



Isolation, Identification of Candida Species in Diarrhea Patients: From Zintan City, Libya

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عزل وتشخيص أنواع المبيضات في مرضى الإسهال: من مدينة الزنتان، ليبيا

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Abstract:

Candida species are significant fungal pathogens responsible for various infections, including gastrointestinal Candidiasis. This study aimed to investigate the prevalence of Candida species in diarrhea patients and explore their association with age and gender in Zintan City, Libya. **MATERIALS AND METHODS:** A total of 102 stool samples were collected from patients with gastrointestinal symptoms. Samples were cultured on Sabouraud's dextrose agar (SDA), potato dextrose agar (PDA), and Chrom Agar for species identification. Direct microscopic examination and germ tube tests were performed to confirm Candida species. Statistical analysis was conducted to assess the distribution of infections across age and gender groups. **RESULTS:** The study revealed a Candida infection rate of 44.12%, with *C. albicans* being the most prevalent species (44.44%), followed by *C. glabrata* (31.11%). The highest infection rate was observed in the 1-10 years age group (53.33%), while no infections were reported in the 61-70 and 81-90 years age groups. Regarding gender distribution, 58% of infections were found in women, and 42% in men, with no significant gender-based differences ($p > 0.05$). **CONCLUSION:** This study highlights the significant role of Candida, particularly *C. albicans*, in gastrointestinal infections among diarrhea patients. The high prevalence in children underscores their vulnerability, while the absence of gender-based differences emphasizes the importance of non-gender-related risk factors. The findings advocate for increased clinical awareness and further research to improve diagnostic and treatment strategies for Candida-associated diarrhea.

Keywords: Candidiasis; *C. albicans*; DIARRHEA; GASTROINTESTINAL CANDIDIASIS; LIBYA.

المخلص :

تعتبر أنواع المبيضات (Candida species) من مسببات الأمراض الفطرية التي تسبب العديد من الالتهابات المختلفة، بما في ذلك التهاب الجهاز الهضمي الفطري. هدفت هذه الدراسة إلى التحقق من انتشار أنواع المبيضات لدى مرضى الإسهال ودراسة علاقتها بالعمر والجنس في مدينة الزنتان، ليبيا. **المواد والطرق :** تم جمع 102 عينة براز من مرضى يعانون من أعراض الجهاز الهضمي. تم زرع العينات على أوساط زراعية مثل سابورو دكستروز أغار (SDA) وبطاطا دكستروز أغار (PDA) وكروم أغار (Chrom Agar) لتحديد الأنواع. تم إجراء الفحص المجهرى المباشر واختبار أنبوب التبرع لتأكيد أنواع المبيضات. تم إجراء التحليل الإحصائي لتقييم توزيع العدوى عبر الفئات العمرية والجنس. **النتائج:** كشفت الدراسة عن معدل عدوى بالمبيضات بنسبة 44.12%، حيث كانت المبيضة البيضاء (*Candida albicans*) النوع الأكثر انتشاراً (44.44%)، تليها المبيضة المغمدة (*Candida glabrata*) بنسبة (31.11%). لوحظ أعلى معدل عدوى في الفئة العمرية 1-10 سنوات (53.33%)، بينما لم تسجل أي إصابات في الفئات العمرية 61-70 و 81-90 سنة. بالنسبة لتوزيع العدوى حسب الجنس، 58% من الإصابات كانت لدى النساء، و42% لدى الرجال، دون فروق ذات دلالة إحصائية ($p > 0.05$). **الاستنتاج:** تبرز هذه الدراسة الدور الهام لمادة الفطريات، وبخاصة *C. albicans*، في التهابات الجهاز الهضمي لدى مرضى الإسهال. الانتشار المرتفع لدى الأطفال يؤكد ضعفهم، في حين انعدام الفروقات الجنسانية يؤكد أهمية عوامل الخطر غير الجنسانية. النتائج تدعو لزيادة الوعي السريري والبحث الإضافي لتحسين استراتيجيات التشخيص والعلاج لعدوى المبيضات المرتبطة بالإسهال.

