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Article

Global Prevalence and Drivers of Dental Students' COVID-19 Vaccine Hesitancy

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Abstract: Background: Acceleration of mass vaccination strategies **Abstract:** Background: Acceleration of mass vaccination strategies is the only pathway to overcome the COVID-19 pandemic. Healthcare professionals and students have a key role in shaping public opinion about vaccines. This study aimed to evaluate the attitudes of dental students globally towards COVID-19 vaccines and explore the potential drivers for students' acceptance levels; Methods: A global cross-sectional study was carried out in February 2021 using an online questionnaire. The study was liaised by the scientific committee of the International Association of Dental Students (IADS), and data was collected through the national and local coordinators of IADS member organizations. The dependent variable was the willingness to take the COVID-19 vaccine, and the independent variables included demographic characteristics, COVID-19-related experience, and the drivers of COVID-19 vaccine-related attitude suggested by the WHO-SAGE; Results: A total of 6639 students from 22 countries representing all world regions responded to the questionnaire properly. Their mean age was 22.06 ± 2.79 (17-40) years, and the majority were females (70.5%), in clinical years (66.8%), and from upper-middle-income economies (45.7%). In general, 22.5% of dental students worldwide were hesitant, and 13.9% rejected COVID-19 vaccines. The students in low- and lower-middle-income (LLMI) economies had significantly higher levels of vaccine hesitancy compared to their peers in upper-middle- and high-income (UMHI) economies (30.4% vs 19.8%; $p < 0.001$); Conclusions: The global acceptance level of dental students for COVID-19 vaccines was suboptimal, and their worrisome level of vaccine hesitancy was influenced by the socioeconomic context where the dental students live and study. The media and social media, public figures, insufficient knowledge about vaccines, and mistrust of governments and the pharmaceutical industry were barriers to vaccination. The findings of this study call for further implementation of epidemiology (infectious diseases) education within undergraduate dental curricula.

Keywords: COVID-19 Vaccines, Cross-Sectional Studies, Decision Making, Dental Education, Dental Students, International Association of Dental Students, Mass Vaccination, Multicenter Study, Social Determinants of Health

1. Introduction

Vaccine hesitancy (VH) is defined by the World Health Organization (WHO) Strategic Advisory Group of Experts on Immunization (SAGE) as "delay in acceptance or refusal of vaccination despite the availability of vaccination services".[1] Given the urgency of

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mass vaccination against severe acute respiratory syndrome – coronavirus 2 (SARS-CoV-2) strategies, VH is increasingly recognized as a serious public health threat that requires thorough investigation among various population groups to fully understand its drivers as well as its prevalence.[2],[3] However, healthcare workers (HCWs) are usually perceived by their patients as the most reliable information source about vaccines; this group sometimes shows different levels of VH.[4],[5] Karafillakis *et al*. 2016 found that the fear of vaccine side effects, apprehension of new vaccines due to lack of safety data, and mistrust of pharmaceutical companies due to financial interests were the most prominent drivers of VH among HCWs in Europe.[6] Unfortunately, all these issues are relevant to the context of coronavirus disease 2019 (COVID-19) vaccines recently produced through intensified manufacturing processes and used based on emergency use authorization (EUA).[7]

Dental students represent a particular subset of the healthcare students population who will play a key role in shaping their patients' health-related attitudes and behaviours in the near future, as they are perceived as role models of a healthy lifestyle.[8] Adopting positive health-related beliefs and attitudes by HCWs increases their preparedness and capacity to counsel patients on behavioural changes.[9] Therefore, self-care is a core competency of medical education and a cost-effective public health policy for sustainable health promotion.[10],[11] Moreover, medical students retain the highest levels of health-related knowledge and attitudes, making them the opinion leaders of public health issues among the university students community.[12]

Additionally, dental students differ from the general university student population because they are prone to an increased risk of contracting infectious diseases as part of their clinical training requirement.[13] Therefore, they are obliged to receive certain vaccines prior to joining the clinical years of their undergraduate courses, including hepatitis B, tetanus, and influenza vaccines.[14] These aggressive policies had led to a significant increase of immunized dentists against a wide array of occupational infections during recent years in some low- and low-middle-income economies.[15],[16] Nevertheless, dental students' knowledge and attitudes towards the relatively novel and nonmandatory vaccines like the human papillomavirus (HPV) vaccine remained suboptimal in countries of various economic capacities, e.g. India, Saudi Arabia, and the United States of America (USA).[17]–[19]

Clinical-year dental students were found to have substantially higher levels of positive attitudes and knowledge towards HPV vaccine and hepatitis B, respectively, compared to their pre-clinical peers.[19],[20] Farsi *et al.* 2020 had found that female dental students showed a significantly higher level of HPV vaccine acceptance than their male peers.[19] Similarly, Rutkoski *et al*. 2020 found that female dental students were more knowledgeable about the HPV vaccine.[18] The conspiracy beliefs and misconception about the immunity system played a decisive role in decreasing the university students' acceptance level of the COVID-19 vaccine.[21] However, there is a lack of worldwide evidence on COVID-19 VH levels and their association with the economy, the indirect evidence suggests that economic hardship is a clear determinant of VH among individuals in the same country.[22] In a recent Italian cross-sectional study, the recovered COVID-19 patients showed substantial levels of VH towards the COVID-19 vaccine (59.2%) and influenza vaccine (54.6%).[23] Older age and previous 2019 influenza shots were the main predictors of positive attitudes towards vaccination.[23]

The primary objective of this study was to estimate the prevalence of COVID-19 VH among a global sample of dental students. The secondary objectives were to explore the potential drivers for VH of dental students and to evaluate their impact on students' acceptance of the COVID-19 vaccine.

2. Materials and Methods

2.1. Study Design

A cross-sectional survey-based study was carried out between February 6th – 28th, 2021 by the national and local member organizations of the International Association of

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Dental Students (IADS).[24] The study utilized an online self-administered questionnaire (SAQ) of multiple-choice items developed through KoBoToolbox (Harvard Humanitarian Initiative. Cambridge, MA. 2021).[25]

After ethical clearance, invitation emails were sent to all the national and local delegates of IADS to participate in this cross-sectional study aiming to evaluate the attitudes of dental students worldwide towards the COVID-19 vaccine. Online orientation sessions were held to demonstrate the study objectives and the role of national and local coordinators in this study who were primarily concerned with survey dissemination and data collection. The Standing Committee on Research and Education (SCORE) of IADS was in charge of supervising the whole project and facilitating communication among the national and local coordinators.[26] The study was conducted and reported according to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement for cross-sectional studies.[27]

2.2. Participants

The target population of this study was the undergraduate dental students in the participating countries. Given the global variability of dental education systems, students of the compulsory training year (dental interns) and the students who graduated within the last 12 months were included. The participation in this study was voluntary, and the participants were not financially compensated and received no other means of incentives to limit selection bias. All participants provided their digital informed consent prior to filling in the questionnaire, and they were offered to withdraw from the study at any moment before submitting their answers without justification.

The national and local coordinators used various methods to circulate the uniform resource locator (URL) of the questionnaire, including social media platforms (Facebook, Twitter, and Instagram), instant messaging groups (WhatsApp, and WeChat), and distribution lists of their organizations and universities.

