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#### ORIGINAL RESEARCH

## Health of Saudi Women in the Post-Pandemic Era: Candidiasis Incidence and Post COVID-19 and COVID-19-Vaccination

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Introduction: Candidiasis, commonly known as yeast infection, affects people worldwide due to the overgrowth of *Candida* species. Of several types, genital candidiasis, particularly vulvovaginal candidiasis (VVC), primarily caused by C. albicans is frequently observed in females of reproductive age. Candidiasis has also become a serious issue in the post-pandemic era, as it occurs as a secondary infection in COVID-19 patients during or after the course of viral illness. Therefore, this study investigated the incidence of C. albicans infections in women of reproductive age, and its relationship with the incidence of COVID-19 and vaccination in Saudi Arabia.

**Objective:** Additionally, this study aimed to determine the awareness of women on candidiasis and its subsequent impact on the occurrence of infection. A survey-based quantitative study was conducted in which primary data were collected from participants using a self-reported questionnaire.

Methods: A total of 200 women aged 18-45 were selected through random sampling. Apart from their sociodemographic characteristics, the history of COVID-19 incidence, COVID-19 vaccination, and candidiasis occurrences among respondents were recorded. Their level of awareness and knowledge of candidiasis, along with their perceptions of strategies for mitigating the risk of incidence, were also evaluated. The collected data were analysed using different statistical tools.

**Results:** The findings of this study revealed a positive correlation between candidiasis, viral infection, and vaccination, regardless of the type and dosage of vaccine administered. Furthermore, both COVID-19 incidence and vaccination had a positive and significant impact on the occurrence of candidiasis among Saudi women.

Conclusion: Despite certain limitations, this study has theoretical and managerial implications for improved management of candidiasis in the post-COVID era.

Keywords: awareness, candidiasis, COVID-19, COVID-19 vaccine, pandemic, incidence

#### Introduction

Over the past three decades, fungal pathogens have become major contributors to life-threatening illnesses and increased mortality in humans.<sup>1</sup> Candidiasis, also referred to as oidiomycosis, poses a significant medical challenge worldwide.<sup>2</sup> Candidiasis is the most prevalent opportunistic yeast infection and encompasses a spectrum of non-life-threatening mucocutaneous and life-threatening invasive diseases.<sup>3</sup> This fungal infection is attributed to yeast species of *Candida* genus, with C. albicans being the most prevalent compared to C. glabrata, C. tropicalis, C. parapsilosis and other non-C. albicans species.<sup>4</sup> These dimorphic yeasts, including C. albicans are commensal in nature and inhabit the skin and gastrointestinal, reproductive and urinary tracts. However, overgrowth of these species can lead to various superficial infections, classified based on the affected area: genital candidiasis (genital parts), mucosal candidiasis (mucous membranes), oropharyngeal candidiasis (mouth and throat), and cutaneous candidiasis (skin).<sup>5</sup> Although Candida species typically exist as commensals within the human host, they display virulence attributes when opportunities arise, particularly in individuals with compromised immune systems.<sup>6</sup> This allows them to enter the bloodstream (systemic

candidiasis or candidemia) and invade vital organs (invasive candidiasis), leading to life-threatening systemic infections. A wide variety of causal factors contribute to yeast infections, including dietary factors, personal hygiene practices, impaired immune systems, and the prolonged use of broad-spectrum antibiotics or immunosuppressive drugs. This complexity highlights candidiasis as a prime example of multifactorial syndrome.<sup>2</sup> The mortality rate associated with invasive candidiasis is estimated to be between 19% and 40%,<sup>7</sup> and it significantly increases to approximately 70% among patients in intensive care units (ICUs),<sup>8</sup> contributing to approximately 1.5 million annual deaths and excess economic costs.<sup>9</sup> The recent emergence of multidrug-resistant strains is also responsible for this higher graph, as it significantly hampers the effectiveness of antifungal treatments.<sup>10</sup>

