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Vaginal candidiasis prevalence, associated factors, and antifungal susceptibility patterns among pregnant women attending antenatal care at bule hora university teaching hospital, Southern Ethiopia

Ibrahim Hussen[1], Alqeer Aliyo[1*], Moorthy Kannaiyan Abbai[1] and Wako Dedecha[1]

Abstract

Background Vulvovaginitis is common in women of reproductive age group characterized by purulent white discharge. The incidence of vulvovaginitis has risen recently due to the resistance of *Candida* species to commonly used antifungal agents and recurrent infections.

Objective The study aimed to determine the prevalence, associated factors, and antifungal susceptibility patterns of vaginal candidiasis among pregnant women attending Bule Hora University Teaching Hospital.

Methods A hospital-based cross-sectional study was conducted from May 2023 to August 2023. Using systematic random sampling, 317 pregnant women participated in the study. Sabouraud Dextrose Agar and Chromogenic *Candida* Differential Agar were used to isolate and identify *Candida* species from clinical samples. Antifungal susceptibility was performed using a modified disc diffusion method. Epi data version 4.6 was used for data entry and Statistical Packages for Social Sciences version 25 was used for statistical analysis. A P-value < 0.05 was declared statistically significant.

Result The prevalence of vaginal candidiasis was 26.8% (95%, CI 21.9–31.72%). History of using contraceptives (AOR = 5.03, 95%CI, 1.21–11.37), past vaginal candidiasis (AOR = 6, 95%CI, 1.61–12.92), pregnant women infected with human immunodeficiency virus (HIV) (AOR = 4.24, 95%CI, 1.23–14.14), diabetic mellitus (AOR = 2.17, 95%CI, 1.02–4.64), history of antibiotic use (AOR = 3.55, 95%CI, 1.67–12.75), pregnant women in third trimester (AOR = 8.72, 95%CI, 1.30–23.07), were the significantly associated factors for vaginal candidiasis. The study revealed that itraconazole, amphotericin B, and miconazole were the most effective antifungal drugs for all *Candida* isolates.

Conclusion The present study has identified a high prevalence of vaginal candidiasis among pregnant women. The isolated *Candida* species showed resistance to fluconazole, ketoconazole, and clotrimazole. Therefore, healthcare providers should increase awareness of the risks of *Candida* infections to reduce *Candida* species among pregnant

*Correspondence:
Alqeer Aliyo
alker438@gmail.com

Full list of author information is available at the end of the article

women. Physicians should prescribe suitable medications based on antifungal drug test outcomes to treat pregnant women with vaginal candidiasis.

Keywords Vaginal candidiasis, Pregnant women, Antenatal care, Bule hora

Introduction

The second most common vaginal infection affecting women of reproductive age is vulvovaginal candidiasis (VVC), which mainly causes inflammation of the vulva and vagina [1]. Worldwide, nearly 5–10 million females seek gynecologic advice for vaginitis every year [2]. Women of childbearing age estimate that approximately 70–75% will have at least one episode of VVC during their lifetime, and 40–50% will suffer recurrence [3]. Recurrent VVC worldwide affects approximately 138 million women annually, ranging from 103 to 172 million, with an annual prevalence of 3871 per 100,000 women worldwide; 372 million women are affected by recurrent VVC over their lifetime [4].

VVC is an infection of the estrogenic vagina and vestibulum, which can extend to the outside of the labia minora, labia majora, and the intercrural region [5]. It is most often by the overabundance of an opportunistic pathogenic yeast, *Candida albicans* (approximately 90%), which is a common member of the vaginal flora [6]. Vulvovaginal candidiasis is caused by *Candida albicans* in almost 80–90% of cases, except that only a minority of cases (10–20%) are caused by non - *C. albicans* species, usually *Candida glabrata* [7]. This dimorphic yeast, a commensal that colonizes the skin and gastrointestinal and reproductive tracts, can be found in the vaginal tracts of 20 to 30% of healthy asymptomatic women at any single point in time. If the balance between the colonizing yeast and the host is temporarily altered, then *Candida* can cause infections such as VVC, associated with clinical signs of inflammation [8].

During pregnancy, VVC is considered more common and difficult to eradicate because of several normal physiological changes such as hormone changes, vaginal pH, and alteration of microflora due to pathogens in the genitourinary tract that favor the growth of *Candida* spp [9]. In vulvovaginal candidiasis, three out of four women had an infection in their lifetime [10]. *Candida albicans* are part of the mucosal flora in many individuals, typically existing as a benign member of the human microbiome for extended periods. However, it can cause superficial infections due to hormonal effects that inhibit anti-*Candida* activities, inadequate hygiene, and compromised immunity. These infections may then develop into severe, life-threatening systemic conditions. Ultimately, this fungal pathogen has the potential to colonize various regions of the body [11, 12].

