

Knowledge, attitudes, and practices toward antibiotic use among adults in Shaqra, Saudi Arabia: a cross-sectional study



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ABSTRACT

Background: Antimicrobial resistance (AMR) is a significant global health concern and a critical threat. This study aimed to evaluate knowledge, attitudes, and practices (KAP) regarding antibiotic use among adults in Shaqra, Saudi Arabia.

Methods: This cross-sectional study was conducted between March 2024 and February 2025. Following the checklist for reporting results of internet e-surveys (CHERRIES) guidelines, a pre-tested online questionnaire was used for data collection. Eleven, seven, and six questions evaluated knowledge, attitude, and practice, respectively. Descriptive statistics summarized socio-demographics, Spearman correlation assessed associations between knowledge and attitudes, and binary logistic regression evaluated predictors of knowledge. A p-value <0.05 was considered significant.

Results: Of 253 participants, 71.1% were male and 28.9% female. Overall, 38.7%, 61.3%, and 60.9% demonstrated good knowledge, positive attitudes, and good practices, respectively. A strong positive correlation was observed between total knowledge and total attitude scores (Spearman's $\rho = 0.585$, $p < .001$). Regression analysis showed that males were more likely to possess good knowledge (OR=2.19; 95% CI: 1.12–4.31; $p=0.023$), while younger respondents (≤ 35 years) had significantly lower odds (OR=0.23; 95% CI: 0.09–0.56; $p=0.001$).

Conclusion: The study identifies critical knowledge gaps regarding appropriate antibiotic use, particularly among younger adults and females. These findings highlight the urgent need for targeted public health campaigns and stricter enforcement of prescription-only antibiotic policies in Shaqra and similar smaller cities in Saudi Arabia.

Keywords: Antibiotics, Antimicrobial Resistance, Knowledge, Attitude, Practice, Saudi Arabia.

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INTRODUCTION

Antibiotics, discovered in the 20th century, have been a major medical breakthrough. They completely changed how we treat bacterial infections, making it easier for doctors to handle tough procedures like chemotherapy and surgery.¹ However, there's now a huge issue called antimicrobial resistance, or AMR. This issue is now a serious global public health problem. AMR spreads quickly because people often misuse antibiotics. They might take them too frequently or use them when they aren't needed.² The growth of AMR is putting many years of medical advancements at risk, making treatments less effective. This results in longer illnesses, causing more deaths, and

increasing healthcare costs.³

Antimicrobial resistance (AMR) is a rapidly escalating global health crisis, responsible for an estimated 4.95 million deaths associated with bacterial AMR in 2019, including 1.27 million deaths directly attributable to resistant infections.⁴ Projections suggest that if left unaddressed, AMR could cause 10 million deaths annually by 2050, surpassing cancer and costing the global economy up to USD 100 trillion.^{4,5} In the Middle East, including Saudi Arabia, the burden is similarly concerning, with resistance rates reported for common pathogens such as *Escherichia coli* and *Klebsiella pneumoniae* often exceeding 50% for third-generation cephalosporins

and showing increasing resistance to carbapenems.^{6,7}

Behavioral and social determinants play a pivotal role in driving this crisis. Misuse and overuse of antibiotics, such as self-medication, incomplete treatment courses, or inappropriate prescriptions for viral infections, are recognized as the leading contributors to AMR.^{8,9} Knowledge, attitude, and practice (KAP) surveys provide critical insights into how public awareness and behaviors shape antibiotic use. Evidence consistently shows that low knowledge levels increase the likelihood of self-medication and inappropriate antibiotic demand, while positive attitudes toward rational use can improve compliance with prescriptions.¹⁰

Conversely, negative practices such as sharing leftover antibiotics or pressuring physicians to prescribe are directly associated with higher community-level resistance patterns.^{11,12}

Understanding KAP at the local level is therefore essential for tailoring interventions to specific populations. In Saudi Arabia, where antibiotics remain widely accessible, including instances of non-prescription dispensing at community pharmacies.^{13,14} The relationship between public knowledge gaps, cultural attitudes, and daily practices has profound implications for AMR containment.

