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Level of knowledge about metalloproteinases in dental students close to graduate from three universities in Peruvian capital city

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Abstract

Background: Metalloproteinases are proteolytic enzymes that degrade dentin and periodontal collagen; therefore, it is of special interest that dental students know its mechanism of action and how its effects can be inhibited. Therefore, the aim of this research was to evaluate the level of knowledge about metalloproteinases in dental students close to graduate from three universities in Peruvian capital city.

Materials and methods: In this analytical, observational, cross-sectional and prospective study, 223 dental students close to graduate in three Peruvian universities were evaluated from September to November 2020. A questionnaire of 20 closed questions with three answers was validated and used to measure the level of general and dental knowledge about metalloproteinases. A *logit* model was used to evaluate the influence of the following variables: "gender" (X1), "type of university" (X2), "marital status" (X3) and "age group" (X4), in the knowledge levels of the students, considering a p-value <.05.

Results: Of the 223 dentistry students, it was obtained that the level of knowledge about metalloproteinases was predominantly low with 82.1%, (95% confidence interval (CI): 77.1%–87.1%) of the total. According to multivariate logistic regression analysis, "type of university" was the only variable that proved to have a significant influence ($p = .022$) on the level of knowledge about metalloproteinases with an odds ratio of (OR = 0.44; CI: 0.21–0.89), whilst the other variables "age group" ($p > .05$), "gender" ($p = .058$) and "marital status" ($p = .114$) were not considered influential factors.

Conclusion: The majority of final year dental students in three Peruvian universities presented a low level of overall knowledge about metalloproteinases. In addition, private university students were 56% less likely to pass the subject knowledge test. On contrary, gender, age group and marital status did not significantly influence the level of knowledge of the students.

KEYWORDS
dental students, dentistry, knowledge, metalloproteinase inhibitors, metalloproteinases, Peru

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1 | INTRODUCTION

Metalloproteinases are enzymes that have the ability to break down or degrade collagen.[1] The study of its functions, its implication in the different biological alterations and its influence in some diseases is of great importance in the training of students in university career of health sciences. Numerous studies have shown the presence of metalloproteinases in chronic diseases linked to environmental factors or by genetic predisposition, such as rheumatoid arthritis, cancer, cardiovascular diseases, multiple sclerosis, cleft lip, cleft palate and amelogenesis imperfecta, amongst others.[2–7]

Metalloproteinases are synthesised by macrophages, fibroblasts and leukocytes, which act on collagen, and are the main responsible for its degradation. Additionally, they are involved in periodontitis and the process of carious lesion, causing the degradation of collagen type I, II and III. Different authors have reported that there are approximately 25 types of metalloproteinases, being the most abundant in the organism, the metalloproteinases of type 1, 3, 8 and 9.[8–10] On contrary, there are endogenous[11] or specific tissue inhibitors[12,13] called TIMPS's (tissue inhibitors of metalloproteinases) that inhibit the mechanism of action of metalloproteinases,[14,15] as well as nonspecific inhibitors[16] or artificial inhibitors[17,18] such as 2% chlorhexidine digluconate solution, EDTA (ethylenediaminetetraacetic acid) and proanthocyanidin[12,17,19–23] that some researchers recommend to inhibit dentin metalloproteinases and prevent collagen degradation, allowing a more stable hybrid layer that increases the chances of successful adhesion and thus a restoration with increased tensile strength.[20,21] These studies applied in the field of restorative dentistry demonstrate the importance for dentistry students to learn, during their professional training, the mechanism of action of metalloproteinases and their nonspecific inhibitors as conditioning agents that allow greater conservation of collagen to achieve a good marginal sealing and optimal adhesion.

