The administration of antibiotic prophylaxis was reportedly given 24 hours before the surgery by 37.5% of the dental surgeons in this study. However, this was not statistically significant. Nevertheless, a 5-day pre- to post-implant surgery use of antibiotic prophylaxis was preferred by 58.3% of the dentist, but this, however, was statistically significant (p -value=0.044). This corroborates the report from the Turkish study²³ where 38.6% of 429 dental surgeons administered antibiotic prophylaxis one hour before implant surgery, while 53.5% of them continued the medication after placing the implants for a total of five days. Also, amongst the 109 dentists that placed implants investigated in a UK study, 50% administered antibiotic prophylaxis one hour before implant surgery and they recorded good results¹. Therefore, results in this study suggest differences in prescribing patterns concerning the duration for pre- and post-operative administration of antibiotics. This could be attributed to the choice of antibiotics, the number of implants placed during the surgery, and probably the

preferred technique of implant surgery (raised flap versus flapless).

A 5-day dose of Clindamycin, 24 hours pre-surgery, was the preferred choice of antibiotic in this study for 30.6% of dental surgeons, although, this was not statistically significant. The second-choice antibiotic recorded was Amoxicillin and this was preferred by 27.8% of dental surgeons. On the contrary, Amoxicillin was the first-choice drug among 50% of dental surgeons in the UK study and they reported success with 3g amoxicillin administered one hour pre-surgery.¹ However, another penicillin product, Aminopenicillin was the preferred antibiotic prophylaxis in the Turkish survey. While 38.6% of the dentists in the study prescribed 2000mg Aminopenicillin one hour before the surgery, 19.3% prescribed 1000mg of Aminopenicillin twice daily, 24 hours before implant surgery.²³ Also, 53.5% of the respondents in the Turkish study prescribed Aminopenicillin at 1000mg twice daily for five days after implant surgery.²³

While there is no global standardization in the use of antibiotics,⁸ there are also no documented reasons for the differences in choice of antibiotics. However, a broad-spectrum antibiotic with the ability to penetrate bone might have favored the use of Clindamycin as the preferred choice in this study. Nonetheless, the American Dental Association (ADA) recommends that Clindamycin should not be used in patients with penicillin allergy because of adverse reactions such as pseudomembranous colitis induced by *C. difficile*.^{25,26} In addition, Salomo-Collet al,²⁷ stated that patients with penicillin allergy who were treated with Clindamycin had a four times higher risk of implant failure. In a fixed-effects meta-analysis conducted by Edibam et al,²⁸ they reported a higher number of implant failures when Clindamycin was administered because of the patient's reported allergy to penicillin. On the other hand, there is sufficient documented evidence that reported an improved outcome when the beta-lactam antibiotics, Amoxicillin are used.²⁹⁻³³ This result on the use of Amoxicillin is also applicable to Aminopenicillin since Amoxicillin is an analogue of Aminopenicillin and it is derived semi-synthetically from the parent drug penicillin.³⁴ A word of caution, however, with the use of Amoxicillin is that prolonged use of this antibiotic has been observed to lead to the elevation of

intracellular reactive oxygen which in turn initiates an oxidative DNA lesion that interferes with osseointegration.^{8,35,36}

The administration of antibiotics with no standardization is a global health challenge resulting in resistant bacteria and side effects like diarrhea, nausea, and vomiting.⁸ Furthermore, in a retrospective study of antibiotic prophylaxis administered to patients with type-2 diabetes mellitus who had 23 implants placed, 500mg Amoxicillin and Potassium Clavulanate were prescribed twice daily for five days, and the result was a 100% success rate.² Thus, it may be safe to conclude that if a 5-day dose of antibiotics prophylaxis could achieve a good success rate among diabetic patients, then a better result with the same dose would be recorded in healthy patients. However, a Turkish study²³ indicated that dental surgeons preferred antibiotic prophylaxis only when placing multiple implants with surgical flap raised. This agrees with a report among some Jordanian dentists who showed a preference for more post-operative antibiotics than pre-operative antibiotics especially when flaps were raised.¹⁸ Moreover, the consensus report of the European Association for Osseointegration (EAO) stated that antibiotic prophylaxis has not shown any benefit in uncomplicated cases of implant placement, however, the case is different with patients that needed graft and in patients with systemic comorbidities like diabetes.³⁸ In our study, which seems to be the first in our country to the best of our knowledge, prophylaxis were given irrespective of whether there were comorbidities or not. The reason could be some patients not knowing their current health status.

