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Distribution of Candida albicans and Non-albicans Candida Species Causing Vaginitis in Iran: A Review

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ABSTRACT

Introduction:
Due to the rising prevalence of non-*albicans Candida* (NAC) species in vulvovaginal candidiasis (VVC), the present study on the geographical distribution of *C. albicans* and NAC species in Iran is of considerable importance. Early identification of rare species can significantly improve prevention and treatment strategies, thereby contributing to meaningful advancements in this field.

Materials and Methods:
This review examined studies conducted in Iran between 2009 and 2024, published in both Persian and English languages in the Google Scholar database. These studies covered reports from various cities, including Zabol, Gorgan, Sari, Damavand, Ilam, Tehran, Jahrom, Ahvaz, Birjand, Mashhad, Kerman, Babol, Qazvin, Ardabil, Babolsar, Shiraz, Yasuj, Gonabad, Kashan, Fasa, Torbat-e Jam, and Neyshabur.

Results:
The NAC species reported in Iran included *C. glabrata, C. krusei, C. tropicalis, C. parapsilosis, C. kefyr, C. africana, C. lusitaniae, C. guilliermondii, C. orthopsilosis, C. dubliniensis, C. sake, C. intermedia,* and *C. famata*. The highest prevalence of VVC in Iran was attributed to *C. albicans*, with a prevalence rate of 66.1% (2,975 out of 4,500 VVC cases), which is relatively high on a global scale. The NAC species accounted for 24.9% of cases (1,121 out of 4,500 VVC cases), with *C. glabrata* being the most common NAC species and exhibiting a prevalence rate of 11.7% (530 out of 4,500 VVC cases).

Conclusion:
The distribution of NAC species across various cities and regions of Iran has revealed significant variations. The reported species not only differ between cities but also within different areas of the same locality, emphasizing the need for localized surveillance and region-specific treatment strategies.

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Introduction

Vaginitis is one of the most common genital infections and is characterized by symptoms, such as abnormal vaginal discharge, odor, irritation, itching, or burning (1,2). The primary infectious causes of vaginitis include bacterial vaginosis, fungal vaginosis, and trichomoniasis (3). Among these, fungal vaginosis, or vulvovaginal candidiasis (VVC), is the second most common cause of vaginal inflammation following bacterial vaginosis (4). Several factors predispose individuals to VVC, including the use of high-estrogen oral contraceptives, hormone replacement therapy, antibiotic use, and underlying diabetes mellitus. By the age of 25, approximately half of all women have experienced at least one episode of VVC, with the onset of sexual activity identified as a key risk factor (5).

Candida albicans is an opportunistic polymorphic fungus naturally present in the vaginal microbiota and has traditionally been recognized as the primary cause of VVC. *C. albicans* can be isolated from the genital tract of 10–55% of healthy, asymptomatic women of reproductive age and may lead to symptomatic infection if the balance between *Candida* and vaginal defenses is disrupted (6, 7). However, in recent years, non-*albicans Candida* (NAC) species have gained increasing scientific and epidemiological interest due to their rising prevalence worldwide (8–10). The most common NAC species include *C. glabrata*, *C. krusei*, *C. parapsilosis*, *C. tropicalis*, and *C. dubliniensis* (11,12), while the less common NAC species are *C. guilliermondii*, *C. famata*, *C. lusitaniae*, *C. norvegiensis, C. nivariensis, C. bracarensis,* and *C. inconspicua* (13,14).

Low socioeconomic status, limited education, non-white ethnicity, and underlying medical conditions are more commonly associated with NAC vaginitis (1). The clinical presentation of NAC vaginitis is highly variable, often with milder symptoms, compared to *C. albicans* infections (2), which may lead to underdiagnosis. Additionally, NAC species are linked to an increased risk of chronic fungal vaginitis (3). Chronic fungal vaginitis, also known as recurrent vulvovaginal candidiasis (RVVC), is defined as the occurrence of four or more episodes of fungal infections within a year (4,5). Recurrent infections are often associated with increased colonization by NAC species, and their persistence is largely due to their resistance to antifungal agents, which can contribute to repeated infections (6).