Pathogenic *Candida* spp have been identified, including the ability to adhere and invade host cells, the secretion of enzyme hydrolases, and biofilm formation [13]. *Candida albicans* has been reported to be resistant to many antifungal drugs and is usually treated with the azole class of antifungal drugs due to their lower toxicity and availability [14, 15]. Vulvovaginal candidiasis is a global concern because of its economic importance and sexually transmitted infection [16]. The mechanisms used by *Candida* spp. to produce vaginal inflammation are not known [17]. Diabetes mellitus is a predisposing factor during pregnancy [18]. Other factors include the use of broad-spectrum antibiotics, high doses of estrogen, and oral contraceptives [19].

During the past several decades, numerous studies have focused on improving standardized antimicrobial susceptibility testing (AST). The Clinical Laboratory Standards Institute (CLSI) serves as a reference method for yeast susceptibility testing. Agar-based susceptibility testing, particularly the classical disk diffusion method, has garnered significant interest among researchers [20]. Antifungal susceptibility tests that correlate with clinical outcomes may forecast treatment failures and contribute to the creation of local antibiograms, aiding in the empirical selection of antifungal agents [21]. Resistance to antifungal drugs, especially in patients previously treated with azole antifungals, poses a significant public health challenge [22].

The community knowledge and evidence on vaginal candidiasis prevalence and associated factors among pregnant women in the study area are limited to access; therefore, the present study will provide important input on the prevalence and associated factors of vaginal candidiasis among pregnant mothers attending antenatal care and help to advance possible recommendations.

Method and materials

Study area and period

This hospital-based cross-sectional study was conducted at Bule Hora University Teaching Hospital from May to August 2023. The hospital is located in Bule Hora town and is one of the towns of the Oromia Regional state in the southern part of Ethiopia. Bule Hora is the capital of the West Guji zone located 467 km from Addis Ababa in the south and is a teaching hospital that provides health services to more than

1.5 million inhabitants in the zone. The hospital's antenatal care (ANC) clinic provides routine antenatal screening services for more than 20 pregnant women per day. This town is bordered on the south by the Borena zone, on the west by the Southern Nations, Nationalities, and Peoples Region, on the north by the Abaya River, which separates it from the SNNPR, and on the east by the Guji zone.

Study design and population

A hospital-based cross-sectional study design was used among pregnant women who attended antenatal care (ANC) at the Bule Hora University Teaching Hospital from May to August 2023. All pregnant women who were randomly selected and attended the antenatal care (ANC) during the data collection period, and met the selection criteria, were included in the study.

Inclusion and exclusion criteria

All randomly selected pregnant women attending Bule Hora University Teaching Hospital ANC aged between 18 and 49 were included in the study, while the pregnant women who had either on/taken intra-vaginally or systemic antifungal therapy within the last 2 or 3 weeks were excluded.

Sample size determination

The sample size for this study was determined using the single population proportion formula. When the proportion of vaginal candidiasis (p=25%) was taken from a previous study conducted at Debra Markos Referral Hospital [23], with the assumption of precision or degree of error 0.05, the confidence interval was 95% and the non-response rate was assumed to be 10%.

$$n = \frac{Z^2\alpha/2P\,(1-p)}{d^2} = \frac{1.96^2\,(1-0.25)}{0.05^2} = 288.12 \approx 288$$

Adding 10% of the non-respondent rate, the final sample size was 317 pregnant women. Where n=Sample size, Z=value corresponding to 95% level of significance=1.96, P=proportion of prevalence vaginal candidiasis in pregnant women=25%, d=marginal error assumed to be 5%.

Sampling technique

Monthly estimated ANC attendant in the Bule Hora University teaching hospital, which was calculated from the antenatal care followers from registration. Then, the total sample size of pregnant women is proportional to their population size based on the previously registered ANC followers. Pregnant women attending ANC at the time of data collection were carefully chosen using a systematic random sampling method. To decide the interval (k), the estimated total number of attendants of ANC 1135 is divided into an allocated sample size of the study, that is, K=N/ n=1,135/ 317=3.58≈4.

where, N=total ANC attendants, n=required sample size, K=sampling interval.

So, all fourth pregnant women attending ANC were included in the sample until the total sample size for this study was obtained in the hospital. Based on the client's sequences, which were used as a sampling frame using systematic random sampling. The process was continued throughout data collection until the required sample size was achieved.

Data collection instruments and procedures

Three Medical laboratory technicians and two midwives were recruited for data collection. Training was provided for the data collector and supervisor. The sociodemographic information, clinical factors, and behavioral factors data were collected using structured questionnaires. The vaginal swab was collected from each participant using a sterile cotton swab moistened with physiological saline and then inserted and rotated gently to pick up the swab. In case an appropriate vaginal swab could not be obtained, alternatively, the participant was informed to collect a first voided urine sample through contamination control using a labeled screw-capped universal container [24].