Before the COVID-19 outbreak, *Candida* infections were a notable concern, with the highest prevalence reaching up to 9% in the most affected group, specifically, those aged 25–34 years.<sup>11</sup> The pandemic further exacerbated the incidence of several fungal infections, such as candidiasis, aspergillosis or mucormycosis from 2020 to 2022.<sup>12,13</sup> COVID-affected patients, especially aged and immunocompromised individuals who recovered from the infection, became highly susceptible to opportunistic fungal infections as a post-Covid effect, often leading to rehospitalization.<sup>14</sup> This exacerbation is linked to the extensive use of interleukin inhibitors during COVID-19 treatments,<sup>15,16</sup> as well as the widespread administration of broad-spectrum antibiotics, especially antimycotics, which promote the selection of resistant species through genomic alterations in normal microbiota.<sup>17</sup> Among these nosocomial infections, invasive yeast infection, particularly candidiasis, is more commonly associated with COVID-19 patients in various countries, but the rate of incidence of COVID-19-associated candidiasis (CAC) is country specific.<sup>20</sup> According to one study, the incidence of candidemia became more than double the rate observed before the pandemic.<sup>21</sup> Before the pandemic, there was a noticeable increase in the prevalence of non-albicans *Candida* species.<sup>22</sup> However, after the pandemic, a shift towards *C. albicans* has been observed, particularly among ICU patients.<sup>16,19</sup> The exact reasons for this shift are still unclear, though it may be related to the overall prevalence of *C. albicans*.

COVID-19 patients, in particular, emerged as a new population at increased risk for developing these infections as coinfections/secondary infections/superinfections.<sup>23</sup> According to scientists, the coronavirus (or SARS-Cov-2) induces immunosuppression in patients, rendering them highly susceptible to secondary opportunistic infections including candidiasis. Moreover, hospitalization in the ICU, widespread use of broad-spectrum antibiotics, corticosteroids, and injection of central venous catheters or vascular catheters in COVID-positive patients create favourable conditions for fungi to invade internal organs and cause candidiasis.<sup>24,25</sup> Underlying chronic diseases such as diabetes mellitus, hypertension, obesity and abdominal infections, along with conditions like ulcerative colitis also play significant role as risk factors for CAC.<sup>20</sup> Additionally, the increased levels of pro-inflammatory and anti-inflammatory cytokines could contribute to a higher risk of fungal co-infections in COVID-19 patients.<sup>26</sup> Furthermore, the majority of COVID-19 patients developed iron deficiency,<sup>27</sup> leading to organ damage and the need for treatment with TNF $\alpha$  antagonists, which further increased their susceptibility to infections.<sup>28</sup>

Vaccination against COVID-19 has been designed and implemented globally to control the pandemic outbreak.<sup>29</sup> The deployment of these vaccines, along with other protective measures, significantly reduces not only new COVID-19 cases but also the severity of illness and mortality rates, thereby proving the efficacy of COVID-19 vaccines. Furthermore, irrespective of the type and dosage of vaccines, most individuals do not experience serious health issues, with side effects limited to muscle pain, fever and headache, indicating the safety of the COVID-19 vaccines.<sup>30</sup> However, Tolani et al<sup>31</sup> observed the occurrence of mucormycosis in individuals following vaccination as a post-COVID sequelae. Therefore, the authors suggested that vaccinated people should remain vigilant against post-COVID fungal infections, even if they are protected from COVID-19.

It has been reported that the overall prevalence of individuals testing serologically positive for COVID-19 in Saudi Arabia was 11%, with noticeable differences across regions. However, an increased prevalence of candidiasis was noted within this country, particularly among women, where *C. albicans* is the most common.<sup>32–34</sup> Despite being recognized as a common fungal infection in both healthy and COVID-19 affected subjects, the occurrence of candidiasis among women in this region in the post-COVID era has not been explored to date. To address the existing research gaps, the present study, focusing on women in Saudi Arabia, was conducted with several objectives. First, we aimed to determine the

incidence of candidiasis among women of reproductive age and its association with the incidence of COVID-19 and vaccination. Second, it assessed the awareness and knowledge of candidiasis, including associated risk factors and symptoms, among women. Third, it aimed to evaluate the impact of COVID-19 incidence and COVID-19 vaccination along with the awareness related to candidiasis on the incidence of this infection. Finally, the study explored the perceptions of women regarding effective strategies to avoid the risk of candidiasis in the post-pandemic era, with the goal of enhancing awareness among the general population.

## Methodology

#### Study Design

This empirical study was a cross-sectional and survey-based quantitative study using a structured and self-administered questionnaire.

