Thi-Qar Medical Journal (TQMJ):Vol.(26),No.(2),2023

Web Site: https://jmed.utq.edu Email: utjmed@utq.edu.iq

ISSN (Print):1992-9218

Effect of Chemothereapy and Radiotherapy on Electrolyte level and PH of Saliva in Cancer Patients with or without Oral Candidiasis in Sulaymani –Iraq

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Abstract

Chemotherapy and Radiotherapy usually impairs the function of the salivary glands; the disruption is both temporary and reversible.To indicate the effect of chemotherapy and radiotherapy treatments on the electrolyte and pH of saliva. Fifty saliva samples from cancer patients were collected with 50 controls. The saliva sample was collected with closed lips within the oral cavity, and then it was expelled into a falcon tube and was centrifugation (5 min at 2500 rpm), we took 250 microliters from the supernatant (clarified saliva), and after that analyzed by (Electrolytes Analyzer machine). The pH of saliva was more acidic in cancer patients in comparison to control individuals (P-value 0.001), and the mean chloride level in cancer patients was recorded (52.05mmo/L), but in ordinary people, the mean showed (46.20mmo/L). In conclusion, cancer treatments are affected by the increase of Chloride levels and decrease of Potassium and pH levels compared with healthy people's saliva.

Key words: chemotherapy, radiotherapy, salivary gland, Oral cavity, chloride

Introduction

Saliva is necessary for oral health because it buffers acids, contains antibodies, helps to prevent gingival mucosal erosions and ulcerations, and promotes tooth remineralization. Patients with impaired salivary function are more likely to develop cavities, denture discomfort, and infections such as candidiasis than those with normal salivary flow rates. (SFRs).(1). The parotid, submandibular, and sublingual glands are the three major salivary glands. (2), which produces and secretes saliva, moistens its intraoral mucosa and teeth, maintains oral hygiene, and aids in tasting, swallowing, speech, and mastication (3). Minor salivary glands are distributed throughout the oral mucosa surfaces, producing mucus saliva containing organic substances even at night and protecting the mouth mucosa from harm. (4).

Chemotherapy usually impairs the function of the salivary glands. The effect is both temporary and reversible. However, it causes discomfort, disrupts with speech, and makes chewing difficult. The patient's saliva quality and quantity are altered. Amylase and peroxidase levels have increased. The chemotherapy causes a simultaneous decrease in the amount of IgA and IgG. As a result, the oral mucosa is more vulnerable to trauma and oral mucositis.(5). However, as chemotherapeutic procedures and agents change, they may cause side effects that impair the lives of patients as well as the treatment of collateral issues. (6). Despite significant advances in the treatment of chemotherapy patients with oral and systemic fungal infections over the last three decades, these infections keep an important clinical problem in this population.(7). Thus, it is essential to identify risk factors for oral infection in chemotherapy patients. Prospective, ongoing investigations with newer cancer chemotherapy regimens are required to identify the underlying causes of increased susceptibility to oral candidiasis. Resistance to opportunistic infections in the oral cavity results from a delicate balance between a complex oral microbiome and the host's protective defenses. The oral microbiome is a diverse community of hundreds of different bacterial and fungal taxa.(8).

Notably, salivary glands secrete large amounts of secretory immunoglobulin (IgA), which protects other IgA from degradation by microbial proteolytic enzymes. (9). These important salivary processes are suppressed when the salivary glands are damaged by Candida infections. Due to its cell adhesion properties and high pathogenic potential, *Candida albicans* is the most common species discovered in oral Candida infections. (10). It has been claimed that the average daily flow of entire saliva in healthy people ranges between 1 and 1.5 L. Despite the presence of several important proteins in saliva, water accounts for 99.5% of its total composition in humans, including electrolytes

sodium, potassium, calcium, chloride, and various enzymes.(11). This study aims to indicate the effect of chemotherapy and radiotherapy treatments on the electrolyte and pH of saliva in cancer patients.

