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KNOWLEDGE AND AWARENESS OF ORTHODONTIC MINI SCREWS AMONG DENTAL STUDENTS IN SAUDI ARABIA: A CROSS-SECTIONAL STUDY

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Abstract

Background: TADs have become increasingly popular in the orthodontic sector latest years as they reduce patient compliance requirements while increasing the number of treatment alternatives to better meet esthetic and occlusal treatment goals. Mini-implants obtain anchorage from jawbone, which increases control over orthodontic tooth movement and helps minimize side effects when treating misaligned teeth. There is little research on micro-screws, and the majority of them indicate that dental students are unaware of them. The aim of this study was to assess the level of knowledge about orthodontic mini screws among dental students in Saudi Arabia.

Materials and Methods: This study uses a structured questionnaire that the authors created as part of a cross-sectional study. The population of this study consists of Saudi dental students (male and female) from all six years of study and seventh year of internship in all dental colleges in Saudi Arabia. The Qualtrics calculator was used for estimating the sample size. The survey was used to gather information from students via Google Form and was then sent around various dental student groups. Those who answered the questionnaire during 2023-2024 AD were selected as participants in our study.

Results: 59.6%, exhibit a low level of knowledge and awareness in this area, while 37.7% demonstrate a moderate level. However, 2.7% of students possess a high level of understanding. There is also statistically significant relation to the level of education (p value= 0.002).

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Conclusion: This study gave us insights about the knowledge associated with the use of orthodontic TADs among the dental students. There is overall low level of knowledge (60%) as regard minimplants among dental students. Thus, introducing the topic of TADs earlier in the undergraduate dental program will enhance the students' case-based learning setup. Hence, the early exposure to use of TADs will improve the students' clinical problem-solving and decision-making skills during their undergraduate clinical years.

Keywords: Mini Implants, Orthodontic Anchorage, Temporary anchorage devices.

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Introduction:

Through the use of force and the conversion of mechanical stimulation into a biologic reaction, teeth can be moved during orthodontic therapy, it takes either inter-arch or intra-arch anchoring to produce differential tooth movement. In orthodontics, anchorage is crucial, and its management is required for the greatest outcomes [1]. To manage anchoring, orthodontists have employed teeth, intraoral, and extraoral appliances. However, before the emergence of mini-orthodontic implants, the field of orthodontics was somewhat unable to resolve this issue [2]. The concept of anchorage refers to stopping unintentional tooth movement. Mini-implants obtain anchorage from jawbone, which increases control over orthodontic tooth movement and helps to minimize side effects when malocclusions are managed [3]. Unlike prosthetic implants, the stability of MIs is primarily derived from mechanical retention with partial osseointegration, whereas prosthetic implants indicate full osseointegration [4]. Mini-screws are also known as TADs (Temporary Anchorage Devices), Micro-implants, or Ortho-implants. With the introduction of TADS, the area of clinical orthodontics faced a huge change [5]. TADs have been increasingly popular in the orthodontic sector due to their potential to decrease the requirement for patient compliance while increasing the number of treatment alternatives to better fit esthetic and occlusal treatment goals [6]. Before the development of mini-implants: Active distalization, increased anchoring, etc. were performed via extra-oral traction, and that need significant for patient compliance. Now regardless of the patient's compliance, a single, continuous force of a mild to moderate size is produced [7]. Gainsforth and Higley gave the first record idea of skeletal anchorage at (1945) [8]. first clinical trial was done for correction of severe deep bite by intrusion of upper incisors using the TAD in the anterior nasal spine, this clinical trial was given by Creekmore and Eklund (1983) [9]. The approach did not immediately become popular since it was too soon to try it in a clinical setting without enough knowledge about reliability or pathophysiology. With the mandibular incisors protruding 6 mm and a mini-screw (1.2 mm in diameter; 6 mm in length), Kanomi reported the first successful case in (1997) [10]. Nowadays, orthodontic mini-implants are used commonly due to their many advantages and variety of treatment possibilities [11]. In 2020, K. Thirumagal et al. carried out a survey regarding the familiarity and understanding of orthodontic mini-implants among dental undergraduates at Saveetha University. The findings indicated that 62% of participants were acquainted with morse taper in implants, while the remaining 38% lacked awareness of this concept. However, the study had certain constraints, including a relatively small sample size and a specific focus on morse implant design [12]. A similar study conducted by Abu Al-Melh et al. at Kuwait University revealed that the survey indicated 65.3% of dental students were educated about orthodontic Temporary Anchorage Devices (TADs) as part of their undergraduate orthodontic curriculum. Furthermore, 11.1% of dental students acquired knowledge about orthodontic TADs through alternative channels like social media and promotional campaigns. However, this study was limited by the distribution of participants, as all participants were from one university [13]. A closely related study was undertaken within the Saudi Arabian population.

