



## Community pharmacists' knowledge and awareness about isotretinoin therapy and its dispensing practice in Jordan

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### ABSTRACT

A validated self-reported questionnaire was used to evaluate pharmacists' knowledge about isotretinoin and their awareness of isotretinoin dispensing practice. The majority were not able to recognize the initial dose of isotretinoin, the potential side effects such as dyslipidemia and liver toxicity, the potential interaction with tetracycline and Vitamin A and the contraindications of isotretinoin. Around 41.3 % of the pharmacists dispensed isotretinoin without a prescription, and the majority did not recognize that isotretinoin should be dispensed for only 30 days, should not be dispensed without an emphasis on the appropriate indication, and did not know the appropriate duration of isotretinoin therapy. Male gender and postgraduate degree were associated with better awareness, while increased work experience and postgraduate degree were associated with better knowledge about isotretinoin therapy. Nevertheless, both male and female pharmacists demonstrated equivalent knowledge levels. The current study demonstrates the need to implement educational programs to improve pharmacists' knowledge and awareness about isotretinoin and its dispensing practice.

### 1. Introduction

Acne vulgaris has been described as the most common skin condition in the US, affecting around 50 % of the American population every year [1], and 45 % of the Jordanian adolescents and young adults in particular [2]. At the beginning of 1982, isotretinoin was approved as the first-line therapy for the treatment of severe, resistant, nodular acne that was unresponsive to conventional therapy [3–5]. Isotretinoin is by far the most cost-effective medication when compared with other medications used for the treatment of severe acne. However, it has been associated with some serious and teratogenic adverse effects that require increased patients' awareness [3–5] such as dryness, dyslipidemia, nosebleeds, dizziness, eye inflammation, joint and back pain, depression, and abnormal liver

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function [6]. A population-based study showed that 9.4 % of the pregnant women who were exposed to isotretinoin during pregnancy gave birth to children with birth defects [7]. Another study reported that among the 154 pregnancies exposed to isotretinoin, 21 infants were born malformed, and 12 spontaneous abortions occurred as a result of isotretinoin exposure [8]. The exposure to isotretinoin during pregnancy can also pose a risk of influencing the function of cephalic neural crest cells, potentially resulting in craniofacial, cardiac, and thymic abnormalities. This may prompt numerous pregnant women to consider elective pregnancy termination [7,9,10]. A retrospective study showed that the majority of the patients (72 %) suffered from dry skin during isotretinoin therapy [11]. Three randomized controlled trials showed that isotretinoin therapy resulted in mild hyperlipidemia and elevations in liver enzymes [12–14]. Most patients were found to have insufficient knowledge about the potential side effects of isotretinoin and how to deal with them in different countries in the Middle East, such as Saudi Arabia [15–17]. Furthermore, there are no specific risk minimization tools other than the warnings in the product leaflet [18], which increase the chance of unwanted adverse effects [15,19,20]. Therefore, it is essential to educate the patients on isotretinoin therapy, its potential side effects, and its proper use.

Pharmacists are the drug experts who play an important role in optimizing drug therapy and providing education about the appropriate use of prescribed medications and their potential side effects [21,22]. In Jordan, in order to get a BPharm (Bachelor in Pharmacy) degree, students need to complete 165 credit hours of university and faculty requirements. They also have to complete 1440 h of practice training over the 5-year pharmacy program in community pharmacies, hospitals, or businesses related to pharmacy [23]. An earlier study reported a 50 % increase in medication adherence among patients with acne vulgaris after receiving pharmacist counseling on isotretinoin [24]. However, earlier studies reported a lack of pharmacists' awareness and poor counseling practice about isotretinoin and its potential side effects. A survey of isotretinoin-exposed pregnancies reported that 24 % of the women surveyed did not recall having contraception counseling before using the medication [25]. An earlier study reported that only 2 % of the pharmacists provided counseling about the expected side effects of isotretinoin therapy [26]. Moreover only 6.2 % of the pharmacists recommended the use of two methods of contraception while on isotretinoin therapy [27] and only one-third recognized that isotretinoin is contraindicated during pregnancy [28]. A systemic review found that pharmacists had very poor medication knowledge and an unsatisfactory level of practice about isotretinoin therapy [29]. The current study is the first to evaluate pharmacists' knowledge about isotretinoin pharmacotherapy and awareness about isotretinoin dispensing practice in Jordan. Findings of the current study should be fed into future educational programs that aim to improve pharmacists' knowledge about this drug and its dispensing practice, hence, enhance safety and treatment outcomes among isotretinoin users.

