



## Awareness about venous thromboembolism among Saudi females who use oral contraceptive pills: a descriptive cross-sectional study

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### Abstract:

**Background:** Oral contraceptive pills (OCPs) are a widely used method of contraception, and use of OCPs is a well-known risk factor for venous thromboembolism (VTE). This study aimed to assess the level of awareness of the association between OCP use and the risk of VTE and the level of knowledge of symptoms and signs of VTE among Saudi females who are users of OCPs.

**Methods:** This cross-sectional study was conducted among the Saudi female population between October and November 2020. Knowledge about VTE risk with the use of OCPs and awareness of VTE symptoms and signs among Saudi females were assessed using a structured online questionnaire distributed through social media platforms.

**Results:** Of 1173 participants, 726 used or had been using OCPs. Only 329 (45%) and 303 (41%) were aware of deep vein thrombosis (DVT) and pulmonary embolism (PE), respectively, as a medical condition, while 312 (43%) were aware of the association of OCPs use with DVT risk. Leg swelling was the most commonly identified symptom of DVT in 297 patients (40%), while shortness of breath was the most common symptom of PE in 331 patients (46%).

**Conclusion:** This study showed that the Saudi female population had a low level of knowledge and awareness of DVT and PE in OCP users. Efforts are needed to increase awareness of these preventable diseases in the Saudi female population.

### Introduction:

Venous thromboembolism (VTE), includes deep vein thrombosis (DVT) and pulmonary embolism (PE), is a common disease that leads to substantial morbidity, mortality, and healthcare costs (1). The worldwide incidence of VTE is 1 per 1000 individuals annually (2). Surgery, hospital admission, immobility, pregnancy, and oral contraceptive pills (OCPs) are independent risk factors for VTE (3). An association between OCP use and increased risk of VTE was observed in the first reported case in 1961 after contraception use gained approval in 1960 (4). This association was later confirmed in many studies (3,5,6). Since then, estrogen doses have been reduced to less than 35 µg in most cases of OCP. Studies also showed a direct correlation between estrogen dose and VTE risk (7). OCPs are the most commonly used method of contraception, with more than 100 million users worldwide (4). A variety of OCPs with different estrogen doses and progestin types are available. The mechanism of estrogen-

induced thrombosis is currently unclear; however, increased levels of von Willebrand factor; factors II, VII, VIII, X; and fibrinogen and decreased levels of protein S were observed in users of OCP containing estrogen (6). Moreover, recent studies have shown an increased risk of VTE among third and fourth generations of progesterone with similar estrogen doses. The frequency of OCP use among Saudi females ranges from 27% to 74.9% (8,9). Globally, public awareness of VTE has been limited (10-12). This study therefore aimed to evaluate the level of awareness of the association between OCP use and VTE risk and the level of knowledge about VTE symptoms and signs among Saudi females who are users of OCPs.

### Methodology:

A descriptive cross-sectional study was conducted to evaluate the level of knowledge about the risk of VTE with the use of OCPs and the level of awareness of VTE symptoms and signs among the Saudi female population. For this purpose, we used a structured online questionnaire

that was distributed through social media platforms and WhatsApp groups to female populations with diverse education levels, socioeconomic status, and background characteristics. All Saudi women aged 14–65 years were included. Ethical approval was granted by the ethical committee of the College of Medicine, Imam Mohammad Ibn Saud Islamic University. Data were collected for one month, from October 7, 2020, to November 7, 2020, and a sample size of 1300 individuals was achieved. One hundred twenty-seven individuals were excluded because they were non-Saudi responders; the final sample was therefore 1173. Data of demographic characteristics, age, education level, occupation, use of OCPs, type and indication of OCPs, and symptoms and signs of PE and DVT were collected. The questionnaire was revised by a thrombosis specialist and gynecologist to increase the reliability and validity of the results. The questionnaire was developed in English and then translated to Arabic; the translated version was reviewed by a specialist in gynecology and thrombosis, and tested on a sample of 46 participants. Before starting the survey, a message stating that answering questions is considered a consent to use the results for medical research. Additionally, a completion message was showed at the end of the survey.

