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Antibiotic prescribing and resistance: knowledge level of medical students of clinical years of University Sultan Zainal Abidin, Malaysia

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Abstract: The innovation of penicillin by Dr Alexander Fleming in 1928 and its use in clinical practice saved many lives, especially during the Second World War. Tuberculosis still carries a significant public health threat and has re-emerged over the past two decades, even in modern countries where tuberculosis was thought to be eliminated. The World Health Organization defines antimicrobial resistance as the resistance of a microorganism to an antimicrobial drug that was initially effective for treatment of infections caused by the microbe. Therefore, the findings of the current study will provide data to enable the design of a new educational program to better equip our students in confronting antimicrobial resistance. This study was a cross-sectional, questionnaire-based survey, which was undertaken in the Faculty of Medicine, Universiti Sultan Zainal Abidin, Kuala Terengganu, Malaysia. The study participants were students of the Bachelor of Medicine and Bachelor of Surgery program (MBBS) of Year III, IV, and V. A total of 142 out of 164 (86%) medical students returned the questionnaire. Specifically, the year-wise breakdown of responses was 29% (41), 39% (55), and 32% (45) for Year III, IV, and V, respectively. Among the study respondents, 28% (40) were male, and the remaining 72% (102) were female. In all, 67% of the participants felt more confident in "making an accurate diagnosis of infection/sepsis." The majority (88%) of the study participants stated that they would like more training on antibiotic selection. This research has found that there is a gap between theoretical input and clinical practice; the students are demanding more educational intervention to face the threat of antimicrobial resistance.

Keywords: antibiotic, prescribing, resistance, medical students, knowledge, Malaysia

Video abstract

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Introduction

Selman Waksman first used the word antibiotic as a noun in 1941 to describe any small molecule made by a microbe that antagonizes the growth of other microbes.[1] Dr Alexander Fleming published his findings of the discovery of penicillin in the *British Journal of Experimental Pathology* in 1929, and by the 1940s penicillin use was commonplace in clinical practice. This saved many lives, especially during the Second World War.[2–4] Penicillin was followed by the invention of a number of antibiotics from 1945 to 1955, namely, streptomycin, chloramphenicol, and tetracycline.[1,4] All of these antimicrobials were produced by microbes, actinomycetes and fungi being the unique resources.[1,4] The development of antimicrobials not only conquered the management of infectious diseases but also raised the average life expectancy and quality of life for humanity. Therefore, this outstanding achievement led to the belief that "infectious diseases would be conquered shortly."[5] Although the history of clinical uses of antimicrobials is quite recent, the antibiotic tetracycline has been identified as far back

as 350–550 CE among the skeletons of the ancient Sudanese Nubia population.[6,7] Similar findings were also reported in femoral bones found in the Dakleh Oasis, Egypt.[8,9] It has led to the notion that both of these ancient communities' diets contained tetracycline. The presence of antimicrobials in foods in these prehistoric societies possibly gave protective effects from microbes. Therefore, these communities suffered either low or no infectious diseases.[6–9]

Tuberculosis (TB) still carries a significant public health threat and has re-emerged over the past two decades, even in modern countries where TB was thought to be eliminated.[10–12] TB was declared a global emergency by the World Health Organization (WHO) in 1993, with around 8–10 million new cases annually and over 2–3 million deaths worldwide.[13] The WHO defines "AR [antimicrobial resistance] as the resistance of a microorganism to an antimicrobial drug that was initially effective for treatment of infections caused by it."[14] Resistance is also defined "as bacteria that are not inhibited by usually an achievable systemic concentration of an agent with the regular dosing schedule and/or fall in the minimum inhibitory concentration ranges."[15] Similarly, multiple drug resistance is defined as the acquired nonsusceptibility to three or more antimicrobial drugs or drug classes.[16,17] The term multiple drug resistance initially was used to identify resistant malignant tumors, and later of *Mycobacterium tuberculosis*. Now it is used for any microbial infections – bacterium, fungus, or parasite.[18] Acquisition of resistance to one antibiotic conferring resistance to another antibiotic, to which the organism has not been exposed, is called cross-resistance.[19–22] In all, 80%–90% of the antibiotics are prescribed for ambulatory patients; the rest in hospital admitted cases.[23] It is also reported that general practitioners prescribe 90% of antimicrobials.[24] It has been estimated in the US by state-sponsored research that 50 of the 150 million prescriptions for antibiotics written for outpatients every year are not evidence-based.[25] It has been also identified that as high as 50% of antimicrobials are used without any scientific basis, and antibiotic was prescribed that was either superfluous or debatable.[26–28] Multiple studies reported that these very dangerous resistant microbes were created due to misuse of antimicrobials.[29–31] The consequences are an increased risk– of additional morbidity and mortality by snowballing the possibility of adverse drug reactions and promotion of AR in community pathogens.[32] Researchers have pointed out that globalization ensures quick spreading of antibiotic resistance, for example, the rapid international spread of New Delhi metallo-blactamase.[33,34] Therefore, there is an urgent need for an international and nationwide platform to control AR.[35–39] European AR Surveillance Network, National AR Monitoring System for Enteric Bacteria (USA), The Surveillance Network (USA), AR Surveillance (Germany), Central Asian and Eastern European Surveillance on AR, and Surveillance of Antibiotic Use and Bacterial Resistance in German Intensive Care Units are the most important investigation programs currently working on AR.[35]

