

# **The prevalence of using prescribed & unprescribed “Roaccutane (Isotretinoin)” among females Riyadh, Saudi Arabia: A cross sectional study**

## **Abstract**

### **Background**

Isotretinoin (Roaccutane) is a synthetic vitamin A derivative, it is one of the most effective medications and one of the common prescribed medications in dermatology for treating acne vulgaris, people should be aware of the side effects of such a medication. side effects of the medications can be mucocutaneous, psychiatric, teratogenic and hepatic.

### **Aims**

**To determine the prevalence of using prescribed and unprescribed Isotretinoin and to assess knowledge of its adverse effects among females in Riyadh, SA.**

### **Materials and methods**

**A questionnaire based cross-sectional study using an online administered. With a sample size of 385 participants. The data will be collected throughout two months by distributing the questionnaire via. social media platforms. Statistical analysis was performed using Rv 3.6.3. Counts and percentages was used to summarize the distribution of categorical variables and data. Chi-square test was used to estimate the association between categorical variables. Hypothesis testing was performed at a 5% level of significance.**

### **Results**

568 respondents completed the questionnaire. Of these, 440 were from Riyadh. The majority of respondents were aged 15 – 20 (46.4%) and 21 – 25 (35.2%). Knowledge regarding some side effects of Roaccutane was significantly higher in respondents who reported using Roaccutane than those who did not. Knowledge of dry and cracked lips as a side effect was significantly higher in users (91.9%) than non-users (73.1%). Similarly, knowledge regarding dry eyes, depression, continuous thirst, nose dryness, bleeds, and effect of Roaccutane on liver biochemical profile, lipid profile, and bones was higher in users than non-users, regarding the teratogenic effect of Roaccutane was insignificantly different between groups.

## **Conclusion**

Females in Riyadh are aware of the side effects of isotretinoin, particularly dryness of the skin, eyes, and lips. Yet there is insufficient knowledge regarding its teratogenic effect. Based on the reported results, a few participants obtained Roaccutane without a prescription from the doctor, and some obtained their information from unreliable sources (i.e., friends/relatives). Our results suggest good practice towards the prescription of isotretinoin.

## **Keywords**

Isotretinoin, Roaccutane, Public health, Awareness, Side effects, Acne vulgaris

UNDER PEER REVIEW

## Introduction

UNDER PEER REVIEW

Isotretinoin, also known as (Accutane or Roaccutane) is a synthetic vitamin A derivative, or retinoid, one of the most common and effective medications for treating acne vulgaris. Acne vulgaris (adolescent acne) is a chronic medical condition affecting the skin, precisely the pilosebaceous follicle, and is mainly characterized by alternating periods of exacerbation and stability, leading to polymorph cutaneous lesions that may leave scars after regression. [1-3] This common condition nearly affects all adolescents. The onset of the appearance of acne among females is usually between 18-20 years, or it may be delayed until 25-30 years. However, it can affect all ages as the risk increases with age, as mentioned in previous literature; in the pediatric population aged 10 to 12 years, 28% to 61% of the population has been clinically diagnosed with acne vulgaris. On the contrary, 79% to 95% of 16 to 18 years old adolescents are affected. [3-8] In 1982, Isotretinoin was proved by FDA (Food and Drug Administration) as a treatment for acne. [1][2] In addition, substantial studies recommended the use of Isotretinoin for treating acne more than other agents, as it is a highly effective agent. As known, this is not the only use of Isotretinoin; it can also act as a chemotherapeutic agent as it can treat various types of cancers, according to literature. [9][10] Moreover, Previous studies showed that the use of Isotretinoin is associated with many said effects; the most observed and identified side effect was mucocutaneous such as retinoid dermatitis, severe retinoid cheilitis, epistaxis, dry eyes, or conjunctivitis, which are dose-dependent predictable side effects. Among adolescents, mood changes, including depression, are commonly reported; other psychiatric manifestations such as anxiety and suicidal thoughts are still controversial. [11-13] Teratogenicity is well known and regarded as one of the most severe and devastating adverse effects. According to FDA and previous literature, Isotretinoin causes congenital disabilities, abortion, and premature births. The recognized and known embryopathy pattern includes severe craniofacial, central nervous system, cardiovascular, and thymic malformations. Ear abnormalities include microtia, low set ears, and anotia; central nervous system defects include microcephalus, hydrocephalus, and reduction malformations of the brain; cardiovascular defects include transposition of the great arteries, tetralogy of Fallot, ventral septal defects, and aortic arch abnormalities. [11],[14-16] Due to this concern, the Saudi Food and Drug Authority (SFDA) started implementing a pregnancy prevention program (PPP) to raise the awareness of females regarding the teratogenic effects of

