SAR Journal of Pathology and Microbiology

Abbreviated Key Title: *SAR J Pathol Microbiol*
Home page: https://sarpublication.com/journal/sarjpm/home
DOI: https://doi.org/10.36346/sarjpm.2026.v07i02.007

OPEN ACCESS

ISSN 2707-7756 (P)
ISSN 2709-6890 (O)

Original Research Article

Immunological and Molecular Study of Oral *Candida dubliniensis* in Children with Orofacial Clefts

Hayder Abdul Hussein Abass[1*], Zainab Abdul Kareem Ataia[2], Hayder Ali Muhammed[3]

[1]Department of Pathological Analyses, College of Science, University of Al-Qadisiyah, Iraq
[2]Department of Biology , College of Education, University of Al-Qadisiyah, Iraq
[3]Department of Microbiology, College of Veterinary Medicine, University of Karbala, Iraq

***Corresponding Author:** Hayder Abdul Hussein Abass
Department of Pathological Analyses, College of Science, University of Al-Qadisiyah, Iraq

Article History: | Received: 10.01.2026 | Accepted: 05.03.2026 | Published: 09.03.2026 |

Abstract: *Candida species are the utmost prevalent opportunistic fungal* pathogens in the immune-compromised patients and bone marrow transplants patients, as well as in Children suffering from orofacial birth defects called Orofacial Clefts that affect the lip, palate, or both, and are more prone to oral candidiasis. Consequently, this study aimed to identify *Candida dubliniensis* and its virulence gene, *Candida dubliniensis* mitochondrial gene using various culture media, PCR, and ELISA. This study was extended between January 2023 to August 2024 at Al-Diwaniya Children's Hospital /Iraq. A 75 oral swab and blood samples were collected from cleft lip/palate patients (with and /without candidiasis). *Candida dubliniensis* was identified via culture om CHROM and Sabouraud agar and PCR targeting the Cdub gene. Serum IL-17/IL-23 levels were measured by ELISA. Statistical analysis used SPSS (chi-square). Among the tested specimens (57.33%) were positive for *C. dubliniensis*, while (42.67%) were negative. All *C. dubliniensis* isolates from patients with orofacial clefts carried the *Candida dubliniensis* mitochondrial gene, whereas no mitochondrial gene was detected in patients without candidiasis. The cytokine levels revealed that oral candidiasis significantly increased the concentration of cytokine Interleukin-17 to 115.91 ± 15.42 pg/ml, in comparison to 68.85 ± 10.59 pg/ml and 21.58 ± 2.33 pg/ml in orofacial cleft patients without candidiasis and the control group respectively. Similarly, Interleukin -23 levels were significantly elevated to 77.28 ± 8.94 pg/ml in the candidiasis group, compared to 53.84 ± 8.93 pg/ml and 8.45 ± 2.46 pg/ml in orofacial cleft patients without candidiasis and the control group respectively. ***In Conclusion*:** This study demonstrates a relatively high prevalence of *Candida dubliniensis* in children with orofacial clefts, with a significant association between the presence of the *Candida dubliniensis* mitochondrial gene and candidiasis. The study also approved the immunological impact of *C. dubliniensis* infections in orofacial clefts patients with *Candida dubliniensis*, as evidenced by significantly elevated levels of Interleukin-17 and Interleukin -23 compared to non-candidiasis orofacial cleft patients and control group.

Keywords: *Candida Dubliniensis*, Mitochondrial Gene, Interleukin -17, Orofacial, Clefts.

INTRODUCTION

Candida species are the most prevalent opportunistic fungal pathogens in the clinical setting's oro-pharyngeal infections, Immune-compromised patients such as AIDS patients, and patients undergoing chemotherapeutic treatment. Bone marrow transplants patients are prone to developing candidiasis [1]. Children with birth defects such as orofacial clefts are known to have structural abnormalities in the mouth and/or facial region. These defects can affect the lip, palate, or both, and are more prone to oral candidiasis [2].

Orofacial clefts can vary in severity and may require surgical interventions and multidisciplinary care to address functional and aesthetic concerns. The most prominent opportunistic *Candida* species encountered in clinical settings is *Candida albicans*, known for its significant virulence factors. *Candida dubliniensis*, closely related to *C. albicans* and *C. africana*, is also a well-recognized pathogen, with an increasing number of

reports documenting its clinical relevance [3]. Molecular studies are still rare in these species. Cleft children, especially infants, are suffering from born with a tendency to infection. Finding a correlation between gene expression of critical virulence factors and OPC pathogenic terms in cleft infants will provide opportunities for molecularly targeted antifungal therapy. However, molecular methods are considered more reliable for differentiating *C. dubliniensis* from *C. albicans, and* may invade oral epithelial cells, form hyphae, and penetrate into epithelial tissues. Additionally, it is capable of changing morphological transitions from budding yeasts to pseudohyphal forms and true hyphae [4].

