RESEARCH ARTICLE

REVISED **Knowledge and practice of community pharmacists towards SGLT2 inhibitors** [version 2; peer review: 2 approved, 1 approved with reservations]
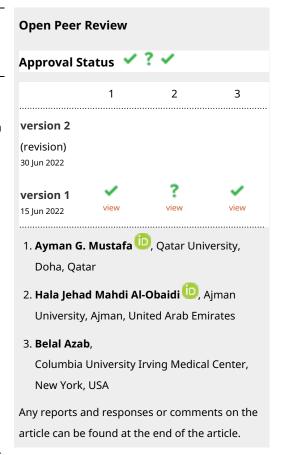
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Abstract

Background: Sodium/glucose cotransporter 2 (SGLT2) inhibitors are a new class of oral anti-diabetic drugs which improve glycaemic control in type 2 diabetes mellitus (T2DM) by preventing the kidney from reabsorbing glucose back to blood. Community pharmacists have long-term relationships with most of their chronic patients, so they play a key role in care for people with diabetes. Therefore, the objective of this study was to assess pharmacists' knowledge and practice towards SGLT2 inhibitors. Thus, improving pharmacists' knowledge about this group of medications could improve the treatment outcome of people with diabetes.

Methods: A cross-sectional study was conducted to meet the study objectives. A convenience sample of 348 community pharmacists in Jordan was recruited. knowledge and practice were assessed using a self-administered questionnaire created for the purpose of this study.

Results: A total of 400 community pharmacists were reached, of whom 348 answered the survey (response rate 87%). The results indicated that SGLT2 inhibitors knowledge score among community pharmacists in Jordan was 6.61 (out of 12). Factors like age, gender, location of the pharmacy, years of pharmacists' experience had no effect on knowledge score; however, pharmacists who attended training courses on diabetes had higher knowledge scores. Additionally, pharmacists' dispensing practice toward SGLT2 inhibitors had insufficient knowledge, such as lack of knowledge about the superiority of SGLT2 inhibitors over other anti-diabetics and inability

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to give the best advice to patients.

Conclusions: Our findings reflect a moderate knowledge among community pharmacists about SGLT2 inhibitors which may negatively affect the patients' outcome; thus, continuous education for the pharmacists is essential.

Keywords
Diabetes, SGLT2 inhibitors, Pharmacists, Jordan

This article is included in the Sociology of Health gateway.

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REVISED **Amendments from Version 1**

1. In the abstract, this sentence was added "Thus, improving pharmacists' knowledge about this group of medications could improve the treatment outcome of people with diabetes."
2. In the introduction, line 6 and 13, two reference were added.
3. In the introduction, the following sentence was added at the end of it ". Improving pharmacists' knowledge about this group of medications could improve the treatment outcome of people with diabetes."
4. The section "Knowledge scale validity and score" is moved up before the statistical analysis, and some modifications were done on it as follows:
   "1 (strongly disagreed), 2(disagreed), 3 (agreed)) and 4 (strongly agreed)."
   "SGLT2 inhibitors knowledge score was 6.61 (SD=2.22, range 1-12) which was calculated as an average of the adequate answers in the knowledge section. Knowledge score was classified as follows:
   -Poor knowledge (1-4)
   -Moderate knowledge (4-8)
   -High knowledge (8-12)"
5. In the methods line 7, "computer-based which was" added.
6. The section "Development of the survey questionnaire " in the methods was changed to "Development of the study instrument". And the word nine in this section was changed to eight.
7. In data analysis section, the "mean and standard deviation" was changed to "frequencies".
8. The statistical test type was added beside each table's title.
9. The first paragraph in the discussion was deleted.
10. The p value was added next to each significant/non-significant words in the discussion.
11. In line 24 in the discussion, the word "low" was changed to "moderate".
12. In line 42 in the discussion the percentage (48.3%) was added.
13. In line 2 in the conclusion the score (6.62) was added.

Any further responses from the reviewers can be found at the end of the article

Introduction

Type 2 diabetes mellitus (T2DM) is a metabolic disorder affecting carbohydrate, fat, and protein metabolism.[1] This condition results from inadequate insulin secretion, insulin resistance, or both, often at later stages in life.[2,3] T2DM is characterised by chronic hyperglycaemia and dyslipidaemia which results in the development of renal disease, cardiovascular disease and microvascular complications.[4] T2DM management should begin in most patients with lifestyle changes which is often followed up by metformin monotherapy.[1] If target blood glucose is not achieved within 3 months, another hypoglycaemic agents can be added.[5]