The pathogenesis of NAC species is less understood, compared to that of *C. albicans*, but key factors, such as adhesion, epithelial invasion, and enzyme secretion are believed to play crucial roles (7). The widespread use of over-the-counter topical azole antifungals has led to a significant challenge, as many NAC species exhibit inherent resistance or reduced susceptibility to low doses of these first-line treatments (8,9). This resistance makes NAC vaginitis, particularly cases caused by *C. glabrata*, more difficult to treat, often resulting in treatment failure. As a result, managing symptomatic NAC vaginitis remains a significant challenge for healthcare providers (10,11).

In recent years, there has been an increase in the incidence of systemic and mucosal infections caused by NAC species, particularly among patients with cancer or human immunodeficiency virus (HIV) in intensive care units. A study performed by Ratner *et al.* analyzed 5,461 vaginal specimens over three years and found that while *C. albicans* accounted for more than 85% of yeast isolates each year, its proportion steadily declined and NAC species became more prevalent (12). Among NAC species, *C. glabrata* was the most commonly isolated, with its prevalence increasing from 2.8% in 2018–2019 to 6.8% in 2020–2021 (13). This trend is not limited to vaginal infections and has also been observed in infections affecting other body sites (14,15).

Consequently, species, such as *C. glabrata, C. krusei, C. parapsilosis,* and *C. tropicalis* are gaining increased clinical recognition (16). Similarly, a study conducted by Wang *et al.* between 2006 and 2013 analyzed 2,204 *Candida* isolates from 2,122 patients with VVC. They found that while *C. albicans* remained the predominant species (80.5%), and its prevalence decreased from approximately 90% in 2006 to 77% in 2013. In contrast, the prevalence of *C. glabrata* increased from approximately 10% in 2003 to 20% in 2013 (17).

Given the concerning rise of NAC species, compared to *C. albicans*, this study aimed to investigate the prevalence of *Candida* species causing VVC as reported in Iran. The objective was to facilitate the early identification of emerging strains to help prevent their further spread.

Materials and Methods

This study reviewed 35 studies on vaginitis, categorized by *C. albicans* and NAC species, conducted in Iran and published in the Google Scholar database. Studies with restricted access were excluded. This review included studies published in English and Persian languages between 2009 and 2024. The collected research projects were conducted in various cities, including Zabol, Gorgan, Sari, Damavand, Ilam, Tehran, Jahrom, Ahvaz, Birjand, Mashhad, Kerman, Babol, Qazvin, Ardabil, Babolsar, Shiraz, Yasuj, Gonabad, Kashan, Fasa, Torbat-e Jam, and Neyshabur.

In total, 4,500 VVC samples were analyzed, with 2,975 (66.1%) identified as *C. albicans*-related vaginitis and 1,121 (24.9%) attributed to NAC species. The remaining 404 samples were either unidentifiable based on the research of the authors, lacked species-specific breakdowns, or contained mixed infections (either *C. albicans* with NAC species or multiple NAC species), which were excluded due to ambiguity in the results. In the present study, some decimal values were rounded due to limited access to original datasets. The keywords used in the literature search included "vulvovaginitis," "non-*albicans*," "*albicans*," "Iran," and "vaginitis."

Results

This review analyzed 35 studies from various cities in Iran that investigated the prevalence of *Candida* species in vaginitis cases. The most common type of VVC reported was *C. albicans*, with a prevalence rate of 66.1% (2,975 cases out of 4,500), which is relatively high, compared to global statistics. The second most common type was NAC, accounting for 24.9% (1,121 cases per 4,500), with *C. glabrata* being the most frequently identified NAC species, contributing to 11.7% (530 cases per 4,500) of all VVC cases (Table 1).