In the field of oral pathology, Diaz et al. carried out a study to determine the levels of metalloproteinases type 1, 2 and 9 in a group of patients with gingival enlargement as a consequence of systemic responses by the intake of drugs or hormonal problems, observing that patients with enlarged gingival tissue presented high levels of metalloproteinases 1, 2 and 9. However, a significant increase of these metalloproteinases was also evidenced in patients submitted to some antihypertensive, anticonvulsant and immunosuppressive drugs.[24] In the field of orthodontics, it has been reported that excessive forces applied to the tooth can generate the activation of metalloproteinases and therefore cause periodontal problems in the future.[25] In the field of endodontics, it has been reported that, in irreversible pulpitis, the activity of metalloproteinase 9 increases, thus causing the degradation of dentin collagen around the dental pulp.[26] In the field of periodontics, it has been reported in some studies through salivary biomarkers that type 8 metalloproteinase is associated with patients with periodontal disease who present as risk factor a systemic disease, such as diabetes, demonstrating specifically in these patients, elevated levels of metalloproteinases in the mouth.[27,28]

In a study conducted on Ecuadorian dental students, a good level of knowledge was reported about a metalloproteinase inhibitor in direct restorations, demonstrating some competence in the knowledge of subject.[29] Currently, there are no studies that have assessed the level of knowledge about metalloproteinases in dental students who are close to completing their professional career. However, the knowledge that students could acquire throughout their university career about metalloproteinases and the understanding of their implications in the different areas of dentistry will serve them in an applicable way to improve their approach to treatment, both locally and systemically, since, as mentioned above, the mechanism of action of metalloproteinases can have an impact on the success or failure of dental treatments performed in different specialties. In addition, know to how to interpret elevated values of metalloproteinases, both at the oral and systemic level, could allow the student to predict possible complications in the performance of dental treatment or to understand the evolution of certain pathologies.

In view of the above, the aim of this study was to evaluate the level of knowledge of metalloproteinases in dental students close to graduate from three universities in Peruvian capital city.

2 | MATERIALS AND METHODS

2.1 | Type of study

An analytical, observational, transversal and prospective study was carried out.

2.2 | Population and selection of participants

The initial population consisted of 278 dental students in their final year of professional dental career from August to December 2020. After considering the inclusion and exclusion criteria, 223 students were left as the final population, of which 79 (35.43%) were from the Universidad Nacional Federico Villareal (UNFV), 36 (16.14%) from the Universidad Alas Peruanas (UAP) and 108 (48.43%) from the Universidad Inca Garcilaso de la Vega (UIGV). Since the entire final population was included in the study, no sample size calculation was required.

Inclusion criteria

1. Students of both sexes of legal age.
2. Dentistry students.
3. Students enrolled in semester 2020–2.
4. Students who accepted virtual informed consent.
5. Dental students who took virtual classes during 2020–2.
6. Dental students close to graduate.

Exclusion criteria

1. Students who did not wish to participate in this study.
2. Students who discontinued the academic term.

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2.3 | Associated Factors

The associated factors considered in the study were the variables: gender (X1), type of university (X2), marital status (X3) and age group (X4).

2.4 | Instrument Development

A questionnaire of 20 closed questions with three answers (Yes/No/I do not know) was developed to evaluate the knowledge of dental students about metalloproteinases in two aspects: general knowledge with 7 questions (Q1–Q7) (Table 2) and dental knowledge with 13 questions (Q8–Q20) (Table 3). The level of global knowledge was defined according to the following range: low (0–10 points), medium (11–13 points) and high (14–20 points).[30,31] One point was awarded for each correct answer.

2.5 | Instrument Validation

The content of the questionnaire was validated by judgement of five experts with more than 10 years of experience, three of them from the area of cariology, periodontics and public health in dentistry, and two dental professors from the research area, who reviewed the conceptual definition and adapted the instrument to the context of research. The test used was the validity coefficient (Aiken's V = 0.89), which was acceptable. For validity of the construct, a confirmatory factorial analysis was made to define the dimensions and group the items, establishing two dimensions: general knowledge (Q1–Q7) and dental knowledge (Q8–Q20). Later, the reliability of the instrument's internal consistency was evaluated by means of the Kuder-Richardson test (KR-20) and a result of 0.82 (CI: 0.63–0.91) was obtained, showing good reliability. As for the stability analysis, the total score was evaluated in 30 students with the same questionnaire at two different moments with a 7-day interval, altering the order of the questions and answers to avoid memory bias (Test - Retest), being the intraclass correlation coefficient (ICC) equal to 0.95 (95% CI: 0.90–0.98), which was considered very good.

