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Ethics
IRB: The study was approved by the institutional ethics committee (No. IEC/SJH/VMMC/Project/August-2017/990).
Consent: Informed consent was taken from all participants of the survey.
Inclusion and Exclusion Criteria
A total of 211 questionnaire were collected, however three of these were incomplete and were excluded from analysis.3.
Attrition
not detected.
Sex as a biological variable
not detected.
Subject Demographics
Age: not detected.
Weight: not detected.
Randomization
not detected.
Blinding
not detected.
Power Analysis
not detected.
Replication
not required.

Table 2: Key Resources Table

Your Sentences	REAGENT or RESOURCE	SOURCE	IDENTIFIER
Software and Algorithms			
Statistical analysis: Data was coded and analyzed using SPSS 16.	SPSS		Suggestion: (SPSS, RRID:SCR_002865)(link)

Other Entities Detected

Your Sentences	Recognized Entity
Statistical Tests	
Continuous variables were assessed for statistical significance using the Kruskal Wallis One Way Analysis of Variance on Ranks.8.4Ethical approvalThe study was undertaken after approval of the institutional ethics committee (No. IEC/SJH/VMMC/Project/August-2017/990).	Analysis of Variance

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The MDAR framework establishes a minimum set of requirements in transparent reporting applicable to studies in the life sciences (see Statement of Task: doi:10.31222/osf.oio/9sm4x.). The MDAR checklist is a tool for authors, editors and others seeking to adopt the MDAR framework for transparent reporting in manuscripts and other outputs. Please refer to the MDAR Elaboration Document for additional context for the MDAR framework.

Materials

Antibodies	Yes (indicate where provided: page no/section/legend)	n/a
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Experimental Animals	Yes (indicate where provided: page no/section/legend)	n/a
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Animal observed in or captured from the field: Provide species, sex and age where possible	Not currently checked by SciScore	
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Human research participants	Yes (indicate where provided: page no/section/legend)	n/a
Identify authority granting ethics approval (IRB or equivalent committee(s), provide reference number for approval.	The study was approved by the institutional ethics committee (No. IEC/SJH/VMMC/Project/August-2017/990).	
Provide statement confirming informed consent obtained from study participants.	Informed consent was taken from all participants of the survey.	
Report on age and sex for all study participants.	**Age:**not detected. **Sex:**not detected.	

Design

Study protocol	Yes (indicate where provided: page no/section/legend)	n/a
For clinical trials, provide the trial registration number OR cite DOI in manuscript.	Not detected.	

Laboratory protocol	Yes (indicate where provided: page no/section/legend)	n/a
Provide DOI or other citation details if detailed step-by-step protocols are available.	Not detected.	

Experimental study design (statistics details)	Yes (indicate where provided: page no/section/legend)	n/a
State whether and how the following have been done, or if they were not carried out		
Sample size determination	not detected.	
Randomization	not detected.	
Blinding	not detected.	
inclusion/exclusion criteria	A total of 211 questionnaire were collected, however three of these were incomplete and were excluded from analysis.3.	

Sample definition and in-laboratory replication	Yes (indicate where provided: page no/section/legend)	n/a
State number of times the experiment was replicated in laboratory	Not detected.	
Define whether data describe technical or biological replicates	Not detected.	

Ethics	Yes (indicate where provided: page no/section/legend)	n/a
Studies involving human participants: State details of authority granting ethics approval (IRB or equivalent committee(s), provide reference number for approval.	The study was approved by the institutional ethics committee (No. IEC/SJH/VMMC/Project/August-2017/990).	
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Studies involving specimen and field samples: State if relevant permits obtained, provide details of authority approving study; if none were required, explain why.	Not detected.	

Dual Use Research of Concern (DURC)	Yes (indicate where provided: page no/section/legend)	n/a
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Analysis

Attrition	Yes (indicate where provided: page no/section/legend)	n/a
State if sample or data point from the analysis is excluded, and whether the criteria for exclusion were determined and specified in advance.	not detected.	