Table 1. Distribution of *Candida albicans* and non-*albicans Candida* (NAC) species isolated from vulvovaginal candidiasis (VVC) in various cities of Iran

Article	City	VVC prevalence	*C. albicans* frequency	NAC species frequency										
				C. glabrata	*C. krusei*	*C. tropicalis*	*C. parapsilosis*	*C. kefyr*	*C. africana*	*C. lusitaniae*	*C. guilliermondii*	*C. orthopsilosis*	*C. dubliniensis*	Rare species
Fouladi *et al.* 2020 (47)	Zabol	30	25	3	1	-	1	-	-	-	-	-	-	-
Nejat *et al.* 2018 (60)	Gorgan	122	87	27	5	-	-	2	-	1	-	-	-	-
Hedayati *et al.* 2015 (26)	Sari	66	~ 28	~ 14	-	-	-	-	-	-	-	-	~ 11	-
Ghajari *et al.* 2018 (28)	Damavand	46	~ 31	~ 12	-	-	-	~ 1	-	-	-	-	-	-
Mohamadi *et al.* 2015 (25)	Ilam	239	150	Not mentioned										
Rad *et al.* 2011 (30)	Tehran	191	128~	~ 35	~ 11	~ 13	~ 3	-	-	-	~ 3	-	-	-
Shokoohi *et al.* 2020 (35)	Jahrom	149	~ 133	~ 8	-	-	-	~ 2	-	-	-	-	-	-
Mahmoudabadi *et al.* 2010 (36)	Ahvaz	147	138	3	Not mentioned								3	-
Rezaei-Matehkolaei *et al.* 2016 (61)	Ahvaz	34	30	3	-	-	-	1	-	-	-	-	-	-
Hashemi *et al.* 2019 (43)	Babolsar	95	42	8	-	-	13	~ 6	2	18	-	1	-	-
Shokoohi *et al.* 2021 (77)	Jahrom	133	119	-	-	-	-	-	11	-	-	-	3	-
Farahyar *et al.* 2020 (62)	Tehran	100	51	36	8	-	-	5	-	-	-	-	-	-
Bonyadpour *et al.* 2016 (63)	Shiraz	105	~ 70	~ 23	~ 3	~ 9	-	-	-	-	-	-	-	-
Khaksar Baniasadi *et al.* 2022 (64)	Kerman	52	21	11	-	9	5	-	3	1	-	-	1	1, *C. famta*
Kiasat *et al.* 2019 (31)	Ahvaz	185	129	28	7	1	-	4	-	3	-	-	-	-
Gharaghani *et al.* 2018 (65)	Yasuj	160	139	6	5	-	-	1	-	-	-	-	-	-
Minooeianhaghighi *et al.* 2020 (37)	Gonabad	145	114	17	11	-	2	-	-	-	-	-	-	-
Nazeri *et al.* 2012 (34)	Kashan	144	112	28	3	Not mentioned								
Aslani *et al.* 2021 (66)	Fasa	125	86	24	8	-	1	2	-	-	-	-	-	-

