Oral Candidal Carriage in Diabetic and Nondiabetic Patients receiving Hemodialysis

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ABSTRACT

Aim: To determine the influence of diabetes on the oral cavity in end-stage renal disease (ESRD) patients undergoing hemodialysis.

Materials and methods: The study was carried out with 100 individuals (50 diabetic and 50 nondiabetic) who were diagnosed with ESRD undergoing hemodialysis, and the influence of diabetes on the oral cavity and oral flora was observed.

Results: The study shows a positive association between severity of oral manifestations, oral lesions, and alterations in the microflora of diabetic ESRD patients, which is in agreement with previous studies. In the present study, we could get encouraging results from the parameters included in the study, providing statistically significant results.

Conclusion: In the patients studied, the impact of ESRD on the oral cavity was evidenced by significant oral changes. The study also reveals that diabetic uremic patients undergoing maintained hemodialysis exhibit a potentially higher risk. Further research is needed to relate the extent of such changes with disease progression.

Keywords: Candida, Dry mouth, End-stage renal failure, Hemodialysis, Oral flora, Oral health.


Sources of support: Nil

Conflict of interest: None

INTRODUCTION

The kidney is a vital organ, which maintains homeostasis. The kidneys perform various functions in the human body like regulation of acid–base and fluid electrolyte balance by filtering blood, reabsorbing water and electrolytes selectively, and excretion of urine. Apart from these functions, the kidneys also have a vital endocrine function like secretion of renin – the active form of vitamin D and erythropoietin. All these hormones are important in the maintenance of blood pressure, metabolism of calcium, and the synthesis of erythrocytes respectively.

Kidney diseases are a major cause of mortality and morbidity.1 End-stage renal disease (ESRD) is the final syndrome for various primary renal diseases and other systemic diseases with renal involvement causing functional loss of kidneys. Manifestations of ESRD involve every system in a clinical condition as uremic syndrome, which is characterized by alteration of water, acid–base, and electrolyte homeostasis, as well as retention of uremia-associated toxins that are normally eliminated through urine, especially protein catabolism nitrogen waste products. Uremic syndrome influences oral health significantly and leads to uremic manifestations, which include xerostomia, alteration in taste, and uremic odor. Dehydration from restricted fluid intake, direct uremic involvement of the salivary glands, and inflammation of salivary glands lead to a decrease in salivary flow. Xerostomia was a prominent finding in these patients.7 The condition is incompatible with life, until and unless the patient begins with dialysis treatment or transplantation of kidneys.2

Dialysis is an artificial mechanism that helps in clearing blood of nitrogen waste and other toxic products of metabolism. Most patients are subjected to dialysis thrice a week. During hemodialysis, patients receive anticoagulation in the form of heparin, to facilitate blood cycling through the dialyzer and ensure permeability of the vascular access.3 These patients remain chronically ill with hematologic, neurologic, metabolic, and cardiovascular problems that are more or less permanent despite optimal dialysis. In very young renal disease patients, growth alterations may be present, particularly if they are maintained on hemodialysis.1

In addition, diabetic patients present a higher tendency for developing renal failure. Diabetes mellitus is a common chronic metabolic disease worldwide. All age groups are affected by diabetes, but it is more common in adults.4 Patients typically are elderly type 2 diabetics with established micro-/macrovascular disease. Hypoglycemia is common due to impaired renal gluconeogenesis,
increased half-life of insulin, hypoglycemic agents, and malnutrition. Patients with diabetes are at higher risk for chronic and acute complications in the oral cavity, such as xerostomia, glossodynia, and various infections, and periodontal diseases. Diabetic patients with ESRD are more prone to develop oral lesions with severe signs and symptoms compared with nondiabetic patients. Abnormalities of soft tissues are also reported to be associated with diabetes mellitus in the oral cavity.

The frequent occurrence of Candida infections in patients with diabetes mellitus has been recognized for many years, and oral candidiasis was thought to be more prevalent among these individuals. The carriage of Candida in the oral cavity of diabetic patients is claimed to be higher. The candidal density has also been reported to be higher in diabetic patients than in nondiabetic patients.

The purpose of this study is to investigate uremia-associated colonization of Candida in the oral cavity of diabetic and nondiabetic patients undergoing hemodialysis. The aim of the study is to determine oral candidal carriage count in the saliva of diabetic and nondiabetic patients on hemodialysis. The primary purpose is to determine the above-mentioned parameter on ESRD patients on hemodialysis, as dialysis patients need comprehensive professional oral care and self-care instructions. The source of infection in the oral cavity can cause a variety of systemic diseases, causing morbidity and mortality in these immunosuppressed patients.