Insufficient use of antibiotics as a result of human activity at the population level is a major force behind the emergence of AMR.¹⁵ Such behaviors include the administration of antibiotics for self-medication using drugs obtained without a prescription, requesting antibiotics for viral infections such as the common cold or flu (which are ineffective), not following prescribed dosing schedules or failing to complete the treatment course.^{16,17} One must realize the determinants of such behavior for solutions to be appropriately formulated. The Knowledge, Attitude, and Practice (KAP) model is a handy tool for public knowledge, beliefs, and behavior assessment of health problems, like the use of antibiotics.¹⁸

In Saudi Arabia, there is a problem with how people use antibiotics and AMR. Many studies show that antibiotics are easily available, sometimes even without a doctor's prescription. People's knowledge about antibiotic usage varies. Some individuals understand a lot, while others have very limited knowledge.^{13,19,20} Research conducted in areas such as several areas of Saudi Arabia reveals significant gaps in understanding and misconceptions. For example, some believe antibiotics can cure viral infections, which they cannot. Also, self-medicating and not following medical advice.^{13,21,22} We need educational campaigns and stricter laws.

Previous research conducted in Saudi Arabia has explored knowledge, attitudes, and practices (KAP) toward antibiotic use in different regions. For instance, a study reported widespread misconceptions and inappropriate practices across the general population¹³, while another

study highlighted poor awareness and self-medication trends in the Western Region.²⁰ More recently, a study examined KAP in Riyadh Province and found that although attitudes were generally positive, significant knowledge gaps and unsafe practices persisted.²² These studies collectively confirm that inappropriate antibiotic use is a national challenge, shaped by varying socio-demographic and cultural factors.

Despite this growing body of literature, little is known about antibiotic KAP in smaller cities such as Shaqra, which has its own distinct socio-cultural and healthcare dynamics. Local variations in knowledge and behavior may not be captured in broader national studies. Therefore, this study aimed to assess knowledge, attitudes, and practices regarding antibiotic use among adults in Shaqra, Saudi Arabia. By providing localized baseline evidence, this work contributes to the development of targeted, culturally sensitive interventions to reduce inappropriate antibiotic use and strengthen AMR stewardship efforts.

METHODS

Study Design, Setting, and Participant

This was a cross-sectional study conducted among adults aged 18 years and above residing in Shaqra city, Saudi Arabia, between March 2024 and February 2025. The study targeted the general adult population living in the city to assess their knowledge, attitudes, and practices (KAP) regarding antibiotic use.

Inclusion and Exclusion Criteria

The study included residents of Shaqra who were ≥18 years old and consented to participate. Individuals who were below 18 years, non-residents of Shaqra, healthcare professionals (including physicians, nurses, and pharmacists), and those who submitted incomplete questionnaires were excluded from the analysis to avoid bias and ensure consistency in the study population.

Sample Size and Sampling Procedure

The required sample size was calculated using the Raosoft sample size calculator, presuming that 20% of the population would have good knowledge, with a 95% confidence level and a 5% margin

of error. The minimum required sample size was 243, which was increased by 10% to account for potential non-response, giving a final target of 267 participants. A convenient non-probability sampling technique was used to recruit participants.

Data Collection Tool

The questionnaire was adapted from a previously validated tool developed by Nepal et al. (25), which has been widely used in assessing antibiotic-related knowledge, attitudes, and practices in both medical and non-medical populations. To ensure cultural appropriateness for the Saudi context, minor modifications were made, followed by translation into Arabic and back-translation to English. It consisted of 11 questions assessing knowledge, 7 questions on attitudes, and 6 questions evaluating practices related to antibiotic use. Responses were in multiple-choice format (Yes/No/I don't know for knowledge; Agree/Disagree/Undecided for attitude; Always/Frequently/Rarely/Never for practice). The questionnaire was pre-tested on 20 individuals to assess clarity and internal consistency. Modifications were made until a Cronbach's alpha score of ≥0.7 was achieved. The final survey was distributed online via Google Forms, following the checklist for reporting results of internet e-surveys (CHERRIES) guidelines.

Variables and measurements

Knowledge was measured by scoring each correct answer as 1 and incorrect or "I don't know" as 0, with scores ranging from 0 to 11. Participants scoring ≥7 were categorized as having "good knowledge," and those scoring <7 as having "poor knowledge." Attitude was measured by assigning a score of 1 for positive responses and 0 for negative or undecided ones, giving a range of 0–7; scores ≥4 were classified as "positive attitude." Practice was measured by assigning a score of 1 to responses of "Always" or "Frequently" and 0 to "Rarely" or "Never," with reverse coding for negative items. The total practice score ranged from 0–6, with ≥4 categorized as "good practice."

