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Impact of Jordanian Pharmacists' Knowledge of the Human Microbiome: Has the Practice of Antibiotics and Probiotics Dispensing Been Affected? A Cross-Sectional Study

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Objective: This study aimed to assess Jordanian pharmacists' knowledge of the human microbiome and the impact of their knowledge on their attitudes and practices toward antibiotics and probiotics.

Methods: A self-administered survey was designed after reviewing the literature. Participants' demographics were collected, and questions to evaluate pharmacists' knowledge, attitudes, and practices toward antibiotic and probiotic dispensing were asked. The data were analyzed using the Statistical Package for the Social Sciences V.26. Pearson correlations and one-way ANOVA were employed to calculate the significance of knowledge, attitudes, and practices. Statistical significance was considered at $p < 0.05$.

Results: Of the 333 respondents, around 75% (n=250) had a high level of general knowledge regarding the human gut microbiome. Almost equal proportions of participants had either intermediate or high levels of knowledge about the role of gut bacteria in health (n=164, 49.2%) (n=166, 49.8%), respectively, while almost two-thirds had an intermediate level of knowledge of the role of gut bacteria in disease (n=197, 59.2%). More than half of the participants had a positive attitude toward antibiotics, probiotics, and the human microbiome (n=179, 53.8%), and the majority (n=239, 71.8%) had an intermediate level of practice with them. There was a significant positive correlation between pharmacists' general knowledge of the human microbiome and their positive attitudes (r=0.306, $p < 0.01$) and practices (r=0.331, $p < 0.01$) toward antibiotics and probiotics.

Conclusion: Study results raise the importance of interventional educational measures to promote healthcare professionals' knowledge of the human microbiome and their potential beneficence on pharmacists' attitudes and practices regarding antibiotics and probiotics dispensing. The results also denote the urgent need for probiotics' clinical guidelines to ensure practice uniformity.

Keywords: human microbiome, antibiotics, probiotics

Introduction

The role of the human microbiome in health and disease keeps unraveling and public awareness of the topic is widely spreading,[1] so healthcare professional's knowledge of microbiome aspects, factors, and interactions has become a necessity in practice.[2] Antibiotic resistance, as a global health threat, has mainly been attributed to the misuse and overuse of antibiotics. Pharmacists' attitudes and practices toward antibiotics greatly impact antibiotic resistance, as they are responsible for dispensing antibiotics and educating the public about their appropriate use.

Many studies have investigated the contributing factors behind public and healthcare professionals' attitudes and practices leading to antibiotic resistance, including antibiotics-self-medication and antibiotic dispensing without a prescription, which are widely disseminated within Arab countries, including Jordan,[3] the United Arab Emirates (UAE),[4] and Saudi Arabia.[5]

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One of the proposed, yet controversial, mechanisms to improve health is the consumption of probiotics; however, there is extensive debate around their safety, efficacy, and suitability for certain groups of people (eg, children, the elderly, and pregnant women), in addition to the absence of clinical and practice guidelines and regulations (ie, target population, dosing, and counseling).[6] Therefore, public acceptability and over-The-counter dispensing of probiotics fall on physicians and pharmacists; hence, pharmacists' knowledge of probiotics is considered crucial in shaping the public understanding of probiotic efficacy and safety. In order to demonstrate the influence of pharmacists in the dispensation of laxatives and probiotics, a study conducted in Spain have found that over 90% of the patients followed the advice of the pharmacist over the advice of their doctors.[7]

In this study, we propose knowledge of the human microbiome as a novel predictor factor contributing to pharmacists' attitudes and behaviors regarding antibiotics and probiotics, and show that providing pharmacists with satisfactory orientation regarding the human microbiome and its role in health and disease could be crucial in our battle against attitudes and practices contributing to antibiotic resistance. An example of knowledge gaps affecting pharmacists' practices is the misconception by some pharmacists that probiotics are primarily intended for gastrointestinal health, as was shown in a recent study conducted in the UAE assessing pharmacists' knowledge, perception, and prescribing practice of probiotics.[8]