Identification of *candida* species

Microscopy examination and culture procedures

The specimens were collected from each pregnant woman and immediately transported to the Bule Hora University Microbiology Laboratory. Smears were prepared from vaginal swabs or urine sediments, stained with Gram's stain, and examined under a microscope using 10x and 40x objectives. The Gram stain revealed Gram-positive yeast-like budding cells, which were then cultured on Sabouraud Dextrose Agar (SDA) containing 2% chloramphenicol. The inoculated plate was incubated at 37 °C and examined after 24 h for cream-colored pastry colonies and budding yeast cells suggestive of *Candida* species. The SDA isolates were inoculated in *Candida* selective agar medium (Chromogenic *Candida* Differential Agar - TM 1977, New Delhi, India) using an inoculating needle and incubated at 37 °C for 72 h to ensure detection of mixed cultures by colon colors such as *C. albicans* (light green), *C. tropicalis* (blue to metallic blue), *C. glabrata* (cream to white), and *C. krusie* (purple-pink). The method is based on the differential release of chromogenic breakdown products from various substrates by *Candida* species after differential exoenzyme activity. It served as the presumptive identification of *C. albicans*, *C. tropicalis*, *C. glabrata*, and *C. krusie* [25].

Germ tube test (GTT)

A colony was transferred from the agar slant using a sterile wire loop and then inoculated into a germ tube test to determine the presence of germ tubes. A germ tube test was performed by mixing 3–4 colonies in 0.5 ml of human serum, incubated at 37 ° C for 2–4 h, and examined under a microscope using 10x and 40x objectives for germ tubes. The presence of *Candida albicans* was confirmed by observation of a short, slender, tube-shaped growth structure (pseudohyphae) [26, 27].

Antifungal susceptibility test

Antifungal susceptibility testing for all *Candida* isolates was performed using a modified disc diffusion method following the 2018 Clinical Laboratory Standards Institute (CLSI) guidelines. The test was carried out by adding 2% glucose and 0.5 µg/mL methylene blue dye to Mueller-Hinton agar. The suspension, prepared with normal saline and four identical colonies, was incubated overnight on Mueller-Hinton agar and then compared to the 0.5 McFarland standard. A cotton swab soaked in the fungal suspension streaked the modified Mueller-Hinton medium. Antifungal discs, including amphotericin B 100 µg, clotrimazole 10 µg, fluconazole 10 µg, itraconazole 10 µg, miconazole, and ketoconazole 30 µg, were placed on the agar using a disc dispenser. The plates were then incubated at 37 ° C for 24 h. Subsequently, the inhibition zones (zone diameters) were measured and interpreted according to CLSI guidelines [28].

Operational definition

Risk behavior

refers to the frequent use of antibiotics and certain types of contraceptives, which can increase the risk of *Candida* infection [29].

Pregnancy-related factor

Refers to the gestational period, which means the time from the beginning of pregnancy to the birth time of the subject that exposed them to the risk of *Candida* infection [30].

Clinical factors

Refers to post-medical diseases such as chronic diseases, such as diabetes mellitus, HIV, and previous episodes of candidiasis [31].

Data quality control

Data collectors received three days of training. The questionnaire was initially prepared in English, then translated into Afan Oromo, and subsequently retranslated into English to maintain the consistency of the questions. 5% of the questionnaires underwent pre-testing at the Bule Hora Health Center. Culture media were prepared following the manufacturer's instructions, and sterility was confirmed by incubating 35% of the batch at 37 °C overnight to check for any microbial growth. Culture medium exhibited growth was discarded and replaced with a new sterile batch. The standard strain of *C. albicans* (American Type Culture Collection (ATCC 10231)) was used for quality control.

Data processing and statistical analysis

Data was entered using EPi data version 4.6 and exported to the SPSS Version-25 Statistical Package for analysis. Descriptive statistics, numbers, frequency, percentages, tables, and odds ratio (OR) were used to describe the findings. In addition, bivariate and multivariate logistic regression was used to assess the association between dependent and independent variables. A P-value less than 0.25 at 95% CI during the bivariate analysis was further calculated using multivariate logistic regression to avoid the effect of confounding. Finally, a p-value <0.05 at 95% CI was considered statistically significant.

Results

Socio-demographic characteristics of study participants

A total of 317 pregnant women were included in this study. The ages of the study participants ranged from 18 to 49 years and the mean age was 28.02 with a standard deviation of ±5.554 years. Regarding marital status, 295 (93.1%) of them were married. Among the study participants, 185 (58.4%) were urban residents. Regarding the status of the educational level, 138 (43.5%) of the women were in elementary school and only 12 (3.8%) were in college (Table 1).

Health-related and risky behavior of study participants

Of the 317 pregnant women who participated in the study, 11(3.5%) were HIV-infected patients, 223 (70.3%) of the participants had a use of contraceptive history while 67(21.1%) women had a history of previous candidiasis. Of the total respondents, 173(54.6%) mothers had a history of using antibiotics. Of the total participants, 188(59.3%) had a history of diabetic mellitus. Regarding the gestation period of respondents, 133(42.0%), 101(31.9%), and 83(26.2%) were 2nd trimester, 3rd trimester, and 1st trimester respectively (Table 2).

