# THESIS ABSTRACT

# Association between Microbial Infections and HßD-3 Gene Expression in Oral Cavity of Children with Leukemia

**Hanan Salman Makii Al-Amri**

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**Background:** Malignant diseases epidemiological studies illustrated an increase in the prevalence and incidence of cancer in Iraqi population. The increase in the incidence and prevalence of malignant diseases are mainly attributed to environmental pollution due to using of depleted uranium in recent Gulf wars.
**Aim:** To determine the microbial infection frequency and its association with HßD-3 Gene Expression in Oral Cavity of Children with Leukemia.
**Materials and methods:** The study was conducted in Basrah Pediatric Hospital during the period between August 2016 and June 2017. The study included testing of 50 samples collected from 25 children with leukemia. Microbial diagnosis achieved by conventional methods and molecular test.
**Results:** Leukemia was more common (40%) in age group of 2-4 years, while it was 4% in the age group of 11-13 years. Acute lymphoid leukemia was the predominant type of leukemia forms 88% of the cases, while myeloid leukemia forms 12%. From total samples (100 samples) before and after chemotherapy, 86% of samples were positive. Before chemotherapy, 53.4% of samples were negative, while 46.5% were negative after chemotherapy. Candida species were the commonly isolated organism from patients with leukemia. From total 32 Candida isolates, 13 (40.6%) were obtained from samples before chemotherapy, while 19 (59.4%) after chemotherapy.
Molecular diagnosis after chemotherapy using internal transcribed spacer ITS1-ITS4 primer showed that 26 (81.24%) isolates of *Candida albicans* with different strains and ATCC 18804 were the most frequent isolate (17). *Candida Africana* form 9.3% (3 isolates) and belong to one strain of 8787. While *Candida krusei* form 6.3% (2 isolates) and the lowest strain was *Candida glabrata* which forms 3.1% (1 isolate). The results of the genetic sequences of the yeast were identical to the results obtained through the API Candida system. The difference was only in 5 isolates. Three were identified by the API Candida system as well as on the centre of CHROM agar medium, where they appeared in light green and the green color to the turquoise, *Candida albicans* 21, 26, and 27 strains respectively. The results of the sequences indicate that *Candida Africa* and the remaining 4 and 7 *Candida albicans* isolates were identified by API as *Trichosporum.* However, the results of the genetic sequence indicate that these isolates were *Candida albicans.* The results of the statistical analysis showed a strong association between yeast infections before and after chemotherapy and without significant difference depending on the determination of the genetic expression of HBD-3 defensive peptide. Additionally, the study showed the effect of chemotherapy on the amount of HBD-3 gene expression in epithelial cells and neutrophil. Present study found a relationship between the amount of HBD-3 and

the neutrophils in children with leukemia. For the expression of genetic development of microbial infections, whether bacterial or fungal, by the monitoring changes in white blood cells including neutrophils, which illustrated a significant decrease in numbers, and follow-up changes in gene expression of HBD-3 in neutrophils and epithelial cells for children with leukemia-induced immunosupression.

Gene expression of the HBD-3 gene in neutrophils and epithelial cells was identified in children with leukemia before and after chemotherapy, which showed a marked decrease in the amount of gene expression. In addition, HBD-3 gene expression was lower in patients than in control and equal to 1. The value of genetic expression before chemotherapy was 0.382182, while after chemotherapy it was 0.4933 and with none significant difference compared to control group. Despite this slight increase in the amount of gene expression resulting from *Candida albicans* infection of the epithelia cells. The HBD-3 gene expression in neutrophils before chemotherapy was 0.86595 and was significantly higher than control group. While after chemotherapy the HBD-3 gene expression in neutrophils was 0.087716 and was significantly differ from the values of before chemotherapy.

Antifungal activity of HBD-3 was evaluated and *Candida albicans* isolates were treated with 7 different concentrations ranged from 1 to 6 μg/ml. The lethal antifungal concentrations was between 3 -6 μg/ml was 94.7% to 99.7%. The killer concentration is LC equal to 90%.

**Conclusion:** *Candida albicans* infections was the common opportunistic infections in leukemic patients as determined in API system and molecular testing. HBD-3 gene expression was with significant association to chemotherapy exposure. Additionally, HBD-3 peptide was with potent anticandidal activity.