Methods

Survey Development

A literature review was performed in preparation for the cross-sectional assessment of community and hospital pharmacists' knowledge, attitudes, and practices toward antibiotic and probiotic dispensing based on their knowledge of the human microbiome. The questionnaire was designed using Google® forms and in paper format both in Arabic (the official language of Jordan) and English. Two academics, fluent in both languages, translated the questionnaire from Arabic to English to ensure similarity and content validity.[9] Content and face validity of the questionnaire were ensured by consulting experts in the field who reviewed the questionnaire and took part in finalizing it. The questionnaire was then piloted on 10 individuals, academics, and non-academics to account for face validity. Their feedback and comments were considered for any unclear questions or jargon, which were removed accordingly. The responses of the pilot samples were not included in the final statistical analyses. The number of registered pharmacists in Jordan was obtained from the Jordanian Pharmacists Syndicate records, and the sample size was calculated using an online calculator with a 95% confidence interval and a 5% margin of error.[10] The target group was all registered pharmacists in Jordan who worked in either a community or a hospital pharmacy. Data collection was performed from June to September 2022 by disseminating the questionnaire either online across different social media groups with member pharmacists or in paper format by visiting pharmacists' workplaces with the aim of manually responding to the questionnaire.

Survey Sections

The questionnaire consisted of four main sections. The first part explored participants' demographics, such as age, gender, place of residence, educational level, the facility sector where they worked (ie, public or private), practice settings (community or hospital pharmacist), and years of experience. The second section evaluated pharmacists' knowledge of bacteria, the human microbiome, and antibiotics in general. Questions about the human microbiome were designed on a 2 point Likert scale, with answers divided between agree and disagree, in which a knowledge score based on a comprehensive literature review was established (see Appendix 1).

Questions in the third section were constructed in three parts and in the first part examined whether pharmacists were able to recognize the role of the microbiome in health and disease based on an agree or disagree scale and a predesigned knowledge score. The role of the microbiome in digestion, nutrient production, activation of immune response, cognitive skills, response to medications, wound healing, fertility, food preferences, physical exercise endurance, and aging was also investigated. The second part of this section asked pharmacists to describe the imbalance of the gut microbiome and the factors that promote its progression using a checkbox of different relevant factors, such as smoking, unhealthy

lifestyle, antibiotic misuse, pollution, and hormonal imbalance. The third part of this section evaluated the participants' knowledge of the microbiome's role in disease states and possible methods to reverse this imbalance.

The last section was designed based on a Likert scale of five degrees ranging from strongly disagree to strongly agree to investigate pharmacists' attitudes and practices regarding antibiotic and probiotic use and their influence on the human microbiome.

Ethics Approval

Research ethics approval was obtained from the Ethics Committee for Scientific Research at Zarqa University, with approval number (Zu-2023/7/5306/37) prior to conducting the study. Informed consent was collected from participants before they recorded their responses to the questionnaire, while ensuring that participant's identities were anonymously maintained. Their responses were treated confidentially, and they were informed that they could withdraw from responding at any time while filling out the questionnaire.

Statistical Analyses

The data were cleared and analyzed using the Statistical Package for the Social Sciences (SPSS) version 26. Simple descriptive statistics were used to present the general characteristics of the research participants and their levels of knowledge, attitudes, and practice. Knowledge questions were scored so that one option was considered the correct answer to yield a score of either[11] for a correct answer or[11] for a wrong answer. Attitudes and practices questions were scored in the direction that implies a positive attitude or practice towards each question. Pearson's correlation coefficient was calculated to detect any significant correlations between knowledge, attitudes, and practices scores at the $p < 0.05$ level. One-way ANOVA and post hoc analysis were used to detect any significant differences between knowledge, attitudes, and practices scores at the $p < 0.05$ level.

Results

An average of 100 electronic responses and 233 paper responses were obtained and statistically analyzed (it was not feasible to calculate the response rate, as the questionnaire link was distributed through social media platforms). The general characteristics of the research participants are listed in Table 1. Around two-thirds of the study participants were in the age group of 25–49 years (n=220, 66.1%). Female respondents comprised 78.4% (n=261) of the study sample. The highest participation rate was from Amman (n=122, 36.6%), followed by Zarqa (n= 91, 27.3%).