Material and method

Fifty clinical samples were collected from people with various types of cancer and Oral candidiasis at Hiwa Hospital in Sulaymaniyah, Iraq, which specializes in treating cancer patients. To compare the effect of cancer treatments on pH and electrolytes levels in saliva patients with control saliva (healthy people), 50 saliva samples from cancer patients and 50 controls were collected. The saliva was collected within the oral cavity with closed lips and then expelled into a falcon tube (Saliva collection, J.ablebio, China). To minimize the contact of saliva with room air, the tube containing the saliva was immediately closed with a plastic stopper at the end of the collection, and saliva samples were stored in an ice box and carried to the laboratory, for centrifugation (5 min at 2500 rpm), we took 250 microliters from the supernatant (clarified saliva), after that analyzed by (Electrolytes Analyzer YACOi- Yarsan, India) for recording Ionized Calcium, Potassium, Sodium, Chloride, and pH.

Statistical analysis:

For storage and statistical analysis, data were entered into computer files using the statistical package for social sciences "SPSS" version 21. The Chi-square test was used to examine the relationship between categorical variables, with a P-value of 0.05 considered significant.

Result

The total cancer cases were used chemotherapy or radiotherapy and some of them applied both. In this study, the maximum duration of treatment among patient with oral candidiasis was 8 years, while the minimum period of treatment was 1 month. The maximum number of Chemotherapy treatment cycles was used 36 times and the minimum cycles were 1 time.The acidity of the mouth and the electrolyte amount of saliva in the mouth were studied to investigate the effect of oral candidiasis on the electrolytes rate of the saliva and its pH changes. The table shows four types of electrolytes (Sodium, Potassium, Chloride, and Calcium) and pH in cases and controls from the current study. (1).

Table (1): Level of electrolytes (mmoI/ L), and pH value between (A) cancer patients (used chemo& radiotherapy), and (B) controls (healthy people)

(A): Electrolyte tests and pH for cancer patients (used chemo& radiotherapy)

Electrolytes Test &Ph	Number Of Samples	Minimum	Maximum	Mean	Standard Deviation
Na(Mmol/L)	50	23.10	50.00	38.8706	7.15758
K (Mmol/L)	50	7.33	27.70	16.1494	6.03399
Cl (Mmol/L)	50	35.70	61.40	52.0529	6.90608
Ca (Mmol/L)	50	0.20	1.10	0.6082	.20427
Ph	50	4.36	6.52	5.4141	.62224

(B): Electrolyte tests and pH for a sample of control

Electrolyte Tests &Ph	Number Of Samples	Minimum	Maximum	Mean	Standard Deviation
Na(Mmol/ L)	50	23.50	59.80	33.52	10.39
K (Mmol/L)	50	16.60	39.36	23.93	6.06
Cl (Mmol/L)	50	29.20	46.20	35.46	4.47
Ca (Mmol/L)	50	0.32	1.49	0.64	0.37
Ph	50	6.23	7.50	6.95	0.43

The results of electrolyte and pH measurements for cancer patients with treatment showed that sodium level has no significant change when compared to control groups (*P*-value 0.263). Mean of Oral candidiasis patients was (38.8) but in control was (35.5), table (1) & figure (1).