Studies³⁹⁻⁴¹ have shown that a combination of amoxicillin and metronidazole is frequently used in dentistry, however, our questionnaire did not include questions on combination of antibiotics and the preferred dose that was used by the respondents. Also, the study did not consider whether the prophylaxis were given in the presence of comorbidities or not. Nevertheless, there seems to be a consensus regarding the use of Clindamycin as prophylaxis antibiotic in Nigeria, which is at variance with studies from Jordan¹⁸ and Turkey²³ where there were no consensus. The authors would, therefore, advise further research with a

larger population in this area in Nigeria, to establish an agreement and guidelines on the choice and dose of antibiotic prophylaxis for dental implant surgery.

CONCLUSION

We found a higher number of dental surgeons using antibiotic prophylaxis compared to those not using it. Clindamycin, given 24 hours before placing implant and continued for 5 days at 150mg 6hourly was the preferred choice of antibiotic prophylaxis, while the second choice was Amoxicillin given 500mg 8hrly, 24 hours before placing implant and continued for 5 days. However, a careful drug history is required to prevent allergies and resistances. Amoxicillin is a good choice when allergies to Clindamycin occur. Prophylactic antibiotics may increase success rate in implant especially when used in patients with comorbidities. This knowledge of dosage for antibiotic prophylaxis may discourage the excessive and unintended use of antibiotics, which may lead to developing resistance, and may ultimately lead to early implant failure.

Acknowledgement: We acknowledge the support and cooperation we received from the National Officers Committee of the Nigerian Dental Association (NDA 2022-2024) ably led by Dr. Tope Adeyemi for the permission to conduct this research among her members. This shows the emphasis the team places on research by members of NDA. We appreciate your encouragement.

We have no conflicting interest to declare.

REFERENCES

1. Ireland RS, Palmer NO, Lindenmeyer A, et al. An investigation of antibiotic prophylaxis in implant practice in the UK. *British dental journal*. 2012 Oct 27;213(8):E14-E14
2. Surapaneni H, Yalamanchili PS, Basha MH, et al. Antibiotics in dental implants: A review of literature. *Journal of pharmacy & Bioallied sciences*. 2016 Oct;8(Suppl 1):S28.
3. Obagbemiro K, Ademola AJ, Yetunde A, et al. Patients' psychosocial well-being and self-reported satisfaction following single implant therapy in Lagos, Nigeria. *Int J Oral Health Dent* 2018;4(3)163-169.