**Isotretinoin.** The program involves signing a medical consent form by the female user, contraceptive guide, and patient guide. The consent aims to prevent potential severe congenital disabilities that Isotretinoin may cause. The consent includes information and warnings about Isotretinoin use [17]. Through intensive literature, there was a couple of previous research with a similar aim around Saudi Arabia; However, there was no study conducted in the capital of Saudi Arabia that Measure the awareness of females and their knowledge about side effects of Isotretinoin, also the prevalence of using prescribed and unprescribed of this type of treatment.

UNDER PEER REVIEW

## **Objectives**

- **To determine the prevalence of using prescribed & unprescribed Isotretinoin (Accutane or Roaccutane) among females in Riyadh, SA.**
- **To assess the knowledge about indication and adverse effects of Isotretinoin (Accutane or Roaccutane) among females in Riyadh, SA.**

## **Methods**

**This study will utilize a cross-sectional design using an online-administered questionnaire distributed over multiple social media platforms. The sample size is estimated to be 385 participants, large enough to reach a confidence interval of 95% as calculated using the Raosoft Sample Size Calculator (Raosoft, Inc. Seattle, WA). The data will be collected throughout two months by distributing the survey over social media platforms. The instrument is derived from an intensive literature review. After developing the questionnaire, it will be translated into Arabic and validated via running a pilot testing on twenty random participants to recognize any issues related to context and content. The questionnaire comprises 16 questions (yes/no questions, multiple choices, short answers, and check-boxes). Those questions were divided into two sections: section A was related to demographic data regarding the participant; section B was to assess their knowledge regarding the use of Isotretinoin and the method of prescription. All participants will receive written consent before completing the questionnaire. Consequently, Statistical analysis will be performed using R v 3.6.3. Counts and percentages will be used to summarize the distribution of categorical variables. A Chi-square test will be used to estimate the association between categorical variables. Hypothesis testing will be performed at a 5% level of significance. Data will be summarized using counts and percentages.**

## **Inclusion criteria**

1. Any Female participants willing to fill the survey.
2. Living in Riyadh, Saudi Arabia.
3. Age 15 years and above.

## **Exclusion criteria**

1. Participants younger than 15 years,
2. Currently living outside of Riyadh Saudi Arabia
3. Participants with disabilities that prevents them from filling the survey

## Results

Table 1. Sociodemographic characteristics of the included respondents

	[ALL]	N
	<i>N=440</i>	
<b>Age:</b>		440
15-20	204 (46.4%)	
21-25	155 (35.2%)	
26-30	29 (6.59%)	
31-35	22 (5.00%)	
41-45	16 (3.64%)	
45+	14 (3.18%)	
<b>Marital status:</b>		440
Divorced	7 (1.59%)	
Married	63 (14.3%)	
Single	369 (83.9%)	
Widowed	1 (0.23%)	
<b>Highest educational level:</b>		440
Middle school	4 (0.91%)	
High school	125 (28.4%)	
Bachelor	293 (66.6%)	
Post-graduate	18 (4.09%)	
Data were summarized using counts and percentages		

Five hundred sixty-eight respondents completed the questionnaire. Of these, 440 were from Riyadh. The majority of respondents were aged 15 – 20 (46.4%) and 21 – 25 (35.2%). Single respondents represented 83.9% of the study sample, and 14.3% were married. Regarding education, 66.6% of the respondents had a bachelor's degree, and 28.4% completed only high school.