The expression of sodium-glucose cotransporter-2 (SGLT2) proteins selectively occurs in the kidney specifically in the proximal convoluted tubule. Roughly, 90% of the absorption of the filtered glucose is under the responsibility of these transporters. Therefore, SGLT2 represents an ideal target and effective options for the treatment of diabetes.[6,7] In patients with T2DM, the renal threshold for reabsorption of glucose is increased above 180 mg/dL (serum glucose concentration), which corresponds to the normal renal threshold reabsorption level of glucose.[2] In addition, it has been reported that the expression of these transporters could be up-regulated in T2DM patients which has the potential to cause a maladaptive response that in turn deteriorates hyperglycaemia.[8] Accordingly, the selective SGLT2 inhibitors can cause a reduction to the respective threshold to as low as 40 to 120 mg/dL.[9] In fact, the combination of metformin and a SGLT2 inhibitor may be beneficial for patients who are at a high risk of experiencing hypogylcemia, because the hypoglycaemic effect of SGLT2 inhibitors is small in comparison to insulin and sulfonylureas.[10] Currently, the Food and Drug Administration (FDA) has approved three SGLT2 selective inhibitors for use in mono, dual, and triple therapy: Canagliflozin, Dapagliflozin and Empagliflozin, and they recently were introduced to the Jordan market.[7,11]

The prevalence of T2DM is high in the Middle East because of the development, diet patterns, and the rapid expansion in economy.[12] Jordan has a high prevalence of T2DM and has been higher than the global average, as the prevalence rate for diabetes among Jordanian population aged between 25 and 70, was increased from 17.1% in 2004 to 23.7% in 2017.[13] Therefore, one treatment approach for improving glycaemic control in T2DM is enhancing the quality of pharmaceutical interventions, increasing patients' compliance, and using the most recently approved anti-diabetic classes SGLT2 inhibitors.[14,15] In fact, community pharmacists have long-term relationships with most of their chronic patients, because patients obtain their chronic medications and diabetes supplies from community pharmacies; therefore, they play a key role in the care of people with diabetes.[3] A large body of evidence revealed that community pharmacists' education about diabetes and its medications has improved patients' glucose and lipid profile in addition to improving cardiovascular outcomes and other complications.[16–18] Thus, the lack of professional pharmaceutical knowledge might have a negative impact on patients with diabetes' outcomes. Accordingly, assessing the current related basic pharmacological knowledge and dispensing practice of community pharmacists of SLGT2 inhibitors, as well as uncovering the weakest areas related to this new anti-diabetic class, has the potential to improve the pharmaceutical outcomes of these medications. Therefore,

the objectives of this study were to assess pharmacists' knowledge and dispensing practice toward SGLT2 inhibitors and explore their perception and dispensing practice. Improving pharmacists' knowledge about this group of medications could improve the treatment outcome of people with diabetes.

Methods

Design and data collection

A cross-sectional design was conducted to meet the study objectives. Data collection was performed between March and September 2020 using a self-administrated questionnaire. The participant pharmacists in our study were visited by the researchers to establish a relationship with them and explain the goals of this research prior to study commencement. Participants were recruited from community pharmacies located among different cities in Jordan including: Amman, Zarqa, Ajloun, Irbid, and Salt, and countryside and city were both targeted based on socio-economic status among each city. The questionnaire was computer-based which was distributed face-to-face with participants at their workplace by four male and female pharmacy students well-trained on data collection and study methods from the Hashemite University. A signed informed consent was obtained from the participants as a pre-requisite to proceed with participation. Participants were interviewed alone for 20-30 minutes to answer the survey questions without anybody beside them and no audio or video recordings were used.

Sample size

The sample size was calculated based on a 95% confidence level, and 5% confidence interval. The total community pharmacies pool in Jordan is 2,864; the sample size calculation revealed the need for at least 346 community pharmacies pharmacists.

Ethical considerations

The study was approved by the Institutional Review Board at the Hashemite University in Jordan (Reference number: 8/5/2019/2020). Participants' involvement in the study was voluntary, and they were informed that they had the right to withdraw from the study at any time.

Development of the study instrument

A self-administered questionnaire was created especially for the purpose of this study, and was validated by a group of experts constituted of two pharmacologists, one endocrinologist, and two pharmacists. This questionnaire was composed of 28 questions which were divided into three sections. The first section consisted of eight questions about demographics data including gender, age, pharmacy location, working time, years of experience, holding a postgraduate degree, attending training courses on diabetes, and the bachelor degree (BSc) of the pharmacists; BSc in Pharmacy or BSc in Pharmacy doctor (Pharm D). The second section was composed of 12 questions regarding the knowledge of community pharmacists about SGLT2 inhibitors as shown in Table 2. The third section was composed of eight question in relation to practice of community pharmacists toward SGLT2 inhibitors including their impression about this group of medications, the frequency at which they received prescriptions for these agents, the best advice for the patients while using these agents, the obstacles they faced while dispensing these agents, how they evaluated their knowledge about SGLT2 inhibitors, how they assessed their need for training courses about SGLT2 inhibitors, how they assessed their need to attend training courses about SGLT2 inhibitors, and what was the source of information they used to improve their knowledge about SGLT2 inhibitors. The questionnaire was pretested for reliability through the pilot study. The views scale was calculated and showed an excellent reliability with a Cronbach's alpha of 0.885. Piloting of the questionnaire was performed to assess the comprehension and accuracy of the questions in relation to the research topic, identify possible redundancy among the 28 questions, and ensure the usability of the data collection method.