Source of Data

The study was conducted in the Dialysis Unit, Department of Nephrology, Choithram Hospital in Indore, Madhya Pradesh. The study was conducted on a total of 100 patients (50 diabetic and 50 nondiabetic) who were diagnosed with ESRD undergoing hemodialysis. The study was conducted by oral examination of the patients undergoing hemodialysis therapy, and the candidal carriage count estimation was performed in the General Pathology Department of Choithram Hospital.

Authorities’ Approval

The study was approved by the Ethical Committee of Modern Dental College and Research Center, Indore, and obtained clearance from the Scientific Research Committee of Devi Ahilya Vishwavidyalaya, Indore. The study groups were divided into two groups:

<table>
<thead>
<tr>
<th>Groups</th>
<th>Type of sample</th>
<th>Number of individuals</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetic</td>
<td>Patients with ESRD on hemodialysis</td>
<td>50</td>
</tr>
<tr>
<td>Nondiabetic</td>
<td>Patients with ESRD on hemodialysis</td>
<td>50</td>
</tr>
</tbody>
</table>

This study comprised 100 individuals with ESRD undergoing hemodialysis and the participants were divided into diabetic and nondiabetic groups.

Inclusion Criteria

- ESRD patients who had been diagnosed with type 2 diabetes and were undergoing hemodialysis.
- ESRD nondiabetic healthy individuals undergoing hemodialysis.

Exclusion Criteria

- Patients with a history of any known systemic diseases other than diabetes and ESRD.
- Patients being seropositive for the human immunodeficiency virus (HIV), hepatitis C virus (HCV), or hepatitis B virus.
- Critically ill patients unable to cooperate.
- Patients with xerostomia.
- Periodontal treatment within the previous year.
- Patients not willing to participate in the study.

GENERAL INFORMATION

The patient’s general information was recorded and relevant data were noted in the proforma. This included the patient’s age, sex, address, and socioeconomic status. The patients included in the study were confirmed as having ESRD. The past medical history of the patient was confirmed, which mainly included major illness like diabetes mellitus and renal diseases.

The medical history of all the 100 patients was recorded in a proforma regarding symptoms and diseases, familial dispositions, education, medication, and previous contacts with the health care system. The personal history of the patient was recorded, which included the type of diet of the patient and whether or not the patient had physical activity. The questionnaire also included the patient’s teeth cleaning habits and tissue abusive habits, mainly smoking and alcohol.

MEDICAL EXAMINATION

The patient had undergone blood investigation for fasting serum glucose, hemoglobin levels, urea, serum creatinine, serum albumin, serum proteins, bilirubin levels, HIV, HCV, and Australian antigen. The values were recorded in the patient’s proforma.

ORAL EXAMINATION (ARMAMENTARIUM USED FOR ORAL EXAMINATION)

- Saliva samples were collected from each patient undergoing hemodialysis with the help of swab technique.
PROFORMA FOR SALIVARY SAMPLE AND CANDIDAL CARRIAGE COLLECTION (FIGS 1 TO 5)

Saliva Sample Collection

Date of Collection: Date of testing:
Time of Collection: Time of testing:
Salivary sample:

For Glucose Estimation

Method: Swab technique

For Candidal Carriage

Method: Phosphate-buffered saline rinse
Amount: 10 mL
Duration: 60 seconds

Saliva Collection and Culture

The palatal mucosa and floor of the mouth have been shown to support a high rate of Candida colonization. So, specimens for candidiasis were taken from these sites. The prevalence of oral yeasts was determined by obtaining fungal cultures from the palatal mucosa and floor of the mouth of each patient by rolling cotton swabs moistened in sterile water along the sterile sites and breaking them into a sterile glass vial containing 2 cc of sterile water for transport to the laboratory. Samples were streaked
using the four-quadrant method with 2 mm wire loop, on Sabouraud’s agar plates for semiquantitative analysis. After 5 to 7 days’ incubation at room temperature, increasing quantities were rated. A streak was made across the yeast colonies initially grown from the samples. These pooled yeast colonies were then streaked on bromocresol green agar plates. Single colonies were picked from each pigmented colony and grown on Sabouraud’s agar slants for examination of morphological and cultural properties. The colony-forming units (CFUs) were counted manually, and the numbers were multiplied by 1000 and expressed as CFU/mL.