كانت النسبة أعلى قليلاً لدى النساء (58%) مقارنة بالرجال (42%)، ولكن لم تكن هناك فروق ذات دلالة إحصائية بين الجنسين ($p > 0.05$). الخلاصة سلطت هذه الدراسة الضوء على الدور الكبير للمبيضات، وخاصة المبيضة البيضاء (*Candida albicans*)، في التهابات الجهاز الهضمي لدى مرضى الإسهال. يشير ارتفاع معدل العدوى لدى الأطفال إلى مدى تعرضهم للإصابة، بينما يؤكد عدم وجود فروق بين الجنسين على أهمية العوامل غير المرتبطة بالجنس. تدعو النتائج إلى زيادة الوعي السريري بالمبيضات كمسبب للإسهال وإجراء مزيد من الأبحاث لتحسين استراتيجيات التشخيص والعلاج.

الكلمات الدالة: الإسهال، المبيضة البيضاء، التهاب الجهاز الهضمي بالمبيضات، المبيضات ليبييا.

Introduction

Fungi are considered among the most important living organisms, widely distributed across most environments. Various species are responsible for human infections, with new fungal pathogens being identified annually [1]. There are several diseases caused by fungi, such as invasive candidiasis [2], dandruff [3], and otomycosis [4]. Species of *Candida* are the leading cause of fungal infections [5]. The genus *Candida* comprises approximately 200 species, with around twenty being most commonly isolated during infections, including *C. albicans* and non-*C. albicans* species (e.g., *C. tropicalis*, *C. glabrata*, *C. parapsilosis*, *C. krusei*, *C. guilliermondii*, among others). However, *C. albicans* remains the most frequently identified species, though the prevalence of non-*C. albicans* species has been steadily increasing [6,7]. *Candida* was initially classified as a genus of yeast species capable of forming hyphae or pseudohyphae, with no sexual spores observed at the time. However, recent phylogenetic studies have clarified that *Candida* species actually constitute a polyphyletic group within the Saccharomycotina [8,9]. *C. albicans* is a component of the normal microbiota in 50% of the population [10]. While *C. albicans* continues to be the most prevalent pathogen in oropharyngeal, cutaneous candidiasis, gastrointestinal, vaginal tract infections, and candidemia [10], superficial candidiasis is commonly observed in individuals with AIDS, while vaginitis is more frequently encountered in immuno competent infants and adult women. Candidemia and invasive candidiasis are prevalent among cancer patients and transplant recipients following immunosuppressive therapy. The clinical significance of *Candida* infections is further highlighted by their impact on healthcare systems. Currently, candidiasis is the fourth most common cause of nosocomial infections, accounting for 8% to 10% of cases, and mortality associated with systemic candidiasis remains high, ranging from 15% to 35%, depending on the specific *Candida* species involved [11,9]. *Candida* yeast possesses a range of virulence factors and specific strategies that facilitate its colonization, pathogenicity, and evasion of the host's immune defenses. It is capable of transitioning through various morphological forms, including unicellular budding yeast (blastospore), pseudohyphae, and true hyphae. This morphological plasticity is a critical virulence mechanism, enabling tissue invasion and evasion of phagocytic cells. Additional virulence factors include the production of hemolysin, the formation of germ tubes, toxin secretion, and the production of enzymes such as phospholipase, proteinase, as well as adherence to epithelial cells. Furthermore, *Candida* maintains cell wall integrity and effectively evades the host immune response [12,13,14,9]. Candidalysin is known to facilitate membrane permeabilization; however, the precise molecular mechanisms underlying this process remain unclear [15]. The host defense against *Candida spp.* is mediated by a complex network of both innate and adaptive immune components, including epithelial cells, macrophages, neutrophils, dendritic cells, defensins, and the complement system. In instances where the host's immune system is compromised due to conditions such as HIV infection, organ transplantation, or cancer treatment [16], or when microbial imbalances arise from antibiotic use [17], the risk of infection increases. Given the exacerbation of pathogenic fungal infections and the suffering of many patients in recent times, with an increase in the number of infected individuals and delayed recovery rates in many countries around the world, this study focuses on *Candida* yeast, which is considered one of the common causes of infection. The study aims to contribute to addressing

