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Oral yeast colonization in peritoneal dialysis and hemodialysis patients and renal transplant recipients

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ABSTRACT

Objective: We aimed to investigate the frequency of oral yeast colonization (OYC) and the risk factors for patients who received continuous ambulatory peritoneal dialysis (CAPD) or hemodialysis (HD) or were renal transplant recipients (RTRs). The patients admitted to the Nephrology Clinic at Ataturk University Medical School from January through April 2013 were included in the study. A questionnaire about risk factors was filled out, and swab cultures were taken from the tongue surface of each participant. OYC was detected in 32.1% of the RTRs, 40% of the HD patients, 20.9% of the CAPD patients, and 18% of the healthy control (HC) group. Of the 42 yeast strains isolated from the renal replacement therapy groups, 26 strains (61.9%) were *Candida albicans*, nine (21.4%) were *Candida glabrata*, two (4.7%) were *Candida krusei*, two (4.7%) were *Candida kefyr*, one (2.38%) was *Candida parapsilosis*, and two (4.7%) were *Geotrichum candidum*. Risk factors for OYC in the RTRs group included antibiotic use and the presence of dental prostheses; however, in patients with chronic renal failure undergoing CAPD, only the presence of dental prostheses was found to be a statistically significant risk factor. Although OYC was mostly detected in patients with chronic kidney disease (undergoing HD, a variety of isolated yeast strains in the RTRs was noted. The rates of OYC and isolated *Candida* species in CAPD were similar to those of the HC group.

1. Introduction

Candida albicans and several non-*albicans Candida* species are opportunistic fungal agents that can maintain survival as commensal organisms in the oral cavities of humans. The ability of *Candida* spp. to colonize on host surfaces through adhesion to epithelial cells and, subsequently, to proliferate is facilitated by the presence of several risk factors [1,2]. Certain systemic and local factors can lead to physiological changes in the host, and these yeasts can become pathogenic [1]. Systemic factors include diabetes mellitus, immune suppression, long-term antibiotic use, leukopenia, and old age, and local factors include xerostomia, a decreased quality and amount of saliva, poor oral hygiene, presence of dental prostheses, and poorly constructed fillings [3–5]. The colonization can cause oral candidiasis, which can progress to its more invasive form, esophageal candidiasis. Moreover, if the immunosuppression continues or becomes stronger, it will continue to be a risk factor for systemic candidiasis [6].

Renal failure can cause defects in cellular and humoral immunity by affecting T-lymphocyte subsets. Uremia causes a decrease in phagocytic activity of macrophages, an increase in neutrophil apoptosis, a depletion of Treg cells and a reduced CD4/CD8 ratio [7]. These changes can be responsible for the persistence of mucosal candida colonization in patients with chronic kidney disease. Additionally, one study claimed that CAPD seems to improve cell-mediated immunity by enhancing the number of T cells, in contrast to other renal replacement therapies [8]. RTRs that are treated with immunosuppressive agents are also more at risk for the development of opportunistic infections. In light of this information, we thought that the immune response of HD, CAPD, and RTR patients against mucosal yeast colonization might be different.

Several studies have investigated OYC in patients with chronic kidney disease who underwent CAPD or HD treatment or who were RTRs [3,9–12]. However, there is no study in the literature that compares the rates of OYC among all such renal replacement therapy (RRT) groups simultaneously. We aimed to detect the rates of OYC and the influential risk factors for these groups simultaneously.

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2. Materials and methods

The study included CKD patients who were admitted to Ataturk University Medical School of Nephrology Polyclinic between January 1, 2013, and May 1, 2013. The CKD patients were undergoing CAPD or HD or were RTRs. Ethics committee approval was given by Ataturk University Medical Faculty Non-pharmacologic Clinical Research Ethics Committee on March 1, 2013; number B.30.2.ATA.0.01.00/35. Forty three CAPD patients (mean age: 48.65 ± 14.82 years), 40HD patients (mean age: 57 ± 14.23 years), 53 RTRs (mean age: 38.19 ± 12.1 years), and 50 age- and sex-matched healthy controls (HCs) were included in the study. Their demographic features are shown in Table 1. RTRs in their first six months after transplantation surgery were excluded from the study because antibiotics and antifungal therapies are used routinely during this period. The inclusion criteria for the study group were as follows: at least 18 years of age, renal transplant recipient at least six months post-transplant, received HD for a minimum of three months, and received CAPD for a minimum of three months. The inclusion criteria for the HC group were as follows: at least 18 years of age, absence of chronic disease (e.g., diabetes mellitus, chronic obstructive lung disease), absence of removable dental prosthesis, and not taking immunosuppressive therapies.

Each study group was given a questionnaire during face-to-face interviews. This questionnaire included age, presence of diabetes mellitus (type 1 or 2), usage of antibiotic and antifungal drugs over the last month, hospitalization history last month, smoking habit, presence of removable oral prosthesis, and number of missing teeth. Additionally, the patients' weight and height were measured, and the Body Mass Index (BMI) was calculated. For mycological analysis, swab samples were taken from the tongue surface of each participant and sent to the mycology laboratory of our hospital. The samples were streaked onto Sabouraud Dextrose Agar with chloramphenicol and incubated at 35 °C for 48 h. At the end of the incubation time, direct microscopic investigations of the yeast colonies grown in this medium were performed. Next, the yeasts were identified with conventional methods, such as germ tube test, chlamydospore formation, shape and arrangement of the blastospores on cornmeal agar with Tween 80, and commercial identification systems, including the API 32C (BioMérieux, France).