As shown in Table 2, more than two-thirds of participants (n=257, 77.2%) considered themselves familiar with the term "human microbiome", and an even higher percentage answered the "most likely description of the human

Table 1 General Characteristics of the Research Participants

	N	%
Age group (years)		
Under 24	113	33.9
25–49	220	66.1
50–64	0	0.0
65–74	0	0.0
Over 75	0	0.0
Gender		
Male	31	9.3
Female	261	78.4

(*Continued*)

Table 1 (Continued).

	N	%
Age group (years)		
Place of residence		
Amman	122	36.6
Zarqa	91	27.3
Irbid	23	6.9
Jerash	6	1.8
Madaba	1	0.3
Ajloun	2	0.6
Ma'an	25	7.5
Mafraq	55	16.5
Karak	2	0.6
Balqa	5	1.5
Aqaba	1	0.3
Educational level		
Diploma	54	16.2
Bachelor's degree	242	72.7
Master's degree	35	10.5
PhD	2	0.6
Workplace sector		
Public	83	24.9
Private	250	75.1
Pharmacy practice setting		
Community pharmacist	245	73.6
Hospital pharmacist	88	26.4
Work experience (years)		
Less than 5 years	178	53.5
5–10 years	87	26.1
More than 10 years	68	20.4

microbiome" question correctly (n=301, 90.4%). When study participants were asked about the factors affecting the composition of the microbiome, the most prevalent answer (n=265, 79.6%) was antibiotics, followed by probiotics (eg, Activia yogurt) (n= 231, 69.4%) and genetics (n= 208, 62.5%). Scores of participants regarding general knowledge of the human microbiome, the role of the human microbiome in health, and the role of the human microbiome in disease are presented in Supplementary Tables 1-3, respectively.

Table 2 Participants' Responses to Microbiome Knowledge Questions

Statement	N	%
Have you ever heard of the term "human microbiome"?		
Yes	257	77.2
No	76	22.8
The most likely description of the human microbiome		
Living bacteria found in the human body	301	90.4
Drugs	16	4.8
Food	14	4.2
Bugs/insects	2	0.6
Factors affecting the composition of microbiome		
Antibiotics	265	79.6
Probiotics (eg, Activia Yogurt)	231	69.4
Diet and nutrition	223	67
Genetics	208	62.5
Disease or hospitalization	206	61.9
Personal hygiene	203	61
Taking care of pets or farm animals	190	57.1
Environment and weather	187	56.2
Feeding method (breast milk or formula milk)	187	56.2
Age	169	50.8
Smoking	167	50.2
Nonantibiotic drugs (eg, antacids)	160	48
Physical activity	153	45.9
Hormones	137	41.1
Stress	124	37.2
Mode of delivery (vaginal or caesarean)	114	34.2
Travel	112	33.6
Body weight	107	32.1
Gender	105	31.5
Sleep	100	30
Mobile phone usage	36	10.8
The most likely the description of imbalance in gut bacteria		
The decrease in number of beneficial bacteria	207	62.2
The increase in number of harmful bacteria	201	60.4
The loss of diversity of the gut bacteria (ie, when you have few different types of bacteria)	162	48.6

(*Continued*)

Table 2 (Continued).

Statement	N	%
Factors leading to imbalance in gut bacteria		
Smoking	268	80.5
Adapting unhealthy diet	268	80.5
Excessive and misuse of antibiotics	266	79.9
Aging	219	65.8
Lack of diversity in diet	211	63.4
Adapting unhealthy lifestyle (eg, lack of exercise or lack of sleep)	193	58
Environmental pollution	190	57.1
Diseases	175	52.6
Excessive use of artificial sweeteners and processed food	154	46.2
Hormonal imbalance	134	40.2
Stress	117	35.1
Excessive caffeine intake (coffee, tea, or energy drinks)	111	33.3
Methods to fix the imbalance in gut bacteria		
Eating healthy food	269	80.8
Taking pills of beneficial bacteria (probiotics)	266	79.9
Eating diverse food	239	71.8
Not using unnecessary antibiotics	236	70.9
Adopting a healthier lifestyle (eg, exercise more, good healthy sleep)	216	64.9
Improving personal hygiene	210	63.1
Quitting smoking	200	60.1
Cutting down artificial sweeteners and processed food	191	57.4
Reducing stress	186	55.9
Reducing caffeine consumption	163	48.9
Spending more time outdoors	152	45.6
Taking antibiotics to kill harmful bacteria	114	34.2

