Original Article

Clinical students' perception of acute rheumatic fever and knowledge of vaccine development in the future: A cross-sectional study

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Abstract

Background & Objective: Acute rheumatic fever (ARF) is a major public health issue among children with increased morbidity and mortality. This study aimed to explore clinical medical students' perceptions and awareness of ARF and the potential for developing a future vaccine, as well as to document the factors associated with these views.

Materials & Methods: This cross-sectional study was conducted in two medical schools in the Enugu metropolis from July 2024 to October 2024. The study enrolled 341 clinical medical students from two medical schools in Southeast Nigeria. Data were collected using a validated interviewer-administered questionnaire. The questionnaire included 11 variables to assess the students' ARF knowledge. The maximum obtainable mark for each respondent was 29. Knowledge of ARF vaccination was assessed using eight variables.

Results: Most respondents (93.0 %) demonstrated awareness of ARF. Just over half (50.7 %) recognized sore throat as a symptom of ARF. Fifty-one point-three per cent of respondents demonstrated good knowledge of ARF. Most respondents (86.8%) knew vaccination could be an effective preventive measure against the disease if available. Fourth-year respondents were five times less likely to possess good knowledge of ARF compared to their sixth-year counterparts, with an Adjusted Odds Ratio (AOR) of 0.2 (95% Confidence Interval [CI]: 0.1-0.5). Respondents under 25 years old were three times less likely to intend to receive the ARF vaccine compared to those 25 years old and above (AOR = 0.3; 95%, CI: 0.1-0.9).

Conclusion: A considerable number of medical students were aware of the development of the ARF vaccine. This serves as a strong call to incorporate the teaching of ARF into the curriculum at all levels of medical education.

Keywords: medical students, acute rheumatic fever, perception, curriculum, knowledge, medical school, vaccination.

Introduction

The incidence of cardiovascular diseases in children is increasing [1-4]. Acute Rheumatic Fever (ARF) is one of the acquired heart diseases with a global burden in Sub-Saharan Africa [1, 2]. Accurate documentation of the epidemiology of ARF and its clinical features in Africa will help to improve diagnosis and enhance secondary prevention [3, 4]. The prevalence of ARF has shown fluctuations over time [5-9]. For instance, over the last 2 decades, the global prevalence rate has increased, and it is projected that by 2030, the rate may increase to 559.88 per 100,000 people [5]. In North-Central Nigeria, ARF prevalence is 21.6 per 1000, with a male preponderance [6]. The morbidity and mortality associated with ARF in 2015 were estimated at 319,400 cases [6]. Some studies have documented that the effective implementation of

surveillance and advocacy programs in the control of ARF is constrained by limited access to primary health care. This is caused by the high cost of microbiological diagnosis of ARF using Anti-Streptolysin O (ASO) titer and throat swabs and the low index of suspicion by physicians coupled with a lack of awareness in the community [10-12]. It is important to note that since Group A Streptococcus (GAS) infections can be prevented with a vaccine developed against organisms that cause sepsis, arthritis, or pyoderma, there is a possibility that such a vaccine could also prevent all manifestations of GAS-related diseases [13]. Vaccination is considered the most effective strategy for reducing the incidence of ARF and curbing the rising prevalence of GAS-related diseases [14]. However, there has been no breakthrough in the clinical trial and development of vaccines. Sheel et al. [14] outlined a framework for vaccine development, emphasizing clinical trial design optimization, phase-specific development strategies and regulatory requirements for vaccine registration [14]. Poor perception and paucity of awareness of the cause, course, morbidity and mortality of ARF among clinical medical students could also contribute to the spread of the disease. A thorough assessment of the level of perception of ARF among clinical students is crucial in reducing the spread of the disease among this population. This study, therefore, aimed to document clinical students' perceptions of ARF and identify associated factors. Furthermore, the study investigated medical students' knowledge and perspectives on the potential for future vaccine development against ARF.

Materials & Methods

Design and setting(s)

This was a cross-sectional study conducted in two medical schools in Southeast Nigeria from 14 March 2024 to 24 October 2024. It involved clinical medical students in their fourth to sixth year of study drawn from two South-eastern Nigerian medical schools: Ebonyi State University, Abakaliki, and Enugu State University of Science and Technology, Enugu.