Knowledge scale validity and score

The knowledge scale was assessed for validity by examining the content validity index (CVI). Five experts were consulted for their opinion for each scale item including relevancy, clarity, and simplicity and scores from 1 (strongly disagreed), 2 (disagreed), 3 (agreed) and 4 (strongly agreed). Questions were tested/re-tested for their clarity and simplicity by interviewing 20 participants. The CVI were ranged from 0.8-0.9 and it was deemed that the scale was valid. SGLT2 inhibitors knowledge score was 6.61 (SD=2.22, range 1-12) which was calculated as an average of the adequate answers in the knowledge section. Knowledge score was classified as follow:

- Poor knowledge (1-4)

- Moderate knowledge (4-8)

- High knowledge (8-12)

Data analysis

Data were coded and incorporated into Statistical Package for Social Sciences (SPSS) version 24.0 (SPSS Inc., Chicago, IL, USA) software after extracting it from Google forms. Demographics numerical variables were described using frequencies. Knowledge difference in demographics with two categories was tested using independent t-tests; however, knowledge difference in demographics with more than two categories was examined using a one-way analysis of variance (ANOVA) followed by a Scheffe posthoc test. Significance was considered when p<0.05.

Results

Demographics

A total of 400 community pharmacists were reached (response rate 87%), and 348 completed this survey. Most of the participant pharmacists were less than 30 years old (n=225, 64.7%). Female participants were slightly predominant (n=203, 58.3%) compared to male participants (n=145, 41.7%). The vast majority of the participants were working in city areas (n=331, 95.1%), their working experience was 0-4 years (n=191, 54.9%), and had no postgraduate degree (n=304, 87.4%). Most participants had not attended training courses on diabetes (n=255, 73.3%) and they had a bachelor's degree in pharmacy (n=307, 88.2%). More details about the sociodemographic characteristics are presented in Table 1.

Pharmacists' knowledge level about SGLT2

Community pharmacists' knowledge score was 6.61 (SD=2.22, range 1-12) which is around the knowledge scale average. The results of this study showed that only 32.5% of the pharmacists provided an adequate answer that SGLT2 inhibitors decrease blood pressure. In addition, 34.5% of the pharmacists knew the best consultation to the patients using SGLT2 inhibitors is to keep genital area clean to avoid infection. Moreover, only 38.5% of them knew that patients with diabetes and hypertension are the best candidates for SGLT2 inhibitor agents. On the other hand, pharmacists provided a good knowledge that SGLT inhibitors are contraindicated in patients with renal failure, and they have a better protective effect in patients with diabetes and hypertension compared to sulfonylurea (63.5% and 63.8%; respectively). The highest knowledge of the pharmacists was for their response to the question related to the dosage form of SGLT2 inhibitors, which is tablets (92.5%). Further details about the pharmacists' knowledge are provided in Table 2.

Community pharmacists' views and dispensing practice toward SGLT2 inhibitors

More than half of the respondent pharmacists thought that SGLT2 inhibitors have a better effect when they are prescribed to a particular group of patients (n=195, 56%). However, more than 20% of them thought that they are slightly better

Table 1. demographical details, n=348 (data are represented as frequencies).

Factor	Categories	Total No. (%)
Age	Up to 29	225 (64.7)
	30 or more	123 (35.3)
Gender	Female	203 (58.3)
	Male	145 (41.7)
Pharmacy location	City	331 (95.1)
	Countryside	17 (4.9)
Working time	Morning	177 (50.9)
	Afternoon or night	171 (49.1)
Years of experience	0-4 years	191 (54.9)
	5-9 years	85 (24.4)
	10 years or more	72 (20.7)
Postgraduate degree	Higher diploma or master	44 (12.6)
	Have no postgraduate degree	304 (87.4)
Training courses in diabetes	Yes	93 (26.7)
	No	255 (73.3)
Bachelor's degree major	Pharmacy	307 (88.2)
	Pharm D	41 (11.8)

Table 2. Community pharmacists' knowledge about SGLT2 inhibitors (data are represented as frequencies).