Interleukin-17 (IL-17) and Interleukin-23 (IL-23) plays a significant role in the immune response against oral candidiasis, which is an infection caused by *Candida* species in the oral cavity. It plays a crucial role in the immune defense against fungal infections, including oral candidiasis, by promoting the recruitment of neutrophils and other immune cells to the site of infection [5]. Children with orofacial cleft (OFC) including cleft lip and cleft palate (CLP) have palatal insufficiency, difficult postoperative management, and require multiple surgeries. They are special care dentistry cases at risk of having susceptibility to oral fungal complications including *Candida* species, which are commonly found in the oral commensals [6].

Patients with orofacial clefts (OFC) have a high risk of oral candidiasis compared to their healthy counterparts. One of the leading causes of oral candidiasis is a species of the *Candida* genus. Prevalence of the fungi in the oral cavity of OFC children is a significant parameter in their susceptibility [7]. Review of literature regarding *Candida dubliniensis* infection in orofacial clefts patients in Al-Diwaniya province / Iraq revealed scarce publications. Consequently, this study intended to identify *C. dubliniensis* and its mitochondrial virulence gene and determine the immunological response.

MATERIALS AND METHODS

Ethical approval and Consent to Participate

Ethical approval was obtained from the Ethical Committee of the Medical College/ University of Al-Qadisiya, (Approval No.: REC/QU/2023/117; Date: 15 December 2023). Written informed consent was obtained from the parents or relatives of all participating children.

Study Design

This study was designed as a cross-sectional that conducted at Al-Qadisiya Teaching Hospital at the period time extended from January 2023 to August 2024.

Sample Collection

The study examined a total of 110 samples, including oral swabs and blood. Among these, 43 OFC patients were confirmed to have candidiasis (positive by culture and PCR), 32 OFC patients did not have candidiasis (negative results), and 35 healthy children served as controls. Therefore, there are 110 participants in total, with 75 OFC patients (43 with candidiasis and 32 without).

Inclusion/Exclusion Criteria

Inclusion Criteria: Participants must meet all of the following criteria to be included in the study, the clinical diagnosis: Patients diagnosed with orofacial clefts (cleft lip, cleft palate, or both) who are scheduled for surgery and Patients presenting with clinical symptoms of oral candidiasis (e.g., white patches, erythematous mucosa).

Exclusion Criteria: Recent Antifungal/Antibiotic use and severe immunocompromising conditions.

Control Group Matching Criteria

Age Matching

Controls should be matched within a narrow age range to the cleft patients (e.g., ± 6 months for infants/childrenCandida colonization is more common in babies and seniors due to weaker immunity, but breastfeeding and a healthy immune system help reduce it. Age and health play key roles in how Candida behaves.

Sex Matching

Controls should be matched by sex because hormones and immune responses differ between males and females, affecting how susceptible someone is to fungal infections.

Candida Dubliniensis Detection

The identification of Candida is based on its morphological features, including colony form, size, color, and texture, as well as its growth characteristics on selective media such as CHROM agar and Sabouraud's Dextrose Agar. These culture media are commonly used in laboratories for the selective isolation and cultivation of yeast, facilitating accurate identification based on distinctive colony appearances and growth patterns. The colonies examined visually to assess their macroscopic characteristics features, such as the overall shape, diameter, coloration, and texture of the yeast colonies. This information can provide initial clues for species identification and differentiation. Another confirmatory tests, such as microscopic analysis and molecular techniques, were done to confirmed the isolated species.

DNA Isolation

The study performed PCR to detect the CDUB gene in all isolates of *C. dubliniensis*. Subsequently, they conducted PCR to detect the presence of the CDUB gene using specific primers listed in the Table 1. The DNA of *C. dubliniensis* isolates was extracted using the QIAGEN DNA extraction Kit® from QIAGEN, USA. Amplification of the CDUB gene was carried out using the Go Taq® Green Master Mix from Promega, USA.

Table 1: Primer sequences for detection of CDUB gene

Gene	Primer Sequence	Amplified Product Size
Cdub-F	5'- TTCTCTGTAAGTAATCCTACAATACAGCGT-3	**357bp**
Cdub-R	5'- ACAATTGATGGAGGTGTCACCATTGGGTTT-3	

A uniplex polymerase chain reaction (PCR) was conducted for molecular detection using the primer specified in Table (1). The PCR reaction mixture for identifying the *C. dubliniensis* virulence gene was prepared according to the specifications outlined in Table (2). The program for PCR thermocycler, was used to identify the virulence genes of *Candida*, as well as using ddH_2O as instead of DNA of *candida* as control negative, followed the parameters detailed in Table (2).