According to study participants, the most frequent descriptions of imbalance in gut bacteria were "the decrease in number of beneficial bacteria" (n= 207, 62.2%) and "the increase in number of harmful bacteria" (n= 201, 60.4%). When asked about the leading causes of imbalance in gut bacteria, the most frequent answers were "smoking" and "adopting an unhealthy lifestyle" (equally, 80.5%), followed by "excessive and misuse of antibiotics" (n= 266, 79.9%). "Eating healthy food" was the most prevalent answer to the question on methods for fixing the imbalance in gut bacteria (n=269, 80.8%), followed by "taking pills of beneficial bacteria probiotics" (n=266, 79.9%).

One-way ANOVA test was applied to detect any differences between knowledge, attitude, and practice scores based on the characteristics of the study sample. Participants who were 24 years or less scored significantly lower than participants in the age group of 25 to 49 years in the following scores: general knowledge scores $F(1331)=17.5$, $p=0.00$; mean knowledge score on the role of gut bacteria in health $F(1331)=4.1$, $p=0.04$; and mean score on attitudes regarding

antibiotics, probiotics, and the human microbiome F(1331)=5.1, p=0.02. Also, there was a statistically significant difference between male and female participants in general knowledge scores, F(3329)=3.8, p=0.01, as it was observed that male participants scored significantly higher than female participants.

Furthermore, a statistically significant difference was observed among residents in the different provinces in scores on practices regarding antibiotics, probiotics, and the human microbiome F(10,322)=2.3, p=0.01; however, post hoc analysis could not be executed due to the low number of respondents from some of the included provinces.

Regarding respondents' attitudes regarding antibiotics, probiotics, and the human gut microbiome, most respondents agreed that it was important to consider the impact of antibiotics on the patient's microbiome (whether it was a short-term (n=281, 84.3%) or long-term effect (n=257, 77.1%)), and the majority believed in the importance of the human microbiome knowledge for pharmacists and healthcare providers (n=281, 84.4%); however, only 60.9% (n=203) considered themselves well informed regarding the significance of the human microbiome with respect to medical practice, a similar percentage (n=212, 63.6%) felt confident in their knowledge discussing the human microbiome with patients, and more than two-thirds of the respondents (n=249, 74.7%) thought that the human microbiome was too "new" as a field for them to consider how it affected patients' health. Most respondents agreed that probiotics (n=266, 79.8%) and healthy lifestyle modifications (n=270, 81%) helped restore the balance of "good" and "bad" bacteria in the gut, and 74.7% (n=249) of respondents agreed that they would take probiotic pills after completing an antibiotic course (Figure 1).

The responses regarding the respondents' practices regarding antibiotics are shown in Figure 2. Around two-thirds of respondents (n=232, 69.6%) never dispended antibiotics without a prescription, around one-third (n=119, 35.7%), on the other hand, would recommend and dispense antibiotics to patients, friends, and family (without a prescription), and 30.6% (n=102) of respondents would take antibiotics as a precaution so they would not get sick. With respect to