Prevalence of vaginal *Candida* species

In this study, the prevalence of vaginal candidiasis among pregnant women attended at ANC was 26.8% (85/317) with (95% CI. 21.9 - 31.72%). Of the total *Candida* species isolates, the predominant was *Candida albicans* 53 (62.4%), followed by *C. glabrata* 13 (15.3%). Non-albicans *Candida* species account for 32 (37.7%) (Fig. 1). The highest frequency of *Candida* isolates was observed in

Table 1 Sociodemographic characteristics among pregnant women who attended ANC at bule hora university teaching hospital, guji zone, southern Ethiopia, 2023

Variables	Category	Frequency	Percent
Age group	18–24	84	26.5
	25–30	146	46.1
	31–36	50	15.8
	> 36	37	11.7
Residence	Urban	185	58.4
	Rural	132	41.6
Marital status	Single	5	1.6
	Married	295	93.1
	Widow	8	2.5
	Divorce	9	2.8
Educational level	Illiterate	5	1.6
	Able to read and write	43	13.6
	Elementary	132	41.6
	High school	125	39.4
	College and above	12	3.8
Religion	Muslim	71	22.4
	Protestant	130	41.0
	Orthodox	116	36.6
Occupation	Employers	14	4.4
	Merchant	53	16.7
	House Wife	239	75.4
	Labor	11	3.5
Monthly income	500–2500	5	1.6
	2501–5000	137	43.2
	5001–7500	159	50.2
	7501–10,000	16	5.0

Table 2 Health-related and risky behavior among pregnant women who attended ANC at bule hora university teaching hospital, west guji zone, southern Ethiopia, 2023

Variables	Category	Frequency	Percent
Contraceptive**s**	Yes	223	70.3
	No	94	29.7
Antibiotics	Yes	173	54.6
	No	144	45.4
Gestation period	1st trimester	83	26.2
	2nd trimester	133	42.0
	3rd trimester	101	31.9
Diabetes mellitus	Yes	188	59.3
	No	129	40.7
HIV/AIDS	Yes	11	3.5
	No	306	96.5
Previous candidiasis	Yes	67	21.1
	No	250	78.9

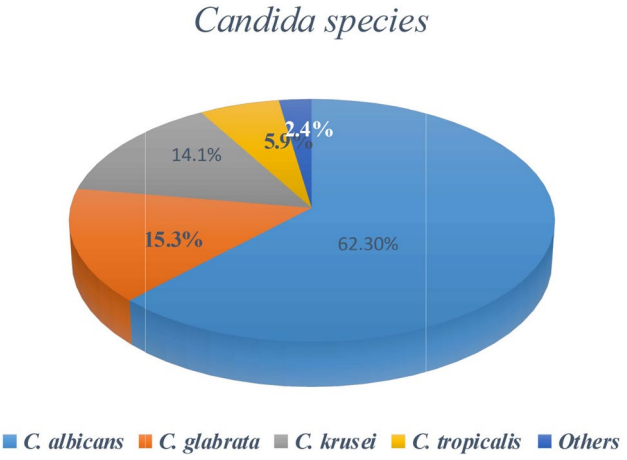

Fig. 1 Proportion of Candida species isolated from pregnant women at Bule Hora University Teaching Hospital, west Guji zone, Southern Ethiopia, 2023

the age range of 25–30 years with 38 (12%), followed by those above 36 years with 18 (9.9%).

Factors associated with the prevalence of vaginal candidiasis

In bivariate logistic regression analysis those variables having a p-value < 0.25 were considered candidate variable for multivariate logistic regression which include married, housewife, use contraceptives, living in urban residence, antibiotics, third trimester, diabetes mellitus, HIV and previous history of candidiasis. Among the variables included in the final model, the odds ratio of vaginal candidiasis infection was about 5 times higher among pregnant mothers who had a history of using contraceptives (AOR = 5.03, 95% CI, 1.21–11.37). Pregnant women who had a history of previous vaginal candidiasis infection were 6 times more likely to have an infection with previous vaginal candidiasis than those who did not have a history of previous vaginal candidiasis infection (AOR = 6, 95%, CI, 1.61–12.92). Human Immunodeficiency Virus (HIV) infection was significantly associated with vaginal candidiasis infection, where HIV-infected pregnant mothers were 4 times more likely to be infected by vaginal candidiasis than non- HIV-infected pregnant women (AOR = 4.24, 95%, CI, 1.23–14.14). Pregnant women who had a diabetes mellitus were approximately two times higher risk when compared to those who had no diabetes mellitus disease (AOR = 2.17, 95%, 1.02–4.64). Pregnant women who had a history of frequently using antibiotics were 3 times more likely to have an infection with vaginal candidiasis than those who had not a history of frequently using antibiotics (AOR = 3.55, 95%, CI, 1.67–12.75). Regarding the gestational period, the pregnant women in the 3rd trimester were 8 times at higher risk when compared to pregnant women in the 1st trimester (AOR = 8.72, 95%CI, 1.30–23.07) (Table 3).