2.6 | Procedure

The questionnaire was distributed to each student through their e-mails using the virtual program Google Classroom®. The informed consent of the students to participate in the study was at the beginning of the questionnaire and followed by the indications to develop it; however, they were free to refuse the evaluation if during the course of the study they did not wish to complete it. Only the principal investigator had access to the data, and no personal details such as telephone number, name and address were required. Only one submission was considered for each student and was limited to 20 min maximum to complete the questionnaire. The research was conducted from September to November 2020. The questionnaire result of each student was sent to their respective e-mail after the entire investigation was completed.

2.7 | Statistical analysis

Data analysis was performed with the Statistical Package for the Social Sciences (SPSS) version 24.0; descriptive statistics were applied to obtain the percentages of the categorical variables and the measures of central tendency and dispersion for the numerical variables. Pearson's chi-square test was used for the bivariate analysis. The risk factors were established with the logistic regression model (logit model) using odds ratio (OR). All analyses were carried out, assuming a 95% confidence level with type I error of 5%.

2.8 | Bioethical considerations

This research respected the bioethical principles for medical research with human beings of the Declaration of Helsinki related to confidentiality, freedom, respect and non-maleficence.[32] This research was approved by the Ethics and Research Committee of the Faculty of Stomatology of the Inca Garcilaso de la Vega University with resolution 253-2020-DFE.

3 | RESULTS

Regarding the sociodemographic variables, the female sex was the most prevalent with 72.2%. Regarding the type of university, 64.6% belonged to a private institution; on contrary, 71.7% were single and 77.1% of the total were between 25 and 35 years old. The mean age of the students was 28.32 ± 4.79 years. The level of knowledge about metalloproteinases in all students was predominantly low (82.1%; CI: 77.1%–87.1%), followed by a regular level (11.2%; CI: 7.1%–15.3%) and a high level (6.7%; CI: 3.4%–9.9%) [Table 1 and Figure 1].

Regarding general knowledge about metalloproteinases, results showed no statistically significant association between the seven questions asked (Q1, Q2, Q3, Q4, Q5, Q6 and Q7) and the variables: gender, type of university, marital status and age group of students [Table 2].

Regarding dental knowledge about metalloproteinases, results showed statistically significant association between the type of university and Q8 (Does the action of metalloproteinases directly influence the formation of cleft palate and cleft lip?) ($p = .012$) and Q11 (Is the dentin bonding agent a TIMP?) ($p = .049$). This last question was also significantly associated with gender ($p = .025$). Finally, the age group was significantly associated with Q17 (Are metalloproteinases activated only in pathological processes of apical periodontitis?) ($p = .034$) [Table 3].

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TABLE 1 Characteristic descriptions of the sociodemographic variables in dental students

Variable	Category	*n*	%	Average Score	SD	CI at 95%
Gender	Female	161	72.2	6.34	4.45	5.65–7.03
	Male	62	27.8	6.63	4.51	5.51–7.75
Type of University	Public (UNFV)	79	35.4	6.72	4.65	5.70–7.75
	Private (UIGV–UAP)	144	64.6	6.26	4.35	5.55–6.97
Marital Status	Single	160	71.7	6.56	4.66	5.83–7.28
	Married o cohabiting	63	28.3	6.06	3.89	5.10–7.02
Age Group	<25 years	31	13.9	6.6	5.45	4.58–8.58
	25–35 years	172	77.1	6.3	6.27	5.61–6.92
	>35 years	20	9	7.5	3.80	5.71–9.28
Age		**Mean**	**SD**			
		28.32	4.79			

Abbreviations: CI, confidence interval; SD, standard deviation.

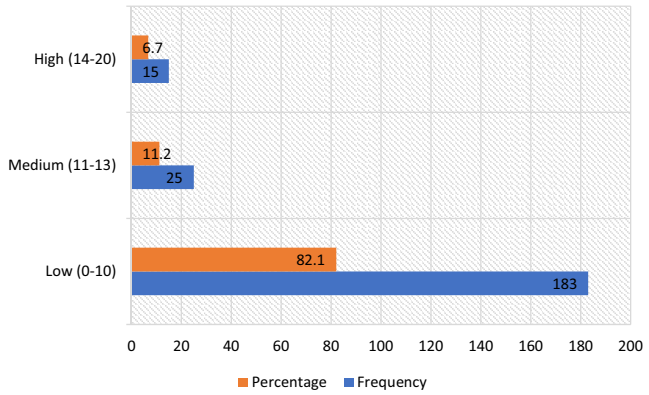


FIGURE 1 Level of knowledge about metalloproteinases according to total score obtained by the students