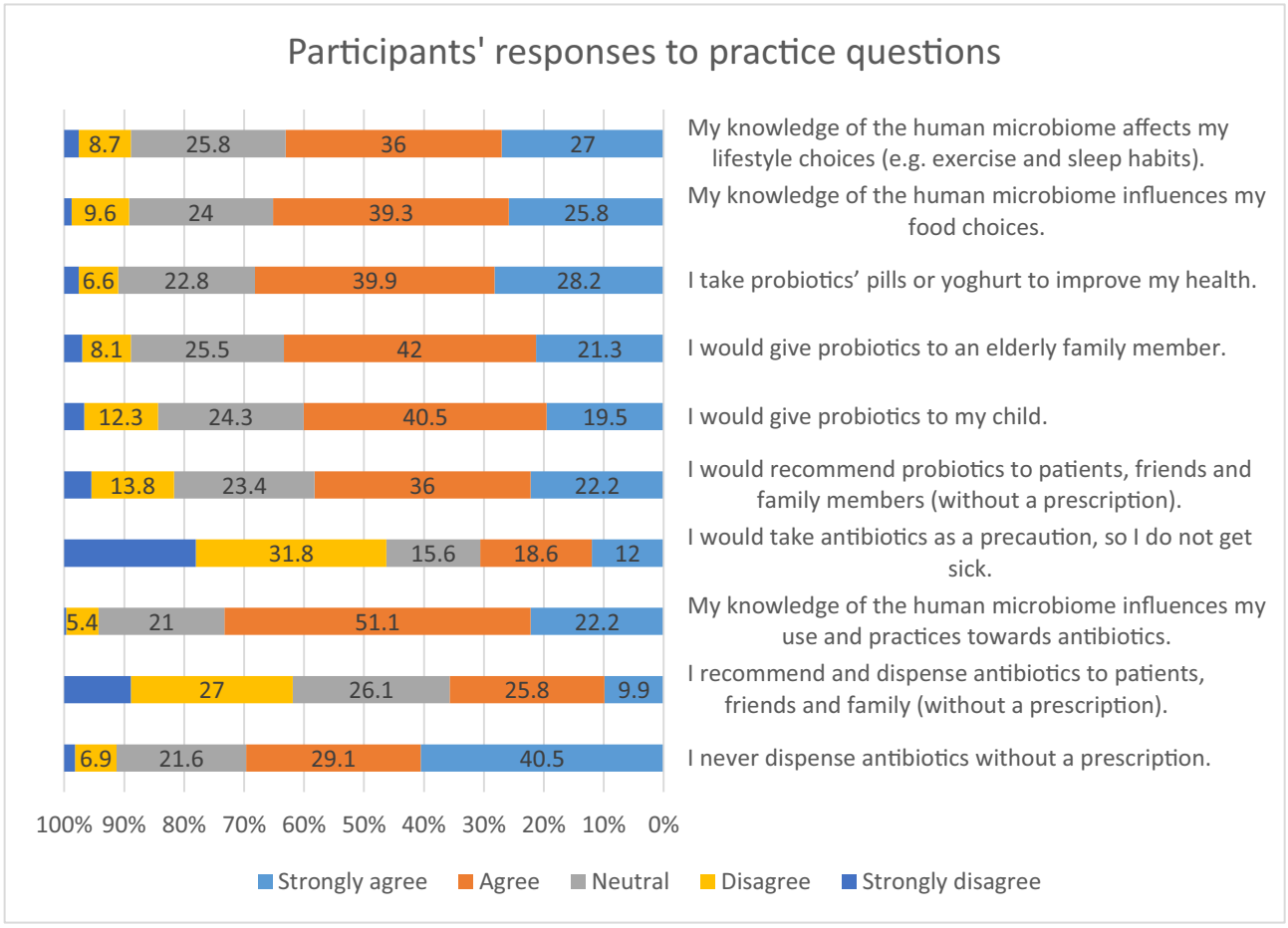

Figure 1 Participants' responses to attitude questions.