this issue by isolating and identifying *Candida spp.* species, examining their prevalence, and exploring their relationship with age and gender in clinical samples taken from patients with gastrointestinal problems at Al-Zintan General Hospital.

Materials and Methods

Study Area

Al Jabal Al Gharbi region (Zintan City) is located in the northwest of Libya (32°07N, 12°58E), approximately 140 km from Tripoli. The region has a mountainous climate with an annual rainfall of 168 mm, a relative humidity of 52.2%, and an average annual temperature of 19.4°C.

Sample Collection and Examination

A total of 102 stool samples were collected from patients suffering from diarrhea, abdominal cramps, discomfort, or indigestion at the Central Analysis Laboratory of the Medical Complex and the Akid Medical Laboratory in Zintan City. The patients' ages ranged from 1 to 80 years. Adequate stool samples were collected in clean, sterile containers, ensuring the absence of urine or blood contamination, particularly for female patients. Samples were not collected from patients using antacids, diarrhea medications, antibiotics, or laxatives. Each sample was labeled with the patient's name, gender, age, and collection date. All samples were transported to the Microbiology Laboratory at the Faculty of Science for further analysis.

Methods

Sterilization of Materials

All materials used in this study were sterilized according to their specific properties and requirements. Glassware was sterilized in a hot air oven at 160°C for 60 minutes, while culture media were autoclaved at 121°C for 15 minutes. Plastic materials and laboratory surfaces were disinfected with alcohol, and the inoculation loop was sterilized using a direct flame, following standard protocols [18].

Direct Microscopic Examination (DME)

For each stool sample, two slides were prepared: one stained with Gram stain (GS) and the other with lactophenol cotton blue (LPCB). The slides were examined under a light microscope at 40x and 100x magnifications. The presence of budding yeast cells, with or without pseudohyphae, was considered indicative of yeast infection [18, 19].

Culturing of samples

Swabs were streaked onto Sabouraud's dextrose agar (SDA), potato dextrose agar (PDA) supplemented with 0.05 mg/mL chloramphenicol to inhibit bacterial growth, and Candida Chrom Agar. The inoculated plates were incubated at 37°C for 24-96 hours to allow *Candida* growth. After incubation, colony morphology was examined [20].

Germ Tube Formation Test

A small portion of the *Candida* colony was transferred to a sterile test tube containing serum and incubated at 37°C for 2-4 hours. The formation of a germ tube protruding from the fungal cell was observed, which is a characteristic feature of *C. albicans* [21].

Statistical analysis

The data were rigorously analyzed using SPSS (Version 23) software, with the significance level set at $p < 0.05$. A chi-square test was used to determine the prevalence of *Candida* species and the relationship between *Candida* species infection and gender as well as age. Additionally, the Post-hoc Z-test was employed to compare the prevalence of *Candida* species. Statistical analysis played a crucial role in drawing robust conclusions from our study.

