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PATTERNS OF IRRATIONAL ANTIBIOTIC USE AND DETERMINANTS OF ANTIBIOTIC RESISTANCE: A CROSS-SECTIONAL STUDY AMONG MEDICAL AND NON-MEDICAL UNIVERSITY STUDENTS IN LAHORE, PAKISTAN

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Keywords

Antibiotic resistance, Irrational use of antibiotics, Medical students, Non-Medical students, self-Medication.

Article History

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Abstract

Background: *Antibiotic resistance (AR) emergence and spread has become one of the global health concerns. Irrational prescribing, improper use and self-medication of antibiotics (AB) are main factors contributing to spread of AR. The main objective of this study is to compare and evaluate irrational AB use and factors contributing to AR among medical and non-medical university students of Lahore, Pakistan.*

Methods*: A comparative cross-sectional study was conducted from May 1 2024 to July 1 2024, among medical and non-medical university students in Lahore. A sample of 500 students (250 medical, 250 non-medicals) was selected. Data were collected via electronic and printed validated questionnaires and analyzed using SPSS version 27, with Chi-square and logistic regression analysis determining statistical significance ($p < 0.05$).*

Results: *Chi-square test revealed gender ($p < 0.001$), study background ($p < 0.001$), and lack of cautiousness about AR ($p = 0.045$) as significant factors contributed to AR. Logistic regression further confirmed gender and study background as significant predictors contributed to AR . So, male students had 70% higher experience of acquiring AR than female students (adjusted odds ratio [AOR] = 1.70). The medical students had 42% lower experience of acquiring AR than the non-medical students (AOR = 0.58).*

Conclusion: *This study concludes that irrational AB use is higher among male students and those from non-medical discipline. It is crucial to implement comprehensive legal regulations for AB control, along with AB stewardship initiatives across different groups of Pakistan.*

INTRODUCTION:

Antibiotic resistance (AR) is likely to develop as a result of ongoing failure to research and discover new antibiotics (AB) as well as the irrational use of already existed AB.(1) It is anticipated that as AR rises death rates and world's economic burden.(2) In 2015, drug-resistant infections caused around 700,000 deaths annually worldwide.(3) In 2019, it was estimated that 4.95 million deaths were linked to bacterial antimicrobial resistance (AMR), of which 1.27 million were attributed to bacterial AMR.(4) It is

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predicted that by 2050 there would be 10 million of them, and the global costs of this could reach up to US $100 trillion.(3) Among 204 nations, Pakistan ranks 29th in terms of age-standardized death rate per 100,000 people associated to AMR.(5) According to World Health Organization WHO, we are around the corner of post AB era where essential AB is not more effective for the treatment of common infections.(6) The WHO defines the rational use of medicine as providing patients with right medication, for right indications, at right doses, for their own individual needs, for a suitable duration, at the minimum possible cost to them and society. When any of these conditions fail to be met, the use of medications becomes irrational.(7) The primary reasons for the irrational AB use include inadequate patient or prescriber education, easy availability of AB without a prescription, pressure on prescribers, pharmaceutical promotion, self-medication and lack in rapid microbial testing. (8) Due to a lack of awareness and education on the role that AB like azithromycin play in treating COVID-19 infections, there was an increase in the irrational AB use during the pandemic.(9) Irrational AB use generally has detrimental impact on quality of medication therapy, which raises morbidity and mortality, waste of resources, psychological effects, and increases the risk of adverse effects and AR.(10) AR develops when bacteria adapt so that AB can't kill them or stop their growth. (11) Three main mechanisms are responsible for the development of AR in bacteria: first, the AB molecule is modified or destroyed; second, the AB target site is altered; and third, binding of AB to target site is decreased due to elimination. Additionally, conjugation, transformation and transduction are other ways that bacteria acquire resistance genes.(12) AR widely spreads in animal, environment and human due to transfer of some particular resistance genes among species result in decrease effectiveness of AB.(13) AR is primarily caused by the following factors: factors related to AB (such as irrational AB use, substandard AB, and availability of over-the-counter OTC AB); factors related to physicians (such as inappropriate prescribing , lack of updated knowledge, and incorrect dosing); factors related to patients (such as poor adherence, financial crises and self-medication); and factors related to the environment (such as overpopulation, frequent mass travel, poor sanitation and widespread AB use for agriculture).(14) Several concerns surround AR, such as how it prevents bacterial infections from being successfully treated, how it compromises the effectiveness of cancer chemotherapy and transplant surgery and how AR infections require more prolonged treatment.(15) Irrational AB use is one of the concerning issues for public health in Pakistan. Different researches find prominent irrational AB use and some factors like social, economic and traditional factors play crucial role (16). In Pakistan, different AB is used irrationally to treat viral infections such as cold and flu, which highlights poor knowledge about rational use of AB.(17) The main objective of this study is to compare and evaluate the irrational AB use and critical factors contributed to AR among medical and non-medical university students in Lahore, Pakistan. The focus of this study was to give practical recommendations about irrational AB use that guide healthcare authorities to make strict policies to alleviate the global issue of AR (18) Extensive approaches like public awareness program, implementation of AB stewardship program and control of OTC sale of AB are required to tackle the issue of irrational AB use. (19)

