Senior Medical Students' Knowledge, Attitude, and Perception Concerning Antibiotic Use and Resistance in Cambodia

- Mr. PHAN Chanarong, MSc.
- Mr. SOPUTHY Chansovannara, MHCD.
- Ms. LAY Sokreaksa, PharmD.
- Assist. Prof. CHAU Darapheak, MD, MPH, PhD

I. Introduction

Emerging and increasing antimicrobial resistance (AMR) poses potential threats to global health, food, and development which requires global multisectoral actions to sustain tomorrow's treatment (1). Antibiotic misuse, overuse, and underuse in both human and animal health are accelerating the process and mechanism of antibiotic resistance in addition to it occurring naturally (1). While the effectiveness of antibiotics is becoming less effective, an increasing number of infectious diseases, including pneumonia, tuberculosis, sepsis, gonorrhea, and foodborne diseases, are becoming sometimes impossible and difficult to treat which are the leading cause of mortality and morbidity mainly in low-and middle-income countries (LMICs) (1). In 2019, AMR directly and indirectly claimed about 5 million human lives and it is predicted that if the recent trend of inappropriate use and excessive use of antimicrobial continue, the mortality rate can rise up to 10 million deaths by 2050 (2–4).

Southeast Asia is particularly vulnerable to the emerging and spreading of antibiotic resistance according to AMR risk assessment in 2017 (5). The upsurge of resistant pathogens negatively impacts the ability to cure common infections and cause the illnesses to become more severe which could lead to prolonged duration of hospitalization, elevate the risk of morbidity and mortality, and increase health care expenditure (3). In Thailand, it is estimated that multidrug resistance bacteria were attributed to an additional 43% of death in patients with hospital-acquired infections (6). In addition, the economic cost of pathogens resistance - such as *Staphylococcus aureus*, *Escherichia coli*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, and *Pseudomonas aeruginosa*- was approximately $0.5 billion in Thailand in 2010 (7). In Cambodia, several pathogenic organisms with high resistance rates including *Escherichia coli*, *Klebsiella pneumoniae*, and *Salmonella spp.* have been reported to WHO Global Antimicrobial Resistance and Use Surveillance System (GLASS); however, there is still inadequate data on AMR to make conclusions on the issue (8).

In the context of healthcare in Cambodia, antibiotic inappropriate use is complex when we consider that it could be driven by various factors including physician prescribing habits, limited diagnostic capacity, lack of microbiology evidence, non-evidence-based clinical guidelines, perceived patient demand, poor hygiene and infection control, antibiotic misconception and accessibility, and perceived bacterial resistance to narrow-spectrum antibiotics (9,10). A national survey of Cambodia physician's study highlighted some concerns that 54% of physicians were aware that antibiotic prescriptions in their healthcare settings were inappropriate, and 93% had experienced difficulty in selecting appropriate antibiotics to treat common infections like common cold and diarrhea (11). Furthermore, 86% and 36% of physicians who participated in the survey prescribed antibiotics to treat the common cold and diarrhea respectively, while most cases were caused by viral infection (11). More importantly, 63% of physicians had not been trained and only 25% had received a little coaching about the rational use of antibiotics and AMR (11). This suggests AMR courses should be included in the health science program curriculum to equip future physicians with adequate knowledge and to promote rational antibiotic use in pre-service training modules.

The WHO emphasizes in the Global Action Plan on AMR in 2016 that member states should improve awareness and understanding of AMR through effective communication, education, and training by making AMR as a key component of professional education, training, certification, continuing education, and development in both human and animal health sectors, as well as agricultural practice (3). In this regard, several countries in LMICs have conducted knowledge, attitude, and perception (KAP) surveys to gain insightful understanding of antibiotic use and resistance among medical health students (12–16). A study in 2014 surveyed senior medical students (SMS) in their final year in Thailand found that respondents had a good perception of AMR problems, whereas they perceived low scores in knowledge sections such as antibiotic use (56%), appropriate antibiotic prescribing (52.8%) and mechanism of resistance (32%) (12). Another study on confidence in antibiotic prescribing intention among SMS in India highlighted that only 35% of participants felt confident in prescribing appropriate antibiotics for their patients in the future which pose a concern to public health leading to increase in the risk of AMR (14). While KAP data on medical students is limited in Cambodia, it is crucial to evaluate Cambodian SMS' knowledge, attitude, and perception toward rational antibiotic use and resistance to better understand the challenges, gaps, and opportunities to improve their performance during pre-service training years.

Rational use of antimicrobials in all clinical settings has become standard practice implementation and it is a major focus of undergraduate and graduate medical science education (17). Also, the fifth of seven

strategies framework to Combat Antimicrobial Resistance in Cambodia's National Policy in 2014 is “to regulate and promote the rational use of medicine” through promoting education on antimicrobial medicine and their proper use by professional society and academic institutions (18). This study aimed to assess the level of knowledge, attitudes, and perceptions regarding antibiotic use and resistance among senior medical students in Cambodia and to identify factors associated with these key indicators. Our research findings will be evidence-based for the medical universities in Cambodia to consider Antimicrobial Stewardship (AMS) as a competency-based approach for future medical professional workers.

II. Methods

1.1. Study design

A cross-sectional study was designed to assess the knowledge, attitude, and perception in relation to antibiotic use and resistance among the final year (year 6) of medical students in Cambodia.

1.2. Survey population

There are 20 higher education institutes in Cambodia that provide training in the field of health sciences, of which seven and thirteen are public and private medical institutes, respectively (20). Among them, only 6 universities provide a degree in Medical Doctor.

For our study, three selected among five universities were invited to participate based on convenient accessibility. Senior medical students from these three selected medical universities in Cambodia were eligible to join the study.

1.3. Sample size calculation

A single population proportion formulation was applied in this study to calculate the sample size. Since there was limited KAP study on antibiotics and resistance among senior medical students in Cambodia. We assumed that the probability of senior medical students having poor knowledge, attitude, and perception was equal to 50%.

Formular $\mathbf{n=z^2(PQ)/d^2}$

Where Z = 1.96 (95% confidence interval), P = 50%, Q= 1-P, D= 0.08 (degree of accuracy =8%)

Based on the calculation, the number of participants in this study was 150 students. To account for the 10% non-response rate, the final sample size for this survey is 165, of which 55 students were randomly selected from each university.