Participants and sampling

Three hundred forty-one clinical medical students from two medical schools in Southeast Nigeria were enrolled consecutively in the study. The students were recruited consecutively until the sample size was reached. Medical students in the clinical class who provided informed consent were included in the study. In contrast, medical students in the pre-clinical class and those without consent were excluded from this study. A two-stage sampling technique was used to select the medical students for inclusion in the study. Six accredited medical schools in southeast Nigeria have clinical medical students. Two medical students were selected out of the six using a simple random sampling technique of balloting. In the second stage, a list of all medical students in the clinical classes (fourth year to sixth year) was made. On each day of data collection, the number of medical students in the three classes in each of the two selected schools who were present served as the sampling frame. The sampling interval was determined by dividing the total number by the sample size of 170, which represented the estimated number of students from each selected school who would participate in the study. Therefore, every medical student was recruited for the study based on the seating arrangement of the students in the three classes on each day of data collection. On each occasion, the index student was selected using a simple random sampling technique of balloting. The formula obtained the sample size: $n = Z^2pq \div d^2$ [15].

A minimum sample size of 347 students was obtained using the formula above.

Tools/Instruments

The study used a validated interviewer-administered questionnaire. Ray et al. [16] adapted this questionnaire using a group of students aged 10-16 randomly selected from different schools. The questionnaire covers questions on knowledge of ARF and willingness to be vaccinated, defined as the preparedness or readiness to receive a vaccine after considering the efficacy, benefits, adverse effects, and barriers associated with receiving such a vaccine [17]. Knowledge of ARF was assessed using 11 variables.

Five items focused on symptoms, with each correct response scoring one and incorrect response scoring 0. The other six variables for the ARF assessment focused on the disease's prevalence, the age group most likely to be affected, impact, diagnosis, treatment options and prevention of the disease. For these six variables, a correct answer by any respondent attracted four marks, while an incorrect answer was scored zero. Thus, the maximum obtainable mark for each respondent was 29. Knowledge of rheumatic fever vaccination was assessed using eight variables. Each correct response from the respondents attracted a score of one, while incorrect responses were scored zero. The maximum score each respondent could obtain is eight.

The questionnaire components related to socioeconomic status were developed using Principal Component Analysis (PCA) in STATA statistical software version 12. The eleven variables listed above served as inputs to the PCA. For the calculation of distribution cut points, quartiles were used. Each respondent was assigned the wealth index score of their family.

The quartiles were Q1 = Poorest, Q2 = The Very Poor, Q3 = The Poor, and Q4 = The Least Poor. The quartiles were further dichotomized into low socioeconomic class, comprising the poorest and very poor, and high socioeconomic class, comprising the poorest and least poor groups.

Cronbach's α was employed to assess the internal consistency of the questionnaire adapted from Ray et al. [18]. A score of 0.8 was achieved, indicating a satisfactory level of reliability. Additionally, Pearson's correlation coefficient was utilized to determine the test-retest reliability, with a score of 0.5 indicating a higher reliability.

Data collection methods

The questionnaires were distributed to the medical students during the didactic lecture period in the first and second semesters of the year of study.

Data analysis

Data entry and analysis were done using the Statistical Product and Service Solutions (IMB-SPSS) statistical software version 25. Continuous variables were represented using mean and standard deviation, while categorical variables were presented using frequencies and proportions. The mean knowledge score of ARF among the categories of independent variables was compared using the Student t-test when the groups were two and with analysis of variance if the groups were more than two.

The mean knowledge score of ARF vaccination among the categories of independent variables was compared using the Student t-test when the groups were two and with analysis of variance if the groups were more than two.

A p-value of <0.05 determined the level of statistical significance. A chi-square test and multivariate analysis through binary logistic regression were employed. Respondents who achieved a score of 50% or higher of the total possible score were considered to have good knowledge.

Results

Table 1 shows the socio-demographic characteristics of the respondents.

The mean ± SD of the age of the respondents was 24.3 ± 2.9 years. The highest proportion of the respondents, 67.2%, were under 25 years old, while the least proportion, 3.8%, were 30 years and above. A higher proportion of the respondents, 51.0%, were male. The majority of the respondents, 96.5%, were single. The highest proportion of the respondents, 64.2%, were in the fifth year of study, while the least proportion, 8.2%, were in the sixth year.