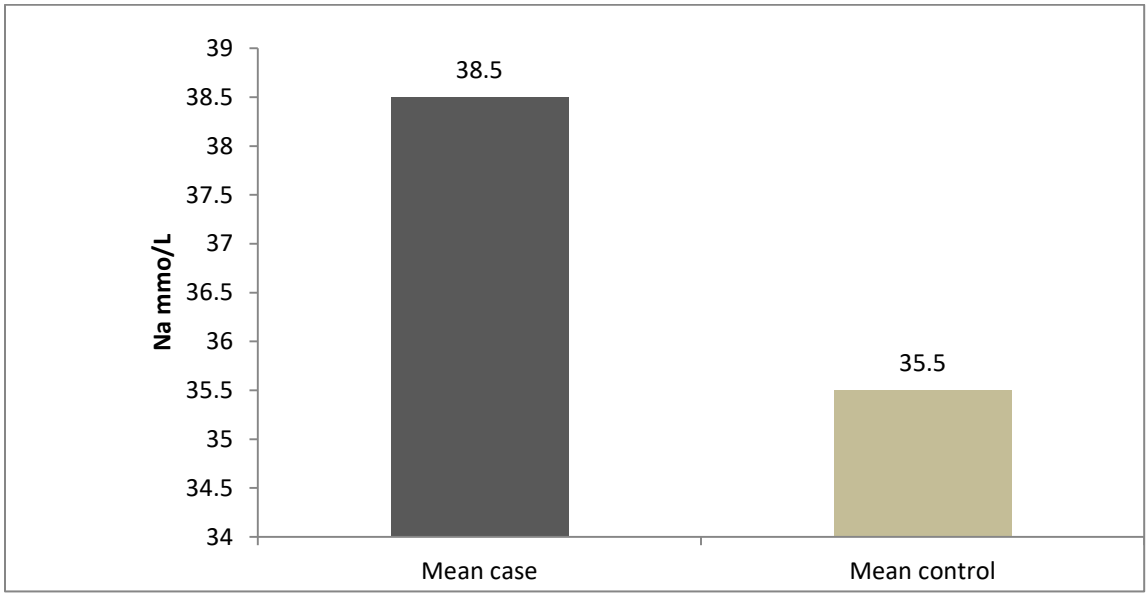

Figure (1): Sodium level distribution between oral candidiasis cases and control

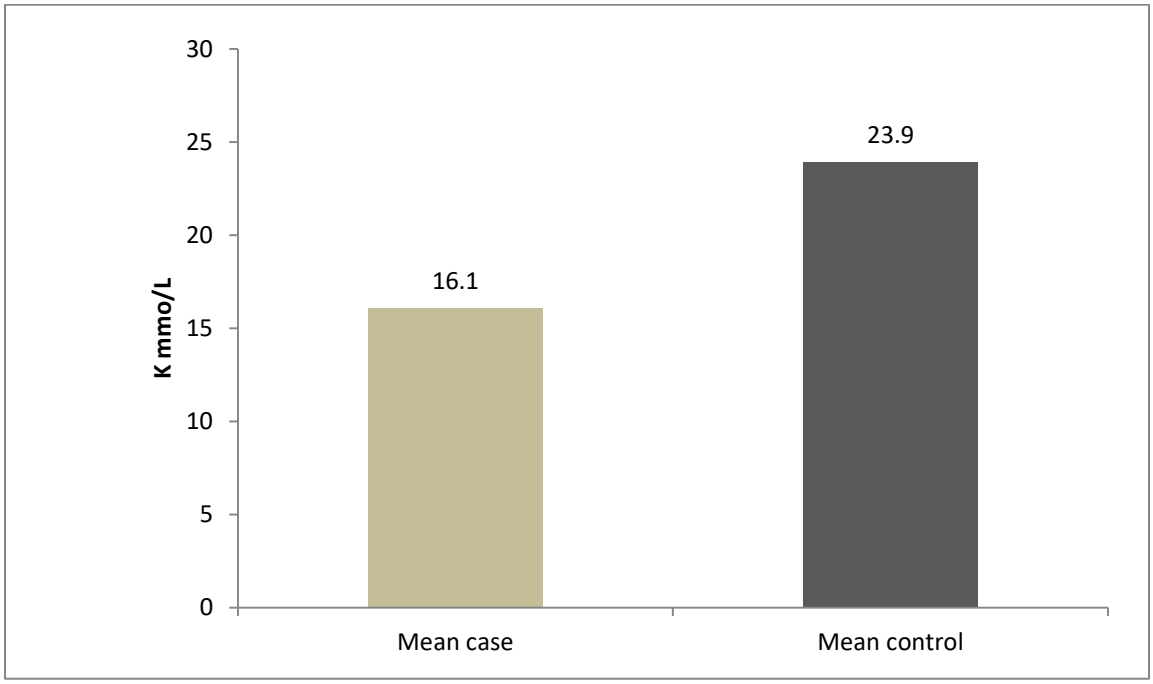

Figure (2): Potassium level between oral candidiasis cases and controls

About potassium, there is significant difference between oral candidiasis cases and control (*P*-value 0.001), when the mean of K (16.1mmo/L), but in control (23.9mmo/L), figure (2).The mean chloride level in cancer patients was recorded (52.05mmo/L), while in normal people, the meant showed (46.20mmo/L). It is significant differences between chloride levels between oral candidiasis and healthy control (*P*-value 0.001). As shown in figure (3).