Statistics	Yes (indicate where provided: page no/section/legend)	n/a
Describe statistical tests used and justify choice of tests.	Continuous variables were assessed for statistical significance using the Kruskal Wallis One Way Analysis of Variance on Ranks.8.4Ethical approvalThe study was undertaken after approval of the institutional ethics committee (No. IEC/SJH/VMMC/Project/August-2017/990).	

Data availability	Yes (indicate where provided: page no/section/legend)	n/a
State whether newly created datasets are available, including protocols for access or restriction on access.	Not detected.	
If data are publicly available, provide accession number in repository or DOI or URL.	Not detected.	
If publicly available data are reused, provide accession number in repository or DOI or URL, where possible.	Not detected.	

Code availability	Yes (indicate where provided: page no/section/legend)	n/a
For all newly generated code and software essential for replicating the main findings of the study:		
State whether the code or software is available.	Not detected.	
If code is publicly available, provide accession number in repository, or DOI or URL.	Not detected.	

Analysis

Adherence to community standards	Yes (indicate where provided: page no/section/legend)	n/a
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By Rajni Gaind

Access Microbiology

6 Antibiotic Use and Antimicrobial Resistance: KAP survey of medical students to evaluate undergraduate training curriculum

--Manuscript Draft--

Antibiotic Use and Antimicrobial Resistance: KAP survey of medical students to evaluate undergraduate training curriculum

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1.4 Keywords

antimicrobial resistance; KAP survey; undergraduate medical students

1.5 **Repositories:** Not applicable

2. Abstract

Introduction: A better understanding of knowledge, attitude and practices of undergraduate medical students towards antimicrobial resistance (AMR) is necessary to identify gaps in current training curriculum.

Methods: A 20-point Likert scale-based questionnaire divided three parts on knowledge, attitude and practices relating to antibiotic use and resistance was devised. Students attending each year of undergraduate medical program were approached to participate in the study over a one-week-period. KAP scores of each year were compared through logistic ordinal regression and Kruskal-Wallis (KW) test.

Results: Two hundred and eight students participated in the study. Overall, knowledge of about intended use of antibiotics, fixed drug combinations and awareness about AMR was good (average score of 5.9 out of a 8). Steady improvement in knowledge scores was observed from first year (-0.441) to final year (0.00). The medical students had favorable attitude towards rational antimicrobial use (Likert score ≥ 4) including the need to spread awareness about AMR amongst students and public and following doctor's prescription. Self-medication was reported by 28.4% of students and hoarding of leftover doses by 49.1%. Attitude score had a direct correlation with the knowledge score on KW test ($\chi^2 = 29.6$, $p \leq 0.5$) but had no significant correlation with antimicrobial practices ($\chi^2 = 3.9$, $p \geq 0.5$).

Conclusion: The gaps identified in students' practices included self-medication, skipping of dosing, hoarding of leftover medication. As improvement in knowledge did not correlate with that of practices, current curriculum needs to include AMR as a focus area to ensure good antibiotic prescribing practices in future practitioners.

3. Data summary

The authors confirm all supporting data have been provided within the article as figures and tables or through excel files with the article.

4. Introduction

Antimicrobial resistance (AMR) is a silent pandemic which adversely impacts patient care with increase in both direct and indirect economic costs , morbidity, mortality in both hospital and simple community acquired infections [1]. WHO has recognized rationalizing antibiotic use through modification in prescription practices and control of over-the-counter purchase as few measures to curtail antibiotic use. This needs a behavioral change on part of the practitioner as well as the community [2]. It also recommended training and education of healthcare workers including medical students on rational antimicrobial use as an integral part of AMR containment strategy [3]. India is one of the largest consumer of antibiotics globally with an increase of 103% from 2000-2015 including those from WHO Watch group of antibiotics [4,5]. India also accounts for a large burden of AMR with alarmingly high level of resistance to reserve antibiotics like carbapenems [6].

Unlike developed countries, India does not have “Infectious diseases” as a recognized specialty with only a few medical colleges offering a structured course in infectious diseases as a postgraduate programme [7]. Medical students after undergraduate training are expected to diagnose and manage patients which include prescribing antibiotics under minimal specialised supervision. A number of studies across the world have shown poor knowledge and practices regarding antibiotic use and prescription amongst medical students [8-11]. Various novel approaches have been used to teach appropriate use of antimicrobials at undergraduate medical level with varying success [12,13].

