Original Article

Pharmacy students' overall knowledge and awareness regarding biofilms

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ABSTRACT

Biofilms have a negative impact on the health of the patients, it is one of the global health concerns that need to be nullified to enhance and improve the health outcome. The knowledge and awareness of biofilms among pharmacy students is very essential. Hence this study aimed to assess the overall knowledge and awareness regarding biofilms among pharmacy/Phar.D. students in multiple universities in Jordan. A descriptive cross-sectional study was conducted in the period between February 1st, 2022, and April 1st, 2022, to assess and evaluate knowledge about biofilms among undergraduate pharmacy/Phar.D. students in Jordanian universities, this was performed by sampling respondents from pharmacy schools in both public and private universities. An online questionnaire-based survey was used to collect the data which were then statistically analyzed using SPSS software. A total of 1,058 undergraduate pharmacy/Phar.D. students are enrolled in this study. Nearly all the students were in their 3rdand 4thyear of study. A high number of participating students (80.7%) have previously been enrolled in or are currently receiving an academic course in pharmaceutical microbiology and around half (48.0%) have been enrolled in or are currently receiving a related course. The study found a significant lack of information in the enrolled students regarding the specifics of biofilms, creating a better understanding of the information needed to be supplemented to raise students' knowledge and avoid common misconceptions.

Keywords: Biofilms, Pharmacy, Students, Knowledge, Infections

Introduction

In the endless battle of survival, bacteria have been known to possess a nifty armor, helping them to always be on top of the survivors' list. Microbial communities are very versatile and can propagate in almost all environmental conditions, as well as easily adapt if new changes occur. This adaptation is mainly attributed to multiple mechanisms such as continuous gene expression regulation and metabolic regulation for planktonic bacterial cells [1, 2]. Another well-known mechanism is biofilm formation. A biofilm is a community consisting of sessile bacteria affixed on a surface or to each other irreversibly. This community is submerged in a matrix of Extracellular Polymeric Substances (EPSs) self-produced by the bacteria. This matrix is a highly self-organized complex three-dimensional structure of polymers in relations to their composition and complex architecture [3]. Members of the biofilm community display an enhanced biological properties, mechanical properties, and phenotypic properties [3-5].

Biofilm formation in healthcare systems is a serious concern; it results in higher morbidity and mortality rates; it is associated with a major impact as an economic burden on the healthcare system. Around 80% of chronic and recurrent infections are due to biofilm-forming bacteria [6]. 50-70% of all nosocomial infections are implant-associated due to biofilm-forming bacteria

Access this article online	
Website: www.japer.in	**E-ISSN:** 2249-3379

How to cite this article: Alsharedeh RH, Alshraiedeh N, Bashatwah R, Huwaitat R, Taybeh E. Pharmacy students' overall knowledge and awareness regarding biofilms. J Adv Pharm Educ Res. 2022;12(4):60-6. https://doi.org/10.51847/GhbRJyJncW

[7, 8]. Biofilms has significant impact in the treatment of biofilms associated infections as it is proving difficult and costly to health care systems [9]. Biofilm bacteria are highly resistant to conventional antimicrobials and are associated with persistent infections [10]. They use Quorum sensing to control every process from proliferation rate and sporulation, maturation of the biofilm, motility, the secretion and use of enzymes, EPS production, horizontal gene transfer, and most importantly; antibiotic resistance and virulence [11]. Moreover wet and dry biofilms are associated with healthcare-associated infections and they may serve as a persistent environmental source of pathogens [12]. Environmental biofilms have also played an important role in the emergence and spread of antibiotic resistance, they must be considered synonymously with antimicrobial resistance due to their innate phenotypic antibiotic tolerance and their excellence in transferring resistance genes [13].

Pharmacists are a vital member of the healthcare team and have a big role in how patients use their medications due to the regular patient counseling about proper drug use and healthcare instructions. Pharmacist education and training havea great impact on the behavior of consumers as well as other members of the healthcare team. Well-educated and trained pharmacists must be able to improve the understanding of antibiotics and their use, raise awareness of the proper use of antibiotics, and aid in the prevention of antibiotic resistance in patients counseled during their visit to the community pharmacy or hospital. Many studies have highlighted that educating and training undergraduate students has a significant impact on their professional attitude and behavior and proper pharmaceutical practice students portray as future pharmacists and part of the healthcare team [14].