## 2. Materials and methods

### 2.1. Patient and public involvement

No patient involved.

### 2.2. Study site and subject

The current cross-sectional survey-based study was conducted on community pharmacists working in both single and chain pharmacies in different cities across Jordan in the period from January through May 2019. The study pharmacists were graduates of Jordanian universities and other universities recognized by the Ministry of Higher Education who are licensed to practice as pharmacists in Jordan. As a criterion for inclusion, the research pharmacist asked the community pharmacist about the indication of isotretinoin therapy, and those who did not know the answer were excluded from the study. The researcher provided the pharmacists with an information sheet describing the study and its' objectives, and those who agreed to participate were asked to sign consent. The pharmacists were informed that participation is voluntary, they have the right to withdraw from the study at any time, and that all the data will be kept confidential.

### 2.3. Study instrument

After an extensive literature review [18,27,30,31] the current study survey was developed. The study pharmacists filled out a structured, three-part questionnaire. The first part was designed to collect socio-demographic variables such as age, gender, years of experience, education level, and working city. The second 15-item part evaluated pharmacists' knowledge in terms of doses, the most common and serious side effects, drug interactions, and contraindications of isotretinoin therapy. A score of one was given for each correct answer, and the scores were summed out of 15. The third part involved 17 yes/no questions that evaluated awareness about the dispensing practice in terms of the availability of prescriptions, the appropriate indication, medication review, treatment duration, appropriate use, potential side effects, follow up with the dermatologist, regular laboratory checks on aspartate aminotransferase, alanine aminotransferase, and triglycerides at baseline and peak dose [32], and isotretinoin use in pregnancy. This part was scored in the same manner as part two, where a score of one was added to each correct answer of the 17 items. The survey was reviewed by experts in the field, including a dermatologist and two professors of pharmacy practice, for face and content validity, and changes were made when deemed appropriate. The study survey was also piloted on fifteen community pharmacists to ensure the clarity of the questionnaire, and the results of the piloted study were excluded from the final analysis. The pharmacists took an average of 10 min to complete the survey.

## 2.4. Sample size calculation

To calculate the minimum required sample size, the Krejcie and Morgan formula [33] was applied. The formula is:

$$s = X^2NP(1 - P) + d^2 (N - 1) + X^2P(1 - P)$$

s = required sample size;

$X^2$  = the table value of chi-square for 1 degree of freedom at the desired confidence level (3.841);

N = the population size;

P = the population proportion;

D = the degree of accuracy expressed as a proportion (0.5).

Krejcie and Morgan composed sample size tables based on the above formula for different population sizes, confidence levels, and margins of error. The population size was assumed to be above 1,000,000 (indefinite), and the minimum required sample was 271 for 90 % CI and a 5 % margin of error.

## 2.5. Statistical analysis

Data were coded and entered into SPSS software version 22 for statistical analysis. Descriptive statistics were made for quantitative variables using frequencies and percentages for categorical variables and the mean and standard deviation for continuous variables. An independent *t*-test was used to find the association between the dichotomous predictors and the continuous outcome knowledge or awareness score, while a one-way analysis of variance (ANOVA) test was used to find the correlation between the categorical predictors of three or more categories and the continuous outcome.

## 2.6. Ethics statement

Ethical approval of this study was obtained from the Institutional Review Board of King Abdullah University Hospital and Jordan University of Science and Technology. The IRB reference is 48/118/2018.

## 3. Results

Out of 356 community pharmacists, a total of 286 completed the survey, with a response rate of 80.3 %. The mean age of the pharmacists was 33 years (SD = 7). Most of the pharmacists were female (64 %), had a BPharm degree (76.6 %), were working in a single pharmacy (64.7 %), had one to three years of working experience (52.8 %), and were working in Amman (49 %). The demographic characteristics of the participating pharmacists are presented in Table 1.