Although the Ministry of Health, Malaysia, has been issuing antibiotic use guidelines for more than two decades, compliance with these guidelines was found to be lacking.[40] The same study also reported that antibiotic resistance is common in Malaysian general hospitals.[40] In 1994, another study reported that ampicillin, cloxacillin, cephalosporins, gentamicin, co-trimoxazole, and tetracyclines were highly resistant in six Malaysian general hospitals. Researchers concluded that AR is a "constant threat and challenge for clinicians" in Malaysia especially in treating nosocomial infections.[41] The *Medical Journal of Malaysia* in 2003 published three articles on the issue of AR in Malaysian communities. All three of these articles were highly concerned about AR and its impact on public health.[42–44] Dr VKE Lim, a very renowned physician in Malaysia, in his recent editorial review of the subject, mentioned that a multifaceted strategy is required to improve antibiotic prescribing and control the emergence of antibiotic resistance. Education of both doctors and patients would form the cornerstone of the strategy.[45] Another three studies of research published in 2004, 2011, and 2013 reported that a significant proportion of antimicrobials were prescribed inappropriately especially in upper respiratory tract infection. These studies concluded that this irrational prescribing would promote more AR.[46–48] These studies accept that more educational intervention will promote rational prescribing and professional responsibility, which will ultimately enlighten health professionals with more expertise against AR.[46–48] A number studies conducted in the general public of Malaysia reported that Malaysians have inadequate knowledge about antimicrobials. These findings reinforce the notion that there is an urgent need for an educational program to raise awareness and advocate a movement among patients.[49–51] Another study reported that a poor knowledge level exists among the general public of Malaysia, and this promotes more frequent and incorrect use of antimicrobials. The same survey also encouraged educational intervention among ordinary citizens.[52] Professor Lim again mentioned in his recent review that the global public threat of AR can only be addressed through good antibiotic stewardship programs. To overcome the global public health threat of AR, all relevant stakeholders of the health service should work in unison.[53]

Rational prescribing is the paramount issue in the struggle against AR. It is tough to convey new ideas to doctors

and other health professionals because they are already entrenched in their own notions and thoughts. Therefore, it is suggested that intervention should be conducted during the early days of medical training. The WHO, in 2012, has emphasized the importance of rational prescribing in the undergraduate medical curriculum.[54] There were different levels of awareness regarding prescribing, but almost every study recommended more educational interventions in the undergraduate curriculum.[55–65] Different studies emphasized that teaching and learning about antimicrobials, both at the undergraduate and postgraduate medical curricula, remain the most noteworthy approach in the fight against AR.[55,66–68] Antimicrobials are "considered among the essential drugs of a core curriculum in clinical pharmacology for undergraduate medical students."[69]

Although there are some related studies conducted throughout the world, there were not many studies specific to Malaysia. One pilot study published in 2014 suggested extensive improvement of the curriculum and education for health care professionals to ensure the rational use of antimicrobials.[70] The first batch of medical students admitted at Universiti Sultan Zainal Abidin (UniSZA) was in 2009, graduated in 2014, to work as house officers in different hospitals for the Ministry of Health, Malaysia.[71] As other universities in Malaysia, UniSZA is subscribed to the integrated curriculum for undergraduate medical education and pharmacology is taught in preclinical years of Year I and II as a lecture-based subject.[72] The Faculty of Medicine, UniSZA, is scheduled to conduct a major revision in the next few years of the undergraduate medical curriculum.[73,74] Therefore, this exercise is to ensure highly professional and committed medical doctors are produced in society.[75–78] Medical students are future doctors for any society, and they are the primary stakeholders in any health care system.[60] Therefore, their beliefs and practices regarding antibiotic prescribing and resistance will have an impact on AR. The current study will provide suitable data to design a new educational program to equip our students in their fight against AR. UniSZA is a new medical school in Malaysia and the first two batches have already graduated and are working as house officers in different government tertiary hospitals of Malaysia. It is mandatory for the faculty of medicine to reorganize and review the curriculum according to the Malaysian Government regulation.[73,74]

Materials and methods

This study was a cross-sectional, questionnaire-based survey, which was undertaken in the Faculty of Medicine, UniSZA, Malaysia. The study participants were students of the MBBS program in Year III, IV, and V. As the total population size was 179, a universal sampling method was applied to select the respondents. Data were collected from May to June 2015 using a validated instrument. The principal author was much impressed with a multicenter study conducted in Europe.[65] He contacted the corresponding author Professor (Dr) Ce´line Pulcini in France and obtained formal permission to use the validated instrument. The questionnaire was again pretested and validated in the local context. The questionnaire was administered to 15 medical students who did not participate in the primary study. Their responses were collected and analyzed for validity and reliability. The Cronbach alpha was calculated as 0.69. A total of 164 (179-15 non-participants) questionnaires were given to the study respondents after a prearranged lecture class. They were asked to complete anonymously the questionnaires. Study respondents were given 15 minutes to complete the questionnaire which was handed over immediately to the principal investigator.

The questionnaire consisted of 21 questions. Initially, demographic features were recorded. The first question was a 5-point Likert scale, where responses ranged from "very unconfident" to "uncertain". It was used to assess the respondent's confidence in prescribing. Six questions were set to give an idea of the student's training in antibiotic prescribing. Out of six, five questions were arranged in the Likert scale-based questions with options of "yes", "no", and "unsure". One question was to assess the total hours of training the respondents had received during their undergraduate study. Then, the next five questions were set to evaluate the respondent's knowledge of AR. Two of these were set out so as to put a tick mark for "yes", "no", or "unsure". The other three questions were arranged in six rows, which indicated the percentage range in the following manner: row 1 was up to 1%, row 2 was >1%–20%, row 3 for 21%–40%, row 4 for 41%–60%, row 5 included 61%–80%, and the last row showed a percentage range from 81% to 100%. The self-reported practices regarding the antibiotic usage of the study population were also assessed by using two questions that consisted of five rows. Each row showed the percentage range in the answer. Ranges of percentage were 1%–20% in the first row, 21%–40% in the second, 41%–60% in the third, 61%–80% in the fourth, and finally 81%–100% in the fifth. The respondent's perception of the factors contributing to antibiotic resistance was assessed by another question that consisted of a 4-point Likert scale, whose responses ranged from "very important" to "not important at all". The next two knowledge-based questions were about the number of new classes of antibiotics that became clinically available in

the last 30 years as well as those that will become available in the next 30 years. The last three questions were used to assess the respondent's perceptions of AR.