Methods:

Study design

This study employed a comparative cross-sectional design to assess the irrational use of AB and factor contributed to AR among medical and non-medical university students. This study was conducted over two months, from 1st May 2024 to 1st July 2024.

Sample size and Sampling method

Raosoft calculator was used for the calculation of sample size. Confidence interval of 95% and margin of error of 5% were used. According to the HEC report (20), the population of university students in Lahore is 4 lacs so the calculated

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sample size for this study was 384. This sample size was increased to 500 to improve robustness in study. Participants were selected with an equal distribution of 250 participants from each category: medical students and non-medical students.

Data collection tool

Data collection tool was used for data collection. The questionnaire for this study was validated for assessment of irrational AB use and factors contributing to AR. This questionnaire was adopted from an open access published study.(21) This included three sections. Section A consisted of Q1 to Q4: Demographics, Section B consisted of Q1 to Q7: AB use related questions and Section C consisted of Q1 to Q3: Parameters contributed to AR among participants**.**

Data collection procedure

Data collection was done by distributing electronic and printed questionnaire. The electronic questionnaire was distributed via Google forms, while printed copies were administered to 250 medical students and 250 non-medical students. Then responses were collected using standardized data collection technique. All the research participants were given details about the objectives and aims of the research.

Ethical considerations

The study was accepted by the Research and Ethics Committee of Gulab Devi Institute of Pharmacy No. REC/GDIP/24/D-CP-18. Informed consent was taken from all participants before data collection. Confidentiality and anonymity were maintained throughout the study.

Study setting

The study was performed in the five universities of Lahore. The universities that were selected for the data collection were a mix of both public and private sectors.

Inclusion and Exclusion criteria

The inclusion criteria were students aged 18 years or more old, understanding the aim, and having voluntary participation, who took any AB within the last year and were either permanent residents of Lahore, Pakistan, or living there for at least the last five years. The exclusion criteria were students who for any reason were not able to answer questions and those students who were intellectually disabled.

Statistical analysis

Firstly, data was entered and evaluated manually using Microsoft Excel. Statistical analysis was done using IBM SPSS version 27. Descriptive statistics was conducted to find count and percentage distribution of sociodemographic factors. Chi-Square (χ^2) test was conducted to analyze significant association of several sociodemographic factors and critical patterns of irrational AB use contributed to AR. Logistic regression test was used for analyzing significant association of irrational AB use related critical patterns contributed to AR after adjusting other factors. A threshold of $p < 0.05$ was set to define statistical significance.

Results:

Demographic characteristics:

In non-medical students, males were in higher numbers (60.8%) than females (39.2%). The students of 3rd / 4th / 5th year among medical field (58%) and non-medical field (58.4%) were in higher numbers compared to 1st / 2nd year among medical field (42%) and non-medical field (41.6%).The age of participants from medical background was 18-20 years (41.2%), 21-25 years (55.2%), 25-30 years (3.6%) and from non-medical background was 18-20 years (41.2%), 21-25 years (49.6 %), 25-30 years (5.2%).

According to the study, (15.6%) of the medical students and (42.6%) of the non-medical students took medications without prescription; they either followed other's suggestion or self-medicated themselves or used AB from previous prescription or past experience. The main reason behind AB use among medical students and non-medical students was fever, common cold and

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cough (approximately 50%). More than (60%) of participants from medical and non-medical background used AB for 1-3 days. The completion of AB course among medical students was (76.4%), which was greater than (62.8%) non-medical students. The main reason behind the discontinuation of AB course was sense of well-being among medical students. The occurrence of side effects was higher among non-medical students (18.1%) than medical students (10.16%). Among medical students who discontinued their AB course, only (57.2%) consulted with a physician or pharmacist before doing so, compared to (30%) of non-medical students. Among non-medical students, (40.8%) reported that AB was ineffective for them compared to (24%) medical students. Almost (74.4%) of non-medical students had no cautiousness about AR than (41.2%) medical students. (Table 1)

Table 1: Demographic factors and typical patterns of rational or irrational AB use among Medical and Non-Medical students.