Table 1. Socio-demographic characteristics of respondents (n = 341)

Variable	Frequency	Percent
Gender		
Male	174	51.02
Female	167	48.97
Marital status		
Single	329	96.48
Married	12	3.52
Class of study		
Fourth year	94	27.57
Fifth year	219	64.22
Sixth year	28	8.21
Educational attainment of father		
No formal education	11	3.23
Primary education	26	7.63
Secondary education	50	14.66
Tertiary education	254	74.49
Educational attainment of mother		
No formal education	12	3.52
Primary education	17	4.99
Secondary education	56	16.42
Tertiary education	256	75.07
Employment status of father		
Unemployed	13	3.81
Self-employed	181	53.08
Paid employment	147	43.11
Employment status of mother		
Unemployed	10	2.93
Self-employed	149	43.70
Paid employment	182	53.37
Family socio-economic status		
Low socio-economic class	176	51.61
High socio-economic class	165	48.39
Age of respondents in years Mean ± SD	4.26 ± 2.94	

Abbreviation: SD, standard deviation.

Table 2 shows awareness of ARF and rheumatic fever vaccine among the respondents. The majority of the respondents, 93.0%, were aware of ARF. The major sources of information included health workers (82.3%), internet/social media (61.8%), and friends (42.3%). Less than one-fifth of the respondents, 17.9%, were aware of the ARF vaccine. The major sources of information on the ARF vaccine included health workers, 77.0%; internet/social media, 50.8%; and friends, 39.3%.

Table 2. Awareness of ARF and rheumatic fever vaccine among the respondents (n = 341)

Variable	Frequency	Percent
Awareness of ARF		
Yes	317	92.96
No	24	7.04
Awareness of rheumatic fever vaccine		
Yes	61	17.89
No	280	82.11

Note: Multiple responses encouraged.

Table 3 shows the respondents' knowledge of ARF and rheumatic fever vaccination. A higher proportion of the respondents, 88.9%, knew that shortness of breath is a symptom of rheumatic fever and rheumatic heart disease. A higher proportion of the respondents, 50.7%, knew that sore throat is a symptom of rheumatic fever. Most respondents, 56.0%, knew the age group 5-15 years were more likely to have rheumatic fever. A higher proportion of the respondents, 81.5%, knew that diagnosis is by history taking and past medical history of sore throat. The mean knowledge of ARF score was 14.8 ± 5.8. Most 86.8% of respondents knew vaccination could be a good measure to prevent diseases. The mean knowledge of ARF vaccination score was 4.5 ± 1.4. Less than half of the respondents, 45.7%, knew they were not in Nigeria's high-priority group for rheumatic fever vaccination. Less than one-tenth of the respondents, 8.5%, were aware of anyone who died from rheumatic fever. A minor proportion of the respondents, 5.6%, intend to receive vaccination for rheumatic fever when available. **Table 4** shows the correlation matrix of variables, including the age of respondents, knowledge of ARF and knowledge of ARF vaccination. A very weak positive correlation existed between knowledge of ARF and rheumatic fever vaccination. Increases in ARF knowledge were associated with increases in ARF vaccination knowledge, and this relationship was statistically significant (n = 341, r = 0.141, p = 0.009). **Table 5** and **6** compared mean scores of knowledge of ARF and knowledge of ARF vaccination. The mean knowledge score of ARF was highest among the sixth-year students, 16.5 ± 5.9, and least among those in the fourth year, 11.6 ± 4.9, and the mean difference was statistically significant (F = 21.836, p < 0.001). The mean knowledge score for ARF was significantly higher among the respondents whose mothers had tertiary education, 15.1 ± 5.9 compared to those whose mothers had secondary education and below, 13.8 ± 5.1 (Student t = 1.990, p = 0.048). The mean knowledge score for ARF was higher among the respondents whose families were in the high socioeconomic class, 15.5 ± 5.6 compared to those in the low socioeconomic class. The mean difference was statistically significant (Student t = 2.374, p = 0.018). The mean knowledge score for rheumatic fever vaccination was significantly higher among respondents who perceived themselves as susceptible to ARF, with a score of 4.9 ± 1.2, compared to those who did not perceive themselves as susceptible, whose score was 4.4 ± 1.5 (Student t = 3.161, p = 0.002). The mean knowledge score for rheumatic fever vaccination was higher among the respondents who intend to receive rheumatic fever vaccination, 5.0 ± 1.3 when compared to those who did not intend to receive the vaccine, 4.4 ± 1.4 and the mean difference was found to be statistically significant, (Student t = 3.718, p < 0.001).

