Available online at www.jpsscientificpublications.com

Life Science Archives (LSA)

ISSN: 2454-1354

Volume – 7; Issue - 2; Year – 2021; Page: 2122 – 2129

DOI: 10.22192/lsa.2021.7.2.5

Research Article

DISTRIBUTION OF MICROORGANISMS IN THE ORAL CAVITY OF CHILDREN WITH LEUKEMIA BEFORE AND AFTER CHEMOTHERAPY

Hanan S. Makki[1], Awatif H. Issa[*2] and Abdullah H. Al Saadoon[2]

[1]*Basra Children Specialty Hospital, Basra Province, Iraq*
[2]*Biology Department, College of Science, University of Basrah, Basra, Iraq*

Abstract

The oral cavity is a unique environment, that gives a critical protective interface between the external and internal environment because it consists of oral mucosa which serves as a barrier to a large number of microbial species present in this moist and warm. So, the hard tissue breaks through the epithelial surface of the oral cavity due to invading by the different microorganisms (bacteria, yeasts), which regarded commensal microorganisms in the oral cavity. Impaired in the immune system in some cases as in patients with leukemia, these microorganisms become pathogens. Current study shows more prevalence for bacteria in oral cavity to patients before receive chemotherapy about 46 (53.4 %) and after take chemotherapy reach to 40 (46.5 %) additional to bacterial prevalence we observed yeasts in oral cavity for children's patients especially *Candida* sp. with increased number of *Candida* sp. After chemotherapy more than before therapy reach to 19 (59.4 %) and 13 (40.6 %) respectively.

Article History

Received : 25.02.2021
Revised : 09.03.2021
Accepted: 30.03.2021

Key words: Oral cavity, Leukemia patients, *Candida* sp. and Commensal microorganisms.

1. Introduction

Leukemia is a group of malignant hematologic diseases with mesenchymal (myeloid or lymphoid) organ originating from the bone marrow, which generates a high number of abnormal hematopoietic cells concerning their proliferation, differentiation, and programmed cell death (apoptosis) (Chandran *et al.*, 2015). The most common type of leukemia among children is (ALL) Acute lymphoblastic leukemia, about 75 % of all childhood leukemia and 25 % of all malignancy in childhood (Wang *et al.*, 2014; Babu *et al.*, 2016). Among some individuals, leukemia first manifests in the oral cavity and the frequent manifestations that occur in leukemia patients include gingival bleeding, oral ulceration, gingival enlargement, candidiasis, and periodontitis (Chamilos *et al*., 2006; Garrett *et al*., 2007; Javed *et al*., 2012). Most children with leukemia suffering from neutropenia that means decreased in absolute neutrophils count less than 500 cell/ mm^3 that play important role in regulating some microbial flora in the oral cavity including bacteria, *Staphylococcus* spp., *Lactobacillus* spp., *Streptococcus* spp., *Klebsiella* spp., *Escherichia coli*, *Enterobacter* spp., *Citrobacter* spp., *Acinetobacter* spp. and yeasts (Zuckermann *et al*., 2012). *Candida* sp. are commensal yeasts with more abundance and colonization in mucus membranes surface in the oral cavity for a patient

***Corresponding author*: Awatif H. Issa**

with leukemia (Alnuaimi *et al*., 2015). Generally, the first manifestation in patients with leukemia occurs in the oral cavity and observed the prevalence *of Candida* spp. and cause candidiasis, pseudomembrane *Candida*, and erythematous (Mushi *et al*., 2016; Javed *et al.*, 2009; Scully, 2004). Previous studies found that oral bacteria are responsible for 25 % to 50 % of systemic infections in neutropenic patients (Wingard, 2001).

2. Materials and Methods

Patients and Specimens

This study was conducted at Basra children's specialty hospital, Basra province, Iraq from August 2016 to June 2017. Fifty specimens were taken from the oral cavity by using sterile cotton swabs from each patient before receiving chemotherapy and lately 4 - 6 weeks after receiving chemotherapy.