Jordan is a small developing country in the Middle East with inadequate supplies of water and natural resources. It is nearly self-sufficient in health services and health education [15]. Currently, little is known about how pharmacy students in low-income countries perceive knowledge about biofilms and their impact on the health system. To date, no study has been conducted in Jordan to determine undergraduate pharmacy students' knowledge about biofilms. Thus, this regionally novel study aims to assess the knowledge and awareness about biofilms among pharmacy/PharmD students in universities in Jordan.

Materials and Methods

Study design and setting

A descriptive cross-sectional study was conducted between February 1st and April 1st, 2022, to assess and evaluate knowledge about biofilms among undergraduate pharmacy/PharmD students in universities in Jordan. Respondents from multiple pharmacy schools in both public and private universities in Jordan have been sampled to fill the survey.

Inclusion and exclusion criteria

All students enrolled in undergraduate pharmacy/PharmDbachelor's degree programs at both public and private universities in Jordan during the study period; irrespective of their age, gender, ethnicity, religion, or social class were eligible to take part in the study. Only participants willing to take part in the study voluntarily were enrolled. All non-pharmacy/non-Pharm D students, in addition to all postgraduate students, were excluded from the study. All pharmacy/PharmD students who have not been enrolled in or are not currently receiving an academic course of pharmaceutical microbiology/related course (i.e. biotechnology, immunology, or advanced microbiology) were excluded from the study.

Data collection

The data collection form was designed after an extensive literature review. Data were collected using a pre-tested standard questionnaire that included 27 questions divided into three sections. A self-administered web-based questionnaire (Appendix 2) was used to collect data to assess the knowledge and awareness about biofilms among pharmacy/PharmD students in universities in Jordan. The Questionnaire consists of a section on socio-demographic data, a section on general knowledge, and awareness of biofilms, and finally a section on the role of biofilms in infections and their behavior. The main methods for participant invitations are Facebook, messages through WhatsApp groups, e-mails, and postings in pharmacy-focused forums. The expected time to complete the questionnaire is 5-10 minutes. No financial inducements were offered to participants.

Informed consent form

An informed consent form (Appendix 1) is required to be signed voluntarily before participating in the questionnaire. The study was described to participants and its importance was clarified in written words. Informed consent must be signed before participating in the questionnaire. Those who signed the informed consent electronically by clicking the agree button were included in the study, while the others were not. Participants were also informed that participation is voluntary, and they can withdraw from the study at any time, as well as being informed that the provided data are treated confidentially with their privacy protected.

Data analysis

SPSS software, V.26 (IBM) was used to analyze the data. Continuous variables were reported as means and standard deviations and categorical variables were reported as frequencies and percentages. The normality of the data was checked using Kolmogorov-Smirnov and Shapiro Wilk tests. The one-way analysis of variance test was used to compare the mean scores between different demographic groups. Tukey post hoc test was conducted to identify the source of significant variation within each group. Significant predictors of knowledge about microbial

biofilm were determined via regression analysis and the level of significance was predetermined as 5%.

Descriptive statistical analyses, such as frequencies and percentages, were used to represent the respondents' demographic information. Student t-test was used for data analysis, to compare the responses of pharmacy students from public and private universities. A statistical significance level of $p<0.05$ was used in all analyses.

Ethical approval

The study protocol was approved by the institutional review board (IRB) committee at King Abdullah University Hospital (KAUH), Irbid, Jordan, after supplying the committee with the requested documents to ensure the protection of human rights, confidentiality, and privacy. (Reference number is 39/136/2020).

State the objectives of the work and provide an adequate background, avoiding a detailed literature survey or a summary of the results.