1.4. Subject selection and inclusion criteria

This study only invited eligible respondents who referred to a medical student enrolling in year 6 of the three selected medical universities in Phnom Penh.

As an exclusion criterion, the research team attempted to contact selected participants from the sampling frame only three times. If we could not reach them by either phone or email, we moved to the next respondent.

1.5. Sample design

The student's name list and contact (telephone and email) information were obtained to develop a sampling frame for each university. Simple randomized selection was used to select participants. 55 students were randomly selected from the sampling frames for each university, then they were asked to join the self-administered questionnaire.

1.6. Data collection tool and procedure

The structured questionnaire was designed in the Khmer language to investigate various aspects of an individual's KAP, consisting of both negative and positive statements. The instrument was adapted from previous studies (12–14,16,21). The structured questionnaire comprised five dimensions with 55 items, including socio-demographic (8 items), education background on antibiotics (8 items), antibiotic consumption (3 items), knowledge (20 items), attitudes and perceptions of antibiotic use, and resistance (16 items). Students spent approximately 20 to 30 minutes to complete the self-administered questionnaire.

The data collectors were trained for data collection, and informed consent. The self-administered questionnaire was distributed to selected medical students at the three universities after seeking approval from the universities. Written consent was obtained for approval from each individual student to ensure that the participation was voluntary prior to the data collection. The study objectives, individual confidentiality information, benefit, and other ethical information were stated in the consent form and

explained by our data collectors/researchers during the data collection period. All students were encouraged to answer all the questions as much as they can.

1.8. Exposure and Outcome

Independent variables

The questions included socio-demographic information (sex, age, address, parent's occupation), antibiotic consumption in the past (frequency, source of antibiotics), and respondent's education background on antibiotics (e.g., attending training at university or participant in research concerning antibiotic use and resistance).

Outcome variable measurement

Knowledge dimension: There were twenty questions to measure the overall levels of senior medical students' knowledge regarding antibiotic use and resistance. There were three subsets in the knowledge dimension: basic knowledge on antibiotics (5 questions), antibiotic resistance mechanism (7 questions), and antibiotic treatment choice based on clinical scenario (8 questions). Twelve of the questions were true/false, while the other eight were scenarios allowing respondents to express their knowledge of appropriate antibiotic treatment. The answer to true/false questions and scenarios was scored as one mark for the correct answer, and zero wa given for the incorrect answer/don't know. The mean was used as the cut-off point to categorize respondents' knowledge into two levels: good (score above mean) and poor knowledge (score below mean).

Attitude and perception toward antibiotic usage and resistance dimension: There was sixteen questions consisting of positive and negative statements, with a 5-Likert scale range score from "strongly agree" to "strongly disagree". Attitude and perception were assessed as binary outcomes. The mean was performed and used as a cut-off point. The respondent with a score below the mean was considered to have a negative perception and attitude, while a score above the mean was categorized as positive.

1.8. Statistical Methods

All data was entered into Epi Data version 3.1 and then exported to STATA for data analysis. Double data entry was employed to ensure the accuracy and completeness of the data. This process helped to minimize data entry errors and increase the reliability of data.

Descriptive statistics was performed to calculate frequencies, means, median, standard deviation, range, and proportion by socio-demographic characteristics, antibiotic consumption, educational background on antibiotics, knowledge, attitude, and perception of antibiotic use and resistance.

A comparative analysis of categorical variables was performed using the Chi-square/fisher exact test to determine the difference in the distribution between those with good and poor knowledge dimension, and negative and positive attitudes and perceptions of antibiotic consumption/resistance based on socio-demographics features (sex, parental education, etc.,) and antibiotic use (antibiotic consumption in the six months, past three months, and a previous month, and source of infection), and education received (perception of the training received so far on the subject).

Logistic regression analysis was performed to assess the association between outcome variables (knowledge, attitude, and perception) and independent variables. Variables presented in the bivariate analysis with a P-value of <0.20 will be added to a multivariate logistic regression model to determine the independent factors associated with poor KAP among SMS. Covariate, such as sex and age, were included in the final model. Odds ratios (ORs) with their 95% confidence intervals (CIs) and p-values will be reported. All data analysis will be performed in STATA version 17 (22).

1.9. Duration of the study

The data collection was carried out from October to November 2023.

III. Ethical consideration

The study was submitted and approved by the National Ethical Committee for Health Research (NECHR) for ethical clearance (reference number: 235 NECHR). Written informed consent was obtained from each individual before the data collection. Participants had the choices to either participate or withdraw at any time during the survey.

IV. Results

Socio-demographic characteristic

The table 1 describes the socio-demographic of respondent participating in this study. A total of 137 (83.5%) out of 165 senior medical students from three medical science universities in Phnom Penh were completed the self-administered questionnaires. Among the participants, 51.5% were below 23 years old, while 48.5% were 24 years old or older. The median age of participants was 23 years, with an interquartile

range of 23 to 25 years.. Gender distribution shows that 62.8% of participants were male, while 37.2% were female. A majority of the participants had parents engaged in non-medical-related occupations, with only a small proportion having parents in medical-related occupations. Regarding educational background related to antimicrobial resistance (AMR), 72.1% had attended AMR training course at the universities. Moreover, most participants (93.4%) knew when to start antibiotic therapy, while fewer knew how to select the best antibiotic for specific infections (59.6%). Understanding the mechanisms of antibiotic resistance was reported by 73.0% of participants. Additionally, 75.2% knew how to find reliable sources of information, but only 52.6% knew how to switch from intravenous to oral antibiotics. Although 72.3% had heard at least three key terms related to AMR including antibiotic resistance, superbugs, antimicrobial resistance, multi-drug resistance, and antibiotic resistance bacteria, 37.2% had used antibiotics in the last 6 months, and 18.2% had used them in the last 3 months. Among those who had used antibiotics, 47.4% of them obtained from private health facilities, followed by 34.2% from public health facilities, and 10.5% self-medication (Table 1).