Razzaghi-Abyaneh *et al.* 2014 (67)	Tehran	173	~ 125	+	+	+	~ 20	-	-	-	+	-	-	1 *C. intermedia*and *C. sake*
Salehi *et al.* 2016 (68)	Neyshabur	421	326	23	12	54	Not mentioned							
Falahati *et al.* 2013 (29)	Tehran	150	67	Not mentioned										
Seifi *et al.* 2015 (76)	Ahvaz	66	32	15	-	1	-	3	-	-	1	-	11	-
Bidaki *et al.* 2024 (44)	Birjand	102	57	20	1	-	24	-	-	-	-	-	-	-
Mahmoudi Rad *et al.* 2010 (70)	Tehran	175	~ 114	~ 23	7	~ 11	-	-	-	-	~ 1	-	-	-
Khorsand *et al.* 2015 (32)	Mashhad	99	77	7	-	4	9	1	-	-	-	-	-	-
Molazade *et al.* 2016 (71)	Kerman	220	90	46	22	-	-	37	-	-	-	-	-	-
Jannati *et al.* 2024 (33)	Neyshabur	167	57	34	5	5	2	6	-	-	1	-	-	-
Sharifynia *et al.* 2017 (72)	Tehran	47	28	12	-	1	1	2	-	1	2	-	-	-
Esmaeilzadeh *et al.* 2009 (42)	Babol	42	34	1	6	-	-	-	-	-	1	-	-	-
Mohammadi *et al.* 2021 (45)	Qazvin	70	47	13	-	3	2	5	-	-	-	-	-	-
Mohammadi-ghalehbin *et al.* 2017 (73)	Ardebil	143	119	+	+	+	-	-	-	-	-	-	-	-
Kord *et al.* (5)	Mashhad	108	84	10	-	1	1	4	-	-	-	-	-	-
Alizadeh *et al.* 2017 (75)	Mashhad	65	38	5	-	11	5	-	-	-	2	-	-	-
Barmar *et al.* 2019 (74)	Torbat-e Jam	309	145	53	33	33	45	-	-	-	-	-	-	-
(-) indicates that the species was not found in the study. (+) indicates that the species was found in the study, but its number is unknown (~) is equivalent to approximate numbers taken from the abstract of the articles (the numbers mentioned in the articles are expressed as percentages)														

The present study, initially conducted under the assumption of uniformity in *Candida* species distribution across different cities and regions, yielded significant findings. It was discovered that not only do the reported species vary between cities, but they also differ within different areas of the same city (Table 2). Furthermore, the incidence and distribution of *Candida* species vary by geographic location, highlighting the importance of regional epidemiological studies in understanding fungal infections.

Table 2. Geographical distribution and prevalence of non-*albicans Candida* species isolated from vulvovaginal candidiasis across different cities in Iran

City	Article	The 1st common species reported	The 2nd common species reported	The 3rd common species reported	The 4th common species reported	The 5th common species reported	The 6th common species reported
Zabol	Fouladi *et al.* 2020 (47)	*C. glabrata*	*C. krusei* *C. parapsilosis*	-	-	-	-
Gorgan	Nejat *et al.* 2018 (60)	*C. glabrata*	*C. krusei*	*C. kefyr*	*C. lusitaniae*	-	-
Sari	Hedayati *et al.* 2015 (26)	*C. glabrata*	*C. dubliniensis*	-	-	-	-
Damavand	Ghajari *et al.* 2018 (28)	*C. glabrata*	*C. kefyr*	-	-	-	-
Ilam	Mohamadi *et al.* 2015 (25)	Not mentioned					
Tehran	Rad *et al.* 2011 (30)	*C. glabrata*	*C. tropicalis*	*C. krusei*	*C. guilliermondii* *C. parapsilosis*	-	-
	Farahyar *et al.* 2020 (62)	*C. glabrata*	*C. krusei*	*C. kefyr*	-	-	-
	Razzaghi-Abyaneh *et al.* 2014 (67)	*C. parapsilosis*	-	-	-	-	-
	Falahati *et al.* 2013 (29)	Not mentioned					
	Mahmoudi Rad *et al.* 2010 (70)	*C. glabrata*	*C. tropicalis*	*C. krusei*	*C. guilliermondii*	-	-
	Sharifynia *et al.* (72)2017	*C. glabrata*	*C. kefyr* *C. guilliermondii*	*C. tropicalis* *C. parapsilosis* *C. lusitaniae*	-	-	-
Jahrom	Shokoohi *et al.* 2020 (35)	*C. glabrata*	*C. kefyr*	-	-	-	-
	Shokoohi *et al.* 2021 (77)	*C. africana*	*C. dubliniensis*	-	-	-	-
Ahvaz	Mahmoudabadi *et al.* 2010 (36)	*C. glabrata* *C. dubliniensis*	-	-	-	-	-
	Rezaei-Matehkolaei *et al.* 2016 (61)	*C. glabrata*	*C. kefyr*	-	-	-	-
	Kiasat *et al.* 2019 (31)	*C. glabrata*	*C. krusei*	*C. kefyr*	*C. lusitaniae*	*C. tropicalis*	-
	Seifi *et al.* 2015 (76)	*C. glabrata*	*C. dubliniensis*	*C. kefyr*	*C. tropicalis* *C. guilliermondii*	-	-