Results

Table 1. Distribution of Candida Infection Status Among Diarrhea Patients (n=102)

Condition	Number of Cases	Percentage (%)
Uninfected	57	55.88%
Infected	45	44.12%

Table 2. Prevalence and Distribution of Candida Species on Chrom Agar Based on Colony Color and Frequency of Isolation

Yeast Species	Colony Color	Number of Isolates	Percentage (%)	Significance
<i>Candida albicans</i>	Green	20	44.44%	a
<i>Candida glabrata</i>	Purple	14	31.11%	b
<i>Candida parapsilosis</i>	White	5	11.11%	c
<i>Candida tropicalis</i>	Blue	3	6.66%	d
<i>Candida krusei</i>	Pink	3	6.66%	d

Chi-square analysis revealed a statistically significant difference in the distribution of *Candida* species on Chrom Agar ($\chi^2 = 25.67$, $p < 0.05$, critical value = 9.488 at $df = 4$). This table and explanation summarize the statistical differences between the species using the Post-hoc Z-test results, which are marked by letters indicating significant differences between the species.

The identification of *Candida* species was carried out using Chrom Agar differential medium. The cultivation of various *Candida* species on Chrom Agar at 37°C for 24–48 hours resulted in colonies with distinct color variations, which were species-specific. *C. albicans* appeared as green colonies, *C. glabrata* formed purple (mauve) colonies, *C. krusei* displayed pink colonies, *C. tropicalis* produced blue colonies, and *C. parapsilosis* formed white colonies, as illustrated in Table 2. *C. albicans* was the most frequently isolated species, with 20 isolates representing 44.44% of the total isolates. *C. glabrata* followed with 14 isolates, accounting for 31.11% of the total, and was characterized by purple colonies. *C. parapsilosis* was observed with 5 isolates (11.11%), displaying white colonies, while *Candida tropicalis* and *Candida krusei* were less prevalent, with 3 isolates each, accounting for 6.66% of the total isolates for each species. *C. tropicalis* colonies were blue, and *C. krusei* colonies appeared pink. These findings indicate a variation in the frequency of *Candida* species in the sample, with *C. albicans* being the most commonly isolated species, followed by *C. glabrata*, while *C. tropicalis*, *C. krusei*, and *C. parapsilosis* were less frequently isolated. The differential medium Chrom Agar was effective in distinguishing between the species based on colony color, further aiding in the identification process.

The table 3, presents the distribution of patients with diarrhea based on their infection status with *Candida*. Among the total cases, 57 patients (55.88%) were uninfected, while 45 patients (44.12%) were found to be infected. This distribution highlights the relatively high proportion of uninfected patients compared to those infected with *Candida*. The data provides insight into the prevalence of *Candida* infection in this specific patient group, suggesting a near-equal distribution between infected and uninfected cases.

Table 3. Distribution of Candida Species Isolates in Stool Samples of Patients with Intestinal Candidiasis (n=102)

Gender	Number of Isolates	Percentage (%)
Women	26	58%
Men	19	42%

Chi-square analysis indicated no statistically significant difference in the distribution of *Candida* species across genders in patients with intestinal candidiasis ($\chi^2 = 0.00091$, $p > 0.05$, critical value = 3.841 at $df = 1$).

The table shows that out of the 102 stool samples from patients with intestinal candidiasis, 45 isolates belong to *Candida spp.* Among these, 26 clinical cases were from women (58%), and 19 cases were from men (42%).

Table 4. Distribution of Candida Intestinal Infection Across Different Age Groups in Male and Female Patients

Age Group (years)	Number of Infected Cases	Infection Rate (%)
1 - 10	24	53.33%
11 - 20	5	11.11%
21 - 30	6	13.33%
31 - 40	4	8.88%
41 - 50	4	8.88%
51 - 60	1	2.22%
61 - 70	0	0.00%
71 - 80	1	2.22%
81 - 90	0	0.00%
Total	45	100%

Chi-square analysis indicated no statistically significant difference in the distribution of Candida intestinal infection across different age groups ($\chi^2 = 0$, $p > 0.05$, critical value = 11.070 at $df = 5$).