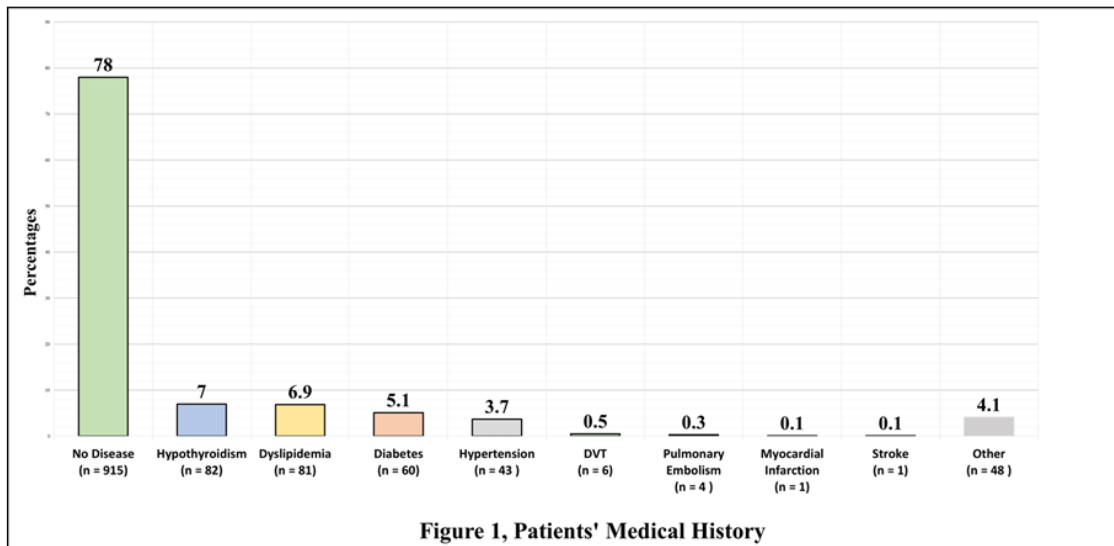
Data analysis was performed using the Statistical Package for the Social Sciences, SPSS 23rd version. Categorical variables were expressed as frequency and percentages. Bivariate and multivariate logistic regressions were also performed to determine factors predicting DVT as a possible complication of using OCPs. P values less than 0.05 were considered statistically significant.

### Results:

A total of 1173 women participated in this study. Almost all the participants were living in Saudi Arabia. The majority of them were living in four major cities (Riyadh, Makkah, Jeddah, and Dammam), and more than half were living in Riyadh. Sixty percent of the participants were aged 18–39 years, followed by 40–60 years (30%). Two-thirds of the participants were married; details of socio-demographic data are shown in Table 1. Hypothyroidism, dyslipidemia, and diabetes, which accounted for 82 (7%), 81 (6.9%), and 60 (5.1%), were the most common chronic diseases in participants; however, 78% had no chronic diseases (Figure 1).

**Table 1: Sociodemographic profile of the participants (n = 1173)**

Table 1: Sociodemographic profile of the participants (n = 1173)		
Age		
14 - 17	112	9.50
18 - 39	705	60.10
40 - 60	349	29.80
> 60	7	0.60
Are you currently living in Saudi Arabia		
Yes	1164	99.2
No	9	0.8
Place of Residency		
Riyadh	771	65.70
Jeddah	103	8.80
Makkah	38	3.20
Dammam	47	4.00
Others	214	18.20
Marital Status		
Single	401	34.2
Married	728	62.1
Divorced	26	2.2
Widowed	18	1.5
Education		
Undergraduate and lower	279	23.8
University Degree	791	67.4
Post-graduates including, Master, and PhD	103	8.8
Occupation		
Unemployed	390	33.2
Student	333	28.4
Employee	369	31.5
Retired	81	6.9
Smoking		
Not smoker	1108	94.5
I was but I quitted Smoking	17	1.4
Yes, I am a smoker	48	4.1



The total number of participants who used OCPs was 726 (62%). At the time of data collection, 232 (19.8%) participants were using OCPs, 494 (42.1%) used OCPs in the past, and 447 (38.1%) never used them. OCPs were prescribed for the first time in 573 (80%) of participants by the physicians, 88 (12%) by the patients themselves, 43 (6%) by non-health care provider recommendation, and 14 (2%) by the pharmacist. Half of the participants used OCPs for more than 18 months (Table 2).

**Table 2: Contraception experience among participants who were users.**

	n	%
Question Directed to Those Who Used Oral Contraception Before		
Less than 3 months	109	15.1
3 - 6 months	79	11
6 - 9 months	33	4.6
9 - 12 months	76	10.5
12 - 18 months	85	11.8
More than 18 months	339	47
A doctor	573	79.8
A pharmacist	14	1.9
I bought it without prescription	88	12.3
A recommendation from a non-health care provider.	43	6
A non-health care provider.	110	15.20
A pharmacist	150	20.70
I bought it without a prescription	190	26.20
Progestin Only	41	5.6
Progesterone and estrogen	248	34.2
I don't know	437	60.2

The most common indications for OCP use were contraception in 626 (86.2%) participants, menstruation regulation in 105 (14.5%) participants, and polycystic ovarian syndrome in 71 (9.8%) participants. The most commonly known side effects were mood swings in 784 (66.8%) participants and headache 597 (50.9%) participants, followed by weight gain in 500 (42.6%), hypertension in 459 (39.1%), and nausea in 434 (37%); however, 50% of participants were not aware of any side effects.