Identification Study

Bacteria and yeasts were identification by used traditional methods that including Macroscopic and Microscopic examination, Routine media (Blood agar, Chocolate agar, MacConkey agar of bacteria, Sabouraud's dextrose agar for fungi and Selective medium (CHROM agar *Candida* medium) of yeasts, all these media were prepared accordance the instructions for manufacture protocol of company procedure. In addition to biochemical test of bacteria (Catalase, Coagulase, Oxidase and API 20 E, API Staph, API 20 Strep from BioMerieux SA, France) and Yeast tests (Germ tube, API Candida from BioMerieux SA, France), Molecular studies including DNA Extraction for yeasts by Commercial kit (from Favorgen company, Canada) was also included in the present research. PCR amplification was performed in a final volume of 25 µl. And each reaction consists of 2.5 µl of Green Master Mix, 0.5 µl $MgCl_2$, 0.5 µl of each forward (ITS1, F-5-TCC GTA GGT GAA CCT GCG G -3) and revers (ITS4, R-5- TCC TCC GCT TAT TGA TAT GC-3), 1.5 µl of template DNA, finally added about 9.5 µl DDH_2O to complete volume into 25 µl. An initial denaturation step at 94 °C for 5 min then the second step was 25 cycles of denaturation at 94 °C for 30 seconds. Annealing at 56 °C for 45 seconds and extension at 72 °C for 1 min, the last final step of 72 °C for 7 min. After that, the amplified products were visualized by 0.8 % agarose gel electrophoresis about (0.2 gm) dissolved in 25 ml of TBE buffer, then stained with 0.2 µl of Ethidium bromide and photographed (Mirhendi *et al*., 2006). After the finished amplification process, the samples of PCR products were sent into sequenced by micro gen company in Korea.

Statistical analysis

Statistical analysis of data was carried out by using the t-test sample (paired samples test and paired samples correlation) with differences at $P<0.05$ which is considered to be statistically significant. This calculation was carried out according to the Statistical Package for Social Science (SPSS version 20) and the least significant difference at a level less than (0.05).

3. Results and Discussion

The oral cavity is a unique environment where contains multiple types of microorganism, whether bacteria or fungi that coexist with the state of ecological balance in healthy individuals (Dale *et al.*, 2005; Kimball *et al*., 2006). Exposure to diseases that cause weakness of the immunodeficiency, leukemia, and other cancers will lead to the imbalance of the oral cavity environment, as there was a decrease in the richness and less diversity of oral microbiota compared to healthy controls (Wang *et al.*, 2014). The patients who use chemotherapy that cause neutropenia and another antimicrobial agent like aminoglycoside agent (gentamycin, amikacin and netilmicin) which used as prophylaxis drug receive to the febrile patient with leukemia to reduce risk of bacterial that invading the body when granulocyte white blood cells(neutrophils) are less than 1500 cell/mm^3 (Andrews *et al*., 2003). In the current study, the results for 50 specimens throat swabs which taken from 25 children with leukemia before and after chemotherapy as shown in Table - 1, where a total

of 86 bacterial isolates were obtained 46 (53.4 %) were isolated before chemotherapy and 40 (46.5 %) were isolated after 4 - 6 weeks of chemotherapy, using the above-mentioned diagnostic methods for diagnosis of bacteria. This result agreed with Wang *et al.* (2014) who proposed that the state number and diversity of bacterial isolation before chemotherapy more than after chemotherapy. As for yeast species that coexisted with bacteria in the oral cavity were all of *Candida* species 32 isolates was obtained 13 (40.6 %) before chemotherapy and about 19 (59.4 %) were isolated after 4 - 6 weeks of chemotherapy, since most children patients in both cases before and after chemotherapy suffering from neutropenia, so this result agreed with Netea *et al*. (2015) who showed the increase in invading opportunistic infections in immune suppression patients, as *Candida* spp. particularly *Candida albicans*.

