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Quick Response Code:

Website: www.jehp.net
DOI: 10.4103/jehp.jehp_940_21

COVID-19 vaccine hesitancy among medical students: A systematic review

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Abstract:

BACKGROUND: Vaccine hesitancy leads to an increase in morbidity, mortality, and health-care burden. Reasons for vaccine hesitancy include anti-vax group statements, misinformation about vaccine side effects, speed of vaccine development, and general disbelief in the existence of viruses like COVID-19. Medical students are future physicians and are key influencers in the uptake of vaccines. Hence, investigating vaccine hesitancy in this population can help to overcome any barrier in vaccine acceptance.

METHODS: In this paper, we review five articles on COVID-19 vaccine hesitancy in medical students and consider potential future research. All published papers relevant to the topic were obtained through extensive search using major databases. Inclusion criteria included studies that specifically investigated COVID-19 vaccine hesitancy in medical students published between 2020 and 2021. Exclusion criteria included studies that investigated vaccine hesitancy in health-care professionals, allied health, and viruses apart from COVID-19. A total of 10 studies were found from our search.

RESULTS: Based on our exclusion criteria, only five studies were included in our review. The sample size ranged from 168 to 2133 medical students. The percentage of vaccine hesitancy in medical students ranged from 10.6 to 65.1%. Reasons for vaccine hesitancy included concern about serious side effects, vaccine efficacy, misinformation and insufficient information, disbelief in public health experts, financial costs, and belief that they had acquired immunity.

CONCLUSION: These results suggest that vaccine hesitancy is an important cause of the incidence and prevalence of COVID-19 cases. Identifying the barriers of vaccine hesitancy in prospective physicians can help increase vaccination uptake in the general public. Further research is necessary to identify the root cause of these barriers.

Keywords:

Coronavirus, COVID-19 vaccine, vaccine hesitancy, medical students

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Received: 26-06-2021
Accepted: 16-01-2022
Published: 29-07-2022

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Introduction

Vaccination is one of the most effective methods for controlling diseases. It prevents approximately 2–3 million deaths per year, and more deaths can be prevented provided coverage of vaccine costs.^[1] Since the invention of the first vaccine against smallpox, several other infections have been controlled through vaccines. Although millions are vaccinated, some are hesitant against vaccinations even after witnessing the raging COVID-19 pandemic. Vaccine hesitancy is defined as a delay in the

acceptance or the refusal of vaccination even in the availability of vaccines.^[2] By November 2020, pharmaceutical companies reported successful results in their large clinical trials.^[3] With mass vaccinations taking place, there are still a large number of the population who are hesitant to take the vaccine, with false news playing a major role. Other reasons for vaccine hesitancy include concern for side effects, vaccine effectiveness, insufficient information, and cost.^[2]

Medical students are most likely exposed to COVID-19-infected patients during their training. They are prospective physicians

How to cite this article: Venkatesan K, Menon S, Haroon NN. COVID-19 vaccine hesitancy among medical students: A systematic review. *J Edu Health Promot* 2022;11:218.

and strong influencers, hence achieving high vaccination rates in this cohort is essential. This, in turn, gains trust in vaccine uptake in the general public. The more vaccinations that take place, the sooner we can control the transmission of the virus, if not eradicate it. In this systematic review, we aim to analyze available evidence on COVID-19 vaccine hesitancy in medical students. We address reasons and implications for vaccine hesitancy in this population and address prospective research. Such research is important as it provides a stepping stone in identifying gaps in public health and current research.

Materials and Methods

Study design and setting

This is a systematic review analyzing COVID-19 vaccine hesitancy in medical students. All published papers relevant to the topic were obtained through extensive search using databases such as Google Scholar, PubMed, and ScienceDirect, using any relevant keywords in different orders: “COVID-19 vaccine” and “medical students” and “COVID-19.”