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Published in 2023 by Alotaibi et al., this study revealed that 61% of the participants expressed their inadequacy in identifying cases that could benefit from orthodontic Temporary Anchorage Devices (TADs). Notably, a considerable proportion of dental students across various academic years advocated for the incorporation of TADs into the fifth-year curriculum. It is worth mentioning, however, that certain participants in this study were unable to provide detailed information about their undergraduate dental curriculum as mentioned by the author [14]. In Saudi Arabia, the topic of mini implants limited attention, particularly among students, with previous research predominantly focusing on orthodontists rather than addressing the students' perspective. Furthermore, existing studies have used varying sample sizes, resulting in divergent outcomes, while incomplete questionnaires have hindered a comprehensive understanding of students' awareness and knowledge. Addressing these limitations through further research encompassing a broader range of dental students and employing more comprehensive surveys is essential to gain valuable insights into the topic's significance and impact within the student community.

Objectives:

The main objective of this study was to assess the knowledge level among general dental students about orthodontics mini screws in Saudi Arabia.

Materials and Methods:

Study design:

This study used a structured questionnaire that the authors had created as part of an across-sectional study questionnaire survey.

Study setting: Participants, recruitment, and sampling procedure:

The population of this study consisted of Saudi undergraduate dental students (both male and female) from all six years of study and the seventh-year internship at all dental colleges in Saudi Arabia. Participants were selected among those who respond to the questionnaire during 2023-2024.

Inclusion and Exclusion criteria:

Adult males and females' dental students from level 3 to level 14 were included. all graduated dental students who completed the seventh internship were excluded.

Sample size:

The required sample size was determined to be 384 individuals based on calculations performed by (Raosoft, Inc., Seattle, WA, USA). This calculation involved using the provided formula and incorporating means and standard deviation. The selection of a 95% confidence interval along with a standard deviation of 1.96 and a maximum acceptable marginal error of 0.05 contributed to this

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determination. Thus, the study necessitates a minimum sample size of $n=(1.96)^2 \times 0.50 \times 0.50 / (0.50)^2$, resulting in 384 participants.

Method for data collection and instrument (Data collection Technique and tools):

The tools used were self-evaluation questionnaires developed by Google Forms first to measure the knowledge and awareness levels of mini-implants among dental students in KSA.

Data collection was done in the form of participants' responses to the questions. the questionnaire included demographic features such as age, gender level of dental student.

Theparticipants were asked about knowledge of temporary anchorage devices' advantages, 'disadvantages, use, and side effects.

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Scoring system of knowledge & awareness:

There were nineteen questions in this part and the students were asked regarding their knowledge and awareness level toward the orthodontic mini-screws in dentistry. Thirteen questions have two options. A correct answer was given (1 score), whereas a (0 score) was given for the wrong answer, Four questions have more than 2 options, but all the answers are wrong it's carry a (score 0) and only one is correct and carries a (score 1), just One question has more than one correct choice and the correct answers of it have (1 score) were as the wrong answer has (0 score). One question had 4 scores (0 score) for No knowledge at all, (1 score) for Poor, (2 score) for Fair, and (3 score) for Well. Total knowledge scores were categorized into 3 levels based on Bloom's cut 80 %-100% (high level),60%-79% (moderate level) and \leq 59% (low level), The scores for knowledge varied from 1 to 22 points, and were classified into three levels as follows: High level (18 points or more.),Moderate level (14-17 points), Low level (13 points or less).