As shown in Table 2, more than half of the pharmacists (54.9 %) did not know the correct initial dose of isotretinoin therapy. The most common recognized side effect of isotretinoin therapy was skin dryness (79 %). However, nearly one third of the pharmacists did not recognize teratogenicity (33.9 %), and more than half of them did not recognize dyslipidemia (52.1 %) and elevation of liver

**Table 1**  
Demographics characteristics of the participating community pharmacists (n = 286).

Characteristics	N (%)	Mean (SD)
Age		33 (7)
Gender		
Male	103 (36)	
Female	183 (64)	
Years of Experience		
1-3	151 (52.8)	
4-6	58 (20.3)	
7-10	30 (10.5)	
More than 10	47 (16.4)	
Education level		
BPharm	219 (76.6)	
PharmD	43 (14.9)	
Master	24 (8.5)	
Place of work		
Single pharmacy	185 (64.7)	
Chain Pharmacy	101 (35.3)	
Working city		
Amman	140 (49)	
Irbid	74 (25.9)	
Al-Zarqa	43 (15)	
Mafraq	29 (10.1)	

**Table 2**  
Pharmacists' knowledge about isotretinoin therapy.

Question	N (%)
Which one of the following is the correct initial dose of isotretinoin?	
0.5–1.0 mg/kg (the correct answer)	129 (45.10 %)
0.5–2.0 mg/kg	121 (42.31 %)
1.0–2.0 mg/kg	5 (1.75 %)
1.5–2.0 mg/kg	21 (7.34 %)
1.0–1.5 mg/kg	5 (1.75 %)
2.0 mg/kg	5 (1.75 %)
Isotretinoin dose should be adjusted in renal failure	
Yes 157 (54.9 %)	
No 129 (45.1 %)	
Which of the following is considered side effect of isotretinoin therapy?	
Skin dryness	
Yes 226 (79 %)	
No 60 (21 %)	
Teratogenicity	
Yes 189 (66.1 %)	
No 97 (33.9 %)	
Dyslipidemia	
Yes 137 (47.9 %)	
No 149 (52.1 %)	
Elevation of liver enzymes	
Yes 142 (49.7 %)	
No 144 (50.3 %)	
Which of the following medication should not be administered concurrently with isotretinoin?	
Tetracycline	
Yes 95 (33.2 %)	
No 191 (66.8 %)	
Vitamin A	
Yes 156 (54.5 %)	
No 130 (45.5 %)	
Which of the following is a contraindication of isotretinoin therapy?	
Pregnancy	
Yes 280 (97.9 %)	
No 6 (2.1 %)	
Breastfeeding	
Yes 278 (97.2 %)	
No 8 (2.8 %)	
Hypervitaminosis A	
Yes 185 (64.7 %)	
No 101 (35.3 %)	
Donation of the blood	
Yes 274 (96.1 %)	
No 12 (3.9 %)	
Excessive hyperlipidemia	
Yes 249 (87.1 %)	
No 37 (12.9 %)	

enzymes (50.3 %) as side effects of isotretinoin therapy. Moreover, 45.5 % of the study pharmacists did not know the potential isotretinoin interaction with vitamin A, and only one third of them (33.2 %) knew the potential interaction with tetracycline. Although most of the pharmacists knew that pregnancy (97.9 %), breastfeeding (97.2 %), blood donation (96.1 %), and excessive hyperlipidemia (87.1 %) are contraindications to isotretinoin therapy, 35.3 % of them did not know that isotretinoin is contraindicated for hypervitaminosis A, and 45.1 % did not know that it needs dose adjustment in patients with renal insufficiency.