Ethical Considerations

The study protocol was approved by the Institutional Review Committee of

Shaqra University (reference number ERC_SU_F_202300035). Informed consent was obtained electronically before participation. Confidentiality and anonymity of participants were maintained throughout the study.

Statistical Analysis

Data were analyzed using SPSS version 20 (IBM Corp., Armonk, NY, USA). Descriptive statistics such as frequencies and percentages were used to summarize demographic characteristics and KAP responses. Bivariate analysis was conducted using Chi-square tests to compare socio-demographic characteristics with knowledge, attitude, and practice categories, which explains the p-values presented in Tables 1 and 2. Spearman's rho correlation was calculated to assess the association between total knowledge, attitude, and practice scores. Binary multiple logistic regression analysis was performed using the ENTER method to identify socio-demographic predictors of good knowledge. A p-value of <0.05 was considered statistically significant.

RESULTS

A total of 253 participants completed the survey, of whom 180 (71.1%) were male and 73 (28.9%) were female. The majority were unmarried (65.6%) and belonged to the younger age group ≤ 25 years (41.9%). More than two-thirds (70.0%) were employed, and the vast majority (90.9%) had a college-level education or higher. Regarding income distribution, 53 (20.9%) participants reported a monthly household income of <5000 SAR, while 24 (9.5%) earned >35,000 SAR. Doctors (28.8%) and multiple sources (38.3%) were the most common sources of information regarding antibiotics.

Chi-square analysis showed significant differences across most socio-demographic variables, including gender, marital status, age group, education, employment, and income (all $p < 0.05$), which suggests that these characteristics were associated with differences in knowledge, attitudes, or practices (Table 1).

Overall, 98 (38.7%) participants demonstrated good knowledge, while 155 (61.3%) had poor knowledge (Table 2). A majority correctly identified that "many

Table 1. Baseline characteristics of the study population and their association with socio-demographic variables

Characteristics	Number (n)	Percentage (%)	p-value
Gender			
Female	73	28.9	<0.001
Male	180	71.1	
Marital Status			
Married	87	34.4	<0.001
Unmarried	166	65.6	
Age group (Years)			
< or equal 25	106	41.9	<0.001
26 to 35	98	38.7	
36 to 45	20	7.9	
> 45	29	11.5	
Educational status			
College and above	230	90.9	<0.001
Intermediate education	23	9.1	
Employment status			
Unemployed	76	30.0	<0.001
Employed	177	70.0	
Family Income			
< 5000	53	20.9	<0.001
5000-14999	83	32.8	
15000-24999	71	28.1	
25000-34999	22	8.7	
>35000	24	9.5	
Source of information regarding antimicrobials			
Awareness camps	2	0.8	<0.001
Doctors	73	28.8	
Family and friends	21	8.3	
Multiple sources	97	38.3	
Nurses	5	1.9	
Pharmacists	14	5.5	
Television and the Internet	41	16.2	

*P-values represent chi-square comparisons across subcategories of each characteristic.

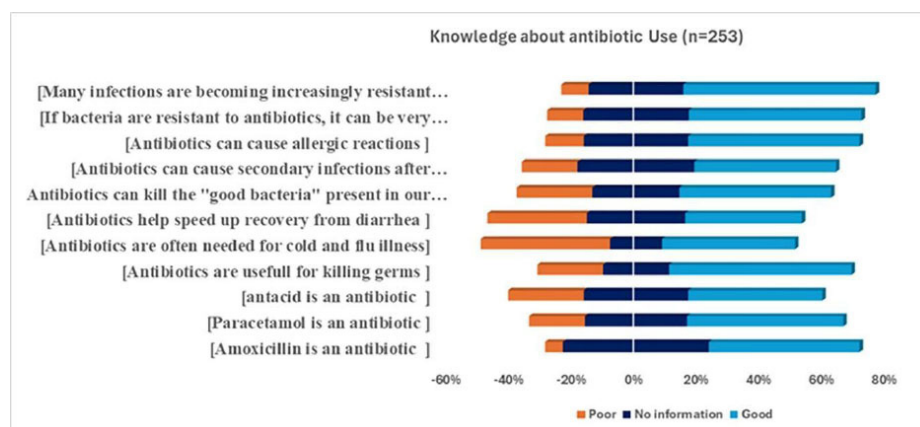


Figure 1. Knowledge about antibiotics among study participants (n=253).

