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Assessment of potential drug–drug interaction knowledge, attitude, and practice among Egyptian hospital and community pharmacists: a cross-sectional multicenter study

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Abstract

Background Pharmacists have an important role in preventing prescribing errors and providing appropriate information. They can detect potential drug–drug interactions (DDIs), which are associated with a more extended hospital stay and higher medical costs that lead to substantial financial burdens on healthcare systems. This study aimed to evaluate and assess the knowledge of community and hospital pharmacists toward drug–drug interaction and their attitude and motivation to find DDI information, in addition to identifying the pharmacist factors affecting this knowledge. A cross-sectional multicenter study was conducted using a self-administered questionnaire. Nineteen drug pairs, that are common in clinical practice, were evaluated. This study aimed to evaluate and assess the knowledge of community and hospital pharmacists toward drug–drug interaction and their attitude and motivation to find DDI information, in addition to identifying the pharmacist factors affecting this knowledge.

Results A total of 4363 pharmacists (2260 community pharmacists and 2103 hospital pharmacists) have completed the survey. The participants' knowledge of DDIs was 58.25%, and there was no significant difference in pharmacist knowledge between community and hospital pharmacists ($p = 0.834$). The highest correct answer was for sildenafil and isosorbide mononitrate pair 78.8%. The most used source of information was the internet or mobile applications, 47.1%. Participants who always considered PDDIs while prescribing detected more drug interactions than those who did not ($p = 0.001$).

Conclusion According to the findings of this study, community and hospital pharmacists had comparable knowledge of DDIs. However, before dispensing uncommon prescriptions, they should consult evidence-based drug information resources and DDI software to identify potential drug interactions.

Keywords Drug–drug interaction, Prescription, Community, Hospital, Pharmacists, Knowledge

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Background

Drug–drug interactions (DDIs) can be defined as a clinical response to drug administration of a combination of two or more drugs that is different from the expected effects of the individual drugs when given alone [1]. DDIs are one of the medication errors that threaten patient safety as a result of pharmacodynamic or pharmacokinetic interaction between the administered drugs, which can lead to failure of treatment strategy or adverse effects or specific toxicity [2, 3]. The consequences of DDIs vary from minor to severe impacts that can be lethal to patients [4, 5]. The recrudescence of DDIs was found to be about 15–45% of hospitalized patients, with many studies linking DDIs with the increase in the length of hospital stay and healthcare costs [6, 7].

Chronic disease prevalence, polypharmacy, elderly, and cancer patients are all associated with an increased incidence of drug interactions [8–11]. The management of DDIs is a complex process that requires understanding the risk rating of DDIs mechanism, severity, and reliability and includes risk–benefit assessment [12, 13]

Computerized provider order entry (CPOE) combined with clinical decision support systems (CDSS) are being widely implemented to prevent adverse drug events (ADEs). Still, the effectiveness of these systems remains unclear and does not appear to avoid clinical ADEs reliably. In Egypt, most works identifying potential DDI depend on pharmacists' knowledge or the usage of online applications for drug–drug interactions. Methods for decreasing the possibility of drug interactions include the improvement of the knowledge of healthcare providers, developing systems for checking DDIs, and improvement of patient education regarding drug use [14].

Pharmacists play essential roles in preventing prescribing errors, providing appropriate information, and detecting potential DDIs. For example, community pharmacists can detect and prevent DDI in their pharmacies by detecting potential interactions and giving advice to patients [15]; in addition, published studies have reported that the rates of potential DDIs in hospitalized patients vary from 2.2% to 30%, so the high knowledge of DDIs among hospital pharmacists is essential in the reduction of DDIs complications that are associated with longer hospital stay [16]. In addition, exposure to potential DDIs can result in unnecessary healthcare costs; for example, a study revealed that the costs due to preventable ADRs in the USA and European countries range from €2,851 to €9,015 [17], and these medical costs represent a financial burden on healthcare systems [18, 19].

Despite drug information resources and online websites that are used to identify potential DDIs, the occurrence of possible DDIs is still high, which is usually due to different causes such as availability of pharmacist time, trustiness of patient to pharmacist, and cooperation between patient and pharmacist [20]. The studies of DDIs and their consequences in Egyptian community pharmacies [21] and hospitals [22, 23] are limited, and these interactions may be associated with severe adverse events. Pharmacists in community settings or hospitals play essential roles in DDI detection; however, their knowledge and attitude toward drug interactions do not appear to be studied sufficiently [24]. Most published studies evaluated the knowledge among prescribers [25]. Our study aimed to evaluate and assess the knowledge of community and hospital pharmacists toward drug–drug interaction and their attitude and motivation to find DDI information, in addition to identifying the pharmacist factors affecting this knowledge.