Question	Adequate answer	Number of adequate answers n (%)
What is the effect of SGLT2 inhibitors on blood pressure?	Decrease blood pressure	113 (32.5)
What is the best advice you can give to the patients who are using SGLT2 inhibitors?	Keep genital area clean to avoid infection	120 (34.5)
To which patients SGLT2 inhibitors group is prescribed the best?	Patients with diabetes and hypertension	134 (38.5)
How do SGLT2 inhibitors work?	Increase glucose renal excretion	143 (41.1)
SGLT2 stands for?	Sodium glucose transporter protein	149 (42.8)
What is the most common side effect of SGLT2 inhibitors?	Urinary tract infection	153 (44)
What is the effect of SGLT2 inhibitors on body weight?	Decrease body weight	175 (50.3)
When SGLT2 inhibitors group is used	After metformin	201 (57.8)
What is the best anti-diabetic agent to be combined with SGLT2 inhibitors?	Metformin	206 (59.2)
SGLT2 inhibitors are contraindicated in?	Patients with renal failure	221 (63.5)
What is the superiority of SGLT2 inhibitors over sulfonylurea?	Have better protective effect in patients with diabetes and hypertension	222 (63.8)
Dosage form?	Tablets	322 (92.5)

than the available anti-diabetic medications (n=76, 21.8%). Moreover, 49.1% of the pharmacists reported that they received one to five SGLT2 inhibitor prescriptions per month, and only 8.3% reported that they received more than ten prescriptions per month. Around half of the pharmacists said that the patient's feedback about SGLT2 inhibitors was very good (n=168, 48.3%). However, very few pharmacists said that the patients had a bad impression of these medications (n=5, 1.4%). A total of 54.9% of the pharmacists revealed that the most common feedback from the patients about these agents is their high price compared to the other anti-diabetic medications. Furthermore, half of the pharmacists thought that their knowledge about SGLT2 inhibitors was good (n=174, 50%), however, 21.6% thought they had a weak knowledge. The vast majority of the pharmacists had not attended a training course about SGLT2 inhibitors before

Table 3. Differences in knowledge based on demographics with two categories (independent t-test).

Demographics	Categories	Mean (SD)	t	DF	P value
Age	Up to 29	6.68 (2.12)	0.79	346	0.43
	30 or more	6.48 (2.38)			
Gender	Female	6.76 (2.27)	1.53	346	0.127
	Male	6.4 (2.12)			
Pharmacy location	City	6.58 (2.24)	0.95	346	0.33
	Countryside	7.11 (1.65)			
Working time	Morning	6.79 (2.18)	1.55	346	0.12
	Afternoon or night	6.42 (2.23)			
Postgraduate degree	Higher diploma or master	6.20 (2.44)	-1.31	346	0.18
	Have no postgraduate degree	6.67 (2.18)			
Training courses in diabetes	Yes	6.78 (2.16)	-2.31	346	0.02
	No	6.16 (2.31)			
Bachelor's degree major	Pharmacy	6.55 (2.22)	-1.48	346	0.13
	Pharm D	7.09 (2.10)			

Table 4. Differences in knowledge based on demographics with more than 2 categories (One-way ANOVA followed by Scheffe post hoc).

Demographics/Dispensing practice	Categories	Mean (SD)	f	DF	P value
Years of experience	0-4 years	6.64 (2.13)	0.07	345	0.93
	5-9 years	6.54 (2.36)			
	10 years or more	6.61 (2.28)			
What is your impression about SGLT2 inhibitors?	Have no superiority over the available medications	5.09 (2.09)	11.98	344	0.0001
	Slightly better than the available medications	6.38 (1.72)			
	Give better effect when they are administered to a particular group of patients	7.12 (2.21)			
	They are expensive medications without any added benefits to the patients	6.14 (2.37)			
How many prescriptions per month do you receive for this group?	One prescription or less	6.29 (2.15)	3.03	344	0.29
	1-5 prescriptions	6.67 (2.19)			
	5-10 prescriptions	6.43 (2.59)			
	More than 10 prescriptions	7.65 (1.56)			
How do you see the feedback of patients who are using these drugs?	Good	6.33 (2.02)	2.27	344	0.080
	Very good	6.89 (2.39)			
	Excellent	6.27 (1.99)			
	Bad impression	7.60 (1.67)			
What are the obstacles you face when you are dispensing these drugs?	Patients lack knowledge	6.25 (1.72)	2.56	344	0.05
	Lack of my knowledge	6.40 (2.00)			
	Patients comments about the price	6.90 (2.35)			
	I have no obstacles	6.09 (2.17)			
What do you think the evaluation of your knowledge about these drugs?	Excellent	7.27 (2.53)	2.64	344	0.04
	Very good	6.71 (2.18)			
	Good	6.70 (2.29)			
	Weak	6.05 (1.84)			