Of 726 OCP users, 312 (43%) were aware of the increased risk of DVT with the use of OCPs, while none of the participants were aware of the increased risk of PE. One-third of all participants, i.e., 417 (35%), were aware that the

use of OCPs increased the risk of DVT, 286 (24.4%) had increased migraine, 199 (17%) had increased breast cancer, and 186 (15.9%) had ectopic pregnancy. Similar to OCP users, none of the participants were aware of the increased risk of PE with the use of OCPs.

Of 1173 participants, 477 (40.7%) and 471 (40.2%) reported knowledge of DVT and PE, respectively as a medical condition, while among participants who used OCPs, 329 (45%) and 303 (41%) reported knowledge of DVT and PE, respectively. More than one-third of all participants (39%) were aware that obesity and family history are additional risk factors for DVT and PE with OCP use, while 32.4% reported age and 31.9% reported smoking as risk factors (Table 3).

**Table 3:**

Comparison of knowledge toward deep vein thrombosis and pulmonary embolism between users of OCP and non-users of OCP

Question	Users of OCP (n=726)	Non-users of OCP (n=447)	P- Value
Yes	329 (45.3%)	148 (33.1%)	< 0.001*
No	397 (54.7%)	299 (66.9%)	
Yes	303 (41.7%)	168 (37.6%)	0.159
No	423 (58.3%)	279 (62.4%)	
Vein thrombosis	414 (57%)	231 (51.7%)	0.001*
Tumors in veins	6 (0.8%)	14 (3.1%)	
Hypoxia	23 (3.2%)	27 (6%)	
I don't know	283 (39%)	175 (39.1%)	
Yes	149 (20.5%)	79 (17.7%)	0.115
No	83 (11.4%)	39 (8.7%)	
I don't know	494 (68%)	329 (73.6%)	
Age	255 (35.1%)	125 (28%)	0.011
Obesity	286 (39.4%)	171 (38.3%)	0.698
Smoking	228 (31.4%)	146 (32.7%)	0.654
Family History of DVT	289 (39.8%)	178 (39.8%)	0.996
I don't know	259 (35.7%)	180 (40.3%)	0.114

OCP: Oral contraceptive pill

\* Significant level at 0.05

Among OCP users, the most commonly recognized symptoms or signs of DVT were leg swelling (41%), followed by leg pain and leg discoloration (32%), while those of PE were shortness of breath (45%), chest pain (34%), and palpitation (18%). Incorrect symptoms or signs were included to validate the measures of awareness. Paralysis of the leg (13%) in DVT and arm pain (12%) in PE were believed to be related symptoms or signs (Table 4).

**Table 4:**

Comparison of knowledge toward signs and symptoms of deep vein thrombosis and pulmonary embolism			
Question	Users of OCP (n=726)	Non-users of OCP (n=447)	P- Value
Leg Swelling	297 (40.9%)	189 (42.3%)	0.643
Leg Discoloration	236 (32.5%)	163 (36.5%)	0.165
Leg Pain	241 (33.2%)	127 (28.4%)	0.086
Leg Paralysis	97 (13.4%)	78 (17.4%)	0.056
Leg Warmth	59 (8.1%)	33 (7.4%)	0.645
Leg Itching	28 (3.9%)	19 (4.3%)	0.738
I Don't Know	298 (41%)	204 (45.6%)	0.123
Shortness of Breath	331 (45.6%)	203 (45.4%)	0.952
Chest Pain	243 (33.5%)	171 (38.3%)	0.096
Palpitation	134 (18.5%)	135 (30.2%)	< 0.001*
Deep Rapid Breathing	130 (17.9%)	100 (22.4%)	0.061
Bloody Cough	63 (8.7%)	87 (19.5%)	< 0.001*
Arm Pain	90 (12.4%)	44 (9.8%)	0.182
Dizziness	62 (8.5%)	53 (11.9%)	0.064
I Don't Know	324 (44.6%)	199 (44.5%)	0.971

OCP: Oral contraceptive pills

\* Significant level at 0.05

In multivariate logistic regression analysis, higher education, residence in major cities, and use of OCPs were associated with high awareness of DVT as a risk factor related to the use of OCPs (Table 5).