Variables	Characteristics	Medical Students		Non-Medical Students	
		n	(%)	N	(%)
		250	50 %	250	50 %
Gender	Male	85	34 %	152	60.8 %
	Female	165	66 %	98	39.2 %
Age (years)	18-20	103	41.2 %	113	45.2 %
	21-24	138	55.2 %	124	49.6 %
	25-30	9	3.6 %	13	5.2 %
Education level	1st / 2nd year	105	42 %	104	41.6 %
	3rd / 4th / 5th year	145	58 %	146	58.4 %
Medication style	Doctor's prescription	211	84.4 %	144	57.6 %
	Self-medication	14	5.6 %	52	20.8 %
	Pre-experience	22	8.8 %	36	14.4 %
	Suggestions from other	3	1.2 %	18	7.2 %
Main reason for AB use	Fever, common cold and cough	121	48.4%	135	54 %
	Infection	83	33.2 %	55	22 %
	Dysentery/diarrhea/ food poisoning	21	8.4 %	39	15.6 %
	Abdominal / other pain	19	7.6 %	12	4.8 %
	Other reasons	6	2.4 %	9	3.6 %
Duration of AB use (days)	1-3	151	60.4 %	162	64.8 %
	4-6	67	26.8 %	61	24.4 %
	7-10	23	9.2 %	16	6.4 %
	Above 10	9	3.6 %	11	4.4 %
Completion of the dosage regimen	Yes	191	76.4 %	157	62.8 %
	No	59	23.6 %	93	37.2 %

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Experience regarding AB was not working on you	Yes No	60 190	24 % 76 %	102 148	40.8 % 59.2 %
Lack of cautiousness about ABR	Yes No	103 147	41.2 % 58.8 %	186 64	74.4 % 25.6 %
No counseling from Doctor or Pharmacist before discontinuation of therapy	Yes No	107 143	42.8 % 57.2 %	175 75	70 % 30 %

In Table 2: (41.2%) of medical students had lack of cautiousness about AR, among them (62.14%) were females, (55.33%) were aged between 21-24 years and (62.14%) were students of 1st/ 2nd year. Among non-medical students, (74.4%) had a lack of cautiousness about AR, (66.67%) were males, (48.92%) were aged between 18-24 years and (54.84%) were student of 3rd /4th/ 5th year. Almost (70%) of the AB users of non-medical background did not seek any counseling from doctor or pharmacist before discontinuation of AB course (Table 2). Among them, (60.57%) were males, (94.28%) were aged between 18–24 years and (60%) were from 3rd /4th/ 5th year. Among medical students these demographic factors varied as (67.28%) were females, (54.20%) were aged between 21-24 years and (52.34%) were from 3rd /4th/ 5th year.

The Chi-square (χ^2) test is a statistical technique used to assess whether a significant relationship exist between categorical variables. It was used to assess whether a significant relationship between potential factors such as gender, age, study background, education level, duration of AB use, lack of knowledge about AR among AB users.

Table 2: Demographic assessment of two key factors contributed to AR among Medical and non-Medical students.

Variables	Characteristics	Lack of cautiousness about Antibiotic resistance (n = 289, 57.8 %)				No counseling from Doctor/ pharmacist (n = 282, 56.4 %)			
		Medical Students (n=103, 41.2%)		Non- Medical Students (n =186, 74.4%)		Medical Students (n =107, 42.8%)		Non- Medical Students (n=175, 70%)	
		N	%	N	%	n	%	N	%
Gender	Male	39	37.86	124	66.67	35	32.71	106	60.57
	Female	64	62.14	62	33.33	72	67.28	69	39.43
Age (years)	18-20	57	55.33	89	47.84	48	44.85	79	45.14
	21-24	43	41.74	91	48.92	58	54.20	86	49.14
	25-30	3	2.91	6	3.22	1	0.93	10	5.72
Education Level	1st /2nd year	64	62.14	84	45.16	51	47.66	70	40
	3rd / 4th/ 5th	39	37.86	102	54.84	56	52.34	105	60