Table 4. *Continued*

Demographics/Dispensing practice	Categories	Mean (SD)	f	DF	P value
How do you assess your need to attend training courses about SGLT2 inhibitors?	High need	6.26 (2.20)	8.91	345	0.0001
	Moderate need	7.12 (2.14)			
	No need currently because it is rarely used	5.81 (2.11)			
What is the source of information which you use to get your knowledge about SGLT2 inhibitors?	Scientific journals	6.22 (2.28)	2.02	344	0.11
	Websites	6.91 (2.23)			
	Pharmaceutical companies	6.61 (2.20)			
	Other sources	6.32 (2.08)			

(n=269, 77.3%). In addition, the vast majority of respondents demonstrated that they were in high (n=150,43.1%) to moderate (n=161, 46.3%) need of training courses about SGLT2 inhibitors.

Factors influencing pharmacists' knowledge about SGLT2

An independent sample t-test was performed to examine the differences in knowledge levels based on the demographics of the pharmacists and other factors with two categories that might affect their knowledge level which are shown in Table 3. The test demonstrated that age and gender of the pharmacists had no significant effect on their knowledge level. In addition, there was no significant difference in pharmacist's knowledge based on pharmacy location, pharmacist's working time (either morning or afternoon or night) and their bachelor's degree major (either pharmacy or pharmacy Doctor). The t-test indicated that holding a postgraduate degree did not affect the pharmacist's knowledge. Interestingly, the test showed that the pharmacists who had attended training courses on diabetes before had a higher knowledge score compared to those who had not attended training courses (p=0.02).

A one-way ANOVA test was used to examine the differences in knowledge level in relation to variables which had more than two categories, and results are shown in Table 4. The results showed that the years of experience of the pharmacists has no significant effect on their knowledge about SGLT2 inhibitors. Similarly, the number of prescriptions received by the pharmacist per month, the feedback of the patients who were using SGLT2 inhibitors, and the source of information that the pharmacists used to gain knowledge about SGLT2 inhibitors, had no significant effect on pharmacist's knowledge. However, pharmacists who thought that SGLT2 inhibitors had no superiority over the other available anti-diabetic medications had lower knowledge scores compared to those who thought the opposite (Scheffe posthoc, p=0.018). In addition, results showed that pharmacists who thought that SGLT2 inhibitors have a better effect when they are administered to a particular group of patients had a higher knowledge score (Scheffe posthoc, 0.0001). Moreover, pharmacists who thought that the best advice they could give for patients who use SGLT2 inhibitors is to keep genital area clean to avoid infection had a higher knowledge score compared to those who thought the best advice was monitoring blood glucose to avoid hypoglycaemia events or monitor body weight to avoid weight gain, or compared to those who had no specific advice to give to the patients (Scheffe posthoc, p=0.0001). Surprisingly, pharmacists who thought they did not face any obstacles while prescribing SGLT2 inhibitors had significantly lower knowledge scores compared to those who thought that the price of these medications is the main obstacle they encounter (Scheffe posthoc, p=0.05). Expectedly, pharmacists who considered their knowledge is excellent had higher knowledge scores compared to those who considered their knowledge was weak (Scheffe posthoc, p=0.04). Furthermore, pharmacists who assessed their need for training courses about SGLT2 inhibitors as moderate had higher knowledge scores compared to those who thought their need for this kind of courses was high or thought there was no need for these courses (Scheffe posthoc, p=0.003, 0.004; respectively).

Discussion

This study revealed a fair knowledge and understanding about SGLT2 inhibitors pharmacotherapy among the study sample. Our results indicate that there was no significant impact of gender (p=0.43) and age (p=0.127) of the pharmacists on their knowledge level. This finding is consistent with a previous study which showed that the knowledge of pharmacists was not affected by their age and gender.[19,20] Notably, the findings showed that there was no significant difference in knowledge level between respondents based on their pharmacy location (cities or countryside) (p=0.33) or their postgraduate degree (0.18). These results are inconsistent with previous reports which showed that pharmacists' knowledge in rural areas was poor compared to pharmacists' knowledge in urban areas.[21,22] This finding could be partly explained by the fact that the majority of the participants in our study were working in urban areas, and they did not hold postgraduate degrees. Additionally, SGLT2 inhibitors were introduced recently to the market in Jordan, which was many years after their graduation (more than 45% of respondents had more than five years of experience). Moreover, possibly due to high price of these agents,[23] they have been introduced selectively to certain pharmacies, so many pharmacists were unexposed to these medications. Consistent with the literature, this research found that community pharmacists who attended training courses on diabetes had a higher knowledge about SGLT2 inhibitors.[24,25] In fact, previous studies have shown that continuous training for pharmacists and engaging them in diabetes self-management training programmes is essential to improve their skills and role in assisting the patients they serve.[24,25] However, the majority of the participants indicated that they were in high or moderate need for training courses about SGLT2 inhibitors.[8] This response was reflected in their average score of knowledge about SGLT2 inhibitors. Moreover, the present study found non-significant differences in the knowledge score of the pharmacists regarding SGLT2 inhibitors based on their demographics data and in association with their different factors. The moderate score of knowledge about SGLT2 inhibitors can be explained by various factors including the insufficient courses about diabetes in pharmacy schools,[26,27] and the inadequate continuous pharmaceutical education for the community pharmacists after graduation,[28,29] particularly, a training program on the newly registered pharmaceutical products such as SGLT2 inhibitors.[30] Taken together, the lack of knowledge about SGLT2 inhibitors might affect community pharmacists' practice, which may lead to negative impact on patients' outcomes.[31,32]