There are four routes available to students to pursue a degree program in Malaysia. The Ministry of Education conducts two qualifying programs to the first degree programs: the first program allows students to matriculate at secondary school. This program is usually a 1-year program, but may extend up to 2 years if necessary. The majority of UniSZA students have completed the 1-year matriculation program. The second route is the Malaysia Certificate of Higher Education, which is a 1.5-year program. Also, a 1-year foundation training is conducted by top Malaysian universities. Finally, students can opt to complete a diploma after secondary school, and later apply for entry into a degree program.[71]

This research obtained UniSZA Research Ethics Committee (UHREC) ethical approval; the certificate was obtained (UniSZA. C/1/UHREC/628-1 [4], March 5, 2015) before the study was conducted. Research ethics were strictly maintained, especially regarding confidentiality. Explanation concerning the purpose of the study was given, and informed consent was obtained verbally from the participants to utilize their data for research purposes. UHREC had examined the questionnaire before the study was started. UHREC was satisfied that there were no sensitive questions. The current research was a questionnaire-based knowledge, attitude, and practice study, which was totally anonymous and voluntary. Thus, researchers thought verbal consent was sufficient. The principal investigator informed UHREC and took permission for the verbal consent procedures before data collection began. This study recovered 86% of the questionnaires as respondents were given total liberty to refuse the study. Simple descriptive statistics were used to generate frequencies and percentages using SPSS Version 20 (IBM Corporation, Armonk, NY, USA).

Results

Demographic profile

A total of 142 out of 164 (86%) medical students returned the questionnaire. Specifically, the year-wise response was 29% (41), 39% (55), and 32% (45) for Year III, IV, and V, respectively. Among the study respondents, 28% (40) were male, and the remaining 72% (102) were female. The majority (92%, 131) of the respondents were single, but the rest were either engaged (5%, 7) or married (2%, 3). Similarly, the majority of the current study population were Malay (82%, 116) and the rest were either Indian (10%, 14) or Chinese (7%, 10) in ethnic origin. The study population had different religious backgrounds; 84% (119) identified as Muslim, Hindu (8%, 11), Buddhist (6%, 8), and Christian (1%, 2). In all, 78% (111) of the present study population have undergone a 1-year matriculation and the rest either a 2-year matriculation (1%, 2) or other (17%, 24) (Table 1).

Levels of confidence in prescribing

The participants felt more confident in "making an accurate diagnosis of infection/sepsis" (67%, 95), "interpreting microbiological results" (55%, 78), "choosing the correct antibiotic" (55%, 78), "choosing the correct dose and interval of administration" (42%, 52), "using a combination therapy if appropriate" (44%, 63), "choosing between intravenous and oral administration" (56%, 79), "deciding not to prescribe an antibiotic if the patient has fever, but no severity criteria, and if you are not sure about your diagnosis" (56%, 79), "planning to streamline/stop the antibiotic treatment according to the clinical evaluation and investigations" (51%, 72), and "planning the duration of the antibiotic treatment" (49%, 69). The respondents felt unconfident in "interpreting microbiological results" (25%, 36), "choosing the correct antibiotic" (30%, 42), "choosing the correct dose and interval of administration" (42%, 60), "using a combination therapy if appropriate" (40%, 57), "deciding not to prescribe an antibiotic if the patient has fever, but no severity criteria, and

Table 1 Demography of study population (n=142)

Variable	n	%
Sociodemographic characteristics		
Sex		
Male	40	28.2
Female	102	71.8
Marital status[a]		
Single	131	92.2
Engaged	7	4.9
Married	3	2.1
Race[b]		
Malay	116	81.7
Chinese	10	7.0
Indian	14	9.9
Religion[b]		
Muslim	119	83.8
Buddhist	8	5.6
Hindu	11	7.7
Christian	2	1.4
Educational characteristics		
Year of study[a]		
Year III	41	28.9
Year IV	55	38.7
Year V	45	31.7
Type of foundation study[c]		
One-year matriculation	111	78.2
Two-year matriculation	2	1.4
Others	24	16.9

Notes: [a]1 missing data; [b]2 missing data; [c]5 missing data.

if you are not sure about your diagnosis" (26%, 37), "planning to streamline/stop the antibiotic treatment according to the clinical evaluation and investigations" (31%, 44), and "planning the duration of the antibiotic treatment" (35%, 49).

The detailed results are shown in Table 2. There were no significant differences ($P>0.05$) observed in any of parameters of confidence of antibiotic prescribing between year and the sex of the respondents (Tables 3 and 4).

Table 2 Levels of confidence in different areas of antibiotic prescribing (n=142)