#### Questionnaire

After consulting relevant literature and expert suggestions, the final questionnaire consisted of seven sections was prepared. Section I primarily focused on the demographic details of the respondents, whereas sections II and III explored their histories of COVID-19 incidence and COVID-19 vaccination, respectively. The following two sections (Sections IV and V) included questions related to respondents' awareness and knowledge of candidiasis caused by *C. albicans*. The questions in Section VI targeted respondents who had experienced this fungal infection (at least once) to gauge the candidiasis occurrence among them and their potential correlation with COVID-19 incidence or vaccination. The last section (Section VII) included items to understand their perceptions of effective strategies for reducing the risk of candidiasis. All questions were structured as close-ended, and the majority were designed in a multiple-choice format that allowed participants to select the most appropriate option(s). A few questions were rating scale type, utilizing a seven-points Likert scale where responses were scored on a scale from 1 (strongly disagree) to 7 (strongly agree). To ensure inclusivity, the questionnaire was initially written in English and subsequently translated into Arabic for native speakers to facilitate understanding and minimize the likelihood of receiving blank responses. This study followed the guidelines of the Declaration of Helsinki and was approved by the ethics committee (2024/196/109 MLT).

#### Sample Population and Sampling Method

This study recruited participants from different regions of Saudi Arabia, using random sampling. Female participants aged between 18 and 45 years, living in Saudi Arabia and willing to participate in the survey were included. As the study objectives were related to *C. albicans*, participants with candidiasis who possessed a valid medical record documenting their experience with *C. albicans* were included in the study. Therefore, the occurrence of candidiasis due to *Candida* species other than *C. albicans* (eg, *C. glabrata*) was not considered in this study.

#### Data Collection

For primary data collection, the questionnaire was administered to the target population in both the online and offline modes between July 2022 and October 2022. Informed consent was obtained from all individuals participating in the survey. In the selected regions of Saudi Arabia (Al Madinah and Riyadh), the women between the age of 18 and 45 years were more than a 100,000 hence Krejcie and Morgan (1970) formula was used to calculate the sample size, with the margin of error of 7%. Of the 245 participants initially recruited, 45 were excluded from the study because they did not meet the required criteria, withdrew from participation, or had incomplete questionnaire submissions. Finally, 200 valid cases with an 81.6% response rate were included in the analysis.

### Data Analysis

Data were analysed using the Statistical Package for Social Sciences (SPSS) software (24.0). Frequencies and simple percentages were computed for categorical variables, whereas descriptive statistics (mean  $\pm$  standard deviation) were calculated for continuous variables. The chi-squared test was used to assess the association between the occurrence of

candidiasis and COVID-19 incidence or vaccination. Linear regression models were used to examine the impact of awareness, COVID-19 incidence, and COVID-19 vaccination on candidiasis incidence. Additionally, one-way ANOVA was conducted to investigate differences in the incidence of *C. albicans* infection based on vaccine type and dosage. In all inferential statistics, statistical significance was set at a p-value less than 0.05.

### Results

#### Demographic Profile of Respondents

<u>Table S1</u> depicts the demographic characteristics of the 200 Saudi Arabian women recruited for the present survey. The selected population was predominantly within the age group-36–45 years (39.5%), followed by those aged 18–25 years (32.5%). The majority of participants were graduates (63%), unemployed (65.5%), and residing in rural areas (59.5%). A significant proportion of the respondents were married (88%) and nearly half of the married women had one or two children (44.5%). In terms of family income, only 36.5% showed a higher socioeconomic status, reporting a monthly income of more than 8000 Saudi Riyals compared to others.

### History of COVID-19 Incidence, COVID-19 Vaccination and C. albicans Infection

Most participants (90.5%) were not diagnosed with COVID-19 (Table 1). Among the COVID-19 positive population (9.5%), a substantial portion confirmed contracting COVID-19, with a moderate level of severity (4%) and required hospitalization (5%). Regardless of the severity of their initial illness, most infected individuals (5%) experienced mild-to -severe post-COVID-19 complications.

The majority (69.5%) received the COVID-19 vaccine, primarily Oxford-AstraZeneca and Moderna-Spikevax vaccines (Table 1). Among them, 63.3% completed the full vaccination course and an additional 10.8% received the booster dose. A significant proportion (60.4%) reported no side effects of vaccination.

