A systematic review and meta-analysis of the prevalence, risk factors, agents and laboratory diagnosis of vulvovaginal candidiasis in Türkiye

Türkiye'de vulvovajinal kandidiyaz prevalansı, risk faktörleri, etkenleri ve laboratuvar tanısına dair sistematik bir derleme ve meta-analizi

İmdat KILBAŞ[1] (ID), Elmas Pınar KAHRAMAN KILBAŞ[2] (ID), İhsan Hakkı ÇİFTÇİ[3] (ID)

ABSTRACT

Objective: Vulvovaginal candidiasis (VVC) is the most common superficial mycosis among women, and it is estimated that 75% of women experience at least one in their lifetime, and about 40-50% have a second exposure. This study aims to determine the prevalence, risk factors, etiological factors and laboratory diagnosis of VVC in Türkiye.

Methods: In the study, original scientific articles for the reporting of VVC epidemiological features published in English and Turkish languages in national and international databases (PubMed, Embase, Scopus, Google Scholar, Web of Science and Turkish Medline) between January 1995 and December 2021 were searched. Electronic databases were searched using various combinations of "vaginal yeast infection", "vaginal candidiasis", "vulvovaginal candidiasis Turkey", "candidal vaginitis", "*Candida* vaginitis", "vaginal candidosis", "Candida species", "epidemiology" key terms.

Results: The mean prevalence of VVC in adult women was found to be 57.91% in all of the 28 included studies, and 68.21% in the 2-18 age group. Considering

ÖZET

Amaç: Vulvovajinal kandidiyazis (VVK), kadınlar arasında en sık görülen yüzeyel mikozdur ve kadınların %75'inin yaşamları boyunca en az bir kez ve bunların da yaklaşık %40-50'sinin ikinci kez maruz kaldığı tahmin edilmektedir. Bu çalışma, Türkiye'de VVK prevalansını, risk faktörlerini, etiyolojik etkenlerini ve laboratuvar tanısını belirlemeyi amaçlamıştır.

Yöntem: Çalışmada, Ocak 1995 ile Aralık 2021 tarihleri arasında ulusal ve uluslararası veri tabanlarında (PubMed, Embase, Scopus, Google Scholar, Web of Science ve Turkish Medline) İngilizce ve Türkçe dillerinde yayınlanan, VVK epidemiyolojik özelliklerinin raporlanmasına yönelik özgün bilimsel makaleler taranmıştır. Elektronik veri tabanlarında "vajinal maya enfeksiyonu", "vajinal kandidiyazis", "vulvovajinal kandidiyazis Türkiye", "kandidal vajinit", "*Candida* vajiniti", "vajinal kandidoz", "*Candida* türleri", "epidemiyoloji"anahtar terimlerinin çeşitli kombinasyonları kullanılarak tarama yapılmıştır.

Bulgular: Dahil edilen 28 çalışmanın tamamında yetişkin kadınlarda VVC prevalansı ortalama %57,91; 2-18 yaş grubunda ise %68,21 olarak bulunmuştur. Etken

[1]Istanbul University, Institute of Health Sciences, Medical Microbiology Doctorate Program, Istanbul
[2]Fenerbahce University, Health Services Vocational School, Department of Medical Laboratory Techniques, Istanbul
[3]Sakarya University, Faculty of Medicine, Department of Microbiology, Sakarya

İletişim / Corresponding Author : Elmas Pınar KAHRAMAN KILBAŞ
Fenerbahçe Üni., Sağlık Hizmetleri MYO, Tıbbi Lab. Teknikleri Bölümü, İstanbul - Türkiye
E-posta / E-mail : elmspnrkk@gmail.com

the causative distribution, the most common *Candida albicans* (54.76%), *Candida glabrata* (24.04%), other *Candida* species (12.29%), *Candida krusei* (3.68%), *Candida kefyr* (3.37%), and *Candida tropicalis* (2.07%) positivity has been reported. In the included studies, the most common predisposing factors of the patients were pregnancy (35.71%) and diabetes (35.71%). When the articles were examined according to the year they were published and the provinces, it was seen that the prevalence of *Candida* did not differ significantly (p>0.05). In the studies, VITEK®2 (bioMérieux, Marcy l'Etoile, France) automatic identification system (15), Germ tube (7) and CHROMagar (7) diagnostic methods were used to identify strains. As a result of the meta analysis, it was determined that there was a high level of heterogeneity among studies (I^2=95.28).

Conclusion: As a result of our meta-analysis study, the prevalence of VVC was found to be high in women and children in Turkey. In addition, it was determined that non-albicans species increased in the etiology of VVK. It has been observed that the incidence of *C. glabrata* species in the etiology of VVC has increased since 1999. Considering that VVK infection increases the susceptibility to other sexually transmitted diseases, as well as the risk of preterm birth and congenital cutaneous candidiasis in pregnant women, it is essential to raise awareness of patients on issues such as treatment follow-up and protection from the disease.

Key Words: Vulvovaginal candidiasis, *Candida albicans*, non-albicans, Türkiye

dağılımına bakıldığında en yaygın *Candida albicans* (%54.76), *Candida glabrata* (%24.04), diğer *Candida* türleri (%12.29), *Candida krusei* (%3.68), *Candida kefyr* (%3.37) ve *Candida tropicalis* (%2.07) pozitifliği bildirilmiştir. Derlenen çalışmalarda hastaların en sık predispozan faktörleri gebelik (%35.71) ve diyabet (%35.71) belirlenmiştir. Makaleler yayınlandıkları yıl ve illere göre incelendiğinde; *Candida* prevalansının anlamlı farklılık göstermediği görülmüştür (p>0,05). Çalışmalarda suşların tanımlanması için VITEK®2 (bioMérieux, Marcy l'Etoile, Fransa) otomatik tanımlama sistemi (15), Germ tüpü (7) ve CHROMagar (7) tanı yöntemleri kullanılmıştır. Meta analiz sonucunda çalışmalar arasında yüksek düzeyde heterojenite olduğu belirlenmiştir (I^2=95,28).