Table 1: Characteristic of study participants in three universitZ in Phnom Penh, 2023 (n=137)

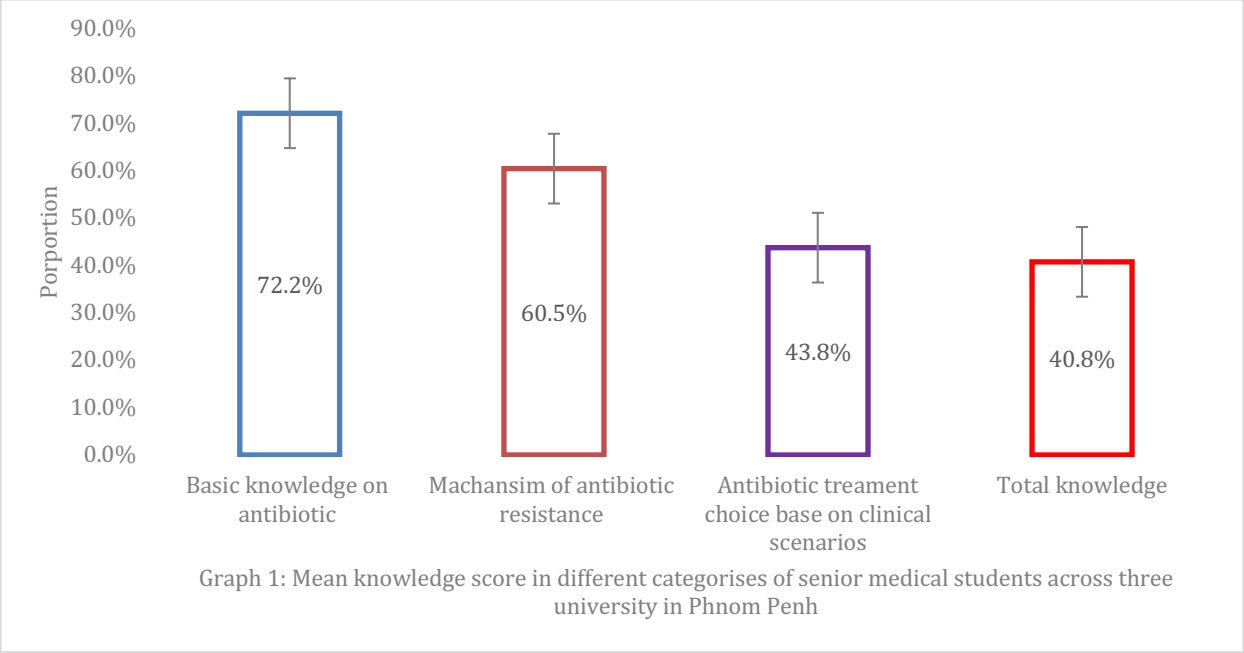
Variables	**Frequency (%)**
Age (Median, IQR)	23 (23-25)
Age group (years)	
≤23	71 (51.5%)
>24	66 (48.5%)
Gender	
Male	86 (62.8%)
Female	51 (37.2%)
Hometown	
Central Plain	88 (64.2%)
Tonel Sap	37 (27.0%)
Coastal, Sea, Plateau & Mountains	12 (8.8%)
Mother occupation	
Medical related	9 (6.6%)
Non-medical related	128 (93.4%)
Father occupation	
Medical related	11 (8.0%)
Non-medical related	126 (92.0%)
Plan to pursue DES*	
No	21 (15.3%)
Yes	116 (84.7%)
Educational background related to AMR	
Attended any training universities (n=136)	
No	38 (27.9%)
Yes	98 (72.1%)
Knew when to start antibiotic therapy	
No	9 (6.6%)

Yes	128 (93.4%)
Knew how to select the best antibiotic for each specific infection (n=136)	
No	55 (40.4%)
Yes	81 (59.6%)
Understood the mechanisms of antibiotic resistance	
No	37 (27.0%)
Yes	100 (73.0%)
Knew how to read and interpret antibiograms	
No	61 (44.5%)
Yes	76 (55.5%)
Knew how to find reliable sources of information	
No	34 (24.8%)
Yes	103 (75.2%)
Knew how to switch from intravenous antibiotic to oral antibiotic	
No	65 (47.4%)
Yes	72 (52.6%)
Had heard at least three AMR key terms	
No	38 (27.7%)
Yes	99 (72.3%)
Antibiotic consumption	
Used antibiotic in the last 6 months	
No	86 (62.8%)
Yes	51 (37.2%)
Used antibiotic in last 3 months	
No	112 (81.8%)
Yes	25 (18.2%)
Used AB in the past month	
No	99 (72.3%)
Yes	38 (27.7%)
Source of antibiotics (n=38)	
Public health facilities	13 (34.2%)
Private health facilities	18 (47.4%)
Self-medication	4 (10.5%)
Obtained antibiotics from more than one source	3 (7.9%)

** DES: Specialized Medical Doctor Degree*

Overall knowledge about antibiotic use and resistance

Among the 137 senior medical students surveyed, only 40.8% (CI: 32.5% - 49.5%) demonstrated overall good knowledge. Specifically, 72.2% (CI: 63.9% - 79.5%) showed a good basic understanding of antibiotics, while 60.5% (CI: 51.8% - 68.8%) exhibited a strong grasp of the mechanisms of antimicrobial resistance. However, only 43.8% (CI: 35.3% - 52.5%) displayed a good understanding of antibiotic treatment based on clinical scenarios. In each knowledge index, the mean score was used as a cut-off to categorize whether respondents had good or poor knowledge on each category (Figure 1).



Graph 1: Mean knowledge score in different categorises of senior medical students across three university in Phnom Penh

Basic knowledge of antibiotic

Regarding the basic knowledge of antibiotic, the mean total score was 3.9 with an SD of 1. About 27.7% (38/137) students received score below overall mean score in basic knowledge on antibiotic index which considered poor knowledge. It is importance to note that about half (54%) of participants conceived that unnecessary use of antibiotic-associated did not have any side effects or risks such as diarrhea, colitis, and allergy (Table 2).