According to bivariate logistic regression analysis, it can be seen that the variables "type of university" and "marital status," in an independent way, have a significant influence ($p = .013$ and .040 respectively) on the level of general and dental knowledge about metalloproteinases in dental students. However, when the multivariate logistic regression analysis is performed (logit model), only the variable type of university (X2) can be considered as a factor that influences general and dental knowledge about metalloproteinases in dental students, so that private university students were 56% less likely to pass the examination (OR = 0. 44; CI: 0.21–0.89). On contrary, "gender" (X1), "marital status" (X3) and "age group" (X4) were not considered as significant influencing factors ($p > .05$) in their exam results [Table 4].

4 | DISCUSSION

In the present research, it was obtained that the global level of knowledge on metalloproteinases in dental students was predominantly low with 82.1%; (CI: 77.1%–87.1%). In addition, there were no statistically significant differences in the level of knowledge according to gender, marital status, type of university and age group. However, the "type of university" variable significantly affected the level of general and dental knowledge about metalloproteinases in students.

The predominantly low level of knowledge about metalloproteinases, presented by dental students, differs from the results reported by Herrera,[29] since in his research, it was obtained that most dental students in the fifth academic year presented mastery and adequate knowledge about a metalloproteinase inhibitor in restorations, demonstrating some expertise in the subject. These differences may be due to the fact that Jimenez et al. only evaluated one aspect of metalloproteinases related to dentin bonding, whilst in the present research, different aspects of knowledge about metalloproteinases related to multiple dental specialties were evaluated, not being found until now (April 2021), similar antecedents in the literature.

In the present study, the sociodemographic variables age, gender and marital status were not an influential factor in the level of knowledge about metalloproteinases of the dental students. This is in agreement with the results of several studies that evaluated other areas of dental knowledge, such as that of Guevara et al.[33] and Cayo et al.,[30] who found that the variables gender and age were not influential factors when measuring the level of knowledge about the dental handling of pregnant patients and the level of dental knowledge about COVID-19. In addition, Núñez et al. reported that there were no differences between sociodemographic characteristics (sex, age group and marital status) when assessing the level of knowledge about sterilisation of dental handpieces.[34] Finally, Zarshenas et al. reported that marital status was not an influential factor when assessing study habits and skills in dental students.[35] On contrary, the variable "type of university" in this study proved to be an influential factor in the level of knowledge about metalloproteinases in dental students.

It is worth mentioning that in this study, a multivariate logistic regression model (logit model) was included in the statistical analysis, because this analysis allowed us to identify the influential

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TABLE 2 Association of general knowledge about metalloproteinases in dental students

Question	Answer		Gender	Type of University	Marital Status	Age Group
	Incorrect	Correct				
	n (%)	*n* (%)	*p*	*p*	*p*	*p*
Q1. Do metalloproteinases depend on calcium to perform their function?	169 (75.8)	54 (24.2)	.297	.486	.434	.228
Q2. Do metalloproteinases depend on phosphorus to perform their function?	174 (78.0)	49 (22.0)	.822	.903	.955	.786
Q3. It is irrelevant that dentists understand the activation of metalloproteinases in the clinical field?	158 (70.9)	65 (29.1)	.335	.752	.655	.83
Q4. Do metalloproteinases destroy cancer cells?	122 (54.7)	101 (45.3)	.381	.732	.647	.521
Q5. Do metalloproteinases degrade collagen?	128 (57.4)	95 (42.6)	.669	.853	.58	.12
Q6. Do metalloproteinases depend on zinc to perform their function?	146 (65.5)	77 (34.5)	.898	.273	.697	.211
Q7. Are the functions of metalloproteinases regulated by TIMPs (Tissue Metalloproteinase Inhibitors)?	148 (66.4)	75 (33.6)	.497	.642	.708	.627