Analyzes and entry method:

Software program for Windows (2016). Then, in order to perform a statistical analysis, the data was transferred to the SPSS application, version 20 (IBM SPSS Statistics for Windows, Version 20.0 Armonk, NY: IBM Corp.). Data was input using the Microsoft Excel application for Windows (2016) after being collected. The Statistical-Package of Social-Science Software (SPSS) application, version 20, was then used to import the data being assessed statistically.

Results:

Table (1): Offers valuable insights into the demographics and academic performance of the participants. The distribution of participants based on age reveals a relatively even spread, with a significant portion (39.2%) falling within the 25 years or older category. The gender distribution skews towards females, comprising 65.3% of the sample. In terms of residential areas, the southern region appears to have the highest representation at 55.9%, while the northern region has the lowest at 5.2%. The level of education is varied, with interns constituting the largest group at 45.6%. Notably, the majority of participants (53.7%) achieved an excellent cumulative GPA, indicating a high level of academic performance.

Table (1): Sociodemographic characteristics of participants (n=406)

Parameter		No.	Percent (%)
Age (in years)	25 years or older	159	39.2
-ge (iii years)	24	76	18.7
	23	69	17.0
	22	56	13.8
	21 or less	46	11.3
Gender	Male	141	34.7
	Female	265	65.3
Residential area	Southern region	227	55.9
	Center region	70	17.2
	Western region	45	11.1
	Eastern region	43	10.6
	Northern region	21	5.2
Level of	3rd year	53	13.1
education	4th year	55	13.5
	5th year	59	14.5
	6th year	54	13.3
	Intern	185	45.6
Current cumulative grade point average (GPA)	Excellent (no less than 3.50 out of 4.00) OR (no less than 4.50 out of 5.00)	218	53.7
	Very good (from 2.75 to 3.49 out of 4.00) OR (from 3.75 to 4.49 out of 5.00)	137	33.7
	Good (from 1.75 to 2.74 out of 4.00) OR (from 2.75 to 3.74 out of 5.00)	26	6.4
	Satisfactory (from 1.00 to 1.74 out of 4.00) OR (from 2.00 to 2.74 out of 5.00)	25	6.2

Figure (1): Illustrates having heard of mini-screws among the participants (n=406)