Birjand	Bidaki *et al.* 2024 (44)	*C. parapsilosis*	*C. glabrata*	*C. krusei*	-	-	-
Mashhad	Khorsand *et al.* 2015 (32)	*C. parapsilosis*	*C. glabrata*	*C. tropicalis*	*C. kefyr*	-	-
	Kord *et al.* (5)	*C. glabrata*	*C. kefyr*	*C. parapsilosis* *C. tropicalis*	-	-	-
	Alizadeh *et al.* 2017 (75)	*C. tropicalis*	*C. glabrata* *C. parapsilosis*	*C. guilliermondii*	-	-	-
Kerman	Molazade *et al.* 2016 (71)	*C. glabrata*	*C. kefyr*	*C. krusei*	-	-	-
	Khaksar Baniasadi *et al.* 2022 (64)	*C. glabrata*	*C. tropicalis*	*C. parapsilosis*	*C. africana*	*C. lusitaniae* *C. dubliniensis* *C. famata*	-
Babol	Esmaeilzadeh *et al.* 2009 (42)	*C. krusei*	*C. guilliermondii* *C. glabrata*	-	-	-	-
Qazvin	Mohammadi *et al.* 2021 (45)	*C. glabrata*	*C. kefyr*	*C. tropicalis*	*C. parapsilosis*	-	-
Ardebil	Mohammadi-ghalehbin *et al.* 2017 (73)	Not mentioned					
Babolsar	Hashemi *et al.* 2019 (43)	*C. lusitaniae*	*C. parapsilosis*	*C. glabrata*	*C. kefyr*	*C. africana*	*C. orthopsilosis*
Shiraz	Bonyadpour *et al.* 2016 (63)	*C. glabrata*	*C. tropicalis*	*C. krusei*	-	-	-
Yasuj	Gharaghani *et al.* 2018 (65)	*C. glabrata*	*C. krusei*	*C. kefyr*	-	-	-
Gonabad	Minooeianhaghighi *et al.* 2020 (37)	*C. glabrata*	*C. krusei*	*C. parapsilosis*	-	-	-
Kashan	Nazeri *et al.* 2012 (34)	*C. glabrata*	*C. krusei*	-	-	-	-
Fasa	Aslani *et al.* 2021 (66)	*C. glabrata*	*C. krusei*	*C. kefyr*	*C. parapsilosis*	-	-
Neyshabur	Salehi *et al.* 2016 (68)	*C. tropicalis*	*C. glabrata*	*C. krusei*	-	-	-
	Jannati *et al.* 2024 (33)	*C. glabrata*	*C. kefyr*	*C. tropicalis* *C. krusei*	*C. parapsilosis*	*C. guilliermondii*	-
Torbat-e Jam	Barmar *et al.* 2019 (74)	*C. glabrata*	*C. parapsilosis*	*C. tropicalis* *C. krusei*	-	-	-