As shown in Table 3, the pharmacists showed a lack of awareness about isotretinoin dispensing practice: where 35.3 % prescribed isotretinoin without a medication review, 41.3 % dispensed isotretinoin without a prescription, 73.8 % did not know that isotretinoin should be dispensed for only 30 days, 70.5 % dispensed isotretinoin without an emphasis on the appropriate indication, 49.8 % dispensed isotretinoin for someone other than the patient, and 41.3 % did not know the appropriate duration of isotretinoin therapy. Although most of the pharmacists (91.2 %) wrote clear instructions on isotretinoin use, results showed that 33.5 % of them did not inform the patients that the drug is better taken with fatty meals. Some pharmacists (14.8 %) did not provide information about the potential side effects of isotretinoin therapy for their patients. With regard to pregnancy instructions, 22 % of the pharmacists did not ask married female patients to perform pregnancy tests on a monthly basis, and only 10.5 % of them informed their patients that pregnancy should be avoided for one month after cessation of isotretinoin treatment. In addition, 17.5 % of the pharmacists did not recommend two different contraceptive methods for women using isotretinoin.

As shown in Table 4, male pharmacists had significantly better awareness about isotretinoin therapy when compared with female pharmacists ( $P < 0.01$ ). Nevertheless, both male and female pharmacists demonstrated equivalent knowledge levels. Having a master's degree was significantly associated with better awareness and knowledge scores when compared with lower educational

**Table 3**  
Awareness about isotretinoin dispensing practice.

Question	Yes	No
I make medication review before prescribing isotretinoin therapy	185 (64.7 %)	101 (35.3 %)
I dispense isotretinoin without prescription <sup>a</sup>	118 (41.3 %)	168 (58.7 %)
I dispense isotretinoin for more than 30 days at one time <sup>a</sup>	211 (73.8 %)	75 (26.2 %)
I dispense isotretinoin only for who are candidates to isotretinoin use	88 (29.5 %)	201 (70.5 %)
I give isotretinoin to the patient in personality and not to any relatives	143 (50.2 %)	141 (49.8 %)
I ask the patient about the period since start using isotretinoin	279 (97.4 %)	7 (2.6 %)
I inform the patient that isotretinoin should not be used for more than 6 months on contentious use	168 (58.7 %)	118 (41.3 %)
I write the instructions of isotretinoin use clearly on the label	259 (91.2 %)	25 (8.8 %)
I counsel the patient to drink large amount of water to avoid dryness during isotretinoin therapy	280 (97.9 %)	6 (2.1 %)
I counsel the patient to take isotretinoin after fatty meals	189 (66.5 %)	95 (33.5 %)
I ask the patient to use sunblock during isotretinoin therapy	263 (92.3 %)	22 (7.7 %)
I inform the patient about expected side effects of isotretinoin	242 (85.2 %)	42 (14.8 %)
I ask the patient to perform regular laboratory checkout during isotretinoin therapy	247 (86.4 %)	39 (13.6 %)
I ask the patient to follow up with dermatologist while using isotretinoin	256 (89.5 %)	30 (10.5 %)
I ask married women to have pregnancy test monthly	223 (78 %)	63 (22 %)
I inform married female patients that pregnancy should be avoided for 1 month after discontinuing isotretinoin therapy	30 (10.5 %)	256 (89.5 %)
I recommend two different contraceptive methods while using isotretinoin	236 (82.5 %)	50 (17.5 %)

<sup>a</sup> Negative questions.

**Table 4**  
Factors associated with knowledge about isotretinoin therapy and awareness of its dispensing practice.

Factor	Total knowledge score (M = 9.12 ± 0.7)		Total awareness score <sup>a</sup> (M = 11.65 ± 3.9)	
	Mean ± SD	P	Mean <sup>a</sup> ± SD	p
Gender				
Male*	8.93 ± 0.5	0.35	12.52 ± 4.6	0.002*
Female	8.93 ± 1.1		11.03 ± 3.6	
Experience years				
1-3	9.12 ± 1.5	0.003*	11.72 ± 4.2	0.88
4-6	8.65 ± 0.6		11.77 ± 3.8	
7-10	9.69 ± 1.4		12.04 ± 5.6	
>10	10.07 ± 0.5		10.77 ± 3.3	
Level of education				
BPharm	8.84 ± 1.4	0.004*	11.83 ± 4.3	0.003*
PharmD	9.03 ± 0.8		11.03 ± 4.2	
Master	9.88 ± 1.1		13.31 ± 2.9	
Working area				
Single Pharmacy	8.93 ± 1.0	0.85	11.09 ± 3.2	0.42
Chain Pharmacy	8.84 ± 1.0		11.62 ± 4.5	
City				
Amman	9.22 ± 0.25	0.47	12.30 ± 1.2	0.34
Irbid	8.65 ± 0.3		10.13 ± 0.58	
Mafraq	9.03 ± 0.5		11.14 ± 0.66	
Alzarqa'a	8.93 ± 0.3		12.47 ± 0.33	