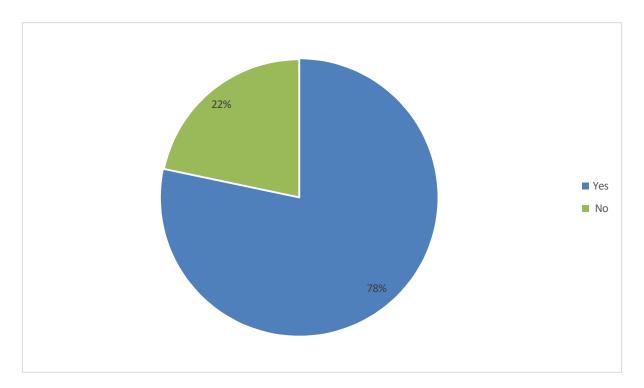


Table (2): Provides valuable insights into the awareness, knowledge, and perceptions of dental students regarding orthodontic mini-implants. The study reveals that a significant majority of the respondents, 78.3%, are aware of mini-implants, also known as micro-implants, mini-screws, and Temporary Anchorage Devices. However, it is noteworthy that 21.7% of the participants indicated a lack of awareness in this regard. Furthermore, 61.1% of the respondents reported receiving information about orthodontic mini-implants during their undergraduate education, while 38.9% did not receive such information, indicating a disparity in exposure to this topic within the curriculum. When asked about their knowledge of micro implants for orthodontics, 36.7% rated their knowledge as fair, 27.6% as well, 23.6% as poor, and 12.1% claimed to have no knowledge at all. This distribution suggests variations in the depth of understanding among the respondents. Additionally, when queried about the main advantages of using orthodontic micro implants, 48.5% cited skeletal anchorage as the primary advantage, while 23.6% mentioned tooth replacement, indicating a substantial awareness of the benefits of these devices. However, 15.5% claimed to have no knowledge in this area, highlighting a knowledge gap that warrants attention. In terms of the material used to make orthodontic micro implants, 31.3% identified pure titanium as the most commonly used material, while 29.6% admitted to not knowing, underscoring the need for further education on this aspect. The data also shed light on potential issues associated with mini-screws, with 51.9% expressing concerns about the loosening of the screw, 33.7% highlighting the risk of trauma to the roots and the periodontal ligament, and 21.2% mentioning carcinogenicity as a potential issue. This indicates a nuanced understanding of the challenges associated with mini-implants. Furthermore, when asked if mini-implants need complete osseointegration, 40.6%

responded affirmatively, 33.7% disagreed, and 25.6% claimed not to know, revealing varying perspectives on this critical aspect.

Moreover, the study highlighted a lack of consensus on certain aspects, such as the placement of orthodontic implants in specific situations and the use of mini-screws as an alternative to traditional anchorage systems in heavy smoker patients. Additionally, the data indicated varying levels of awareness regarding the relationship between insulin-dependent diabetes and the failure of orthodontic mini-implants, as well as the consideration of disadvantages associated with micro-implants. Notably, 47.5% of respondents believed that doctors can apply micro-implants in a patient's mouth without worrying about infection control, while 25.6% disagreed with this statement, underscoring differing perceptions in this area. Finally, the overwhelming preference for orthodontic implants as a source of anchorage in uncooperative patients, as indicated by 83.3% of the respondents, highlights the potential significance of mini-implants in addressing specific patient needs. Overall, the data from this study provides valuable insights into the current knowledge, awareness, and perceptions of dental students in Saudi Arabia regarding orthodontic mini-implants, highlighting areas of strength and opportunities for further education and clarification. This information can serve as a foundation for enhancing the understanding and utilization of mini-implants within the dental education curriculum and clinical practice, ultimately contributing to improved patient care and outcomes in the field of orthodontics.

Table (2): Parameters related to knowledge and awareness score among the participants. (n=406).

	0 1		,
Parameter		No.	Percent
1- Are you aware of mini-implants? Other name: micro-implant, mini-	Yes	318	78.3
screws, and Temporary Anchorage Device	No	88	21.7
2-During your orthodontic undergraduate education, did you	Yes	248	61.1
get any information about orthodontic mini-implants?	No	158	38.9
3- How much do you know about	Fair	149	36.7
micro implants (screws) for orthodontics?	Well	112	27.6
	Poor	96	23.6
	No knowledge at all	49	12.1
4- What are orthodontic	Implants for orthodontic treatment	259	63.8
(Temporary Anchorage Devices)	Implants for orthognathic surgeries	81	20.0