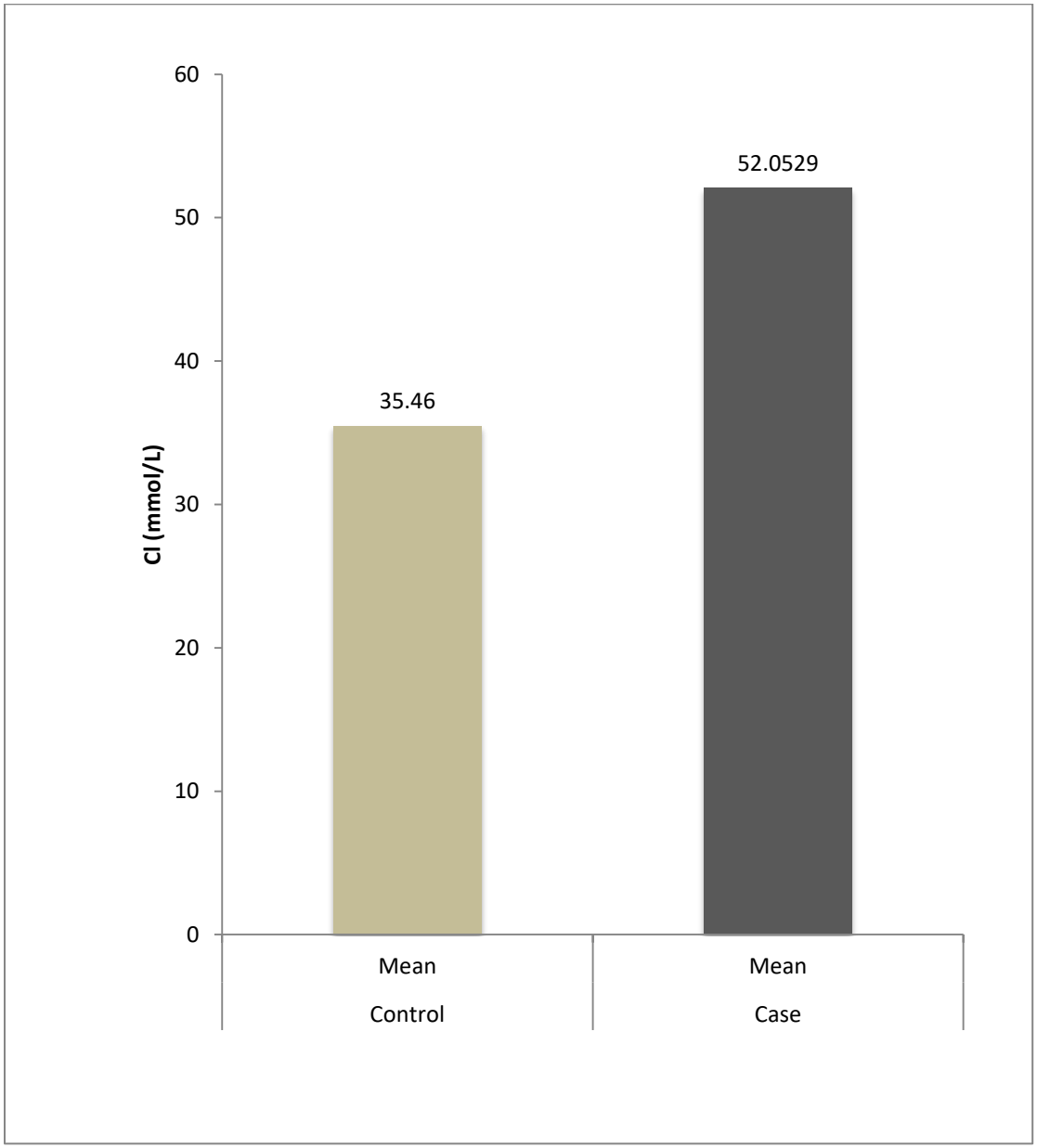

Figure (3): Chloride level from Oral candidiasis cases and controls

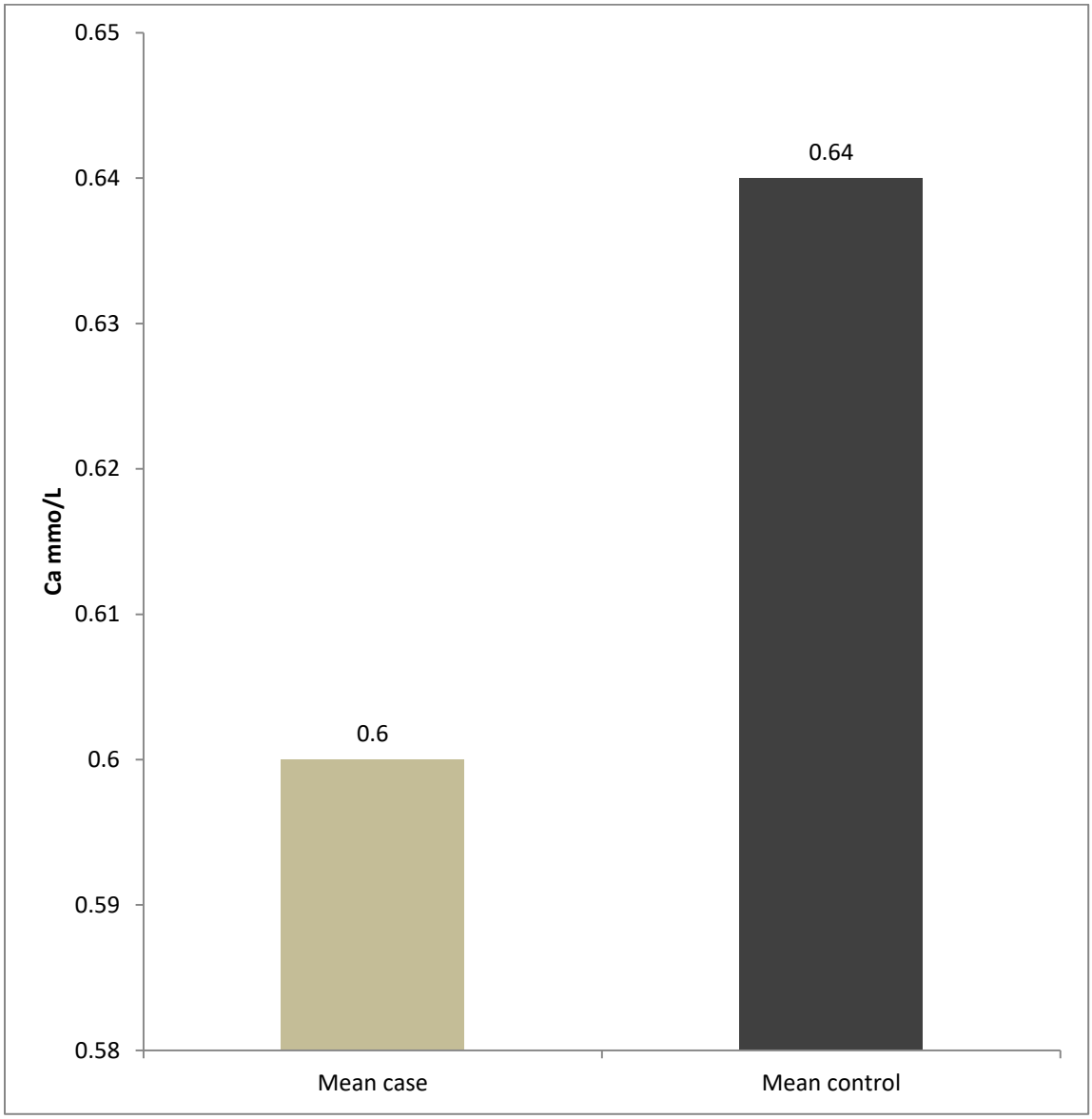

Figure (4): levels of calcium saliva between cancer patients and controls

Calcium is another type of electrolyte that is not different significantly between cancer patients and control. (*P*-value 0.518), the mean level recorded in case (0.60 mmoI/L), comparative with control the mean level (0.64mmo/L)**, f**igure (4).

pH has a signification infection between oral candidiasis case level compared with control (*p*-value 0.001). In this case, the mean level showed (5.4), but in the control showed (6.95), as showed figure (5).