Furthermore, this study highlights the views and dispensing practice of community pharmacists in Jordan towards SGLT2 inhibitors. More than half of the respondent pharmacists supported that SGLT2 inhibitors have a better effect when they are prescribed to a particular group of patients. This view concords with the fact that SGLT2 inhibitors are useful for a particular group of patients such as obese or hypertensive patients with diabetes, or patients who are at higher risk of hypoglycaemia.[33,34] Importantly, SGLT2 inhibitors provide greater HbA1c reduction when compared with sulphonylureas or other oral anti-diabetic agents.[35,36] Our results demonstrated that most pharmacists think that these agents have no superiority over the other available anti-diabetic medications; however, many studies show the superiority of SGLT2 inhibitors and different classes of new anti-diabetic agents in reducing the HbA1c,[37–39] which could be explained by their lack of knowledge about these anti-diabetic agents. Around half of the patients (48.3%) provided positive feedback about these agents. This finding is consistent with that of previous studies which indicated that SGLT2 inhibitors improved clinical treatment satisfaction in people with diabetes.[40,41] However, positive and negative feedback from patients about these agents have been reported.[42] Note that the last American Diabetes Association (ADA) guideline in 2018 has recommended to combine SGLT2 inhibitors with metformin for their benefits in decreasing the risk of cardiovascular events.[43] Therefore, with this recommendation, more physicians are expected to prescribe these medications,[44] which supports the need for increasing pharmacists' knowledge about SGLT2 inhibitors.

Furthermore, only about one third of the pharmacists in this study could give the proper advice for patients with diabetes who are using SGLT2 inhibitors, which is to keep genital area clean to avoid infection.[35] This is an important advice that should be given to the patients who use SGLT2 inhibitors, because these agents increase the glucose excretion in the urinary tract, which pre-dispose patients to genital tract infections. These infections are usually fungal in nature, and can present as vulvitis in women, and balanaposthitis or balanitis in men.[45–47]

Conclusions

The findings of this study demonstrated that pharmacist's knowledge about SGLT2 inhibitors is moderate (6.62), which may negatively affect the outcomes of this medication on patients. In addition, it shed light on the importance of continuous education for the community pharmacists on these new anti-diabetic agents, because pharmacists have essential roles in the healthcare system due to their accessibility to patients. The findings of this study encourage to conduct further research on the awareness of pharmacists of these medications in all healthcare settings.

Data availability
Underlying data
Open Science Framework. Knowledge and Practice of Community Pharmacists towards SGLT2 Inhibitors, https://doi.org/10.17605/OSF.IO/W928T.

This project contains the following underlying data:

- SGLT2 inhibitors data.sav

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Open Peer Review

Current Peer Review Status: ✓ ? ✓

Version 1

Reviewer Report 27 June 2022

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✓ **Belal Azab**

Department of Pathology and Cell Biology, Columbia University Irving Medical Center, New York, NY, USA

A well-written manuscript that assessed the knowledge practice of community pharmacists about SGLT2 inhibitors in Jordan. This manuscript gets to a great conclusion that is well supported by extensively analyzed data. I have some minor comments below that won't affect the robustness of the manuscript, but they are just opportunities for improvement.

- In paragraph 3 in the introduction, add a reference after "people with diabetes" line number 9.

- At the end of the introduction, it would be better to elaborate more on the impact of this study which explains the aims of this study.

- The section entitled "Development of the survey questionnaire" in the methods should be amended to "Development of study instrument"

- I think the first paragraph in the discussion is a repetition, so, should be deleted.

Overall, this is an interesting study and the authors have collected and analyzed a good dataset using appropriate methodology. The paper is generally well written and structured, and I recommend it for indexing.

Is the work clearly and accurately presented and does it cite the current literature?
Yes

Is the study design appropriate and is the work technically sound?
Yes

Are sufficient details of methods and analysis provided to allow replication by others?