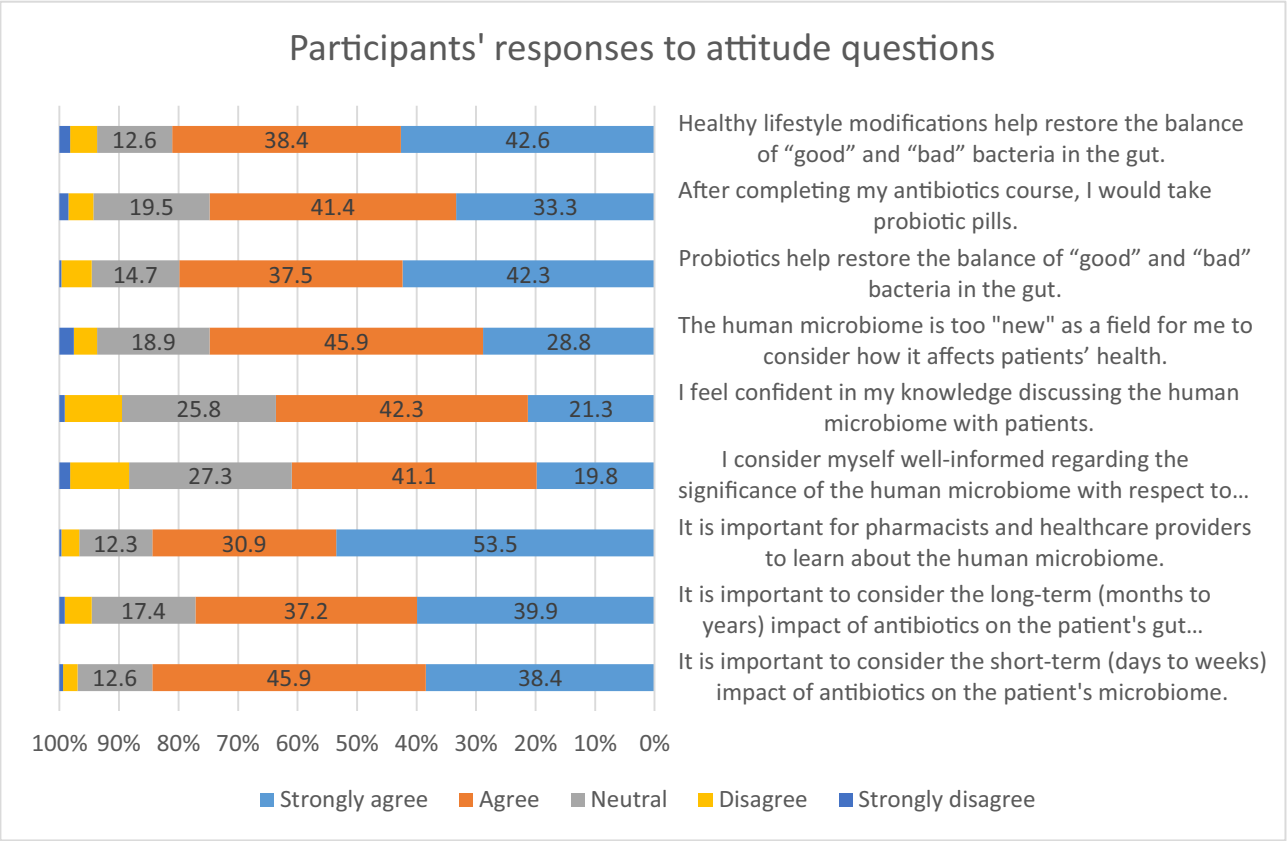

Figure 2 Participants' responses to practice questions.

respondents' practices regarding probiotics, over half of those surveyed (n=194, 58.2%) indicated that they would recommend probiotics to patients, friends, and family members (without a prescription), (n= 200, 60%) would give probiotics to their child, (n=211, 63.3%) would give probiotics to an elderly family member, and an even higher percentage (n=227, 68.1%) would personally take probiotics' pills or consume yogurt to improve their health. Knowledge of the human microbiome was reported to influence respondents' use and practices toward antibiotics and respondents' food and lifestyle choices (eg, exercise and sleep habits) by 73.3% (n= 244), 65.1% (n= 217), and 63% (n= 210) of respondents, respectively.

With respect to the levels of knowledge, attitude, and practice scores among the research participants, around 75% (n=250) had a high level of general knowledge regarding the human microbiome (Supplementary Table 4). Almost equal proportions of research participants had either intermediate or high levels of knowledge about the role of gut bacteria in health (n=164, 49.2%) (n=166, 49.8%) respectively, while almost two-thirds had an intermediate level of knowledge of the role of gut bacteria in disease (n=197, 59.2%) (Supplementary Table 4). More than half of the research participants had a positive attitude toward antibiotics, probiotics, and the human microbiome (n=179, 53.8%), and the majority (n=239, 71.8%) had an intermediate level of practice toward the same.