Table 2: Basic knowledge of antibiotic (n=137)

True/False statement (Answer)	**Incorrect n (%)**	**Correct n (%)**
1. Antibiotics are effective against viruses *(False)*	15 (10.9%)	122 (89.1%)
2. Antibiotics are effective against the common cold and influenza virus *(False)*	18 (13.1%)	119 (86.9%)
3. Antibiotics have the same effects as anti-inflammatory drugs *(False)*	35 (25.5%)	102 (74.5%)
4. Unnecessary use of antibiotic-associated side effects or risks such as diarrhea, colitis, and allergy *(True)*	74 (54.0%)	63 (46.0%)
5. Once the symptoms are relieved, one should immediately stop using antibiotics *(False)*	6 (4.4%)	131 (95.6%)

Knowledge of the mechanism of antimicrobial resistance

The Table 3 displays participants' responses regarding their knowledge of the mechanism of antimicrobial resistance. The mean score obtained from our study was 2.9, with an SD of 1.3. Out of the total 137 students, 54 (39.5%) scored below the mean, indicating poor knowledge of mechanisms of antimicrobial

resistance. More than half of the respondents provided incorrect responses to four out of seven statements in this component (Table 3).

Table 3: Knowledge on antimicrobial resistance mechanism (n=137)

True/False statement (Answer)	**Incorrect n (%)**	**Correct n (%)**
1. Healthy individuals can carry antibiotic-resistant bacteria *(True)*	97 (70.8%)	40 (29.2%)
2. The unnecessary use of antibiotics makes them ineffective *(True)*	27 (19.7%)	110 (80.3%)
3. Antibiotic resistance bacteria could spread from one person to another person *(True)*	76 (55.5%)	61 (44.5%)
4. Every person treated with antibiotics is at an increased risk of antibiotic-resistant infection *(True)*	61 (44.5%)	76 (55.5%)
5. The mechanism of resistance to beta-lactams in K. pneumoniae is mainly enzymatic *(True)*	86 (62.8%)	51 (37.2%)
6. The mechanism of resistance to methicillin resistant S. aureus is by efflux pumps *(False)*	116 (84.7%)	21 (15.3%)
7. The mechanism of resistance to vancomycin resistant E. faecalis is alteration of binding sites *(True)*	97 (70.8%)	40 (29.2%)

Knowledge of antibiotic treatment based on clinical scenarios

The index score of knowledge based on clinical scenarios was 3.2 with an SD of 1.4. Among the respondents, 60 students (43.8%) demonstrated good knowledge by scoring above the mean. In addition, 125 students (91.2%) reported that they would treat diarrhea without antibiotics, which is deemed as a good practice by prescribing only oral rehydration salts. However, a significant proportion of students (83.9%) suggested prescribing antibiotics to treat viral upper respiratory infections, which is not a recommended practice. Additionally, a large percentage of students (88.3% and 77.4%) answered incorrectly when asked about switching antibiotics to treat Staphylococcus aureus and Escherichia coli, respectively. (Table 4).

Table 4: Knowledge on antibiotic treatment choice base on clinical scenarios (n=137)

Multiple choices (Answer)	**Incorrect n (%)**	**Correct n (%)**
1. A 4-year-old child had diarrhea for 4 days (3 stools daily). She had no fever during the past days nor at consultation. What is your treatment choice? *(No antibiotics, just oral rehydration salts)*	12 (8.8%)	125 (91.2%)
2. A 6-year-old child had fever (38^{o}C), nasal discharge, and a painful throat for two days. At the general examination, the throat is reddish. What is your treatment choice? *(No antibiotic)*	115 (83.9%)	22 (16.1%)
3. During your ward round, you see two patients with severe renal failure. Patient A is a 68-year-old man suffering from serious cellulitis at the leg, he is treated with clindamycin. Patient B is a 64-year-old diabetic woman who is blindly (empirically) treated for septicemia with Ceftriaxone. Dosage reduction is needed for *(Neither patient A nor patient B)*	108 (78.8%)	29 (21.2%)

4. Which one of the following antibiotics is safe during pregnancy? *(Amoxicillin)*	56 (40.9%)	81 (59.1%)
5. Which of the following antibiotics has the best activity against anaerobes? *(Metronidazole)*	49 (35.8%)	88 (64.2%)
6. Methicillin resistant – Staphylococcus aureus is susceptible to *(None of those antibiotics)*	121 (88.3%)	16 (11.7%)
7. Which one of the following antibiotics most effectively crosses the blood-brain barrier? *(Ceftriaxone)*	77 (56.2%)	60 (43.8%)
8. A patient in the surgical ward develops a fever post-operatively. ESBL producing E. coli is isolated from a blood culture and a pus swab. The patient is currently on ceftriaxone. What is the best way to manage this patient? (Meropenem)	106 (77.4%)	31 (22.6%)

Attitude and perception toward antibiotic use and its resistance

The Table 5 summarizes the findings, indicating that the mean score for questions related to attitude and perception was 63.3, with a SD of 5.8. Notably, approximately 46% of students exhibited a positive attitude and perception towards antibiotic use and resistance. It is noteworthy that the majority of students (89.1%) agreed that antibiotics are overused in Cambodia. However, only slightly more than half of the respondents (51.6%) disagreed with the practice of prescribing broad-spectrum antibiotics when equally effective narrower-spectrum antimicrobials are available, which could potentially increase antibiotic resistance (Table 5).

Table 5: Perception and attitude toward appropriate antibiotic use, its resistance among senior medical student in Phnom Penh, 2023 (n=137)

Perception and attitude	Disagree n (%)	Agree n (%)
1. Antibiotics are overused in Cambodia	15 (10.9%)	122 (89.1%)
2. Antibiotics are overused in hospitals/health facilities where I have trained	95 (69.3%)	42 (30.7%)
3. Antibiotic resistance is not a significant problem in Cambodia	126 (92.0%)	11 (8.0%)
4. Antibiotic resistance is not a significant problem in hospitals/health facilities where I have trained	116 (84.7%)	21 (15.3%)
5. New antibiotics will be developed in the future to solve antibiotic resistance	31 (22.6%)	106 (77.4%)
6. Prescribing broad-spectrum antibiotics when equally effective narrower-spectrum antimicrobials are available to increase antibiotic resistance	70 (51.1%)	67 (48.9%)
7. Better use of antibiotics will reduce problems with the mechanical resistance organism	9 (6.6%)	128 (93.4%)
8. Inappropriate use of antibiotics can pose potential harm to patients	10 (7.3%)	127 (92.7%)
9. Inappropriate use of antibiotics causes antimicrobial resistance	3 (2.2%)	134 (97.8%)
10. Poor adherence to hand hygiene practices by physicians and other healthcare workers cause the spread of antibiotic resistance	67 (48.9%)	70 (51.1%)