Data collection tool and technique

Inclusion criteria included studies that specifically investigated COVID-19 vaccine hesitancy in medical students published between 2020 and 2021. Exclusion criteria included studies that investigated vaccine hesitancy in health-care professionals, allied health, and viruses apart from COVID-19. We investigated the following parameters: reported rates of vaccine hesitancy, self-perception of risk of exposure to COVID-19, acceptance rates of COVID-19 vaccine, reasons and determinants for vaccine hesitancy, and motivating factors. Two authors (KV and SM) conducted the literature search, and another author (NNH) verified the data. We did a quality assessment using the Newcastle–Ottawa Scale [Appendix A]. This scale assesses the quality of nonrandomized studies. It consists of eight items with three subscales with a total maximum score of 9 in each of the three subsets. A score of 7 or more is considered a high-quality study.

Ethical code consideration

The procedures followed were in accordance with the ethical standards.

Results

Initial search retrieved 10 studies. We excluded five studies based on our exclusion criteria after a review of the abstract. This left five studies meeting the inclusion criteria.^[4-8] Studies were conducted in the USA, Uganda, Egypt, and India. The sample sizes varied from 168 to 2133 medical students. The methods used to collect data were online questionnaires. Results from these studies

are evident in Appendix B. The search strategy is shown in Appendix C.

Vaccine hesitancy

The percentage of vaccine hesitancy in medical students ranged from 10.6 to 65.1%. The study by Lucia *et al.* was the first to evaluate COVID-19 vaccine hesitancy among American medical students. Online surveys were distributed to 168 medical students in the USA. Results revealed that even though over 98% of the medical students acknowledged the importance of developing the COVID-19 vaccine, approximately one-quarter of students (23%) were hesitant to take the vaccine as soon as it was approved by the FDA.^[4] Similarly, Kelekar *et al.* revealed that out of the 167 medical students in the USA, 23% were hesitant about receiving the COVID-19 vaccine.^[8]

Saied *et al.* explored beliefs and barriers in 2133 Egyptian medical students which revealed that 34.9% of the students accepted the COVID-19 vaccination, 45.7% were hesitant, and 19.4% refused the vaccine.^[5] The study by Kanyike *et al.* was the first study of its kind in Uganda and the African continent to investigate COVID-19 vaccine hesitancy and acceptance. They reported that out of the 600 medical students, approximately 376 (62.7%) were not willing to be vaccinated and 30.7% displayed vaccine hesitancy.^[6] The study by Jain *et al.* had similar parameters but investigated 1068 medical students in India. Results revealed that 10.6% of the students were hesitant in taking the COVID-19 vaccine.^[7]

Self-perception of risk of exposure to COVID-19

Self-perception of increased risk of exposure to COVID-19 was reported by many medical students. This indirectly acted as a motivating factor for taking the vaccine. Lucia *et al.* reported that 98% of the students agreed they are likely to be exposed to COVID-19.^[4] Jain *et al.* noted that 80% of the medical students believed they had a higher chance of getting infected with COVID 19..^[7]

Kanyike *et al.* reported that 31% of the medical students perceived a slight risk of being infected with COVID-19, and 35% of the students felt that COVID-19 posed a moderate risk to them, respectively.^[6] In addition, Kelekar *et al.* illustrated that 98.2% of the medical students and 95.1% of the dental students who participated in vaccine hesitancy opined that they were likely to be exposed to COVID-19 as a future health-care practitioner.^[8]

Acceptance of COVID-19 vaccine

The percentage of medical students accepting the importance of the COVID 19 vaccine across the five studies varied from 45.4% to 99.4%. However, fewer students were willing to take the vaccine once it was available (53%,^[4] 34.9%,^[5] 37.3%,^[6] and 89.4%^[7]). Kelekar *et al.* reported that

all the medical students who were hesitant to take the COVID-19 vaccine ($n = 37$) were positive about receiving the influenza vaccine the same season.^[8]