The present study was designed to assess the knowledge, attitude and practices regarding antimicrobial resistance and good antibiotic practices of undergraduate medical students in a large tertiary care teaching hospital. The study was aimed at identifying the present gaps that can be addressed in the revised medical curriculum.

5. Methods

Setting: Our hospital was established in 1942 and affiliated to the medical college in 2002. Every year 180 students are admitted to the undergraduate medical (MBBS) course. The students are selected from across India through a national level entrance test. MBBS (Bachelor of Medicine and Bachelor of Surgery) in India encompasses four and a half years of study and one-year internship. The undergraduate course includes study of basic sciences in first year, training in allied sciences in second and third year and clinical rounds with bedside teaching commences from second year. A cross-sectional study was conducted in August 2019 over a one-week-period to understand the perception of students towards antimicrobial resistance. The study was approved by the institutional ethics committee (No. IEC/SJH/VMMC/Project/August-2017/990).

Questionnaire: A pre-designed, 20-point questionnaire divided into three parts: knowledge, attitude and practices was used for collection of data. Part I, focused on knowledge regarding antibiotics and antibiotic resistance and consisted of seven dichotomous questions with yes or no answers and one multiple choice question. Part II and Part III consisted of six questions based on 5-point Likert scale. Part II was designed to assess attitude towards judicious use of antibiotics with responses varying from strongly disagree to strongly agree. Part III assessed antibiotic practices of students with answers ranging from never to always. The questionnaire was vetted by experts before starting the study. Cronbach's Alpha (an estimate of internal consistency and scale reliability) was 0.90. Scores were created by summing the scores for respective items such that a higher score indicated more positive knowledge.

The questionnaires were distributed in classrooms after a lecture. All ongoing MBBS batches were surveyed within a time frame of one week. Participation in the study was purely voluntary and anonymous. A total of 211 questionnaire were collected, however three of these were incomplete and were excluded from analysis.

Statistical analysis: Data was coded and analyzed using SPSS 16 (RRID :SCR_002865). Descriptive statistics were used to summarize the numerical variables (mean) and categorical variables (expressed as frequencies and percentages). Ordinal regression was applied for categorical variables to test for significance. Continuous variables were assessed for statistical significance using the Kruskal Wallis One Way Analysis of Variance on Ranks.

6. Results and Discussion

MBBS course in Indian medical curriculum includes four and half years (9 semesters) and one year of compulsory internship. During the survey, a total of 208 MBBS students from 1st year to final year participated in the study. Interns were not included as they can be considered practitioners with license to prescribe medication in limited capacity within the hospital. Medical students from 1st year to final year belonged to an age range of 18-24 years. Among the 211 students enrolled, approximately 42 students were enrolled from each year of the course.

6.1 Knowledge

Table 1 shows knowledge of the medical students regarding antibiotics, their use and resistance during the different phases of MBBS curriculum. Majority of our students were aware of antibiotic resistance (92-100%) in the study period. This is similar to a study from Italy conducted on 1050 medical students and the awareness was 90% [11]. Knowledge of other aspects of antibiotics such as their efficacy in bacterial rather than viral infections, effect of antibiotic use on normal bacterial flora, awareness about AMR as a concept was also correctly understood by majority of students (92.4 – 99.5%) (Table 1). This is in contrast to the study among medical students from Jordan where the awareness was comparatively low (70.4%) [14]. Our findings are in concordance with the knowledge of antibiotics and antimicrobial resistance amongst medical students from Italy (95.2%) and China (92.9%) [11,15]. In comparison to these three studies where a higher percentage of students (17% - 35%) were reportedly unaware of inefficiency of antibiotics for viral illnesses, only 7.6% (n=16) of our medical students believed that antibiotics could be used to treat viral infections [11,14,15]. In countries like India many febrile illness are caused by viruses like Dengue, Japanese Encephalitis , seasonal flu and Chikungunya and are self-limiting. An interesting finding was that awareness in this regard was high. Only 2.4% (n=5) of medical students in our study responded that antibiotics should be taken for all febrile episodes which is similar to the Italian (1.8%) study [11]. In contrast, the Chinese and Jordanian studies had reported that 22 – 50% of medical students agreed that antibiotics could be used for every febrile episode [14,15]. WHO has reported a common misconception among general public (76%) that humans develop resistance to antibiotic rather than bacteria [16]. Nearly 40% (n=85) of students in our study also held this belief in comparison to the Italian study where only 7% were unclear on this concept [11]. Antibiotics use create imbalance in the microbial flora and thus selects resistance [17-19]. Medical students in our study were largely (95.7%, n=199) aware of this fact like the Italian study (90.2%) [11]