Methods

Study design

This cross-sectional multicenter study was conducted using a self-administered questionnaire distributed with pharmacy students' aid between February 1, 2021, and June 30, 2021. Pharmacists working in a private or chain community pharmacy and Ministry of Health or university or private hospital pharmacy were included in the study; those in other sectors, such as industry and academia, were excluded.

Survey questionnaire and data collection

The DDI questionnaire was designed and developed from previous studies that assessed the knowledge of healthcare professionals about DDIs [5, 26, 27]. The structured questionnaire consisted of two sections. The first one was demographic data of the participant pharmacists, including pharmacists' educational level, age, gender, setting, and experience years. The second one contains 19 pairs of common drug interactions in clinical practice [24]. Pharmacists' knowledge was assessed as "No interaction, Contraindication, May be used together with monitoring, and Not sure."

After finishing the questionnaire, participants were supplied with the correct answers to raise their awareness and knowledge about these potential drug–drug interactions. Participants were informed that their responses and the information was kept securely.

Outcome measures

The primary objectives were to assess the knowledge of community and hospital pharmacists toward potential drug–drug interactions (PDDIs) that reflect the quality of health systems in pharmacies, while the secondary outcomes were to determine the predictor factors impacting pharmacist knowledge of drug interactions.

Sample size calculations

According to Egyptian pharmacists' syndicate records, there are approximately 216,072 registered pharmacists in Egypt, with a confidence level of 97% and a margin of error of 5%. If 50% of the pharmacists would have good knowledge, the minimum acceptable sample size is 470 participants.

Statistical analysis

The data were analyzed using SPSS software version 24 for Analysis. For descriptive Analysis, results were presented as frequencies and percentages. Mann–Whitney test was used for independent nonparametric data. A linear regression model was used to determine the potential predictors of (potential drug–drug interactions) PDDIs knowledge, including participant's age, education, settings, years of practice, and attitude toward PDDIs. For all tests, $p < 0.05$ was considered statistically significant.

Results

Characteristics of the participants

A total of 4363 pharmacists (2260 community pharmacists and 2103 hospital pharmacists) have completed the survey. As shown in Table 1, the majority (58.4%) aged from 20 to 29 years old. Most (61.1%) had bachelor's degrees, and 69.1% of the participants were from urban regions. About 79.6% of the participants had practiced up to 10 years. There is no significant difference in age and years of practice between community and hospital pharmacists as shown in Table 2.

Knowledge of pharmacists of DDIs

The participant's knowledge of DDIs was 58.25% (average of correct answers about DDIs). Table 3 summarizes participants' responses to the DDI questions, presenting the frequencies (percentages) of respondent answers for each of the 19 drug pairs. The lowest correct answer was between alprazolam and itraconazole ($n = 778$, 17.8%). In contrast, most participants answered the remaining 18 drug pairs questions correctly, and the most correct answer was for sildenafil and isosorbide mononitrate pair ($n = 3438$, 78.8%).

As shown in Table 4, the highest frequency of correct answers among the community pharmacists was 17 questions, and 0.8% of the community pharmacists answered all the questions incorrectly. However, the highest frequency of correct answers among the hospital pharmacists was 13 questions, and 0.9% answered all 19 questions incorrectly. None of the pharmacists knew all the 19 questions correctly in both groups. The mean rank of the sum of correct answers for the community and hospital pharmacists was 2178.14 and 2186.14, respectively, with a p value of 0.834 (the difference in knowledge between community pharmacists and hospital pharmacists was nonsignificant).