### Incidence of C. albicans Infection

Fifty percent of the participating population had a history of candidiasis affecting the genital areas (45%), oral parts (25%) and gastrointestinal tract (20%) (Table 1). Most patients experienced candidiasis only once, with no history of recurrence (82%). While candidiasis was noted in 32.5% of women following the COVID-19 pandemic, those who had

| Parameters                    | Category  | Frequency (%)                                       |  |  |  |  |
|-------------------------------|---|---|--|--|--|--|
| History of COVID-19 incidence |   |   |  |  |  |  |
| Diagnosed with COVID-19       | No<br>Yes   | 181 (90.5)<br>19 (9.5)                              |  |  |  |  |
| Severity of COVID-19 illness  | Insignificant<br>Mild<br>Moderate<br>Severe         | 3 (1.5)<br>4 (2.0)<br>8 (4.0)<br>4 (2.0)            |  |  |  |  |
| Hospitalized during COVID-19  | No<br>Yes   | 9 (4.5)<br>10 (5.0)                                 |  |  |  |  |
| Post-COVID-19 complications   | None<br>Insignificant<br>Mild<br>Moderate<br>Severe | 4 (2.0)<br>5 (2.5)<br>2 (1.0)<br>4 (2.0)<br>4 (2.0) |  |  |  |  |

Table I History of COVID-19 Incidence, COVID-19 Vaccination and Candidiasis

(Continued)

| Parameters                      | Category  | Frequency (%)                                    |  |  |  |
|---------------------------------|---|--|--|--|--|
| History of COVID-19 vaccination |   |  |  |  |  |
| Received Covid-19 vaccination   | No<br>Yes   | 61 (30.5)<br>139 (69.5)                          |  |  |  |
| Dosage                          | Fully vaccinated<br>Partially vaccinated<br>Booster dosage  | 63.3 (63.3)<br>25.9 (25.9)<br>10.8 (10.8)        |  |  |  |
| Туре                            | Pfizer-BioNTech<br>Oxford-AstraZeneca<br>Moderna-Spikevax<br>Janssen (Johnson & Johnson)-Jcovden  | 29 (20.9)<br>42 (30.2)<br>44 (31.7)<br>24 (17.3) |  |  |  |
| Experienced side effects        | No<br>Yes   | 84 (60.4)<br>55 (39.6)                           |  |  |  |
| Inci                            | dence of C. albicans infection  |  |  |  |  |
| Diagnosed with infection        | Never<br>Before COVID-19 pandemic<br>After COVID-19 pandemic<br>Both  | 100 (50.0)<br>17 (8.5)<br>65 (32.5)<br>18 (9.0)  |  |  |  |
| History of recurrences          | No<br>Yes   | 82 (82)<br>18 (18)                               |  |  |  |
| Frequency of experience         | Only once<br>2–3 times<br>4–5 times<br>More than 5 times  | 82 (82)<br>9 (9)<br>7 (7)<br>2 (2)               |  |  |  |
| Affected body part(s)           | Genital tracts (vulva, vagina)<br>Protective coverings (nail, skin)<br>Oral parts (mouth, tongue)<br>Respiratory tract (larynx, pharynx)<br>Gastro-intestinal tract | 45 (45)<br>3 (3)<br>25 (25)<br>7 (7)<br>20 (20)  |  |  |  |

Table I (Continued).

contracted COVID-19 expressed a neutral stance regarding their experience with *Candida*-related symptoms soon after testing positive for COVID-19 ( $2.64 \pm 1.73$ ). However, they disagreed with the idea of experiencing such symptoms soon after being vaccinated ( $2.44 \pm 1.60$ ).