Reasons for vaccine hesitancy

Common reasons for vaccine hesitancy included concerns for serious side effects,^[4-8] vaccine effectiveness,^[7,8] misinformation,^[4,6] insufficient information,^[5] financial costs,^[5] belief that they had acquired immunity,^[6] and lack of trust in public health experts,^[4,5,7] which discouraged students from participating in vaccine clinical trials, odds ratio (OR), 95% confidence interval (CI) = 2.33 (1.71–3.17), $P < 0.001$.^[7]

Kanyike *et al.* found significant parameters for acceptability for the vaccine which included being male, being single, receiving any other vaccine in the past 5 years, and moderate or very high perceived risk of getting infected with COVID-19.^[6] Moreover, students who were hesitant to get vaccinated in the past were less likely to get the COVID-19 vaccine this time around.^[6]

Similar trends have been observed in dental students as well. Kelekar *et al.* demonstrated that even though 78.8% of the dental students accept that the COVID-19 vaccine is important to them as future health-care providers, 65% of the dental students did not consider themselves at risk for severe COVID-19 infection possibly due to preexisting use of personal protective equipment in the dental field. In this study, implementation of the COVID-19 vaccine mandate has been cited as an important motivating factor for students to take the vaccine (63% reported that they were willing to take the vaccine if mandated by the health system/dental school).^[8]

Determinants of COVID-19 vaccine hesitancy

Lucia *et al.* and Saied *et al.* both demonstrated that demographic variables and experience with COVID-19 did not predict COVID-19 vaccine uptake.^[4,5] Kanyike *et al.* and others reported that males were twice as likely as females to take up the COVID-19 vaccine.^[6,9,10]

It is interesting to note that Kelekar *et al.* reported more underrepresented minorities among dental students (21%; 44 Hispanic and eight Black students) than among medical students (7.4%; 10 Hispanic and two Black students). Once these demographic variables were controlled, personal vaccination behaviors, experience with COVID-19, and being medical or dental students were no longer predictive of the willingness to get vaccinated.^[8]

In the study by Jain *et al.*, students who were hesitant to take the COVID-19 vaccine were not confident in the vaccine in reducing transmission in the community. They

also viewed that the vaccine should not be mandated for health-care workers and travelers.^[7]

Motivating factors

Common motivating factors for vaccine uptake included protecting oneself and fear of infecting families.^[5,6] Students who had trust in public health experts had fewer concerns about the vaccine side effects and supported vaccine mandates.^[4] Jain *et al.* noted that the concern among Indian medical students getting infected with COVID-19 was associated with lower hesitancy in receiving the COVID-19 vaccine, as well as for participating in COVID-19 vaccine trials. The majority of these students who chose to be vaccinated were fuelled by the desire to attend in-person classes and resume normal lives.^[7]

According to Kelekar *et al.*, even though medical students were not directly involved in the care of COVID-19 patients (due to pandemic restrictions), it is possible that vaccine acceptance rates were higher in them compared to dental students since they witnessed the residents and attending physicians heavily involved in the care of critically ill patients infected with COVID-19 daily.^[8]

Discussion

The findings from these five studies document the existence of vaccine hesitancy among medical students. As strong influencers in health-care and prospective physicians, the perceptions and interests of medical students in the vaccine have a crucial impact on vaccine uptake in the general public. The major findings from these five studies illustrate that the majority of the students are likely to receive the COVID-19 vaccine once available. In addition, most medical students understand the importance of developing a COVID-19 vaccine, and only a few percentage of students are hesitant in receiving the vaccine. Popular reasons for vaccine hesitancy include lack of trust in public health experts, vaccine side effects, and misinformation. Similar trends have been observed in students from other graduate schools, such as dental students.