Table 1 Frequencies and percentage of the demographic characteristics of the study participants ($n = 4363$)

Character	Number of participants (%)
Age	
20–29	2550 (58.4)
30–39	1287 (29.5)
40–49	405 (9.3)
≥ 50	121 (2.8)
Gender	
Male	2198 (50.4)
Female	2165 (49.6)
Education	
Bachelor	2666 (61.1)
Postgraduate certificate holders	453 (10.4)
Master	370 (8.5)
Pharm D	426 (9.8)
Board-certified pharmacists	91 (2.1)
PhD	357 (8.2)
Geographic region	
Rural	1347 (30.9)
Urban	3016 (69.1)
Years of practice	
5 <	2178 (49.9)
05-Oct	1296 (29.7)
Oct-15	542 (12.4)
15–20	199 (4.6)
>20	148 (3.4)
Settings	
Community pharmacists	2260 (51.8)
Hospital pharmacists	2103 (48.2)

Table 2 Comparison of the demographic characteristics of community and hospital pharmacists

Character	Mean rank (community pharmacist)	Mean rank (hospital pharmacist)	*p* value
Age	2165.35	2199.89	0.304
Gender	2096.62	2273.75	0.00 (< 0.05)*
Education	1925.94	2457.17	0.00 (< 0.05)*
Geographic region	2097.77	2272.52	0.00 (< 0.05)*
Years of practice	2178.99	2185.23	0.859

Mann–Whitney test was used

*For this test, $p < 0.05$ was considered statistically significant

Table 3 Frequencies and percentages of participants' response to potential DDIs

Drug–drug interaction pairs	No interaction *n* (%)	Used with monitoring *n* (%)	Contraindication *n* (%)	Not sure *n* (%)
Acetaminophen/codeine and amoxicillin	**3395 (77.8)**	580 (13.3)	167 (3.8)	22 1 (5.1)
Warfarin and sulfamethoxazole/trimethoprim	403 (9.2)	**2432 (55.7)**	1241 (28.4)	287 (66)
Warfarin and digoxin	**2431 (55.7)**	887 (20.3)	794 (18.2)	251 (5.8)
Digoxin and amiodarone	353 (8.1)	**2240 (51.3)**	1434 (32.9)	336 (7.7)
Cyclosporine and rifampicin	718 (16.5)	**2147 (49.2)**	1014 (23.2)	484 (11.1)
Digoxin and itraconazole	447 (10.2)	**2552 (58.5)**	942 (21.6)	422 (9.7)
Digoxin and sildenafil	**2884 (66.1)**	457 (10.5)	768 (17.6)	254 (5.8)
Simvastatin and itraconazole	359 (8.2)	716 (16.4)	**2906 (66.6)**	382 (8.8)
Sildenafil and isosorbide mononitrate	262 (6)	363 (8.3)	**3438 (78.8)**	300 (6.9)
Conjugated estrogens and raloxifene	**2224 (51)**	681 (15.6)	760 (17.4)	698 (16)
Theophylline and ciprofloxacin	522 (12)	**2119 (48.6)**	1339 (30.7)	383 (8.8)
Pimozide and ketoconazole	371 (8.5)	594 (13.6)	**2876 (65.9)**	522 (12)
Warfarin and Fluconazole	412 (9.4)	**2529 (58)**	1054 (24.2)	368 (8.4)
Alprazolam and itraconazole	413 (9.5)	326 (7.5)	**778 (17.8)**	2846 (65.2)
Digoxin and clarithromycin	404 (9.3)	**2502 (57.3)**	1087 (24.9)	370 (8.5)
warfarin and sulfinpyrazone	443 (10.2)	**2519 (57.7)**	795 (18.2)	606 (13.9)
Dopamine and phenytoin	567 (13)	**2388 (54.7)**	995 (22.8)	413 (9.5)
Fexofenadine HCL and metoprolol	**3025 (69.3)**	453 (10.4)	349 (8)	536 (12.3)
Itraconazole and quinidine	329 (7.5)	620 (14.2)	**2916 (66.8)**	498 (11.4)

The boldness indicates the correct ones

Table 4 Frequencies and percentages of the community pharmacists and hospital pharmacists correct answers

Number of correct answers	Frequency (%) (community pharmacist)	Frequency (%) (hospital pharmacy)
0	18 (0.8)	19 (0.9
1	25 (1.1)	13 (0.6)
2	54 (2.4)	36 (1.7)
3	79 (3.5)	57 (2.7)
4	84 (3.7)	85 (4)
5	102 (4.5)	108 (5.1)
6	139 (6.2)	123 (5.8)
7	134 (5.9)	127 (6)
8	142 (6.3)	153 (7.3)
9	151 (6.7)	143 (6.8)
10	182 (8.1)	176 (8.4)
11	194 (8.6)	137 (6.5)
12	164 (7.3)	166 (7.9)
13	145 (6.4)	180 (8.6)
14	140 (6.2)	124 (5.9)
15	138 (6.1)	126 (6)
16	143 (6.3)	173 (8.2)
17	221 (9.8)	153 (7.3)
18	5 (2)	4 (2)
19	0 (0)	0 (0)
Total	2260 (100)	2103 (100)

Source of potential DDI information

The sources of DDI information are shown in Fig. 1. The internet or mobile applications were the most used source of information ($n=2057$, 47.1%). The least commonly used sources were knowledge bases in Arabic and package inserts (2.2% and 1.2%, respectively).