## Association Between C. albicans Infection and Diagnosis of COVID-19 and Receipt of COVID-19 Vaccination

As depicted from Table 2, the frequency of women reporting candidiasis after the pandemic was significantly higher than before the pandemic, regardless of COVID-19 incidence and vaccination status. Secondly, there was a significant positive association between *C. albicans* infection and COVID-19 diagnosis ( $\chi 2 = 12.801$ , p < 0.05). Most women infected with *C. albicans* after the pandemic (68.4%) were diagnosed with COVID-19. Similarly, the correlation between *C. albicans* infection and reception of COVID-19 vaccination was significant and positive ( $\chi 2 = 10.095$ , p < 0.05). Among *Candida*infected participants during post pandemic period, those who were vaccinated reported candidiasis at a higher frequency (38.1%) than those who did not receive the vaccination (19.7%). These findings suggest a possible link between COVID-19 infection, vaccination and increased susceptibility to *C. albicans* infections. However, the association between

|                   |     |            | Diagnosed with Cand             | Total                          | Chi       | p Value |        |       |
|-------------------|-----|------------|---------------------------------|--------------------------------|-----------|---------|--------|-------|
|                   |     | Never      | Before the COVID-19<br>Pandemic | After the COVID-19<br>Pandemic | Both      |         | Square |       |
| Diagnosed with    | No  | 95 (52.5%) | 17 (9.4%)                       | 52 (28.7%)                     | 17 (9.4%) | 181     | 12.801 | 0.005 |
| Covid-19          | Yes | 5 (26.3%)  | 0 (0%)                          | 13 (68.4%)                     | l (5.3%)  | 19      |        |       |
| Received Covid-19 | No  | 40 (65.6%) | 3 (4.9%)                        | 12 (19.7%)                     | 6 (9.8%)  | 61      | 10.095 | 0.018 |
| vaccination       | Yes | 60 (43.2%) | 14 (10.1%)                      | 53 (38.1%)                     | 12 (8.6%) | 139     |        |       |

 Table 2 Association Between Candidiasis, COVID-19 Incidence and Its Vaccination

COVID-19 infection and candidiasis cannot be fully established due to the low percentage of COVID-positive participants in this study. Therefore, further investigation is needed to draw a definitive conclusion.

#### Awareness Level Regarding Candidiasis

Approximately 74% of the respondents asserted that their overall knowledge of *C. albicans* was very high (Table S2). They agreed that they had heard of this fungus before taking this survey  $(4.04 \pm 1.10)$ , understand the meaning of candidiasis  $(3.98 \pm 1.07)$ , know all symptoms  $(3.97 \pm 1.19)$  and risk factors  $(3.97 \pm 1.07)$  of candidiasis and are aware of its transmission mode  $(3.83 \pm 1.25)$  (Table S3). Regarding sources of information, approximately 48.5% gained information from others who were either healthcare professionals (doctors) or non-professionals (friends, family) (Table S2). Both broadcast and digital media were also identified as sources of information for another 35% of the individuals.

#### Knowledge on C. albicans

When respondents were assessed for their knowledge of *C. albicans*, the majority identified the disease as fungal (74.5%), which was transmitted through direct contact with contaminated surfaces (79.5%) (Table S2). They considered factors such as pregnancy, poor eating habits, lack of personal hygiene, uncontrolled diabetes, irregular menstrual cycle, stress, lack of sleep, overuse of antibiotics, and a weak immune system as major causes of candidiasis. A significant proportion (76.5%) of the participants believed that all females were likely to experience this infection at least once in their lifetime. However, almost all respondents, except for a few (94.5%), agreed that candidiasis was treatable.

## Impact of Candidiasis Awareness, COVID-19 Incidence and COVID-19 Vaccination on Candidiasis Occurrence

Linear regression was conducted to assess the influence of awareness of candidiasis, COVID-19 incidence and COVID-19 vaccination (independent variables) on candidiasis incidence (dependent variable) among Saudi Arabian women. Respondents acknowledged that there was a significant level of awareness of *C. albicans* among women in Saudi Arabia  $(3.63 \pm 0.71)$  (data not included). However, despite this increased awareness, the regression model demonstrated no significant effect of awareness on the incidence of candidiasis (Tables 3). In contrast, both COVID-19 incidence and COVID-19

|                                   |        | ndardized<br>ficients | т      | Sig.  |
|-----------------------------------|--------|-----------------------|--------|-------|
|                                   | В      | Std. Error            |        |       |
| Diagnosed with COVID-19           | 0.176  | 0.070                 | 2.530  | 0.012 |
| COVID-19 vaccination              | 0.180  | 0.070                 | 2.562  | 0.011 |
| Awareness of C. albicans in women | -0.004 | 0.070                 | -0.053 | 0.958 |

 Table 3 Impact of COVID-19 Occurrence, Vaccination and Awareness About C. Albicans

 on Candidiasis Infection

**Note**: r<sup>2</sup> = 0.072; F(3196)=5.084; p<0.01.

vaccination significantly and positively influenced the occurrence of candidiasis in Saudi Arabian women. The 7.2% of the variations in candidiasis incidence was explained by COVID-19 incidence, COVID-19 vaccination and awareness *C. albicans* in women. Furthermore, the beta coefficient value indicated that for every unit increase in COVID-19 occurrence and vaccination, candidiasis incidence increased by 0.176 and 0.180 times, respectively (p < 0.05).