Table - 1: Distribution of Bacteria species in Oral cavity for Children with Leukemia in Study Group

Bacterial species	No. % of isolates before chemotherapy		No. % of isolates after chemotherapy	
Viridans group of *Streptococci*	(7)	15.2%	(5)	12.5%
Streptococcus mitis	(4)	8.7%	(4)	10%
Streptococcus trails	(3)	6.5%	(3)	7.5%
Streptococcus spp.	(2)	4.4%	(2)	5%
Globicatelia sanguinis	(2)	4.4%	(1)	2.5%
Enterococcus spp.	(3)	6.5%	(4)	10%
Staphylococcus aureus	(2)	4.4%	(2)	5%
Staphylococcus xylosus	(3)	6.5%	(2)	5%
Staphylococcus spp.	(4)	8.7%	(3)	7.5%
Staphylococcus lugdunesis	(0)	0%	(1)	2.5%
Staphylococcus sciuri	(0)	0%	(2)	5%
Staphylococcus cohnii	(0)	0%	(1)	2.5%
Leuconostac spp.	(0)	0%	(1)	2.5%
Lactobacillus	(1)	2.2%	(0)	0%
Diphtheroid	(3)	6.5%	(1)	2.5%
Klebsiella pneumoniae	(2)	4.4%	(3)	7.5%
Klebsiella spp.	(3)	6.5%	(1)	2.5%
Escherichia coli	(1)	2.2%	(1)	2.5%
Pseudomonas oryzihabstans	(1)	2.2%	(0)	0%
Pseudomonas luteola	(1)	2.2%	(0)	0%
Enterobacter cloacae	(1)	2.2%	(1)	2.5%
Acinetobacter lwoffii	(2)	4.4%	(0)	0%
Ochrabacterium anthropi	(1)	2.2%	(0)	0%
Serratia marcesence	(0)	0%	(1)	2.5%
Enterococcus sakazakii	(0)	0%	(1)	2.5%
Total = 86 99.9 %	46	53.4%	40	46.5%

Table - 2: Distribution of *Candida* Species in Oral Cavity for Children with Leukemia in Study Group

Candida Species	No. of isolates % Before chemotherapy		No. of isolates % After chemotherapy	
Candida albicans	10	31.3%	16	50%
Candida africana	1	3.1%	2	6.3%
Candida krusei	1	3.1%	1	3.1%
Candida glabrata	1	3.1%	0	0%
Total = 32 100%	13	40.6%	19	59.4%

Table - 3: Statistical Analysis of Cultured of *Candida* species for Children That Calculate Twice Before and After Chemotherapy

No.	Type sample	Correlation coefficient	P-value
1	*Candida* spp.	0.658	0.491

P > 0.05 No significant difference

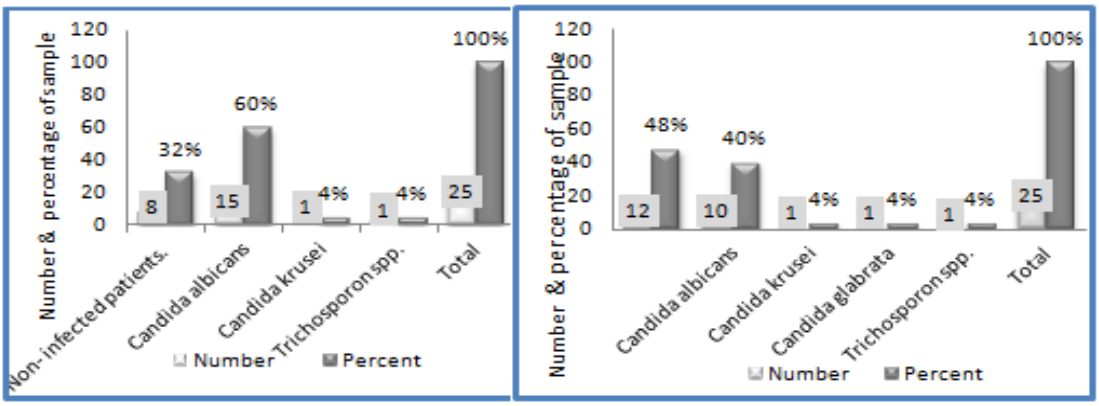

Figure - 1: Types of *Candida* species identified by API system (A) before chemotherapy and (B) after chemotherapy in a patient with leukemia