Table 3 Bi-variable and multivariable analysis of associated factors with vaginal candidiasis among pregnant women who attended ANC at bule hora university teaching hospital, west guji zone, southern Ethiopia, 2023

Variables	Category	VC (+) *N* (%)	VC (-) *N* (%)	COR (95% CI)	*P*-value	AOR (95% CI)	*P*-value
Age group	18–24	16(5%)	68(21.5%)	1	0.346	1	0.136
	25–30	38(12%)	108(34.1%)	0.67(0.268–1.136)		0.606(0.314–1.171)	
	31–36	19(6%)	37(11.7%)	0.050(0.104–0.676)	0.896	0.534(0.236–1.212)	0.41
	> 36	12 (3.8%)	19 (6.0%)	0.372(0.243–1.457)	0.256	0.208(0.083–0.519)	0.231
Residence	Urban	57 (30.8%)	128 (69.2%)	1.654(0.823–2.239)	0.324	2.023(0.746–2.018)	0.231
	Rural	28 (21.2%)	104 (78.8%)	1		1	
Marital status	Married	72 (24.4%)	223 (75.6%)	0.215(0.171–9.848)	0.269	5.354(1.875–15.286)	0.066
	Widow	3 (37.5%)	5 (62.5%)	0.4(0.260–7.961)	0.6	2.083(0.396–10.948)	0.386
	Divorce	7 (77.8%)	2 (22.2%)	2.33(0.91–2.513)	0.36	3.00(0.676–13.309)	0.14
	Single	3(60.0%)	2(40.0%)	1		1	
Educational level	Illiterate	2(40%)	3(60%)	1	0.639	1	0.547
	Able to read and write	22 (51.2%)	21 (48.8%)	0.636(0.096–4.197)		0.528(0.351–3.893)	
	Elementary	28 (21.2%)	104 (78.8%)	2.476(0.394–15.548)	0.333	1.389(0.241–11.532)	0.294
	High school	25 (20%)	100 (80%)	2.667(0.423–16.826)	0.297	1.223(0.327–12.928)	0.258
	College and above	8 (66.7%)	4 (33.3%)	0.333(0.039–2.874)	0.318	0.295(0.287–1.245)	0.262
Religion	Protestant	46 (35.4%)	84 (64.6%)	1.882(0.274–1.931)	0.61	0.389(0.256–1.001)	0.412
	Orthodox	23 (19.8%)	93 (80.2%)	0.850(0.573–2.416)	0.65	1.079(0.498–1.532)	0.324
	Muslim	16(22.5%)	55(77.5%)	1		1	
Occupation	Employers	10 (71.4%)	4 (28.6%)	3.00(0.204–5.572)	0.891	0.546(0.133–2.235)	0.40
	Merchant	23 (43.4%)	30 (56.6%)	0.92(0.486–16.807)	0.789	1.443(0.418–4.983)	0.56
	House Wife	47 (19.7%)	192 (80.3%)	0.294(0.248–9.65)	0.189	2.558(0.840–7.794)	0.098
	Labor	5 (45.5%)	6 (54.5%)	1		1	
Monthly income	500–2500	1(20.0%)	4(80.0%)	1	0.74	1	0.08
	2501–5000	20 (14.6%)	117 (85.4%)	1.462(0.155–13.766)		8.80(0.772–10.22)	
	5001–7500	53 (33.3%)	106 (66.7%)	0.5(0.055–4.585)	0.54	12.87(4.040-40.998)	0.187
	7501–10,000	11 (68.75%)	5 (31.25%)	0.113(0.095–3.585)	0.34	4.40(1.454–13.316)	0.83
Contraceptive	Yes	65(29.1%)	158(70.9%)	1.52(1.106–2.371)	0.015	5.032(1.206–11.371)	**0.021**
	No	20(21.3%)	74(78.7%)	1		1	
Antibiotics	Yes	54(31.2%)	119(68.8%)	1.65(1.379–3.327)	0.038	3.550(1.668–12.749)	**0.03**
	No	31(21.5%)	113(78.5%)	1		1	
Gestation period	1st Trimester	16(19.3%)	67(80.7%)	1	0.87	1	0.21
	2nd Trimester	21(15.8%)	112(84.2%)	1.273(0.436–2.638)		4.830(2.63–8.872)	
	3rd Trimester	48(47.5%)	53(52.5%)	0.263(0.134–0.723)	0.007	8.23(1.299–23.066)	**0.012**
Diabetes mellitus	Yes	60(46.5%)	69(53.5%)	5.67(3.288–9.777)	0.03	2.172(1.019–4.644)	**0.040**
	No	25(13.3%)	163(86.7%)	1		1	
HIV	Yes	9(81.8%)	2(18.2%)	13.6 (5.285–18.462)	0.0123	4.235(1.229–14.141)	**0.020**
	No	76(24.8%)	230(75.2%)	1			
Previous Candidiasis	Yes	46(68.7%)	21(31.3%)	11.851(6.382–22.008)	0.021	6.00(1.605–12.924)	**0.031**
	No	39(15.6%)	211(84.4%)	1		1	