Table 2. prevalence and awareness regarding the use of Roaccutane

	[ALL]	N
	<i>N=440</i>	
<b>Ever used Roaccutane</b>		440
No	279 (63.4%)	
Yes	161 (36.6%)	
<b>Any relatives use Roaccutane</b>		161
No	23 (14.3%)	
Yes	138 (85.7%)	
<b>Source of information regarding Roaccutane and its uses</b>		161
Dermatologist	79 (49.1%)	
Friends and relatives	74 (46.0%)	
Social media	8 (4.97%)	
<b>Roaccutane prescribed by a physician</b>		161
No (Available without prescription)	3 (1.86%)	

Yes	158 (98.1%)	
<b>Laboratory investigations performed before using Roaccutane</b>		161
No	8 (4.97%)	
Yes	153 (95.0%)	
<b>Duration of Roaccutane use:</b>		161
< 2 months	10 (6.21%)	
2 - 3 months	21 (13.0%)	
3 - 5 months	65 (40.4%)	
6 - 12 months	49 (30.4%)	
1+ year	16 (9.94%)	
<b>Roaccutane use:</b>		161
Continuous	137 (85.1%)	
Intermittent	24 (14.9%)	
<b>Aware of Roccutane's side effects:</b>		161
No	10 (6.21%)	
Yes	151 (93.8%)	
Data were summarized using counts and percentages		

One-third of the respondents reported using Roaccutane (n = 161, 36.6%) and 63.4% did not. Of those who used Roaccutane, 85.7% reported knowing relatives who used it. The source of information regarding Roaccutane and its uses varied between respondents. The dermatologist was the main source of information in 49.1% of the cases, while friends and relatives were the main sources in 46%. Social media was the main source of information in the remaining 4.97% of the respondents. All but three respondents (98.1%) mentioned that a physician prescribed Roaccutane. The great majority of the respondents reported doing laboratory investigations before using Roaccutane (95%). The duration of use varied between respondents, with only 6.21% and 9.94% reporting its use for < 2 months and 1+ year, respectively. The majority of the respondents reported using Roaccutane for 3 – 5 months (40.4%) and 6 – 12 months (30.4%), respectively. The use of Roaccutane was continuous in 85.1% of the cases and intermittent in the remaining 14.9%. Most of the respondents were aware of the side effects of Roaccutane (93.8%).