Table 2: PCR reaction volume

Content	Volume (µl)
Master Mix	7.5
DNA template	5
Forward Primer	2.5
Reverse Primer	2.5
Nuclease Free Water	2.5
Total	**20**

In the immunological analysis, blood samples were collected and centrifuged at 3000 rpm for 5 minutes to separate the serum. The levels of IL-17 and IL-23 in the patient serum were detected by Enzyme-Linked Immunosorbent Assay (ELISA) using diagnostic kit and according to instruction of the company (Sunlong biotechnology / Korea). The assay allows accurate quantification of IL-17 and IL-23 levels in the children's serum, all samples were tested in duplicate or triplicate.

Statistical Analysis

The Statistical Package for the Social Sciences (SPSS) software was used to analyze the data. The statistical difference between groups was established using the Pearson chi-square test.

RESULTS

The current study included totally, 110 oral cotton swabs that were collected and analyzed between January 2023 and August 2024. Samples were obtained from patients with orofacial clefts (cleft lip and/or cleft palate), including cases with and without candidiasis, in addition to 35 oral swabs collected from healthy control individuals. The distribution of study participants included 39 cleft lip cases, 36 cleft palate cases, and 35 controls. All specimens cultured on Sabouraud Dextrose Agar (SDA) supplemented with chloramphenicol revealed small, white to cream-colored smooth colonies (Figure 2). Along time of culture, the colonies revealed feet or rough appearance. Additionally, sub cultured on CHROM agar revealed dark green to deep blue-green colonies after 48 hours at 37 ºC, this agar used as a presumptive identification of *Candida* species based on colony morphology and pigmentation (Figure 3). Out of the total swabs examined, 43 (57.33%) were identified as positive for *Candida dubliniensis*, whereas 32 (42.67%) were negative.

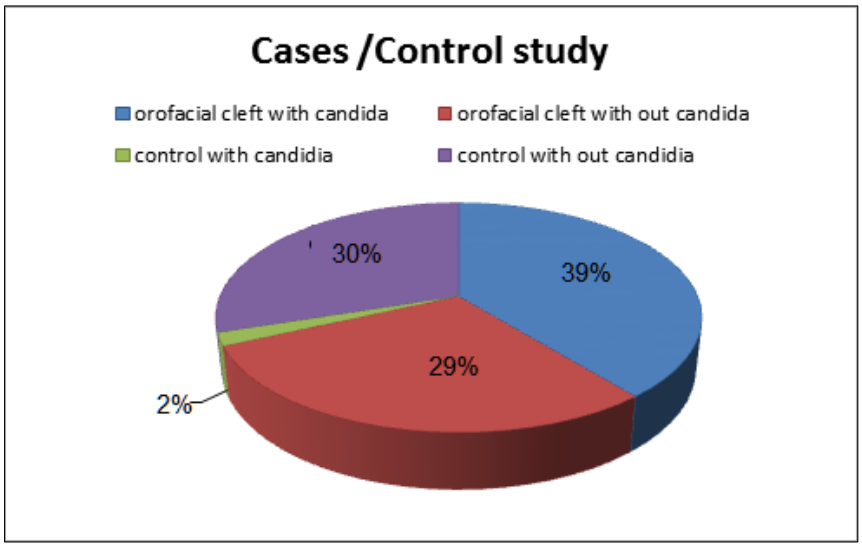

Figure 1: illustrates the distribution of *Candida dubliniensis* in both the patient and control groups

The data reveal that 39% of individuals with cleft lip are positive for *C. dubliniensis*, compared to 30% of those without clefts. Similarly, 29% of individuals with cleft palate exhibit *C. dubliniensis* presence, whereas only 2% of the control group are affected. These findings suggest a higher prevalence of *C. dubliniensis* among individuals with orofacial clefts compared to the control population.

