Clinical and Immunological Insights into Oral Candidiasis: *Candida* Biofilms and Host Cytokine Responses, Koya-Iraq

Sawan M. Mirkhan[1,2†] and Taha J. Zrary[2]

[1]Department of Biology, Faculty of Science and Health, Koya University, Koya 44023, Kurdistan Region - F.R. Iraq

[2]Department of Medical Microbiology, Faculty of Science and Health, Koya University, Koya 44023, Kurdistan Region - F.R. Iraq

***Abstract*—Oral candidiasis (OC) is a widespread opportunistic fungal disease primarily caused by *Candida albicans*, with non-albicans *Candida* species progressively recognized as new pathogens. Previous studies have typically focused on a single microbial feature, such as the frequency of *Candida* species or biofilm formation, or on host immune responses, including cytokine activity, but have rarely investigated both simultaneously. These gaps have limited understanding of how fungal virulence factors interact with host immunity and have hindered the identification of reliable disease biomarkers. The present investigation examined the prevalence, species distribution, biofilm activity, and host immune responses in OC participants in Kurdistan, Iraq. A total of 154 suspected cases were directly cultured on Sabouraud Dextrose Agar and HiCrome™ *Candida* Differential agar and analyzed with the VITEK 2 system. Among them, 61 participants (39.6%) tested positive for OC, with *C. albicans* as the predominant isolate (59.4%), followed by *Candida kefyr*, *Candida dubliniensis*, *Candida parapsilosis*, *Candida tropicalis*, and *Candida krusei*. More than half of the isolates produced biofilm, and *C. tropicalis* exhibited the strongest biofilm-forming capacity. Immunological profiling revealed significantly higher neutrophil counts and elevated serum interleukin (IL)-10 and IL-17 in OC-positive participants. Diabetes mellitus appeared as the most common comorbidity. By integrating *Candida* species characterization with host immune profiling, this research provides new insights into the interaction between host defense mechanisms and fungal pathogenicity. In contrast to earlier work, the current analysis directly related species-specific biofilm capacity with neutrophil and cytokine dynamics, establishing IL-17 as a potential biomarker of OC activity.**

***Index Terms*—Biofilm, *Candida albicans*, Interleukin-17, Neutrophils, Oral candidiasis.**

ARO-The Scientific Journal of Koya University
Vol. XIV, No.1(2026), Article ID: ARO.12632. 8 pages
DOI: 10.14500/aro.12632
Received: 21 September 2025; Accepted: 11 January 2026
Regular research paper; Published: 10 April 2026
†Corresponding author's e-mail: sawan.majid@koyauniversity.org

I. Introduction

Oral candidiasis (OC), also known as oral thrush, is a common opportunistic fungal infection caused predominantly by *Candida* species and characterized by excessive fungal growth on the oral mucosa (Vila, et al., 2020). Although OC is most frequently observed in immunocompromised individuals, it also occurs in otherwise healthy populations under conditions such as poor oral hygiene, denture use, prolonged antibiotic therapy, and systemic disease (Hellstein and Marek, 2019). Globally, OC prevalence is high, reaching up to 90% in patients with HIV/AIDS, 60% among denture wearers, and 30–40% in individuals receiving long-term immunosuppressive treatment (Nuncã, Coculescu, and Coculescu, 2022). Beyond its high prevalence, the etiological profile of OC has evolved over recent years.

Among the *Candida* genus, *Candida albicans* remains the most common etiological agent of OC; however, non-albicans *Candida* (NAC) species, including *Candida tropicalis*, *Candida kefyr*, *Candida parapsilosis*, *Candida dubliniensis*, and *Candida krusei*, are increasingly reported in clinical practice (Alrayyes, et al., 2019; Singh, et al., 2024). This epidemiological shift is clinically significant because NAC species often exhibit distinct virulence traits and reduced susceptibility to commonly used antifungal agents, complicating disease management. This shift in species distribution highlights the importance of examining pathogenic characteristics that contribute to disease persistence and treatment challenges.

Biofilm formation is a critical virulence factor contributing to the persistence of OC. Biofilms protect *Candida* cells from host immune defenses and antifungal therapy, thereby promoting chronic infection, recurrence, and antifungal resistance (Pereira, et al., 2021; Cho, et al., 2021; Rodrigues, Gomes, and Rodrigues, 2019). However, fungal virulence factors alone are insufficient to explain disease development and clinical outcomes fully.

Several studies have investigated biofilm formation among oral *Candida* isolates; however, most have focused primarily

on microbial characteristics without parallel assessment of host immune responses.