(-) indicates that the species was not found in the study

The NAC species reported in Iran included *C. glabrata, C. krusei, C. tropicalis, C. parapsilosis, C. kefyr, C. africana, C. lusitaniae, C. guilliermondii, C. orthopsilosis, C. dubliniensis, C. sake, C. intermedia,* and *C. famata.* The frequency of each NAC species, based on the data collected from 35 studies and a total of 1,121 NAC-positive cases, is as follows: *C. glabrata* (47.2%), *C. tropicalis* (13.9%), *C. krusei* (13.2%), *C. parapsilosis* (11.9%), *C. kefyr* (7.3%), *C. dubliniensis* (2.5%), *C. lusitaniae* (2.1%), *C. africana* (1.4%), *C. guilliermondii* (0.9%), *C. famata* (0.08%), *C. orthopsilosis* (0.08%), *C. intermedia* (unknown), *C. sake* (unknown). This distribution highlights the predominance of *C. glabrata* among NAC species and underscores the need for continued monitoring of emerging strains.

The present research, based on the 35 reviewed studies, revealed a significant finding: there was a strong correlation between age and the incidence of VVC. Notably, vaginal infections were more prevalent in women of reproductive age, underscoring the influence of age and estrogen levels on the occurrence of vaginitis. The lowest frequency of VVC was observed in individuals over 50 years old, further supporting this age-related trend. The women most affected in this study were those with diabetes, underlying health conditions, and a history of antifungal treatments. It is also noteworthy that itching was identified as the most common symptom among VVC patients in this study.

Findings of the present study also highlighted that the increased incidence of NAC species is primarily driven by the use of immunosuppressants and broad-spectrum antibiotics, which have contributed to resistance against first-line treatments, specifically azoles.

Additionally, this research emphasized the urgent need for education on VVC. A significant link was found between sexual health knowledge and education, underscoring the importance of recognizing VVC types and educating women accordingly. Given the global rise in NAC species due to antifungal and antibiotic resistance, rapid identification of species and their prevalence in different geographic locations is crucial for the effective treatment and prevention of this type of vaginitis.

Discussion

The VVC is an infection caused by *Candida* species, affecting over 130 million women annually. This condition leads to significant psychosocial issues and incurs high healthcare costs (18, 19). *Candida* species, including *C. albicans*, the primary cause of VVC (20, 21), are part of the normal mucosal flora in most healthy women, residing in the gastrointestinal and genitourinary tracts. Under favorable conditions, these fungi can adhere to the vaginal epithelium and colonize the vulvovaginal mucosa, resulting in symptomatic VVC, as reported in the study performed by Odds FC (7,22-24).

Denning *et al*. performed a study that examined the prevalence of vaginitis in 50 populous countries worldwide, and Iran ranked 17th in terms of the prevalence of this disease, with 4,630 cases per 100,000 women. This high prevalence rate can be attributed to the relatively widespread occurrence of vaginitis in Iran (19). According to available studies, the prevalence of VVC in Iran was estimated at 51.4% among 8,738 suspected cases of vaginitis. For example, a study performed by Mohamadi *et al*. found that 239 out of 385 individuals suspected of having vaginitis tested positive, indicating a high likelihood of diagnosing vaginitis in women with similar symptoms (25).

Hedayati *et al*. (26) in their study found no significant relationship between age and the occurrence of VVC. However, the present research demonstrated a significant relationship between age and VVC, with vaginal infections being more common in women of reproductive age and rare in postmenopausal or adolescent females. This finding suggests a hormonal influence on the infection, as estrogens can disrupt the balance between *Candida* species and the host, leading to infection (27,28). Falahati *et al*. reported that most patients with vaginitis were in the 20-30 age group (29). In another study, the mean age of patients was 32.4 ± 8.2 years (30). Additionally, a study conducted by Kiasat *et al*. showed that VVC occurred most frequently in the 21-30 age group, followed by the 31-40 age group. The lowest incidence rate of VVC was observed in individuals over 50 years of age, further confirming the influence of age and estrogen levels on the occurrence of vaginitis (31). Certain groups of women are at higher risk of developing vaginitis, including females with diabetes, frequent antibiotics use, cystic fibrosis, or a history of RVVC. These women require better education, support, and often suppressive antifungal therapy (19). The present review of reported cases of vaginitis in Iran revealed a significant association between the incidence of vaginitis and factors, such as diabetes, underlying diseases, and a history of antifungal treatment (32-38). For instance, a study performed by Rad *et al*. found that 14.5% of patients with recurrent VVC were using antibiotics, 12% had diabetes, and 2.4% were immuno- compromised (30).