Note Bold indicates statistically significant at $p < 0.05$, Reference = 1. VC (+) is vaginal *Candida* positive and VC (-) is vaginal *Candida* negative. COR is crude odds ratio and AOR is adjusted odds ratio. N is the number of respondents and % is the percentage of respondents

Antifungal susceptibility patterns of *Candida* species

For antifungal susceptibility testing was performed on 85 vaginal isolates of *Candida* species. Among the antifungal drug susceptibility amphotericin B and Miconazole were the most effective antifungal drugs for all *Candida* isolates. The species isolates of *C. albicans* 16(30.2%) was resistant to fluconazole. The species isolates of *C. glabrata* were 100% sensitive to itraconazole, miconazole, and amphotericin B, whereas; 3(23.1%), 2(18.4%), 1(7.7%) of the isolates were resistant to fluconazole, ketoconazole, and clotrimazole, respectively. All isolates of *C. tropicalis* were 100% sensitive to all antifungal drug tests and only fluconazole resisted in 2(7.7%) of isolates. All unidentified *Candida* isolates were 100% sensitive to all six antifungal drugs. Most of *C. krusei* was resistant to fluconazole 5(41.7%), ketoconazole 5(41.7%), clotrimazole 2 (16.7%), and only 11(91.7%) was sensitive to amphotericin B (Table 4).

Of the total six antifungal drugs; the resistance proportion was highest for fluconazole and ketoconazole with 26(30.6%) and 17(20%) (Table 5).

Table 4 Antifungal susceptibility patterns of Candida species isolated from pregnant women at bule hora university teaching hospital, west guji zone, southern Ethiopia, 2023

Antifungal drug	Antifungal susceptibility pattern	C. albicans number (%)	C. glabrata number (%)	C. tropicals number (%)	C. krusie number (%)	Other sp number (%)
Itraconazole	S	46(86.8%)	13(100%)	5(100%)	10(83.3%)	2(100%)
	I	2(3.8%)	0(0.0%)	0(0.0%)	1(8.33%)	0(0.0%)
	R	5(9.4%)	0(0.0%)	0(0.0%)	1(8.33%)	0(0.0%)
Miconazole	S	47(88.7%)	13(100%)	5(100%)	11(91.7%)	2(100%)
	I	4(7.5%)	0(0.0%)	0(0.0%)	0(0.0%)	0(0.0%)
	R	2(3.8%)	0(0.0%)	0(0.0%)	1(8.3%)	0(0.0%)
Fluconazole	S	36(67.9%)	10(76.9%)	3(60%)	6(50%)	2(100%)
	I	1(1.9%)	0(0.0%)	0(0.0%)	1(8.3%)	0(0.0%)
	R	16(30.2%)	3(23.1%)	2(40%)	5(41.7%)	0(0.0%)
Ketoconazole	S	39(73.6%)	10(76.9%)	5(100%)	7(58.3%)	2(100%)
	I	4(7.5%)	1(7.7%)	0(0.0%)	0(0.0%)	0(0.0%)
	R	10(18.9%)	2(15.4%)	0(0.0%)	5(41.7%)	0(0.0%)
Clotrimazole	S	44(83%)	12(92.3%)	5(100%)	10(83.3%)	2(100%)
	I	5(9.4%)	0(0.0%)	0(0.0%)	0(0.0%)	0(0.0%)
	R	4(7.5%)	1(7.7%)	0(0.0%)	2(16.7%)	0(0.0%)
Amphotericin B	S	47(88.7%)	13(100%)	5(100%)	11(91.7%)	2(2.6%)
	I	4(7.5%)	0(0.0%)	0(0.0%)	1(8.3%)	0(0.0%)
	R	2(3.8%)	0(0.0%)	0(0.0%)	0(0.0%)	0(0.0%)

Table 5 Total susceptibility pattern of Candida species isolated from pregnant women at bule hora university teaching hospital, west guji zone, southern Ethiopia, 2023

Antifungal Drug	Sensitive		Intermediate		Resistance	
	Number	%	Number	%	Number	%
Itraconazole	76	89.4	3	3.5	6	7.1
Fluconazole	57	67.1	2	2.4	26	30.6
Ketoconazole	63	74.1	5	5.9	17	20
Miconazole	78	91.8	4	4.7	3	3.5
Clotromazole	72	84.7	5	5.9	8	9.4
Amphotericin B	76	89.4	5	5.9	4	4.7

S- Sensitive I- Intermediate R- Resistance

Discussion

The present study showed that the overall prevalence of *Candida* species among pregnant women 26.8% (95% CI, 21.9–31.72) was in line with the study done in Daber Markos referral hospital 25% [23]. It is less than the study conducted in Senegal at 31.93% [32], Lebanon at 39% [33], Dakar Senegal at 32% [34], Kenya at 42.7% [25], and Cameroon at 55.4% [35]. This great variation might be due to geographical environmental factors and differences in lifestyle that affect *Candida* infection from country to country.