Attitude toward potential DDIs

As shown in Fig. 2, about 86.98% of the participants consider DDIs when prescribing, with 48.38% agreeing with the statements and 38.60% strongly agreeing, respectively, and only about 1.5% do not consider it when prescribing. More than 88% of participants said that DDI information is essential for their practice. In addition, more than 85% always check DDI when unsure about it, and about 80% are willing to learn about it.

Predictors of PDDIs knowledge

As shown in Table 5, the linear regression model indicates that significant predictors of a higher number of recognized drug pairs were age, education, and attitude toward PDDIs. Participants who always considered PDDIs while prescribing detected more drug interactions than those who did not ($p=0.001$). In addition, those

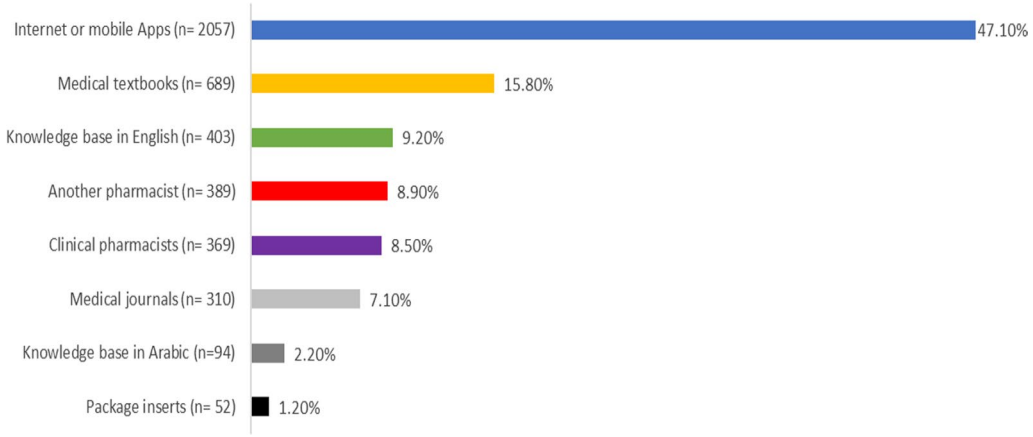

Fig. 1 Source of PDDIs information

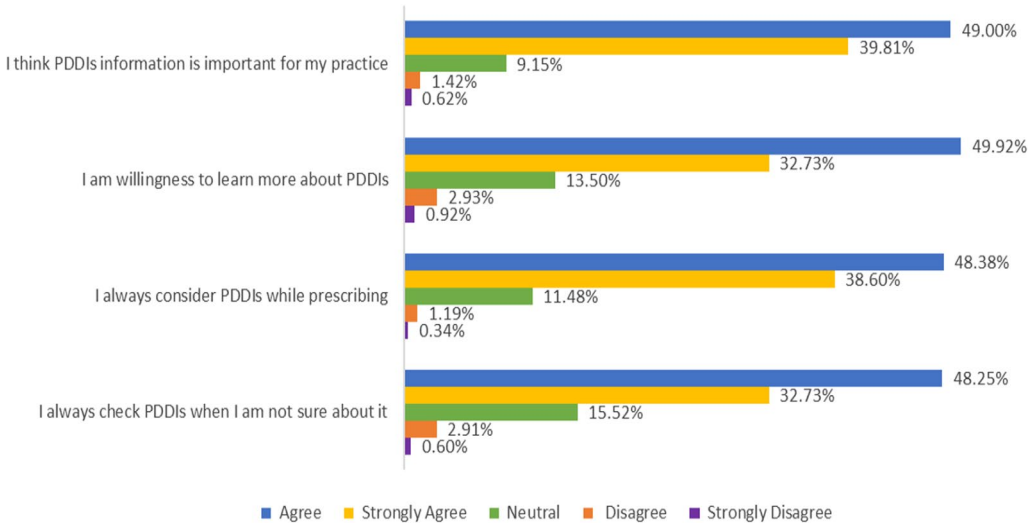

Fig. 2 Participants attitude toward PDDIs

Table 5 Predictors of the knowledge level of the study participants for PDDIs

Character	Unstandardized β coefficient	*p* value
Constant	6.252	< 0.001
Age	0.297	0.034*
Geographic region	0.145	0.308
Education	− 0.121	0.004*
Setting	− 0.146	0.28
Years of practice	0.052	0.618
Attitude I always consider PDDIs while prescribing	0.351	0.001*
I think PDDIs information is important for my practice	0.145	0.204
I always check PDDIs when I am not sure about it	0.379	< 0.001*
I am willingness to learn more about PDDIs	0.09	0.356

Linear regression test was used

*For this test, $p < 0.05$ was considered statistically significant

who did not check PDDIs when not sure about it had lower scores for PDDIs than those who did ($p < 0.001$).

Discussion

The recognition of interacting drugs is critical for any healthcare providers, including pharmacists, to decrease the DDIs and, consequently, reduce the drug-related morbidity and mortality that may occur as a result of these interactions [5, 28]. Although thousands of articles on drug interactions have been published and numerous computerized screening systems have been developed, patients continue to suffer from adverse drug interactions. It was found that about twenty percent of the adverse drug effects in the developed countries, which are responsible for more than 700,000 deaths, are due to drug–drug interactions [14]. Possible methods for reducing the risk of drug interactions include improving healthcare providers' knowledge, improving computerized screening systems, providing information on patient risk factors, increasing pharmacogenetic information, more attention to drug administration risk factors, and improving patient education on drug interactions.

In this survey, we assessed the ability of pharmacists to recognize clinically significant drug combinations. It was found that among DDI information sources, internet or mobile applications and medical textbooks were the most used sources of information. The majority of the participants (47.1%) tended to receive information regarding DDIs from electronic sources, which is consistent with a previous study conducted in Iran [29]. The possible explanation for this finding may be the high percentages of young participants in the present study, and people in this age group are usually interested in technology and use it in many fields. A small percentage of the participants in our survey (1.2%) reported that they use package inserts, which is a risk factor for incorrect use of drugs [30].