#### Difference in Incidence of Candidiasis Based on Vaccine Type and Dosage

One-way ANOVA was performed to assess the difference in candidiasis incidence based on the type and dosage of COVID-19 vaccine. Table 4 shows no statistically significant differences in the incidence of candidiasis based on dosage (F = 0.121, p > 0.05) or vaccine type (F = 2.001, p > 0.05). This suggests that, while COVID-19 vaccination significantly influenced the incidence of candidiasis in Saudi Arabian women, the type and dosage of the vaccine did not have a significant impact on the occurrence of candidiasis.

# Perception of Respondents Regarding Effective Strategies to Reduce the Risk of Candidiasis

Participants were assessed to gauge their understanding of strategies that could effectively reduce the risk of candidiasis following the COVID-19 incidence and vaccination. According to them, consuming protein- and vitamin-rich food; avoiding sugary, junk, or fungal-based items; taking broad-spectrum medications; adopting preventive measures; following a proper diet; practicing good personal hygiene during menstruation; and maintaining a healthy lifestyle can lower the chances of *C. albicans* infection (Table 5). However, they remained neutral regarding other aspects, such as

|                                     |    | •             |       |         |
|-------------------------------------|----|---------------|-------|---------|
|                                     | Ν  | Mean ± SD     | F     | p Value |
| Dosage                              |    |               |       |         |
| Fully vaccinated                    | 88 | 2.701 ± 1.625 | 0.121 | 0.886   |
| Partially vaccinated                | 36 | 2.861 ± 1.624 |       |         |
| Booster dosage                      | 15 | 2.800 ± 1.222 |       |         |
| Vaccine type                        |    |               |       |         |
| Pfizer-BioNTech                     | 29 | 2.897 ± 1.502 | 2.001 | 0.117   |
| Oxford-AstraZeneca                  | 42 | 2.690 ± 1.649 |       |         |
| Moderna-Spikevax                    | 44 | 2.409 ± 1.578 |       |         |
| Janssen (Johnson & Johnson)-Jcovden | 24 | 3.354 ± 1.433 |       |         |

| Table 4 Difference in | Candidiasis | Incidence | Based | on | Vaccine | Туре | and |
|-----------------------|-------------|-----------|-------|----|---------|------|-----|
| Dosage                |             |           |       |    |         |      |     |

 Table 5 Effective Strategies to Reduce Risk of Candidiasis

| Items  | Mean  | Std. Deviation |
|--|-------|----------------|
| Knowing the infection and its associated signs or symptoms   | 2.995 | 1.059          |
| Understanding the potential risk factors   | 3.405 | 1.061          |
| Adopting preventive measures   | 3.705 | 0.934          |
| Following good personal hygienic practices during menstruation   | 3.470 | 1.138          |
| Following a proper diet and lifestyle practices.   | 3.410 | 1.237          |
| Adopting proper sexual practices   | 3.395 | 1.022          |
| Taking broad spectrum medications (Reverse coding)   | 3.485 | 1.165          |
| Avoiding sugary beverages and junk food.   | 3.660 | 1.158          |
| Avoid items derived from fungi or yeast sources (alcoholic beverages, cheese, bread, fermented products) | 3.565 | 0.965          |
| Avoiding foods made of refined sugars (cakes, desserts, candies, pastries, honey, jam etc.)              | 3.425 | 1.054          |
| Avoiding high content lactose food items.  | 3.225 | 1.072          |
| Consuming food rich in dietary fibre (whole grains, ground flaxseeds, leafy vegetables).                 | 3.295 | 1.190          |
| Consuming food rich in protein sources (Fish, meat, poultry, pulses)                                     | 4.055 | 1.361          |
| Consuming food rich vitamins (citrus fruits, blueberries, nuts and seeds)                                | 3.880 | 1.384          |

knowing the infection, its associated symptoms or risk factors, adopting proper sexual practices, and consumption of food rich in dietary fibre or lactose, indicating a knowledge gap in these areas.