Results and Discussion

Participants' characteristics

The sample consists of 1,058 undergraduate pharmacy/PharmD students from all pharmacy schools in Jordan (n=14). Of those, 83.2% (n=880) were female students. The majority of the students were in their 3rd and 4th year of study with 41.1% (n=435) and 25.2% (n=267), respectively. More than half (57.6%) of the students' ages ranged between 20 and 21 years. As shown in **Table 1**, the majority of participants (90.6%) were from public schools of pharmacy, and (91.8%) majored in Pharmacy.

A high number of participating students (80.7%) have been enrolled in or are currently receiving an academic course in pharmaceutical microbiology and around half (48.0%) have been enrolled in or are currently receiving a related course i.e. biotechnology, immunology, or advanced microbiology.

Table 1. Demographic Characteristics of the Study Sample (N= 1,058)

Character	Frequency (%)
Gender	
Male	178 (16.8%)
Female	880 (83.2%)
Age (Year)	
18-19	72 (6.8%)
20-21	609 (57.6%)
22-23	277 (26.2%)
>23	100 (9.5%)
Year of study	
First-year	23 (2.2%)
Second-year	55 (5.2%)
Third-year	435 (41.1%)
Fourth-year	267 (25.2%)
Fifth-year	252 (23.8%)
Sixth year	26 (2.5%)
Major	
Pharmacy	971 (91.8%)
Pharm D	87 (8.2%)
University type	
Public	959 (90.6%)
Private	99 (9.4%)
Receiving pharmaceutical microbiology course	
Yes	854 (80.7%)
No	204 (19.3%)
Receiving pharmaceutical microbiology-related courses*	
Yes	508 (48%)
No	550 (52%)

*Biotechnology, immunology, or advanced microbiology

The study found that less than half of the participants (43.4%) reported themselves to have sufficient knowledge about microbial biofilms, with the majority (83.9%)agreeing their knowledge was exclusively from their undergraduate microbiology-related courses. A considerable percentage of students (65.3%) displayed their willingness to improve their knowledge about microbial biofilms and three-quarters of the students (74.8%) exhibited a greater sense of the importance of microbial biofilm-related research **(Figure 1)**.

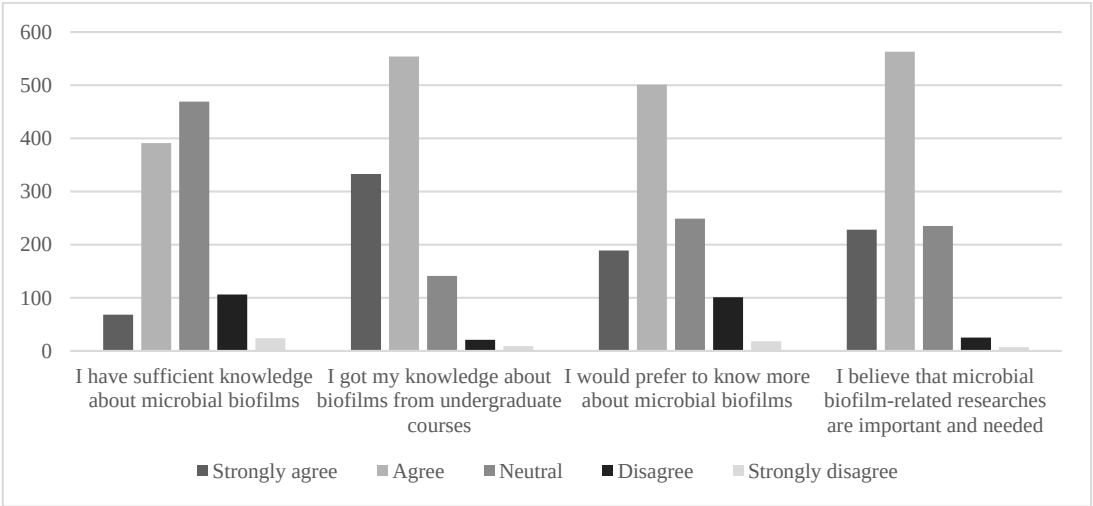

Figure 1. Students' perception of "Microbial biofilms"

Perception towards "Microbial biofilms"

Students' knowledge about "Microbial biofilms"