Additionally, a study conducted by Minooeianhahighi *et al*. revealed that 55% of patients with vaginitis had anxiety and stress, 35% had decreased self-esteem, 5% were dissatisfied with life, and 5% had other psychological symptoms (37). This suggests that anxiety and stress may increase the risk of developing vaginitis. In support of this, Harville *et al*. found that women with high stress levels were more likely to develop bacterial vaginosis, compared to those with lower stress levels (39). In the study carried out by Paladine *et al*., itching was identified as the most common symptom of VVC (40).

Similarly, the most common symptoms reported in this study were itching, abnormal discharge, and burning, respectively (31,41,42). Other symptoms, such as vaginal irritation, dyspareunia, curd-like vaginal discharge, painful intercourse, lower abdominal pain, and inflammation were also observed (28,37, 43-45). Although *C. albicans* is considered the primary cause of VVC, the identification rate of NAC species is steadily increasing (46). In a study performed by Makanjuola *et al*., NAC vaginitis was evaluated as milder in terms of clinical manifestation, often affecting patients with chronic underlying diseases. However, its symptoms tend to be more recurrent or chronic, compared to *C. albicans* vaginitis. The aforementioned study also noted that extensive research has focused on the pathogenicity of *C. albicans,* compared to the NAC strain. *C. albicans* are capable of expressing all virulence factors, while NAC strains exhibit variable combinations of virulence factors depending on the specific strain (7). Two factors that have contributed significantly to the rise in NAC strains are the use of immunosuppressants and broad-spectrum antibiotics (24). Similar results were found in Iran, where the groups most at risk for vaginitis included women with diabetes, underlying diseases, or a history of antifungal treatment or the use of broad-spectrum antibiotics (47).

As shown by Salehei *et al*., the susceptibility patterns of *Candida* isolates vary across studies conducted in different countries. Most NAC species exhibit higher minimum inhibitory concentrations for antibiotics, compared to *C. albicans,* and show greater resistance to first-line drugs, particularly azoles. This resistance has made the treatment of NAC-induced vaginitis significantly more challenging (46).

This section provides a more detailed examination of *C. albicans* and NAC species. *C. albicans* is a common cause of mucosal infections, a polymorphic fungus capable of growing in yeast, hyphal, and hyphal-like forms. The hyphal form penetrates the epithelium and endothelium, causing tissue damage and facilitating access to the bloodstream (48). In the United States, *Candida* species are now the second most common cause of vaginal infections, following bacterial infections, while in Europe, they are cited as the leading cause (49).

The adherence of *Candida* species to the epithelial surface of the vagina is key to successful colonization or infection. The *C. albicans* adheres more efficiently than many NAC species. This adherence mechanism contributes to the persistence of *C. albicans* in the host, playing a critical role in the establishment of both colonization and infection. The process is mediated by specific cellular proteins called adhesins, which typically recognize host ligands, the extracellular matrix, and enhance attachment to non-living surfaces (50).

In a study performed by Mohanty *et al*., the primary cause of VVC was NAC, specifically *C. glabrata* (51). However, in a total of 35 studies conducted in Iran, *C. albicans* was identified as the leading cause of VVC, with a higher prevalence of 66.1% (2,975 out of 4500 VVC patients). These findings align with the of previous studies (23,46,52). This suggests that geographical location may play a significant role in the incidence of vaginitis. As Kent *et al*. have noted in their study, despite the global rise in NAC species, the incidence of candidiasis in Scandinavia has remained relatively stable over the past five years. This may support the idea that geographical factors influence the incidence of this condition (27).