In the current study, the predominant *Candida* species isolated was *Candida albicans*; it accounted for 62.35% which is comparable to the study done in Kenya 63.83% [25] and Senegal 62% [32]. The highest frequency of *Candida* colonization 38 (12%) was observed in the age group of 25–30 years, followed by the age group above 36 (>36) years 18(9.9%). This finding is compared to the study conducted in Nigeria that showed that pregnant women in the age group 26–30 years had the highest prevalence of infection at 15.4% [36]. This result is in contrast to a study conducted at Debre Markos referral hospital in the northern part of Ethiopia, *Candida* colonization of 38.5% was observed in the age group of 30–36 years, followed by the age group of 26–33 (31.1%) [23]. The difference may be due to environmental, ethnic, socioeconomic, religious, and cultural factors.

Furthermore, the current study showed that the age group of women between 25 and 30 years of age had a high prevalence of *Candida* colonization, which is similar to a study conducted in northern Nigeria and Palakkad, India, which showed that pregnant women aged 26 to 30 years recorded the highest prevalence of *Candida* colonization 37.1% [36] and 39.08% [37]. The reason for this could be related to women in this age group secrete high reproductive hormones that can suppress the immune

system and create favourable conditions for *Candida* colonization [38]. The other possible reason is related to the use of antibiotics that kill bacteria, including normal floras, there by *Candida* will have an opportunity to colony in the vaginal wall [19].

The present study revealed that the prevalence of vaginal candidiasis infection was about 5 times higher among pregnant mothers who had a history of using contraceptives than non-using contraceptive pregnant mothers. This finding was similar to the report from Tobago University of West India that vaginal candidiasis is higher in pregnant mothers who had a history of using contraceptives than in non-users [29]. The reason for this might be the contraceptive causes many changes in the vaginal environment that might decrease the ability to resist *Candida* infection.

Moreover, this study showed that pregnant women who had a history of using antibiotics were 3 times more likely to have an infection with vaginal candidiasis than those who had not a history of frequently using antibiotics. This finding is similar to the study conducted at the University of Buena in Cameroon [39]. The reason might be that antibiotics disturb (kill) the normal flora of the human body, which is important for protecting the pathogenic organism, and as a result, high *Candida* colonization will occur [19].

The findings of this study revealed that HIV infection was significantly associated with vaginal candidiasis infection, where HIV-infected pregnant mothers were 4 times more likely to be infected by vaginal candidiasis than non- HIV-infected pregnant women. The results of this report were consistent with the study carried out at the Debra Markos referral hospital [23]. This reason might be in immunosuppressed patients, vaginal candidiasis can be correlated well with reduced cell-mediated immunity [40]. The findings of the present study reported that pregnant women who had a history of previous vaginal candidiasis infection were 6 times more likely to have an infection with vaginal candidiasis than those who had not a history of previous vaginal candidiasis infection. This result agreed with the study conducted in Uganda that showed that the majority of respondents had previously had vaginal candidiasis [41]. The possible reason might be due to the shortage of health facilities disseminating information about the cause and effects of vaginal candidiasis and testes.

The present study revealed that pregnant women who had a history of diabetic mellitus were approximately two times at higher risk compared with those who had no history of diabetes mellitus disease. This result report agrees with the study conducted in India [42] and the Debra Markos referral hospital [23]. This could be in diabetes mellitus; glucose concentrations increase in the vaginal secretions that stimulate the adherence of epithelial cells [43]. The present study showed that the gestational period pregnant women in the 3rd trimester were 8 times at higher risk when compared with pregnant women in the 1st trimester. This report is compared to the study conducted in Kenya [25] and Nigeria [36]. However, our findings were in contrast to another study conducted in Uganda which revealed that the 2nd trimester has the highest number of VVC and the least positivity was taken from 3rd trimester pregnant women [41]. This difference might be due to the study design and sample size of the study participants that we used.