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mini screws?	I don't know	66	16.2
5- What are the main advantages of	Skeletal anchorage	197	48.5
using orthodontic micro implants (screws)?	Tooth replacement	96	23.6
	I don't know	63	15.5
	Soft tissue anchorage	50	12.3
6- Which material is most often	Pure titanium	127	31.3
used to make orthodontic micro implants (screws)?	I don't know	120	29.6
	Titanium and chrome	95	23.4
	Titanium and copper	64	15.8
7- What potential issues might arise	Loosening of the screw	211	51.9
with Mini-screws?**	Loosening of the screw and trauma to the roots and the PDL	137	33.7
	Trauma to the roots and the PDL	229	56.4
	Carcinogenicity	86	21.2
	Creates gray to black gingival pigmentation	132	32.5
8- Do you think the mini-implants need complete osseointegration?	Yes	165	40.6
need complete observategration	No	137	33.7
	I don't know	104	25.6
9- Can developing patients with	Yes	144	35.5
mixed dentition use orthodontic	No	137	33.7
mini-screws	I don't know	125	30.8
10- Do you think that micro	Yes	196	48.3
implants (screws) cost a lot of money compared to traditional	I don't know	119	29.3
anchorage devices?	No	91	22.4
11- In what all situations	Correction of canted occlusal plane, Molar intrusion, Molar	138	34.0

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orthodontic implants are placed?	mesialization, Molar distalization, and Intrusion of incisors		
	I don't know	114	28.1
	Closure of extraction spaces, Molar intrusion, Molar mesialization, intrusion of incisors	87	21.4
	Correction of canted occlusal plane, molar intrusion,molar distalization, intrusion of incisors	67	16.5
v	Yes	208	51.2
implants often have a diameter of less than 3mm?	I don't know	135	33.3
	No	63	15.5
13- Are mini-screws (Temporary	I don't know	193	47.5
Anchorage Devices) used as an alternative to traditional anchorage systems in heavy smoker patients?	Yes	109	26.8
	No	104	25.6
14 - is there a relationship between	Yes	205	50.5
insulin-dependent diabetes and failure of orthodontic mini-	I don't know	133	32.8
implants?	No	68	16.7
15- Did you consider whether	Yes	247	60.8
micro-implants had any disadvantages?	I don't know	115	28.3
	No	44	10.8
16-One advantage of using a micro-	True	193	47.5
implant is that doctors can apply it in a patient's mouth without	I don't know	109	26.8
worrying about infection control?	False	104	25.6
17- From your perspective, which	Orthodontic implant	338	83.3
one would you recommend as a source of anchorage in uncooperative patients?	Extra oral anchorage	68	16.7

^{**=} Results may overlap.

Table 3 shows that the majority of the participant dental students, comprising 59.6%, exhibit a low level of knowledge and awareness in this area, while 37.7% demonstrate a moderate level. However, it is encouraging to note that 2.7% of students possess a high level of understanding. These figures underscore the importance of further educational initiatives and resources aimed at enhancing the knowledge and awareness of orthodontic mini screws among dental students in Saudi Arabia.

Table (3): Shows knowledge and awareness about orthodontic mini-screws score results.

	Frequency	Percent
High level	11	2.7
Low level	242	59.6
Moderate level	153	37.7
Total	406	100.0

Figure (2): knowledge and awareness about orthodontic mini-screws score results among participants (n=406)

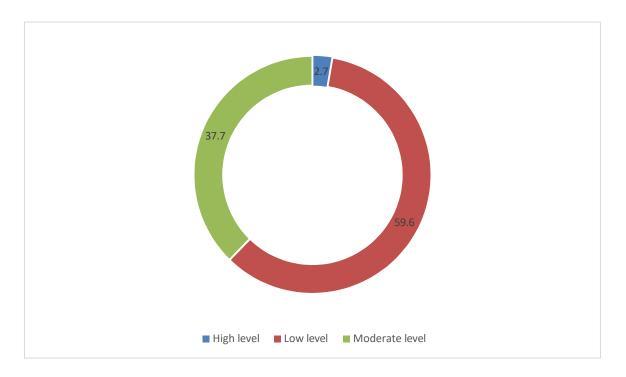


Table 4 shows that the level of knowledge and awareness of mini-implants among dental students is statistically significant related to their level of education (p value= 0.002). It also shows statistically insignificant relation to gender, residential area, and current cumulative GPA.

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Table (4): Relation between level of knowledge and awareness and sociodemographic parameters. (n=406).