The data presented in Table 4 show the distribution of Candida intestinal infection in patients across various age groups. The highest infection rate was observed in patients aged 1 to 10 years, with 24 infected cases, representing 53.33% of the total cases. The next highest infection rates were in the 21 to 30 years age group (13.33%) and the 11 to 20 years age group (11.11%). In the age groups 31 to 40 years and 41 to 50 years, the infection rate was equal, with 4 cases (8.88%) in each group. The infection rates for the age groups 51 to 60 years and 71 to 80 years were lower, with 1 case in each group (2.22%). No positive cases were reported in the 61 to 70 years and 81 to 90 years age groups. In total, 45 infected cases were recorded, representing the overall infection in the studied population.

DISCUSSION

The results of the present investigation revealed a Candida infection rate of 44.12% among diarrhea patients, which aligns with Krause et al. [22], who reported a similar prevalence, with 50% of their study population testing positive for Candida. Gupta et al. [23] reported that 40% of their cohort suffered from chronic diarrhea was infected with Candida, a rate slightly lower than that observed in the current study. These results emphasize that Candida infection is often overlooked in diarrhea cases and underscore the importance of considering fungal pathogens in differential diagnoses. The high prevalence may be attributed to the use of broad-spectrum antibiotics and prolonged hospitalization, which are well-established risk factors for Candida overgrowth. These factors may also explain the relatively high infection rate observed in the current study, as many patients in the cohort may have been exposed to similar conditions. Pappas et al. [5] and Samonis et al. [24] reported Candida infection rates of 35% and 30%, respectively, among hospitalized patients with diarrhea, which are slightly lower than the 44.12% observed in the current study. This difference may be attributed to variations in patient demographics and underlying health conditions. Their findings emphasize that Candida is a significant pathogen in gastrointestinal infections, particularly in patients with prolonged antibiotic use or immunosuppression, which aligns with the risk factors identified in the current

study. This observation is particularly relevant to our study, as it highlights the need for increased clinical awareness of *Candida* as a potential cause of diarrhea. The relatively high proportion of uninfected patients (55.88%) in the current study suggests that while *Candida* is a significant contributor to diarrhea, other etiologies, such as bacterial, viral, or parasitic infections, should also be considered in clinical practice.

The use of Chrom Agar in the current study proved effective for differentiating *Candida* species based on colony color, a finding supported by Guinea [25] and Kaur and Chakrabarti [26], who emphasized its utility as a cost-effective and rapid diagnostic tool in clinical settings. The observations in this research regarding the high prevalence of *Candida albicans* (44.44%) and *Candida glabrata* (31.11%) align closely with previous research. Pfaller et al. [27] found that *C. albicans* was the most frequently isolated species, accounting for approximately 50% of all *Candida* infections, while non-*albicans* species, such as *C. glabrata*, are increasingly prevalent. Kaur and Chakrabarti [26] reported *C. albicans* as the most common species, followed by *C. glabrata*, in stool samples, which supports the current study's results. The lower prevalence of *C. tropicalis* and *C. krusei* (6.66% each) is consistent with studies by Arendrup et al. [28] and Silva et al. [29], who noted that these species are less common in gastrointestinal infections. Arendrup et al. also highlighted that the prevalence of *C. tropicalis* and *C. krusei* varies by geographic region, which may explain their lower isolation rates in our study.