11. Patients' demand for antibiotics contributes to the overuse of antibiotics in the community	39 (28.5%)	98 (71.5%)
12. I would like more education on antibiotic resistance	3 (2.2%)	134 (97.8%)
13. I would like more education on hospital infection control	7 (5.1%)	130 (94.9%)
14. I would like more education on how to use antimicrobials appropriately	1 (0.7%)	136 (99.3%)
15. I believe that the antibiotics I will prescribe as a doctor will contribute to the problems of resistance	78 (56.9%)	59 (43.1%)
16. I thought that I am a key role in helping control antibiotic resistance	10 (7.3%)	127 (92.7%)

Factors associated with poor knowledge of antibiotic use and its resistance

The Table 6 describes determinate factors associated with poor knowledge of antibiotic use and its resistance. It is observed that 66.6% of female medical students demonstrate poor overall knowledge about antibiotic and its resistance compared to male respondents (55.7%); however, there was no statistically significant. A large proportion of students who did not attend any training or seminars about antimicrobial use/resistance was 71.7% exhibited a poor knowledge, higher compared to students who attended training (54.8%), while there was no statistically significant difference. Notably, a significant proportion of students (72.7%) reported that they didn't know how to prescribe the best antibiotic for each specific infection and perceived a poor knowledge compared to students who knew how to select the best antibiotic for treatment, with a p-value of 0.007. In addition, approximately 73.5% of respondents who had heard less than three AMR key terms was poor knowledge compared to students had heard at least three AMR key terms (53.4%), with statistically significant p-value =0.032.

After adjusting for covariates, in multivariate analysis indicated that three predictors were independently associated with poor knowledge on antibiotic use and its resistance, including not knowing how to read and interpret antibiogram (aOR 2.3, 95% CI: 1.05 - 5.19, p-value = 0.038), had heard less than three AMR key terms (aOR: 2.75, 95% CI: 1.12 - 6.75, p-value = 0.027), and used antibiotic in the past month (aOR: 2.72, 95% CI: 1.12 - 6.63, p-value = 0.027) (Table 8).

Table 6: Determinant factor associated with poor knowledge of antibiotic use and its resistance among senior medical students in three universities in Phnom Penh, 2023 (n=137)

Variables	n=137	Poor overall Knowledge n=81 (%)	P-Value
Age group (years)			

≤23	71	39 (55.7%)	0.347
>24	66	42 (63.6%)	
Gender			
Male	86	47 (54.6%)	0.167
Female	51	34 (66.6%)	
Hometown†			
Central Plain	88	52 (59.0%)	0.859
Tonel Sap	37	21 (56.7%)	
Coastal, Sea, Plateau & Mountains	12	8 (66.6%)	
Mother occupation†			
Medical related	9	4 (44.4%)	0.486
Non-medical related	128	77 (60.1%)	
Father occupation†			
Medical related	11	7 (63.6%)	1.000
Non-medical related	126	74 (58.7%)	
Plan to pursue DES*			
No	21	10 (47.6%)	0.244
Yes	116	71 (61.2%)	
Educational background related to AMR			
Attended any training at universities (n=136)			
No	38	27 (71.0%)	0.071
Yes	98	53 (54.8%)	
Knew when to start antibiotic therapy†			
No	9	7 (77.7%)	0.309
Yes	128	74 (57.8%)	
Knew how to select the best antibiotic for each specific infection (n=136)			
No	55	40 (72.7%)	**0.007**
Yes	81	40 (49.3%)	
Understood the basic mechanisms of antibiotic resistance			
No	37	25 (67.5%)	0.221
Yes	100	56 (56.0%)	
Knew how to read and interpret antibiograms			
No	61	40 (65.5%)	0.169
Yes	76	41 (53.9%)	
Knew how to find reliable sources of information			
No	34	21 (61.7%)	0.718
Yes	103	60 (58.1%)	
Knew how to switch from intravenous antibiotic to oral antibiotic			
No	65	44 (67.6%)	0.053
Yes	72	37 (51.3%)	
Had heard at least three AMR key terms			
No	38	28 (73.5%)	**0.032**
Yes	99	53 (53.4%)	
Antibiotic consumption			
Used antibiotic in the last 6 months			

No	86	52 (60.4%)	0.678
Yes	51	29 (56.8%)	
Used antibiotic in last 3 months			
No	112	67 (59.8%)	0.725
Yes	25	14 (56.0%)	
Used antibiotic in the past month			
No	99	54 (54.5%)	0.078
Yes	38	27 (71.0%)	
Source of antibiotics† (n=38)			
Public health facilities	13	9 (69.2%)	0.729
Private health facilities	18	12 (66.6%)	
Self-medication	4	4 (100.0%)	
Obtained antibiotics from more than one source	3	2 (71.0%)	

**DES: Specialized Medical Doctor Degree*

†Fisher exact test

Factors associated with negative attitude and perception toward antibiotic use and its resistance

The Table 7 illustrates determinant factors linked to negative attitude and perception towards antibiotic use and resistance. The analysis revealed that slightly more than half of the participants (52.9% of females and 54.6% of males) exhibited a negative attitude and perception. Additionally, a significant proportion (70.2%) of students who did not have a basic understanding of the antibiotic resistance mechanism had a negative attitude towards antibiotic use and resistance, compared to those (48.0%) who had a basic understanding of the mechanism, with a statistically significant a p-value of 0.02. Furthermore, a higher percentage (72.6%) of students who were not familiar with less than three key terms related to antibiotic resistance had a negative attitude towards antibiotic use and resistance, compared to those who were familiar with at least three terms (p-value=0.004) (Table 7).

In multivariate analysis, factors found to be significantly associated with negative attitude and perception were not understand the basic mechanism of antibiotic resistance (aOR: 2.80, 95% CI: 1.21 - 6.49, p-value = 0.016), and had heard less than three AMR key terms (aOR: 0.36, 95% CI: 1.53 - 8.87, p-value = 0.004), after adjusting for covariates (Table 8).