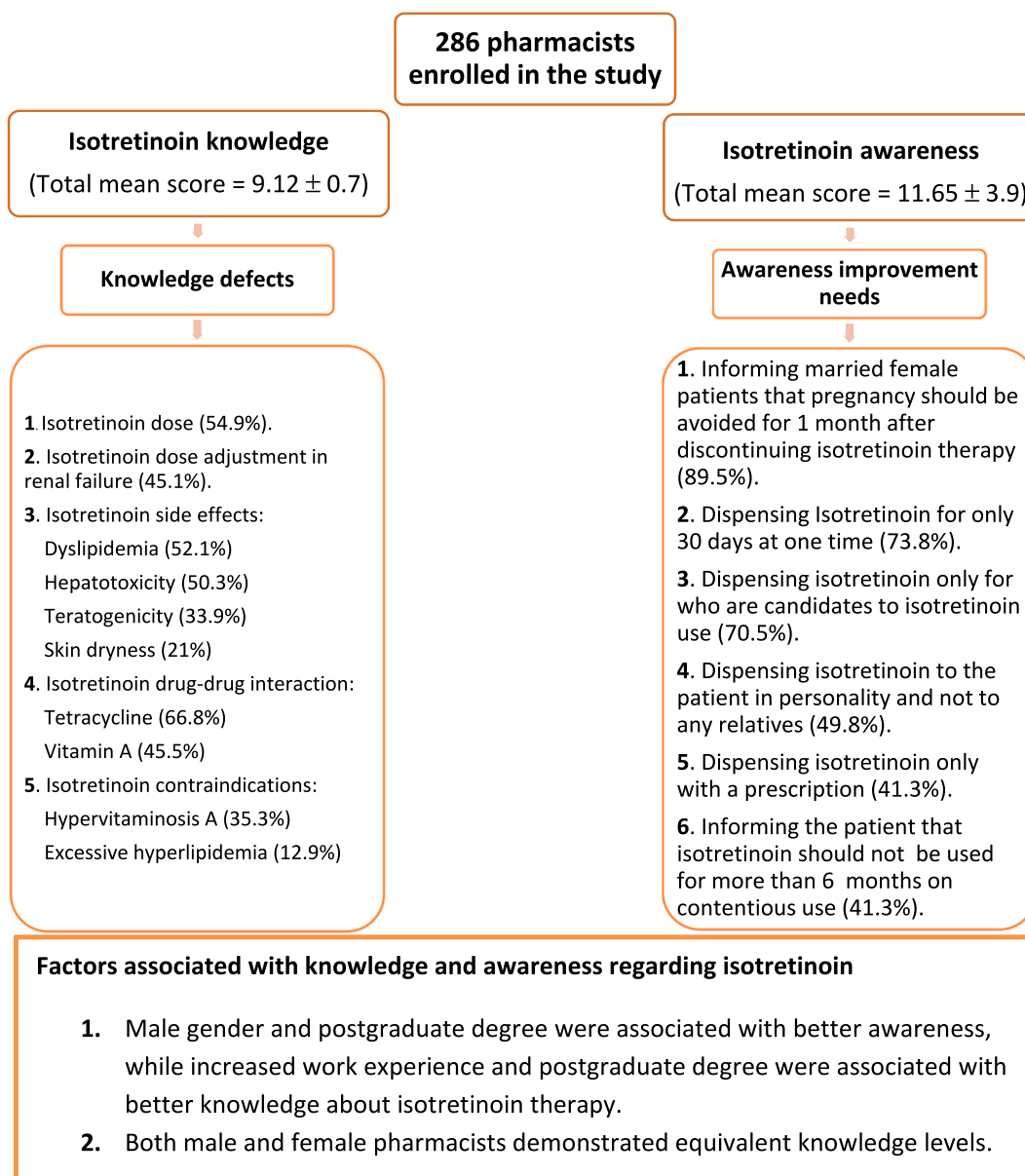
\*P < 0.05 significant difference compared to other groups.