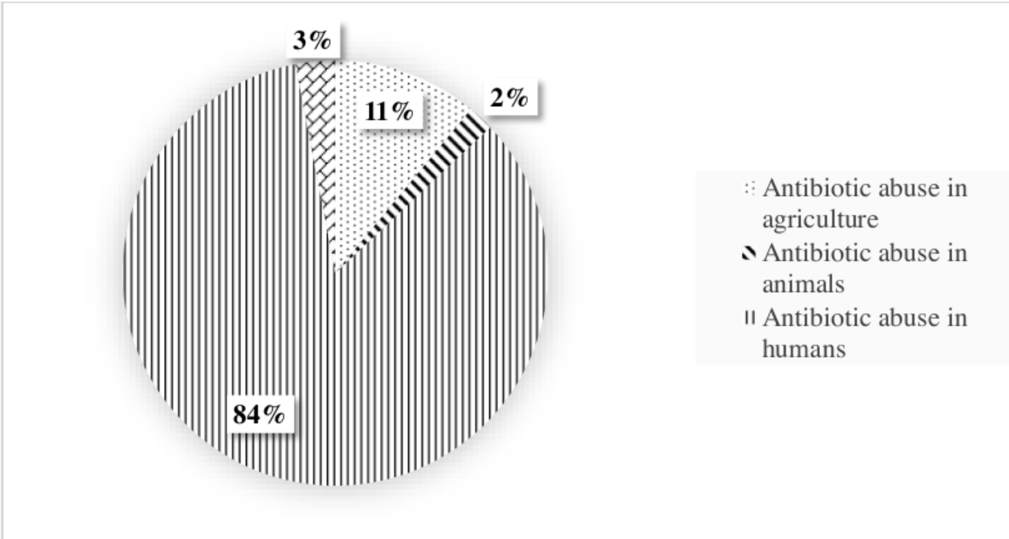
Table 1: Knowledge of medical students about antibiotic use and antimicrobial resistance (Percentage of respondents answering ‘Yes’)

Question	1st Year (n=40)	2nd Year (n=47)	3rd Year (n=40)	4th Year (n=40)	5th Year (n=41)	Total (n=208)
Have you ever heard of bacterial resistance to antibiotics?	92.5%	97.9%	100%	100%	97.5%	98.1%
Do you think antibiotics can be used to treat bacterial infections?	97.5%	100%	100%	100%	100%	99.5%
Do you think antibiotics can be used to treat viral infections?	0	6.4%	12.5%	5%	14.6%	7.7%
Do you think antibiotics should be taken every time you have fever?	7.5%	4.3%	0	0	0	2.4%
Do you think antibiotics can cause an imbalance in the body’s normal bacterial flora?	90%	89.36%	100%	100%	97.5%	95.7%
Have you ever heard of fixed-drug combinations?	32.5%	55.3%	95%	95%	92.7%	73.6%
Do you think humans can become resistant to antibiotics?	65%	59.6%	20%	20%	36.6%	40.9%

Fixed dose combinations (FDC) consists of two or more approved drugs combined in a single dosage form in a fixed ratio, manufactured and distributed in specified doses to treat either single ailment or multiple co-morbid conditions [20].Their commercial success has led to introduction of many irrational newer combinations. These irrational FDCs often have pharmacokinetic and pharmacodynamic mismatch associated with reduced efficacy and enhanced toxicity [21]. The fixed dose antibiotics may not contain effective dose of individual drugs leading to mutations and selection pressure proliferating resistant strains [20]. On 14th September 2018, Government of India banned 328 irrational FDCs on the recommendation of the Drug Technical Advisory Board (DTAB) [22]. It was heartening to find that awareness about these fixed doses antibiotic combination was high (73.5%, n = 153) amongst our students.