Figure 2: Colony morphology of the *C. dublicansis* was grown on Sabouraud chloramphenicol medium

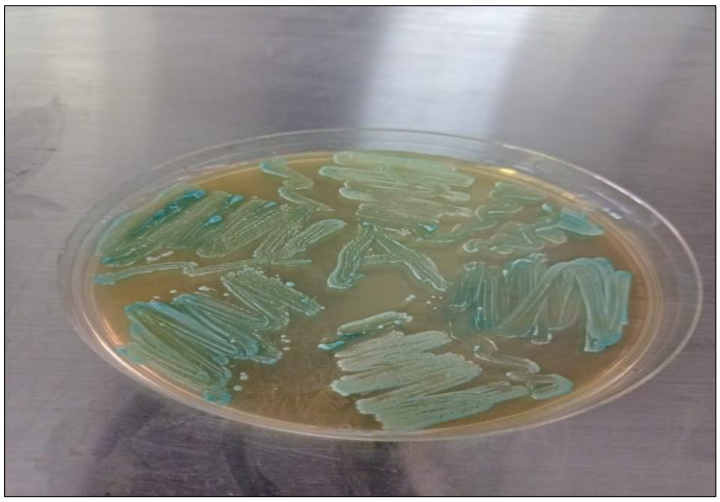

Figure 3: The colony morphology and identification of pure *Candida dubliniensis* isolates cultivated on CHROM agar

The distinct colony coloration and morphology observed on this medium facilitate differentiation *Candida dubliniensis* from other *Candida* species. Chrom agar is a selective and differential medium commonly used for yeast identification, providing a rapid and reliable method for distinguishing *C. dubliniensis* based on its unique pigmentation and growth characteristics.

Association between Cleft Type and Candida Dubliniensis Detection

The distribution of cleft type according to *Candida dubliniensis* positivity is presented in Table 3. The distribution of oralfacial cleft with and without candidiasis in both cleft (lips and palate cleft), the study found the more prevalence of *C. dubliniensis* (62.79%) in patient have palate cleft (27.21%) rather than lips cleft among 43 patient with statistical differences ($P< 0.05$), while among 32 patient of orolfacial cleft without candidiasis, 20 (62.5%) have lips cleft more than palate cleft (37.5%). Among the *C. dubliniensis*-positive cases (n = 43), cleft palate was more frequent (27, 62.79%) than cleft lip (16, 37.21%). In contrast, among the *C. dubliniensis* -negative cases (n = 32), cleft lip predominated (20, 62.5%) compared with cleft palate (12, 37.5%). A statistically significant association was observed between cleft type and *C. dubliniensis* detection ($\chi^2 = 4.701$, df = 1, P = 0.031).

Table 3: Distribution of oralfacial cleft with and without candidiasis in both cleft (lips and palate cleft)

Oral disease cases	Orofacial cleft with *C. dubliniensis* No. (%)	Orofacial cleft without *C. dubliniensis* No. (%)	Statistical analysis
Palate Cleft	27 (62.79%)	12 (37.5%)	$X^2 = 4.701$ DF=1 P= 0.031
Lips Cleft	16 (37.21%)	20 (62.5%)	
Total	**43 (57.33%)**	**32 (42.67%)**	

*Candida dubliniensis was more prevalent in cases of cleft palate (62.79%) compared to cleft lip (27.21%) among the 43 patients with candidiasis (P < 0.05). Conversely, among the 32 orofacial cleft cases without candidiasis, cleft lip was more common (62.5%) than cleft palate (37.5%). These results suggest a higher susceptibility to C. dubliniensis colonization in individuals with cleft palate, while cleft lip cases were more frequently observed in the absence of candidiasis.
** X2: chisquare test; DF: degree of freedom, P: P value.

Figure 4: Representative clinical presentation of orofacial clefts: (A) cleft lip and (B) cleft palate.

Relationship between Oral Plaque and Candida dubliniensis Infection

The association between oral plaque conditions and *C. dubliniensis* positivity is summarized in Table (4). Among the *C. dubliniensis*-positive group (n = 43), dental plaque was the most frequently observed condition (25 cases, 58.14%), followed by periodontal plaque (11 cases, 25.58%), while 7 cases (16.28%) showed no plaque appearance. Conversely, among the *C. dubliniensis*-negative group (n = 32), periodontal plaque was most common (18 cases, 56.25%), followed by dental plaque (9 cases, 28.13%), and no plaque appearance (5 cases, 15.62%). A statistically significant association was found between oral plaque status and *C. dubliniensis* infection ($\chi^2 = 8.114$, df = 2, P = 0.017). There is a significant relationship between oral disease cases and fungal infections in the group of children suffering from cleft palate.

Table 4: Distribution of *C. dubliniensis* among orofacial clefts with dental caries and periodontal plaque

Oral disease cases	Orofacial cleft without C. *dubliniensis* No. (%)	Orofacial cleft with *C. dubliniensis* No. (%)	Statistical analysis
Periodontal plaque	18 (56.25%)	11 (25.58%)	$X^2= 8.114$ DF=2 P= 0.017
Dental plaque	9 (28.13%)	25 (58.14%)	
No plaque appearance	5 (15.62%)	7 (16.28%)	
Total	**32 (42.67%)**	**43 (57.33%)**	

*Table shows a strong link between oral diseases and fungal infections in cleft palate children, while periodontitis was more common (56.25%) in non-*C. dubliniensis* patients.
**X2: chisquare test; DF: degree of freedom, P: P value.