2.3. Instrument

The SAQ consisted of 20 multiple-choice items that required on average 7 – 9 minutes to be completed, and it was divided into four categories; a) demographic data including gender, age, academic level, and country; b) COVID-19-related experience including the previous infection, providing care to a COVID-19 patient, having a COVID-19 patient within the social circle, and having a deceased COVID-19 patient with the social circle; c) willingness to take COVID-19 vaccine determined by a 5-point Likert scale, and d) the drivers of COVID-19 vaccine-related attitude. The items of the fourth category were adopted from the compendium validated by the WHO-SAGE.[2]

The impact of media/social media, influential leaders and gatekeepers, trust in government, trust in pharmaceutical companies, and personal, religious, and cultural values were selected as the contextual drivers, while the beliefs of health and natural immunity, and perceived knowledge sufficiency were depicted as the individual drivers. Out of the vaccine-specific drivers' group, the risk to benefit ratio of administering the COVID-19 vaccine, introducing a new vaccine, and the vaccine availability were selected.

A panel of experts in medical education and public health were invited to review the relevance, appropriateness, and clarity of the suggested questionnaire to determine its content validity. Consequently, 18 dental students were recruited to fill in the questionnaire twice with a minimum interval of 48 hours to evaluate its reliability. The mean Cohen's kappa coefficient of the test re-test was 81.83 ± 0.16 (0.55 – 1), indicating that the questionnaire retained a perfect level of reliability. (Table 1)

Table 1. The results of test re-test reliability.[1]

Participant	κ coefficient	Participant	κ coefficient
No. 1	0.81	No. 10	0.55

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No. 2	0.82	No. 11	1.00
No. 3	0.91	No. 12	0.70
No. 4	1.00	No.13	1.00
No. 5	1.00	No. 14	0.79
No. 6	0.61	No. 15	0.71
No. 7	0.57	No. 16	1.00
No. 8	1.00	No. 17	0.81
No. 9	0.63	No. 18	0.82

[1] Cohen's Kappa statistic *(κ)*; 0.01 – 0.20 as none to slight, 0.21 – 0.40 as fair, 0.41 – 0.60 as moderate, 0.61–0.80 as substantial, and 0.81–1.00 as perfect agreement. [28]

2.4. Ethical Considerations

The study protocol had been reviewed and approved by the Ethics Committee of the Faculty of Medicine, Masaryk University (MUNI) on January 20th, 2021 with reference No. 4/2021. The questionnaire collected no identifying personal data from the participants. The study data were collected and managed by MUNI in full compliance with the European General Data Protection Regulation 2016/679 (GDPR).[29]

2.5. Statistical Analysis

The Statistical Package for the Social Sciences (SPSS) version 27.0 (SPSS Inc. Chicago. IL. 2020) was used to perform all the statistical tests.[30] Primarily, descriptive analysis was performed for the demographic variables, COVID-19-related experience, willingness to take COVID-19 vaccine, and the drivers of COVID-19 vaccine-related attitude represented by frequencies, percentages, cumulative percentages, means, and standard deviations. Consequently, the students had been classified according to their academic level as pre-clinical (1st year and 2nd year) and clinical (3rd year – fresh graduate). The participating countries were also stratified into four groups according to the latest ranking of the World Bank (the fiscal year 2021) as low-income economies, lower-middle-income economies, upper-middle-income economies, and high-income economies.[31] Inferential statistics were carried out to evaluate the association of COVID-19 vaccine acceptance level and demographic variables using the Mann-Whitney U test and the Kruskal-Wallis test. Similarly, the vaccine acceptance level and its associated drivers were evaluated using the Mann-Whitney U test with a confidence level of 95% and significance value (p) ≤ 0.05.

3. Results

3.1. Demographic Characteristics

A total of 6680 students participated in this study, with 41 students filled in the questionnaire improperly; therefore, they were excluded from the final analyses. Out of the 6639 included students, 4682 (70.5%) females, 1836 (27.7%) males, 53 (0.8%) non-binary, and 68 (1%) preferred not to disclose their gender. The mean age of participants was 22.06 ± 2.79 (17–40) years. While 2206 (33.2%) participants were pre-clinical students, 4433 (66.8%) were in clinical years.

The participating students were from 22 countries; 57 (0.9%) from Albania, 183 (2.8%) from Canada, 169 (2.5%) from Croatia, 381 (5.7%) from Ecuador, 78 (1.2%) from Estonia, 416 (6.3%) from Indonesia, 388 (5.8%) from Iran, 354 (5.3%) from Iraq, 492 (7.4%) from Italy, 129 (1.9%) from Latvia, 107 (1.6%) from Lebanon, 291 (4.4%) from Lithuania, 350 (5.3%) from Malaysia, 153 (2.3%) from Nepal, 379 (5.7%) from Pakistan, 417 (6.3%) from Palestine, 389 (5.9%) from Portugal, 596 (9%) from Russia, 467 (7%) from Sudan, 283 (4.3%) from Tunisia, 386 (5.8%) from Turkey, and 174 (2.6%) from USA.

According to the latest ranking of the World Bank (the fiscal year 2021), 467 (7%) of the participants were from low-income economies, 1232 (18.6%) from lower-middle-income economies, 3035 (45.7%) from upper-middle-income, and 1905 (28.7%) from high-

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income economies.[31] According to the World Dental Federation (FDI) geographical categorization, 750 (11.3%) were from Africa, 738 (11.1%) from the Americas, 1298 (19.6%) from Asia-Pacific, 1266 (19.1%) from Eastern-Mediterranean, and 2587 (39%) from Europe.[32] (Table 2)

Table 2: Demographic characteristics of the participating dental students worldwide, February 2021

Variable	Outcome	Frequency	Percentage	Cumulative Percentage
Gender	Female	4682	70.5%	70.5%
	Male	1836	27.7%	98.2%
	Non-binary	53	0.8%	99%
	Prefer not to say	68	1%	100%
Age	17 – 22 years	4218	63.5%	63.5%
	23 – 40 years	2421	36.5%	100%
Academic Level	1st Year	979	14.7%	14.7%
	2nd Year	1227	18.5%	33.2%
	3rd Year	1422	21.4%	54.6%
	4th Year	1259	19%	73.6%
	5th Year	817	12.3%	85.9%
	6th Year	240	3.6%	89.5%
	Internship	322	4.9%	94.4%
	Fresh Graduate	373	5.6%	100%
Country	Albania	57	0.9%	0.9%
	Canada	183	2.8%	3.6%
	Croatia	169	2.5%	6.2%
	Ecuador	381	5.7%	11.9%
	Estonia	78	1.2%	13.1%
	Indonesia	416	6.3%	19.3%
	Iran	388	5.8%	25.2%
	Iraq	354	5.3%	30.5%
	Italy	492	7.4%	37.9%
	Latvia	129	1.9%	39.9%
	Lebanon	107	1.6%	41.5%
	Lithuania	291	4.4%	45.9%
	Malaysia	350	5.3%	51.1%
	Nepal	153	2.3%	53.4%
	Pakistan	379	5.7%	59.2%
	Palestine	417	6.3%	65.4%
	Portugal	389	5.9%	71.3%
	Russia	596	9.0%	80.3%
	Sudan	467	7.0%	87.3%
	Tunisia	283	4.3%	91.6%
	Turkey	386	5.8%	97.4%
	USA	174	2.6%	100%
	Africa	750	11.3%	11.3%