#### Discussion

The present study provides a comprehensive assessment of the health outcomes of Saudi Arabian women in the context of candidiasis occurrence by considering both the COVID-19 incidence and COVID-19 vaccination. In this study, only 9.5% of women participated in the survey reported a history of COVID-19 infection, reflecting a low incidence in the country. Previous studies showed a similarly low prevalence, ranging from 1.78% to 24.45% depending on the region.<sup>35</sup> This low prevalence may be attributed to the high number of asymptomatic COVID-19 cases that went unreported. Additionally, the Saudi Arabian government implemented preventive measures and conducted awareness campaigns against the viral infection to curb the disease transmission.<sup>36</sup> These proactive steps, along with effective healthcare practices, vaccination against COVID-19 and treatment protocols played a crucial role in controlling the spread of COVID-19 within the country.<sup>37</sup>

In the present study, half of the women in the reproductive age group had a history of candidiasis, mostly in their genital and oral parts, during the pre- and/or post-pandemic eras. The occurrence of vulvovaginal candidiasis among reproductive-aged women, especially during pregnancy, in different regions of the world was also reported by Disha and Haque.<sup>38</sup> According to a review, the evidence of VVC in expecting mothers is higher in African and Middle Eastern countries, particularly Kenya (90.38%), followed by Saudi Arabia (70.2%). Similarly, *C. albicans*-induced VVC has been noted in 68% of women aged 15–64 years living in the central region of Saudi Arabia.<sup>34</sup> In addition to genital candidiasis, colonization of *Candida* species has also been observed in 43.4% of subjects.<sup>39</sup> Among the different species, *C. albicans* was identified as the causative yeast in 55.6% of adults carrying oral *Candida*, indicating its predominance over non-*Candida albicans* species. Incidents of asymptomatic *Candida* infections have also been reported at a higher percentage, ranging from 61.9% (Argentina) to 70.74% (Burkina Faso).<sup>38</sup> This suggests that women who were not diagnosed in this study may harbor *Candida* colonization in their body parts without exhibiting any symptoms. Consequently, some of them may be unaware, potentially leading to an increase in the frequency of candidiasis.

Most previous studies have established a higher occurrence of candidiasis in COVID-19 patients.<sup>40</sup> However, there has been limited focus on candidiasis incidence in vaccinated individuals. One study found that non-vaccinated participants were at higher risk of infection with non-albicans *Candida* species,<sup>41</sup> but this study primarily involved diabetic patients with post-COVID-19 infections. This indicates that the association between COVID-19, vaccination and Candida infection has not been thoroughly evaluated in women, who are commonly affected by this type of fungal infection. In this context, the present research offers important insights, showing that more than half of the C. albicanspositive group experienced the infection following the outbreak. Most patients infected with C. albicans after the pandemic had also contracted COVID-19 and received vaccination. This pattern suggests a possible correlation between candidiasis, viral infection and vaccination, regardless of the type or dosage of the vaccine administered. However, due to the low percentage of COVID-positive participants in this study, the association between COVID-19 infection and candidiasis cannot be fully established. Therefore, further investigation is necessary to reach a definitive conclusion. Additionally, both the COVID-19 incidence and COVID-19 vaccination had a positive and significant impact on the occurrence of candidiasis among Saudi women. This is in agreement with earlier studies that demonstrated co-infection with candidiasis in patients with COVID-19.42,43 According to many authors, post Covid-19 has become a serious condition, as it develops into different types of candidiasis (candidemia, oropharyngeal candidiasis, oral candidiasis and intra-abdominal candidiasis) as secondary infections.<sup>28,44</sup> The diagnosis of CAC in immunosuppressed patients is challenging for healthcare practitioners. Consequently, the treatment of CAC becomes difficult, leading to an increased death rate (19–40%).<sup>44</sup> A 100% mortality rate was observed among CAC patients who took antifungal medications,<sup>42</sup> underscoring the seriousness of this infection. One of the primary reasons for their susceptibility to such fungal infections is their impaired immune system.<sup>20</sup> In addition to immunodeficiency, several other factors, such as ICU stay for a prolonged period, corticosteroid and antibiotic intake or mineral deficiency, trigger the entry of Candida spp. and their overgrowth or switching from commensal to pathogenic forms, thereby predisposing COVID-19 patients to candidiasis. Pre-existing chronic diseases, such as diabetes, hypertension and obesity, can also increase the risk of fungal infection for these vulnerable patients. Apart from this, high number of candidiasis cases may also be linked with other potential causes, such as poor hygiene, hormonal changes, immunosuppression due to treatments unrelated to COVID-19, diet or underlying health conditions of the candidiasis affected participants. However, the present study did not evaluate predisposing factors for such infection in women with or without COVID-19, suggesting the abovementioned factors as possible mechanisms involved in candidiasis. Conversely, the impact of COVID-19 vaccination on candidiasis incidence has not been reported in the literature. There is only one case report in which a COVID-19 vaccinated male with diabetes was affected by mucormycosis in the maxilla as a post-COVID sequel.<sup>31</sup> Nevertheless, the lack of empirical research in this area necessitates further investigation to determine the relationship between the two factors.