Out of the five studies, two studies were done in the USA.^[4,8] The other three studies were done in Egypt, Uganda, and India.^[5-7] This allows us to analyze vaccine hesitancy behavior across different regions in the world. The rate of vaccine acceptance in the Uganda study was 37.3% which was slightly higher than the acceptance rates reported in Egyptian medical students.^[5,6] Approximately 30.7% of the medical students were hesitant about the COVID-19 vaccine.^[6] These findings were much lower than Egyptian (46%), Michigan (23%), and Indian medical students (10.6%).^[4,5,7] This discrepancy can be attributed

to the less severe form of the disease and fewer cases in Uganda owing to the variable impact of COVID-19 across the world. This could directly affect an individual's risk perception of COVID-19 and compromise their decision to take up the vaccine.^[6]

In the study by Saied *et al.*, the high percentage of vaccine hesitancy among medical students was correlated with a high level of perception of increased risk of COVID-19.^[5] Similar findings are also evident with Lucia *et al.* in which over two out of ten medical students were hesitant to take the COVID-19 vaccine despite self-perception of increased risk of exposure to COVID-19.^[4] Simultaneously, this finding is in contrast with a prior study that demonstrates risk perception as a predictor in disease prevention.^[11]

Kelekar *et al.* showed that medical students were more likely than dental students to vouch for vaccine mandates for the general public and health-care providers, more likely to acknowledge the importance of COVID-19 vaccination for themselves as health-care providers, and willing to be involved in a COVID-19 vaccine trial.^[8] However, medical students were also more likely to express concerns about the COVID-19 vaccine efficacy compared to dental students. This vaccine hesitancy despite self-perception of increased risk of exposure to COVID-19 is in contrast with another study that shows risk perception as a key positive predictor of preventive health behaviors.^[11]

Expanding on the study by Kelekar *et al.*, students from minority groups were more likely to accept the vaccine, which is in contrast to the popular notion that minority groups are less likely to accept the vaccine.^[8] Those with lower educational backgrounds and socioeconomic statuses report greater vaccine hesitancy compared to those with higher education and socioeconomic status.^[12,13] This discrepancy pertains to several factors such as distrust in health-care professionals and concerns regarding the efficacy and side effects of the vaccine. This illustrates that ethnic minority groups do not have equal health-care access or knowledge about the COVID-19 vaccine. Further research is necessary to identify methods to alleviate these barriers. It must be noted that in the study by Kelekar *et al.*, a large portion of minority students was Hispanic (13%) followed by only 2.5% of the African American students. This could have explained the difference in results.^[8]

A study by Sun *et al.* investigated COVID-19 vaccine hesitancy among university students in China which revealed that reasons for vaccine hesitancy and/or refusal to take the vaccine included demographic variables such as lower socioeconomic status, female gender, societal stigma, informed consent hesitancy, and time needed to

be set apart for a medical study. Key motivating factors included COVID-19 prosocial behaviors and perceived likelihood of infection.^[14] Rostkowska *et al.* conducted a study to evaluate attitudes of European medical students and early graduates and self-reported vaccination coverage, which revealed that 96.9% got vaccinated as part of the vaccination program in their country, and 99% of the respondents accepted and acknowledged the usefulness and need of vaccines.^[15] However, 1st- and 2nd-year students declared being vaccinated less often in the national vaccination programs and less willing to get booster doses compared to senior students and junior doctors. This discrepancy and knowledge gap among 1st- and last-year students amplify the need to include various vaccine awareness courses in the medical curriculum from the start.^[15] These studies combined suggest that vaccine hesitancy is a global phenomenon in medical students.^[14] Creating target-based health education to emphasize the importance of vaccinations is essential to boost confidence.^[16,17]

Limitations and recommendations

One limitation of this review is that it lacked meta-analysis due to the small number of studies included. Another limitation is that this study used only three databases (Google Scholar, PubMed, and ScienceDirect). Hence, we suggest that studies be carried out in other databases as well. In addition, our search terms only had three terms (COVID-19 vaccine, medical students, and COVID-19). Other terms could also have been used to enhance the search.