Sonuç: Meta-analiz çalışmamız sonucunda; Türkiye'de kadınlarda ve çocuklarda VVK prevalans oranı yüksek bulunmuştur. Ayrıca VVK etiyolojisinde albicans dışı türlerin arttığı tespit edilmiştir. 1999 yılından günümüze geldikçe VVK etiyolojisinde *C. glabrata* türlerinin görülme sıklığının arttığı görülmüştür. VVK enfeksiyonunun cinsel yolla bulaşan diğer hastalıklara karşı duyarlılığı ve ayrıca gebelerde erken doğum, konjenital kütanöz kandidiyaz riskini arttırdığı göz önünde bulundurulduğunda, tedavi takibi ve hastalıktan korunma gibi konularda hastaların bilinçlendirilmesi esastır.

Anahtar Kelimeler: Vulvovajinal kandidiyaz, *Candida albicans*, non-albicans, Türkiye

INTRODUCTION

Vulvovaginal candidiasis (VVC) is a significant health problem that includes signs and symptoms associated with infections caused by Candida species. VVC is the most common superficial mycosis among women, and it is estimated that 75% of women experience at least one exposure in their lifetime, and about 40-50% have a second exposure (1).

Although *C. albicans*, *C. glabrata*, *C. parapsilosis*,

C. krusei and *C. tropicalis* are the most frequently reported VVC agents, it has been stated that *C. albicans* is a species responsible for 80-95% of all VVC infections. However, it has been reported that the rate of cases caused by *C. glabrata* has increased significantly in the last two decades (2,3). Although there is usually only one type of causative agent in the etiology of VVC, two or more Candida species were found to be causative in 1-10% of women. The association of *C. albicans* and *C. glabrata* is more common in VVC infections with more than one agent (2).

In the formation of VVC; different factors such as hygienic habits, pregnancy, diabetes, immunosuppressive diseases and the administration of hormonal contraceptives, hormone replacement therapy, chemotherapy, reproductive age, use of broad-spectrum antibiotics and steroids can play a predisposing role for infections (4,5).

Although VVC is common, the exact incidence of this infection is unknown. Because there is no notification requirement, it can be diagnosed clinically without laboratory confirmation. Also, due to the widespread use of over-the-counter treatments, many VVC patients do not apply to the hospital. The primary diagnostic method of this infection is the fungal examination (direct examination of vaginal discharge with 10% KOH together and culture). It should be noted that culture-based epidemiological reports alone increase the incidence of the disease. Because 10% of women are colonized and culture-positive but asymptomatic (6,7).

VVC emerges as a problem that has increasing importance for our country and the whole world and needs to be taken seriously. Unfortunately, it is a disease with almost no clinical-laboratory cooperation. There is no standard treatment scheme in many clinics, and there is no algorithm for diagnosis in the relevant guidelines. In addition, non-culture-based diagnostic tests are used irregularly in our country to diagnose of VVC. Molecular tests are not available in routine laboratories. This study, in order to draw attention to current problems and contribute to solution-oriented approaches; It is aimed to examine the prevalence of VVC in Turkey, the distribution of the agents, the predisposing factors, the demographic characteristics of the patients and the methods used in the diagnosis by systematic review and meta-analysis method.

MATERIAL and METHOD

This systematic review and meta-analysis were conducted based on the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines (8). In the study, original scientific articles published in English and Turkish languages in national and international databases (PubMed, Embase, Scopus, Google Scholar, Web of Science and Turkish Medline) between January 1995 and December 2021 were searched.

For all English and Turkish population-based studies reporting the prevalence of VVC in women in Turkey; in all electronic databases, "vajinal maya enfeksiyonu", "vajinal kandidiyazis", "vulvovajinal kandidiyazis Türkiye", "kandidal vajinit", "Candida vajiniti", "vajinal kandidoz", "Candida türleri", "epidemiyoloji", "vaginal yeast infection", "vaginal candidiasis", "vulvovaginal candidiasis Turkey", "candidal vaginitis", "Candida vaginitis", "vaginal candidosis", "Candida species", "epidemiology" various combinations of the key terms were used. Scanning and collection of related articles were done by three authors. The authors independently evaluated the publications for inclusion in the study, and inconsistencies were discussed and agreed upon by the authors.

Inclusion criteria for the study consisted of original articles reporting the prevalence of vulvovaginal candidiasis and causative organisms diagnosed according to laboratory results of women living in Turkey.

Studies with a sample group of fewer than 20 cases, not reporting the total number of patients or

isolates, not reporting the agent at the species level, only colonization or sporadic VVC studies reporting recurrent vulvovaginitis/chronic vulvovaginitis/atrophic vaginitis, reviews without original data, theses, case reports, case series, letters to the editor, studies with inconsistent data and congress papers were excluded from the scope of the study within the framework of exclusion criteria (Figure 1).

The titles and abstracts were evaluated in the pre-reading process, and the full texts of the studies that the authors found appropriate by consensus were reached. Microsoft Excel spread sheets were

Figure 1. PRISMA flowchart showing the literature search and study selection strategy

| Total studies searched by keywords |
| (1227) |
| PubMed, Embase, Scopus, Google Scholar, Web of Science, Türk Medline |