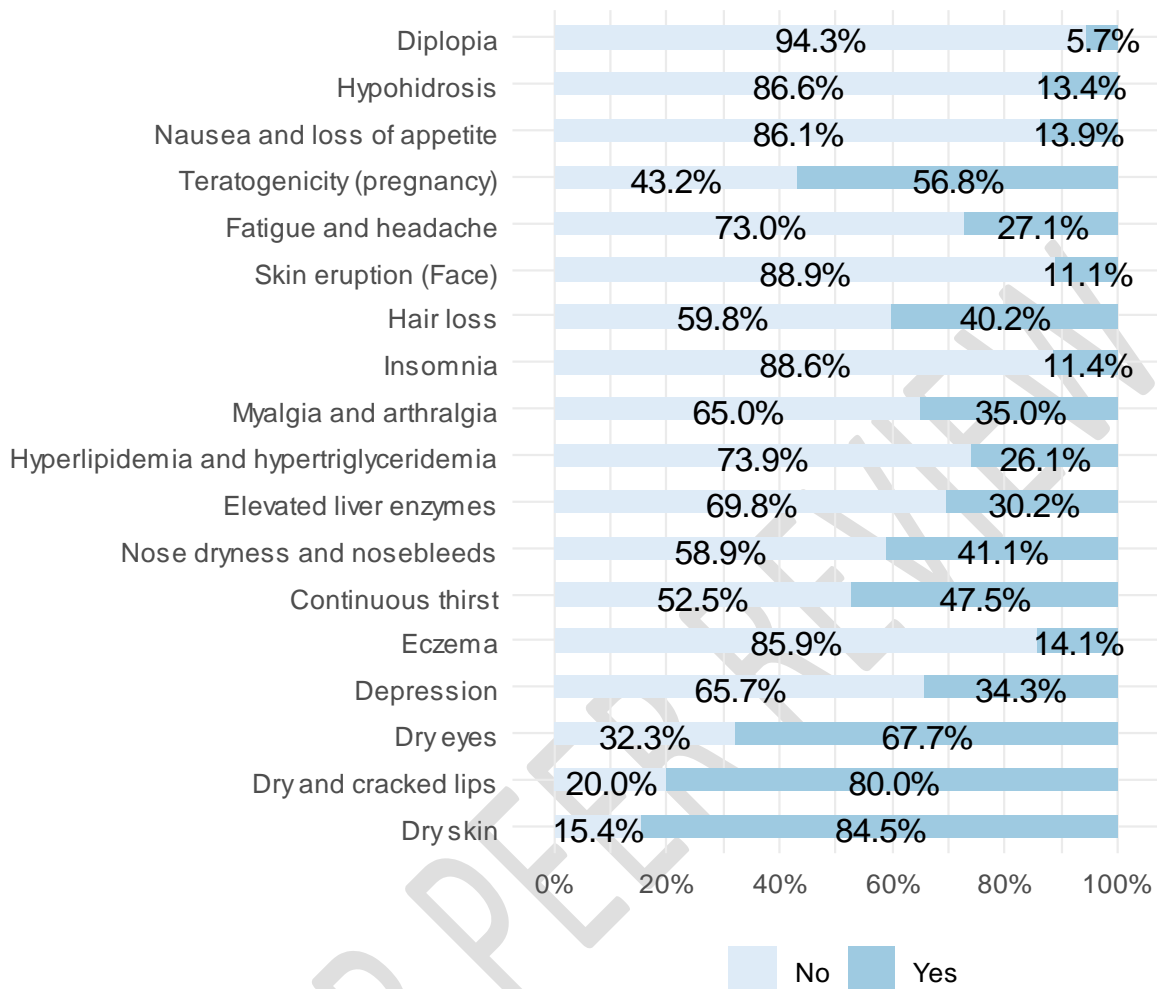


Figure 1. Awareness regarding side effects of Roaccutane

All respondents were asked to identify the side effects of Roaccutane (n = 440). The most commonly identified side effects of Roaccutane were dry skin (84.5%), dry/cracked lips (80%), and dry eyes (33.6%). The least commonly identified side effects were diplopia (5.7%), hypohidrosis (13.4%), and nausea/loss of appetite (13.9%).

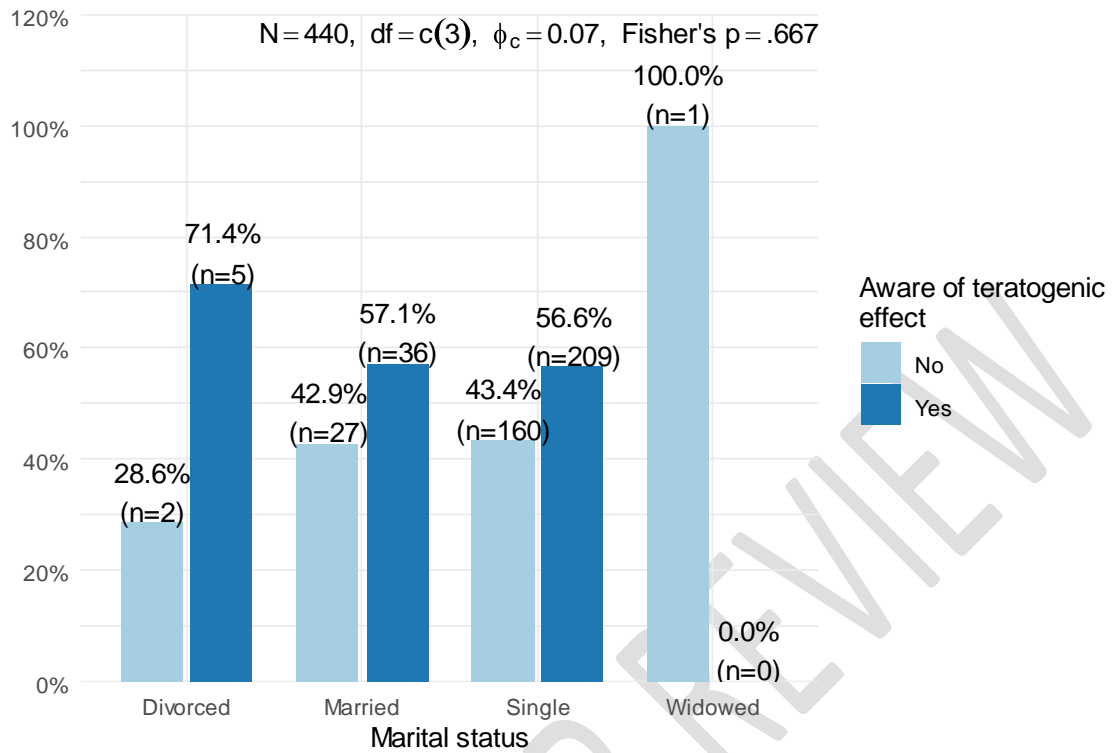


Figure 2. Knowledge regarding the teratogenic effect of isotretinoin stratified by marital status

Results showed that knowledge regarding the teratogenic effect of Isotretinoin was low across all age groups and was lowest in respondents aged 15 – 20 years old.