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Geographic Region	Americas	738	11.1%	22.4%
	Asia-Pacific	1298	19.6%	41.9%
	Eastern-Mediterranean	1266	19.1%	61%
	Europe	2587	39%	100%
Economic Level	Low-income Economy	467	7%	7%
	Lower-middle-income Economy	1232	18.6%	25.6%
	Upper-middle-income Economy	3035	45.7%	71.3%
	High-income Economy	1905	28.7%	100%

3.2. COVID-19-related Experience

A total of 1105 (16.6%) students reported that they had been previously infected by severe acute respiratory syndrome coronavirus–2 (SARS–CoV–2). The students from low- and lower-middle-income economies (LLMI) were significantly ($\chi 2$ = 13.81; p < 0.001) more infected by COVID-19 compared to the students from upper-middle- and high-income economies (UMHI), 19.5% vs 15.6% respectively. While 538 (31.7%) students from LLMI provided care to COVID-19 patients, 1270 (25.7%) students from UMHI provided such care with a statistically significant difference ($\chi 2$ = 22.64; p < 0.001).

The same pattern was found with having COVID-19 patients within students' social circles, as 1515 (89.2%) students from LLMI versus 4286 (86.8%) students from UMHI knew personally COVID-19 patients ($\chi 2$ = 6.65; p = 0.01); and with having deceased COVID-19 patients within students' social circles, as 945 (55.6%) students from LLMI versus 2086 (42.2%) students from UMHI reported to knew someone died from COVID-19 infection ($\chi 2$ = 91.41; p < 0.001). (Table 3)

The clinical students were significantly more affected by COVID-19 pandemic than their preclinical peers; as 17.6% vs 14.7% were previously infected ($\chi 2$ = 9.12; p = 0.003), 28.1% vs 25.5% provided care to COVID-19 patients ($\chi 2$ = 5.15; p = 0.023), 88.9% vs 84.2% knew personally COVID-19 patients ($\chi 2$ = 29.78; p < 0.001), and 47.4% vs 42.2% knew someone died from COVID-19 infection ($\chi 2$ = 15.86; p < 0.001).

Male students were significantly ($\chi 2$ = 22.67; p < 0.001) more infected by COVID-19 compared to their female peers, 19.8% vs 14.9% respectively. Also, 584 (31.8%) males versus 1170 (25%) females provided care to COVID-19 patients ($\chi 2$ = 31.18; p < 0.001). Contrarily, female students had knew personally COVID-19 patients more than male students, 87.8% vs 86.8% respectively ($\chi 2$ = 1.26; p = 0.268). Similarly, more females knew deceased COVID-19 patients, 45.9% vs 45.1% ($\chi 2$ = 0.32; p = 0.57).

The highest countries with previously infected students were Albania (43.9%), Iran (34.3%), Tunisia (31.1%), Lebanon (29%), Ecuador (24.9%), Russia (23.7%), and USA (20.1%). The highest countries with students providing care to COVID-19 patients were Iran (49.7%), Albania (49.1%), Tunisia (42%), Iraq (38.4%), Lebanon (36.4%), Palestine (35.3%), and Russia (33.4%).

Table 3: COVID-19-related experience of the dental students stratified by economic level, February 2021

Variable	LLMI	UMHI	Total	Sig.[1]
I had been infected by SARS-CoV-2	332 (19.5%)	773 (15.6%)	1105 (16.6%)	< 0.001
I had been caring for someone with COVID-19 infection	538 (31.7%)	1270 (25.7%)	1808 (27.2%)	< 0.001
I know someone who had COVID-19 infection	1515 (89.2%)	4286 (86.8%)	5801 (87.4%)	0.010
I know someone who had died from COVID-19 infection	945 (55.6%)	2086 (42.2%)	3031 (45.7%)	< 0.001

[1] Chi-squared test was used with a significance level ≤ 0.05.

3.3. COVID-19 vaccine-related attitudes

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Regarding their attitudes towards the COVID-19 vaccine, 491 (7.4%) students totally disagreed with taking the vaccine, 434 (6.5%) disagreed, 1494 (22.5%) were hesitant about taking the vaccine, 1495 (22.5%) agreed, and 2725 (41%) totally agreed. (Table 4)

The LLMI students were significantly ($\chi 2 = 82.26$; $p < 0.001$) more hesitant to take the vaccine than their UMHI peers, 30.4% vs 19.8%, respectively. The highest percentage of hesitant students from low-income economies (37.5%), followed by lower-middle-income economies (27.8%), upper-middle-income economies (25.2%), and high-income economies (11.1%). Similarly, the highest percentage of resistant students were from low-income economies (18.6%), and the lowest percentage was from high-income economies (7.3%). Contrarily, the lowest agreement level was in low-income economies (43.9%), followed by lower-middle-income economies (56.9%), upper-middle-income economies (58%), and high-income economies (81.6%).

Table 4: Dental students' attitudes towards COVID-19 vaccine stratified by economic level, February 2021

Variable	Outcome	LLMI	UMHI	Total	Sig.[1]
I am willing to take the COVID-19 vaccine once it becomes available to me.	Totally Disagree = 1	150 (8.8%)	341 (6.9%)	491 (7.4%)	0.009
	Disagree = 2	126 (7.4%)	308 (6.2%)	434 (6.5%)	0.089
	Not Sure = 3	517 (30.4%)	977 (19.8%)	1494 (22.5%)	< 0.001
	Agree = 4	441 (26%)	1054 (21.3%)	1495 (22.5%)	< 0.001
	Totally Agree = 5	465 (27.4%)	2260 (45.7%)	2725 (41%)	< 0.001
	Total (1-5)	3.56 ± 1.21	3.93 ± 1.23	3.83 ± 1.24	< 0.001

[1] Chi-squared and Mann-Whitney U test were used with a significance level ≤ 0.05.

3.4. Drivers of COVID-19 Vaccine-related Attitude

The LLMI students were more significantly ($U = 3436031$; $p < 0.001$) influenced by the reports they heard and read in media and social media compared to their UMHI peers, 42% vs 30.4%, respectively. They were also more significantly ($U = 3832308$; $p < 0.001$) influenced by celebrities, religious and political leaders, 21.3% vs 14.5%.

In terms of confidence in government and pharmaceutical companies, the UMHI students (37.9% and 51% respectively) were more significantly ($U = 3608480, 3526701$; $p < 0.001, < 0.001$ respectively) confident than their LLMI peers (27.1% and 37% respectively). While the UMHI students were more aware of people with religious and cultural values that retain them from taking vaccines, 25% vs 17% respectively; the LLMI students were more agreeable with this antivaccination stand, 18% vs 10.9% respectively.

Regarding the individual drivers, 38.1% of LLMI students thought that there was better were ways to prevent COVID-19 than using vaccines versus 22.4% of UMHI students $U = 3514137$; $p < 0.001$). Additionally, the UMHI students were significantly ($U = 3707403$; $p < 0.001$) more confident that they had enough information about COVID-19 vaccines and their safety compared to their LLMI peers, 33.1% vs 27%, respectively.