↓

| Repetitive and irrelevant studies were eliminated |
| (631) |

↓

| Articles with full text available |
| (542) |

↓

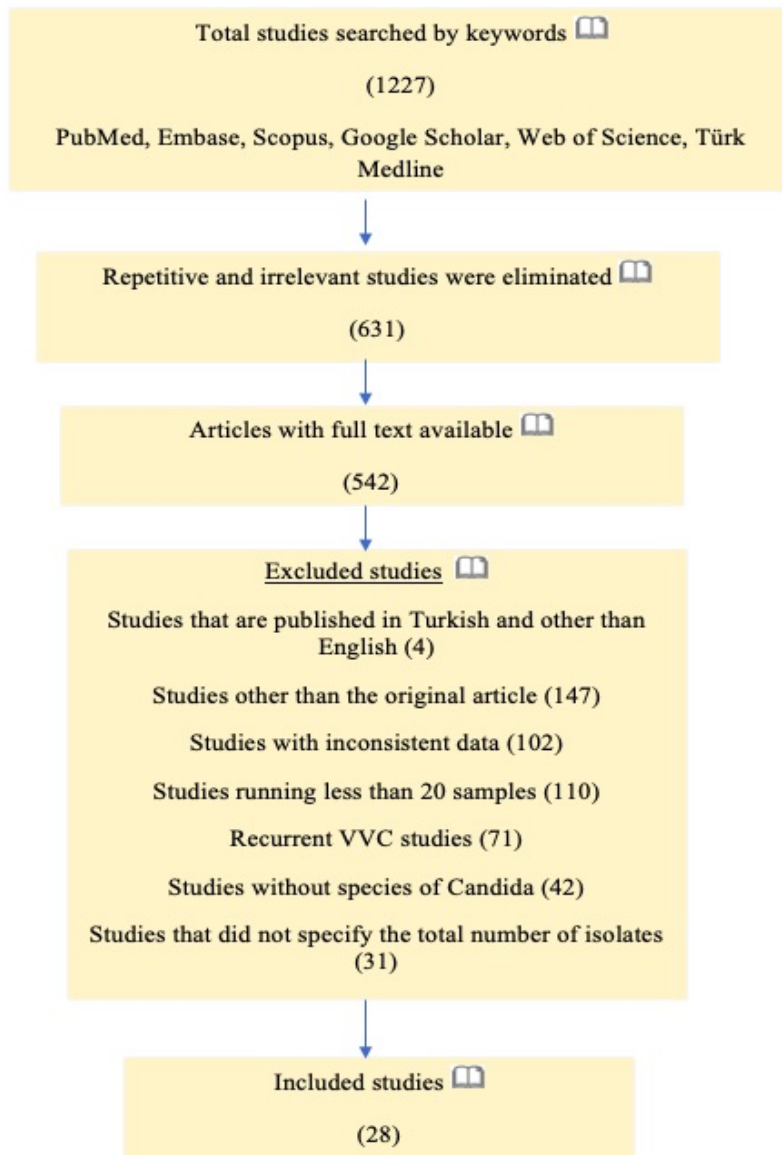| Excluded studies |
| Studies that are published in Turkish and other than English (4) |
| Studies other than the original article (147) |
| Studies with inconsistent data (102) |
| Studies running less than 20 samples (110) |
| Recurrent VVC studies (71) |
| Studies without species of Candida (42) |
| Studies that did not specify the total number of isolates (31) |

↓

| Included studies |
| (28) |

Figure 1. PRISMA flowchart showing the literature search and study selection strategy

prepared to collect data; the surname of the first author, the publication year of the article, study duration, study location, sample size, number of confirmed cases, causative types, age of patients, predominant risk factors, predominant clinical symptoms, and laboratory diagnostic methods of VVC were listed.

The data obtained from the literature review were analyzed in the IBM SPSS (Version 25.0) statistical package program. While evaluating the data, normal distribution analysis (Kolmogorov-Smirnov) was performed in addition to descriptive statistical methods (frequency, percentage, mean, standard deviation). Tests (t-test and One Way-ANOVA) were conducted to measure whether *Candida* species differ according to various variables. The study's effect sizes and heterogeneity were calculated with the Comprehensive Meta-Analysis (CMA, Version 2) program, and Forest plot analyzes were performed.

RESULTS

The results were evaluated at the 95% confidence interval, at the $p < 0.05$ significance level. Since eight of the 28 included studies only worked with Candida-positive samples (candida prevalence would appear to be 100%, it would be misleading), they were not included in the statistical analysis. The methodological evaluation of the study was made with the criteria shown in Table 1. These quality criteria were not considered an exclusion criterion. The qualitative review of studies accepted for meta-analysis was

scored according to a checklist designed with critical evaluation by three independent researchers. These criteria were determined as the test method used, the number of patients included, and the time period in which the study was conducted (Table 1).

During the search of publications related to VVC, 1227 titles and abstracts were found. After the pre-reading evaluation, 542 full texts were included in the review, a total of 28 original articles were included in the study after the inclusion and exclusion criteria were applied (Figure 1). The characteristics of all original articles reviewed within the scope of the review are presented in detail in Table 1. The clinical characteristics of the patients in the included studies were variable; The most common predisposing factor reports were pregnancy (10/28) and diabetes (10/28).

In all 28 studies included, the most common *C. albicans* (54.76%), *C. glabrata* (24.04%), other *Candida* species (12.29%), *C. krusei* (3.68%), *C. kefyr* (3.37%) and *C. tropicalis* (2.07%) positivity were reported. The change graph of the *Candida* species by years is given in Figure 2. When the articles were analyzed according to the years and cities in which they were published, it was determined that the prevalence of *Candida* did not show a statistically significant difference. ($p=0.59$, $p=0.23$; $p>0.05$) It was seen that most of the notifications were made from Adana (8/28) and Ankara (6/28) provinces. In addition, it was determined that the publications we included in the review about VVC were made between 1999-2005 at the most and that these publications decreased between 2014-2021.