Discussion

This study aimed to explore the perception and awareness of ARF among clinical medical students and to document associated factors. A high level of awareness (93.3%) was noted among medical students. This may be attributed to the fact that most information on ARF was derived from health professionals. The level of awareness of ARF among medical students was significantly higher than that reported by Alnemari et al. [18] in Saudi Arabia, where a level of awareness of 55.2 % was reported in students in the College of Medicine and 33.3% in the College of Dentistry, 44.8% in the College of Pharmacy, 21.4% in the college of applied Medical sciences and 45.9% among college of nursing students. The present study's findings were higher than those of Nkoke et al. [19] and Chelo et al. [20]. The variation in awareness of ARF may be attributed to the differing medical curricula employed by the participating medical schools, the year of study of the medical students involved, and potentially the methodologies used by the authors. The study also showed that 56% of medical students know that ARF commonly affects children between the ages of 5 and 15 years. Similarly, only

41.6% noted that skin rash could trigger ARF. This was also similar to the study of Fakieha et al. [21], where 54.8% of the subjects knew that children aged 5 to 15 years old are susceptible to ARF. The association between skin rash (bacterial dermatitis) and ARF was noted in 46.1% of the reportage of Fakieha et al. [21]

Table 3. Knowledge of ARF and rheumatic fever vaccination among the respondents (n = 341)

Variable	Correct response	Frequency (Percent)
Prevalence of rheumatic fever has decreased over time	Yes	63 (18.47)
Shortness of breath is a symptom of rheumatic fever and rheumatic heart disease	Yes	303 (88.86)
Joint pain/swelling is a symptom of rheumatic fever	Yes	149 (43.70)
Leg swelling is a symptom of rheumatic fever	Yes	93 (27.27)
Skin rash is a symptom of rheumatic fever	Yes	142 (41.64)
Sore throat is a symptom of rheumatic fever	Yes	173 (50.73)
Treatment of sore throat and primary prophylaxis is ideal preventive measure	Yes	199 (58.36)
Age group (5-15 years) more likely to have rheumatic fever	Yes	191 (56.01)
Treatment is by use of non-steroidal anti-inflammatory drugs, antibiotics and steroids	Yes	185 (54.25)
Impact of the disease is in poor socio-economic groups	Yes	129 (37.83)
Diagnosis is by history taking and past history of sore throat	Yes	278 (81.52)
Vaccination could be a good measure to prevent diseases	Yes	296 (86.80)
Rheumatic fever vaccine may be of immense help in the fight against the disease	Yes	273 (80.05)
One could be expected to wear a face mask even after receiving rheumatic fever vaccine	Yes	55 (16.13)
There is no disease called rheumatic fever hence rheumatic fever vaccine is false	No	265 (77.71)
There is no rheumatic fever in Nigeria hence no need for rheumatic fever vaccine	No	250 (73.31)
Side effects of rheumatic fever vaccine may be reported after administering the vaccine	Yes	43 (12.61)
There has been no vaccine developed for the prevention of rheumatic fever	Yes	258 (75.66)
Nigeria is not interested in rheumatic fever vaccination	No	103 (30.21)
Intention to receive rheumatic fever vaccination		
I could be infected with Rheumatic fever		
Yes	87	25.51
No	254	74.49
Have been tested for rheumatic fever		
Yes	8	2.3
No	333	97.7
Aware of anyone that was tested for rheumatic fever		
Yes	32	9.38
No	309	90.62
Aware of anyone infected with rheumatic fever		
Yes	50	14.66
No	291	85.34
Aware of anyone that died from rheumatic fever		
Yes	29	8.50
No	312	91.50
Intend to receive vaccination for rheumatic fever when available		
Yes	19	5.57
No	322	94.43
Knowledge of rheumatic fever/rheumatic heart disease		
Mean ± SD	14.8 ± 5.8	
Knowledge of rheumatic fever vaccination		
Mean ± SD	4.5 ± 1.4	

Abbreviation: SD, standard deviation.

Table 4. Correlation matrix of variables including age of respondents, knowledge of ARF and knowledge of rheumatic fever vaccination (n = 341)

Variable	Correlation co-efficient r, p-value		
	Age of respondents in years	**Knowledge of ARF (total score)**	**Knowledge of rheumatic fever vaccination (total score)**
Age of respondents in years	1		
Knowledge of ARF (total score)	r = 0.001 p = 0.984	1	
Knowledge of rheumatic fever vaccination (total score)	r = 0.062 p = 0.256	r = 0.141 p = 0.009	1

Abbreviations: r, correlation co-efficient; p-value, probability value.