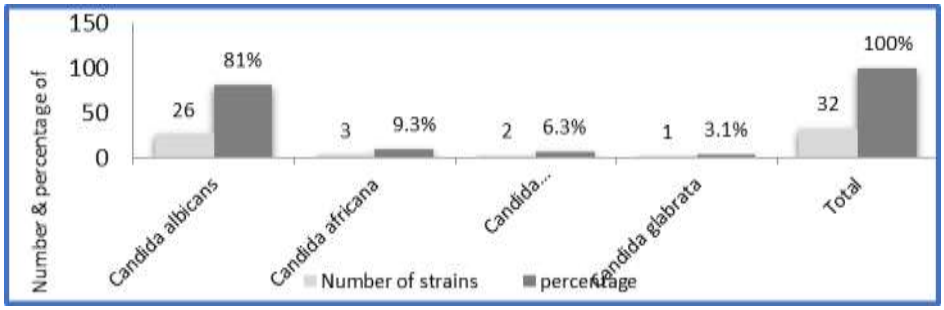

Figure - 2: Results of the gene sequence of *Candida* species and their strains before and after chemotherapy

Table – 4: Results of API Candida and Result Data for *Candida* Species Sequence Before and After Chemotherapy

Before chemotherapy				After chemotherapy	
No.	Results of API	Results of Sequence	No.	Results of API	Results of Sequence
1	*Candida albicans*	*Candida albicans* strain h3b	2	*Candida albicans*	*Candida albicans* strain CBS:2735
3	*Candida albicans*	*Candida albicans* strain ATCC18804	4	*Trichosporon spp*	*Candida albicans* strain h10a
5	*Candida krusei*	*Pichia kudriavzevii* CBS:5147	6	*Candida krusei*	*Pichia kudriavzevii* CBS:5147
7	*Trichosporon spp*	*Candida albicans* isolate 79209	8	*Candida albicans*	*Candida albicans isolate IMICRO* 142
9	*Candida albicans*	*Candida albicans* strain d9b	10	*Candida albicans*	*Candida albicans* strain d9b
11	*Candida albicans*	*Candida albicans* strain ATCC 752	12	*Candida albicans*	*Candida albicans* strain ATCC 752
	/		13	*Candida albicans*	*Candida albicans* strain Hb13
14	*Candida albicans*	*Candida albicans* strain H245B	15	*Candida albicans*	*Candida albicans strain ATCC 18804*
16	*Candida glabrata*	*Candida glabrata CBS:138*	17	*Candida albicans*	*Candida albicans strain ATCC 18804*
	/		18	*Candida albicans*	*Candida albicans strain ATCC 18804*
19	*Candida albicans*	*Candida albicans strain ATCC 18804*	20	*Candida albicans*	*Candida albicans strain ATCC 18804*
	/		21	*Candida albicans*	*Candida africana* CBS 8781
22	*Candida albicans*	*Candida albicans strain ATCC 18804*	23	*Candida albicans*	*Candida albicans strain ATCC 18804*
	/		24	*Candida albicans*	*Candida albicans strain ATCC 18804*
25	*Candida albicans*	*Candida albicans strain ATCC 18804*	26	*Candida albicans*	*Candida africana* CBS 8781
27	*Candida albicans*	*Candida africana* CBS 8781	28	*Candida albicans*	*Candida albicans strain ATCC 18804*
29	*Candida albicans*	*Candida albicans strain ATCC 18804*	30	*Candida albicans*	*Candida albicans strain ATCC 18804*
	/		31	*Candida albicans*	*Candida albicans strain ATCC 18804*
	/		32	*Candida albicans*	*Candida albicans strain ATCC 18804*

*Total No. for patient = 25 , % for patient before chemotherapy= (13)52% , % for patient after chemotherapy= (19)79%

* Total No. for isolate =32 , % for isolates before chemotherapy= (13) 40.6% , % for isolates after chemotherapy= (19)59.37%