Table 1. Criteria for the quality assessment of studies

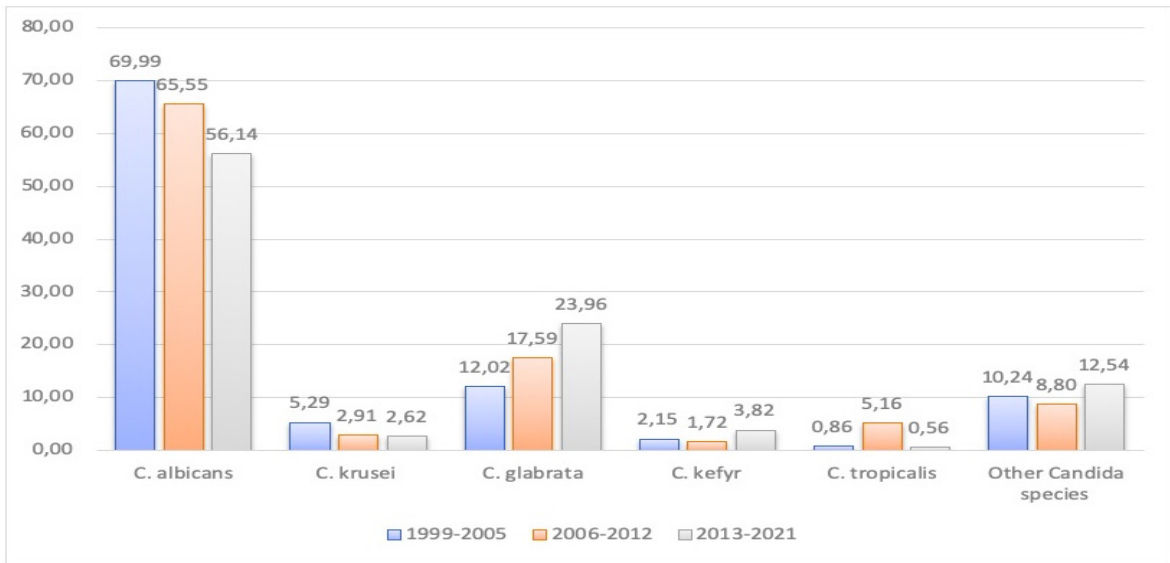|	3 point	2 point	1 point
Identification method	AU+CN	AU	CN
Number of patients	>500	100-500	<100
Time period	≥3 year	2 year	≤1 year

AU: Automatised, CN: Convention

Figure 2. Distribution of Candida species by years

It has been reported that *Candida* strains isolated from VVC patients were studied from vaginal swab samples in 23 studies and vaginal discharge samples in fve studies. A statistically significant difference was found between the prevalence of *C. tropicalis* and the sample type, and it was found that all strains were isolated from the vaginal swab samples, and there was no *C. tropicalis* strain isolated from the vaginal discharge sample. (p=0.007; p<0.05)

VITEK®2 (bioMérieux, Marcy l'Etoile, France) was used to identify of strains in 15 of the original articles, Germ tube was used in 7, CHROMagar in 7, and other diagnostic methods listed in Table 2. No statistically significant difference was found between the diagnostic methods and the prevalence of *Candida* species. (p=0.31; p>0.05)

Table 2a shows the data sets of the studies that included patients aged 16 and over, and in 2b, the data sets of the studies that included patients aged 2-18 years. When the data of two studies involving patients aged 2-18 years were examined, it was seen that Type 1 DM was detected as the underlying disease. In the studies in Table 2.b, the most frequently isolated species was *C. albicans*, followed by *C. glabrata*. When the prevalence was analyzed according to years and cities in the studies in Table 2.b, a statistically significant difference was found (p=0.76, p=0.56). In addition, no statistically significant difference was found between the diagnostic methods and the prevalence of *Candida* species (p=0.09). In qualitative studies, studies were scored between 3 and 9. The qualitative mean score of the studies was calculated as 5.28 ± 1.33. It is shown in Table 2.

In the random-effect model, it is assumed that the studies can predict different true effects. The actual effect sizes of all studies are different. The effect sizes estimated in the meta-analysis predict the mean of all studies' effect sizes. The difference can also be caused by the sample and method differences in the studies. Therefore, the random-effects model was used in our meta-analysis. As a result of the analysis, it was determined that there was a high level of heterogeneity between studies (I2=95.28) (Figure 3).