Serum Cytokine Levels (IL-17 and IL-23)

Serum concentrations of IL-17 and IL-23 were measured in three groups: orofacial cleft patients with *C. dubliniensis* infection, orofacial cleft patients without *candidiasis*, and healthy controls (Table 5). IL-17 levels were significantly higher in patients with *C. dubliniensis* infection (115.91 ± 15.42 pg/ml) compared to orofacial cleft patients without candidiasis (68.85 ± 10.59 pg/ml), and the control group (21.58 ± 2.33 pg/ml) (P = 0.0046). Similarly, IL-23 levels were significantly elevated in the *C. dubliniensis*-positive group (77.28 ± 8.94 pg/ml) compared to the non-candidiasis group (53.84 ± 8.93 pg/ml) and controls (8.45 ± 2.46 pg/ml) (P = 0.0035).

Table 5: Shows mean and SD of IL-17 and IL-23 levels in the Orofacial cleft patients and the control group. Cytokine 17 and 23 levels were highest in orofacial cleft patients with candidiasis, lower in those without candidiasis, and lowest in the control group

Interleukins	Patients With *C. dubliniensis*	Patients Without *C. dubliniensis*	Control	*P. value Tukey pairwise ANOVA test
IL -17	115.91 ± 15.42 Pg ml A	68.85± 10.59 Pg/ml B	21.58 -2.33 pg ml C	**0.0046**
IL-23	77.28 ± 8.94 pg ml A	53.84± 8.93 Pg/ml B	8.45 -2.46 pg ml C	**0.0035**

The CDUB gene was successfully amplified for all strains using new specific primers and generated PCR products ranging in size from 357 bp for *C. dubliniensis* (Figure. 6). This investigation identified the presence of the CDUB virulence gene in 100 % of the 43 *C. dubliniensis* isolates tested from orofacial cleft patients. On the other hand, the study did not record any PCR product in patients without candidiasis cases.

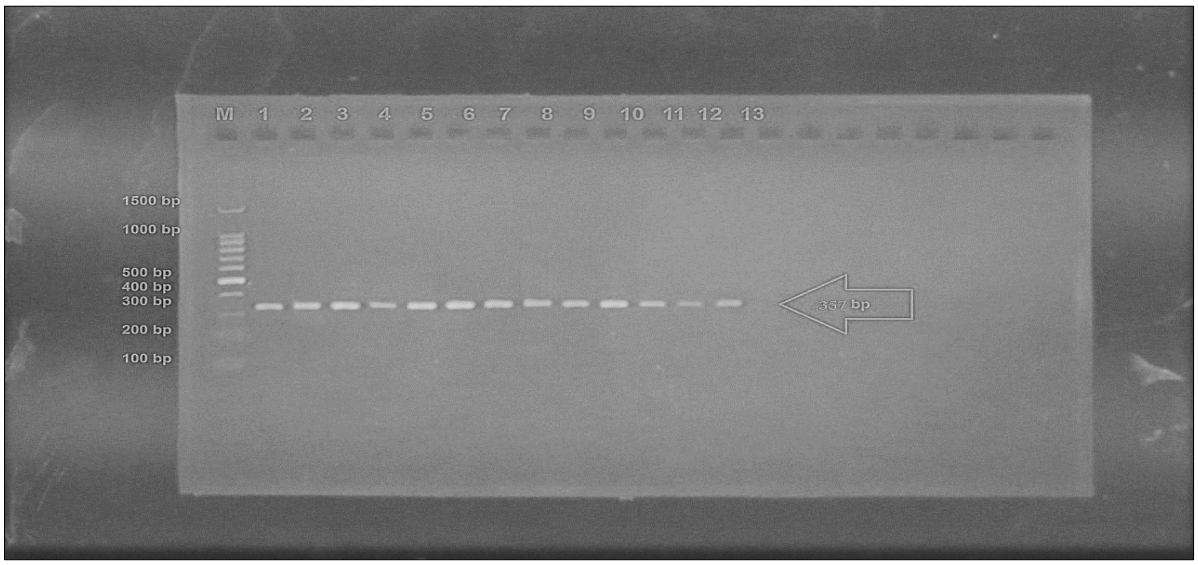

Figure 5: Shows the Gel electrophoresis of PCR amplicon (*CDUB* genes (357 pb) in (*C. dubliniensis*) on 1.5% agarose gel at 7 V/cm for 30 min. Lane 1: 1500 bp DNA ladder

DISCUSSION

The present study demonstrated a significantly higher prevalence of oral candidiasis among children with orofacial clefts, particularly those with cleft palate, compared to children without candidiasis. *Candida dubliniensis* was identified as the predominant species, showing a statistically significant association with cleft palate cases ($P < 0.05$). The text discusses that children with orofacial clefts and candidiasis show increased levels of IL-17 and IL-23, suggesting activation of the Th17 immune pathway. It also highlights a notable link between fungal infections and oral diseases like dental caries [21].