Host defense against OC involves both innate and adaptive immune mechanisms, including epithelial barrier function, neutrophil recruitment, and T-helper cell responses (Pavlova and Sharafutdinov, 2020). Interleukin (IL)-17 plays a central role in antifungal immunity by enhancing neutrophil recruitment and mucosal protection, whereas IL-10 functions as an anti-inflammatory cytokine that limits immune-mediated tissue damage (Jiang, et al., 2020; Halimi, et al., 2022). Despite their recognized importance, these immune mechanisms are frequently studied in isolation from fungal virulence factors.

Importantly, previous investigations have typically examined either the distribution of *Candida* species and biofilm formation or host immune responses in isolation. This separation has limited understanding of the interaction between fungal virulence and host immunity, hindering the identification of reliable biomarkers of disease activity. This lack of integration underscores the need for studies that simultaneously evaluate microbial and host factors.

Therefore, this study aimed to investigate the distribution of *Candida* species and their biofilm-forming capacity in participants with OC and to integrate these findings with host immune responses, including neutrophil counts and serum IL-10 and IL-17 levels, to evaluate IL-17 as a potential biomarker of disease activity.

II. Participants and Methods

A. Sample Collection

This study was conducted at Shahid Dr. Khalid Hospital in the Koya region of Kurdistan, Iraq, from December 2024 to May 2025, as part of a broader multicenter research project, with the present manuscript reporting data from this center only. A total of 154 participants, including both men and women, were enrolled across a broad age range, from 7 months to 70 years. Oral swabs were collected for mycological analysis. In addition, peripheral blood samples were obtained from participants and centrifuged at 3,000 rpm for 10 min to separate serum, which was stored for subsequent immunological analysis. The serum was stored at −20°C until further analysis. The collected data involved details about the participants, such as age, gender, and marital status. On December 12, 2024, the Faculty of Science and Health Ethics Committee at Koya University approved ethical permission for the project, designated as DMMB-9-24. Before data and sample collection, all study participants or their parents were informed of the ethical approval. Participants were classified as OC-positive based on clinical findings and positive *Candida* culture, while those with negative cultures and no clinical signs were classified as OC-negative controls.

Examination and culturing Candida species

Oral swabs were obtained from each participant with suspected oral infections to detect oral *Candida*. Swab samples were cultured on sabouraud dextrose agar (SDA) medium (Himedia, India) supplemented with chloramphenicol (5 mg/mL; Amman Pharmaceutical Industries Co., Amman, Jordan) and incubated at 37°C for 48 h. For preliminary identification, isolated single colonies were cultured on HiCrome™ *Candida* agar (Himedia, India) and incubated at 37°C for an additional 48 h. The development of the colony was then assessed, enabling the separation of *Candida* species based on distinct colorations and the presence (Jan, et al., 2022; Mehta and Wyawahare, 2016).

Confirmation and identification of Candida species applying the VITEK 2 system

While HiCrome™ *Candida* agar provides rapid presumptive differentiation of *Candida* species, VITEK 2 was used for confirmatory identification. After culturing on SDA, pure colonies were transferred to a system that uses biochemical tests to distinguish species based on enzymatic reactions and fermentation profiles, providing results within 24–48 h (Melhem, et al., 2013).

B. Assessment of Biofilm Formation by Candida Isolates

Qualitative detection of biofilm generation using the Congo red agar (CRA) method

Sharma, et al. (2017), Basnet, et al. (2023), and Furtuna, Debora, and Warsito (2018) stated that the CRA was designated as a qualitative and basic technique for identifying biofilm generation, through subsequent modifications. To formulate the CRA medium, brain heart infusion (BHI) broth at 37 g/L was combined with 50 g/L glucose, 20 g/L agar No. 1, and 0.8 g/L Congo red indicator. Congo red stain was used as a concentrated aqueous solution, autoclaved at 121°C for 15 min, then mixed into the autoclaved BHI glucose agar base after the base had cooled to 55°C.

Sixty-four *Candida* isolates were examined using this method. Fresh isolates were initially cultured on SDA and incubated at 37°C for 24 h to get uncontaminated colonies. The colonies were next streaked onto CRA plates and incubated at 37°C for 48 to 72 h. Black colonies with a dry crystalline texture were determined to be positive for biofilm generation, while pink to red colonies were classified as negative. The assays were conducted in triplicate.