<sup>a</sup> One-way analysis of variance (ANOVA) and independent t-test were applied where applicable.

degrees (P < 0.05). Moreover, pharmacists with seven or more years of experience demonstrated a significantly higher knowledge than those with less years of experience (P < 0.01). The main study findings are summarized in Fig. 1.

#### 4. Discussion

In the current study, pharmacists reported a lack of knowledge about isotretinoin therapy and a lack of awareness about the dispensing practice. It is well known that isotretinoin can cause several side effects, including dryness, teratogenicity, dyslipidemia, and elevations in hepatic enzymes [20]. Most of the current study pharmacists recognized skin dryness as a side effect of isotretinoin therapy, which was consistent with the finding from a study conducted in the UAE [26] and more than that of a Saudi study finding [27]. Around one-third of the pharmacists in the current study did not recognize teratogenicity as a side effect of isotretinoin, which was much higher than what was found in an earlier Saudi study [27]. Nearly half of the pharmacists in the current study did not recognize dyslipidemia and elevation of liver enzymes as side effects of isotretinoin; similar results were reported in an earlier study [26]. Additionally, a study conducted in Saudi Arabia reported that around one-third of the participating pharmacists did not recognize that isotretinoin can cause hepatic side effects [27]. In terms of drug-drug interactions, only 54.5 % of the pharmacists in the current study knew about the isotretinoin interaction with vitamin A, and 66.8 % failed to identify the interaction with tetracycline



**Fig. 1.** Summary of the study findings.

therapy. An earlier study reported that only 2.38 % of the pharmacists were able to recognize the interaction between isotretinoin and vitamin A [34]. In order to avoid potential drug-drug interactions, pharmacists should perform a medication review in order to identify the presence of any medication that could interact with isotretinoin and thus prevent further toxicities. However, nearly one third of the participating pharmacists in this study did not perform a medication review or evaluate the risk of isotretinoin interaction with other medications, which was consistent with the findings of an Emirati study, where only 32 % of the participating pharmacists asked their patients about the medications or supplements that used concurrently with isotretinoin [26]. The reported lack of knowledge about isotretinoin's potential side effects and drug-drug interactions in this study sheds light on the necessity to equip pharmacists with updated information about isotretinoin's therapy by conducting training programs, workshops, scientific conferences, seminars, and medical posts using social media, with an emphasis on conducting medication reviews before dispensing isotretinoin.

In the current study, more than one-third of the pharmacists dispensed isotretinoin without a prescription, which is about double the percentage found in a study conducted in Saudi Arabia [27]. Furthermore, most of the pharmacists in this study were not aware that isotretinoin should be dispensed for only 30 days. Earlier studies in the Netherlands, Belgium, and France found that 81.8 %, 43.1 %, and 60 % of pharmacists, were aware of this fact, respectively [31,35]. In Ireland, 39.5 % of healthcare professionals, including pharmacists limited isotretinoin prescriptions to 30 days to support regular follow-up [36]. The implementation of an isotretinoin