Although extensive research has been conducted to identify the pathogenic features of *C. albicans*, relatively less is known about the pathogenicity of NAC species (53). While hyphal production is a major factor in *C. albicans* infections, it plays a minor role in the majority of NAC vaginitis cases (7). It is important to note the increasing percentage of infections caused by NAC species over the past three decades (54).

This rise is concerning due to their growing resistance to azole antifungals, which are the first-line treatments, and the fact that NAC infections can result in more severe disease and higher mortality rates. Additionally, the affected patients tend to be younger, making it crucial to recognize and investigate the increased prevalence of NAC in recent decades (55,56).

As Taei *et al*. have pointed out, the increasing number of NAC species may be linked to factors, such as prior exposure to polyenes and azoles, the use of indwelling catheters, malignancies, age, advancements in biochemical and molecular diagnostic methods, and geographical factors (57,58). In a study carried out by Kennedy *et al*., *in vitro* and *in vivo* data demonstrated that different NAC species identified in the lower genital tract vary significantly in terms of epidemiology, vaginal virulence or pathogenicity, and susceptibility to antifungal drugs. As a result, the accurate identification of clinical isolates is crucial for more effective treatment of infections (59).

Previous studies have identified *C. glabrata*, *C. parapsilosis*, *C. tropicalis*, and *C. krusei* as the most common NAC species, in that order (20). In the present study, the most common species identified were *C. glabrata* (5,26,28, 30–37,42–45,47,60–75), *C. tropicalis* (5, 30–33, 45,63,64,67, 68,70,72,74–76), *C. krusei* (30–34,7,42,44,47, 60, 62, 63, 65–68, 70, 71, 73, 74), and *C. parapsilosis* (5,30,32,33, 37,43–45,47,64,66,67,72,74,75).

In a study conducted by Makanjuola *et al*., less common NAC species involved in vaginitis were *C. guilliermondii*, *C. famata*, *C. lusitaniae*, *C. norvegiensis*, *C. nivariensis*, *C. bracarensis*, and *C. inconspicua* (7). However, the present study found that the less common species in Iran were *C. orthopsilosis*, *C. famata*, *C. guilliermondii*, and *C. africana* (30,33,42,43, 64,70,72,75–77).

In many studies, *C. glabrata* is identified as the primary cause of vaginitis caused by NAC (10,31,52,74,78,79). However, in the study performed by Hashemi *et al*. in Babolsar City, Iran, the highest prevalence was observed for *C. lusitaniae* (43). Similarly, in a study conducted by Shokoohi *et al*. in Jahrom City, Iran, *C. africana* was the most prevalent species (77). In two other studies in Mashhad and Neyshabur, Iran, *C. tropicalis* was found to be the most common NAC species (68,75).

A study carried out by Esmaeilzadeh *et al*., also in Babol City, identified *C. krusei* as the most prevalent species (42). Additionally, in studies conducted in Mashhad and Birjand, Iran, *C. parapsilosis* was the predominant species (32,44). These findings suggest that geographical location not only influences the prevalence of vaginitis but also affects the specific types of vaginitis seen in patients.

Conclusion

The rising prevalence and antifungal resistance of NAC species in Iran, particularly among individuals with diabetes or immunocompromised conditions, highlight the need for early identification and geographical mapping.

These efforts are essential for effective treatment and prevention. However, most available data are derived from large cities, indicating a potential gap in our understanding. Future research should prioritize smaller cities and rural areas to bridge this gap and provide a more comprehensive overview of NAC vaginitis across the country.

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Disclosure

The authors declare that they have no relevant material or financial interests that relate to the research described in this paper.

Ethical Statement

Ethics approval is not applicable as this is a review paper and does not involve direct research on animals or humans.

Conflicts of Interest

The authors declare no conflicts of interest.

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