infections are becoming increasingly resistant to antibiotics" (61.3%), and that "antibiotics are useful for killing germs" (58.1%). However, misconceptions

persisted, with 41.1% believing that antibiotics are needed for colds and flu, and 31.6% thinking that antibiotics speed up recovery from diarrhea. In addition,

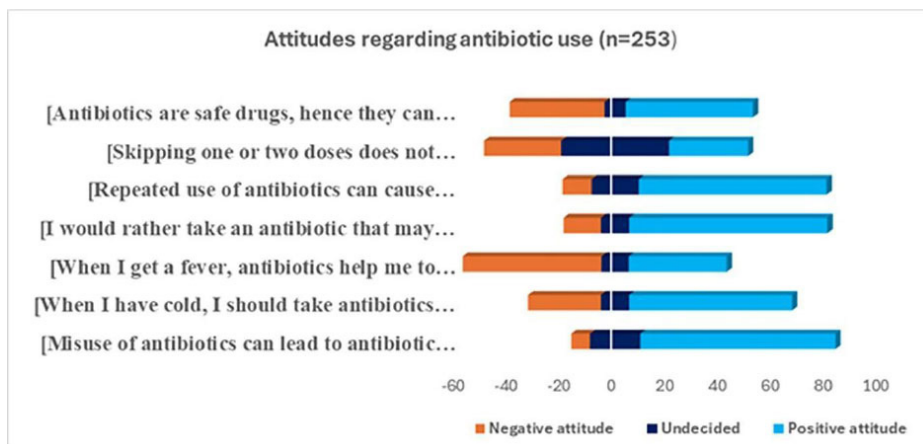


Figure 2. Attitudes regarding antibiotics among study participants (n=253).

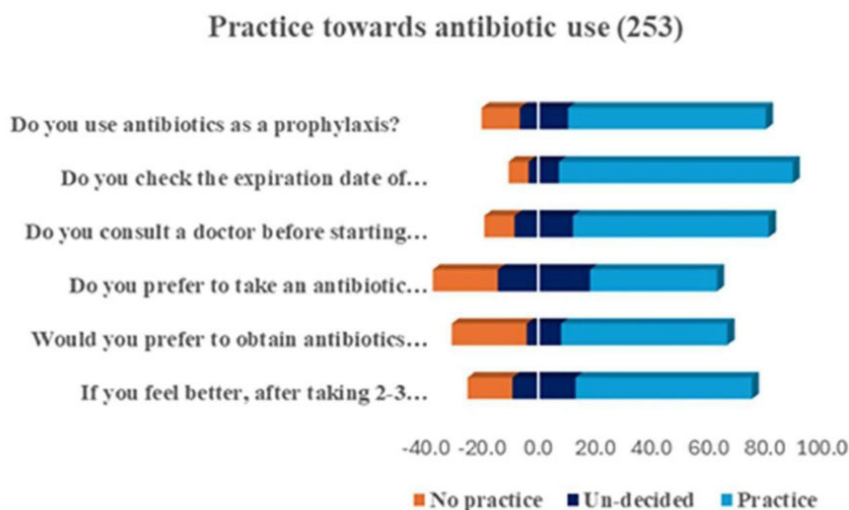


Figure 3. Practice towards antibiotic use (n=253).

one-third of participants could not differentiate between antibiotics and non-antibiotics (e.g., confusing amoxicillin or paracetamol). These findings highlight substantial gaps in understanding (Figure 1).

Positive attitudes were reported by 155 (61.3%) participants, while 98 (38.7%) demonstrated negative attitudes (Table 2). Encouragingly, 73.9% agreed that misuse of antibiotics contributes to resistance, and 75% disagreed with the statement that they would rather take an unnecessary antibiotic than wait to see if they improve without it. On the other hand, 35.9% still believed antibiotics were “safe for common use,” and 40.7% were undecided about whether skipping doses contributes to resistance. These findings suggest that while awareness of AMR exists, misconceptions about safety remain common (Figure 2).