dispensing education program in these countries could explain the gap in awareness about isotretinoin dispensing practices when compared with Jordan. Furthermore, the current study revealed that some pharmacists need knowledge improvement in isotretinoin dispensing practice with regard to the appropriate indication of isotretinoin, the necessity to dispense isotretinoin to the patient in particular, the administration and duration of isotretinoin therapy, the importance of performing pregnancy tests monthly, and isotretinoin use in female patients of childbearing age. Moreover, some pharmacists did not ask female patients to use two different contraceptive methods while using isotretinoin in the present study. An earlier study reported that only 6.2 % of the participating pharmacists recommended the use of two methods for contraception while on isotretinoin therapy [27]. Another study showed that only 27 % of the participating pharmacists provided education about the importance of using two methods of contraception while on isotretinoin therapy [26]. In light of the teratogenic effects associated with isotretinoin, it is imperative to implement risk-minimization measures to prevent unintended pregnancies during its use. Several Western countries have successfully implemented programs like the Pregnancy Prevention Programme (PPP) in Europe and iPledge in the USA to address this concern [37,38]. In Jordan, pharmacists should proactively develop and implement similar risk-minimization programs. This may involve educating patients about effective contraception methods, conducting regular pregnancy testing before, during, and after the treatment, and adhering to a strict dispensing protocol. By doing so, pharmacists can significantly reduce the risk of unintended pregnancies during treatment.

When exploring the variables associated with improved knowledge and awareness about isotretinoin therapy, male pharmacists reported a significantly higher awareness score when compared with female pharmacists. Female pharmacists in our society have home obligations in addition to their working hours, which makes them less available to search for drug information such as isotretinoin. Results also showed that pharmacists with seven or more years of experience demonstrated a significantly higher knowledge than those with less years of experience. Pharmacists with master's degrees showed significantly better knowledge and awareness about isotretinoin use when compared with those who had lower educational degrees. It is worth noting that no significant association was found between area of residence and either knowledge or awareness about isotretinoin therapy.

The current study has some limitations. The use of a self-reported questionnaire in this study may have influenced the accuracy of participants' responses due to social desirability bias. Furthermore, even though the target sample size was achieved, the use of a larger sample size would aid in drawing conclusions that are more robust from the current study and increase the generalizability of the study findings. Moreover, the lack of decoys in the proposed answers to the knowledge questions might limit an accurate assessment of the participants' knowledge. On the other hand, given the scarcity of the data in the literature, the current study should provide further insight on the community pharmacists' information needs about isotretinoin therapy and its dispensing practice, as well as help narrow down the variables that should be targeted to enhance knowledge and dispensing practice and enhance safety among this medication candidate. Furthermore, according to the latest statistics [39], 85 % of the population in Jordan is urban, with approximately 75.4 % concentrated in Amman, Zarqa, Irbid, and Mafraq. This suggests that our study results may indeed be representative of the whole Jordanian community.

## 5. Conclusions

The current study clearly demonstrates the lack of pharmacists' knowledge about isotretinoin therapy and the need to implement educational and training programs in order to improve pharmacists' awareness of several aspects of isotretinoin dispensing practice. This includes ensuring the availability of prescriptions, the appropriate indication, making medication reviews, the appropriate duration of isotretinoin use, isotretinoin administration, and counseling on isotretinoin use with regard to pregnancy, particularly for female pharmacists, pharmacists with fewer years of work experience, and those who do not have a postgraduate degree in pharmacy.

## Ethical statement

Ethical approval of this study was obtained from the Institutional Review Board of King Abdullah University Hospital and Jordan University of Science and Technology. The IRB reference is 48/118/2018.

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## Data availability statement

Data will be made available on request.

## CRedit authorship contribution statement

**Anan S. Jarab:** Writing – review & editing, Validation, Supervision, Project administration, Methodology, Conceptualization. **Sayer I. Al-Azzam:** Visualization, Resources, Project administration, Methodology, Formal analysis, Conceptualization. **Shriefa Al-Mutairi:** Writing – original draft, Resources, Investigation, Formal analysis, Data curation, Conceptualization. **Shrouq Abu Heshmeh:** Writing – original draft, Methodology, Formal analysis, Data curation. **Tareq L. Mukattash:** Writing – review & editing, Validation, Methodology, Conceptualization. **Walid AL-Qerem:** Writing – review & editing, Validation, Formal analysis, Conceptualization. **Rami**

**Beiram:** Writing – review & editing, Validation, Methodology, Conceptualization. **Salah Aburuz:** Validation, Supervision, Project administration, Methodology, Conceptualization.

### Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

### Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.heliyon.2023.e22354>.

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