Parameter		Level of knowledge and awareness		Total (N=406)	P value*
		Moderate or	Low	-	
		high level	level		
Gender	Male	77	64	141	0.082
		31.8%	39.0%	34.7%	_
	Female	165	100	265	_
		68.2%	61.0%	65.3%	_
Residential area	Western region	27	18	45	0.726
		11.2%	11.0%	11.1%	_
	Southern region	138	89	227	_
		57.0%	54.3%	55.9%	_
	Northern region	12	9	21	_
		5.0%	5.5%	5.2%	_
	Eastern region	28	15	43	_
		11.6%	9.1%	10.6%	_
	Center region	37	33	70	_
		15.3%	20.1%	17.2%	_
Current cumulative grade point average	Very good (from 2.75 to 3.49 out of 4.00) OR (from 3.75 to	81	56	137	0.487
(GPA)	4.49 out of 5.00)	33.5%	34.1%	33.7%	
	Satisfactory (from 1.00 to 1.74	12	13	25	_
	out of 4.00) OR (from 2.00 to 2.74 out of 5.00)	5.0%	7.9%	6.2%	_
	Good (from 1.75 to 2.74 out of	18	8	26	_
	4.00) OR (from 2.75 to 3.74 out of 5.00)	7.4%	4.9%	6.4%	_

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	Excellent (no less than 3.50 out of 4.00) OR (no less than 4.50 out of 5.00)	131	87	218	
		54.1%	53.0%	53.7%	
Level of education	Intern	105	80	185	0.002
		43.4%	48.8%	45.6%	_
	6th year	26	28	54	_
		10.7%	17.1%	13.3%	
	5th year	37	22	59	
		15.3%	13.4%	14.5%	_
	4th year	30	25	55	_
		12.4%	15.2%	13.5%	
	3rd year	44	9	53	
		18.2%	5.5%	13.1%	_

^{*}P value was considered significant if ≤ 0.05 .

Discussion:

Orthodontic anchorage is commonly known as resistance to unwanted tooth movement [15]. Orthodontic skeletal Temporary Anchorage Devices (TADs), also known as miniscrews or miniimplants, are small titanium screws that are placed in the vestibular or palatal mucosa through the bone to create an independent rigid anchor unit. Moreover, TADs can be connected to nearby teeth to reinforce anchorage [16, 17]. TADs are commonly used in orthodontic treatment for a variety of reasons to enhance anchorage [18, 19]. TADs allow dental movement to be achieved at the transverse, vertical, and anterior-posterior planes without adverse effects and are sometimes necessary for optimal treatment [20, 21]. It has been shown that TADs are well accepted by the orthodontists and patients, and they are safe and effective treatment options for comprehensive orthodontic treatments [22, 23]. TADs are used for several purposes which include the retraction of anterior teeth, molar protraction or distalization, intrusion of the dentition, extrusion of impacted teeth, expansion of the arch, and orthopaedic correction of cases with maxillary deficiency. Other uses of TADs involve molar uprighting, enhancing anchorage in periodontally compromised dentition and correction of occlusal cants [24, 25]. Nowadays, orthodontic mini-implants are used commonly due to their many advantages and variety of treatment possibilities. The major drawback while using mini-screws appears to be failure due to mini-screw loosening. The reason for loose screws appears to be multi-factorial and is a disconcerting and unpredictable reality which we have to embrace in our clinical practice.

The main objective of this study is to measure the knowledge level among general dental students about orthodontics mini screws in Saudi Arabia.