Table 2a. Datasets of studies included in the review

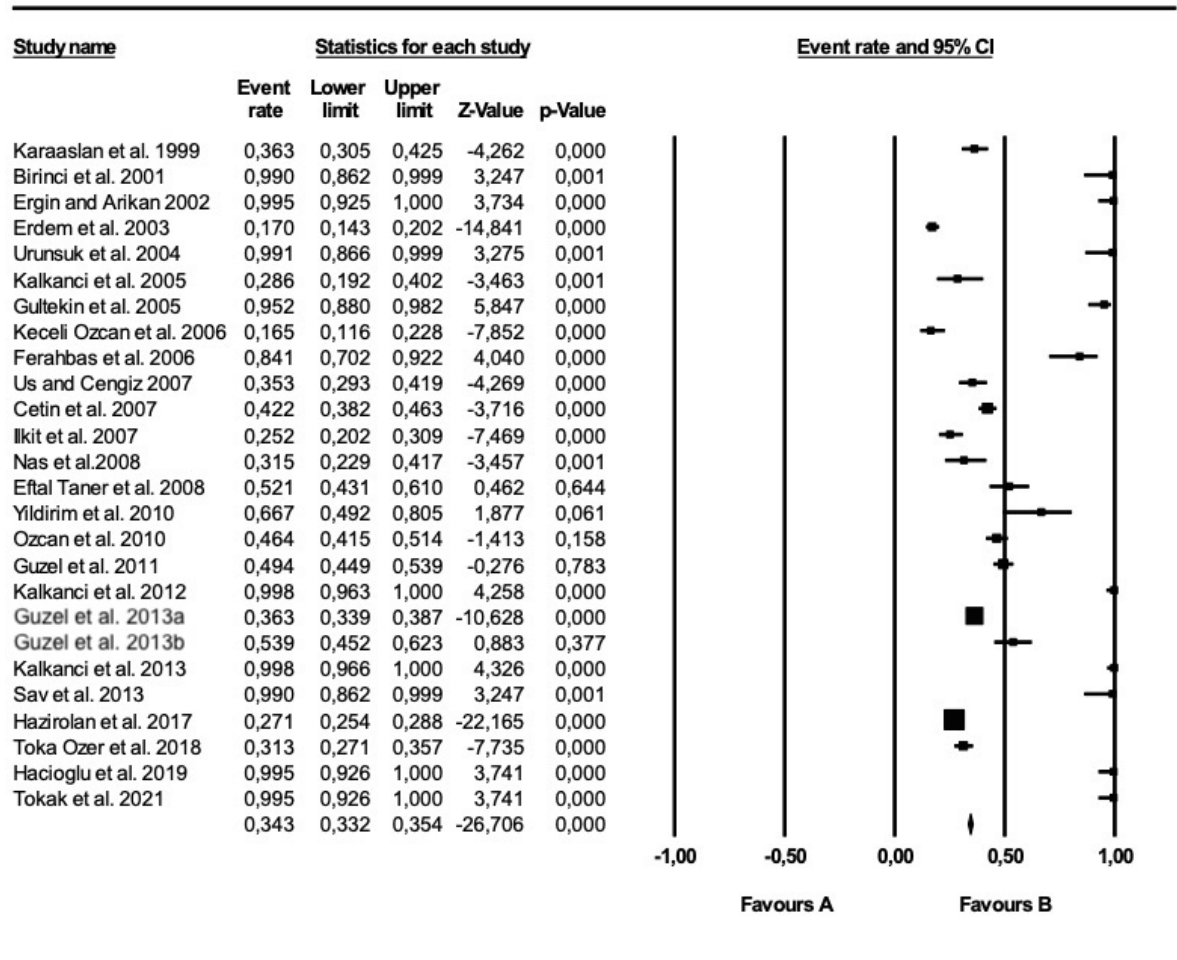| Author	City	N	n	Alb + (%)	N-alb + (%)	PF	ST	DMT	AR	QS
Karaaslan et al. 1999 (9)	Ankara	248	90	76.67	23.33	-	VD	Fungichrom I	18-51	4
Birinci et al. 2001 (10)	Samsun	50	50	100	0	-	VS	CHROMagar, VITEK®2	-	5
Ergin ve Arikan 2002 (11)	Ankara	99	99	67.67	32.33	-	VS	VITEK®2, GT	-	7
Erdem et al. 2003 (12)	Sivas	622	106	63.21	36.79	PR, DM, IF	VS	CANDIFAST	-	6
Urunsak et al. 2004 (13)	Adana	52	52	76.92	23.08	PR, DM, IF, CC	VS	VITEK®2	20-47	6
Gultekin et al. 2005 (14)	Aydin	84	80	56.25	43.75	-	VD	CHROMagar, GT	-	4
Kalkanci et al. 2005 (15)	Ankara	70	20	60	40	-	VS	VITEK®2	-	4
Ozcan et al. 2006 (16)	Kocaeli	170	28	75	25	DM, PR, AB, KK	VS	VITEK®2	25-35	5
Ferahbas et al. 2006 (17)	Kayseri	44	37	84.09	15.91	PR, LF, KF	VS	CHROMagar, VITEK®2	17-54	5
Cetin et al. 2007 (18)	Hatay	569	240	44.17	55.83	PR, DM	VS	VITEK®2	21-59	6
Ilkit et al. 2007 (19)	Adana	250	63	23.81	76.19	-	VS	Albicans ID2		5
Us ve Cengiz 2007 (20)	Ankara	218	77	53.25	46.75	PR	VS	CHROMagar, VITEK®2	-	6
Nas et al. 2008 (21)	Ankara	29	29	100	0	DM, P-MEN	VS	Asp pro	-	3
Eftal Taner et al. 2008 (22)	Izmir	117	61	57.38	42.62	-	VS	VITEK®2	-	5
Yildirim et al. 2010 (23)	Ankara	33	22	100	0	DM, PR	VS	VITEK®2	22-57	4
Ozcan et al. 2010 (24)	Adana	392	182	57.14	42.86	-	VS	CHROMagar, GT	-	5
Guzel et al. 2011 (25)	Adana	474	234	36.42	63.58	DM, HPO, HP	VS	CHROMagar, VITEK®2	18-49	6
Kalkanci et al. 2012 (26)	Adana	207	207	60	40	PR	VS	Fos	18-49	4
Guzel et al. 2013a (3)	Adana	1543	560	43.21	56.79	DM, PR, OCP	VD	CHROMagar, VITEK®2	-	9
Guzel et al. 2013b (27)	Adana	495	129	45	55	VI	VS	Fos	-	4
Kalkanci et al. 2013 (28)	Adana	228	228	50	50	-	VS	VITEK®2, GT	18-49	6
Sav et al. 2013 (29)	Kayseri	50	50	77.55	22.44	-	VD	VITEK®2, GT	-	5
Hazirolan et al. 2017 (30)	Malatya	2534	686	53.94	46.06	-	VS	GT, HWP1 gene polymorphisms	16-82	7
Toka Ozer et al. 2018 (5)	Konya	448	140	35.71	64.29	DM, PR, AB, CH	VD	GT	16-78	4
Hacioglu et al. 2019 (31)	Istanbul	100	100	84	16	-	VS	Fos and Pro	-	4
Tokak et al. 2021 (2)	Konya	100	98	57	43	HP, PR	VS	VITEK®2, API20	-	7
TOTAL		26	8922	3606						

N: Number of samples, n: Number of positive samples, Alb +: *C. albicans* positive, N-Alb+: Non-Albicans positive, PF: Predisposing factor, ST: Sample type, DMT: Diagnostic method, AR: Age range, QR: Qualitiy scale, DM: Diabetes mellitus, PR: Pregnancy, CH: Chemotherapy, IF: Immunodeficiency, OCP: Oral contraceptive pill, AB: Antibiotic use, CC: Corticosteroid use KF: Kidney failure, LF: Liver failure, VS: Vaginal swab, VD: Vaginal discharge, DR-M: Direct microscopy, HP: Hyperthyroidism, HPO: Hypothyroidism, VI: Vaginal itching, P-MEN: Postmenopausal period, GT: Germ tube, Fos: Phospholipase activity, Pro: Proteinase activity, Asp pro: Aspartyl proteinase expression.