Table 2 shows the knowledge of students about microbial biofilms. A significant percentage of students (71.2%) knew the definition of biofilms as an organized community of microorganisms, enveloped in an extracellular polymeric substance (EPS). Whereas, only 12.7% of the students knew that the discovery of biofilms is not new. Regarding the microbial effect of biofilms on surfaces, less than half of the participants (44.0%) knew that biofilms can initiate and colonize on both living and non-living surfaces. Approximately half of the participants (52.9%) knew that biofilms can delay wound healing. Finally, regarding the removal of biofilms, the majority of students (73.8%) falsely reported that biofilms are easily eradicated by antimicrobials compared to planktonic infections.

Table 2. Pharmacy students' total and mean knowledge about microbial biofilms scores

	Knowledge statement	Correct answer N (%)	Mean score (± SD)
1	Biofilms are organized communities of microorganisms (particularly bacteria), enveloped in an extracellular polymeric substance (EPS)	766 (71.2%)	0.72 (0.44)
2	Planktonic and biofilms are very similar	312 (29.0%)	0.31 (0.46)
3	Biofilms theory has been proposed in the last 10 years	137 (12.7%)	0.29 (0.46)
4	Bacteria in biofilms replicated at a slower rate compared to planktonic cells and this is the reason why planktonic cells are easier to be treated	177 (16.4%)	0.13 (0.34)
5	Only Gram-negative bacteria can form biofilms while Gram-positive bacteria cannot	391 (36.3%)	0.37 (0.48)
6	In general biofilms are beneficial to humans	333 (30.9%)	0.45 (0.50)
7	Infections related to biofilms are only device- related	395 (36.7%)	0.27 (0.44)
8	Biofilms can initiate and colonize only on living surfaces and not on non-living ones	473 (44.0%)	0.16 (0.36)
9	Biofilms are very common in both acute and chronic infections	164 (15.2%)	0.54 (0.50)
10	Biofilms can delay wound healing	569 (52.9%)	0.17 (0.38)
11	Biofilms form an external film only on the surface of injured skin but not internally	378 (35.1%)	0.17 (0.37)
12	Biofilms are beneficial for the wound as they form a film and cover it, thus preventing it from being contaminated when it's exposed to the external environment	253 (23.5%)	0.36 (0.48)
13	Biofilms are easily eradicated by antimicrobials compared to planktonic infections	282 (26.2%)	0.37 (0.48)
14	Physical removal of biofilms is not recommended as clinical practice in biofilms management	185 (17.2%)	0.25 (0.43)
15	Recommended clinical practice in treating wound infection is the same whether biofilms are formed or not, only the dose is higher in the case of biofilms	265 (24.6%)	0.24 (0.43)
	Total		4.8 (3.10)

Effect of students' characteristics on their knowledge about microbial biofilm

Table 3 presents the effect of the students' demographics on their knowledge of microbial biofilm scores. Students' scores significantly changed with students' age, academic year, and previous or current enrollment in pharmaceutical microbiology courses (P<0.001). Tukey's HSD posthoc test confirmed that those aged 18-19 years in their first or second academic year have different scores than other participants.

Table 3. Pharmacy students' knowledge about microbial biofilm score by students' characteristics

Variable		Students' knowledge score		P-value
		Mean	SD	
Gender				
	Male	4.65	3.25	0.463
	Female	4.83	1.41	
Age (Year)				
	18-19	3.03	2.84	0.001*
	20-21	4.84	3.05	
	22-23	5.29	3.06	
	>23	4.49	3.21	
Year of study				
	First-year	2.74	2.45	<0.001*
	Second-year	2.40	2.86	
	Third-year	4.83	3.03	
	Fourth-year	5.09	3.00	
	Fifth-year	5.10	3.10	
	Sixth-year	5.50	3.72	
Major				

Pharmacy	4.80	3.06	0.906
Pharm D	4.84	3.51	
University type			
Public	4.82	3.07	0.649
Private	4.67	3.38	
Receiving pharmaceutical microbiology course			
Yes	5.13	3.08	<0.001*
No	3.42	2.77	
Receiving pharmaceutical microbiology-related courses			
Yes	4.88	3.11	0.417
No	4.73	3.08	