Level of confidence-based on domain	Number of respondents, n (%)			Total
	Year III	Year IV	Year V	
Making an accurate diagnosis of infection/sepsis				
Very unconfident	0 (0)	1 (1.8)	0 (0)	1 (0.7)
Unconfident	8 (19.5)	10 (18.2)	3 (6.7)	21 (14.8)
Confident	**27 (65.9)**	**35 (63.6)**	**32 (71.1)**	**95 (66.9)**
Very confident	4 (9.8)	6 (10.9)	9 (20.0)	19 (13.4)
Uncertain	2 (4.9)	3 (5.5)	1(2.2)	6 (4.2)
Interpreting microbiological results				
Very unconfident	1 (2.4)	1 (1.8)	0 (0)	2 (1.4)
Unconfident	12 (29.3)	18 (32.7)	6 (13.3)	36 (25.4)
Confident	**20 (48.8)**	**26 (47.3)**	**31 (68.9)**	**78 (54.9)**
Very confident	5 (12.2)	7 (12.7)	7 (15.6)	19 (3.4)
Uncertain	3 (7.3)	3 (5.5)	1 (2.2)	7 (4.9)
Choosing the correct antibiotic				
Very unconfident	1 (2.4)	1 (1.8)	0 (0)	2 (1.4)
Unconfident	10 (24.4)	21 (38.2)	10 (22.2)	42 (29.6)
Confident	**24 (58.5)**	**26 (47.3)**	**28 (62.2)**	**78 (54.9)**
Very confident	6 (14.6)	5 (9.1)	6 (13.3)	17 (12.0)
Uncertain	0 (0)	2 (3.6)	1 (2.2)	3 (2.1)
Choosing the correct dose and interval of administration				
Very unconfident	1 (2.4)	1 (1.8)	1 (2.2)	3 (2.8)
Unconfident	15 (36.6)	**24 (43.6)**	**21 (46.7)**	**60 (42.3)**
Confident	**22 (53.7)**	20 (36.4)	17 (37.8)	59 (41.5)
Very confident	2 (4.9)	5 (9.1)	3 (6.7)	10 (7.0)
Uncertain	1 (2.4)	5 (9.1)	3 (6.7)	9 (6.3)
Using a combination therapy if appropriate				
Very unconfident	1 (2.4)	2 (3.6)	0 (0)	4 (2.8)
Unconfident	14 (34.1)	**26 (47.3)**	17 (37.8)	57 (40.1)
Confident	**22 (53.7)**	19 (34.5)	**22 (48.9)**	**63 (44.4)**
Very confident	3 (7.3)	6 (10.9)	4 (8.9)	13 (9.2)
Uncertain	1 (2.4)	2 (3.6)	2 (4.4)	5 (3.5)
Choosing between intravenous and oral administration				
Very unconfident	0 (0)	1 (1.8)	0 (0)	1 (0.7)
Unconfident	15 (36.6)	9 (16.4)	8 (17.8)	32 (22.5)
Confident	**16 (39.0)**	**34 (61.8)**	**28 (62.2)**	**79 (55.6)**
Very confident	8 (19.5)	10 (18.2)	8 (17.8)	26 (18.3)
Uncertain	2 (4.9)	1 (1.8)	1 (2.2)	4 (2.8)
Deciding not to prescribe an antibiotic if the patient has a fever, but no severity criteria, and if you are not sure about your diagnosis[a]				
Very unconfident	0 (0)	2 (3.6)	0 (0)	2 (1.4)
Unconfident	12 (29.3)	16 (29.1)	9 (20.0)	37 (26.1)
Confident	**23 (56.1)**	**25 (45.5)**	**30 (66.7)**	**79 (55.6)**
Very confident	4 (9.8)	6 (10.9)	3 (6.7)	13 (9.2)
Uncertain	2 (4.9)	5 (9.1)	3 (6.70)	10 (7.0)
Planning to streamline/stop the antibiotic treatment, according to clinical evaluation and investigations				
Very unconfident	0 (0)	0 (0)	0 (0)	0 (0)
Unconfident	13 (31.7)	19 (34.5)	12 (26.7)	44 (31.0)
Confident	**18 (43.9)**	**24 (43.6)**	**29 (64.4)**	**72 (50.7)**
Very confident	9 (22.0)	5 (9.1)	2 (4.4)	16 (11.3)
Uncertain	1 (2.4)	7 (12.7)	2 (4.4)	10 (7.0)
Planning the duration of the antibiotic treatment				
Very unconfident	1 (2.4)	2 (3.6)	1 (2.2)	4 (2.8)
Unconfident	14 (34.1)	16 (29.1)	18 (40.0)	49 (34.5)
Confident	**21 (51.2)**	**24 (43.6)**	**24 (53.3)**	**69 (48.6)**
Very confident	5 (12.2)	8 (14.5)	2 (4.4)	15 (10.6)
Uncertain	0 (0)	5 (9.1)	0 (0)	5 (3.5)

Notes: The highest frequency is bold. [a]1s missing data.

Table 3 Comparison among Year III, IV, and V in levels of confidence of antibiotic prescribing

	Areas of confidence in prescribing	Mean (SD)			*F* stat	*P*-value*
		Year III	Year IV	Year V		
1	Making accurate diagnosis of infection	3.00 (0.71)	3.00 (0.77)	3.18 (0.58)	0.67	0.571
2	Decide not to prescribe antibiotic	2.90 (0.77)	21.04 (134.31)	3.00 (0.74)	0.52	0.669
3	Choose correct antibiotic	2.85 (0.69)	2.75 (0.80)	2.96 (0.67)	1.13	0.339
4	Choose correct dose	2.68 (0.72)	2.80 (0.97)	2.69 (0.90)	1.46	0.228
5	Use combine therapy	2.73 (0.74)	2.64 (0.87)	2.80 (0.79)	1.84	0.143
6	Choose route of administration	2.93 (0.88)	3.02 (0.71)	3.04 (0.67)	0.19	0.901
7	Interpret microbe result	2.93 (0.91)	2.87 (0.86)	3.07 (0.62)	0.50	0.686
8	Planning to stop antibiotic	2.95 (0.81)	3.00 (0.98)	2.87 (0.69)	0.21	0.891
9	Planning duration of antibiotic	2.73 (0.71)	2.96 (0.98)	2.60 (0.62)	2.08	0.106

Note: *One-way analysis of variance.
Abbreviation: SD, standard deviation.

Training in antibiotic prescribing

The majority (88%, 124) of the study participants stated that they would like more training in the antibiotic selection, seven students (5%) did not want further education, and another eleven students (8%) were unsure. Most of the respondents (87%, 123) felt prescribing inappropriate or unnecessary antibiotics to be professionally unethical. In all, 72% (102) of the respondents were confident that their current teaching Hospital Sultanah Nur Zahirah (HSNZ) has antibiotic guidelines, but 23% (33) students were unaware, and 5% (7) students indicated that there are no antibiotic guidelines for HSNZ. In all, 50% (71) of the respondents do not possess a copy of HSNZ antibiotic guidelines or found it on the internet while 34% (48) of students said they received a copy and 16% (23) students were unsure about it. Personally consulting antibiotic guidelines when considering an antibiotic for a patient was only practiced by 45% (64) students, and the rest, 39% (56) and 16% (22) students, were either not practiced or unsure (Figure 1). There were statistically (P=0.018) significant differences observed among Year of Study of the respondents regarding the question "How many hours of training in the principles of prudent antibiotic use do you think you have received during your undergraduate study?"

Knowledge that may shape perceptions of AR

Most students (83%, 118) felt that antibiotic resistance was a national problem, and 63% (90) felt that the situation also exists in the teaching hospital (Figure 2). In all, 42% (59) of respondents stated that methicillin-resistant *Staphylococcus aureus* was responsible for a greater proportion (21%–40%) of *S. aureus* bacteremia in Malaysia, while 35% (50) respondents stated that it was <1% 10 years ago. In all, 49% (65) respondents thought that over 1%–20% of *S. aureus* bacteremias were caused by vancomycin-resistant bacteria in Malaysia, and 40% (57) respondents believed that over 21%–40% of all bacterial infections in Malaysia (excluding TB) were resistant to all known antibiotics (Figure 3). There were no significant differences (P>0.05) observed in any of parameters regarding knowledge that may shape the perception of AR between year and sex of the respondents.