Quantitative evaluation of biofilm formation by microtiter plate assay

Biofilm generation was assessed using the 96-well microplate method as described by Amran, et al. (2024), with some modifications. Biofilm evaluation was performed on 64 *Candida* isolates. Pure cultures in tryptic soy broth at 37°C for 24 h were adjusted to 0.5 McFarland (~1.5×10^8 CFU/mL) and diluted 1:100 to approximately 10^6 CFU/mL. Aliquots (200 μL) were dispensed into sterile 96-well polystyrene microplates and incubated at 37°C for 48 h. The microplate wells were then washed twice with PBS, air-dried, stained with 0.5% Safranin for 20 min, rinsed, and dried (Ramos, et al., 2020). The bound stain was solubilized with a 20:80 (v/v) acetone: Ethanol mixture, and the absorbance was measured at 590 nm. The classification of biofilm emergence abilities by the microtiter plate system is based on the cut-off value (ODc) as described by Pokhrel, et al. (2022).

C. Immunological Profiling in OC

Neutrophil count by complete blood count (CBC)

A total of 154 peripheral blood serum samples were collected, including those from participants with OC and uninfected participants as controls. CBCs, including neutrophil quantification, were performed using the Mindray BC-2800 automatic hematology analyzer (Mindray Bio-Medical Electronics Co., Shenzhen, China). Neutrophil counts were quantified in $\times 10^9$/L, with levels ranging from 2.0 to 7.5 $\times 10^9$/L deemed normal according to recognized reference ranges.

Serum IL-10 and IL-17 quantification by enzyme-linked immunosorbent assay (ELISA)

Serum samples from 90 participants (60 oral *Candida*-positive and 30 negative controls) previously stored at −80°C were examined. IL-10 and IL-17 concentrations were measured using commercial human sandwich ELISA kits: IL-10: ELK1142; range 7.82–500 pg/mL; sensitivity three pg/mL; IL-17: ELK2610; range 15.63–1,000 pg/mL; sensitivity 5.5 pg/mL; ELK Biotech, China, according to the producer's directions. Both standards and samples have been assessed in duplicates. Optical density has been determined at 450 nm by means of a microplate reader, and cytokine concentrations were calculated from standard curves and stated in pg/mL (Halimi, et al., 2022; Chimenz, et al., 2022).

D. The Statistical Evaluation

The categorical variables were presented as frequency and percentage. The Chi-square test isolates the distribution across confidence levels. Relations between patients' status and cytokine concentrations (IL-10, IL-17) were examined using linear regression, with model fit indices described. Normality tests (Kolmogorov–Smirnov and Shapiro-Wilk) indicated non-normal distributions. Neutrophil counts were compared using Welch's t-test. Analyses were led in the Statistical Package for the Social Sciences v25, with $p < 0.05$ considered significant.

III. Results

A. Sample Distribution

Overall, among 154 participants, 61 (39.6%) were positive for OC, while 93 (60.4%) were negative (Fig. 1). Of the positive cases, females accounted for 57.4% (n = 35) and males for 42.6% (n = 26).

Diabetes was the most common comorbidity among positive cases (24 participants), followed by hypertension, which was observed in 12 cases, although other chronic diseases were infrequent. Whereas other illnesses may appear only sporadically, as shown in Table I.

B. Direct Microscopy and Culture Results

A clinical examination of participants with suspected OC revealed adherent white patches on the tongue surface, indicative of a fungal infection (Fig. 2). Culture on SDA supplemented with chloramphenicol and incubated at 37°C for 24–48 h produced creamy, smooth, convex colonies characteristic of *Candida* spp. (Fig. 3). Differentiation on HiCrome™ *Candida* Differential Agar revealed distinctive colony colors, enabling accurate species-level identification consistently (Fig. 4). Overall, 64 isolates were obtained from

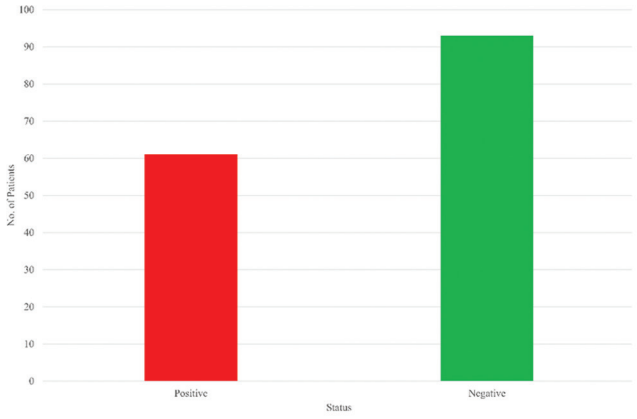

Fig. 1. Distribution of oral candidiasis cases among study participants (n = 154).