Prospective studies can focus on investigating COVID-19 vaccine hesitancy in medical students of various ethnicities, gender differences, and socioeconomic statuses. To address misinformation, prospective studies can investigate methods to circulate accurate information through major platforms, such as social media, to clarify misconceptions and address the importance of vaccines. Medical schools should structure a curriculum that prepares prospective physicians against the fight of diseases and to avoid falling prey to anti-vax campaigns and false information. Another prospective research would involve utilizing a larger sample size of medical students to enhance external validity. Trust in health-care professionals and the health-care system is one of the factors that play a pivotal role in vaccine acceptance. A robust multidisciplinary approach is indispensable in combating the rising challenge of infodemics, in addition to the practical challenges wrought by the pandemic itself.

Conclusion

The COVID-19 pandemic has led to an increase in the health-care burden. To alleviate the disease burden, the

general public must be vaccinated accordingly. Vaccine hesitancy represents a major issue in this pandemic, and medical students are among one of the cohorts that have displayed hesitancy. Reasons for this include mistrust and concern regarding the side effects and efficacy of the vaccine. Prospective studies should focus on identifying and investigating methods to alleviate these barriers. To control vaccine hesitancy takes a combination of trust in public health experts, willingness to be vaccinated, and appropriate education surrounding the vaccine.

Acknowledgments

The authors would like to thank the reviewers for their helpful comments.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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Appendix A: Quality Assessment of Studies Newcastle-Ottawa Scale

Study	Total score	Selection			Comparability	Outcome		
		Representativeness of the sample	Sample size	Nonrespondents	Ascertainments of exposure	Based on design and analysis	Assessment of outcome	Statistical test
Lucia <i>et al.</i> , 2020	3				*	*	*	
Saied <i>et al.</i> , 2020	8	*	*	*	*	**	*	*
Kanyike <i>et al.</i> , 2021	8	*	*	*	*	**	*	*
Jain <i>et al.</i> , 2021	7	*	*		*	**	*	*
Kelekar <i>et al.</i> , 2021	4	*			*	*	*	

*Indicates presence of item

Appendix B: Characteristics of included studies

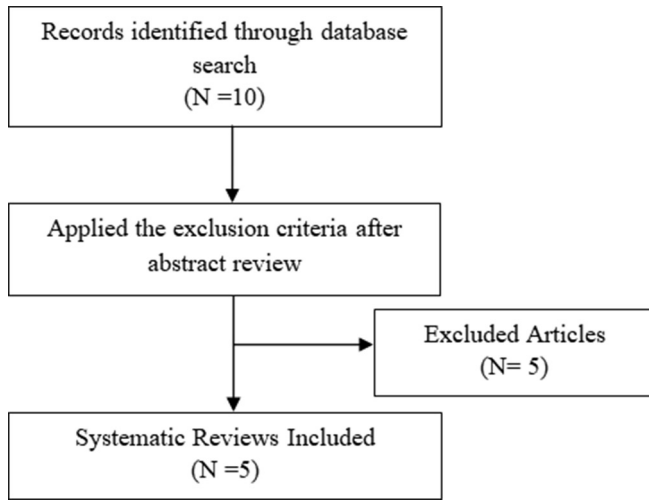
Name of study	Study type and sample size	Location	Survey method	Percentage of students willing to receive COVID-19 vaccine	Percentage of students hesitant to receive COVID-19 vaccine	Percentage of students accepting the importance of COVID-19 vaccine	Reasons for hesitancy	Motivating factors
COVID-19 vaccine hesitancy among medical students ^[4]	Cross-sectional survey (n=168)	Michigan, USA	Online questionnaire. Logistic regression was used to identify COVID-19 vaccine uptake predictors and willingness to participate in the vaccine trial	53% of clinical students were significantly more likely to participate in a vaccine trial compared to nonclinical students (62% vs. 44%, P=0.02)	23%	>98%	54.6% expressed concerns about serious vaccine side effects; student concerns also included lack of transparency as well as undue politicization of the vaccine. The speed of vaccine development affecting vaccine efficacy is also a major concern	Realizing the importance of COVID-19 vaccine to stay healthy as a future physician=99.4% Students willing to take the vaccine had fewer concerns about side effects and were more likely to trust the public health system and agreed with vaccine mandates (P<0.05)
Vaccine hesitancy: Beliefs and barriers associated with COVID-19 vaccination among Egyptian medical students ^[5]	Cross-sectional study (n=2133)	Egypt	Online questionnaire. Logistic regression analyses used to identify predictors of willingness to take the COVID-19 vaccine	34.9%	45.7% were hesitant, and 19.4% refused	Accepted importance of COVID-19 vaccine=90.5%	Main vaccination barriers were insufficient information regarding the vaccine (72.76%), potential unknown adverse effects (56.31%), insufficient trust in the vaccination source (55.09%), and fear of high financial costs of the vaccine (68%)	Main motivating factors: Fear of infecting family (77.73%), fear of being infected (35.11%), and availability of free vaccines (11.72%)