*P<0.05

Simple linear regression analysis showed that students' age, academic year, and previous or current enrollment in pharmaceutical microbiology courses were significantly associated with students' knowledge scores with a p-value less than 0.01. Multiple linear regression analysis to predict student knowledge from student age, academic year, and previous or current enrollment in pharmaceutical microbiology courses showed that these variables statistically significantly predicted student knowledge score, $F(3, 1058) = 20.123$, $p < 0.001$, $R2 = 0.054$. However, only academic year and previous or current enrollment in pharmaceutical microbiology course variables added statistically significantly to the prediction ($p = 0.011$ and $p < 0.001$, respectively) **(Table 4)**.

Table 4. Multiple linear regression analysis predicting students' knowledge about microbial biofilm

Variable	B	SE	β	95% CI	P-value*
Age (Year)	-0.219	0.178	-0.053	-0.568-0.130	0.218
Year of study	0.345	0.135	0.115	0.081-0.609	0.011*
Receiving pharmaceutical microbiology course	1.482	0.255	0.189	0.981-1.982	<0.01*

B: The unstandardized beta; SE: The standard error for the unstandardized beta; β: The standardized beta; P-value: The probability value

The current study aims to identify the levels of knowledge and awareness of undergraduate pharmacy/PharmD students towards biofilms. The sample collected is from different pharmacy schools in Jordan and covers all years of study. The preponderance of students (80.7%) have attended the pharmaceutical microbiology course and approximately half of them (48%) have attended pharmaceutical microbiology-related courses, such as biotechnology, immunology, or advanced microbiology. Analysis of pharmacy/PharmD students' knowledge shows that more than half were not sufficiently informed about biofilms. However, a significant percentage of the students (83.9%) are interested in improving their knowledge about microbial biofilms, and around three-quarters of participants agreed that more biofilm-related research should be performed.

The results also indicated that the year of study affects the knowledge of the students. From Third- to sixth-year undergraduate students significantly showed a better theoretical knowledge about biofilms ($p<0.01$). These results could be explained by the fact that pharmaceutical microbiology and its related courses are introduced after the second year of study.

More than two-thirds of the students agreed that biofilms are organized communities of microorganisms, enveloped in an EPS and that planktonic cells and biofilms are not similar. Despite that, the majority of the students reported that biofilms have been only recently identified. This is utterly incorrect as the term "Biofilm" was reported by Costerton *et al*. in 1978, he later defined them as "a structured community of bacterial cells enclosed in a self-produced polymeric matrix, adherent to a surface." in 1999 [16].

In this study, 44% of the students knew that biofilms can initiate and colonize on living and non-living surfaces and this is true as bacterial biofilm formation is a complex cycle of a multi-step process where multiple microbial species irreversibly attach to and grow on animate and inanimate surfaces [17-20]. However, only about 36% of students knew that biofilms are not only-device related as microorganisms can develop biofilms on a variety of surfaces both biotic and abiotic [21].

Both Gram-negative and Gram-positive bacteria can indeed form biofilms in response to environmentally harsh conditions, such as extreme temperature and desiccation. The alteration in the phenotype of the organisms concerning growth rate and gene transcription also contributes to making these communities difficult to treat by conventional antibiotics. Nevertheless, only around 36% of students knew that both gram-negative bacteria and Gram-positive bacteria can form biofilms.

From another point of view, less than 50% of the responders knew that biofilms have a beneficial use. It has been reported that biofilms have been used agriculturally in bioremediation, as biofertilizers, and in pest control, as well as used in wastewater treatment. Biofilms can also be used industrially for ore mining and biofuel production [22, 23].

The fact that bacteria in biofilms are sessile and replicate at a lower growth rate in addition to the reduced metabolism may make the systemic antibiotics, which target metabolic processes in growing bacteria, ineffective [17, 24]. Sadly, only around 16% of students knew this information.