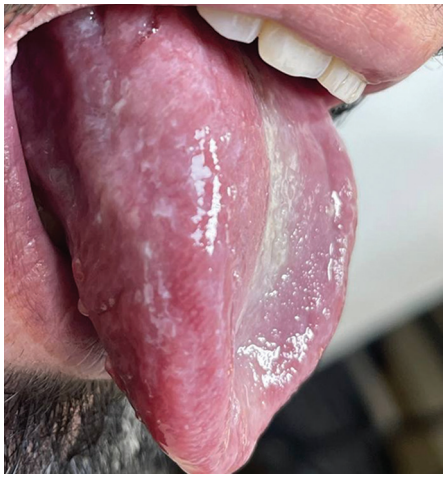

Fig. 2. Clinical presentation of oral candidiasis showing adherent white pseudomembranous plaques on the dorsal surface of the tongue, characteristic of *Candida* infection.

TABLE I
Distribution Of Chronic Diseases Among Oral Candidiasis-Positive Participants (n=61)

Chronic disease	Number of participants (n)
Diabetes	24
Hypertension	12
Migraine	2
Rheumatoid arthritis	1
Autism	1
Renal failure	1
Gastroenteritis	1
Thyroid disease	1
Heart disease	1
Cancer	1
Goiter	1

http://dx.doi.org/10.14500/aro.12632

61 participants, as some samples yielded more than one *Candida* species. *C. albicans* was the most prevalent (59.4%), followed by *C. kefyr* (18.8%), *C. dubliniensis* (7.8%), *C. parapsilosis* (6.3%), *C. tropicalis* (4.7%), and *C. krusei* (3.1%). In addition, two isolates of *Rhodotorula* spp. were detected (Fig. 5).VITEK 2 identified 61 positive samples, mostly at high confidence. In the 96–99% range, *C. albicans* (29 isolates) dominated alongside a single *C. parapsilosis*, confirming high reliability for *C. albicans*. At lower ranges, NAC were more frequent: six species appeared in the 94–95.9% band, *C. kefyr* (11) and *C. tropicalis* (2) clustered mainly at 90–91.9%, while the lowest band (88–89.9%) included two *C. albicans* and one *C. kefyr*. As observed in Table II, 31 isolates were rated as excellent, 16 as Very Good, 14 as Good, and only three as acceptable. These findings confirm that VITEK 2 provides reliable identification, with *C. albicans* consistently detected at the highest probability levels, whereas NAC species showed greater variability at lower probability ranges.

Fig. 3. Typical colony morphology of *Candida* species cultured on sabouraud dextrose agar after 48 h of incubation at 37°C, showing creamy, smooth, convex yeast colonies.

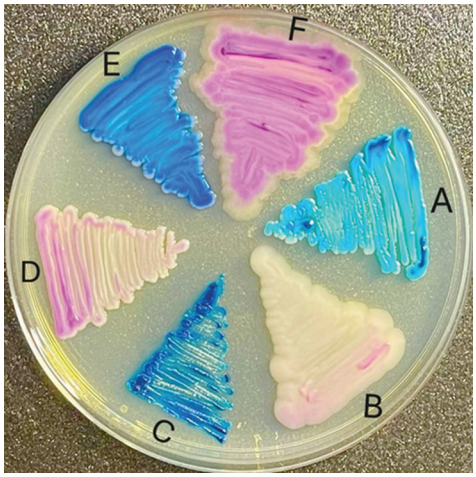

Fig. 4. Differentiation of *Candida* species on HiCrome™ Candida differential agar showing species-specific colony colors: *Candida albicans* (A), *Candida kefyr* (B), *Candida dubliniensis* (C), *Candida parapsilosis* (D), *Candida tropicalis* (E), *Candida krusei* (F).

C. Biofilm Formation in Candida Isolates

Out of 64 *Candida* isolates tested on CRA (Table III), *C. albicans* was the most common species (59.3%), followed by *C. kefyr* (18.7%). In contrast, other species, such as *C. dubliniensis*, *C. krusei*, *C. parapsilosis*, and *C. tropicalis*, each accounted for <10% of the total. Stratification by CRA outcomes revealed that *C. albicans* was present in both biofilm-positive and biofilm-negative groups, whereas *C. tropicalis* was exclusively found in the biofilm-positive group (10.3%), and *C. krusei* was present only in the biofilm-negative group (5.7%). After 48–72 h of incubation at 37 C, CRA plates revealed distinct morphologies: Black, dry crystalline colonies of *C. tropicalis* indicated positive biofilm production. In contrast, smooth red colonies of *C. albicans* confirmed the absence of biofilm (Fig. 6).