All the vaccine-specific drivers were significantly in favour of UMHI, as 54.4% of UMHI students had higher levels of beliefs that the benefits of COVID-19 vaccines outweigh their reported side effects compared to only 40.2% of LLMI students. Also, 45.2% of UMHI students were more inclined to take a newly introduced vaccine versus 37.6% of LLMI students. Similarly, 43.2% of UMHI students felt confident that their health centres would have COVID-19 vaccine whenever needed compared to only 33.6% of LLMI students. (Table 5)

Males had significantly higher levels of belief of natural immunity superiority over vaccines and perceived knowledge sufficiency ($U = 4139866, 3758515$; $p = 0.013, < 0.001$ respectively). Females had lower levels of confidence in government (34.6% vs 37.4%), confidence in pharmaceutical companies (47.5% vs 47.9%), belief that COVID-19 benefits outweigh its reported side effects (50.1% vs 53.5%), and inclination to take newly introduced vaccines (42.1% vs 46.8%). Across academic levels, the fresh graduates were the

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least informed about COVID-19 vaccine safety, and they were the most supportive of the belief of natural immunity superiority over vaccines.

Table 5: Dental students' vaccine-related attitudes drivers stratified by economic level, February 2021

Variable	Outcome	LLMI	UMHI	Total	Sig.[1]
Contextual Drivers					
Do reports you hear/read in the media/ on social media make you re-consider the choice to take the COVID-19 vaccine?	Yes = 2	713 (42%)	1504 (30.4%)	2217 (33.4%)	
	Not Sure = 1	464 (27.3%)	1055 (21.4%)	1519 (22.9%)	
	No = 0	522 (30.7%)	2381 (48.2%)	2903 (43.7%)	
	Total (0-2)	1.11 ± 0.85	0.82 ± 0.87	0.9 ± 0.87	< 0.001
Do celebrities, religious or political leader influence your decision about getting vaccinated?	Yes = 2	362 (21.3%)	716 (14.5%)	1078 (16.2%)	
	Not Sure = 1	227 (13.4%)	600 (21.1%)	827 (12.5%)	
	No = 0	1110 (65.3%)	3624 (73.4%)	4734 (71.3%)	
	Total (0-2)	0.56 ± 0.82	0.41 ± 0.73	0.45 ± 0.76	< 0.001
Do you trust that your government is making decisions in your best interest with respect to what vaccines are provided (e.g., your government purchases the highest quality vaccines available)?	Yes = 2	460 (27.1%)	1871 (37.9%)	2331 (35.1%)	
	Not Sure = 1	550 (32.4%)	1580 (32%)	2130 (32.1%)	
	No = 0	689 (40.6%)	1489 (30.1%)	2178 (32.8%)	
	Total (0-2)	0.87 ± 0.81	1.08 ± 0.82	1.02 ± 0.82	< 0.001
Do you trust pharmaceutical companies to provide credible data on COVID-19 vaccine safety and effectiveness vaccines?	Yes = 2	629 (37%)	2521 (51%)	3150 (47.4%)	
	Not Sure = 1	579 (34.1%)	1462 (29.6%)	2041 (30.7%)	
	No = 0	491 (28.9%)	957 (19.4%)	1448 (21.8%)	
	Total (0-2)	1.08 ± 0.81	1.32 ± 0.78	1.26 ± 0.79	< 0.001
Do you know anyone who does not take a vaccine because of religious or cultural values?	Yes = 2	289 (17%)	1234 (25%)	1523 (22.9%)	
	Not Sure = 1	181 (10.7%)	649 (13.1%)	830 (12.5%)	
	No = 0	1229 (72.3%)	3057 (61.9%)	4286 (64.6%)	
	Total (0-2)	0.45 ± 0.77	0.63 ± 0.86	0.58 ± 0.84	< 0.001
If "Yes", do you agree with these people?	Yes = 2	52 (18%)	135 (10.9%)	187 (12.3%)	
	Not Sure = 1	30 (10.4%)	162 (13.1%)	192 (12.6%)	
	No = 0	207 (71.6%)	937 (75.9%)	1144 (75.1%)	
	Total (0-2)	0.46 ± 0.78	0.35 ± 0.67	0.37 ± 0.69	< 0.001
Individual / Group Drivers					
Do you think that there are better ways to prevent COVID-19 than using vaccines (e.g., developing immunity by getting sick and recovered)?	Yes = 2	647 (38.1%)	1109 (22.4%)	1756 (26.4%)	
	Not Sure = 1	432 (25.4%)	1523 (30.8%)	1955 (29.4%)	
	No = 0	620 (36.5%)	2308 (46.7%)	2928 (44.1%)	
	Total (0-2)	1.02 ± 0.86	0.76 ± 0.8	0.82 ± 0.82	< 0.001
Do you feel you have enough information about COVID-19 vaccines and their safety?	Yes = 2	458 (27%)	1633 (33.1%)	2091 (31.5%)	
	Not Sure = 1	399 (23.5%)	1439 (29.1%)	1838 (27.7%)	
	No = 0	842 (49.6%)	1868 (37.8%)	2710 (40.8%)	
	Total (0-2)	0.77 ± 0.85	0.95 ± 0.84	0.91 ± 0.845	< 0.001
Vaccine-specific Drivers					
Do you think that the benefits of COVID-19 vaccines outweigh their reported side effects / adverse reactions?	Yes = 2	683 (40.2%)	2686 (54.4%)	3369 (50.7%)	
	Not Sure = 1	661 (38.9%)	1421 (28.8%)	2082 (31.4%)	
	No = 0	355 (20.9%)	833 (16.9%)	1188 (17.9%)	

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In general, when a new vaccine is introduced, are you inclined to consent on your vaccination?	**Total (0-2)**	1.19 ± 0.76	1.38 ± 0.76	1.33 ± 0.76	< 0.001
	Yes = 2	638 (37.6%)	2233 (45.2%)	2871 (43.2%)	
	Not Sure = 1	556 (32.7%)	1606 (32.5%)	2162 (32.6%)	
	No = 0	505 (29.7%)	1101 (22.3%)	1606 (24.2%)	
Do you feel confident that the health center or doctor's office will have the COVID-19 vaccine you need, when you need them?	**Total (0-2)**	1.08 ± 0.82	1.23 ± 0.79	1.19 ± 0.8	< 0.001
	Yes = 2	571 (33.6%)	2132 (43.2%)	2703 (40.7%)	
	Not Sure = 1	617 (36.3%)	1541 (31.2%)	2158 (32.5%)	
	No = 0	511 (30.1%)	1267 (25.6%)	1778 (26.8%)	
	Total (0-2)	1.04 ± 0.8	1.18 ± 0.81	1.14 ± 0.81	< 0.001

[1] Mann-Whitney U test was used with a significance level ≤ 0.05.

3.5. Demographic Determinants of COVID-19 Vaccine-related Attitude

The acceptance level of the COVID-19 vaccine ranged between 1 denoting "totally disagree", and 5 denoting "totally agree". The mean acceptance level of males was significantly (U = 4165947; p = 0.042) higher than females; it was also higher than non-binary students (3.47 ± 1.42) and the students who did not disclose their gender (3.44 ± 1.43).