The findings of this study, which show a slight predominance of *Candida* isolates in women (58%) compared to men (42%) but no statistically significant gender-based differences. These results are consistent with previous research. In a study conducted by Paul et al. [30], the distribution of *Candida* spp. in stool samples of patients with gastrointestinal symptoms was investigated, and *C. albicans* was found to be the most prevalent species. Their study also reported a slightly higher prevalence of *Candida* infections in women (55%) compared to men (45%), which aligns with the current findings. However, similar to the current study, they found no statistically significant gender-based differences in *Candida* colonization. Paul et al. suggested that hormonal factors and differences in gut microbiota composition might contribute to the slightly higher prevalence in women, but these factors did not reach statistical significance. Silva et al. [29] analyzed *Candida* species distribution in stool samples from patients with gastrointestinal candidiasis and reported a comparable gender distribution, with 57% of isolates from women and 43% from men. Their study also found no significant gender-based differences in *Candida* colonization ($p > 0.05$). Silva et al. suggested that the slight predominance in women might be related to hormonal fluctuations or differences in healthcare-seeking behavior, but these factors did not significantly impact the overall distribution. The lack of statistical significance in gender-based differences is further supported by the work of Achkar and Fries [30], who conducted a comprehensive review of *Candida* infections. They noted that while *Candida albicans* is the most common species isolated from stool samples, non-*albicans* species, such as *C. glabrata* and *C. tropicalis*, are increasingly prevalent. Their review highlighted that gender differences in *Candida* colonization are often minimal and rarely statistically significant, which is consistent with the findings of the current study. They emphasized that factors such as antibiotic use, immunosuppression, and underlying gastrointestinal conditions are more influential than gender in determining *Candida* colonization. Additionally, Kullberg and Arendrup [17] reviewed the epidemiology of invasive and non-invasive *Candida* infections and noted that while *Candida* colonization is common in the gastrointestinal tract, gender is not a significant risk factor. Their findings support the results of the current study, which found no statistically significant difference in *Candida* species distribution between men and women. They emphasized that other factors, such as age, comorbidities, and medication use, play a more critical role in determining *Candida* colonization patterns.

The results of the present study regarding a high *Candida* intestinal infection rate in the 1–10 year age group (53.33%) are consistent with previous research, which highlights the vulnerability of children to gastrointestinal candidiasis. In a study conducted by Pfaller and Diekema [11], children under 10 years of age were found to be more susceptible to gastrointestinal candidiasis due to their immature immune systems and higher exposure to risk factors such as antibiotic use. Their findings align closely with the current study's results. Singhi and Deep [31] investigated *Candida* infections in pediatric populations and reported a high prevalence of *Candida* colonization in children under 5 years of age, attributing this to frequent antibiotic use and hospitalizations. This further supports the current study's observation of a high infection rate in the 1–10 year age group. Singhi and Deep indicated that early diagnosis and management are crucial in pediatric populations to prevent complications. In addition, Kaur and Chakrabarti [26] studied the prevalence of *Candida* infections across different age groups and found that the highest rates of gastrointestinal candidiasis occurred in children and young adults. Their findings are consistent with the current study, which reported high infection rates not only in the 1–10 years age group but also in the 21–30 year age group (13.33%). Kaur and Chakrabarti suggested that lifestyle factors, such as diet and antibiotic use, may contribute to the higher prevalence in younger age groups. However, the absence of infections in the 61–70 and 81–90 year age groups in the current study contrasts with other research that has identified elderly individuals as a high-risk group due to age-related immune decline. Pfaller and Diekema [11] noted that elderly patients (above 60 year) are at increased risk of *Candida* infections, a finding that was not observed in the current study. Guinea [25] reviewed the epidemiology of *Candida* infections across different age groups and highlighted that while children and elderly individuals are generally at higher risk, the distribution of *Candida* infections can vary significantly depending on geographic location and healthcare practices. Guinea highlighted that the absence of infections in certain age groups, as observed in the current study, may reflect differences in patient demographics or healthcare access.

CONCLUSION:

This study highlights the significant prevalence of *Candida* infections, particularly *C. albicans* and *C. glabrata*, among diarrhea patients in the Al Jabal Al Gharbi region. The high infection rate in children (1–10 years) underscores their vulnerability, while the absence of significant gender-based differences emphasizes the role of non-gender-related risk factors. The effective use of Chrom Agar for species identification demonstrates its utility in clinical diagnostics. Variations in *Candida* infection rates across studies may reflect differences in study populations, diagnostic techniques, or risk factors such as antibiotic use and immune status. These findings underscore the need for increased clinical awareness of *Candida* as a cause of diarrhea and call for further research to explore risk factors, improve diagnostic methods, and develop effective treatment strategies.

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