Result of API *Candida* system that performed for 32 isolates that recovered from 25 patients. These include 13 (40.6 %) isolates before chemotherapy and 19 (59.4 %) isolates after chemotherapy showed a positive result. All the results of the API *Candida* system were compatible with sequence results proportion 84.4 % except 5 isolates about 15.6 % was not compatible with sequence result as shown in Table - 3. The result before chemotherapy showed that (12) 48 % patients with leukemia did not have an infection with *Candida* spp., and (10) 40 % patients were infected with *Candida albicans* and (1) 4 % patients for each *Candida krusei*, *Candida glabrata*, and *Trichosporon* spp. as shown in Figure - 1. While the result after chemotherapy showed that (8) 32 % for patients with leukemia did not have an infection with *Candida* sp., (15) 60 % for *Candida albicans*, (1) 4 % for *Candida krusei* and *Trichosporon* spp. as shown in Figure - 2. Only the isolates 4 and 7 showed discrepancies between Api and the sequence results for the previous isolates were identified as *Trichosporon* spp. with API *Candida* system, while by using sequence techniques they identified as *Candida albicans* of strains h10a and 79209 respectively, both isolates have the same characteristic morphology on SDA and reaction on CHROM agar medium. Also, there were some differences among the isolates 21, 26, 27 respectively when API *Candida* system identified as *Candida albicans* and sequence results was *Candida africana* CBS 8781, both isolates have the same characteristic features on SDA and CHROM agar medium. Also, in this study revealed disappeared *Candida glabrata* strain CBS:138 of the isolate (16) was not recovered before chemotherapy while *Candida albicans* strain ATCC 18804 of isolate (17) reported after chemotherapy for the same patient as shown in Table - 4, this difference may be due to chemotherapy effects on *Candida* spp. that agrees with (Teoh and Pavelka, 2016).

The patient's chance of survival was increased through clinicians administer better treatment decisions by used early diagnosis of invasive fungal infections such as candidiasis. The molecular biology methods are more confident than traditional phenotyping methods (Shokohi *et al*., 2010; Shokohi *et al*., 2011). For substance, *Candida* species were identified by Molecular biology methods. Such as multiplex PCR, standard PCR, PCR with species-specific probes, PCR-RFLP, real-time PCR (Mirhendi *et al*., 2008). The current study using the universal primers ITS1 and ITS4, which amplified between 510 - 870 bp of the ITS1 - 5.8 S-ITS2 region. As well as the result for *Candida* species sequence before and after chemotherapy in this study has been shown that *Candida albicans* reach 81.25 % including 26 strains were 15. *Candida albicans* strain ATCC 18804, 2 *Candida albicans* strain ATCC 752, 2

Candida albicans strain d9b and 1 number for each next strain H245B l, 79209 l, LMICRO142, h10a, Hb13, h3b, and CBS:2735). While *Candida africana* reaches to (3) 9.30 % consists of one type of strain CBS 8781, *Candida krusei* (*Pichia kudriavzevi*i) reach to (2) 6.30 % in one type of strain CBS:5147 and the last strain was *Candida glabrata* (1) 3.10 % CBS:138. This study showed that the proportion of infected children with *Candida* species increased from 52 % before to 76 % after chemotherapy. *Candida albicans* represent about 40 % - 60 % proportion of infected children with *Candida* species before and after chemotherapy respectively. This result is confirmed by the results sequence that refers to 81.25 % belong to *Candida albicans* with different strains, the ATCC 18804 strain is the most common among strains, the second species identified by the results sequence technique was *Candida africana* which reached 9.37 %. This species did not identify by the Api *Candida* system which was diagnosed as *Candida albicans* in isolates (21, 26, 27) respectively, while the results sequence for *Candida krusei* (teleomorph *Pichia kudriavzevi*i) reach 6.25 %. The results of the current study revealed a high correlation between *Candida* species, as well as *Candida albicans* more prevalence from other non - *Candida albicans* in the oral cavity of children with leukemia before and after chemotherapy. This finding agrees with Subramaniam *et al.* (2008), Badiee *et al.* (2009), Mokaddas *et al.* (2010) and Darbandi *et al.* (2014) who demonstrated that the most often *Candida* spp. that is associated with oral lesions was *Candida albicans*, and other *Candida* spp. have also been isolated from the oral cavity. fungi were caused about 40 % to 50 % of fatal infections among cancer patients. This study shows that a correlation between *Candida* spp. before and after chemotherapy reach to 0.658 with no significance different P> 0.05.