Table 4 Comparison between sexes in levels of confidence of antibiotic prescribing

	Areas of confidence in prescribing	Mean (SD)		Mean difference	*t*-stat (*df*)	*P*-value*
		Male	Female	(95% CI)		
1	Making accurate diagnosis of infection	3.18 (0.64)	3.01 (0.71)	0.17 (–0.09, 0.42)	1.28 (140)	0.202
2	Decide not to prescribe antibiotic	3.03 (0.86)	12.68 (98.63)	–9.65 (–40.55, 21.25)	–0.62 (140)	0.538
3	Choose correct antibiotic	2.93 (0.76)	2.8 (0.72)	0.12 (–0.15, 0.39)	0.89 (140)	0.376
4	Choose correct dose	2.75 (0.98)	2.71 (0.85)	0.04 (–0.28, 0.37)	0.27 (140)	0.791
5	Use combine therapy	2.75 (0.90)	2.69 (0.78)	0.06 (–0.24, 0.37)	0.42 (140)	0.677
6	Choose route of administration	3.00 (0.75)	3.00 (0.75)	0 (–0.28, 0.28)	0.00 (140)	1.000
7	Interpret microbe result	3.00 (0.60)	2.93 (0.87)	0.07 (–0.19, 0.32)	0.54 (103.02)	0.593
8	Planning to stop antibiotic	2.98 (0.83)	2.93 (0.85)	0.04 (–0.27, 0.36)	0.28 (140)	0.782
9	Planning duration of antibiotic	2.75 (0.87)	2.78 (0.79)	–0.03 (–0.34, 0.27)	–0.23 (140)	0.822

Note: *Independent *t*-test.
Abbreviations: SD, standard deviation; CI, confidence interval.

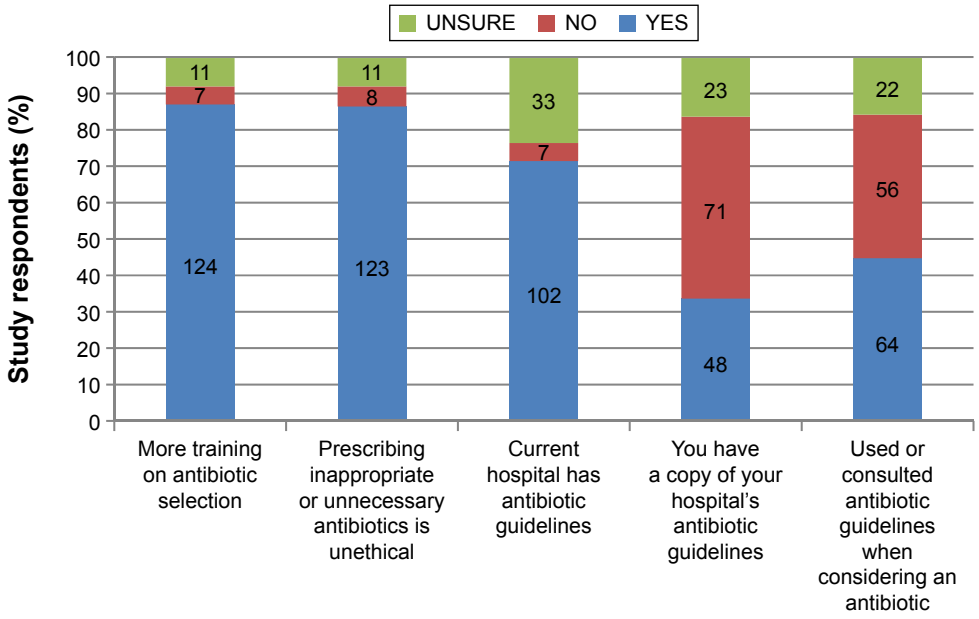

Figure 1 Questions on training in antibiotic prescribing.

Antibiotic usage

About 35% (49) of the respondents felt that the proportion of all clinical antibiotic use in a hospital in Malaysia comprised of 41%–60% of cases when compared to the community. In all, 37% (52) of the respondents agreed that the clinical antibiotic usage in this country is probably unnecessary or inappropriate by 1%–20% (Figure 4).

Contributors to resistance

The majority of the respondents agreed that "too many antibiotic prescriptions" (55%, 78), "too many broad spectrum antibiotics used" (50%, 71), and "excessive use of antibiotics in livestock" (43%, 61) were leading contributors to AR (Table 5). Another group felt that "too long durations of antibiotic treatment" (42%, 59), "dosing of antibiotics are too low" (36%, 51), "poor hand hygiene" (27%, 38), "not removing the focus of infection" (41%, 58), and "paying too much attention to pharmaceutical representatives/advertising" (37%, 53) were moderately important factors contributing to AR (Table 5). The rest of the study participants gave the opinion for slightly important and not important contributors to generate AR (Table 5). There were no significant differences ($P>0.05$) observed in any of parameters of confidence of antibiotic prescribing between years and the sex of the respondents (Tables 6 and 7).

Development of antibiotics

In all, 44% (63) of the respondents believed that six to ten antibiotic classes were available during the period 1980–2011, and 23% (45) of students thought that there would be six to ten new antibiotic classes in 2011–2020 (Figure 5).

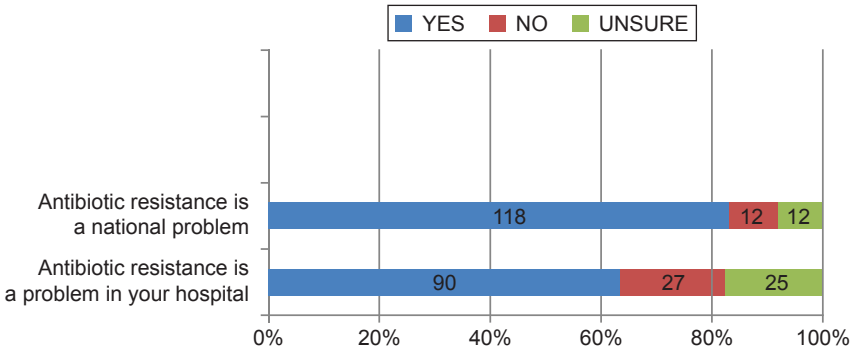

Figure 2 Students' perceptions of antimicrobial resistance.