Table 2b. Characteristics of studies with pediatric patients included in the review

Author	City	N	n	Alb + (%)	N-Alb + (%)	PF	ST	DMT	AR	QS
Tunger et al. 2000 (32)	Manisa	801	266	68.00	32.00	-	VS	Mycotube (Roche)	10-18	8
Kendirci et al. 2004 (33)	Kayseri	35	25	72.00	28.00	Type 1 DM	VS	VITEK®2	2-17	4
TOTAL		2	836	291						

N:Number of samples, n:Number of positive samples, Alb +:*C. albicans* positive, N-Alb+:Non-Albicans positive,

PF:Predisposing factor, ST:Sample type, DMT:Diagnostic method, AR:Age range, QR:Qualitiy scale, DM:Diabetes Mellitus

Study name	Event rate	Lower limit	Upper limit	Z-Value	p-Value
Karaaslan et al. 1999	0,363	0,305	0,425	-4,262	0,000
Birinci et al. 2001	0,990	0,862	0,999	3,247	0,001
Ergin and Arikan 2002	0,995	0,925	1,000	3,734	0,000
Erdem et al. 2003	0,170	0,143	0,202	-14,841	0,000
Urunsuk et al. 2004	0,991	0,866	0,999	3,275	0,001
Kalkanci et al. 2005	0,286	0,192	0,402	-3,463	0,001
Gultekin et al. 2005	0,952	0,880	0,982	5,847	0,000
Keceli Ozcan et al. 2006	0,165	0,116	0,228	-7,852	0,000
Ferahbas et al. 2006	0,841	0,702	0,922	4,040	0,000
Us and Cengiz 2007	0,353	0,293	0,419	-4,269	0,000
Cetin et al. 2007	0,422	0,382	0,463	-3,716	0,000
Ilkit et al. 2007	0,252	0,202	0,309	-7,469	0,000
Nas et al.2008	0,315	0,229	0,417	-3,457	0,001
Eftal Taner et al. 2008	0,521	0,431	0,610	0,462	0,644
Yildirim et al. 2010	0,667	0,492	0,805	1,877	0,061
Ozcan et al. 2010	0,464	0,415	0,514	-1,413	0,158
Guzel et al. 2011	0,494	0,449	0,539	-0,276	0,783
Kalkanci et al. 2012	0,998	0,963	1,000	4,258	0,000
Guzel et al. 2013a	0,363	0,339	0,387	-10,628	0,000
Guzel et al. 2013b	0,539	0,452	0,623	0,883	0,377
Kalkanci et al. 2013	0,998	0,966	1,000	4,326	0,000
Sav et al. 2013	0,990	0,862	0,999	3,247	0,001
Hazirolan et al. 2017	0,271	0,254	0,288	-22,165	0,000
Toka Ozer et al. 2018	0,313	0,271	0,357	-7,735	0,000
Hacioglu et al. 2019	0,995	0,926	1,000	3,741	0,000
Tokak et al. 2021	0,995	0,926	1,000	3,741	0,000
	0,343	0,332	0,354	-26,706	0,000

Figure 3. Forest plot analysis of the prevalence of VVC in the included studies

DISCUSSION

This study is the first systematic research and meta-analysis to examine the prevalence of VVC, the distribution of causative agents (*C. albicans*/non-albicans) and predisposing factors in adult women and children (2-18 years of age) in Turkey over a 26 year period. In the light of the available data, the prevalence of VVC in adult women was found to be 57.91% on average and 68.21% in the 2-18 age group. Compared to the literature, it has been reported that the prevalence of VVC in Iranian women is 45% on average (6). Nurat et al. (34) reported that the general prevalence of VVC was 25%, that the prevalence of VVC was 33.8% in women aged 20-29, and 24.3% in women aged 30-39. Konadu et al. (35) reported the prevalence of VVC as 31.1% in children under the age of 19 in Ghana. In the study conducted by Emeklioglu et al. (36) in Kayseri, they found that the prevalence of VVC in children aged 3-18 was 55.2%. Differences in results in studies may be due to factors such as clinical diagnosis without laboratory confirmation, patients' lifestyles, contraceptive methods they use, and predisposing factors.

In our study, the most common species of VVC were; *C. albicans* (54.76%), *C. glabrata* (24.04%), other *Candida* species (12.29%), *C. krusei* (3.68%), *C. kefyr* (3.37%), and *C. tropicalis* (2.07%) was detected. Gamarra et al. (37) reported the most frequently isolated *Candida* species in 118 patients with VVC, respectively; *C. albicans* (85.9%), *C. glabrata* (4.9%), *C. tropicalis* (0.8%) and *C. krusei* (0.8%). Richter et al. (38) reported that *C. albicans* was most common with 76% in patients with VVC in the USA, followed by *C. glabrata* with 16%.

The most common risk factors for VVC in the patients included in our study were pregnancy (35.71%) and diabetes (35.71%). Sasani et al. (6) reported that oral contraceptive use was the most common risk factor for the development of VVC in Iranian women. It has been reported that VVC is mostly associated with pregnancy, systemic diseases such as diabetes, and

antibiotic and oral contraceptive use, respectively (39). In addition, in studies involving patients aged 2-18 years, the most common risk factor was reported as Type 1 DM. When high blood sugar levels are not controlled, the pH of the vaginal area increases and the concentration of glucose and vaginal glycogen increases with the proliferation of yeasts. It is known that vaginal colonization with *Candida* is higher in women using insulin or oral hypoglycemic agents (40).

This study showed that the mean age of those with VVC infection (11 of the included studies reported a mean age) was 32.26, which was consistent with other studies in the literature (5, 9, 13, 16, 18, 22, 23, 25, 26, 28, 30). Emeribe et al. (41) reported that it is most common in women aged 25-34 years. Konate et al. (42) reported the rate of patients between 21-40 as 42.7% . The VVC is seen frequently in this age range may be due to factors such as sexual activity, higher pregnancy rates in this range, hormonal changes, and use of oral contraceptives.

Our study has some limitations. These:

• Only 11 of the included studies reported the mean age, and only age ranges were reported in the other studies,

• High heterogeneity of studies and

• Inadequate reporting of important information such as clinical and demographic data of patients, and these limitations are due to the included studies.