Widespread antibiotic use in livestock and agriculture has led to rapid emergence and dissemination of AMR [2,23]. Most of this use involves addition of low dose antibiotics to animal feed as growth promoters or at higher doses for disease prevention. We found that students were unaware about abuse of antibiotics in animals and agriculture as contributing factors to AMR, with 84% identifying abuse in humans as the most important cause. (Figure1)

Figure 1: Response of students to the question “What do you think is the most common cause of spread of antibacterial resistance?”



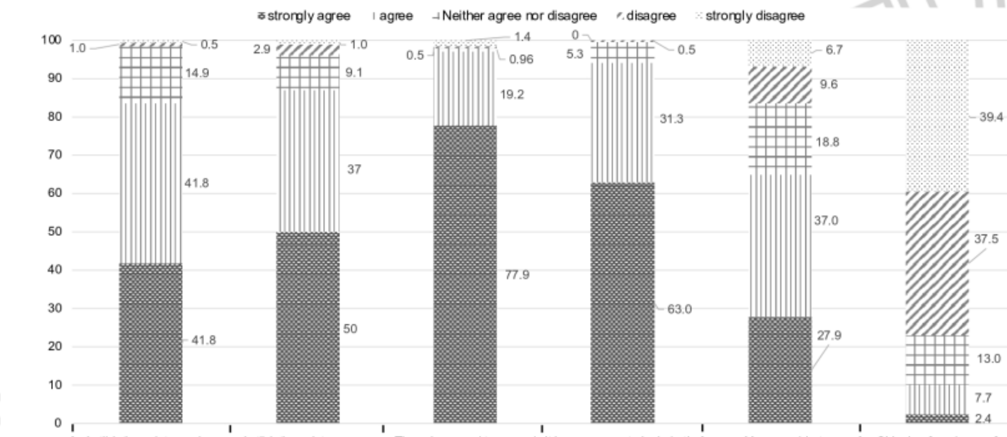
Knowledge of medical students on all aspects of antimicrobial resistance was overall good with an average score of 5.9 out of a possible 8. On ordinal regression scale, overall knowledge score showed steady improvement from first year (-0.441) to final year (0.00) medical students with p value ≤0.5. Although the knowledge regarding awareness about antibiotic resistance and use was similar among students in different years of the curriculum, however awareness regarding fixed drug combinations increased year-on-year from 32.5% to 92.7% . Similarly, awareness regarding the misconception that humans can become resistant to antibiotics improved (Table 1) from 65% to 36.5% (p value = 0.01).

The 3rd and 4th year of medical education is more clinically oriented with involvement in patient diagnosis and management. This clinical exposure of students with patients has a positive impact and helps clarifying many preformed notions and prejudices amongst students regarding antibiotic over time [11,24].

6.2 Attitude

In the present study, attitude of students towards antimicrobial use was favourable with score of 4 or more on Likert scale (LS) (Figure 2). The scores did not vary over the years of study. In a multicenter European study on 338 medical students, 92% had agreed that AMR is a national problem in their country [24]. Amongst our students 85% (n=177) recognized antibiotic resistance as a problem that could adversely affect their health (87%, n=181). An overwhelming majority of students favored the need to spread public awareness about AMR (97%, n=202) as well as increased focus on AMR in undergraduate teaching (94%, n=195). Previous studies from Malaysia (88%), USA (75%) and China (89%) had reported that most medical students felt the need for more comprehensive teaching on antibiotics for better prescribing practices [15,25,26].