Biofilm formation was evaluated using the microtiter plate assay. Among 64 *Candida* isolates, 25 (39.1%) were non-biofilm producers, 32 (50%) showed weak biofilm formation, 3 (4.7%) were moderate producers, and 4 (6.2%) exhibited strong biofilm formation. This distribution is presented in Fig. 7. The overall mean OD for all isolates was 0.27. Species-wise, *C. albicans* (n = 38) had a mean OD of 0.25, with most isolates being weak producers. *C. dubliniensis* (n = 5) averaged 0.15 and was largely non-biofilm producing, while *C. Kefyr* (n = 12) showed a mean OD of 0.26, reflecting predominantly weak activity. *C. krusei* (n = 2) averaged 0.25, and *C. parapsilosis* (n = 4) 0.31, including one moderate producer. Importantly, *C. tropicalis* (n = 3) showed the highest biofilm-forming capacity (mean OD of 0.90), with all isolates classified as strong producers. Representative wells showing negative, weak, moderate, and strong biofilm formation are illustrated in Fig. 8.

Descriptive statistics of NEU: Shows mean, standard deviation (SD), confidence interval (CI), interquartile range (IQR), skewness, and kurtosis of NEU counts for OC-negative (n = 93) and OC-positive (n = 61) groups. As shown in Table IV and Fig. 9, NEU levels were substantially higher in OC-positive participants (M = 8.17, SD = 1.37, n = 61) compared with OC-negative controls

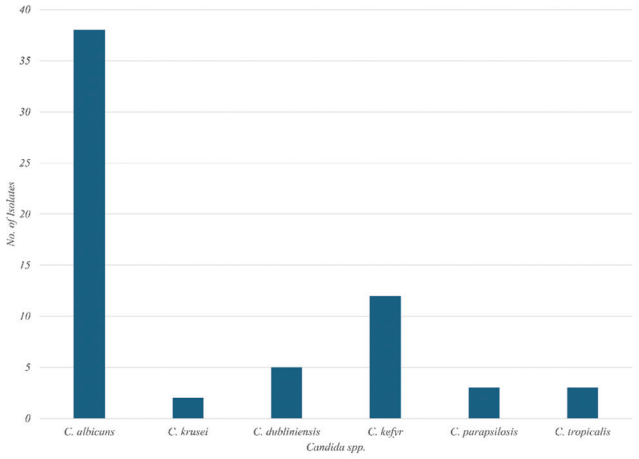

Fig. 5. Frequency of *Candida* spp. and related yeast species isolated from oral swabs.

(M = 5.20, SD = 1.65, n = 93). Notably, 52 of 61 OC-positive participants (85.2%) exhibited neutrophil counts exceeding the upper standard reference limit (7.5 × 10^9/L). The narrower IQR in the positive group (0.77 vs. 2.60) indicates strong clustering around the mean. The negative group exhibited a distribution that approximated normality, whereas the positive group showed evidence of non-normal concentration.

Table V shows that NEU counts were significantly higher in participants with OC-positive (n = 61) than in OC-negative controls (n = 93). Welch's t (141.5) = 12.08, p < 0.001, mean difference = 2.96 × 10^9/L (95% CI [2.48, 3.45]). The effect size was considerable (Cohen's d = 2.16, Hedge's g = 2.15), indicating minimal overlap between the two groups. The result remained highly significant under the assumption of equal variance.

TABLE II
CONFIDENCE CATEGORIES IN THE IDENTIFICATION OF *CANDIDA* SPECIES USING VITEK 2

Candida spp.	Confidence rate (%)					
	88–89.9	90–91.9	92–93.9	94–95.9	96–99	Number of isolates (n)
Candida albicans	2	0	2	5	29	38
Candida dubliniensis	0	1	2	2	0	5
Candida kefyr	1	11	0	1	0	13
Candida krusei	0	0	0	2	0	2
Candida parapsilosis	0	0	0	2	1	3
Candida tropicalis	0	2	0	1	0	3
Total	3	14	4	13	30	64

TABLE III
CONGO RED AGAR ASSAY RESULTS FOR BIOFILM FORMATION AMONG *CANDIDA* SPECIES

Congo red agar	*Candida* spp.						Number of isolates (n)
	Candida albicans	*Candida dubliniensis*	*Candida kefyr*	*Candid. krusei*	*Candida parapsilosis*	*Candida tropicalis*	
Negative	21	4	6	2	2	0	35
Positive	17	1	6	0	2	3	29
Total	38	5	12	2	4	3	64