**Table 5:**

Multivariate logistic regression analysis of factors predicting the identification of DVT as a possible complication of OCP use.				
Age (Older than 40 vs Younger than 40)	0.94	1.01	0.76	1.32
Education (Graduate and above vs Undergraduate)	0.04*	1.38	1.00	1.91
Place of Residency (Major cities vs Non-Major cities)	0.04*	1.42	1.00	2.01
OCP Using State (Used OCP before vs Never used OCP)	< 0.001*	2.30	1.53	3.46
Who Prescribed OCP (A Doctor vs Not a Doctor)	0.58	0.90	0.63	1.3

OCP: Oral contraceptive pill

\* Significant level at &lt;0.05

### Discussion:

OCPs are a widely used method of contraception. In the present study, the frequency of OCP use was 62% among Saudi females. Saudi females were found to have a low level of awareness of DVT and PE as a risk factor related to OCP use. DVT was a known risk factor for OCP use in 34% of all participants and 312 (43%) of participants who used OCP, while PE was not a known risk factor in all participants. However, 40% participants had awareness of DVT and PE as a medical condition. Similar to our result, a global public awareness study reported a low level of awareness of VTE in the general population (44% for DVT and 54% for PE) (10). In a recent cross-sectional study conducted in Riyadh City, Saudi Arabia, evaluated the level of awareness and knowledge of signs and symptoms of VTE and reported relative lack of awareness (38% for PE

and 19% for DVT) [11]. In 340 Saudi pregnant women, the level of knowledge of DVT and PE was determined in 26% and 13% of participants, respectively (12). Lack of awareness was also consistent with the finding of a previous study conducted in Al-Qassim, Saudi Arabia, among women who have attended primary health care centers. That study showed that 50% of participants had a low level of knowledge regarding OCP use (13).

One important factor for evaluating OCP is the current usage or history of usage of OCPs. Our study showed that, among 62% of participants using or have used OCPs in the past, similar to a study conducted in the Riyadh region, 57% used OCP during their lifetime (14). Other studies showed similar numbers, between 40% and 70% (13,15,16). In this study, 20% of the participants were using OCP at the time of the survey, compared to a study that showed 34% of their

respondents were using OCPs (17). Our study showed that the majority of participants who used OCPs had used them for more than 18 months (47%), while 15.1% used them for less than three months. A study conducted in Jeddah reported that in those who used OCP, there was a variation in the duration of use, with 22% having used OCPs for less than a year, 32.7% having used between two and five years, and only 13.1% having used for >5 years (18).

In the present study, the first use of OCPs was prescribed by physicians in the majority of participants (80%), while 88 (12.3%) participants bought the medications without a prescription; for 6% and 1.9% of participants, OCPs were recommended by a non-health care provider and by a pharmacist, respectively. Similarly, another study conducted in Riyadh showed that 15% of the participants used OCPs without medical prescriptions (14).

Estrogen and progestin or progestin-only OCPs are the main types of OCPs prescribed. Of those who used OCPs, 34.2% believed that their medication contained estrogen and progestin and 5.6% thought it contained only progestin, while the majority were unaware of the type of OCPs. The most common indication for OCPs in this study was contraception (86%). Two studies from Saudi Arabia showed the same indications in 70% and 62% of participants (14,18).

Similar to non-OCP users, almost half of OCP users were unaware of any symptoms or signs of DVT or PE. The most commonly identified symptoms of DVT were leg swelling, followed by pain and discoloration. Similar to our results, two studies from Saudi Arabia showed that the most identified symptoms of DVT were leg swelling, followed by pain. Similarly, the most common identified symptoms of PE were shortness of breath, followed by chest pain, in both studies (11,12). The least identified incorrect symptoms of DVT were leg paralysis and leg itching, in 15% and 4%, respectively, while in a global public study, leg paralysis and itching were identified in 35% and 22% of participants, respectively (10).

The limitations of this study include the use of closed-ended questions and survey distribution through social media platforms and WhatsApp groups. However, the sample size of this study was large (n=1173) and included participants from multiple cities in Saudi Arabia, while similar studies were conducted in one city. This study assessed the level of knowledge of VTE risk among OCP users, which has not been assessed previously in Saudi Arabia.

In conclusion, this study showed that Saudi females have a low level of awareness and knowledge about the association between VTE and use of OCPs; moreover, they had a low level of awareness about VTE as a medical condition in addition to knowledge on the symptoms and signs. It is important to encourage physicians/pharmacists to educate patients about the risk of VTE with use of OCPs and increase awareness about the symptoms and signs of VTE through public campaigns and social media.

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