The data obtained were recorded using SPSS 15.0. Chi-square test, Pearson's correlation analysis, and Fisher's exact test were performed. P values <0.05 were considered statistically significant.

3. Results

OYCs were detected in 32.1% of the RTRs, 40% of the HD patients, 20.9% of the CAPD patients, and 18% of the HC group ($p = 0.075$). Of the 42 yeast strains isolated from the RRT groups, 26 strains (61.9%) were *C. albicans*, nine (21.4%) were *Candida glabrata*, two (4.7%) were *Candida krusei*, two (4.7%) were *Candida kefyr*, one (2.38%) was *Candida parapsilosis*, and two (4.7%) were *Geotrichum candidum*. Nine *Candida* strains were isolated in the HC group; seven of the strains were *C. albicans*, and the other two were *C. glabrata*. The distributions of the isolated yeast strains are shown in Table 2.

The comparison of the OYC rates for the RTR, HD, CAPD, and HC groups according to age and gender is shown in Table 3. Senility (>40 years old) was detected as a statistically significant risk factor for the RTR, HD, and CAPD groups ($p < 0.05$). When this rate was evaluated with respect to gender, a statistically significant difference was not detected among any of the groups (Table 3).

Other risk factors for OYC were evaluated for each study group, including BMI for the RTR group, removable oral prostheses for the RTR and CAPD groups, and the duration of RRT (period from transplantation until the present) for the RTR group (directly proportional) and the HD group (inversely proportional); all factors were determined to be statistically significant risk factors. However, diabetes mellitus, history of antibiotic use, history of hospitalization, a smoking habit, and the number of missing teeth were not statistically significant for these three groups. An evaluation of the risk factors for the RRT groups is shown in Table 4.

When the risk factors for *C. albicans* or non-*albicans Candida* spp. were evaluated among all individuals who were shown to have OYC, diabetes mellitus, old age, antibiotic use, and prolonged RRT duration were found to increase the *C. albicans* rates. However, male gender, hospitalization, >10 missing teeth, and a smoking habit increased the non-*albicans Candida* spp. rates. Additionally, *C. glabrata* from non-*albicans Candida* spp. had the highest rate in the HD group, whereas five different species of *Candida* were isolated in the RTRs, and two strains of *G. candidum* were detected only in the RTR group.

When the laboratory findings for the CKD patients with OYC were compared with the RTRs, the C-reactive protein (CRP) values (mean ± SD) were found to be significantly higher ($p = 0.007$) in the CKD patients who underwent dialysis treatment, but no difference was detected in terms of the other laboratory findings, as shown in Table 5.

4. Discussion

Candida constitute a component of the gut, mouth, and vaginal flora in humans and normally present with no symptoms or clinical findings. However, *Candida* spp. can cause life-threatening fungal infections when they occur as opportunistic pathogens, particularly in situations of immunosuppression or impairment of the normal mucosal microbiota. The oral mucosal colonization of *Candida* species can occur via adhesion to structures, such as epithelial surface molecules, extracellular matrix proteins, and dental acrylic; thus, they can maintain viability against mechanical and immunological clearance mechanisms [13]. In addition, their virulence mechanisms such as hydrolytic enzyme activity can evade the mucosal barrier, which is one of the important components of innate immunity. In particular, *Candida* colonization in the gastrointestinal tract can result in penetration into the vascular system and hematogenous dissemination in the presence of facilitating factors such as humoral or cellular immunodeficiency, senility, and xerostomia [6,14]. Additionally, the oral cavity is an important source of sepsis in immunosuppressed patients, and cytotoxic drugs and the transplant procedure itself can have direct effects on the oral environment [15]. If the condition referred to as invasive candidiasis is not diagnosed in a timely manner and appropriate therapy is not initiated as soon as possible, death may occur [16].

C. albicans is the most frequently isolated fungal species both in healthy persons and in patients with underlying disease. According to data obtained from several reports, oral carriage of *C. albicans* occurs in 17.7% of healthy individuals, with no underlying disease affecting their immunity, and it is present in 40.6% of hospitalized patients [1,17]. *C. albicans* was the most frequently isolated species reported in studies performed on groups such as those of different geographic locations [18], the elderly [4], diabetic vs nondiabetic patients [10], renal failure vs healthy patients [9], cancer patients [19], and patients with solid organ transplantations [11,13]. Non-*albicans Candida* species such as *C. glabrata*, *C. krusei*, *C. parapsilosis*, *Candida dubliniensis*, *Candida tropicalis*, *C. kefyr*, and *Candida lusitaniae* were also reported to be frequently isolated from the oral flora [20]. Godoy et al. [9] found that the most frequent *Candida* variates isolated from CKD patients were *C. albicans* (63%), *C. glabrata* (16.1%), *C. tropicalis* (8.7%) and *C. kefyr* (3.7%). Garcia et al. (K8) found these rates to be as follows: *C. albicans* (74.6), *C. glabrata* (22.0%), *C. tropicalis* (15.2%), and *C. parapsilosis* (3.4%). In our study, the per-