4. Conclusion

The current study observed that the increased infection with opportunistic microorganisms in patients under immune suppression such as different species of bacteria and *Candida* spp. particularly *Candida albicans*, result from the effect of chemotherapy in an environmental oral cavity so the most common species of *Candida* identified was *Candida albicans* with different strains and the most common strain was ATCC 18804. Other species w*ere Candida africana*, *Candida krusei* (*Pichia kudriavzevi*), and *Candida glabrata* respectively.

Acknowledgment

The authors represent deep thanks to everyone who helped us during this study. Deep thanks to all the children suffering from leukemia at the Basra specialist child hospital and to their parents for allowing us to take samples from their children despite their suffering.

5. Reference

1) Alnuaimi, A.D., Wiesenfeld, D., O'Brien-Simpson, N.M., Reynolds, E.C. and McCullough, M. J. (2015). Oral Candida colonization in oral cancer patients and its relationship with traditional risk factors of oral cancer: a matched case-control study. *Oral Oncology*, 51(2):139 - 145.
2) Andrews, T. and Sullivan, K. E. (2003). Infections in patients with inherite defects in phagocytic function. *Clinical Microbiology Reviews*, 16(4): 597 - 621.
3) Babu, K.L.G., Mathew, J., Doddamani, G.M., Narasimhaiah, J. K. and Naik, L.R.K. (2016). Oral health of children with acute lymphoblastic leukemia: A review. *Journal of Orofacial Sciences*, 8(1): 3 - 8.
4) Badiee, P., Kordbacheh, P., Alborzi, A., Zakernia, M. and Haddadi, P. (2009). Early detection of systemic candidiasis in the whole blood of patients with hematologic malignancies. *Japan Journal of Infectious Disease*, 62(1): 1 - 5.
5) Chamilos, G., Luna, M., Lewis, R.E., Bodey, G.P., Chemaly, R., Tarrand, J.J., Safdar, A. and Kontoyiannis, D. P. (2006). Invasive fungal infections in patients with hematologic malignancies in a tertiary care cancer center: an autopsy study over a 15-

year period (1989-2003). *Haematologica*, 91(7): 986 - 989.