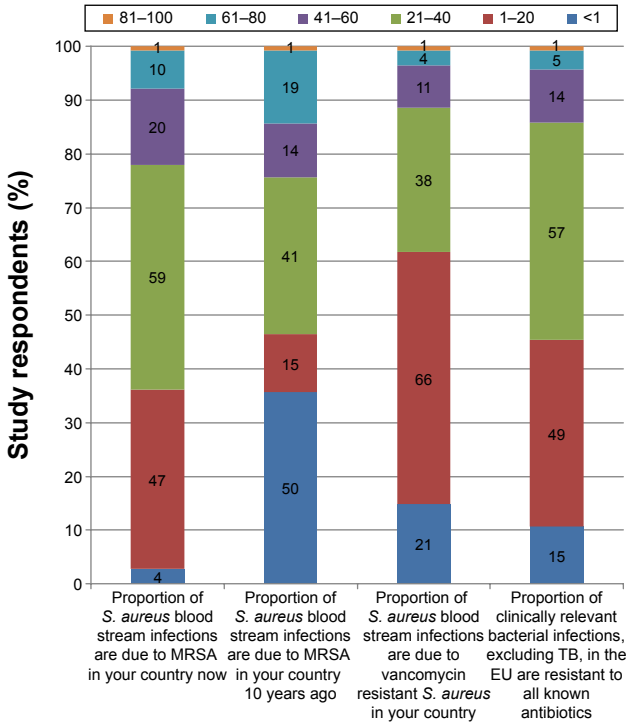

Figure 3 Knowledge of students that may shape perceptions of antimicrobial resistance.

Abbreviations: EU, European Union; MRSA, methicillin-resistant *Staphylococcus aureus*; *S. aureus*, *Staphylococcus aureus*; TB, tuberculosis.

Perceptions of AR

Resistant bacteria are believed to cause 25,000 deaths per year in Europe.[79] Road traffic accidents (RTAs) and lung cancer are responsible for around two to three and ten times as many deaths, respectively.[80] Overall, 27% (38) and 36% (51) of research participants think that deaths due to AR were four to eight times higher than RTA and lung cancer, respectively (Figure 6). In all, 23% (33) medical students in the study were able to answer correctly for estimation of RTAs while 36% (51) answered correctly the reasonable estimate for comparison between deaths due to lung cancer and AR. Most of the respondents (45%, 65) felt that the antibiotics they would prescribe as doctors would likely contribute to the problem of AR later, and 42% (60) students believed that antibiotic resistance would become a possible clinical problem during their career.

Discussion

Demographic profile

The response rate of the students for the current study was 86%, which is very similar to that of a Danish recommendation.[81] Universal sampling was adopted because of small population size (179) and 15 of them participated in the pilot study. Consequently, 164 was the total population to whom the questionnaire was distributed; among them, 142 (86%) returned and 22 did not participate in the study. The study respondents are able to enjoy complete freedom to participate or not. Hence, it is hard to answer why they did not return the questionnaire. Furthermore, a total of 157 (15+142) joined the current work. So, actually among 179 clinical students of UniSZA, 88% participated in this cross-sectional research. In this study, there were more female medical students than male colleagues; this finding is analogous to that in many other studies.[75–78,82–84]

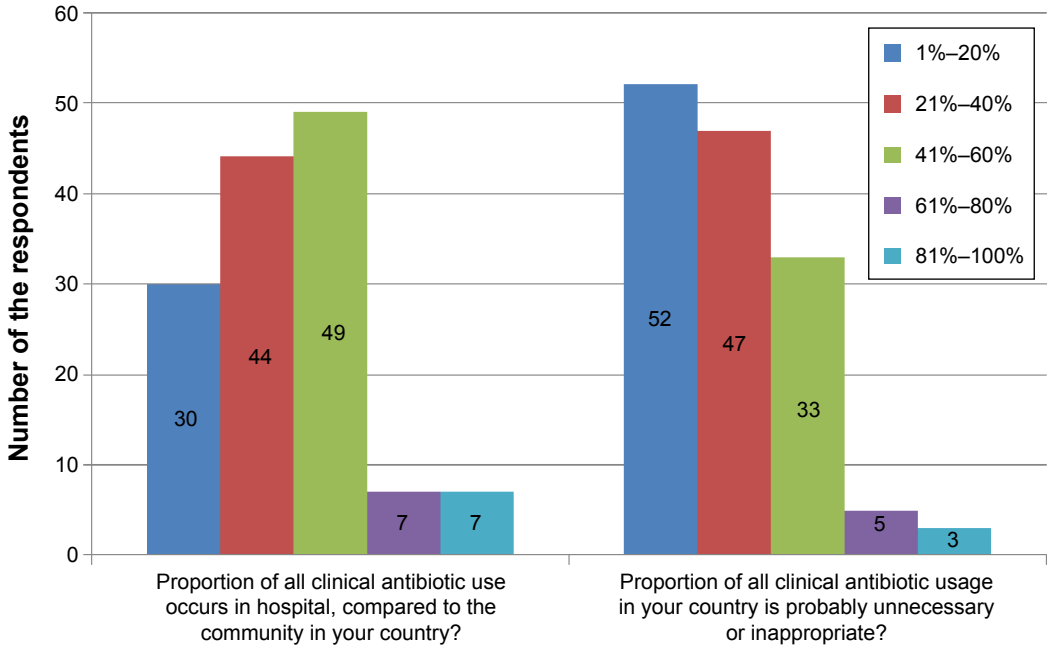

Figure 4 Knowledge of proportion of all clinical antibiotic usage.

Table 5 Perceptions of the importance of potential contributors to antibiotic resistance (n=142)

Statements	Number of respondent, n (%)			
	Very important	Moderately important	Slightly important	Not important
Too many antibiotic prescriptions	**78 (54.9)**	47 (33.1)	14 (9.9)	3 (2.1)
Too many broad spectrum antibiotics used	**71 (50.0)**	51 (35.9)	16 (11.3)	4 (2.8)
Too long durations of antibiotic treatment[a]	43 (30.3)	**59 (41.5)**	30 (21.1)	9 (6.3)
Dosing of antibiotics are too low	29 (20.4)	**51 (35.9)**	50 (35.2)	12 (8.5)
Excessive use of antibiotics in livestock	**61 (43.0)**	45 (31.7)	28 (19.7)	8 (5.6)
Poor hand hygiene	31 (21.8)	**38 (26.8)**	37 (26.1)	36 (25.4)
Not removing the focus of infection (eg, medical devices or catheters)	53 (37.3)	**58 (40.8)**	24 (16.9)	7 (4.9)
Paying too much attention to pharmaceutical representatives/advertising[b]	31 (21.8)	**53 (37.3)**	35 (24.6)	21 (14.8)

Notes: The highest frequency is bold. [a]1 missing data; [b]2 missing data.