4. Jung RE, Pjetursson BE, Glauser R, et al. A systematic review of the five-year survival and complication rates of implant-supported single crowns. *Clin Oral Implants Res* 2008; 19: 119–130.
5. Goodacre CJ, Kan JY, Rungcharassaeng K. Clinical complications of osseointegrated implants. *J Prosthet Dent* 1999; 81: 537–552.
6. Narby B, Kronström M, Söderfeldt B, Palmqvist S. Changes in attitudes toward desire for implant treatment: a longitudinal study of a middle-aged and older Swedish population. *Int J Prosthodont* 2008; 21: 481–485.
7. Ng PC, Pow EH, Ching SH, et al. Dental implant practice among Hong Kong general dental practitioners in 2004 and 2008. *Implant Dent* 2011; 20: 95–105.
8. Giro G, In J, Witek L, et al. Amoxicillin administrations and its influence on bone repair around osseointegrated implants. *Journal of Oral and Maxillofacial Surgery*. 2014 Feb 1; 72(2):305-e1.
9. Esposito M, Grusovin MG, Loli V, Coulthard P, Worthington HV. Does antibiotic prophylaxis at implant placement decrease early implant failures? A Cochrane systematic review. *European journal of oral implantology*. 2010 Jun 1; 3(2).PMC 20623035.
10. Baqain ZH, Moqbel WY, and Sawair FA. Early dental implant failure: risk factors. *British Journal of Oral and Maxillofacial Surgery*. 2012 Apr 1; 50(3):239-43.
11. Rodriguez-Argueta OF, Figueiredo R, Valmaseda-Castellon E, Gay-Escoda C. Postoperative complications in smoking patients treated with implants: a retrospective study. *Journal of Oral and Maxillofacial Surgery*. 2011 Aug 1; 69(8):2152-7.
12. Lodi G, Azzi L, Varoni EM, Pentenero M, Del Fabbro M, Carrassi A, Sardella A, Manfredi M. Antibiotics to prevent complications following tooth extractions. *Cochrane Database of Systematic Reviews*. 2021(2)..
13. Chirouze C, Hoen B, and Duval X. Infective endocarditis prophylaxis: moving from dental prophylaxis to global prevention? *European journal of clinical microbiology & infectious diseases*. 2012 Sep; 31:2089-95..
14. Schwartz AB, Larson EL. Antibiotic prophylaxis and postoperative complications after tooth extraction and implant placement: a review of the literature. *Journal of Dentistry*. 2007 Dec 1; 35(12):881-8.
15. Ramu C, Padmanabhan TV. Indications of antibiotic prophylaxis in dental practice—Review. *Asian Pacific Journal of Tropical Biomedicine*. 2012 Sep 1; 2(9):749-54..
16. Sykara M, Maniatakos P, Tentolouris A, Karoussis IK, Tentolouris N. The necessity of administering antibiotic prophylaxis to patients with diabetes mellitus prior to oral surgical procedures—a systematic review. *Diabetes & Metabolic Syndrome: Clinical Research & Reviews*. 2022 Oct 1; 16(10):102621.
17. Hedrick TL, Adams JD, Sawyer RG. Implant-associated infections: an overview. *Journal of Long-Term Effects of Medical Implants*. 2006; 16(1).
18. AbuKaraky AE, Afifeh KA, Khatib AA, Khdairi NO, Habarneh HM, Ahmad WK, Hamdan AA, Sawair FA. Antibiotics prescribing practices in oral implantology among Jordanian dentists. A cross-sectional, observational study. *BMC Research Notes*. 2011 Dec; 4:1-8.
19. Camacho-Alonso F, Muñoz-Cámara D, Sánchez-Siles M. Attitudes of dental implantologists in Spain to prescribing antibiotics, analgesics and anti-inflammatories in healthy patients. *Medicina Oral, Patología Oral y Cirugía Bucal*. 2019 Nov; 24(6):e752.
20. Ata-Ali J, Ata-Ali F. Do antibiotics decrease implant failure and postoperative infections? A systematic review and meta-analysis. *International Journal of Oral and Maxillofacial Surgery*. 2014 Jan 1; 43(1):68-74.
21. Hasan TH, Al-Harmoosh RA. Mechanisms of antibiotic resistance in bacteria. *Sys Rev Pharm*. 2020 Jun 1; 11(6):817-23. Researchgate