Table 7: Determinant factor associated with negative attitude and perception on antibiotic use and its resistance among senior medical students in three universities in Phnom Penh, 2023 (n=137)

Variables	n=137	Negative attitude and perception n=74	P-Value
Age group (years)			
≤23	71	38 (53.2%)	0.904
>24	66	36 (54.5%)	
Gender			
Male	86	47 (54.6%)	0.846
Female	51	27 (52.9%)	
Hometown			

Central Plain	88	47 (53.4%)	0.950
Tonel Sap	37	20 (54.0%)	
Coastal, Sea, Plateau & Mountains	12	7 (58.3%)	
Mother occupation†			
Medical related	9	5 (55.5%)	1.000
Non-medical related	128	69 (53.9%)	
Father occupation			
Medical related	11	7 (63.6%)	0.504
Non-medical related	126	67 (53.7%)	
Plan to pursue DES* (n=136)			
No	21	14 (66.6%)	0.206
Yes	116	60 (51.7%)	
Educational background related to AMR			
Attended any training at universities (n=136)			
No	38	24 (63.1%)	**0.167**
Yes	98	49 (50.0%)	
Knew when to start antibiotic therapy†			
No	9	5 (55.5%)	1.000
Yes	128	69 (53.0%)	
Knew how to select the best antibiotic for each specific infection (n=136)			
No	55	28 (50.9%)	0.499
Yes	81	46 (56.7%)	
Understood the basic mechanisms of antibiotic resistance			
No	37	26 (70.2%)	**0.020**
Yes	100	48 (48.0%)	
Knew how to read and interpret antibiograms			
No	61	34 (55.7%)	0.717
Yes	76	40 (52.6%)	
Knew how to find reliable sources of information (hospital, or national guidelines) to treat infections			
No	34	22 (64.7%)	0.149
Yes	103	52 (50.4%)	
Knew how to switch from intravenous antibiotic to oral antibiotic			
No	65	34 (52.3%)	0.703
Yes	72	40 (55.5%)	
Had heard any following AMR key terms			
No	38	28 (72.6%)	**0.004**
Yes	99	46 (46.4%)	
Antibiotic consumption			
Used antibiotic in the last 6 months			
No	86	43 (50.0%)	0.221
Yes	51	31 (60.7%)	
Used antibiotic in last 3 months			

No	112	61 (54.4%)	0.823
Yes	25	13 (52.0%)	
Used AB in previous month			
No	99	51 (51.5%)	0.343
Yes	38	23 (60.5%)	
Source of antibiotics†			
Public health facilities	13	9 (69.2%)	0.174
Private health facilities	18	8 (44.4%)	
Self-medication	4	4 (100.0%)	
Obtained antibiotics from more than one source	3	2 (60.5%)	

**DES: Specialized Medical Doctor Degree*

Table 8: Logistic regression for the senior medical students' characteristics associated with poor knowledge and negative attitude and perception toward antibiotic use and its resistance in Phnom Penh, 2023 (n=137)

	Poor Knowledge		**Negative attitude and perception**	
Variables	**aOR (95% CI)**	**P-value**	**aOR (95% CI)**	**P-value**
Age group (years)				
≤23	Ref.		Ref.	
>24	1.51 (0.7 - 3.28)	0.295	0.9 (0.43 - 1.88)	0.784
Gender				
Male	Ref.		Ref.	
Female	2.13 (0.95 - 4.78)	0.065	1.22 (0.57 - 2.64)	0.604
Mother occupation				
Medical related	Ref.		-	-
Non-medical related	2.76 (0.63 - 12.17)	0.18	-	-
Plan to pursue DES				
Yes	-	-	Ref.	
No	-	-	2.14 (0.75 - 6.09)	0.154
Educational background related to AMR				
Attended any training at universities (n=136)				
Yes	Ref.		-	-
No	1.8 (0.73 - 4.43)	0.204	-	-
Understood the basic mechanisms of antibiotic resistance				
Yes	-	-	Ref.	
No	-	-	2.80 (1.21 - 6.49)	**0.016**
Knew how to read and interpret antibiograms				
Yes	Ref.		-	-
No	2.33 (1.05 - 5.19)	**0.038**	-	-

Have heard at least three AMR key terms				
No	Ref.		Ref.	
Yes	2.75 (1.12 - 6.75)	**0.027**	3.68 (1.53 - 8.87)	**0.004**
Antibiotic consumption				
Used AB in the past month				
No	Ref.		-	-
Yes	2.72 (1.12 - 6.63)	**0.027**	-	-

CI: Confident Interval
aOR: Adjusted Odd Ratio

V. Discussion

Medical students who are future task forces in the healthcare system play a profound role in reducing the rate of AMR. It is, therefore, essential to better understand their level of knowledge and perception regarding rational antibiotic use and antimicrobial resistance. This study aimed to explore the baseline level of knowledge, attitude, and perception towards the proper use of antibiotics and their resistance among sixth-year medical students before introducing the Antimicrobial Stewardship (AMS) course in medical science education. The findings of a study indicate that only 40.8% of students exhibited good overall knowledge of antibiotic use and its resistance. Poor knowledge was attributed to factors such as lack of understanding in interpreting antibiograms, limited familiarity with AMR key terms, and recent use of antibiotics in the past month. In addition, positive attitudes and perceptions towards AMR were observed in nearly half (46%) of the students. In contrast, determinant factors with negative attitudes and perceptions had insufficient knowledge of the primary mechanism of antibiotic resistance and were familiar with fewer than three AMR key terms.

The overall knowledge level regarding antibiotic use and resistance among year-six medical students in Cambodia was considered low (40.8%). Similarly, a study conducted by M Lubwama et al. in 2021 showed even a low proportion of students (36.6%) in East Africa demonstrate good overall knowledge, and the scores in the subdivided knowledge index decreased respectively(23). Indeed, the poor knowledge rate was more prevalent across different subsections, with basic knowledge of antibiotics (27.8%), antibiotic resistance mechanisms (39.5%), and antibiotic treatment based on clinical scenarios (56.2%). A recent systematic review in Cambodia reported a high prevalence of resistant pathogens like Escherichia coli and Staphylococcus aureus in human samples (24). On the other hand, our study evidenced that only 60% asserted in prescribing the best antibiotic to treat each specific infection. 77.4% and 88.3% of students incorrectly responded to questions regarding switching antibiotics to treat patients with Escherichia coli and Staphylococcus aureus, respectively. This highlights the importance of having adequate knowledge on selecting the right antibiotics to treat specific infections or pathogens, as it can significantly impact improving and rationalizing antibiotic prescription.