Contd...

Appendix B: Contd...

Name of study	Study type and sample size	Location	Survey method	Percentage of students willing to receive COVID-19 vaccine	Percentage of students hesitant to receive COVID-19 vaccine	Percentage of students accepting the importance of COVID-19 vaccine	Reasons for hesitancy	Motivating factors
Acceptance of the COVID-19 vaccine among medical students in Uganda ^[6]	Cross-sectional survey (n=600)	Uganda	Structured online questionnaires via Google Forms. Fisher's exact test/Chi-square test, and logistic regression were used	37.3%	62.7%	45.5% accept that the COVID-19 vaccine is important to protect them from the disease	Concerns about adverse effects=64.4% having heard or read negative information about the vaccine=53.5%. Students believed they had acquired immunity against COVID-19=30.7%	Demographic variables related to increased vaccine acceptability included male gender (aOR=1.9, 95% CI 1.3-2.9, P=0.001) and being single (aOR=2.1, 95% CI 1.1-3.9, P=0.02) Main motivating factors: To protect oneself=85.3% and others=63.4% from COVID-19
COVID-19 vaccine hesitancy among medical students in India ^[7]	Cross-sectional survey (n=1068)	India	Structured anonymous online questionnaires using Google Forms. Determinants of vaccine hesitancy were identified using multivariate logistic regression	89.4%	10.6% (4.0% disagreed and 6.6% were "not sure")	84.9% accepted that the COVID-19 vaccine will help slow the community's spread of disease Cumulative vaccine hesitancy showed a significant declining trend (P<0.05) from 15.5% (end of the 1st week of the survey) to 10.6% (end of the 5th week)	Concern about vaccine effectiveness (43.8%) and concern about adverse effects (58.1%) (n=1068) Lack of trust in public health experts/ government officials (OR: 2.33 (95% CI: 1.71-3.17), P<0.001) Among the hesitant group (n=113), the predominant source of information regarding the vaccine was the internet (69.9%), social media (67.3%)	97.6% realized the importance of being up to date about upcoming vaccines as future physicians The high chance of getting infected with COVID-19 in the near future as a medical student (80.4%) was also a motivating factor to receive the vaccine
COVID-19 vaccine acceptance and hesitancy among dental and medical students ^[8]	Cross-sectional study (n=406) (158 medical students)	Florida, Michigan, Utah	An online platform (Qualtrics XM online survey). Multiple logistic regression was used to identify COVID-19 vaccine uptake predictors	Medical students=77.3%	Medical students=23%	99.4% of medical students accept that COVID-19 vaccine is important to them as a future health-care provider	6.1% of medical students believed that people get more vaccines than are good for them Concern about efficacy (medical students=76.7%) and concern about serious adverse effects (medical students=54.6%)	Trust in the information about the COVID-19 vaccine from public health experts (medical students=87%)

OR=Odds ratio, aOR=Adjusted OR, COVID-19=Coronavirus disease 2019, CI: Confidence interval



Appendix C: Search strategy for eligible studies