Yes

If applicable, is the statistical analysis and its interpretation appropriate?
Yes

Are all the source data underlying the results available to ensure full reproducibility?
Yes

Are the conclusions drawn adequately supported by the results?
Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Molecualar biology, pharmacogenetics, human genetics

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Author Response 28 Jun 2022
Abdelrahim qudhah, Hashemite University, Zarqa, Jordan

The authors would like to thank you for your positive valuable feedback on the manuscript which will improve the quality of it.

C1: In paragraph 3 in the introduction, add a reference after "people with diabetes" line number 9.

 R1: A reference is now added.

C2: At the end of the introduction, it would be better to elaborate more on the impact of this study which explains the aims of this study.

 R2: The impact of this study is added now.

C3:The section entitled "Development of the survey questionnaire" in the methods should be amended to "Development of study instrument"

R3: The title of this section is amended as recommended.

C4: I think the first paragraph in the discussion is a repetition, so, should be deleted.

R4: This paragraph is now deleted.

Competing Interests: No competing interests were disclosed.

Reviewer Report 27 June 2022

? **Hala Jehad Mahdi Al-Obaidi** (ID)

College of Pharmacy and Health Sciences, Ajman University, Ajman, United Arab Emirates

The study is very well designed and well written. I enjoyed reading it. Decision made: Approved with only minor changes are required as follows:

Method:

In the data analysis section, it is stated that the "*Data were analysed by using SPSS software after extracting it from Google forms*", this means that the questionnaire was computer-based, i.e. iPads/PCs were used, however, in the design and data collection section, you've mentioned that the questionnaire was distributed face-to-face with participants at their workplace, which made me think that the questionnaire was a paper-based survey. Please clarify this point.

Development of the survey questionnaire:

It is mentioned that the questionnaire was composed of 28 questions which were divided into three sections: The first section consisted of eight questions; the second section was composed of 12 questions and the third section was composed of nine questions. The total number of 8, 12, and 9 is 29, not 28. Please check the accurate number of the questions under each section accordingly.

Data Analysis:

It is mentioned (in data analysis section) that '*Demographics numerical variables were described using **mean and standard deviation**'. This was used in Table 3 and Table 4 (Knowledge difference in demographics with two categories) i.e. the mean (±SD). While in other Tables, i.e. Table 1 (demographic details) and Table 2 (Community pharmacists' knowledge about SGLT2 inhibitors) the total number and percentages (no.; %) were used not Mean and SD. You can specify those separately. Also, it is recommended to mention the name of the statistical test used either under each Table or in the data analysis section.

Knowledge scale validity and score:

In this section, full details of the scores are needed, i.e. not only from 1 (not all) to 4 (strongly agreed). It is well explained how the knowledge scale is validated but it is not clear how the SGLT2 inhibitor's knowledge was calculated to 6.61 (SD=2.22, range 1-12). You may explain here more about it and state the range of the high, moderate, or low/poor knowledge scores to compare your findings with the knowledge scale average. And explain how the pharmacist's knowledge is

considered a low or moderate level.

Discussion:

Across the discussion part, it is recommended to add the *P*-value for each significant/not significant finding. Also, in the discussion section, it is stated that **"*Around half of the patients provided positive feedback about these agents*"**. It is better to write the exact percentage and reference to support this statement.

Conclusion:
In the conclusion, it is stated that the findings of this study demonstrated that pharmacists' knowledge about SGLT2 inhibitors is Moderate. It is recommended to add the score for this evaluation.

Is the work clearly and accurately presented and does it cite the current literature?
Yes

Is the study design appropriate and is the work technically sound?
Yes

Are sufficient details of methods and analysis provided to allow replication by others?
Partly

If applicable, is the statistical analysis and its interpretation appropriate?
Partly

Are all the source data underlying the results available to ensure full reproducibility?
Yes

Are the conclusions drawn adequately supported by the results?
Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Diabetic patient's knowledge, attitude and Practice using questionnaire in a cross sectional method.

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

> Author Response 28 Jun 2022
> **Abdelrahim qudhah**, Hashemite University, Zarqa, Jordan
>
> The authors would like to thank you for your positive valuable feedback on the manuscript which will improve the quality of it.

The study is very well designed and well written. I enjoyed reading it. Decision made: Approved with only minor changes are required as follows:

Method:

C1: In the data analysis section, it is stated that the "*Data were analysed by using SPSS software after extracting it from Google forms*", this means that the questionnaire was computer-based, i.e. iPads/PCs were used, however, in the design and data collection section, you've mentioned that the questionnaire was distributed face-to-face with participants at their workplace, which made me think that the questionnaire was a paper-based survey. Please clarify this point.

R1: Thank you for your comment. The questionnaire was computer-based, however, it was distributed to the participants face-to-face, not over social media platforms.