Table 6 Comparison among Year III, IV, and V in levels of contributors to resistance

	Contributors to resistance	Mean (SD)			*F* stat	*P*-value*
		Year III	Year IV	Year V		
1	Too many antibiotic prescriptions	1.73 (0.78)	1.51 (0.77)	1.58 (0.72)	0.90	0.444
2	Too many broad spectrums used	1.73 (0.78)	1.71 (0.88)	1.58 (0.69)	0.57	0.635
3	Too long duration	2.15 (0.79)	20.25 (134.42)	1.84 (0.85)	0.53	0.662
4	Dosing too low	2.44 (0.74)	2.25 (0.95)	2.31 (0.95)	1.07	0.364
5	Excessive use of antibiotics	1.95 (0.87)	1.93 (0.94)	1.78 (0.95)	0.62	0.605
6	Poor hand hygiene	2.29 (1.06)	2.55 (1.05)	2.76 (1.15)	1.90	0.132
7	Not removing focus of infection	2.07 (0.85)	1.89 (0.94)	1.76 (0.74)	1.36	0.256
8	Pay too much on attention advertising	26.41 (155.69)	20.42 (134.40)	2.56 (0.97)	0.33	0.806

Note: *One-way analysis of variance.
Abbreviation: SD, standard deviation.

Table 7 Comparison between sexes on their view regarding contributors to resistance

	Contributors to resistance	Mean (SD)		Mean difference	*t*-stat (*df*)	*P*-value*
		Male	Female	(95% CI)		
1	Too many antibiotic prescriptions	1.68 (0.80)	1.56 (0.74)	0.12 (–0.16, 0.4)	0.82 (140)	0.411
2	Too many broad spectrums used	1.80 (0.91)	1.62 (0.73)	0.18 (–0.11, 0.47)	1.24 (140)	0.216
3	Too long duration	26.98 (157.63)	2.03 (0.92)	24.95 (–25.47, 75.36)	1.00 (39.00)	0.323
4	Dosing too low	2.38 (0.84)	2.29 (0.92)	0.08 (–0.25, 0.41)	0.48 (140)	0.629
5	Excessive use of antibiotics	1.90 (0.84)	1.87 (0.95)	0.03 (–0.31, 0.37)	0.16 (140)	0.873
6	Poor hand hygiene	2.50 (1.06)	2.57 (1.11)	–0.07 (–0.47, 0.34)	–0.34 (140)	0.738
7	Not removing focus of infection	1.85 (0.80)	1.91 (0.88)	–0.06 (–0.38, 0.26)	–0.39 (140)	0.701
8	Pay too much attention on advertising	2.38 (0.98)	21.85 (138.88)	–19.48 (–62.99, 24.03)	–0.89 (140)	0.378

Note: *Independent *t*-test.
Abbreviation: SD, standard deviation.

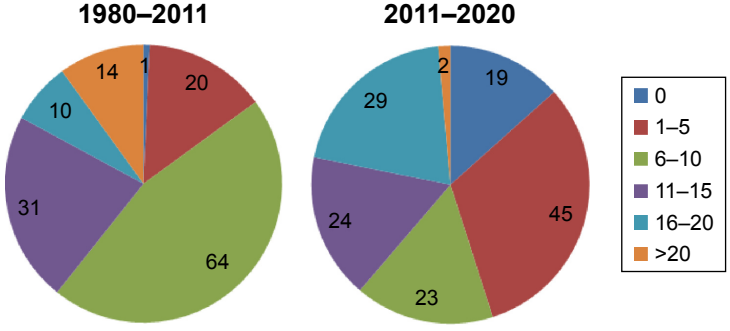

Figure 5 New classes of antibiotics that students think became clinically available at years 1980–2011 and 2011–2020.

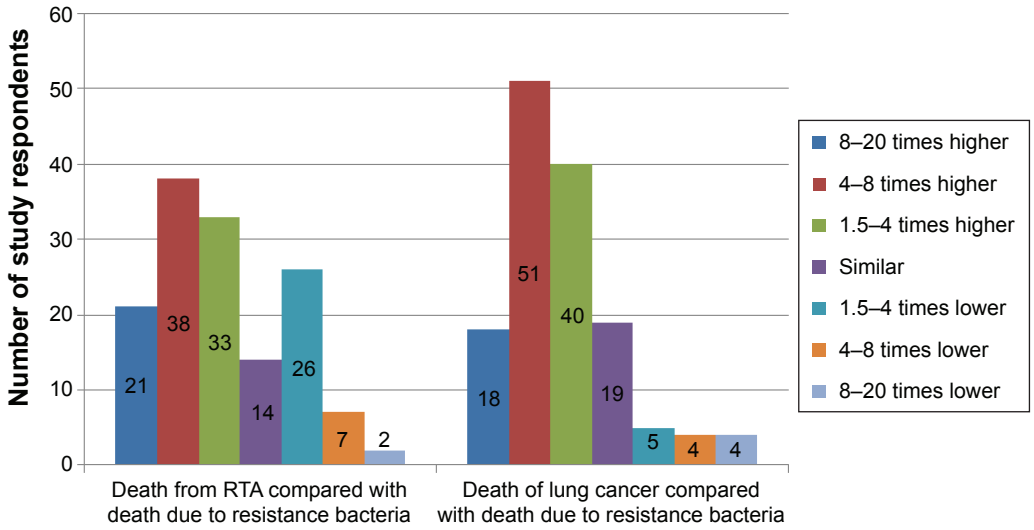

Figure 6 Student's perception of death from road traffic accidents and lung cancer compared with death due to bacterial resistance to antimicrobials.
Abbreviation: RTA, road traffic accident.