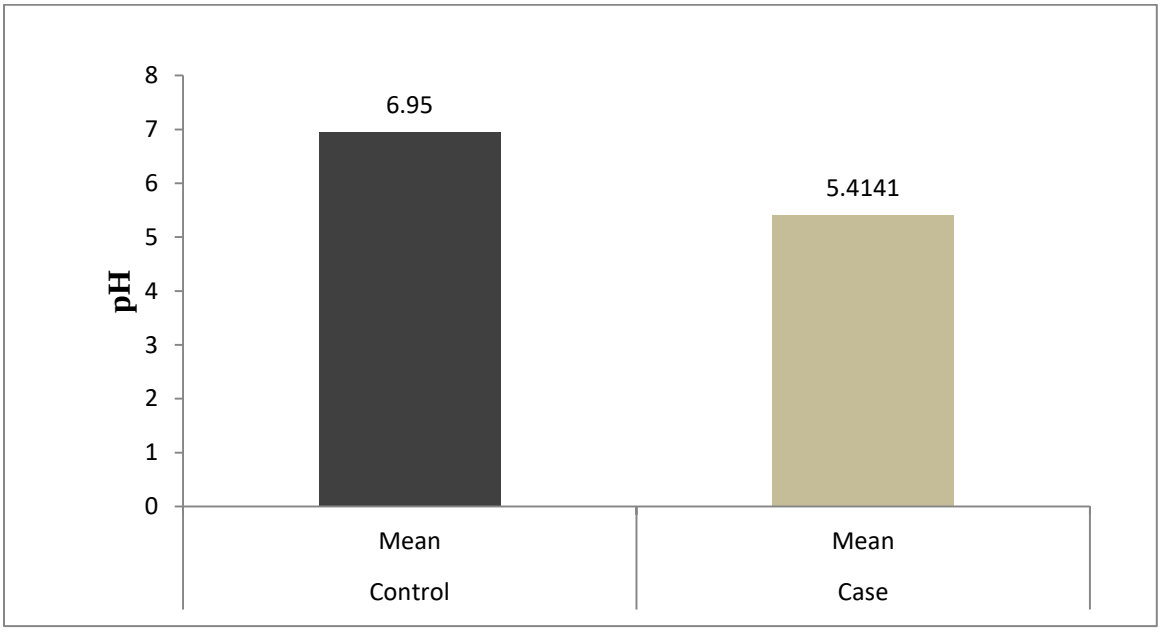

Figure (5): Levels of pH saliva between oral candidiasis cases and control

Discussions

Chemotherapeutic drugs are now classified as either cytostatic or cytotoxic. Cytostatic drugs prevent malignant cell proliferation, whereas cytotoxic drugs cause cell death. (6). The duration of treatment in this study ranged from one month to eight years, and the cycles of treatment in both chemo and radiation ranged from one to 36 cycles. Another study found that approximately (60%) of chemotherapy patients had at least one or more oral manifestations. The most common appearance in our study was xerostomia (29.71%), while the least common was lichenoid reaction (0.72%). Dysgeusia (21.74%) and candidiasis (18.84%) are two other symptoms. The number of oral indications had no relationship with the number of chemotherapy treatment cycles. It did, however, show a significant relationship with chemotherapy treatment duration, implying that the incidence of oral symptoms was higher in people who had a longer period of chemotherapy and a lower quality of life.(12). Patients must pay more attention to keeping their mouths clean after cancer treatment in order to reduce the risk and prevalence of oral candidiasis.

Chemotherapy-induced dry mouth impacts 10-80% of patients getting chemotherapy or radiation treatments. (13) Regardless of the type of cancer. In contrast with radiotherapy-

induced salivary gland dysfunction, which persists for years after radiation therapy is completed, the onset of oral symptoms generally begins on the 7th to 10th day after the administration of chemotherapy and resolves after the completion of chemotherapy. Dry oral mucosa with subsequent oral pseudomembranous candidiasis, halitosis, oral dysesthesia, hypogeusia, and chewing, swallowing, and speaking difficulties are among the symptoms.(14).