The EPS plays an important role in biofilms' tolerance to antimicrobial agents. In addition to forming a protecting environment for bacterial cells from the host immune systems,

such as phagocytosis, EPS can also shield them from antibiotics. The high viscosity of the biofilm structure limits or prevents the diffusion of antibiotics to deeper layers in the bacterial community [25].

According to Mandell *et al.* , there is a phenotypic and non-specific change in antibiotics tolerance occurs between planktonic and biofilms as a significant decrease in antibiotic sensitivity is notice in biofilms compared to planktonic bacteria [26].

However, nearly three-quarters of the students agreed that biofilms are easily eradicated by antimicrobials when compared to planktonic infections. A similar percentage of almost 75% of the students also agreed that recommended clinical practice in treating wound infections is the same whether biofilms are formed or not, only the dose is higher in the case of biofilms. This proves that only one-quarter of students have adequate knowledge of the mechanism of action of antibiotics and the resistance and/or tolerance mechanisms adapted in biofilm communities.

In addition to the difficulty of biofilms' eradication by conventional antibiotics, the association of these communities in perpetuating the inflammatory phase of wound healing is another obstacle for health care professionals. Biofilms of mixed microorganisms with different bacterial and fungal species were characterized in 60% of chronic wounds and are present in 6% of acute wound specimens and they are responsible for more than 60% of all nosocomial infections [27, 28]. A study performed by Wolcott *et al.* demonstrated that immature biofilms growing within the first 24 hours of formation were more susceptible to antibiotics, but after up to 48 hours became mature thus increasingly more tolerant [29]. Biofilms not only form on the surface of the wound but also invades deep into the infected or burnt tissue [30]. One of the current key methods for wound care management is the biofilms clearance through debridement. In debridement, enough pressure and shear force is applied to remove biofilm and to expose healthy tissue. This procedure is performed using various removal methods such as sharp debridement, autolytic enzymes debridement, biological debridement, mechanical debridement and chemical debridement. After debridement, topical antimicrobial agents may be used on the infected wound to kill remaining planktonic bacteria, and prevent reformation of biofilm [31-33].

This study has proven that a knowledge gap exists between the causes and effects of the prevalence of biofilm in chronic wounds. Even though almost half of the students reported that wound healing is delayed if containing a biofilm, only 15% knew that biofilms are more common in chronic infections compared to acute infections. Two-thirdsof the students also thought that biofilms develop only on the surface of the wound and three-quarters answered that the externally formed film will protect the wound from the external environment with only a small percentage of 17% of responders agreed that physical removal of biofilms is recommended as clinical practice in biofilms management.

This lack of knowledge the students suffer from can be attributed to the fact that most universities in Jordan have only one mandatory pharmaceutical microbiology course students must be enrolled in before graduation, while other courses such as advanced microbiology areelective courses, so any given lecturer will only have one course (3 credit hours) to cover headlines of the most important aspect of pharmaceutical microbiology without the ability to go into meticulously detailed information for any of them.

This study has revealed the extent of students' awareness of the process of biofilm formation and the impact it has on clinical decision-making, and therefore a better understanding of the information that should be supplemented to raise students' knowledge and avoid misconceptions.

Conclusion

The study concludes that the knowledge and awareness of biofilms among pharmacy/PharmD students in Jordanian universitiesare considerably poor and the level of knowledge is not adequate nor satisfactory. To our knowledge, this is the first study in Jordan and near regions focusing on biofilms knowledge and awareness among pharmacy students. Thus, the results could be the leading to future studies on this topic. The results from this study raise an alarm about the need for appropriate and improved education about biofilms and the impact it has on human health. The need to provide future pharmacists with proper knowledge and skills is vital to emphasize their role in the continuous battle for infection control and the required appropriate treatment. Proper education and guidance from pharmacists to their patients will lead to enhanced awareness and consciousness of biofilm-related infections in patients within the community or hospital-dwellers and an overall improvement in health outcomes for counseled and educated patients on how to carry on their treatment regimens correctly.

Acknowledgments: The authors thank the students who participated in this study.

Conflict of interest: None

Financial support: None

Ethics statement: None

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