Levels of confidence in prescribing

The participants felt more confident in "making an accurate diagnosis of infection/sepsis" (67%), "interpreting microbiological results" (55%), "choosing the correct antibiotic" (55%), "choosing the correct dose and interval of administration" (42%), "using a combination therapy if appropriate" (44%), "choosing between intravenous and oral administration" (56%), "deciding not to prescribe an antibiotic if the patient has fever, but no severity criteria, and if you are not sure about your diagnosis" (56%), "planning to streamline/stop the antibiotic treatment according to the clinical evaluation and investigations" (51%), and "planning the duration of the antibiotic treatment" (49%). Overall, 50% or more of current study participants were confident of six of nine issues of the level of confidence in prescribing. Current study findings regarding knowledge level of antibiotic prescribing and resistance were not satisfactory, but research participants were medical students of Years III–V. Again, at UniSZA, from year III, students are first exposed to the hospital and patients. As in first 2 years, they go to preclinical subjects with only little early clinical exposure. Therefore, study participants have at least 3 months to 2 years and 3 months extra time to learn more regarding antibiotic prescribing in their clinical years. Moreover, after graduation, according to Malaysian regulations, they will be working as a house officer for another 2 years under strict supervision. Consequently, there is time for improvement. Our study findings were lower than some European studies and Bangladeshi studies conducted on interns or house officers.[65,85–87] But regarding "using a combination therapy if appropriate," our respondents obtain an almost similar score to the studies, although our participants were medical students and those were trainee doctors.[85,87]

Training in antibiotic prescribing

The majority (88%) of the respondents stated that they would like more training on antibiotic selection. Most of the respondents (87%) felt prescribing antibiotics irrationally was unethical. About 72% of study respondents were sure that HSNZ had antibiotic guidelines, but 50% of them did not possess a copy of the guide, and only 45% had consulted the antibiotic guidelines (Figure 1). Study findings showed that the respondents have realized there is a gap between their theoretical lecture-based input,[72] regarding antimicrobials, and clinical practice. Similar studies from different countries also indicated demand for more educational intervention.[55–65,70,87] The total antimicrobials class hours at the faculty of medicine is 7 hours during the first 2 years of the preclinical stage. All are lecture-based teaching hours. UniSZA's medical curriculum does not currently possess any class for teaching antimicrobial selection. Therefore, students when started clinical clerking they comprehend that there is an urgent need for training of drug, including antimicrobial selection procedure.

Knowledge that may shape perceptions of AR

Most students (83%) felt that antibiotic resistance is a national problem, and 63% felt that the situation also exists in HSNZ (Figure 2). In all, 42% of our medical students stated that 21%–40% *S. aureus* infections were due to methicillin-resistant *Staphylococcus aureus* while 35%

thought it was <1% 10 years ago. In all, 49% research participants thought that over 1%–20% of *S. aureus* bacteremias were caused by vancomycin-resistant bacteria in Malaysia, and 40% students believed that over 21%–40% of all bacterial infections in Malaysia (excluding TB) were resistant to all known antibiotics (Figure 3). These findings were more or less similar to Bangladeshi and European studies.[85,87]

Antibiotic usage

About 35% and 23% of the research participants thought that 41%–60% antimicrobials used in hospitals in Malaysia and the antibiotic chosen were inappropriate (Figure 4). Current study findings regarding antimicrobial usage in the hospital are lower than the US study[23] but the irrational use of antibiotics was quite similar to a number of studies.[25–28]

Contributors to resistance

The majority of this study respondents agreed that "too many antibiotic prescriptions" (55%), "too many broad spectrum antibiotics used" (50%), and "excessive use of antibiotics in livestock" (43%) were primary contributors to AR (Table 5). These findings were similar to some studies conducted in different parts of the world.[85,88–90] Another group felt that "too long durations of antibiotic treatment" (42%), "dosing of antibiotics are too low" (36%), "poor hand hygiene" (27%), "not removing the focus of infection" (41%, 58), and "paying too much attention to pharmaceutical representatives/advertising" (37%) were moderately important factors contributing to AR (Table 5). A good number of research participants were quite aware of poor hand hygiene as a contributor to AR. A lot of studies have reported that poor hand hygiene contributes to AR.[90–92] Since our respondents were still students and remain within the university, they have yet to be exposed to the persuasions of the pharmaceutical industries.[76,87,93]

Development of antibiotics

In all, 45% and 32% of the research participants believed that six to ten and eleven to 15 antibiotic classes became available during the period 1980–2011 and 2011–2020, respectively (Figure 5). The present study findings were different from a European study. In this study, respondents believed that more antimicrobials were available during 2011–2020.[65]

Perceptions of AR

About 23% and 10% of research participants think that death due to RTA and lung cancer is four to five and eight to 20 times higher than AR, respectively (Figure 6). These findings were only 9% in a multicenter European study.[65] Research respondents (10–13%) thought that death due to RTA and lung cancer were similar with AR but a European study reported that 51% of study respondents believed there are similar mortality numbers in AR, RTA and lung cancer (Figure 6).[65]

Limitation of the study

This is a cross-sectional study. Therefore, the findings are only the snapshot of the current clinical batches of medical students in UniSZA, Malaysia. Again, the sample size was small because the UniSZA MBBS program has only 179 clinical medical students. Therefore, it will be difficult to generalize the findings for the whole country.

Conclusion

Taking into account the limitation of a cross-sectional study, this study was able to find the prevailing perception of respondents regarding antimicrobial prescribing and resistance. This research has evidently concluded that there is a gap between theoretical input and clinical practice. Students have demanded more educational intervention to face this potential threat of AR. Clinical competency regarding antibiotic prescribing during their housemanship was mainly acquired by emulating senior colleagues, and this should be replaced by P-drug selection program in the MBBS curriculum and also during housemanship. Both national and local guidelines for antibiotic prescribing should be made available more easily, preferably as a free download from the university or hospital website. Moreover, care must be taken to update the guidelines regularly. In summary, AR is a multifactorial problem. Therefore, much integration and cooperation among all health professionals, including patients, is needed to eliminate and reduce the risk of bacterial resistance developing to antimicrobials.

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Disclosure

The authors report no conflicts of interest in this work.

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