The fifth-year students were the most accepting (3.93 ± 1.25); however, the interns were the least accepting (3.59 ± 1.26). Overall, the clinical students were significantly (U = 4655705; p = 0.001) more accepting compared to the pre-clinical students. (Table 6)

Table 6: Dental students' demographic determinants of COVID-19 acceptance, February 2021

Variable	Outcome	Acceptance Level	Sig.[1]
Gender	Female	3.83 ± 1.23	0.013
	Male	3.87 ± 1.26	
	Non-binary	3.47 ± 1.42	
	Prefer not to say	3.44 ± 1.43	
Academic Level	1st Year	3.73 ± 1.28	0.110
	2nd Year	3.81 ± 1.19	
	3rd Year	3.91 ± 1.19	
	4th Year	3.90 ± 1.25	
	5th Year	3.93 ± 1.25	
	6th Year	3.80 ± 1.31	
	Internship	3.59 ± 1.26	
	Fresh Graduate	3.66 ± 1.26	
Clinical Training	Preclinical (1st year & 2nd year)	3.77 ± 1.32	0.001
	Clinical (3rd year – Graduate)	3.86 ± 1.24	
Country	Albania	3.14 ± 1.27	< 0.001
	Canada	4.41 ± 1	
	Croatia	3.73 ± 1.26	
	Ecuador	3.86 ± 1.19	
	Estonia	3.62 ± 1.22	
	Indonesia	4.37 ± 0.89	
	Iran	3.38 ± 1.38	
	Iraq	3.27 ± 1.17	
	Italy	4.7 ± 0.8	

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	Latvia	3.8 ± 1.37	
	Lebanon	3.86 ± 1.18	
	Lithuania	4.18 ± 1.12	
	Malaysia	4.33 ± 0.91	
	Nepal	3.91 ± 1.04	
	Pakistan	3.97 ± 1.01	
	Palestine	3.72 ± 1.27	
	Portugal	4.57 ± 0.85	
	Russia	2.85 ±1.12	
	Sudan	3.37 ± 1.17	
	Tunisia	2.88 ± 1.2	
	Turkey	3.99 ± 1.11	
	USA	4.53 ± 1.04	
Geographic Region	Africa	3.18 ± 1.2	< 0.001
	Americas	4.15 ± 1.15	
	Asia-Pacific	4.19 ± 1	
	Eastern-Mediterranean	3.5 ± 1.29	
	Europe	3.91 ± 1.26	
Economic Level	Low-income Economy	3.37 ± 1.17	< 0.001
	Lower-middle-income Economy	3.63 ± 1.23	
	Upper-middle-income Economy	3.66 ± 1.25	
	High-income Economy	4.36 ± 1.07	

[1] Mann-Whitney U and Kruskal-Wallis tests were used with a significance level ≤ 0.05.

In the high-income group, Italy was the most accepting country (4.7 ± 0.8), followed by Portugal (4.57 ± 0.85) and USA (4.53 ± 1.04), while Estonia was the least accepting one (3.62 ± 1.22). In the upper-middle-income group, Indonesia was the most accepting country (4.37 ± 0.89), followed by Malaysia (4.33 ± 0.91) and Turkey (3.99 ± 1.11), while Russia was the least accepting one (2.85 ±1.12). Pakistan was the most accepting lower-middle-income country (3.97 ± 1.01), and Tunisia was the least accepting lower-middle-income country (2.88 ± 1.2). (Figure 1)

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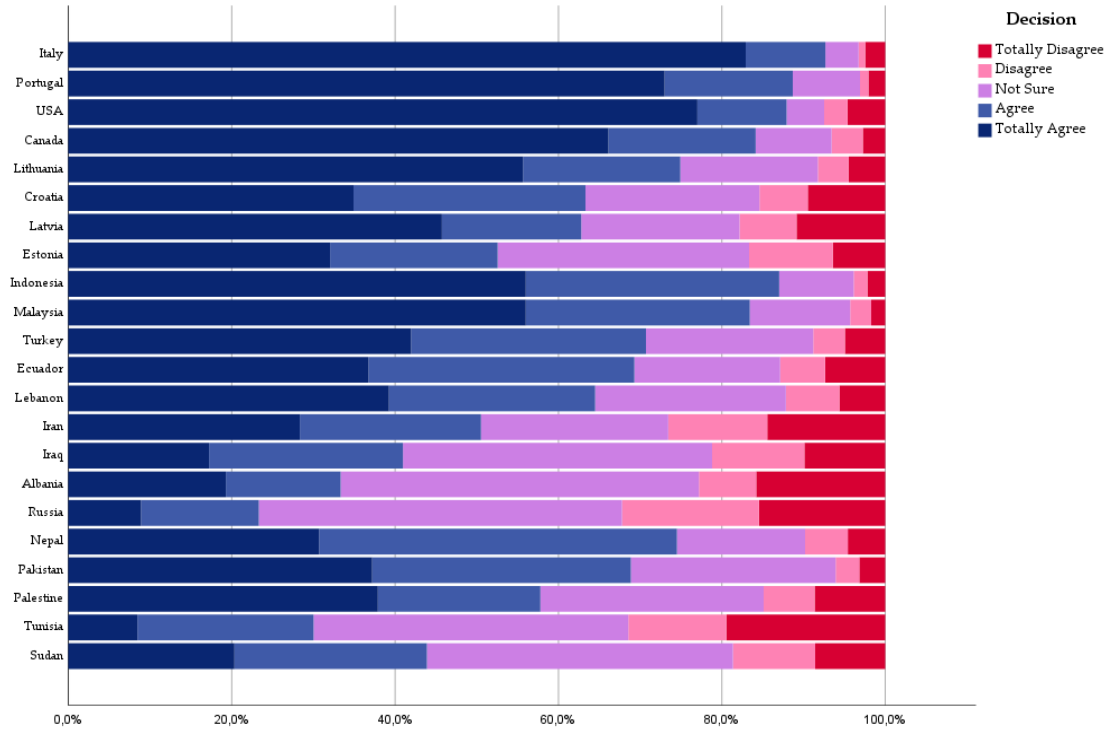
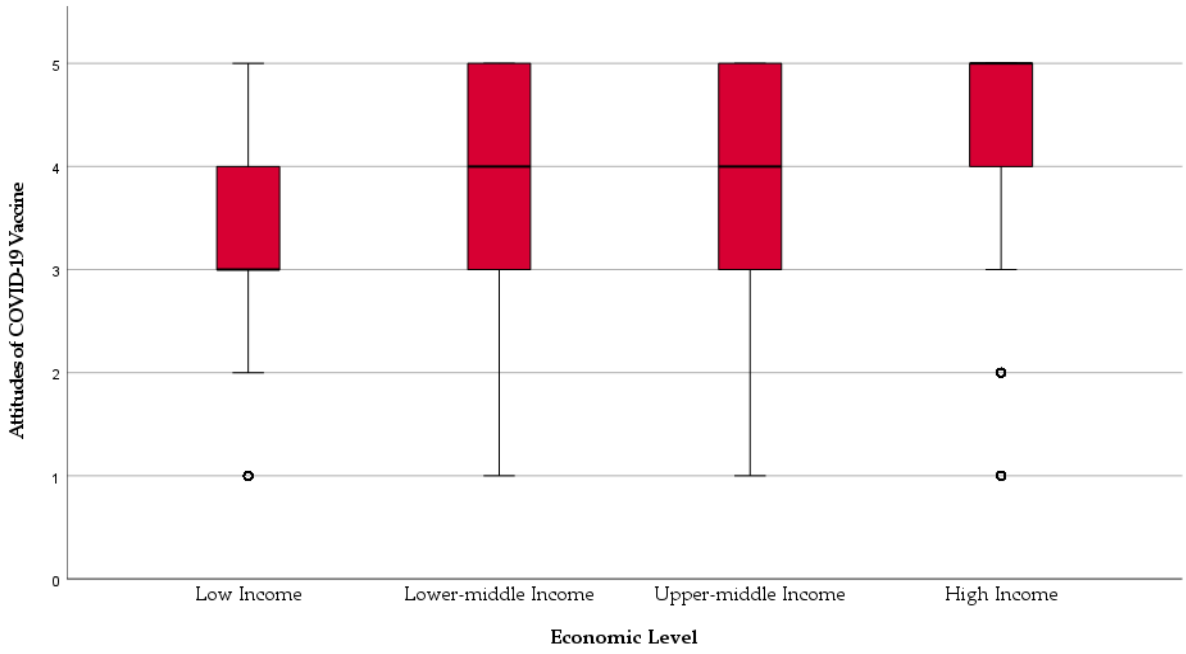