Table 5. Comparison of mean scores of knowledge of ARF and knowledge of rheumatic fever vaccination (n = 341)

Variable	n	Mean ± SD	Sig.
Age of respondents in groups			
< 25 years	229	14.8 ± 5.8	t = 0.007, p = 0.994
≥ 25 years	112	14.8 ± 5.7	
Gender			
Male	174	14.5 ± 5.7	t = 0.973, p = 0.331
Female	167	15.1 ± 5.8	
Marital status			
Single	329	14.7 ± 5.8	t = 0.747, p = 0.456
Married	12	16.0 ± 4.2	
Year of study			
Fourth year	94	11.6 ± 4.9	F = 21.836, p <0.001
Fifth year	219	15.9 ± 5.6	
Sixth year	28	16.5 ± 5.9	
Educational attainment of father			
Tertiary education	254	14.7 ± 5.8	t = 0.218, p = 0.827
Secondary education and below	87	14.9 ± 5.8	
Educational attainment of mother			
Tertiary education	256	15.1 ± 5.9	t = 1.990, p = 0.048
Secondary education and below	85	13.8 ± 5.1	
Employment status of father			
Unemployed	13	13.8 ± 4.6	F = 0.446, p = 0.640
Self-employed	181	15.0 ± 6.0	
Paid employment	147	14.6 ± 5.6	
Employment status of mother			
Unemployed	10	14.5 ± 5.9	F = 0.089, p = 0.915
Self-employed	149	14.7 ± 5.6	
Paid employment	182	14.9 ± 5.9	
Family socio-economic status			
Low socio-economic class	176	14.1 ± 5.9	t = 2.374, p = 0.018
High socio-economic class	165	15.5 ± 5.6	
Intend to receive rheumatic fever vaccine			
Yes	90	14.0 ± 5.1	t = 1.647, p = 0.101
No	251	15.1 ± 6.0	
Comparison of mean scores of knowledge of rheumatic fever vaccination			
	n	**Mean ± SD**	**Sig.**
Age of respondents in groups			
< 25 years	229	4.5 ± 1.4	t = 1.150, p = 0.251
≥ 25 years	112	4.7 ± 1.4	
Gender			
Male	174	4.5 ± 1.5	t = 0.278, p = 0.781
Female	167	4.5 ± 1.4	

Abbreviations: t, t-test statistic; F, analysis of variance statistic; SD, standard deviation; n, number of participants; Sig., Significance; p, probability value.

Table 6. Comparison of mean scores of knowledge of ARF and knowledge of rheumatic fever vaccination (n = 341)

Variable	n	Mean ± SD	Sig.
Marital status			
Single	329	4.5 ± 1.4	t = 2.130, p = 0.053
Married	12	5.1 ± 0.9	
Year of study			
Fourth year	94	4.3 ± 1.7	F = 2.881, p = 0.057
Fifth year	219	4.7 ± 1.3	
Sixth year	28	4.3 ± 1.7	
Educational attainment of father			
Tertiary education	254	4.5 ± 1.4	t = 0.029, p = 0.977
Secondary education and less	87	4.5 ± 1.6	
Educational attainment of mother			
Tertiary education	256	4.5 ± 1.3	t = 1.352, p = 0.177
Secondary education and less	85	4.7 ± 1.6	
Employment status of father			
Unemployed	13	4.9 ± 1.6	F = 0.556, p = 0.574
Self-employed	181	4.5 ± 1.4	
Paid employment	147	4.5 ± 1.4	
Employment status of mother			
Unemployed	10	4.6 ± 2.1	F = 0.591, p = 0.554
Self-employed	149	4.4 ± 1.5	
Paid employment	182	4.6 ± 1.3	
Family socio-economic status			
Low socio-economic class	176	4.4 ± 1.5	t = 1.253, p = 0.211
High socio-economic class	165	4.6 ± 1.3	
Perceived susceptibility to rheumatic fever			
Yes	87	4.9 ± 1.2	t = 3.161, p = 0.002
No	254	4.4 ± 1.5	
Have been tested for rheumatic fever			
Yes	8	4.0 ± 1.3	t = 1.054, p = 0.293
No	333	4.5 ± 1.4	
Aware of someone tested for rheumatic fever			
Yes	32	4.9 ± 1.3	t = 1.725, p = 0.085
No	309	4.5 ± 1.4	
Aware of someone infected with rheumatic fever			
Yes	50	4.8 ± 1.4	t = 1.371, p = 0.171
No	291	4.5 ± 1.4	
Aware of someone that died from rheumatic fever			
Yes	29	4.6 ± 1.4	t = 0.378, p = 0.706
No	312	4.5 ± 1.4	
Intend to receive rheumatic fever vaccination			
Yes	90	5.0 ± 1.3	t = 3.718, p < 0.001
No	251	4.4 ± 1.4	