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	year								

In Table 3, demographics and critical pattern contributed to AR among the AB users were analyzed. AR was found higher among males (40.1%) compared to females (25.4%). The relationship between gender and AR was identified as statistically significant (**p < 0.001**). AR was found to be higher among non-medical students (40.8%) compared to medical students (24.0%). The relationship between study background and AR was identified as statistically significant (**p < 0.001**). AR was found to be higher among those individuals who were not cautious about AR (36.0%) compared to those who were cautious (27.5%).The relationship between lack of cautious about AR and AR was identified as statistically significant (**p < 0.045**). Logistic regression is used to assess relationships between the binary dependent variable and each independent variable while controlling for the other independent variables. In this study, this test was carried out to assess the effect of gender, age, study background, education level, medication style, reason for AB use, duration of AB, lack of cautiousness about AR and completion of prescribe AB course on the development of AR among AB users.

Table 3: Chi-Square (χ^2) test for analyzing various sociodemographic and irrational AB use related critical patterns contributed to ABR among Medical and Non-Medical students. Note: Statistically significant values are written in bold.

Variables	Characteristics	Experience on "Antibiotics were not working"				p-value
		Yes		No		
		n	%	n	%	
Gender	Male Female	95 67	40.1 % 25.4 %	142 196	59.9 % 74.6 %	**< 0.001**
Age (years)	18-20 21-24 25-30	73 81 8	33.8 % 30.9 % 36.3 %	143 181 14	66.2 % 69.1 % 63.7 %	0.736
Study Background	Medical Non-Medical	60 102	24.0 % 40.8 %	190 148	76.0 % 59.2 %	**< 0.001**
Education Level	1st /2nd year 3rd / 4th / 5th year	64 98	30.6 % 33.6 %	145 193	69.4 % 66.4 %	0.472
Medication style	Doctor's prescription Self-medication Pre-experience Suggestions from other	109 28 15 10	30.7 % 42.4 % 25.9 % 47.6 %	246 38 43 11	69.3 % 57.6 % 74.1 % 52.4 %	0.077

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Main reason for AB use	Fever, common cold , cough	89	34.8 %	167	65.2 %	0.345
	Dysentery/diarrhea/ food poisoning	23	38.3 %	37	61.7 %	
	Infection	38	27.5 %	100	72.5 %	
	Abdominal / pain Other	7	22.6 %	24	77.4 %	
	reasons	5	33.3 %	10	66.7 %	
Duration of AB use (days)	1-3	100	31.9 %	213	68.1 %	0.893
	4-6	42	32.8 %	86	67.2 %	
	7-10	12	30.8 %	27	69.2 %	
	Above 10	8	40.0 %	12	60.0 %	
Completion of the dosage regimen	Yes	112	32.2 %	236	67.8 %	0.876
	No	50	32.9 %	102	67.1 %	
Lack of cautiousness about ABR	Yes	104	36.0 %	185	64.0 %	**0.045**
	No	58	27.5 %	153	72.5 %	

P-value equals to or less than 0.05 considered statistically significant.

In an adjusted logistic regression model (Table 4), gender was statistically significant predictor of AR (p = 0.011). The risk of developing AR was 1.7 times higher in males compared to females (adjusted odds ratio [AOR] = 1.70, 95% confidence interval [CI]: 1.13 to 2.58). Study background was a statistically significant predictor for the development of AR (p = 0.017). The risk of developing AR was 42% lower in medical students compared to non-medical students ([AOR] = 0.58, 95% [CI]: 0.372 to 0.906).

Table 4: Logistic regression test for analyzing various sociodemographic and irrational AB Use related critical patterns contributed to ABR among Medical and Non-Medical students.

Variables	Characteristics	p-value	AOR	95% CI	
				Lower	Upper
Gender	Male vs female [R]	**.011**	1.709	1.131	2.582
Study background	Medical vs Non-medical [R]	**.017**	0.580	0.372	0.906
Age (years)	18-20 vs Above 20 [R]	.437	0.855	0.575	1.270
Level of education	1st / 2nd year vs 3rd / 4th / 5th year [R]	.196	0.740	0.468	1.168
Medication style	Doctor's prescription vs Suggestions from other [R] Self-medication vs	.347	0.640	0.253	1.621
	Suggestions from other [R] Pre-experience vs	.756	0.850	0.305	2.369
	Suggestions from other [R]	.189	0.485	0.165	1.427