C2: Development of the survey questionnaire:

It is mentioned that the questionnaire was composed of 28 questions which were divided into three sections: The first section consisted of eight questions; the second section was composed of 12 questions and the third section was composed of nine questions. The total number of 8, 12, and 9 is 29, not 28. Please check the accurate number of the questions under each section accordingly.

R2: Thank you for your comment. The third section was composed of eight questions. It is now corrected.

C3: Data Analysis:

It is mentioned (in data analysis section) that '*Demographics numerical variables were described using **mean and standard deviation***'. This was used in Table 3 and Table 4 (Knowledge difference in demographics with two categories) i.e. the mean (±SD). While in other Tables, i.e. Table 1 (demographic details) and Table 2 (Community pharmacists' knowledge about SGLT2 inhibitors) the total number and percentages (no.; %) were used not Mean and SD. You can specify those separately. Also, it is recommended to mention the name of the statistical test used either under each Table or in the data analysis section.

R3: Thank you for your comment. The "mean and standard deviation is amended to "frequencies". The test used is now added beside the title of each table.

C4: Knowledge scale validity and score:

In this section, full details of the scores are needed, i.e. not only from 1 (not all) to 4 (strongly agreed). It is well explained how the knowledge scale is validated but it is not clear how the SGLT2 inhibitor's knowledge was calculated to 6.61 (SD=2.22, range 1-12). You may

explain here more about it and state the range of the high, moderate, or low/poor knowledge scores to compare your findings with the knowledge scale average. And explain how the pharmacist's knowledge is considered a low or moderate level.

R4: Thank you for your comment. This section is now amended. Full details of the scores were added. The knowledge score was calculated as an average for the adequate answers of the participants. Knowledge score was classified as poor (1-4), moderate (4-8), and high (8-12).

C5: Discussion:

Across the discussion part, it is recommended to add the *P*-value for each significant/not significant finding. Also, in the discussion section, it is stated that ***"Around half of the patients provided positive feedback about these agents"***. It is better to write the exact percentage and reference to support this statement.

R5: Thank you for your comment. P value and percentage are now added.

C6: Conclusion:
In the conclusion, it is stated that the findings of this study demonstrated that pharmacists' knowledge about SGLT2 inhibitors is <u>Moderate.</u> It is recommended to add the score for this evaluation.

R6: The score is added now.

Competing Interests: No competing interests were disclosed.

Reviewer Report 23 June 2022

✓ **Ayman G. Mustafa** (iD)
Department of Basic Medical Sciences, College of Medicine, QU Health, Qatar University, Doha, Qatar

This paper discusses community pharmacists' knowledge and practices toward a group of a new anti-diabetic group, SGLT2 inhibitors, in Jordan which is an important topic that gives new insight into this group of medications.

The paper is well-written and of high quality, however, I have some minor comments that would improve the paper:

○ In the abstract, Add the expected impact of this study, for example; Improving pharmacists' knowledge about this group of medications could improve the treatment outcome of people with diabetes.

○ In the introduction, in the first paragraph, line 5, insert reference after "metformin monotherapy"

○ Also in the second paragraph of the introduction, line 5, insert reference after "glucose level"

○ In methods, the section entitled 'Knowledge scale validity and score" is best be moved up before the statistical analysis section.

The results of this study are quite novel which could help the pharmacists to improve their knowledge about this group of medications that will improve the quality of life for people with diabetes. I think the study is of good value and I recommend it for indexing.

Is the work clearly and accurately presented and does it cite the current literature?
Yes

Is the study design appropriate and is the work technically sound?
Yes

Are sufficient details of methods and analysis provided to allow replication by others?
Yes

If applicable, is the statistical analysis and its interpretation appropriate?
Yes

Are all the source data underlying the results available to ensure full reproducibility?
Yes

Are the conclusions drawn adequately supported by the results?
Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Free radicals in biology and medicine

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Author Response 28 Jun 2022

Abdelrahim qudhah, Hashemite University, Zarqa, Jordan

The authors would like to thank you for your valuable feedback on the manuscript which

will improve the quality of it.

C1: In the abstract, Add the expected impact of this study, for example; Improving pharmacists' knowledge about this group of medications could improve the treatment outcome of people with diabetes.

R1: The expected impact of this study was added to the abstract.

C2: In the introduction, in the first paragraph, line 5, insert reference after "metformin monotherapy"

R2: A reference is now added.

C3: Also in the second paragraph of the introduction, line 5, insert reference after "glucose level"

R3: A reference is now added.

C4: In methods, the section entitled 'Knowledge scale validity and score" is best be moved up before the statistical analysis section.

R4: The title of this section is amended as recommended.

Competing Interests: No competing interests were disclosed.

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