Candida species are commensal yeasts commonly present in the oral cavity as part of the normal microbiota. Under physiological conditions, their growth is controlled by host immunity, saliva, and microbial competition. However, disturbances in the oral environment may promote fungal overgrowth, leading to oral candidiasis [17]. In the current study, children with orofacial clefts showed increased susceptibility to Candida colonization, which is consistent with previous findings reported in regional and international studies [2-10].

Anatomically, cleft palate defects result in irregular surfaces, deep fissures, and communication between the oral and nasal cavities. These structural abnormalities promote food retention and plaque accumulation, thereby complicating oral hygiene efforts [22].

Similar findings were reported in studies conducted in Middle Eastern and European populations, where cleft palate patients demonstrated significantly higher oral Candida colonization compared to cleft lip patients and healthy controls [10]. The present results align with these observations, as *C. dubliniensis* prevalence was notably higher in cleft palate cases (62.79%) compared to cleft lip cases (27.21%).

In addition to anatomical factors, biological mechanisms may further explain this association. Saliva plays a critical protective role through mechanical cleansing and antimicrobial components such as immunoglobulin A and defensins. Cleft palate may

impair normal salivary flow and distribution, resulting in localized dryness and reduced antifungal defense [5]. This altered microenvironment favors Candida adherence, biofilm formation, and persistent colonization.

The significant association between *C. dubliniensis* and dental caries observed in this study (approximately 60% of oral disease cases) may be explained by synergistic microbial interactions. Candida species can co-aggregate with cariogenic bacteria such as *Streptococcus mutans*, enhancing biofilm virulence and acid production. Similar associations have been documented in international studies highlighting the contributory role of *Candida* in caries progression [3]. Conversely, periodontitis was more prevalent among patients without *C. dubliniensis* (56.25%), although *Candida* species are known to colonize periodontal pockets and potentially exacerbate inflammatory destruction.

From an immunological perspective, significantly elevated IL-17 levels were observed in children with both orofacial cleft and candidiasis compared to those without candidiasis. IL-17 is a key pro-inflammatory cytokine produced mainly by Th17 cells (pro-inflammatory $CD4+$ T helper cells) and plays a central role in mucosal defense against fungal infections [1]. *Candida* antigens stimulate dendritic cells to produce IL-23, which promotes Th17 differentiation and sustained IL-17 production. This explains the parallel elevation of IL-23 (77.28 ± 8.94 pg/ml) observed in the infected group. Similar immunological patterns have been described in studies investigating oral candidiasis in immunocompromised and pediatric populations [12].

The combined presence of structural abnormalities and fungal infection may amplify inflammatory signaling pathways. IL-17 promotes neutrophil recruitment and enhances antimicrobial peptide production, but excessive activation may also contribute to tissue inflammation [15]. Therefore, the elevated IL-17 and IL-23 levels detected in this study likely reflect an intensified mucosal immune response to persistent *Candida* colonization in anatomically compromised tissues.

Molecular identification using PCR targeting the *CDUB* gene provided specific detection of *Candida dubliniensis*. The *CDUB* gene represents a species-specific genetic marker distinguishing *C. dubliniensis* from closely related species such as *Candida albicans*. Molecular techniques improve diagnostic accuracy and overcome limitations associated with phenotypic identification methods [11].

Despite these important findings, several limitations should be acknowledged. First, the relatively small sample size (n = 43) may limit generalizability. Second, this was a single-center study, which may not fully represent the broader pediatric population. Third, the cross-sectional design does not allow assessment of longitudinal changes in cytokine levels or Candida colonization over time. Future multicenter studies with larger cohorts and longitudinal follow-up are recommended to better clarify the causal relationship between cleft anatomy, fungal colonization, and immune response.

CONCLUSION

In conclusion, the current study revealed a significant association between cleft palate anatomy and increased *Candida* colonization, particularly *C. dubliniensis*, accompanied by activation of the IL-23/IL-17 immune axis. Structural, microbiological, and immunological factors collectively contribute to the increased susceptibility to oral candidiasis in children with cleft palate.