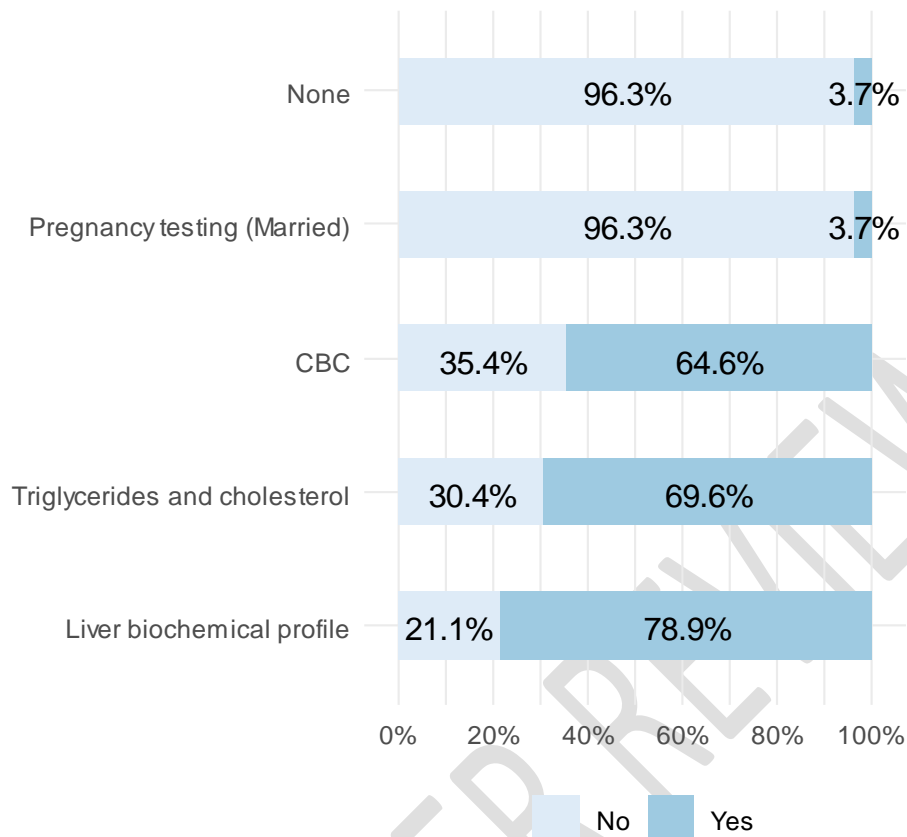


Figure 3. Laboratory investigations performed before using Roaccutane

Respondents who used Roaccutane were asked to identify the laboratory investigations performed before its use (n = 161). Liver biochemical profile was performed by 78.9% of the users. Triglycerides and cholesterol levels were checked by 69.6% of the respondents, and CBC was performed by 64.6% of the users. Pregnancy testing was performed by 3.7% of the users.