Figure 1: Dental students' COVID-19 vaccine acceptance level by state, February 2021

Africa was the least accepting region (3.18 ± 1.2), followed by Eastern-Mediterranean (3.5 ± 1.29), and the Americas was the most accepting region (4.15 ± 1.15). Across the economic ranking, vaccine acceptance level was gradually distributed with the least accepting was the low-income group (3.37 ± 1.17), and the most accepting was the high-income group (4.36 ± 1.07). The difference between lower-middle-income group (3.63 ± 1.23) and upper-middle-income group (3.66 ± 1.25) was slight and statistically insignificant (U = 1833237; p = 0.302). (Figure 2)



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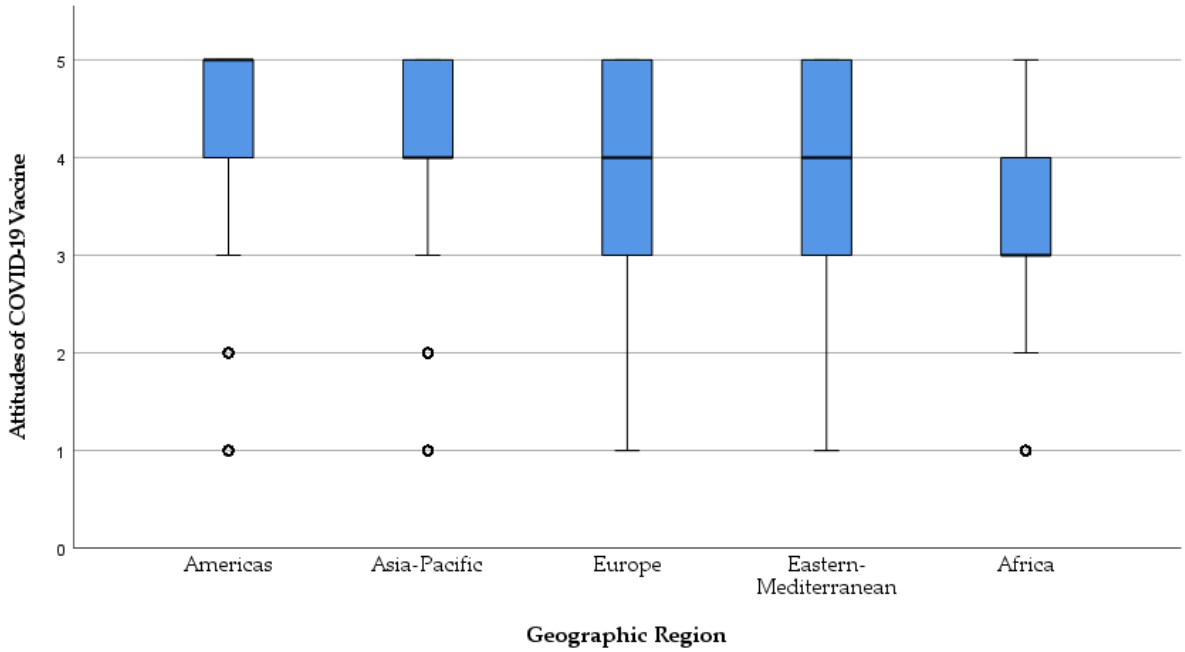

Figure 2: Dental students' COVID-19 vaccine acceptance by (a) economic level and (b) geographic region, February 2021

Regarding their COVID-19-related experience, the students who had been previously infected were significantly ($U = 2677855$; $p < 0.001$) less accepting (3.57 ± 1.36), also the students who provided care to COVID-19 patients were significantly ($U = 4004539$; $p < 0.001$) less accepting (3.68 ± 1.31). However, having a COVID-19 patient within students' social circles was significantly ($U = 2219499$; $p < 0.001$) associated with a higher acceptance level of COVID-19 vaccine (3.86 ±1.24), having a deceased COVID-19 patient within students' social circles was significantly ($U = 5175777$; $p < 0.001$) lowering the COVID-19 vaccine acceptance (3.77 ± 1.26). (Table 7)

Table 7: Dental students' COVID-19 vaccine acceptance and COVID-19-related experience, February 2021

Variable	No	Yes	Sig.[1]
I had been infected by SARS-CoV-2	3.88 ± 1.21	3.57 ± 1.36	< 0.001
I had been caring for someone with COVID-19 infection	3.89 ± 1.21	3.68 ± 1.31	< 0.001
I know someone who had COVID-19 infection	3.68 ± 1.25	3.86 ±1.24	< 0.001
I know someone who had died from COVID-19 infection	3.89 ± 1.22	3.77 ± 1.26	< 0.001

[1] Mann-Whitney U test was used with a significance level ≤ 0.05.

3.6. Drivers of Dental Students' COVID-19 Vaccine Acceptance

3.6.1. Contextual Drivers

Globally, the dependence on media and social media to inform vaccine-related decision was significantly ($U = 2678371$; $p < 0.001$) associated with a decreased level of vaccine acceptance (3.71 ± 1.21). Similarly, the reliance on public figures and opinion leaders was insignificantly ($U = 2495719$; $p = 0.236$) associated with a lower level of vaccine acceptance (3.82 ± 1.27).

The confidence in government was significantly ($U = 1467912$; $p < 0.001$) associated with a higher level of vaccine acceptance (4.29 ± 1.10), also the confidence in pharmaceutical companies improved vaccine acceptance (4.31 ± 1.06) significantly ($U = 1041773$; $p <$

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0.001). The students who agreed with the antivaccination stand based on cultural and religious values had significantly (U = 43532; p < 0.001) much lower levels of vaccine acceptance (2.75 ± 1.44).