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Regarding the knowledge and awareness about orthodontic mini-screws score, 59.6%, exhibit a low level of knowledge and awareness in this area, while 37.7% demonstrate a moderate level. However, it is encouraging to note that 2.7% of students possess a high level of understanding. When asked about their knowledge of micro implants for orthodontics, 36.7% rated their knowledge as fair, 27.6% as well, 23.6% as poor, and 12.1% claimed to have no knowledge at all. In terms of the material used to make orthodontic micro implants, 31.3% of our study participants identified pure titanium as the most commonly used material, while 29.6% admitted to not knowing. On the other hand, a study conducted by Manal M. Abu Al-Melh et.al [26], revealed that the overall knowledge about TADs were 29.2, 38.9, and 13.9% of the participants obtained poor, fair, and satisfactory knowledge scores, respectively. About the composition of the orthodontic TADs, around half of all dental students (48.6%) selected the correct answer "pure titanium" and one-third (36.1%) did not know the answer which is higher than our results. Another study conducted in Saudi arabia, revealed that approximately 35.6% chose the material composition of orthodontic TAD as "titanium and stainless steel," whereas 36.9% did not know the answer which is higher than our results. [27]

In 2020, K. Thirumagal et al. [28] carried out a survey regarding the familiarity and understanding of orthodontic mini-implants among dental undergraduates at Saveetha University. The findings indicated that 62% of participants have satisfactory knowledge about TADs, while the remaining 38% lacked awareness of this concept which is relatively lower than our findings in this topic. A similar study conducted at Kuwait University [29], revealed that the survey indicated 65.3% of dental students were educated about orthodontic Temporary Anchorage Devices (TADs) as part of their undergraduate orthodontic curriculum. Furthermore, 11.1% of dental students acquired knowledge about orthodontic TADs through alternative channels like social media and promotional campaigns. A closely related study was undertaken within the Saudi Arabian population. Published in 2023 by Alotaibi et al. [30], this study revealed that 61% of the participants expressed their inadequacy in identifying cases that could benefit from orthodontic Temporary Anchorage Devices (TADs). Notably, a considerable proportion of dental students across various academic years advocated for the incorporation of TADs into the fifth-year curriculum. Regarding the main advantages of using orthodontic micro implants, 48.5% of our study participant cited skeletal anchorage as the primary advantage, while 23.6% mentioned tooth replacement, indicating a substantial awareness of the benefits of these devices. However, 15.5% claimed to have no knowledge in this area. However, another study conducted in Saudi arabia [31], revealed that the third-, fourth-, and fifth-year students did not know the advantage of orthodontic TADs. Findings suggest that junior students lack basic knowledge about TADs. As regard TADs usage among developing patients, our study revealed differing opinions regarding the use of mini-screws in developing patients with mixed dentition, as well as the cost comparison between micro implants and traditional anchorage devices, demonstrating the need for further education and clarification. On the contrary, the literature review showed that TADs combined with intraoral elastics in growing patients had significant benefits in terms of esthetic, functionality, and long-term stability. [32,33,34,35] regarding the disadvantages of micro implants, 51.9% of our study participants expressed concerns about the loosening of the screw, which is similar to the results of other surveys. [36, 37]

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Conclusion:

This study gave us insights about the knowledge associated with the use of orthodontic TADs among the dental students, there is 59.6%, exhibit a low level of knowledge and awareness in this area, while 37.7% demonstrate a moderate level. However, it is encouraging to note that 2.7% of students possess a high level of understanding. There is also statistically significant relation to the level of education (p value= 0.002), and there is a statistically insignificant relation to gender, residential area, and current cumulative GPA. There is overall low level of knowledge (60%) as regard mini-implants among dental students. Thus, introducing the topic of TADs earlier in the undergraduate dental program will enhance the students' case-based learning setup. Hence, the early exposure to use of TADs will improve the students' clinical problem-solving and decision-making skills during their undergraduate clinical years.

Acknowledgement:

We thank the participants who all contributed samples to the study.

Ethical approval

Ethical approval was obtained from the research ethics committee of King Abdulaziz university. An informed consent was obtained from each participant after explaining the study in full and clarifying that participation is voluntary. Data collected were securely saved and used for research purposes only.

Funding

The study did not receive any external funding.

Conflict of interests

The authors declare that there are no conflicts of interest.

Informed consent:

Written informed consent was obtained from all individual participants included in the study.

Data and materials availability

All data associated with this study are present in the paper.

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