DECLARATIONS

Acknowledgment: None

Ethics Statement: The authors declare that this study was conducted in accordance with the ethical standards and guidelines outlined in the journal's "Ethics Approval" section of the author guidelines. As this work is a narrative review, formal ethical approval was not required. All clinical images (e.g., cleft lip/palate figures) were anonymized by obscuring identifying features, and consent for publication was obtained from participants' guardians.

Funding: The authors declare that this research supported by University of Al-Qadisiya.

Competing Interest's Statement: The authors declare that they have no competing interests.

Author Contributions

HAHA provided the concepts, molecular experiments, data analysis, and writing of the manuscript; ZAKA Conducted microbiological culture and identification (CHROM agar, Sabouraud's dextrose agar), analyzed data, and reviewed the manuscript; HAM Supervised immunological assays (ELISA for IL-17/IL-23), contributed to statistical analysis (SPSS), and critically revised the final manuscript. Worked with data collection and analysis; RHJ revised the manuscript and analyzed the data.

HAHA, ZAKA, HAM read, approved, and incorporated feedback into the final version for submission.

REFERENCES

1. Scorzoni L, Fuchs BB, Junqueira JC, Mylonakis E. Current and promising pharmacotherapeutic options for candidiasis. Expert Opin Pharmacother. 2021 May;22(7):867-887. doi:

10.1080/14656566.2021.1873951. Epub 2021 Feb 4. PMID: 33538201; PMCID: PMC8122024.