3.6.2. Individual Drivers

The students who thought COVID-19 should be better prevented by natural immunity than by vaccines had a significantly (U = 1698349; p < 0.001) lower level of vaccine acceptance (3.35 ± 1.38). Additionally, the students with insufficient knowledge about COVID-19 vaccine safety had a significantly (U = 1766800; p < 0.001) lower level of vaccine acceptance (3.48 ± 1.19).

3.6.3. Vaccine-specific Drivers

The COVID-19 vaccine acceptance level was significantly decreased in the students who did not think that vaccine's benefits outweigh its reported side effects, the students who were not inclined to take newly introduced vaccines, and the students who were not confident of finding the vaccine in their local health centre when needed (U = 1010578, 974557, 1608552; p < 0.001, < 0.001, < 0.001) respectively. (Table 8)

Table 8: Drivers of dental students' COVID-19 vaccine acceptance worldwide, February 2021

Category	Driver	No	Yes	Sig.[1]
Contextual	Media	3.99 ± 1.31	3.71 ± 1.21	< 0.001
	Public Figures	3.87 ± 1.25	3.82 ± 1.27	0.236
	Government	3.37 ± 1.30	4.29 ± 1.10	< 0.001
	Pharmaceuticals	3.06 ± 1.30	4.31 ± 1.06	< 0.001
	Values	4.30 ± 1.05	2.75 ± 1.44	< 0.001
Individual / Group	Natural Immunity	4.16 ± 1.11	3.35 ± 1.38	< 0.001
	Sufficient Knowledge	3.48 ± 1.19	4.21 ± 1.23	< 0.001
Vaccine-specific	Risk/Benefit Ratio	3.14 ± 1.37	4.31 ± 1.06	< 0.001
	New Vaccine	3.06 ± 1.28	4.37 ± 1.03	< 0.001
	Availability	3.44 ± 1.3	4.17 ± 1.15	< 0.001

[1] Mann-Whitney U test was used with a significance level ≤ 0.05.

4. Discussion

Globally, 22.5% of dental students within our sample were hesitant about taking COVID-19 vaccines. Verger *et al.* 2021 found that 28.39% of healthcare workers in France and French-speaking parts of Belgium and Canada were hesitant about COVID-19 vaccines.[33] The findings of Verger *et al.* 2021 were a bit close to what had been found in Malta (22%), Portugal (21%), Germany (20%), Netherlands (19%), and Italy (19%).[34],[35] On the other hand, the studies that sampled general university students showed a wide range of hesitancy about COVID-19 vaccines ranging between Egypt (46%), Jordan (25.5%), Malta (25.3%), USA (19.3%), and India (10.6%).[21],[36]–[39]

As representatives of the healthcare student population, Dental students have a crucial role in disseminating robust information about COVID-19 vaccines effectiveness and safety.[6] This social role is backed by the prevailing evidence on healthcare professionals' impact on shaping public opinion regarding health issues, including vaccination.[8],[9] Dental students are also threatened by an array of occupational infections due to their clinical training; therefore, compulsory vaccination strategies for pre-clinical students had been increasingly implemented in recent years.[15] Although positive attitudes are predicted from dental students towards vaccines as they are used to receive them, they demonstrated suboptimal levels of knowledge and attitudes towards new vaccines.[18],[19]

In the current study, the economic level was a significant determinant of dental students' VH, as 37.5% of low-income, 27.8% of low-middle-income, 25.2% of upper-middle-income, and 11.1% of high-income economies students were hesitant about COVID-19

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vaccines. This socioeconomic gradient of VH has been recently found among population groups in Italy, where perceived levels of economic hardship were significantly associated with VH.[22] However, there is a lack of evidence on the relationship between economic level and vaccines acceptance from a global perspective; a recent systematic review showed that the highest acceptance level among healthcare workers was in a high-income country, Israel (78.1%), while the lowest level was in a low-income country, the Democratic Republic of the Congo (27.7%).[40] Regardless of their methodological heterogeneity, cross-sectional studies showed that acceptance levels of medical students in UMHI countries like Italy (86.1%), Poland (92%) were much higher than LLMI countries like Egypt (35%).[36],[41],[42]

The socio-economic gradient of VH can be better understood in the light of the contextual, individual, and vaccine-specific driver endorsed by the WHO-SAGE. The students of UMHI countries have significantly had lower levels of dependance on media/social media (30.4% vs 42%; $p < 0.001$), been less influenced by public figures (14.5% vs 21.3%; $p < 0.001$), had less mistrust of government (30.1% vs 40.6%; $p < 0.001$), less mistrust pharmaceutical industry (19.4% vs 28.9%; $p < 0.001$), less readiness to reject vaccines based on personal/ cultural/ religious values (10.9% vs 18%; $p = 0.003$), and less misconception about natural immunity (22.4% vs 38.1%; $p < 0.001$) that their colleagues of LLMI countries. Contrarily, the students of UMHI countries had significantly higher levels of sufficient knowledge (33.1% vs 27%; $p < 0.001$), knowledge of vaccine risk/benefit ratio (54.4% vs 40.2%; $p < 0.001$), willingness to take new vaccine (45.2% vs 37.6%; $p < 0.001$), and confidence about local availability of vaccines (43.2% vs 33.6%; $p < 0.001$).

Almost 70% of our sample was composed of female students, and this represents the actual female/male ratio of dental students globally. According to the latest report of the Council of European Dentists (CED), the dental profession is majorly practised by females in Europe.[43] The Health Policy Institute (HPI) of the American Dental Association (ADA) revealed that female dental practitioners had increased from 16% in 2001 to 34.5% in 2020, and this pattern is projected to continue given the steady increase of female dental students from 11.7% in 1979 to 51.6% in 2019.[44],[45] The global phenomenon of "feminization of dentistry" is profoundly evident in low-income settings, including Central Asia, Africa, and South America.[46]–[48]

Female dental students had a statistically significant higher level of COVID-19 VH ($\chi 2 = 9.18$; $p = 0.02$) than their male colleagues. This finding is in agreement with the recent systematic review of Sallam 2021 on COVID-19 vaccines, which revealed that males were more likely to accept vaccines.[40] In both LLMI and UMHI countries, female students had higher levels of VH (32% and 20.3%, respectively) than their male colleagues (25.6% and 18.3%, respectively). The emerging evidence on COVID-19 VH among general population groups shows that females are less accepting for COVID-19 vaccines in UMHI countries like the US, United Kingdom (UK), Portugal, Jordan, Kuwait, and Saudi Arabia and LLMI countries like Nigeria, Bangladesh, and Ethiopia.[21],[49]–[54]

Pre-clinical dental students had a statistically significant higher level of COVID-19 VH ($\chi 2 = 7.39$; $p = 0.007$) than their clinical colleagues. Lucia *et al.* 2020 found that clinical medical students (62%) were significantly more inclined to participate in vaccine trials than their pre-clinical colleagues (44%) in Michigan, USA.[55] This pattern was also found among medical students in India and Poland and dental students in the USA.[39],[42],[56] Apart from COVID-19 vaccines, the clinical medical students had higher acceptance levels of influenza vaccine in Brazil, Germany and Saudi Arabia, and human papillomavirus vaccine in India than their pre-clinical colleagues.[57]–[60] One reason to explain this is what Wicker *et al.* found in their 2013 study where clinical students had higher levels of perceived occupational risk than pre-clinical students due to their proximity to blood- and air-borne infections, thus explaining their increased likelihood to accept vaccination.[60]