The current frequency of fungal infections that occur every year in Turkey and the economic burden it brings to the country are not clearly known. As a result of our meta-analysis study, the prevalence of VVC in Turkey was found to be higher than in other studies in the literature. It has been determined that non-albicans species are on the increase in the etiology of VVC in our country, and it will be helpful to determine the agent at the species level in patients diagnosed with VVC, and to investigate the antifungal susceptibility levels, in terms of treatment effectiveness and to prevent the development of antifungal resistance. Demographic characteristics of patients and reporting

of underlying disease or accompanying symptoms are essential in determining VVC risk factors in studies. For this reason, it is recommended to report the characteristics of the patients entirely in the relevant publications. Monitoring the prevalence of VVC, planning national epidemiological surveillance studies, creating prevention/prevention training programs can contribute to the protection of public health, the country's economy, and the creation of standard diagnosis/treatment algorithms.

ETHICS COMMITTEE APPROVAL

* This study does not require Ethics Committee Approval.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

REFERENCES

1. Faraji R, Rahimi MA, Rezvanmadani F, Hashemi M. Prevalence of vaginal candidiasis infection in diabetic women. Afri J Microbiol Res, 2012; 6:2773-8.

2. Tokak S, Kılıç IH, Eriç Horasanli J, Mutlu EG, Tasbent FE, Karagoz ID. Vaginal candidiasis in Konya area: Etiology, risk factors, virulence patterns, and antifungal susceptibilit. Rev Romana Med Lab, 2021; 29 (2): 201-15.

3. Guzel AB, Aydın M, Meral M, Kalkancı A, Ilkit M. Clinical characteristics of Turkish women with candida krusei vaginitis and antifungal susceptibility of the C. krusei isolates. Infect Dis Obstet Gynecol, 2013a; 1–7.

4. Sardi J, Silva D, Anibal PC, Baldin JJCMC, Ramalho SR, Rosalen PL, et al. Vulvovaginal candidiasis: epidemiology and risk factors, pathogenesis, resistance, and new therapeutic options. Curr Fungal Infect Rep, 2021; 15 (1): 1-9.

5. Toka Özer T, Cengiz T, Yılmaz H. Prevalence of vulvovaginal candidiasis and treatment with isoconazol nitrate. J Immunol Clin Microbiol, 2018; 3 (1): 8-14.

6. Sasani E, Rafat Z, Ashrafi K, Salimi Y, Zandi M, Soltani S, et al. Vulvovaginal candidiasis in Iran: A systematic review and meta-analysis on the epidemiology, clinical manifestations, demographic characteristics, risk factors, etiologic agents and laboratory diagnosis. Microb Pathog, 2021; 154: 104802.

7. Jeanmonod R, Chippa V, Jeanmonod D. Vaginal Candidiasis. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing, 2024. Available from: https://www.ncbi.nlm.nih.gov/books/NBK459317/.

8. Moher D, Shamseer L, Clarke M, Ghersi D, Liberati A, Petticrew M, et al. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 Statement. Syst Rev, 2015; 4: 1-9.

9. Karaaslan A, Cengiz L, Boyacıoğlu İ, Cengiz AT, Özsan M. Vulvovajinal kandidiazisli olgulardan izolen edilen maya türlerinin dağılımı ve antifungallere duyarlılıkların saptanması. Bull of Microbiol, 1999; 33 (4): 319-25.

10. Birinci A, Sanıç, A, Durupınar B. Determination of determination of minumum inhibitory concentrations of candida species isolated from vaginal swab specimens by using broth macrodilution and e-test. J Chem, 2001; 13 (1): 43-6.

11. Ergin A, Arikan S. Comparison of microdilution and disc diffusion methods in assessing the in vitro activity of fluconazole and Melaleuca alternifolia (tea tree) oil against vaginal Candida isolates. J Chemother, 2002; 14 (5): 465-72.

12. Erdem H, Cetin M, Timuroglu T, Cetin A, Yanar O, Pahsa A. Identification of yeasts in public hospital primary care patients with or without clinical vaginitis. ANZJOG, 2003; 43 (4):312-6.

13. Urunsak M, Ilkit M, Evruke C, Urunsak I. Clinical and mycological efficacy of single-day oral treatment with itraconazole (400 mg) in acute vulvovaginal candidosis. Mycoses, 2004; 47 (9): 422-7.

14. Gültekin B, Yazici V, Aydin N. Vajinal örneklerden izole edilen candida suşlarının dağılımı ve chromagar candida besiyerinin değerlendirilmesi. Mikrobiyol Bul, 2005; 39 (3): 319-24.

15. Kalkancı A, Biri A, Bozdayı G, Kuştimur S. Vulvovaginal kandidoz olgularından elde edilen candida spp. örneklerinin bazı antifungallere duyarlılıkları. J Clin Obstet Gynecol, 2005; 15 (2): 87-90.

16. Ozcan SK, Budak F, Yucesoy G, Susever S, Willke A. Prevalence, susceptibility profile and proteinase production of yeasts causing vulvovaginitis in Turkish women. APMIS, 2006; 114: 139-45.

17. Ferahbas A, Koc AN, Uksal U, Aygen E, Mistik S, Yildiz S. Terbinafine versus itraconazole and fluconazole in the treatment of vulvovaginal candidiasis. Am J Ther, 2006; 13 (4): 332-6.

18. Cetin M, Ocak S, Gungoren A, Ulvi Hakverdi A. Distribution of Candida species in women with vulvovaginal symptoms and their association with different ages and contraceptive methods. Scand J Infect Dis, 2007; 39 (6-7): 584-8.

19. Ilkit M, Hilmioğlu Polat S, Tasbakan M, Aydemir S. Evaluation of Albicans ID2 and Biggy agar for the isolation and direct identification of vaginal yeast isolates. JJ Med Microbiol, 2007; 56 (6): 762-5.

20. Us E, Cengiz SA. Prevalence and phenotypic evaluation of Candida dubliniensis in pregnant women with vulvovaginal candidosis in a university hospital in Ankara. Mycoses, 2007; 50 (1): 13-20.