Saliva plays a crucial role in oral health. It buffers acids, has antibodies, helps prevent gingival mucosal erosions and ulcerations, and aids in tooth remineralization. When the salivary function is diminished, there is more risk of patients developing caries, experiencing denture discomfort, and having diseases such as candidiasis than in people who have normal salivary flow rates (SFRs)(1).

To some extent, all salivary electrolytes, including sodium, are thought to have antimicrobial properties. In this study, the sodium concentration in cancer patients was higher than in controls, but there was no significant difference in sodium levels between oral candidiasis patients and healthy people (P-value 0.26). Unlike previous studies, sodium concentrations were kept constant before and after intensity-modulated radiation therapy treatment. (15). like previous studies, it shows that there are differences in the ranks(16). It may be due to the taken treatment of cancer patients.

Calcium is secreted into saliva along with proteins, and the concentration of calcium increases as flow rate increases; the calcium concentration in plasma is approximately two times that of saliva.18 Sewon et al. discovered a link between gingival bleeding and saliva calcium levels.(17). Most electrolyte concentrations are also affected by salivary flow rate. Both acini and secretory duct epithelial cells are severely damaged by radiation. (18). In this study, the calcium concentrations in oral candidiasis cases and controls were comparable, and there was no significant difference in calcium levels between patients and healthy people (P-value 0.518). Unlike previous studies, calcium concentrations were lower in cancer patients, and lower calcium ion concentrations lead to less effective demineralization of teeth, contributing to rampant caries in patients after radiotherapy.(15).

Potassium and chloride levels differ significantly between oral candidiasis patients and controls (P-value 0.001). The underlying mechanisms for saliva electrolyte alteration identified in the previous study could be multifaceted and complex. First, the lower potassium and calcium concentrations could be due to radiation-induced damage to the plasma membrane and the associated ion channels in acinar cells. The radiotherapy group

had a potassium concentration that was approximately 30% higher than the controls in the previous study. (17).

This was consistent with our previous findings that a membrane stabilization agent protected salivary gland secretory function during radiotherapy. (19). Second, the decreased potassium concentrations could be attributed to a decrease in salivary flow rate. When primary isotonic saliva was passed through the salivary ducts at a lower flow rate following Intensity-Modulated Radiation Therapy (IMRT), electrolytes were thoroughly reabsorbed, resulting in a lower concentration. Third, the cause of increased chloride and decreased potassium could be radiation-induced ductal system damage. The main function of the ductal system in producing hypotonic saliva is the reabsorption of NaCl secreted by acinar cells. In the second stage of saliva secretion, potassium is primarily secreted by ductal cells, primarily intralobular ducts, though extralobular ducts also contribute to potassium secretion.(20).

A pH of around neutral is ideal for the growth of microorganisms related to oral health. (17). A pH below neutral encourages the growth of cariogenic microorganisms and other acid-tolerant species associated with mucosal infections, whereas a pH above neutral favors periodontitis-causing microorganisms.(17). In 39-62% of cases, patients with hypofunctioning salivary glands may develop a secondary Candida infection while receiving cancer treatment. (21). Salivary gland dysfunction (SGD) is a common and debilitating complication that affects nearly two-thirds of cancer patients. Early diagnosis and management of (SGD) may result in reduced morbidity and improved well-being. The current approach to SGD management is mostly palliative, with the goal of increasing saliva production while reducing the risk of secondary effects such as dental caries, dysgeusia, and fungal infections. (22).

The pH difference between oral candidiasis cases and controls is significant (p-value 0.0001). The combination of host and fungal risk factors, as in the previous study, causes a decrease in pH, and the decreased saliva flow rate and pH value may increase the risk of rampant dental caries in patients undergoing IMRT for nasopharyngeal carcinoma.(15).

Conclusion

The study concluded that cancer patients had significantly higher chloride levels than controls, while patients had lower potassium and pH levels than controls. When comparing patients to healthy subjects, sodium, and calcium ions do not differ significantly.

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