Our study showed no significant differences in the proportion of community pharmacists and hospital pharmacists who correctly answered the same number of questions about DDIs. The level of the participants' knowledge of DDIs was 58.25% (average of correct answers about DDIs), and this finding is comparable to another study (53.3%) [31]. However, our results are not consistent with another study [24] that revealed a level of knowledge among pharmacists of about 37.3%, but the later study included 26 drug pairs; however, our study included 19 pairs, and these differences in drug pairs may be the cause of the differences in the level of the participant's knowledge on DDIs.

Among the drug pairs selected to assess DDIs knowledge, sildenafil, and isosorbide mononitrate were the most highly recognized drug pairs (78.8%), which is consistent with another study [32]. The lowest recognized pairs were alprazolam and itraconazole (17.8%), which are contraindicated with each other. In accordance with another study [5], even if one justified that the drug combinations classified as contraindicated could be used with close monitoring and considered both choices to be correct, up to 65% of the participants remained unsure if there was a potential interaction or not. In our study, we tried to investigate the predictors of DDI knowledge of participants, including age, education, setting, years of practice, and the participants' attitudes toward DDIs. It was found that a significant correlation exists between participants' age and their knowledge level in DDIs. The older participants answered more DDI questions than younger ones, which is consistent with another study that used identical drug pairs as our study [33]. Another study, in contrast to ours, found no connection between age and DDI knowledge level [34], but this may be explained as the later study involved participants of relatively the same age.

Another predictor of DDI knowledge is the education level, which was found to have a significant correlation with the level of knowledge of DDIs. Unexpectedly, participants with bachelor's and postgraduate certificate holders recognized a higher number of interactions than did those with Ph.D. and board-certified pharmacists, and this finding was in accordance with a study carried out in Khartoum state and showed that pharmacists with bachelor's recognized higher number of DDIs than those with master [31]. The results of our study were in contrary to a previous study [33] that reported that participants' education level did not affect the knowledge level of DDIs. These findings could be due to several factors, including the fact that Ph.D. holders are not recent graduates and may not have as good recall of DDIs, as well as the fact that the majority of pharmacists have bachelor's or postgraduate diploma degrees rather than PhDs and board certifications.