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Main reason for AB use	Fever , common cold and cough vs other reasons [R]	.771	1.189	0.371	3.810
	Dysentery / diarrhea / food poisoning vs other reasons [R]	.693	1.287	0.387	4.518
	Abdominal /other pain vs other reasons [R]	.592	0.677	0.163	2.817
	Infection vs other reasons [R]	.920	0.941	0.283	3.126
Duration of AB therapy (days)	1-3 vs above 10 [R]	.496	0.712	0.268	1.893
	4-6 vs above 10 [R]	.694	0.694	0.294	2.263
	7-10 vs above 10 [R]	.703	0.796	0.247	2.566
Lack of cautiousness about AR	Yes vs No [R]	.632	1.114	0.717	1.730
Completion of prescribed course of AB	Yes vs No [R]	.322	1.250	0.804	1.944

P-value equals to or less than 0.05 considered statistically significant, [R] Reference values.

Discussion:

In this research, we estimated various factors like gender, age, education level, study background, medication style, duration of AB and reasons of AB usage and factors contributed to AR. Based on research findings; gender, educational background and lack of cautiousness were identified as critical factors of AR among the students. Around (40.1%) of the males and (25.4%) of the female's student among study participants had experienced AR. We found males were 1.7 times more likely to exhibit AR compared to females. The study findings were also in line with other studies.(22) Males behaviors and attitudes towards AB use may also play a role and associated with a higher risk of AR .(22) Some studies indicate that men might be more prone to engaging in behaviors that heighten their risk of acquiring drug-resistant infections.(23)

In this study finding, the educational background was also significant factor of AR. Students with a medical background were significantly less likely to exhibit the AR compared to those with a non-medical background which is similar to the findings of Nopadol Precha et al., 2024.(24) Non-Medical students had about (42%) higher likelihood of AR compared to non-medical students. The knowledge and awareness regarding AR in medical students had higher levels of knowledge, attitude, and practice (KAP) correlated with AB use and AR compared to non-medical students.(24)

Lack of cautiousness about AR among study participants was also one of the significant predictors in developing AR. AR was found to be higher (36%) of individuals who were not cautious about AR and the association between lack of cautiousness about AR and AR was found to be statistically significant. This result was supported by Dopelt et al., 2023.(25). The remaining variables in this study were found not significant. According to the study, (42.6%) of the non-medical students and (15.6%) of the medical students took AB without prescription. According to Ayub et al., 2023 (26), significant proportion non-medical students take AB without a prescription.

Almost (18.1%) of non-medical students had experienced side effects from AB compared to (10.1%) of medical students and this was their reason to discontinue the course of AB. Ayub et al., stated that non-medical students haven't better understanding of AB and are more non-compliant with therapy compared to medical students.(26) Among medical students, (76.4%)

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had completed the prescribe AB course which was higher than (62.8%) non-medical students. Only (57.2%) of medical students consulted with a physician or pharmacist before the discontinuation of their AB course compared to (30%) of non-medical students. Almost (70%) of the non-medical students did not consult any counseling from doctor or pharmacist before discontinuation of AB course. The lack of awareness about rational AB use may also contribute to non-medical student's reluctance to consult physician or pharmacist before the discontinuation of AB course.(27) Among medical students who had lack of cautiousness about AR, (62.14%) been student of 1st/ 2nd year. A comparative study by Gupta et al., found that 1st/ 2nd year medical undergraduate students lacked awareness about AR as it may lead to the misuse of AB and contribute to the growing problem of AR.(28)

Conclusion:

This study established a significant relationship between genders, study background with AR. Because irrational use of AB leads to AR which is a growing serious issue of concern across the world, various innovative methods are being implemented globally like AB stewardship program to tackle this widespread health issue. Consequently, there is a pressing need for robust legal regulations to control the distribution of AB to the public. Additionally, there should be efforts focused on educating people, and surveillance of AB use across different communities in the country.

Conflict of Interest:

The authors declare no conflict of interest.

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Authors Contributions:

Iram Aman Ullah: Supervision, Validation, Project Administration, Conceptualization, Writing - Review & Editing. Ayesha Aleem: Supervision, Project Administration. Hasnat Tariq: Project Administration, Conceptualization, Methodology, Writing, Original Draft. Khadija Shaikh Conceptualization, Methodology, Investigation, Writing - Original Draft. Fatima Ebad: Data Curation, Visualization, Investigation. Muhammad Abdullah: Data Curation, Investigation. Arzal Saeed: Data Curation, Resources. Ahsan Amir: Resources, Software. Aqsa Mutahhir: Formal Analysis, Validation. Omer Ijaz Butt: Critical review and administration. Dr. Mobasher Ahmad Butt: Critical review and administration

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