Previous infection with SARS-CoV-2 might be a barrier for vaccination, as the students in our study who recovered from COVID-19 were considerably more resistant (20.4% vs 12.6%) and slightly more hesitant (24.1% vs 22.2%) to get vaccinated than their colleagues who were not infected. This finding confirms the results of a recent Italian

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cross-sectional study, where the recovered COVID-19 patients showed substantial levels of VH towards COVID-19 vaccine (59.2%) and influenza vaccine (54.6%).[23] Similarly, providing care to COVID-19 patients was also a barrier for vaccination, as the students who looked after COVID-19 patients were considerably more resistant (18.2% vs 12.3%) and slightly more hesitant (23% vs 22.3%) about vaccination. This can be explained by the fact that more than one-third of the students in our sample who provided care to COVID-19 patients had a high level of misconception about immunization.

Using media and social media as the primary source of vaccine-related information was found to be another barrier to be willing to get vaccinated for dental students, as VH levels were significantly higher among the students who used media and social media in both UMHI countries and LLMI countries as their primary source of information. Li HO *et al*. 2020 found that 27.5% of the most popular videos about COVID-19 on YouTube contained misleading information, thus necessitating urgent interventions by health organizations to work proactively with content creators to disseminate high-quality videos.[61] The vaccine opposing content on Twitter was steadily increasing during the first half of 2020 thus requiring thematic analysis of such content.[62] The discourse analysis of Griffith *et al*. 2021 for COVID-19 VH tweets found that concerns over safety, mistrust of governments and drug manufacturers, and insufficient knowledge about vaccines were the critical drivers of VH.[63]

Trust in governments and their capacity to provide the best available vaccine was a significant suppressor of VH among dental students, as VH was reported by only 11.3% of the students who trusted their governments compared to 29.7% of the students who did not trust their governments. One of the lessons learned from the swine flu (H1N1) pandemic of 2009 was that vaccine acceptance levels during contagious outbreaks are prominently influenced by public confidence in the governments' technical and organizational skills.[64] Similarly, trust in the pharmaceutical industry had a promoter role in COVID-19 vaccine acceptance, as VH was reported by only 11% of the students who trusted the pharmaceutical industry compared to 33% of the students who did not trust it. In the recent meta-analysis of Díaz Crescitelli *et al.* 2020, the lack of trust in the pharmaceutical industry was found to be triggered by suspicions about their financial interests and their relationships with governments.[65]

Perceived level of knowledge sufficiency about vaccines and their effectiveness was a significant determinant of COVID-19 vaccine acceptance among dental students globally. Male students had higher levels of sufficient knowledge than their female colleagues (39.8% vs 28.3%; $p < 0.001$), and UMHI students were slightly more knowledgeable than LLMI students (33.1% vs 27%; $p < 0.001$). VH was reported by 10.8% of the students with sufficient knowledge, while it was reported by 32.8% of the students with insufficient knowledge. For a better understanding of the role of perceived knowledge in vaccine acceptance, the perceived knowledge level was found to be associated with increased awareness about the risk/benefit ratio of COVID-19 vaccination ($U = 1719706.5$; $p < 0.001$), a higher level of readiness to take new vaccines ($U = 1773557$; $p < 0.001$), and a lower level of misconception about immunization ($U = 2808567$; $p = 0.576$). Therefore, the results of this study call for urgent and further implementation of the epidemiology of infectious diseases education and vaccination trends within undergraduate dental curricula for better preparation of dental students for future outbreaks.[66]–[69]

Availability of vaccines was a significant promoter for COVID-19 vaccines acceptance among dental students globally, as the students who believed that COVID-19 vaccines would be available for them were less hesitant (28.1% vs 14.4%; $p < 0.001$). In the USA, COVID-19 vaccine acceptance levels increased gradually over the last months, which indicates that increasing trends of vaccine acceptance may correlate positively with the shift from hypothetical vaccines to the availability of real-world vaccines with substantial effectiveness and safety.[70] In the UMHI group, Italy was the most accepting country (4.7 ± 0.8), while Russia was the least accepting country (2.85 ± 1.12). On March 1st, 2021, 5.08% of the Italian population and only 2.48% of the Russian population received at least one dose of COVID-19 vaccines.[71] In the LLMI group, Pakistan was the most accepting

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country (3.97 ± 1.01), while Tunisia was the least accepting country (2.88 ± 1.2). On March 16th, 2021, 0.6% of the Pakistani population and 0% of the Tunisian population were vaccinated.[71]

4.1. Study Strengths

To the best of the authors' knowledge, this is the first study to assess the prevalence of COVID-19 VH among dental students globally. The study also provides coherent evidence on the impact of gender, clinical training, economic level on the attitudes of dental students towards COVID-19 vaccination. The drivers of VH endorsed by the WHO-SAGE were explored for the first time in the population of healthcare students, and they yielded revealing and conclusive results.

4.2. Study Limitations

The first limitation of this study is its sample which is not equally distributed across gender, but this can be simply justified as the sample aimed to be as representative as possible. The second limitation is the imbalanced representation of economic levels, and this occurred mainly due to the disproportionate geographic representation of the IADS. Lastly, the study is naturally limited as a cross-sectional study by its snapshot scope; however, VH levels had been dynamically changing over time, requiring ideally prospective cohort studies to monitor these trends.

4.3. Study Implications

Future research on VH among healthcare students should explore the role of university curricula on students' knowledge about vaccines effectiveness and safety. Also, future research will benefit from prospective cohort studies as they can record the dynamics of attitudes towards vaccines influenced by the emerging achievements and disruptions. The undergraduate dental curricula have to functionally integrate components on infectious diseases epidemiology, especially air-borne infections and vaccination trends, as part of their dental public health and infection control modules. Dental education needs to empower students with sufficient knowledge for making them ambassadors of high-quality health information and to spread the culture of trusting science.

5. Conclusions

The overall acceptance level (63.5%) of dental students for COVID-19 vaccines worldwide was suboptimal. The worrisome level of VH (22.5%) was impacted by the economic context where the dental students live and study, as the students from high-income setting were more confident of receiving COVID-19 vaccines. The male gender and clinical training were also associated with an increased level of vaccines acceptance. The media and social media, public figures, insufficient knowledge about vaccines and their safety, and mistrust of governments and the pharmaceutical industry were barriers for vaccination. The findings of this global study call for further implementation of infectious diseases epidemiology education and vaccination trends within undergraduate dental curricula.

Supplementary Materials: The following are available online at www.mdpi.com/xxx/s1, Table S1: Global Questionnaire of Dental Students' Attitudes Towards COVID-19 Vaccines.docx

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Institutional Review Board Statement: The study was conducted according to the guidelines of the Declaration of Helsinki and approved by the Ethics Committee of the Faculty of Medicine, Masaryk University Ref. 4/2021 on January 20th, 2021.

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