Figure 2: Year-on-year comparison of attitude of medical students towards antibiotic use and antimicrobial resistance (In percentage and Likert scores)



LIKERT SCALE	Antibiotic resistance is a problem in India.	Antibiotic resistance can affect your health and of those around you.	There is a need to spread information about when to use antibiotics among the public.	It is necessary to include the teaching of rational use of antibiotics in the medical curriculum at the undergraduate level.	You are able to purchase antibiotics over the counter easily without a doctor's prescription.	Skipping few doses of antibiotics should not affect or hasten the development of antibiotic resistance.
Y1	3.5	4.0	4.5	4.3	2.8	4.1
Y2	4.0	4.1	4.7	4.6	2.4	4.0
Y3	4.4	4.2	4.5	4.5	2.1	3.7
Y4	4.7	4.7	4.8	4.6	1.9	4.4
Y5	4.5	4.5	4.8	4.7	2.3	3.8
Avg	4.2	4.3	4.7	4.5	2.3	4.0

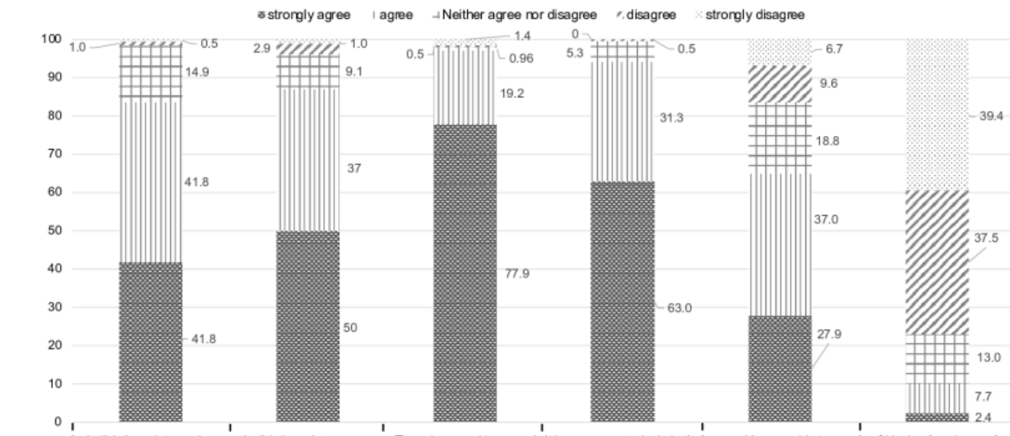
With reports of unregulated pharmacies and unethical practices, availability of over the counter antibiotics, antibiotics misuse in India is now staggering. This was reflected in our study, where two-thirds (65%) of medical students (Likert score 2.3) also agreed that antibiotics can be bought without a valid prescription. Seventy percent of our students identified that skipping of doses contributes to development of AMR. This is higher than a previous Indian study (57% of students) [27], but comparatively lesser than the response from Jordanian study where 84.3% medical students were able to identify skipping of doses as a contributing factor for AMR [14].

6.3 Practices

Good antibiotic practices include taking antibiotics after doctor's consultation, following the dosing schedule and avoiding self-medication. James et al, 2006 had reported medical students were prone to self-medication as well as irrational drug usage [28]. Upper respiratory tract ailments and diarrhea were the most common illness for which people tend to self-medicate. However, commonest causative organisms in both these ailments are viruses and antibiotics hardly have any role in treatment.

For questions regarding antimicrobial practices, Likert score fell behind attitude ranging from 2.1-3.4. Average Likert score for different years remained consistent for practices in question. (Figure 3). Overall response to self-medication was satisfactory with an average Likert score of 3.8. Only 28% of students said they always consult a doctor before taking antibiotics whereas 43% said that they did very often (Figure 3). In contrast, in a previous report from India by Afzal et al, 2013 only 10% of medical students admitted to self-medicate with antibiotics [27]. Sore throat was the most common illness for which our students take antibiotics (Figure 3). Similar findings were seen in the Chinese study where common cold was the leading cause of self-medication [15]. Self-medication is more evident in older students (average LS≤3 for both sore throat and diarrheal diseases) than first year students (1st year, LS≥3.5 for sore throat and 3.3 for diarrhea).