Unnecessary antibiotic use among medical health profession students is considered a global issue that is more likely to increase the rate of AMR, adverse events, and economic burden. Our study found that students who used antibiotics prior one month before the survey increased odds of demonstrating poor knowledge of antibiotic use and its resistance. Likewise, a study conducted by Hu et al. in China in 2021 highlighted that students with a high score in knowledge, attitude, and practice are less likely to demand antibiotics and use antibiotics for prophylaxis (25).

The adherence to an antibiogram is crucial for providing support and guidance for the selection of optimal empirical antimicrobial therapy and a better understanding of the efficiency of each antibiotic response to specific pathogens, as well as assisting health facilities in monitoring changes in antimicrobial resistance (26). The findings of our study indicate that students who demonstrate less proficiency in reading and interpreting antibiograms are 2.3 times more likely to exhibit poor overall knowledge compared to those who claim proficiency in this area (95% CI 1.05 – 5.19). The study conducted in South Africa supported that only 2% of medical students felt prepared to interpret an antibiogram, while a study conducted in Malawi reported that only 11% of students proclaimed the subject of antimicrobial stewardship education and preparedness as good or very good (27,28). Also, students who were familiar with less than three AMR key terms were found to be a predictor of poor knowledge in relation to antibiotic use and its resistance. Approximately 73.5% demonstrate poor overall knowledge compared to those knowing more than three AMR key terms. It is likely that students who are exposed more to AMR key terms acquire more knowledge through classes, in-service training, workshops, and research. This suggested increasing clinical experience in either in-service training, classroom, or research class may be the most effective way to increase clinical knowledge, which can affect confidence in future prescribing (29).

Of the senior medical students who participated in our study, only 46% had a positive perception and attitude toward antibiotic use and its resistance. Approximately 69.3% of students agreed that antibiotics were overused in hospitals or health facilities where they had trained. This could be explained by the fact that antibiotics are widely used in communities and health facilities. The national cross-sectional study with Cambodian physicians conducted by Om et al. (2016) addressed that more than half (54%) proclaimed that antibiotic prescription was inappropriate in their hospital (30). Students who lack knowledge of the basic mechanism of antibiotic resistance and are familiar with less than three AMR key terms increased the odds of negative attitudes and perceptions. There are studies that reported quite low scores of knowledge on the basic mechanism of AMR among final-year medical students (31,32). A system review reported even though the majority of students asserted that AMR is a problem worldwide, a large proportion of students still lack knowledge and confidence in antibiotic prescription (31). It is likely that proficiency in AMR foundation knowledge could be helpful for further prescribers and dispensers, and with adequate training, it will increase positive attitudes and perceptions. This suggested incorporating novel and effective training in the classroom and in-service training on all aspects of AMS and AMR in the medical curriculum.

It is important to note that this study has certain limitations that should be taken into consideration. While it sheds light on the factors that contribute to poor knowledge and negative attitudes towards antibiotic use and resistance, it is difficult to establish a causal relationship. Furthermore, there is a possibility of

respondent bias, as students who were more interested in the AMR topic were more likely to participate in the study after receiving an orientation and background information. Additionally, social pressure may have influenced respondents to overestimate their level of prescribing confidence when reporting their AMR education background.

VI. Conclusion

This study was considered as a baseline assessment of sixth-year medical students' knowledge, attitude, and perception about antibiotic use and resistance before the Ministry of Health incorporated AMS training into the medical health science curriculum. The finding indicated that the majority of sixth-year medical students had overall inadequate scores in knowledge and attitude toward antibiotic use and resistance, which was quite unsatisfactory. This evidence suggests an urgent need to incorporate AMR learning materials into medical health science curricula to equip future healthcare workers with the adequate knowledge and skills to address these issues. Given the pivotal role that medical students closely interact with patient care and community health in the near future, it is imperative to provide them with comprehensive AMR education through both university and in-service training programs. By doing so, we can effectively combat the growing threat of AMR and ensure the sustainability of our healthcare systems. Further study is needed to assess this area with a large sample size after the implementation of the AMS competency education program.

VII. Reference

1. World Health Organization. Antibiotic resistance [Internet]. [cited 2023 May 31]. Available from: https://www.who.int/news-room/fact-sheets/detail/antibiotic-resistance

2. UN Environment Programme. UNEP - UN Environment Programme. 2023 [cited 2023 May 31]. Bracing for Superbugs: Strengthening environmental action in the One Health response to antimicrobial resistance. Available from: http://www.unep.org/resources/superbugs/environmental-action

3. World Health Organization. Global action plan on antimicrobial resistance [Internet]. Geneva: World Health Organization; 2015 [cited 2023 May 30]. 28 p. Available from: https://apps.who.int/iris/handle/10665/193736

4. Shallcross LJ, Howard SJ, Fowler T, Davies SC. Tackling the threat of antimicrobial resistance: from policy to sustainable action. Philos Trans R Soc Lond B Biol Sci. 2015 Jun 5;370(1670):20140082.

5. Chereau F, Opatowski L, Tourdjman M, Vong S. Risk assessment for antibiotic resistance in South East Asia. BMJ. 2017 Sep 5;358:j3393.

6. Lim C, Takahashi E, Hongsuwan M, Wuthiekanun V, Thamlikitkul V, Hinjoy S, et al. Epidemiology and burden of multidrug-resistant bacterial infection in a developing country. Abdool Karim Q, editor. eLife. 2016 Sep 6;5:e18082.

7. Shrestha P, Cooper BS, Coast J, Oppong R, Do Thi Thuy N, Phodha T, et al. Enumerating the economic cost of antimicrobial resistance per antibiotic consumed to inform the evaluation of interventions affecting their use. Antimicrobial Resistance & Infection Control. 2018 Aug 9;7(1):98.