6) Chandran, P., Le, Y., Li, Y., Sabloff, M., Mehic, J., Rosu-Myles, M and Allan, D. S. (2015). Mesenchymal stromal cells from patients with acute myeloid leukemia have altered capacity to expand differentiated hematopoietic progenitors. *Leukemia research*, 39(4): 486 - 493.
7) Dale, B. A and Fredericks, L. P. (2005). Antimicrobial peptides in the oral environment: expression and function in health and disease. *Current Issues in Molecular Biology*, 7(2): 119 - 134.
8) Darbandi, B., Salem, K., Rahbarnikoukar, V. and Ansari, S. (2014). Estimating the Density of *Candida albicans* in Children with Acute Lymphoblastic Leukemia (A Pilot Study). *Journal of Dentomaxil lofacial*, 3(1): 29 - 36.
9) Garrett, W. S., Lord, G.M., Punit, S., Lugo-Villarino, G., Mazmanian, S.K., Ito, S., Glickman, J. N and Glimcher, L. H. (2007). Communicable ulcerative colitis induced by T-bet deficiency in the innate immune system. *Cell*, 131(1): 33 - 45.
10) Javed F., Utrija A and Bello Correa F. O. (2012). Oral health status in children with acute lymphoblastic leukemia. *Critical Reviews in Oncology and Hematology*, 83: 303 - 309.
11) Javed, F., Klingspor, L., Sundin, U., Altamash, M., Klinge, B and Engström, P. E. (2009). Periodontal conditions, oral *Candida albicans* and salivary proteins in type 2 diabetic subjects with emphasis on gender. *BMC Oral Health*, 9(1): 1 - 8.
12) Khan, S. A. and Wingard, J. R. (2001). Infection and mucosal injury in cancer treatment. *JNCI Monographs*, 29: 31 - 36.
13) Kimball, J. R., Nittayananta, W., Klausner, M., Chung, W. O and Dale, B. A. (2006). Antimicrobial barrier of an *in vitro* oral epithelial model. *Archives of Oral Biology*, 51(9): 775 - 783.
14) Mirhendi, H., Makimura, K., Khoramizadeh, M. and Yamaguchi, H. (2006). A one-enzyme PCR-RFLP assay for identification of six medically important *Candida* species. *Nippon Ishinkin Gakkai Zasshi*, 47(3): 225 - 229.
15) Mokaddas, E., Burhamah, M. H., Khan, Z. U and Ahmad, S. (2010). Levels of (1→3)-β-D-glucan, *Candida* mannan and *Candida* DNA in serum samples of pediatric cancer patients colonized with *Candida* sp. *BMC Infectious Diseases*, 10(1): 1 - 6.
16) Mushi, M. F., Mtemisika, C. I., Bader, O., Bii, C., Mirambo, M.M., Groß, U. and Mshana, S.E., 2016. High oral carriage of non-albicans *Candida* spp. among HIV-infected individuals. *International Journal of Infectious Diseases*, 49: 185 - 188.
17) Netea, M. G., Joosten, L.A., Van Der Meer, J.W., Kullberg, B.J. and Van De Veerdonk, F.L. (2015). Immune defence against *Candida* fungal infections. *Nature Reviews Immunology*, 15(10): 630 - 642.
18) Scully, C. (2004). Oral and maxillofacial medicine: The basis of diagnosis and treatment. *British: Wright Elsevier*, 10: 287 - 310.
19) Shokohi, T., Soteh, M. H., Pouri, Z. S., Hedayati, M. T. and Mayahi, S. (2010). Identification of *Candida* species using PCR in cancer patients in Iran. *Indian Journal of Medical Microbiology*, 28(2): 147 - 151.
20) Shokouhi, T., Bandalizadeh, Z., Hedayati, M. T and Mayahi, S. (2011). *In vitro* antifungal susceptibility of Candida species isolated from oropharyngeal lesions of patients with cancer to some antifungal agents. *BMC Infectious Diseases*, 10(1): 10 - 16.
21) Subramaniam, P., Girish Babu, K. and Nagarathna, J. (2008). Oral manifestations in acute lymphoblastic leukemic children under chemotherapy. *Journal of Clinical Pediatric Dentistry*, 32(4): 319 - 324.
22) Teoh, F. and Pavelka, N. (2016). How chemotherapy increases the risk of systemic Candidiasis in cancer patients. *Pathogens*, 5(1): 6 - 10.

23) Wang, Y., Xue, J., Zhou, X., You, M., Du, Q., Yang, X., He, J., Zou, J., Cheng, L., Li, M. and Li, Y. (2014). Oral microbiota distinguishes acute lymphoblastic leukemia pediatric hosts from healthy populations. *PloS one*, 9(7): 102116.

24) Zuckermann, J., Stoll, P., Meneghel, R. L., Kuchenbecker, R. S., Santos, R. P and Moreira, L. B. (2012). Microbiological findings in febrile neutropenic patients in a tertiary hospital of Southern Brazil. *Clinical and Biomedical Research*, 32(3): 1115 - 1124.

Access this Article in Online

Quick Response Code	
Website	**www.jpsscientificpublications.com**
DOI Number	**DOI: 10.22192/lsa.2021.7.1.5**
Thomson Reuters Researcher ID	**L – 5547 – 2016**
ISI Impact Factor	**4.206**

How to Cite this Article:

Hanan S. Makki, Awatif H. Issa and Abdullah H. Al Saadoon. 2021. Distribution of Microorganisms in the Oral Cavity of Children with Leukemia Before and After Chemotherapy. *Life Science Archives*, 7(2): 2122 – 2129.

DOI: 10.22192/lsa.2021.7.1.5