Figure 3: Year-on-year comparison of practices of medical students regarding antibiotic use (In percentage and Likert scores)



LIKERT SCALE	Antibiotic resistance is a problem in India.	Antibiotic resistance can affect your health and of those around you.	There is a need to spread information about when to use antibiotics among the public.	It is necessary to include the teaching of rational use of antibiotics in the medical curriculum at the undergraduate level.	You are able to purchase antibiotics over the counter easily without a doctor's prescription.	Skipping few doses of antibiotics should not affect or hasten the development of antibiotic resistance.
Y1	3.5	4.0	4.5	4.3	2.8	4.1
Y2	4.0	4.1	4.7	4.6	2.4	4.0
Y3	4.4	4.2	4.5	4.5	2.1	3.7
Y4	4.7	4.7	4.8	4.6	1.9	4.4
Y5	4.5	4.5	4.8	4.7	2.3	3.8
Avg	4.2	4.3	4.7	4.5	2.3	4.0

Skipping of doses, buying more than required add to another problem of "left over antibiotics". WHO had recommended that left over antibiotics should neither be used nor shared without consulting doctors first. Over half of surveyed students (50.9%) affirmed to skipping doses as well as hoarding of antibiotics at home and this practice was consistent (LS 2.4 – 3.1) across all years. Afzal et al, 2013 reported 41% students had admitted having skipped doses, 36% agreed they never discard left-over antibiotics and above 50% had shared these antibiotics with family and friends [27]. Although there is a year on year increase in tendency for self-medication amongst students, it is also accompanied with better adherence to dosing schedule. Previous studies have attributed clinical training of older students in disease etiology and management which enables them to diagnose and self-treat many illnesses [14,15].

On March 1 2014, Schedule H1 notification came into force with the intent to control the rampant misuse and over-the-counter sale of antibiotics [29]. Schedule H stipulates retail dispensing of drugs only against a valid prescription. Currently, 46 drugs have been placed under this restricted category, which mainly comprises third and fourth generation cephalosporins, carbapenems, newer fluoroquinolones and first- and second-line antitubercular drugs. The packaging of these drugs have mandatory Schedule H1 warning printed on the label in a box with red border and the Rx symbol in red [29]. Only 13.5% students acknowledged that they always pay attention to the red line on packaging. This practice was observed uniformly over the years with LS=2.7 in first year as well as in final year students (average LS=2.6).

To know the correlation between knowledge and attitude as well as knowledge and practices of students, Kruskal-Wallis One Way Analysis of Variance on Ranks test was performed. Total attitude and total practice scores of students were calculated by summation of individual Likert score for each response. Favorable responses were awarded a higher score. Maximum attitude score and practice score that could be achieved was 30 each. Knowledge scores had no correlation to attitude score (p value = 0.082) or practices score (p=0.698). In a study conducted on high school students and teachers in Delhi, it was found that students had poor knowledge about antibiotic use and resistance while the teachers had only a basic understanding [30]. Our first year students thus represent this population and we can see a gradual increase in knowledge score of medical students. To improve antibiotic practices, innovative teaching learning methods like regular workshops in prescribing practices, role plays, competitions etc. need to be introduced. Students should be encouraged to actively participate and feedback from the students should be obtained for further improvement to the curriculum.

7. Conclusion:

Knowledge of medical students regarding AMR steadily improved over the years of study. However, some incorrect concepts and practices like misconceptions about development of AMR, self-medication, skipping of dosing, hoarding of leftover medication etc. formed in the first year persist through their final year. The present study highlights a lack of correlation between knowledge, attitude and practices. As improvement in behavior lagged behind that in knowledge, the authors conclude that the current curriculum is unable to change practices of students. With the revised competency based medical education (CBME) for undergraduate medical students in India, it is hoped that above gaps will be bridged.

8. Author statements

8.1 Author Contributions

Conceptualization- RS and RG; Data curation- MJ; Methodology – RS, RG and MJ; Investigation – RS, AP and MJ; Formal Analysis – RS and AP; Validation – RS and AP; Supervision – RG; Writing – original draft – RS and AP; Writing – Review & Editing - RG

8.2 Conflicts of interest

The author(s) declare that there are no conflicts of interest.

8.3 Funding information

This work received no specific grant from any funding agency.

8.4 Ethical approval

The study was undertaken after approval of the institutional ethics committee (No. IEC/SJH/VMMC/Project/August-2017/990). Informed consent was taken from all participants of the survey.

8.5 Consent for publication

No participants' identifiers have been included in the article.

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