21. Nas T, Kalkanci A, Fidan I, Hizel K, Bolat S, Yolbakan S, et al. Expression of ALS1, HWP1 and SAP4 genes in Candida albicans strains isolated from women with vaginitis. Folia Microbiol (Praha), 2008; 53 (2): 179-83.

22. Taner CF, Elveren B, Balsak B, Polat SH, Aygören MO. Mikotik vajinitlerde sertakonazol nitratın etkinliği ve tolerabilitesi. Trakya Üniv Tıp Fak Derg, 2008; 25 (3): 204-8.

23. Yildirim Z, Kilic N, Kalkanci A. Fluorometric determination of acid proteinase activity in Candida albicans strains from diabetic patients with vulvovaginal candidiasis. Mycoses, 2010; 54 (5): e463-7.

24. Ozcan K, Ilkit M, Ates A, Turac-Bicer A, Demirhindi H. Performance of Chromogenic Candida Agar and CHROMagar Candida in recovery and presumptive identification of monofungal and polyfungal vaginal isolates. Med Mycol J, 2010; 48 (1): 29-34.

25. Guzel AB, Ilkit M, Akar T, Burgut R, Demir SC. Evaluation of risk factors in patients with vulvovaginal candidiasis and the value of chromID Candida agar versus CHROMagar Candida for recovery and presumptive identification of vaginal yeast species. Med Mycol J, 2011; 49 (1): 16-25.

26. Kalkanci A, Güzel AB, Jabban IIK, Aydin M, Ilkit M, Kuştimur S. Yeast vaginitis during pregnancy: susceptibility testing of 13 antifungal drugs and boric acid and the detection of four virulence factors. Med Mycol J, 2012; 50 (6): 585-93.

27. Guzel AB, Küçükgöz-Güleç Ü, Aydin M, Gümral R, Kalkanci A, Ilkit M. Candida vaginitis during contraceptive use: The influence of methods, antifungal susceptibility and virulence patterns. J Obstet Gynecol, 2013b; 33 (8): 850-6.

28. Kalkanci A, Güzel AB, Jabban IIK, Aydin M, Ilkit M, Kuştimur S. Candida vaginitis in non-pregnant patients: A study of antifungal susceptibility testing and virulence factors. J Obstet Gynecol, 2013; 33 (4): 378-83.

29. Sav H, Demir G, Atalay MA, Koç AN. Klinik örneklerden izole edilen candida türlerinin değerlendirilmesi. Turk Hij Den Biyol Derg, 2013; 70 (4): 175-80.

30. Hazirolan G, Altun HU, Gumral R, Gursoy NC, Otlu B, Sancak B. Prevalence of Candida africana and Candida dubliniensis, in vulvovaginal candidiasis: First Turkish Candida africana isolates from vulvovaginal candidiasis. JMM, 2017; 27 (3): 376-81.

31. Hacioglu M, Guzel CB, Savage PB, Tan ASB. Antifungal susceptibilities, in vitro production of virulence factors and activities of ceragenins against Candida spp. isolated from vulvovaginal candidiasis. Med Mycol, 2019; 57 (3): 291-9.

32. Tünger Ö, Özbakkaloğlu B, Ecemiş T, Koyuncu F. Vulvovajinitli kadınlarda maya mantarının sıklığı ve türlere göre dağılımı. TMC Derg, 2000; 30 (3-4): 127-30.

33. Kendirci M, Koç AN, Kurtoglu S, Keskin M, Kuyucu T. Vulvovaginal candidiasis in children and adolescents with type 1 diabetes mellitus. J Pediatr Endocrinol Metab, 2004; 17 (11): 1545-9.

34. Nurat AA, Ola BG, Olushola SM, Mikhail TA, Ayodeji AS. Detection and epidemiology of vulvovaginal candidiasis among asymptomatic pregnant women attending a tertiary hospital in Ogbomoso, Nigeria. Nigeria Int J Biomed Res, 2015; 6 (7): 518-23.

35. Konadu DG, Owusu-Ofori A, Yidana Z, Boadu F, Iddrisu LF, Adu-Gyasi D, et al. Prevalence of vulvovaginal candidiasis, bacterial vaginosis and trichomoniasis in pregnant women attending antenatal clinic in the middle belt of Ghana. BMC Pregnancy Childb, 2019; 19 (1): 341.

36. Emeklioğlu B, Çakır N, Çakır I, Kendirci M, Koç AN. Assessment of fungal genital infection frequency, antifungal sensitivity, and the impact of hemoglobin a1c levels on these infections in diabetic children. Erciyes Med J, 2021; 43 (5): 427-32.

37. Gamarra S, Morano S, Dudiuk C, Mancilla E, Nardin ME, Mendez E, et al. Epidemiology and antifungal susceptibilities of yeasts causing vulvovaginitis in a teaching hospital. Mycopathologia, 2014; 178 (3-4): 251-8.

38. Richter SS, Galask RP, Messer SA, Hollis RJ, Diekema DJ, Pfaller MA. Antifungal Susceptibilities of candida species causing vulvovaginitis and epidemiology of recurrent cases. J Clin Microbiol, 2005; 43 (5): 2155-62.

39. Balcı O, Çapar M. Vajinal enfeksiyonlar. Vajinal enfeksiyonlar. Turk J Obstet Gynecol, 2005; 2 (5): 14-20.

40. Bassyouni RH, Wegdan AA, Abdelmoneim A, Said W, Aboelnaga F. Phospholipase and aspartyl proteinase activities of candida spe- cies causing vulvovaginal candidiasis in patients with type 2 diabe- tes mellitus. J Microbiol Biotechnol, 2015; 25 (10): 1734-41.

41. Emeribe AU, Nasir IA, Onyia J, Ifunanya AL. Prevalence of vulvovaginal candidiasis among nonpregnant women attending a tertiary health care facility in Abuja, Nigeria. Res Rep Trop Med, 2015; 6: 37-42.

42. Konaté A, Yavo W, Kassi FK, Djohan V, Angora EK, Barro-Kiki PC, et al. Aetiologies and contributing factors of vulvovaginal candidiasis in Abidjan (Cote d'Ivoire). JMM, 2014; 24 (2): 93-9.