A significant weak positive correlation was found between participants' knowledge of the role of gut bacteria in health and their attitudes regarding antibiotics, probiotics, and the human microbiome (r=0.186, $p < 0.01$). Also, a weak positive correlation was found between participants' knowledge of the role of gut bacteria in disease and their practices regarding antibiotics, probiotics, and the human microbiome (r=0.188, $p < 0.01$). A significant moderate positive correlation was found between participants' general knowledge and each of the following: participants' knowledge of the role of gut bacteria in health (r=0.317, $p < 0.01$) and attitudes (r=0.306, $p < 0.01$) and practices (r=0.331, $p < 0.01$) regarding antibiotics, probiotics, and the human microbiome. Also, a significant moderate positive correlation was found between participants' knowledge of the role of gut bacteria in health and their practices regarding antibiotics, probiotics,

and the human microbiome (r=0.321, p<0.01). Furthermore, a significant strong positive correlation was found between participants' knowledge of the role of gut bacteria in health and their knowledge of the role of gut bacteria in disease (r=0.591, p<0.01) and between participants' attitudes regarding antibiotics, probiotics, and the human microbiome and their practices regarding the same (r=0.539. p < 0.01) (Supplementary Table 5).

Discussion

The study provides unique and valuable insights into the impact of pharmacists' knowledge of the human microbiome and its role in health and disease as an influential factor driving their attitudes and practices regarding antibiotics and probiotics. Here, we present knowledge of the human microbiome as a powerful tool to modulate public and healthcare professionals' mind-sets regarding their attitudes and practices regarding antibiotics and probiotics. Our results show that the prevalence of self-medication with antibiotics and the propensity to dispense antibiotics without a medical prescription was lower among pharmacists with a higher knowledge score of the human microbiome. Also, pharmacists with higher knowledge scores were also more likely to take or recommend probiotics to patients, friends, and family members (without a prescription).

In addition, the study results show that the higher the score of participants' knowledge (either general or specific knowledge), the less likely they were to take or dispense antibiotics without a prescription, and the more likely they were to take and recommend probiotics to patients, friends, and family members (without a prescription). Despite the high or intermediate levels of knowledge (either general or specific knowledge) of participants of the human microbiome, correlations of knowledge (either general or specific knowledge) with either pharmacists' attitudes or practices were either moderately or weakly significant, which might be attributed to a number of impediments, such as the lack of clinical and practice guidelines and regulations (ie, target population, dosing, and counseling) regarding the use of probiotics.

Two of the major behaviors contributing to antibiotic resistance are self-medicating with antibiotics and the propensity to dispense antibiotics without a medical prescription,[12,13] especially with the high prevalence rates of self-medication with antibiotics in Jordan.[3] The results of this study indicated that of the 333 participants, around one-third (n=119, 35.7%) would recommend and dispense antibiotics to patients, friends, and family (without a prescription), and a similar proportion (n=102, 30.6%) would take antibiotics as a precaution so they would not get sick. In a study conducted in Jordan in 2021 evaluating community pharmacists' knowledge of and attitudes toward antibiotic use, resistance, and self-medication, almost all respondents (97%) agreed that community pharmacists were qualified to prescribe antibiotics to patients with bacterial infections, and most respondents (95.2%) practiced antibiotic self-medication.[14] Another study conducted in Portugal to investigate factors associated with a propensity to dispense antibiotics without a medical prescription found that agreement with the dispensing of antibiotics without a medical prescription was highest in cases of dental diseases, followed by urinary tract infections.[15]

Probiotics are still considered over-The-counter medications;[16–18] therefore, pharmacists play a great role in dispensing probiotics and shaping public knowledge and awareness regarding them. In the present study, it was found that the higher the score of participants' knowledge, the more likely they were to take probiotic pills or recommend them to others. This is similar to a study conducted in Jordan in 2019 to evaluate Jordanian healthcare providers' knowledge, attitudes, and practice patterns toward probiotics, which reported that half of the healthcare professionals included in the study (51.5%) had fair knowledge about probiotics (pediatricians were more knowledgeable), and around 59% of healthcare professionals had positive attitudes toward probiotics. However, only 41% had ever recommended or prescribed them to patients.[19] Another regional study conducted in Muscat, Oman, showed that pharmacists have a good background knowledge of probiotics.[20]