A majority of participants (60.9%) demonstrated good practices (Table 2). Most respondents reported checking expiry dates before use (82.2%) and consulting doctors before initiating antibiotics (68.8%). However, 26.5% admitted to obtaining antibiotics directly from pharmacies without prescriptions, and 32.4% were undecided about taking antibiotics for cough or sore throat. These practices reflect a persistent “know-do” gap, where knowledge does not always translate into safe behaviors (Figure 3).

Table 2 shows the distribution of knowledge, attitude, and practice scores. χ^2 analysis demonstrated that 61.3% of participants had poor knowledge, while 61.3% and 60.9% demonstrated positive attitudes and good practices, respectively, with significant differences observed across demographic subgroups (all $p < 0.05$). Overall, 155 (61.3%) and 154

(60.9%) were categorized as having poor knowledge and good attitudes toward antibiotic use, respectively. 154 (60.9%) displayed good practice towards antibiotic use (Table 2).

Correlation analysis revealed a strong positive relationship between knowledge and attitude (Spearman's $\rho = 0.585$, $p < 0.001$), and a moderate positive relationship between attitude and practice ($\rho = 0.408$, $p < 0.001$). Knowledge and practice were weakly correlated ($\rho = 0.238$, $p < 0.001$). These results suggest that improving knowledge could positively influence attitudes, which in turn may shape practices (Table 3).

Two questions assessed perceptions of the doctor–patient relationship. A majority (69.7%) reported being satisfied even when antibiotics were not prescribed, while 21.3% expressed dissatisfaction. Moreover, 73.1% indicated they would not consult another doctor if antibiotics were not prescribed, whereas 16.2% said they would, and 10.7% were unsure. These findings highlight trust in physicians, although a notable minority still equates antibiotic prescribing with quality care.

Binary logistic regression identified two significant predictors of good knowledge (Table 4). Males were more likely to demonstrate good knowledge compared to females (OR = 2.19, 95% CI: 1.11–4.31, $p = 0.023$). Conversely, younger adults aged ≤ 35 years had significantly lower odds of good knowledge (OR = 0.23, 95% CI: 0.09–0.56, $p = 0.001$). Marital status, education, employment, and income were not significant predictors (Table 4).

DISCUSSION

This study provides Shaqra-specific evidence on the knowledge, attitudes, and practices (KAP) of antibiotic use among adults, highlighting that while the majority demonstrated positive attitudes (61.3%) and good practices (60.9%), a significant proportion (61.3%) exhibited poor knowledge. These findings underscore the presence of a knowledge–practice gap, where individuals may endorse responsible attitudes and even follow rational behaviors, yet still lack a fundamental understanding of appropriate antibiotic use. This gap has important implications for antimicrobial resistance (AMR), as

Table 2. Distribution of knowledge, attitude, and practice (KAP) scores and their associations with socio-demographic variables

Item	Number	Percentage	P-value
Knowledge Score			
Good	98	38.7	<0.001
Poor	155	61.3	
Attitude Score			
Negative	98	38.7	<0.001
Positive	155	61.3	
Practice Score			
No Practice	99	39.1	<0.001
Practice	154	60.9	

*P-values represent chi-square comparisons between KAP categories (good vs. poor knowledge, positive vs. negative attitude, and good vs. poor practice). and socio-demographic characteristics

Table 3. Correlation between Knowledge, attitudes, and practice

		Total Knowledge Score [TKS]	Total Attitude Score [TAS]	Total Practice Score [TPS]
TKS	Pearson's r	—		
	df	—		
	p-value	—		
	Spearman's rho	—		
	df	—		
TAS	Pearson's r	0.590***	—	
	df	251	—	
	p-value	<.001	—	
	Spearman's rho	0.585***	—	
	df	251	—	
TPS	Pearson's r	0.237***	0.417***	—
	df	251	251	—
	p-value	<0.001	<0.001	—
	Spearman's rho	0.238***	0.408***	—
	df	251	251	—
	p-value	<0.001	<0.001	—

*Note. * p < 0.05, ** p < 0.01, *** p < 0.001

incomplete or inaccurate knowledge can translate into inappropriate demand, misuse, and ultimately fuel resistance trends.