	Non-users	Users	p.overall
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	<i>N=279</i>	<i>N=161</i>	
Dry skin:	231 (82.8%)	141 (87.6%)	0.230
Dry and cracked lips:	204 (73.1%)	148 (91.9%)	<b>&lt;0.001</b>
Dry eyes:	162 (58.1%)	136 (84.5%)	<b>&lt;0.001</b>
Depression:	78 (28.0%)	73 (45.3%)	<b>&lt;0.001</b>
Eczema:	34 (12.2%)	28 (17.4%)	0.171
Continuous thirst:	144 (51.6%)	65 (40.4%)	<b>0.030</b>
Nose dryness and nosebleeds:	84 (30.1%)	97 (60.2%)	<b>&lt;0.001</b>
Elevated liver enzymes:	67 (24.0%)	66 (41.0%)	<b>&lt;0.001</b>
Hyperlipidemia and hypertriglyceridemia:	45 (16.1%)	70 (43.5%)	<b>&lt;0.001</b>
Myalgia and arthralgia:	66 (23.7%)	88 (54.7%)	<b>&lt;0.001</b>
Insomnia:	31 (11.1%)	19 (11.8%)	0.949
Hair loss:	98 (35.1%)	79 (49.1%)	<b>0.006</b>
Skin eruption (Face):	36 (12.9%)	13 (8.07%)	0.163
Fatigue and headache:	55 (19.7%)	64 (39.8%)	<b>&lt;0.001</b>
<b>Teratogenicity (pregnancy):</b>	<b>154 (55.2%)</b>	<b>96 (59.6%)</b>	<b>0.422</b>
Nausea and loss of appetite:	38 (13.6%)	23 (14.3%)	0.959
Hypohidrosis:	43 (15.4%)	16 (9.94%)	0.139
Diplopia:	16 (5.73%)	9 (5.59%)	1.000
Counts and percentages were used to summarize the responses statistical analysis was performed using Chi-square test of independence			

Table 3. Association between Roaccutane use and its side effects

Results showed that knowledge regarding some side effects of Roaccutane was significantly higher in respondents who reported using Roaccutane than those who did not. Knowledge regarding dry and cracked lips was significantly higher in users (91.9%) than non-users (73.1%). Similarly, knowledge regarding dry eyes, depression, continuous thirst, nose dryness, and bleeds was higher in users than non-users. Knowledge regarding the effect of Roaccutane on liver biochemical profile, lipid profile, and bones was also higher in users than non-users. Knowledge regarding the teratogenic effect of Roaccutane was not significantly different between groups.

## Discussion

Emotional, Physical, and scarring are significant burdens of acne in patients of various ages. Effective regimens are readily available. However, consistent and accurate use of these regimens is required for effective disease management, reduced risk for scarring, and enhancing various factors that affect the quality of life [18]. The rise in hormonal levels during puberty causes the formation of acne. The presence of other diseases such as polycystic ovary syndrome (PCOS) can also affect the appearance of acne [19]. Sensitive skin, lifestyle-related stress, using full-coverage foundations, and discontinuation of oral contraceptives increase the severity of acne [20]. Roaccutane or Isotretinoin is an oral vitamin A derivative, considered one of the most effective options for managing severe acnes [21]. Advantages of Isotretinoin include cost-effectiveness, especially when compared with other medications used to treat severe acne. However, it is teratogenic when used during pregnancy and can cause congenital disabilities,

such as severe cardiovascular, craniofacial, thymic, and central nervous system malformations [16]. Patients who suffer from acne know about isotretinoin drugs in one way or other. However, some patients may hesitate from starting this drug due to a lack of information about the drug. Proper understanding and awareness regarding the drug and its side effects help minimize adverse effects and increase compliance. The current study aimed to assess the use and awareness regarding the side effects of Isotretinoin in female patients in Riyadh. A similar study was conducted in Riyadh recently. However, the distribution of age was similar to that observed in the current study. In the study conducted by Ibrahim and colleagues, the majority of the respondents were aged 20 – 30 years old [22]. In this study, one-half of the respondents were aged 15 – 20 years old, and 42% were aged 21 – 30 years old, which adds to the existing knowledge regarding Isotretinoin and awareness regarding its side effects. Nonetheless, a discrepancy was observed in the knowledge regarding the teratogenic effect of Isotretinoin. A previous study was done in Riyadh showed that ~90% of the respondents were aware of the side effects of Isotretinoin [22]. Also, a study conducted in Eastern Saudi Arabia showed that 88% of the respondents were aware of the teratogenic effect of Isotretinoin [23]. The results in this study were not comparable to these two previous studies, which showed that 56.8% of the respondents were not aware of the teratogenic effect of Isotretinoin [22]. The insufficient knowledge regarding the teratogenic effect of Roaccutane can be explained by the high number of single participants included in this study (83%) compared to other studies and the low number of isotretinoin users included in the current study (36%). Thus, it can be expected that knowledge regarding Isotretinoin and its teratogenic effect would be higher if the users were married, of childbearing age, previously used, or are currently using Isotretinoin as was the case in a cross-sectional study conducted in Makkah [24]. Another explanation would be the source of information regarding Isotretinoin, with 50% of the respondents relying on relatives/friends or social media as a source of information. Nonetheless, our results are also consistent with those reported in another cross-sectional study in Western Saudi Arabia which showed even lower knowledge regarding the teratogenic effect of Isotretinoin [25]. The similarity in knowledge can be explained by the similarities in the demographic characteristics (marital status and age), particularly the lower age of the included participants. These results suggest that knowledge regarding the teratogenic effect of Isotretinoin is still suboptimal, a finding which is supported by evidence from another recent cross-sectional study [26]. Dryness of the skin, eyes, and lips were the top three side effects identified by the respondents, followed by nose dryness and bleeding. These results are similar to those reported in several cross-sectional studies [24,25,27], where the dryness of the eyes, lips, and skin were the most common side effects. On the other hand, the least experienced side effect was depression; this result is consistent with what was observed in previous studies [13,28]. In this study, most respondents who used Isotretinoin (95%) performed at least one of the needed laboratory investigations before using Isotretinoin. A study conducted in 2019 in Eastern Saudi Arabia showed that half of the participants (44.2%) used Isotretinoin with only mild acne as their first choice, which is not consistent with the current guidelines. The study also showed that one-fifth of the respondents did not assess the blood glucose level, lipid profile, liver enzymes before starting isotretinoin [23]. These results are in line with what was observed in this current study. One-third of the respondents did not assess cholesterol or