Interestingly, the number of years of experience of the participants was not a significant predictor of DDI knowledge level, and this is consistent with other studies that used different drug pairs for DDI knowledge assessment [5, 31].

Regarding attitudes toward DDIs and their relation to the level of DDI knowledge, it was found that participants who always consider DDIs while prescribing and checking about DDIs when not sure about them recognized a more significant number of DDIs than those who did not, and these results are consistent with previous study conducted in China [33]. This indicates the strong association between the participants' tendency to check references and their knowledge of PDDIs, as proved by the correct recognition of the drug pair interactions.

Astonishingly, this study revealed no significant association between setting (whether community or hospital pharmacists) and the level of their knowledge of DDIs.

The findings of the present study have several implications for practice. This article highlights an important issue that requires urgent attention in Egypt which is the improvement of drug–drug interaction knowledge among community and hospital pharmacists. It is crucial for improving patient safety and healthcare outcomes in the country to ensure the rational and optimal use of drugs. By raising awareness of this issue and identifying potential solutions, this study makes an important contribution to the field of healthcare in Egypt and beyond. Our study has identified some recommendations to improve the knowledge and practice of hospital and community pharmacists regarding DDIs. Based on the study's findings, it is recommended that continuing education and training programs should be developed for hospital and community pharmacists in Egypt to improve their knowledge of DDIs. The Egyptian Ministry of Health should develop guidelines and protocols for the management of DDIs in hospitals and community pharmacies to ensure consistency in practice. Additionally, these pharmacies should have access to electronic databases that provide up-to-date information on DDIs to support their practice. This study highlights the need for ongoing education and training programs, updated guidelines, and increased resources to support pharmacists in their efforts to provide safe and effective care to patients. Finally, future studies should be conducted to assess the impact of education and training programs on hospital and pharmacists' knowledge and practice regarding DDIs.

The limitation of our study is that the 19-drug pairs might not be adequate to reflect the extent of knowledge applicable to the vast number of PDDIs. In addition, the study's sample size may limit the generalizability of the findings. The sample size is small or not representative of the entire population of hospital and community pharmacists in Egypt, so, the results may not accurately reflect the overall knowledge level of pharmacists in the country. Additionally, the study's reliance on self-reported data from pharmacists introduces the possibility of response bias. Participants may overestimate their knowledge to present themselves in a more favorable light or may underreport their knowledge about DDIs due to various reasons, such as social desirability bias. Furthermore, the study focuses solely on assessing the pharmacists' knowledge without considering other factors that may influence their ability to apply that knowledge in practice, such as time constraints, workload, or access to resources.

In addition, future studies of larger sample sizes of pharmacists and more drug pairs are required to face the challenges and limitations of this study taking into consideration other factors such as time constraints, workload, or access to resources that may affect their ability to apply that knowledge in practice,

Conclusion

According to our study findings, community and hospital pharmacists had comparable knowledge of DDIs. Pharmacists should improve their knowledge of drug–drug interactions (DDIs) to ensure patient safety**.** Also, they should consult evidence-based drug information resources and DDI software to identify potential drug interactions before dispensing prescriptions. Developing a system for checking DDIs is necessary.

Abbreviations

PDDIs	Potential drug–drug interactions
DDIs	Drug–drug interactions
CPOE	Computerized provider order entry
CDSS	Clinical decision support systems
ADEs	Adverse drug events

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Author contributions

Study conception and design were done by EAW, MA, and AE. Data analysis and interpretation were performed by AEAW, AE, YSAD, and EMS. EAW, AEAW, MA, AE, and EMS helped in drafting, revision of the paper, and final approval of the published version.

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Availability of data and materials

The datasets generated and analyzed during the current study are available from the corresponding author on a reasonable request.

Declarations

Ethics approval and consent to participate

All procedures performed in the study involving human participants were in accordance with the ethical standards of Faculty of pharmacy October 6 University ethics committee and with the 1964 Declaration of Helsinki and its later amendments. The study was received approval from the Ethics Committee and institutional review boards of October 6 University (Approval Number: PR-Ph-2112005). Pharmacist's participation in this survey was voluntary. Informed consent was obtained from all participants. They were asked before questionnaire if they participate in this study, and they able to refuse take part in the research or exit the survey at any time without penalty. Pharmacists were only required to complete the questionnaire once. Participants informed that their personal details were not linked to their responses and the information were kept securely.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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