Our results align with previous research conducted in different regions of Saudi Arabia. Alnasser et al. (2021) reported widespread misconceptions in a national web-based survey, particularly the belief that antibiotics could treat viral infections.¹³ Similarly, Shatla et al. (2022) in the Western Region observed low knowledge levels but relatively favorable attitudes.²⁰ More recently, Alotaibi et al. (2025) examined KAP in Riyadh Province, finding that despite generally positive attitudes, unsafe practices such

as self-medication remained common.²² Together with our findings in Shaqra, these studies suggest that although awareness campaigns may have improved public perceptions of AMR, accurate knowledge remains limited.

In Shaqra, 41.1% of participants incorrectly believed that antibiotics are effective for viral illnesses such as colds and flu. This is concerning because it mirrors misconceptions seen globally and indicates that public health messaging has not sufficiently penetrated smaller Saudi cities. Given that community pharmacies in Saudi Arabia have historically dispensed antibiotics without prescription, such misconceptions likely reinforce patterns of

inappropriate antibiotic access and use.²¹

The misconception that antibiotics can treat viral infections is not unique to Saudi Arabia. Napolitano et al. (2013) in Italy found that over one-third of respondents held this belief.¹⁶ Similarly, Nepal et al. (2019) reported that community members often misuse antibiotics due to a poor understanding of their indications.²³ These parallels suggest that while AMR is a global challenge, local healthcare system structures, such as over-the-counter availability in Saudi Arabia, may exacerbate misuse.

The issue of self-medication also reflects a global problem. In our study, 26.5% of participants reported using antibiotics without physician consultation. This is consistent with findings from Saudi Arabia, where Alghadeer et al. (2018) reported high rates of self-medication²⁴, and Bin Abdulhak et al. (2011) documented that pharmacies frequently dispensed antibiotics without prescriptions.²⁵ Such practices undermine stewardship and highlight the need for stronger regulatory enforcement and community-level education.

Our regression analysis revealed important demographic differences. Males were significantly more likely to have good knowledge (OR=2.19), while younger participants (≤ 35 years) were less knowledgeable (OR=0.23). Similar trends have been observed internationally. Alex (2019) reported that male medical students in Nigeria demonstrated higher antibiotic knowledge than females.²⁶ The lower knowledge among youth in Shaqra may be attributed to reliance on informal sources, particularly social media, which often propagate health misinformation. Kwon and Kwon (2025) highlighted that health literacy patterns differ by age, with younger individuals more likely to rely on digital platforms, while older individuals depend on formal healthcare sources.²⁷ This suggests that youth-targeted, digitally tailored interventions are urgently needed in Saudi Arabia to correct misconceptions and promote appropriate antibiotic use.

Despite knowledge gaps, attitudes toward antibiotics in this study were generally positive, with 73.9% acknowledging that misuse contributes to resistance. However, over one-third

Table 4. Multi-logistic regression showing socio-demographic predictors of good knowledge

Predictor	Estimate	SE	Z	p-value	OR	95%CI	
						Lower	Upper
Intercept	0.47178	0.450	1.0482	0.295	1.603	0.6634	3.873
Gender:							
Male – Female	0.78556	0.345	2.2782	0.023	2.194	1.1160	4.312
Marital status:							
Un Married – Married	-0.22430	0.393	-0.5707	0.568	0.799	0.3699	1.726
Age:							
≤35 Years – > 35 Years	-1.48249	0.463	-3.2012	0.001	0.227	0.0916	0.563
Education status:							
Intermediate education – College and above	-0.01638	0.473	-0.0346	0.972	0.984	0.3890	2.488
Employment status:							
Employed – Unemployed	0.00618	0.328	0.0188	0.985	1.006	0.5293	1.913
Income:							
> 15000 SAR – < 15000 SAR	-0.39340	0.288	-1.3682	0.171	0.675	0.3841	1.185

*Note. Estimates represent the log odds of “Knowledge categories = Good” vs. “Knowledge categories = Poor”

(35.9%) still considered antibiotics inherently safe for common use. This reflects a dangerous normalization of antibiotics as “cure-all” medicines. Similar contradictory attitudes have been reported in Lebanon, where Mouhieddine et al. (2015) found that while many acknowledged resistance risks, antibiotics were still perceived as safe for frequent use. Such findings suggest that awareness of AMR does not necessarily translate into rational decision-making, and culturally embedded perceptions of antibiotics remain a barrier to change.²⁸