TABLE IV
DESCRIPTIVE STATISTICS OF NEU (×10^9/L) FOR NEGATIVE (N) AND POSITIVE (P) ORAL CANDIDIASIS GROUPS

Group	Mean (SD)	95% CI	IQR	Skewness	Kurtosis
OC-negative	5.20 (1.65)	4.87–5.54	2.60	−0.40	−0.28
OC-positive	8.17 (1.37)	7.81–8.52	0.77		

SD: Standard Deviation, CI: Confidence Interval, IQR: Inter quartile range

TABLE V
INDEPENDENT-SAMPLES T-TEST COMPARING NEUTROPHIL COUNTS (×10^9/L) BETWEEN ORAL CANDIDIASIS NEGATIVE AND POSITIVE GROUPS

Test assumption	t-value	df	p (2-tailed)	Mean difference	95% CI for difference
Equal variances assumed	11.60	152	< 0.001	2.96	(2.46, 3.47)
Equal variances not assumed	12.08	141.46	< 0.001	2.96	(2.48, 3.45)

df: Degree of freedom, CI: Confidence interval

D. Linear Regression Analyses of IL-10 and IL-17 Serum Levels

Results of linear regression examining the effect of OC status (positive = 60, negative = 30; total n = 90) on IL-10 serum levels.

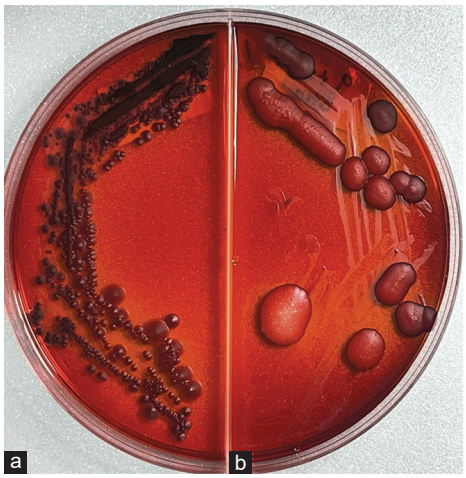

Fig. 6. Representative Congo red agar outcomes: (a) *Candida tropicalis* positive biofilm formation, (b) *Candida albicans* negative biofilm formation.

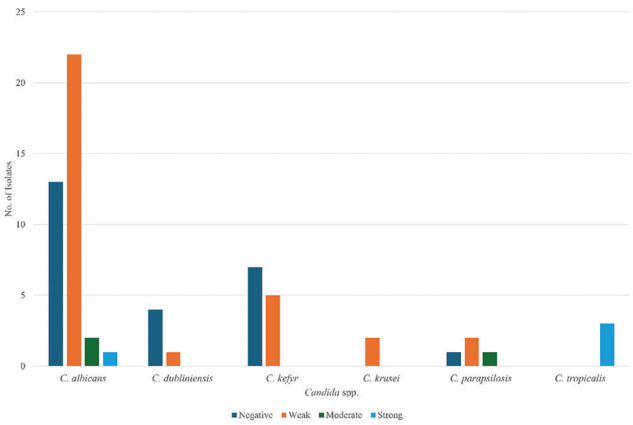

Fig. 7. Distribution of biofilm formation abilities among *Candida* species by the microtiter plate assay.

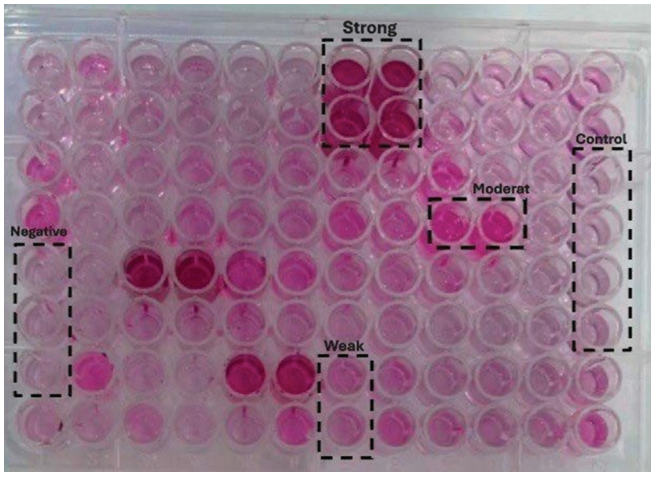

Fig. 8. Quantitative assessment of biofilm formation by *Candida* isolates using the microtiter plate assay stained with 0.5% Safranin.