factor in the level of knowledge about metalloproteinases, indicating that dental students from private universities were 56% less likely to pass the examination than students from a public university. Although this result should be taken with caution, these findings are likely due to the fact that public university students passed a complex and rigorous entrance examination that allowed those universities to filter out students with better study habits.[36] However, it is important to clarify that the differences in knowledge between students from both types of universities are not statistically significant in the total score, as can be seen in Table 1. On contrary, it is possible that the differences in the level of knowledge between public and private university students are also due to the difference in the length of their curricula, even though it has similar subjects. Students at the public university (UNFV) complete their dental studies in 6 years, whilst those at the private universities (UIGV and UAP) complete it in 5 years. In this sense, UNFV students have one more year of preparation in basic and preclinical sciences, which allows them to develop the subjects in greater depth and with much more time to carry out research on various applications of the theoretical field in the clinical field, allowing them to review more updated scientific information and discuss it through seminars or journal reviews. To cite an example, UNFV students take an extension of courses in pathology, periodontics, orthodontics, implantology, surgery and paediatric dentistry, unlike the private universities considered in this study. In the aforementioned subjects, after reviewing the study plans of the three universities, it can be observed that it is rare to include seminars and group exhibitions, where the importance of the theoretical concepts learned in the basic sciences can be discussed and their application analysed in the clinical setting, as an example of how high values of certain MMPs can influence the manifestation of some systemic or oral pathologies. Therefore, the results obtained in this research must be taken into consideration by professor of the different subjects in dental specialties, since students, by understanding the mechanism of action of metalloproteinases and the knowledge of their endogenous and exogenous inhibitors, will be able to develop lines of research to optimise the durability of biomaterials, avoiding the degradation of dentin collagen in the field of restorative dentistry[8–10,12,17,19,20] or to relate the increase of some types of metalloproteinases with possible risks of developing periodontal diseases[1,8,9] and take appropriate actions in time. In addition, it is important for the dental student to know which types of metalloproteinases are associated with chronic diseases that directly and indirectly affect oral health.[2–5,13]

Our research had some limitations. For example, we were only able to evaluate dental students from three universities in Peruvian capital city who were in their final year of their professional careers. On contrary, we applied the hetero-administered questionnaire in a virtually asynchronous manner with a time limit of 20 min and without the possibility of repetition, to avoid greater bias, since at the time of this evaluation the country was in a national emergency and in obligatory social isolation.[37] Regarding the validated instrument,

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TABLE 3 Association of dental knowledge about metalloproteinases in dental students

	Answer					
	Incorrect	Correct	Gender	University type	Marital Status	Age group
Question	*n* (%)	*n* (%)	*p*	*p*	*p*	*p*
Q8. Does the action of metalloproteinases directly influence the formation of cleft palate and cleft lip?	156 (70.0)	67 (30.0)	.838	.012	.763	.054
Q9. Is the agent EDTA (ethylenediaminetetraacetic acid) a TIMP?	156 (70.0)	67 (30.0)	.596	.699	.186	.066
Q10. Does 2% chlorhexidine digluconate inhibit the action of metalloproteinases when applied to dentin?	142 (63.7)	81 (36.3)	.411	.433	.114	.699
Q11. Is the dentin bonding agent a TIMP?	159 (71.3)	64 (28.7)	.025	.049	.494	.878
Q12. Are metalloproteinases not related to the field of orthodontics, but rather to periodontics?	159 (71.3)	64 (28.7)	.553	.303	.762	.691
Q13. When applying self-etching adhesive with 10-MDP on exposed dentin, is the collagen still degraded by the action of metalloproteinases?	128 (57.4)	95 (42.6)	.631	.639	.146	.269
Q14. Do metalloproteinases promote the progression of carious lesions?	127 (57.0)	96 (43.0)	.417	.395	.971	.413
Q15. Are metalloproteinases involved in Amelogenesis Imperfecta?	170 (76.2)	53 (23.8)	.926	.941	.992	.309
Q16. Do metalloproteinases help counteract periodontal disease?	152 (68.2)	71 (31.8)	.091	.145	.764	.567
Q17. Are metalloproteinases activated only in pathological processes of apical periodontitis?	148 (66.4)	75 (33.6)	.189	.446	.187	.034
Q18. After performing the SRP (scaling and root planning) with the addition of antibiotics, do the levels of metalloproteinases decrease?	172 (77.1)	51 (22.9)	.949	.982	.55	.348
Q19. Is metalloproteinase 9 mostly found in dental and periodontal pathologies?	166 (74.4)	57 (25.6)	.155	.123	.82	.59
Q20. Is metalloproteinase 7 mostly found in dental and periodontal pathologies?	148 (66.4)	75 (33.6)	.963	.108	.187	.337