On a positive note, participants in Shaqra reported rational practices such as checking expiry dates (82.2%) and consulting doctors before antibiotic use (68.8%). These align with stewardship objectives and demonstrate some progress in public behaviors. However, the persistence of self-medication reflects the classic “know–do gap,” where individuals may recognize the risks of resistance yet continue unsafe practices. Addressing this requires not only education but also structural interventions, including stricter enforcement of prescription-only laws, pharmacist-led counseling, and public campaigns that emphasize behavior change rather than knowledge alone.

Saudi Arabia has adopted a National Action Plan on AMR²⁹, in line with the WHO Global Action Plan³⁰, which emphasizes multi-sectoral collaboration. Our findings provide Shaqra-specific baseline data to inform you of these efforts. Interventions should prioritize

younger populations and women, who have demonstrated lower knowledge levels. Pharmacists should be engaged as key frontline actors, given their role in dispensing practices. Community leaders and religious figures may also be leveraged as trusted sources to reshape cultural perceptions about antibiotics.

Framing these results within the global AMR crisis underscores their importance. Murray et al. (2022) estimated that AMR was associated with 4.95 million deaths in 2019, including 1.27 million directly attributable to resistant infections.³¹ More recent data indicate 4.71 million AMR-associated deaths in 2021, with concerning shifts toward older populations.² In this landscape, even modest improvements in local KAP can contribute to global stewardship goals, especially in regions with high antibiotic consumption and access challenges.

This study has several strengths, including the use of a validated questionnaire, adherence to the checklist for reporting results of internet e-surveys CHERRIES guidelines, and focus on a previously unstudied population in Shaqra. However, limitations must be acknowledged. The cross-sectional design precludes causal inference, self-reported data may be subject to recall and social desirability bias, and the use of convenience sampling limits generalizability to other regions. Despite these limitations, this study adds valuable insight into antibiotic use in a smaller Saudi city, complementing evidence from larger metropolitan areas.

CONCLUSION

This study assessed the knowledge, attitudes, and practices regarding antibiotic use among adults in Shaqra, Saudi Arabia. While the majority of participants demonstrated positive attitudes and good practices, a substantial proportion exhibited poor knowledge, particularly misconceptions about the effectiveness of antibiotics for viral illnesses. Younger adults (≤35 years) and females were more likely to have knowledge gaps, while males were more knowledgeable. These findings highlight the existence of a knowledge–practice gap and underscore the risk of self-medication, which remains prevalent in the community. Our results emphasize the urgent need for targeted interventions to improve public understanding of antibiotic use and to reduce inappropriate behaviors that contribute to antimicrobial resistance.

DECLARATION

Ethics approval and consent to participate

This study was approved by the Institutional Review Committee of Shaqra University (Reference No. ERC_SU_F_202300035, February 2024). Informed consent was obtained electronically from all participants before survey completion. Participation was voluntary, and responses were collected anonymously.

Consent for publication

Not applicable.

Conflict of interest

The author declares that there are no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Authorship Contribution

Abdulrahman Saad Alfaiz (corresponding author) contributed to the study concepts, design, definition of intellectual content, literature search, data analysis, statistical analysis, manuscript preparation, editing, review, and guarantor of the study. Feras Mansour Almarshad contributed to the concepts, design, literature search, data acquisition, data analysis, manuscript preparation, editing, and review. Abdulmajeed Mohammed Almansour was involved in data acquisition, literature search, clinical studies, and manuscript editing and review. Abdulaziz Saad Althiabi contributed to data acquisition, literature search, clinical and experimental studies, and manuscript editing. Fahad Abdullah Algassim participated in data acquisition, clinical and experimental studies, literature search, and manuscript editing. Altaf Hussain Bandy contributed to data analysis, statistical analysis, manuscript preparation, and review. Ramaprabha Prabhakar Venkataswamy was involved in statistical analysis, manuscript editing, and review. Aqeel Ahmed Jaleel contributed to the study concepts, design, definition of intellectual content, data analysis, statistical analysis, manuscript review, and served as guarantor. All authors read and approved the final version of the manuscript.

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