8. Reed TAN, Krang S, Miliya T, Townell N, Letchford J, Bun S, et al. Antimicrobial resistance in Cambodia: a review. International Journal of Infectious Diseases. 2019 Aug;85:98–107.

9. Om C, Daily F, Vlieghe E, McLaughlin JC, McLaws ML. "If it's a broad spectrum, it can shoot better": inappropriate antibiotic prescribing in Cambodia. Antimicrob Resist Infect Control. 2016 Dec;5(1):58.

10. Om C, Daily F, Vlieghe E, McLaughlin JC, McLaws ML. Pervasive antibiotic misuse in the Cambodian community: antibiotic-seeking behaviour with unrestricted access. Antimicrobial Resistance & Infection Control. 2017 Mar 24;6(1):30.

11. Om C, Vlieghe E, McLaughlin JC, Daily F, McLaws ML. Antibiotic prescribing practices: A national survey of Cambodian physicians. Am J Infect Control. 2016 Oct 1;44(10):1144–8.

12. Rattanaumpawan P, Chuenchom N, Thamlikitkul V. Perception, attitude, knowledge and learning style preference on challenges of antimicrobial resistance and antimicrobial overuse among first year doctors in training and final year medical students. Antimicrob Resist Infect Control. 2019 Dec;8(1):142.

13. Seid MA, Hussen MS. Knowledge and attitude towards antimicrobial resistance among final year undergraduate paramedical students at University of Gondar, Ethiopia. BMC Infectious Diseases. 2018 Jul 6;18(1):312.

14. Ritchie O, Shetty V, Prabhu S, Shetty AK. Confidence in Antibiotic Prescribing Intentions among Senior Medical Students in India. The American Journal of Tropical Medicine and Hygiene. 2020 Dec 2;103(6):2561–7.

15. Nogueira-Uzal N, Zapata-Cachafeiro M, Vázquez-Cancela O, López-Durán A, Herdeiro MT, Figueiras A. Does the problem begin at the beginning? Medical students' knowledge and beliefs regarding antibiotics and resistance: a systematic review. Antimicrob Resist Infect Control. 2020 Dec;9(1):172.

16. Thriemer K, Katuala Y, Batoko B, Alworonga JP, Devlieger H, Geet CV, et al. Antibiotic Prescribing in DR Congo: A Knowledge, Attitude and Practice Survey among Medical Doctors and Students. PLOS ONE. 2013 Feb 18;8(2):e55495.

17. McNulty CAM, Cookson BD, Lewis MAO. Education of healthcare professionals and the public. Journal of Antimicrobial Chemotherapy. 2012 Jul 1;67(suppl 1):i11–8.

18. Ministry of Health, Cambodia. National Policy to Combat Antimicrobial Resistance. 2014.

19. Ministry of Health, Cambodia. Antimicrobial Stewardship (AMS) Competency Based Curriculum. 2023.

20. Cambodia Ministry of Education, Youth Sport. Education Strategic Plan 2019-2023 [Internet]. Cambodia Ministry of Education, Youth Sport; 2019 Jun. Available from: http://moeys.gov.kh/en/policies-and-strategies/education-strategic-plan-2019-2023/

21. Lubwama M, Onyuka J, Ayazika KT, Ssetaba LJ, Siboko J, Daniel O, et al. Knowledge, attitudes, and perceptions about antibiotic use and antimicrobial resistance among final year undergraduate medical and pharmacy students at three universities in East Africa. PLoS One. 2021;16(5):e0251301.

22. StataCorp. Stata Statistical Software: Release 17. College Station, TX: StataCorp LLC.

23. Lubwama M, Onyuka J, Ayazika KT, Ssetaba LJ, Siboko J, Daniel O, et al. Knowledge, attitudes, and perceptions about antibiotic use and antimicrobial resistance among final year undergraduate medical and pharmacy students at three universities in East Africa. Di Gennaro F, editor. PLoS ONE. 2021 May 7;16(5):e0251301.

24. Reed TAN, Krang S, Miliya T, Townell N, Letchford J, Bun S, et al. Antimicrobial resistance in Cambodia: a review. International Journal of Infectious Diseases. 2019 Aug;85:98–107.

25. Hu Y, Wang X, Tucker J, Little P, Moore M, Fukuda K, et al. Knowledge, Attitude, and Practice with Respect to Antibiotic Use among Chinese Medical Students: A Multicentre Cross-Sectional Study. IJERPH. 2018 Jun 4;15(6):1165.

26. Truong WR, Hidayat L, Bolaris MA, Nguyen L, Yamaki J. The antibiogram: key considerations for its development and utilization. JAC Antimicrob Resist. 2021 May 25;3(2):dlab060.

27. Kamoto A, Chapotera G, Suleman F. Knowledge, attitude and perception on antimicrobial use and antimicrobial resistance among final year medical students in the College of Medicine, Malawi. Malawi Med J. 2020 Sep;32(3):120–3.

28. Nowbuth AA, Monteiro FJ, Sheets LR, Asombang AW. Assessment of the knowledge, attitudes and perceived quality of education about antimicrobial use and resistance of medical students in Zambia, Southern Africa. JAC Antimicrob Resist. 2023 Jun 12;5(3):dlad073.

29. Ritchie O, Shetty V, Prabhu S, Shetty AK. Confidence in Antibiotic Prescribing Intentions among Senior Medical Students in India. The American Journal of Tropical Medicine and Hygiene. 2020 Dec 2;103(6):2561–7.

30. Om C, Vlieghe E, McLaughlin JC, Daily F, McLaws ML. Antibiotic prescribing practices: A national survey of Cambodian physicians. Am J Infect Control. 2016 Oct 1;44(10):1144–8.

31. Efthymiou P, Gkentzi D, Dimitriou G. Knowledge, Attitudes and Perceptions of Medical Students on Antimicrobial Stewardship. Antibiotics. 2020 Nov;9(11):821.

32. Augie BM, van Zyl RL, McInerney PA, Miot J. Knowledge and perceptions about antibiotic resistance and prudent antibiotic prescribing among final year medical students in two African countries. International Journal of Pharmacy Practice. 2021 Oct 1;29(5):508–14.