TABLE 4 Bivariate analysis and multivariate logistic regression model of general and dental knowledge about metalloproteinases according to associated factors

		Associated Factors		Bivariate Analysis		Multivariate Analysis	
Variables	Categories	*p*-value	OR	95% CI	*p*-value	OR	95% CI
(X1) Gender	Female	-	1.00	-	-	1.00	-
	Male	.057	1.99	0.97–4.06	.058	2.05	0.98–4.29
(X2) Type of University	Public	-	1.00	-	-	1.00	-
	Private	.013	0.42	0.21–0.84	.022	0.44	0.21–0.89
(X3) Marital Status	Single	-	1.00	-	-	1.00	-
	Married or Cohabiting	.040	0.39	0.16–0.98	.114	0.41	0.13–1.24
(X4) Age Group	<25 years	.468	1.40	0.56–3.53	.124	5.54	0.63–49.02
	25–35 years	.633	1.23	0.53–2.87	.160	4.34	0.56–33.64
	>35 years	-	1.00	-	-	1.00	-

Note: Abbreviations: 95% CI, 95% confidence interval; OR, odds ratio.

Logit model: all the variables were entered into the statistical analysis of the multivariate model and were accepted because it obtained a significance of $p = .012$ according to Omnibus test of the model's coefficient.

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the lack of criteria analysis was presented as a limitation, since there was no gold standard test or similar questionnaire to evaluate the level of general and dental knowledge about metalloproteinases.

It is recommended to carry out more studies regarding the level of knowledge about metalloproteinases applied to different dental specialties, both at undergraduate and postgraduate levels, in different populations, nationally and internationally, whilst considering the sociodemographic variables in a logit model. On contrary, it is also recommended to evaluate the level of knowledge about metalloproteinases in longitudinal studies, to identify whether the level of knowledge improves over time, especially in specialty courses such as orthodontics, periodontics and implant dentistry, dental surgery, oral pathology and endodontics.[12] In addition, it would also be advisable to replicate the study in dental students from public and private universities with the same number of years in their curricula.

5 | CONCLUSIONS

In sum, the level of knowledge about metalloproteinases of dental students from three universities in Peruvian capital city was predominantly low. In addition, students from private universities were 56% less likely to pass the knowledge test on that subject. However, "gender," "age group" and "marital status" did not prove to be an influential factor in the level of knowledge from students, either for passing or failing the test. It is important that dental professor of different specialties, sensitise and influence the study and feedback of metalloproteinases, since understanding its high values in the mouth or its mechanism of action and the way to neutralise its effects using exogenous inhibitors, becomes clinically relevant in dental practice.

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CONFLICT OF INTEREST

The authors declare they have no conflicts of interest.

AUTHOR CONTRIBUTIONS

They conceived the research idea (CFCR), elaborated the manuscript (CFCR, LCSC, MJCM, NCL, GBV), collected, tabulated the information (CFCR, SMMC, CLG), carried out the bibliographic search (LACG, MILC, LCSC), interpreted the statistical results and helped in the development from the discussion (CFCR, CLG, MJCM, NCL, GBV), he performed the critical revision of the manuscript (CFCR, LCSC, JMCM, SMMC, NCL, GBV, CLG, MILC, LACG). All authors approved the final version of the manuscript.

ETHICAL POLICY AND INSTITUTIONAL REVIEW BOARD STATEMENT

This research respected the bioethical principles for medical research with human beings of the Declaration of Helsinki related to confidentiality, freedom, respect and non-maleficence. This research was approved by the Ethics and Research Committee of the Faculty of Stomatology of the Inca Garcilaso de la Vega University with resolution 253–2020-DFE.

PATIENT DECLARATION OF CONSENT

None.

DATA AVAILABILITY STATEMENT

The data that support the study results are available from the author (Dr. César F. Cayo-Rojas, e-mail: cesar.cayo@upsjb.edu.pe) on request.

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