22. Kraemer SA, Ramachandran A, Perron GG. Antibiotic pollution in the environment: from microbial ecology to public policy. *Microorganisms*. 2019 Jun 22;7(6):180.
23. Yalcin-Ülker GM, Cakir M, Meral DG. Antibiotic prescribing habits of the clinicians dealing with dental implant surgery in Turkey: a questionnaire study. *International Journal of Implant Dentistry*. 2020 Dec;6:1-2.
24. Ahmad N, Saad N. Effects of antibiotics on dental implants: a review. *J Clin Med Res*. 2012;4:1-6PMC 3279494
25. Azher S, Patel A. Antibiotics in Dentoalveolar surgery, a closer look at infection, alveolar Osteitis and adverse drug reaction. *Journal of Oral and Maxillofacial Surgery*. 2021 Nov 1;79(11):2203-14.
26. Santamaría Arrieta G, Rodríguez Sánchez F, Rodríguez-Andrés C, et al. The effect of preoperative clindamycin in reducing early oral implant failure: a randomised placebo-controlled clinical trial. *Clinical Oral Investigations*. 2023 Mar;27(3):1113-22.
27. Salomó-Coll O, Lozano-Carrascal N, Lázaro-Abdulkarim A, et al. Do penicillin-allergic patients present a higher rate of implant failure? *International Journal of Oral & Maxillofacial Implants*. 2018 Nov 1;33(6).
28. Edibam NR, Lorenzo-Pouso AI, and Caponio VC. Self-reported allergy to penicillin and clindamycin administration may be risk factors for dental implant failure: A systematic review, meta-analysis and delabeling protocol. *Clinical Oral Implants Research*. 2023 Apr 27.
29. Blumenthal KG, Parker RA, Shenoy ES, Walensky RP. Improving clinical outcomes in patients with methicillin-sensitive *Staphylococcus aureus* bacteremia and reported penicillin allergy. *Clinical Infectious Diseases*. 2015 Sep 1;61(5):741-9.
30. Elliott DJ, Zaoutis TE, Troxel AB, Loh A, Keren R. Empiric antimicrobial therapy for pediatric skin and soft-tissue infections in the era of methicillin-resistant *Staphylococcus aureus*. *Pediatrics*. 2009 Jun 1;123(6):e959-66.
31. MacFadden DR, LaDelfa A, Leen J, Gold WL, Daneman N, Weber E, Al-Busaidi I, Petrescu D, Saltzman I, Devlin M, Andany N. Impact of reported beta-lactam allergy on inpatient outcomes: a multicenter prospective cohort study. *Clinical Infectious Diseases*. 2016 Oct 1;63(7):904-10.
32. Koliscak LP, Johnson JW, Beardsley JR, Miller DP, Williamson JC, Luther VP, Ohl CA. Optimizing empiric antibiotic therapy in patients with severe β -lactam allergy. *Antimicrobial agents and chemotherapy*. 2013 Dec;57(12):5918-23..
33. Murphy J, Isaiah A, Dyalram D, Lubek JE. Surgical site infections in patients receiving osteomyocutaneous free flaps to the head and neck. Does choice of antibiotic prophylaxis matter?. *Journal of Oral and Maxillofacial Surgery*. 2017 Oct 1;75(10):2223-9.
34. Kewicz HA, Feezle H, and Richardson M. Thermostability Determination of Broad Spectrum Antibiotics at High Temperatures by Liquid Chromatography-Mass Spectrometry. 2013 NCUR. 2013 Aug 5.
35. Melhus A, Ryan AF: Effects of amoxicillin on cytokine and osteocalcin expression in bone tissue during experimental acute otitis media. *Cytokine* 25:254, 2004
36. Arabski M, Kazmierczak P, Wisniewska-Jarosinska M, Poplawski T, Klupinska G, Chojnacki J, Drzewoski J, Blasiak J. Interaction of amoxicillin with DNA in human lymphocytes and *H. pylori*-infected and non-infected gastric mucosa cells. *Chemico-Biological Interactions*. 2005 Feb 28;152(1):13-24.
37. Klinge A, Khalil D, Klinge B, Lund B, Naimi-Akbar A, Tranaeus S, Hultin M. Prophylactic antibiotics for staged bone augmentation in implant dentistry. *Acta Odontologica Scandinavica*. 2020 Jan 2;78(1):64-73.