Self-reported data indicated that most participating women had heard about *C. albicans*, had very high knowledge of it and were aware of this fungal infection, including its risk factors, modes of transmission and associated symptoms. However, no significant effect of awareness on its incidence was observed. In terms of protective strategies against *C. albicans*-mediated candidiasis, women demonstrated a positive perception of the significance of dietary habits, medication use, personal hygiene and maintaining a healthy lifestyle. However, their understanding that knowing associated symptoms or risk factors and adopting proper sexual practices could mitigate this risk is uncertain. This is possibly because almost all participants had no knowledge of the mode of disease transmission mode, adopting safe sexual practices and maintaining good personal hygiene to enhance awareness among women. By being more knowledgeable and aware of candidiasis, women can avoid this infection and its associated complications by adopting correct measures and manage candidiasis effectively.<sup>45</sup>

The present study had certain limitations. First, the study sample was geographically restricted to Saudi Arabia; therefore, the findings cannot be generalized to other populations. Second, the analysis was based on self-reported data, which introduces the risk of response bias and raises questions regarding the reliability of the data for awareness levels regarding candidiasis. Third, several other factors (such as underlying health conditions and antibiotic use during the pandemic) that may influence the observed incidences of candidiasis have not been explored and can influence the accuracy of the study's conclusions. Furthermore, the pandemic may exert delayed or persistent effects on the immune system and the microbial balance within an individual's body. However, this cross-sectional study was conducted within a specific time frame and was therefore unable to capture the long-term consequences of the COVID-19 outbreak and its vaccination on the incidence of candidiasis. The present study included a low percentage of COVID-positive patients, which limits the ability to fully justify the relationship between COVID-19 incidence and candidiasis infection among these women.

#### Conclusion

In conclusion, *C. albicans*-induced candidiasis was a common yeast infection in Saudi Arabian women after the pandemic. Both COVID-19 incidence and COVID-19 vaccination significantly and positively influenced the occurrence of candidiasis. Simultaneously, high number of candidiasis cases among covid-negative individuals may indicate other potential causes underlying this disease condition. Furthermore, a lack of knowledge about the mode of disease transmission through sexual contact and the importance of adopting proper sexual practices to reduce infection risk highlights the need for education in these areas among women.

Overall, this study provides a comprehensive understanding of the interplay between viral infection, vaccination and candidiasis incidence. It also contributes to advancing scientific knowledge in this field and establishes a foundation for future research. This study provides valuable insights for policymakers by offering cues for increasing the awareness level of women to reduce the risk of infection as well as for enhancing public health policies and guidelines related to post-COVID-19 care. Moreover, by evaluating the influence of COVID-19 vaccination on candidiasis, this study allows them to monitor vaccination policy considerations. Taken together, this study holds profound significance for women's health, particularly in the context of managing fungal infections in individuals following both the COVID-19 incidence and vaccination.

#### **Ethics Approval and Consent to Participate**

Ethical approval for this study was obtained from the Scientific Research Ethics Committee of the College of Applied Medical Sciences, Taibah University (2024/196/109 MLT).

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