Statistical Analysis

After the data collection, statistical analysis was performed to identify differences. The students’ t test was used to compare the difference in gender, age, duration of hemodialysis, saliva pH value, and visual analog scale (VAS) scores between diabetic and nondiabetic hemodialysis groups.

Additionally, Tukey test was performed to examine the difference between each of the two subgroups.

To describe the linear association between salivary glucose and random blood glucose, a statistical procedure called regression was used to construct a model. Regression is used to assess the contribution of one or more “explanatory” variables (called independent variables) to one “response” (or dependent) variable. It also can be used to predict the value of one variable based on the values of others.

OBSERVATIONS AND RESULTS

The statistical analysis of the study was done on 100 subjects, out of whom 44 were diabetic and 57 were nondiabetic, data were evaluated, accounting for a total of 100 patients. The study was designed as a cross-sectional study. Both diabetic and nondiabetic patients who underwent hemodialysis were recorded by case history evaluation. Each patient’s questionnaire was recorded and the relevant medical history and habit history were noted. The master chart of all the relevant information was prepared and values of all the parameters were written in the preformed format. The oral examination of all the patients was done and the candidal carriage was estimated for all the patients.

From Table 1 and Graph 1, it can be seen that in the present study, males [75 (74.3%)] accounted for the maximum number of patients, and females were 26 (25.7%). Thus, there was a preponderance of males over females.

From Table 2 and Graph 2, it can be clearly seen that in both the diabetic and nondiabetic groups, there was a male preponderance. In the nondiabetic group, there were 43 (75.5%) males and 14 (24.5%) females, while in the diabetic group, there were 32 (72.7%) males and 12 (27.3%) females.
Table 3: Subjects with positive Candida culture in nondiabetic ESRD and diabetic ESRD groups under hemodialysis

<table>
<thead>
<tr>
<th>Total subjects</th>
<th>Subjects with positive growth</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nondiabetics</td>
<td>57</td>
<td>12</td>
</tr>
<tr>
<td>Diabetics</td>
<td>44</td>
<td>33</td>
</tr>
</tbody>
</table>

Table 4: Candida colony counts in the two groups

<table>
<thead>
<tr>
<th>Diabetes status</th>
<th>Mean ± SD (CFU/mL) Median Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nondiabetic ESRD</td>
<td>1065.45 ± 2202.45 0 0–7800</td>
</tr>
<tr>
<td>Diabetic ESRD</td>
<td>5033.33 ± 2852.98  5000 0–9800</td>
</tr>
</tbody>
</table>

The present study has attempted to examine the oral flora, in particular candidal species on diabetic patients on hemodialysis.

This study comprised 100 subjects of whom 25% were females and 75% were males; and out of 100 subjects, 57 were nondiabetic and 44 were diabetic (Table 1).

Results from the present study showed that diabetic patients on hemodialysis have a more complicated medical condition that leads to compromised dental health.

Previous research has shown that salivary pH value in hemodialysis patients was higher than in controls. Diabetic patients on hemodialysis exhibited lower salivary pH value. The decreased saliva pH value may result from the diabetic complication of acidosis. The salivary pH may fluctuate at different times and vary depending on the dietary habits and oral conditions.

Immunocompromised conditions increase the risk of opportunistic Candida infections. Other known risk factors for candidiasis are xerostomia, low saliva flow, total dental prosthesis, poor oral hygiene, age, and diabetes. In agreement with other reports, candidiasis was found associated with xerostomia in diabetic patients. The association of candidiasis with pale mucosa and smooth tongue could suggest malnutrition predisposing to Candida infection. Pseudomembranous candidiasis was the most common type in most of the cases (Table 4). The prevalence of candidiasis found higher in the diabetic group could mean a stronger association of candidiasis to diabetics with ESRD. On the contrary, habit (cigarette
smoking and tobacco chewing)-associated candidiasis was prevalent in the nondiabetic group (Table 4). The reported prevalence of oral Candida infections in patients undergoing hemodialysis was 5.7 to 37%, differences probably being caused by the diagnostic criteria discrepancy. Klassen and Krasko, for instance, reported a 1% central rhomboid glossitis and 12% erythematous patch prevalence in dialysis patients, both probably equivalent to candidiasis.