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A subsample of 90 participants (60 positives, 30 negatives) was tested for IL-10. Linear regression analysis demonstrated that disease status was a significant predictor of IL-10 levels (Table VI). Being OC-positive was associated with a marked increase in IL-10 (B = 188.32, SE = 30.28, β = 0.553, t = 6.22, p < 0.001), and the model clarified 30.5% of the variance (R^2 = 0.305).

IL-17 was also analyzed in the same subsample (60 positive, 30 negative). Regression analysis revealed that OC status strongly predicted IL-17 levels (Table VII). Being disease-positive was associated with an increase of 340.34 units (SE = 41.03, β = 0.662, t = 8.30, p < 0.001), with the model explaining 43.8% of the variance (R^2 = 0.438).

Taken together, these findings suggest that OC positivity is strongly associated with elevated IL-10 and IL-17 levels, with IL-17 showing the stronger predictive relationship. This indicates that both cytokines, particularly IL-17, may play a dominant role in the disease progression and could serve as potential biomarkers, as shown in Fig. 10.

IV. Discussion

The research demonstrated an OC prevalence of 39.6% among participants, with higher rates among females and middle-aged individuals. *C. albicans* constituted the primary isolate at 59.4%, although NAC species, including *C. kefyr*, *C. dubliniensis*, *C. parapsilosis*, and *C. tropicalis*, were also prevalent. The expanding recognition of NAC species, which often demonstrate intrinsic resistance to both azoles and other antifungal agents, has been documented in clinical settigs (Hwang, et al., 2024; Kitaya, et al., 2023). These findings indicate that species distribution alone does not fully explain OC's clinical behavior.

Moreover, biofilm formation was identified as an essential virulence factor, with over half of the isolates exhibiting weak to strong biofilm capacity. Notably, *C. tropicalis* demonstrated the highest biofilm production, consistent with previous reports linking this species to enhanced persistence and antifungal resistance (Malinovská, Čonková, and Váczi, 2023; Butassi, et al., 2021).

These results underscore the therapeutic significance of addressing biofilm-associated diseases through alternative or combined treatment. Nevertheless, fungal virulence represents only one component of disease pathogenesis.

In addition, Neutrophil counts were significantly elevated in participants with OC compared with controls (8.17 × 10^9/L vs. 5.20 × 10^9/L; p < 0.001). Given that the normal reference range for peripheral blood neutrophils is approximately 2.0–7.5 × 10^9/L (Al-Jafar, 2016). The patient group in this study demonstrated clear neutrophilia, supporting previous reports that neutrophils are rapidly recruited in a biphasic (dual wave) pattern to control *Candida* infection (Zhu, et al., 2023). Their antifungal functions, for instance, phagocytosis, extracellular trap release, and generation of reactive oxygen species, are well established (Gazendam, et al., 2016). Recent reviews further highlight neutrophils as key players in fungal immunity, consistent with our findings (Kayongo, et al., 2023).

In addition to cellular immune responses, cytokine-mediated mechanisms play a critical regulatory role. Furthermore, Serum IL-10 and IL-17 levels showed elevation in participants with OC compared to healthy controls (IL-10: 39.9 vs. 228.2 pg/mL; IL-17: 39.8 vs. 380.1 pg/mL). Although OC is a localized mucosal infection,

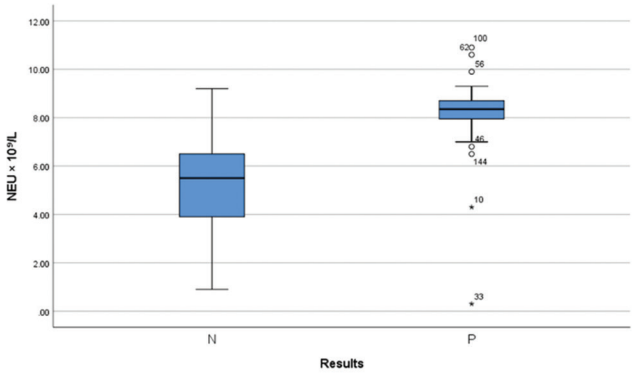

Fig. 9. Descriptive statistics of NEU (×10^9/L) for negative (N) and positive (P) oral candidiasis groups.