2. Verma AH, Zafar H, Ponde NO, Hepworth OW, Sihra D, Aggor FEY, Ainscough JS, Ho J, Richardson JP, Coleman BM, Hube B, Stacey M, McGeachy MJ, Naglik JR, Gaffen SL, Moyes DL. IL-36 and IL-1/IL-17 Drive Immunity to Oral Candidiasis via Parallel Mechanisms. J Immunol. 2018 Jul 15;201(2):627-634. doi: 10.4049/jimmunol.1800515. Epub 2018 Jun 11. PMID: 29891557; PMCID: PMC6039262.
3. de Souza PTDR, Gonçalves-Wilhelmsen NCV, Rosa RT, Correia CFKN, Pereira TM, Kitahara ABP, Ignácio SA, Azevedo-Alanis LR, Rosa EAR. Oral Colonization and Virulence Factors of *Candida* spp. in Babies With Cleft Palate. Cleft Palate Craniofac J. 2022 Aug;59(8):1056-1063. doi: 10.1177/10556656211030437. Epub 2021 Jul 14. PMID: 34259068.
4. Vila T, Sultan AS, Montelongo-Jauregui D, Jabra-Rizk MA. Oral Candidiasis: A Disease of Opportunity. J Fungi (Basel). 2020 Jan 16;6(1):15. doi: 10.3390/jof6010015. PMID: 31963180; PMCID: PMC7151112.
5. Farronato G, Cannalire P, Martinelli G, Tubertini I, Giannini L, Galbiati G, Maspero C. Cleft lip and/or palate: review. Minerva Stomatol. 2014 Apr;63(4):111-26. English, Italian. PMID: 24705041. https://pubmed.ncbi.nlm.nih.gov/24705041
6. De-La-Torre J, Quindós G, Marcos-Arias C, Marichalar-Mendia X, Gainza ML, Eraso E, Acha-Sagredo A, Aguirre-Urizar JM. Oral Candida colonization in patients with chronic periodontitis. Is there any relationship? Rev Iberoam Micol. 2018 Jul-Sep;35(3):134-139. doi: 10.1016/j.riam.2018.03.005. Epub 2018 Aug 3. PMID: 30082174.
7. Machorowska-Pieniążek A, Mertas A, Skucha-Nowak M, Tanasiewicz M, Morawiec T. A Comparative Study of Oral Microbiota in Infants with Complete Cleft Lip and Palate or Cleft Soft Palate. Biomed Res Int. 2017;2017:1460243. doi: 10.1155/2017/1460243. Epub 2017 Mar 14. PMID: 28393073; PMCID: PMC5368409.
8. Conti HR, Shen F, Nayyar N, Stocum E, Sun JN, Lindemann MJ, Ho AW, Hai JH, Yu JJ, Jung JW, Filler SG, Masso-Welch P, Edgerton M, Gaffen SL. Th17 cells and IL-17 receptor signaling are essential for mucosal host defense against oral candidiasis. J Exp Med. 2009 Feb 16;206(2):299-311. doi: 10.1084/jem.20081463. Epub 2009 Feb 9. PMID: 19204111; PMCID: PMC2646568.
9. Silva JJD, Silva TAD, Almeida H, Rodrigues Netto MF, Cerdeira CD, Höfling JF, Boriollo MFG. Candida species biotypes in the oral cavity of infants and children with orofacial clefts under surgical rehabilitation. Microb Pathog. 2018 Nov;124:203-215. doi: 10.1016/j.micpath.2018.08.042. Epub 2018 Aug 20. PMID: 30138757.
10. Yue H, Hu J, Guan G, Tao L, Du H, Li H, Huang G. Discovery of the gray phenotype and white-gray-opaque tristable phenotypic transitions in Candida dubliniensis. Virulence. 2016 Apr 2;7(3):230-42. doi: 10.1080/21505594.2015.1135287. Epub 2015 Dec 29. PMID: 26714067; PMCID: PMC4871672.
11. Jabri B, Iken M, Ait-Ou-Amar S, Rida S, Bouziane A, Ennibi OK. *Candida albicans* and *Candida dubliniensis* in Periodontitis in Adolescents and Young Adults. Int J Microbiol. 2022 Jan 11;2022:4625368. doi: 10.1155/2022/4625368. PMID: 35058983; PMCID: PMC8766183.
12. Kagami S, Rizzo HL, Kurtz SE, Miller LS, Blauvelt A. IL-23 and IL-17A, but not IL-12 and IL-22, are required for optimal skin host defense against Candida albicans. J Immunol. 2010 Nov 1;185(9):5453-62. doi: 10.4049/jimmunol.1001153. Epub 2010 Oct 4. PMID: 20921529; PMCID: PMC3076054.
13. Khan I, Ahmad T, Manzoor N, Rizvi MA, Raza U, Premchandani S. Evaluating the role of local host factors in the candidal colonization of oral cavity: A review update. Natl J Maxillofac Surg. 2020 Jul-Dec;11(2):169-175. doi: 10.4103/njms.NJMS_161_20. Epub 2020 Dec 16. PMID: 33897176; PMCID: PMC8051668.
14. Mancera E, Nocedal I, Hammel S, Gulati M, Mitchell KF, Andes DR, Nobile CJ, Butler G, Johnson AD. Evolution of the complex transcription network controlling biofilm formation in *Candida* species. Elife. 2021 Apr 7;10:e64682. doi: 10.7554/eLife.64682. PMID: 33825680; PMCID: PMC8075579.
15. Saunus JM, Wagner SA, Matias MA, Hu Y, Zaini ZM, Farah CS. Early activation of the interleukin-23-17 axis in a murine model of oropharyngeal candidiasis. Mol Oral Microbiol. 2010 Oct;25(5):343-56. doi: 10.1111/j.2041-1014.2010.00570.x. PMID: 20883223.
16. Sangar, S., Ravindran, V., & Ramanathan, V. (2021). Oral mucosal lesions in children with and with out cleft palate: a case control study. Turkish Online Journal of Qualitative Inquiry, 12(5). https://www.tojqi.net/index.php/journal/article/view/1325
17. Vyas T, Gupta P, Kumar S, Gupta R, Gupta T, Singh HP. Cleft of lip and palate: A review. J Family Med Prim Care. 2020 Jun 30;9(6):2621-2625. doi: 10.4103/jfmpc.jfmpc_472_20. PMID: 32984097; PMCID: PMC7491837.
18. Vila T, Sultan AS, Montelongo-Jauregui D, Jabra-Rizk MA. Oral Candidiasis: A Disease of Opportunity. J Fungi (Basel). 2020 Jan 16;6(1):15. doi: 10.3390/jof6010015. PMID: 31963180; PMCID: PMC7151112.
19. Yue H, Hu J, Guan G, Tao L, Du H, Li H, Huang G. Discovery of the gray phenotype and white-gray-opaque tristable phenotypic transitions in Candida dubliniensis. Virulence. 2016 Apr 2;7(3):230-42.

doi: 10.1080/21505594.2015.1135287. Epub 2015 Dec 29. PMID: 26714067; PMCID: PMC4871672.

20. Akram, Z. M., & Al-Taee, A. M. (2024). Evaluation of salivary IL-17 and IL-23 in children with orofacial cleft and oral candidiasis. Journal of Medical and Oral Biosciences, 1(1). https://jmob.aliraqia.edu.iq
21. Wu, Q., Li, Z., Zhang, Y., Peng, X., & Zhou, X. (2023). Dental caries and periodontitis risk factors in cleft lip and palate patients. Frontiers in Pediatrics, 10, Article 1092809. https://doi.org/10.3389/fped.2022.1092809.