The presence of Candida infections and the density of candidal growth in the oral cavity is often said to be increased in ESRD patients with diabetes. Several studies have reported that the prevalence of yeast carriage among diabetic patients with ESRD could reach up to 54% and that Candida albicans could account for 25 to 69% of the isolates. Oral colonization with Candida species occurs more frequently in diabetic patients compared with nondiabetic individuals. In this study, candidal carriage is observed in the saliva of ESRD diabetic and nondiabetic patients. Only a few studies have been done to compare candidal carriage both in diabetic and nondiabetic patients. The study constituted the collection of salivary samples from a population of 100 patients, of which 50 patients (50%) were nondiabetics, 50 patients (27.50%) were diabetics (Table 5).

Table 5 shows that in nondiabetic patients, only 21.01% showed positive yeast culture; however, out of diabetic patients, 75% showed positive yeast culture. A study conducted by Safia et al also showed a higher frequency of candidal growth in diabetic patients, and the candidal density was also higher in ESRD diabetic group. A similar study conducted by Khaled Abu-ELleen also showed that positive yeast was detected in 58.3% of diabetics compared with 30% of healthy controls (p < 0.001). This is also in agreement with numerous previous studies, which have all indicated that diabetes mellitus enhances Candida colonization and proliferation in ESRD. Tapper-Jones et al have shown that 42% of healthy nondiabetics harbor C. albicans in their mouths compared with 60% of diabetics. Have suggested that 16.2% of the controls and 40.2% of the diabetics carry C. albicans in their mouth.

In our study, the mean CFUs were significantly higher in diabetic patients compared with nondiabetic patients. Similar results were found by Tapper-Jones et al. They have stated that Candida becomes more easily established in the mouth of diabetics than in nondiabetics with ESRD. Local factors like denture wearing and smoking favor the carriage of Candida. Kumar et al have also confirmed similar results in their study. There were significantly higher CFUs of Candida in type II diabetic subjects than nondiabetics, and it has been shown to be associated with increased concentration of glucose in saliva.

Adhesion of an organism to the host is a prerequisite for colonization and subsequent infection. Oral epithelia in diabetes favor adhesion and colonization of Candida unlike in nondiabetic individuals. It is possible that there may be intrinsic qualitative changes on the cell surface receptors modulating Candida adhesion in ESRD diabetic subjects. Conducted a study in which they have concluded that the carriage rate of Candida was significantly higher in ESRD diabetic subjects than in nondiabetic subjects.

A study done by Radhika concluded that there was a positive correlation between diabetics and Candida CFU in the overall study population, confirming the results. This is explained by the fact that high levels of blood glucose increase candidal adherence to buccal epithelial cells. This study also showed that diabetes mellitus is not in itself usually responsible for significant increase in candidal population, but it is only when interacting with the local factors, such as denture wearing and smoking. In our study, candidal carriage was found to be highly significant in diabetics. Studies on the candidal carriage are often contradictory, which may be a result of a variety of sampling techniques employed. There is effect of some local and systemic factors, which could potentially influence candidal carriage rate and density in ESRD diabetic patients.

The carriage of Candida in the oral cavity of diabetic subjects is claimed to be higher. The candidal density has also been reported to be higher in diabetic ESRD than in nondiabetic ESRD subjects, confirmed by other investigators. Hence, in view of the above facts, the present study was undertaken and from the facts and findings, the following are the observations:

- The incidence of diabetic kidney disease (DKD OR ESRD) was higher in male patients compared with female patients.
- The incidence of pseudomembranous candidiasis, angular cheilitis, ulcerative stomatitis, and smooth tongue was statistically significant and higher in the diabetic compared with the nondiabetic group.
- Total 75% of diabetic subjects had positive isolates of C. albicans species in candidal culture, the mean candidal colony count was significantly higher, i.e., 5033.33 ± 2852.98, and the range was 0 to 9800 CFU/mL. The comparison between mean candidal CFUs of nondiabetic ESRD and diabetic ESRD was statistically significant.

The following conclusion can be drawn from the present study:

- ESRD diabetic patients had a significantly higher prevalence of signs, symptoms, and oral lesions compared with nondiabetic ESRD patients. Diabetes is known to affect oral microflora. Furthermore, complications that include renal failure can also significantly alter
the microflora of oral cavity. The isolation of *C. albicans* and candidal CFU in the overall study population was significantly higher in diabetic ESRD patients compared with nondiabetic ESRD patients, which might be due to the immunodeficiency state in these patients.

Thus, the study showed a positive association between severity of oral manifestations, oral lesions, and alterations in the microflora of diabetic ESRD patients, which is in agreement with previous studies. In the present study, we could get encouraging results from the parameters included, providing statistically significant results.

However, the comparison of oral manifestations in a larger population with ESRD and at molecular level needs further exploration.

REFERENCES