Abbreviations: t, t-test statistic; F, analysis of variance statistic; SD, standard deviation; n, number of participants; Sig., Significance; p, probability value.

The current study noted no association between gender and the perception of ARF. However, Fakieha et al. [21] noted gender as the only important factor affecting knowledge of ARF in their study. Other studies noted that females have better knowledge than males [22-29].

The study noted that fewer medical students (50.7%) knew that sore throat was a symptom of ARF. Concerning the association between bacterial sore throat and ARF, Kulik et al. [25] noted that over 79.5% of their subjects were aware of the link between a sore throat and ARF, which was also similar to the study of Manase et al. [26] where 73.1% of health workers were aware of this relationship between sore throat and ARF [25]. This poor awareness of the association between sore throat and ARF highlights the need for specific training and potential curriculum revisions.

Though 93.0% of the clinical medical students were aware of ARF, only a minor population had good knowledge of ARF in terms of epidemiology, spread and management. This indicates a serious and urgent need to intensify the dissemination of information on the epidemiology and spread of the diseases, especially among clinical medical students. This information should also be introduced to pre-clinical medical students to curb the militating effects of this disease. Besides, information on primary and secondary prevention and disease awareness should be provided in the early years of medical school [30].

It is noted in this study that students who were in the 6th year of study had more knowledge of ARF than those in a lower class. It is expedient to introduce the lecture on the awareness and prevention of ARF in the introductory class of the medical school. This finding contrasts with those of other studies [28–30]. Furthermore, students from high socioeconomic classes had a higher knowledge of ARF than those from a lower economic class. This finding was at variance with Machluf et al. [31], who documented the association of ARF with lower socioeconomic classes. The study showed that a major proportion of medical students (81.5%) were well-informed about the rising prevalence of ARF. Some studies have documented a rising prevalence of ARF, with 300,000–500,000 new cases diagnosed annually and approximately 230,000 related deaths [31].

About half (54.3%) of the medical students in the current study noted that the management of ARF includes using non-steroidal anti-inflammatory drugs, antibiotics and steroids. Fakieha et al. [21] corroborated the same results when they noted that 56.5% of their subjects were aware of using antibiotics to manage sore throat. Interestingly, the current study found that 75.7% of the medical students recognized the non-availability of rheumatic fever vaccine, yet 78.9% were aware of the ongoing effort to develop such a vaccine. This good level of awareness could be explained by the correlational matrix, which showed a positive correlation between knowledge of ARF and knowledge of rheumatic fever vaccination.

Conclusion

There is a poor perception of ARF's clinical correlates and management among clinical medical students. Many medical students are aware of the development of an ARF vaccine. This is a clarion call to add the teaching of ARF to the curriculum at all levels in the medical school. This could reduce the burden and complications associated with the disease. Vigorous campaigns and changes in medical curricula, which should include lectures on ARF across all levels of medical school, may significantly increase the perception and management of ARF among medical students [45].

Ethical considerations

This was obtained from the Research and Ethics Committee of Enugu State University Teaching Hospital (Parklane) Enugu, Nigeria. Additionally, verbal informed consent was obtained from the participating medical students of the studied medical schools. The study adhered to established ethical principles and institutional guidelines throughout. The code for the approved work was ESUTHP/C-MAC/RA/034/158.

Artificial intelligence utilization for article writing

Not applicable..

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Conflict of interest statement

The authors declare that they have no competing interests.

Author contributions

MC, ATC, OCN, ENO, ICN, JTO, NOO, and CNO conceived and designed this study, while JMC helped with the critical revision of the article. JMC and ENO

also did the Data analysis/interpretation. All authors have read and approved the manuscript.

Supporting resources

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Data availability statement

Data are, however, available from the authors upon reasonable request and with permission of the corresponding author.

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