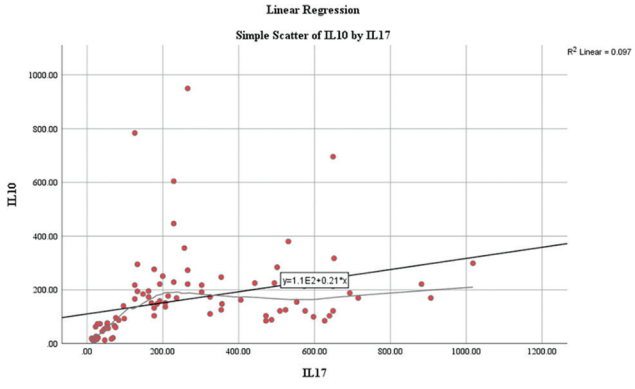

Fig. 10. Linear regression analysis showing the relation between interleukin (IL)-10 and IL-17 serum levels in oral candidiasis.

TABLE VI
Linear Regression Analysis Of Il-10 Serum Levels By Oral Candidiasis Status (Subsample: 60 Positives, 30 Negatives)

Predictor variable	B	SE B	β	T	p-value	95% CI for B
Constant	39.91	24.72	-	1.61	0.110	−9.22, 89.04
Status (positive vs. negative)	188.32	30.28	0.553	6.22	<0.001	128.15, 248.49

Model Fit: R=0.553, R^2=0.305, Adjusted R^2=0.297, Std. Error=135.40, analysis of variance: F (1, 88)=38.69, p<0.001. B: Unstandardized regression coefficient, SE B: Standard Error of B, β (Beta): Standardized regression coefficient, T: The t-statistic

TABLE VII
Linear Regression Analysis Of Il-17 Serum Levels By Oral Candidiasis Status (Subsample: 60 Positives, 30 Negatives)

Predictor variable	B	SE B	β	T	p-value	95% CI for B
Constant	39.81	33.50	-	1.19	0.238	−26.76, 106.39
Status (positive vs. negative)	340.34	41.03	0.662	8.30	<0.001	258.80, 421.88

Model Fit: R=0.662, R^2=0.439, Adjusted R^2=0.432, Std. Error=183.49, analysis of variance: F (1, 88)=68.81, p<0.001. B: Unstandardized regression coefficient, SE B: Standard Error of B, β (Beta): Standardized regression coefficient, T: The t-statistic

systemic cytokines such as IL-10 and IL-17 reflect immune activation through mucosal-systemic immune cross-talk and immune cell trafficking, thereby providing clinically relevant information on host immune responses.

These results highlight the critical involvement of both cytokines in the host response to fungal infection. Control IL-10 levels were comparable to those reported in previous studies in healthy adults, whereas IL-17 concentrations exceeded the commonly cited reference range (<2.6 pg/mL), likely due to assay variability or population-specific differences (Vanpouille, et al., 2022).

Concurrently, the increase in IL-10 suggests *Candida* may trigger anti-inflammatory pathways to limit immune-mediated damage and enhance persistence, a mechanism described in recent immunological studies (Pavlova and Sharafutdinov, 2020; Shen, et al., 2020). Underlying systemic conditions may further influence these immune alterations.

Likewise, the high frequency of comorbidities, particularly diabetes mellitus, highlights systemic disease as a significant risk factor associated with OC, as hyperglycemia-associated immune dysfunction predisposes individuals to fungal colonization and recurrent infection (Novianti and Sufiawati, 2023). This distribution suggests that metabolic disorder may be a significant underlying risk factor. OC-negative controls were not formally matched by age, sex, or comorbidities; therefore, potential confounding factors, including diabetes mellitus, cannot be excluded.

Overall, the findings show that OC arises from the combined effects of fungal virulence, particularly species-specific biofilm formation, and host immune modulation. Elevated neutrophils, IL-10, and especially IL-17 illustrate how protective and regulatory pathways shape disease progression. Unlike earlier studies that examined microbial or immune factors separately, this integrated approach reveals IL-17 as a promising biomarker of disease activity, underscoring the need to address both microbial and host components when designing diagnostic and therapeutic strategies.

V. Conclusion

This study demonstrates that OC is driven by the combined effects of the distribution of *Candida species*, biofilm-forming capacity, and host immune responses. While *C. albicans* remains the predominant species, *C. tropicalis* showed strong biofilm-forming potential. OC-positive participants exhibited significantly elevated neutrophil counts and increased serum levels of IL-10 and IL-17. These findings highlight the importance of integrating microbial and immunological factors in OC and suggest that IL-17 may serve as a potential biomarker of disease activity. However, further studies adjusting for confounding factors are warranted.

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