In the present study, a high resistance rate was observed for fluconazole, ketoconazole, clotrimazole, and itraconazole with (30.6%), (20%), (9.4%) and (7.1%) respectively. This finding was similar to a study done in Uganda, which reported high resistance (37.6%), (25.5%) (and 9.6%), fluconazole, itraconazole, and clotrimazole, respectively [44]. The present study revealed that the species isolates of *C. glabrata* were 100% sensitive to itraconazole, miconazole, and amphotericin B, whereas; 3(23.1%), 2(18.4%), 1(7.7%) of the isolate were resistance to fluconazole, ketoconazole, and clotrimazole respectively. This finding was compared to the study conducted at the Beijing Centre, China, which showed that the C. *glabrata* resisted clotrimazole 16.6%, fluconazole 19.2%, ketoconazole 15.2%, and only miconazole was active against 56.5% of isolates [45].

Furthermore, the present study showed that of the total of six antifungal drugs; the resistance proportion was highest for fluconazole (30.6%), ketoconazole (20%) and clotrimazole (9.6%). This result was in contrast to the study conducted in Pakistan which indicated that most *Candida* spp. tested were resistant to fluconazole (62%), clotrimazole (59.3%), ketoconazole (58.3%), and itraconazole (40.7%) [46]. The possible reason for this high resistance might be due to the inappropriate use of antifungal drugs during the diagnosis of fungal infection.

The strengths and limitations of the study

The strength of the study was the data collected from patients and it was the primary data that increased the completeness and consistency of the data. The limitations of the study are the cross-sectional design of the study makes it challenging to establish causal relationships. Molecular-level species identification wasn't performed due to resource constraints. Differentiating *Candida* species solely by the color of colonies on Chromagar *Candida* may result in incorrect identification. In addition, not all antifungal susceptibility was achieved due to resource constraints, and no more reagents were found in the country was limited only by the limited number of drugs.

Conclusion and recommendation

The study findings indicated a high prevalence of vaginal *candidiasis* in the study. The most common species was *C. albicans*, followed by *C. glabrata*, *C. krusei* and *C. tropicalis*. The proportion of *Candida* among pregnant women with previous candidiasis was significantly higher than those without previous candidiasis. Factors such as prior use of antibiotics, diabetes mellitus, and HIV (immunocompromised state) before candidiasis and before pregnancy were significantly associated with vaginal candidiasis. Furthermore, the prevalence of *Candida* was notably high among women aged 25–30. In terms of antifungal drug susceptibility, Amphotericin B and Miconazole were found to be the most effective for all *Candida* isolates. Resistance proportions were highest for fluconazole and ketoconazole out of the six antifungal drugs tested. Notably, *C. glabrata* isolates showed 100% sensitivity to itraconazole, miconazole, and amphotericin B, with varying degrees of resistance to fluconazole, ketoconazole, and clotrimazole. It is recommended that healthcare providers implement infection prevention strategies during admissions to healthcare facilities to mitigate *Candida* infections. Furthermore, health education regarding the risks of *Candida* infections is advised at both zonal and healthcare facility levels to reduce vaginal candidiasis among pregnant women. A population-based study is warranted to ascertain the exact prevalence of vaginal candidiasis among pregnant women in the study area.

Abbreviations

ANC	Antenatal Care
AOR	Adjusted odds ratio
AST	Antimicrobial Susceptibility Testing
ATCC	American Type Culture Collection
COR	Crude odds ratio
CLSI	Clinical Laboratory Standards Institute
DM	Diabetes Mellitus
GTT	Germ Tube Test
HCAM	Hi- Chrome Agar Media
HIV	Human Immunodeficiency Virus
KOH	Potassium Hydroxide
MICs	Minimum Inhibitory Concentrations
NAC	Non- Albicans Candida
SDA	Sabroud Dextrose Agar
VVC	Vulvo Vaginal Candidiasis

Supplementary Information

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Supplementary Material 1

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Author contributions

Ibrahim Hussen: Conceptualization, developed proposal, resource, project administration, investigation, and supervision, performed data analysis and interpretation, and wrote, read and approved the final manuscript. Alqeer Aliyo and Moorthy Kannaiyan Abbai: Data curation, formal analysis, software, investigation, and supervision; performed data analysis and interpretation; and wrote, read and approved the final manuscript. Wako Dedecha: Data curation, software, investigation, and supervision; performed data analysis and interpretation; and wrote, read and approved the final manuscript.

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Data availability

All data relevant to the study are included in the article or uploaded as supplementary information.

Declarations

Ethical approval and consent to participate

Ethical approval of this study was reviewed and approved by Bule Hora University's Institutional Review Committee (Ref no: BHUIRC04/2022). Official letters were sent to the health office and supporting letters to Bule Hora University. Written informed consent was obtained from participants in their simple language about the infection, the purpose of the investigation, and the benefits of the study. To ensure the confidentiality of participants' information, codes were used and any identifier of the participants were not written on the questionnaire. Participants were interviewed alone to ensure privacy. Only voluntary participants were asked, and they had a right to refuse to participate in the study. The results were given to the healthcare provider who was working in the ANC room of the hospital for further diagnosis and treatment.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

Author details

[1]Medical Laboratory Science Department, Institute of Health, Bule Hora University, P.O. Box 144, Bule Hora City, Ethiopia

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