triglyceride levels, one-third did not perform a complete blood count (CBC), and one-fifth did not perform a liver biochemical profile. Interestingly, only 3.7% of the respondents did pregnancy testing before using the medication. A study conducted in Riyadh found that knowledge regarding the teratogenic effects of Isotretinoin was low and recommended improvement in the risk reduction counseling skills [29]. Many women using Isotretinoin do not monitor for pregnancy before and during the use of Isotretinoin. Only 44%–67% of women reported doing a pregnancy test before starting Isotretinoin, and only 20% reported taking a repeated pregnancy test [30]. Moreover, most women use over-the-counter (OTC) pregnancy tests for human chorionic gonadotropic (HCG) hormone, which is characterized by low sensitivity and may cause false-negative results, especially if done shortly after conception [31]. Repeat testing may help detect pregnancy and earlier termination of treatment or pregnancy [32]. We suggest that the difference regarding the teratogenic effect of Isotretinoin can somewhat be explained by the source of information regarding Isotretinoin, where dermatologists were the primary source of information in only 50% of the included respondents. At the same time, friends, relatives, and social media were the primary source in the remaining 50%. It has also been suggested that a contraceptive information sheet can significantly improve the knowledge of the patients regarding contraception and may prevent isotretinoin-induced congenital disabilities [33]. The knowledge regarding the side effects of Isotretinoin was significantly higher in users than non-users previously reported in the literature [12,25].

## **Limitations**

The current study had several limitations. First, the data were self-reported. Thus, it is subjected to inaccuracy. The nature of the study design limits and may affect the generalizability of the results due to the introduction of different types of biases. This issue might cause selection or sampling bias. We did not assess the knowledge regarding contraceptive methods employed when using isotretinoin according to the Pregnancy Prevention Program (PPP) guidelines employed by the Saudi Food and Drug Authority (SFDA). We also did not assess the severity of the acne in the included respondents, which might affect the use of isotretinoin. Moreover, this paper only focused on females and males were not included. The side effects of Roaccutane were presented as a check-box question. Thus, the teratogenicity option might have been missed by some respondents.

## **Conclusion**

Results suggest that women in Riyadh, Saudi Arabia, are somewhat aware of the side effects of isotretinoin, particularly dryness of the skin, eyes, and lips. Results also showed insufficient knowledge regarding its teratogenic effect. Based on the reported results, some of the included patients did not do the needed tests such as pregnancy tests and blood tests before starting isotretinoin. Moreover, some study participants obtained Roaccutane without a prescription from the doctor, and some obtained their information from unreliable sources (i.e., friends/relatives ,internet). In conclusion, our results suggest good practice towards the prescription of isotretinoin. Knowledge regarding isotretinoin and its use should be disseminated in the community to prevent possible teratogenicity from its use. Therefore, we encourage rising awareness regarding Saudi FDA pregnancy prevention program to prevent future incidents.

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