However, these results contrast with the results of other studies conducted earlier in other countries. For example, a study from Nigeria reported limited knowledge of probiotics by healthcare professionals (pharmacists were more knowledgeable).[21] Two other studies have also reported limited knowledge of probiotics by healthcare professionals in Lagos State[22] and Pakistan.[23] Furthermore, in an online international survey that included 1066 health professionals from 30 countries, most respondents evaluated their knowledge of probiotics as medium (36.4%) or good (36.2%), and only 8.9% of respondents rated it as excellent.[24] As good knowledge is frequently

correlated with positive attitudes and good practices, according to our results, we propose knowledge of the human microbiome as a predictor factor of healthcare professionals' attitudes and practices regarding antibiotics and probiotics.

Linking healthcare professionals' knowledge of the human microbiome with their attitudes and clinical practice has been addressed in a few studies in the literature. An online survey distributed in Rhode Island, US, to address the knowledge and opinions of antibiotic prescribing regarding the importance of the human microbiome and its relation to antibiotics and the immune system, found that clinicians considered the health of the human microbiome when prescribing antibiotics; however, they did not feel well informed or confident in their knowledge about the microbiome or its relevance to patient health.[25] The study also reported that a higher level of knowledge of the microbiome was associated with the increased importance placed on the microbiome and its relevance to medical practice. Likewise, in this study, most of the participants (n=281, 84.4%) believed in the importance of pharmacists and healthcare providers learning about the human microbiome. However, although a significant proportion of the participants (n=249, 74.7%) believed that the human microbiome was too "new" as a field for them to consider how it affected patients' health 60.9% (n=203), they considered themselves well informed regarding the significance of the human microbiome with respect to medical practice, and a similar percentage (n=212, 63.6%) felt confident in their knowledge discussing the human microbiome with patients.

Regarding the link between participants' attitudes and practices regarding antibiotics, probiotics, and the human microbiome, a significant positive strong correlation was found (r=0.539. $p < 0.01$). This alignment of a high level of knowledge with positive attitudes and practices is not always the case in the literature. Another knowledge, attitude and practices (KAP) survey in Jordan regarding probiotics reported fair knowledge and a positive attitude that did not reflect a positive practice.[19]

To the best of our knowledge, this study is the first of its kind in Jordan linking pharmacists' knowledge of the human microbiome to their attitudes and practices regarding antibiotics and probiotics. However, the study had a number of caveats that needed to be noted, including convenience sampling and the low number of respondents from some of the included provinces. Despite convenient sampling, the sample was fairly representative, given that, gender-wise, there are more female pharmacists in Jordan (more females were included in the study sample (78.4%) than males). Also, residency-wise, more pharmacists are situated in the middle governorates compared to north and south (63.9% of respondents were from the middle governorates). In addition, more pharmacists work in the private sector than in the public sector (75.1% of respondents were from the private sector).[26] Another limitation of our study is that the data were self-reported and that healthcare professionals may admit less negative attitudes and practices than in which they really engage.

Conclusion

This study highlighted the importance of knowledge of the human microbiome and its role in health and disease for pharmacists, in their attitudes and practices toward antibiotics and probiotics, and in their personal lives regarding food and lifestyle choices, which ultimately reflected positively on knowledge of the general population of the human microbiome, which in turn might help rectify public behaviors leading to antibiotic resistance. Future directions include interventional studies to assess the effect of educating pharmacists (or pharmacy students) of the human microbiome on their attitudes and practices regarding antibiotics and probiotics.

Data Sharing Statement

All data were provided within the manuscript and supplementary tables.

Ethical Approval

Research ethics approval was obtained from the Ethics Committee for Scientific Research at Zarqa University, with approval number (Zu-2023/7/5306/37) prior to conducting the study. Informed consent was collected from participants before they recorded their responses to the questionnaire, while ensuring that participant's identities were anonymously maintained.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors state no conflicts of interest in this work.

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