

A retrospective study comparing oral health in cancer patients and healthy people

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Abstract

The purpose of this study was to investigate the relationship between oral and dental health in cancer patients and control group, which was conducted in Tabriz Shahid Gazi hospital. A researchers-made and validated questionnaire including oral and dental health criteria, was filled by the cancer patients (201 cases) and healthy controls (199 cases). Then, the results of the study were analyzed by SPSS software, and reported as Odds ratios (95 % confidence intervals) in tow groups. The results indicate that comparison of filled tooth, tooth extraction, dental caries, and gingival problems including bleeding, gum surgery and inflammation in cancer and controls were significantly meaningful. However, the comparison between the two groups was not significant in terms of the type of the tooth (natural or denture) and the number of daily toothbrushes, but they were considered as risk factors due to statistical results. Environmental factors, and especially oral hygiene, can play an important role in the incidence of different cancers. Among these, the type of oral microorganisms, and their overgrowth and released antigens should be studied further in the emergence of different kinds of cancer in humans.

Key Words: Oral cancer; oral health; microorganisms.

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For over a century, scientists have claimed the role of various forms of microbes in cancer induction. Nevertheless, this claim has always been considered false and baseless.¹⁻⁴ As we know, human body is more prokaryotic than eukaryotic from viewpoint of microbial counts, which in the literature have been described by terms like that microbiome, microbiota and metagenome.⁵ The so-called microbiota has main roles in manipulation of immune system (toward ill or health states), and many studies have being conducted for treating human diseases with microbiota.^{4,6,7} Some of the microbes have direct carcinogenicity in humans including *H. pylori*, HBV, HIV and HPV viruses, causing cancer in humans.⁸⁻¹⁰ Microbiome (microbial population) of intestine and mouth could affect all activities of cells and organs near or far of intestines with creating different kinds of diseases including systemic inflammatory events, rheumatoid arthritis, localized disease, oral and pharyngeal cancers.^{5,11-13} Poor oral and periodontal health has also been proposed to increase malignant tumors in parts other than the oral or gastrointestinal system.¹⁴ Presence of *P. gingivalis* in saliva have been proposed as a predictor of head and

neck squamous cell carcinoma (HNSCC), colon cancer, and a risk of cancer death.¹⁵⁻¹⁷ It has also been proposed that demographics, including gender, education levels, lifestyle, diet and environmental exposures, influence intra- and interpersonal microbiome differences, which in turn affect human health.⁵ Conversely, it has been proposed that the abundance and patterns of the oral microbiota change in patients with oral cancer.^{18, 19}

In particular, emphasis was placed on the role of dental and oral health such as brushing, flossing and mouthwashes to improve the parameters of the mouth and gums.^{8,20} Carcinogenicity synergism of oral bacteria including *F. nucleatum* and *P. gingivalis* have been reported in the oral and colon malignancies.²¹

The purpose of this study conducted in Tabriz Shahid Gazi hospital was to investigate the relationship between oral and dental health in cancer patients and a control group.

Materials and Methods

Design, sampling and duration

This cross-sectional study was done at the Department of Microbiology, Maragheh University of Medical

Oral health in cancer patients and healthy people

Eur J Transl Myol 32 (4): 10672, 2022 doi: 10.4081/ejtm.2022.10672

Sciences, Maragheh, Iran in collaboration with Oncology Centers of Hematology and Oncology Research Centers of Shahid Ghazi, and Imamreza Hospitals of Tabriz University of Medical Sciences, two approved cancer patients centers in north-west of Iran. Informed consent was obtained from all patients. In addition, due to the small number of patients, all types of cancer patients referred to referral cancer centers from the northwest of the country were included in the study. A total of 201 cancer patients and 199 healthy individuals were included in this study.

All of the patients were confirmed in the cancer registry system of west Azerbaijan state from June 2016 to June 2018 (Tabriz, Iran) under supervision of the Tabriz University of Medical Sciences. The 199 controls of the healthy group were selected from patient's family members especially for matching and preventing intervening factors. Healthy controls were included if they do not have chronic or known diseases and were apparently healthy. Considering that the statistical population was in different classes of gender, age, education, occupation, and other variables, so, stratified random sampling method was used for selecting controls. Considering that the so-called cancer centers were two reference oncology centers of north-west of Iran, both of the patients and controls were representatives of north-west of country.

Data collection and analysis

Data collection was done by a standardized questionnaire, whose validity and reliability were reconfirmed by content validity, and Cronbach's Alpha of Likert scales. Questions were set to measure the oral health of individuals for aim of a retrospective study of the role of microbes in cancer induction. All of the questionnaires were filled by direct supervisory of two educated nurses in the so-called sections after approving and getting ethic code of Maragheh University of Medical sciences. (TBZMED.REC.1394.632) from regional ethical committee.

Designing of the questionnaire

The questionnaire was researcher-made, but questions were selected from viewpoint of the life quality in the healthy or unhealthy conditions of oral health, as reported in previous studies.²⁻⁴ The questionnaire content validity was supervised and confirmed by a group of experts. Based on the aim of the study, clearness, relevancy, suppleness, and the necessity of questions have been considered in designing and

confirmation of validity. As pre-test, 30 individuals filled questionnaire and the internal consistency was assessed in a pilot evaluation. Cronbach alpha was measured to 0.81, which indicated the questionnaire is acceptable for such a study. Odd ratio and confidence intervals between groups were calculated by SPSS software. P-value < 0.05 was considered as significance threshold.

Results

Oral and dental scores distribution in studied groups have been indicated in Table 1. Means and standard deviations of oral and dental health scores in cancer and health groups are calculated as 26.8, 11.4, and 34.2, 13.7, respectively. Statistics indicate that healthy groups have a better and higher oral and health scores in comparison with cancer patients in this study. Frequency and percent of different criteria including toothbrush, dental kinds, filled, extracted, and decayed teeth, and gums health in cancer and healthy groups were indicated in Table 2. Out of 201 cancer patients (94) 47% don't using daily dental brushing, 33% and 8% were stated that they are using brushes one and more than two times daily respectively. Twelve percent of patients do not respond to the questions. In comparison, out of 199 healthy people (19) 10% don't using daily dental brushing, 27% and 59% were using brushes one and more than two times daily respectively. Four percent of patients do not respond to the questions. Of the 201 cancer patients, and 199 healthy people, 42%, and 58% had dentures and 7% and 93% had natural teeth, respectively. In cancer patients, the percentage of dentures was 6 times greater than healthy people. High percentage of patients were in the adult age, but the majority of healthy people were in middle age groups, which can be partly interpreted as cancer being a chronic phenomenon and frequently occurs at older age groups. In cancer patients 0-1(23%), 2-3(26%), 4-10(12%), and 11-15(8%) of teeth were filled, respectively. In 31% of cancer, patients were filled all of the teeth. However, in the healthy group, 0-1(61%), 2-3(26%), 4-10(3.5%), and 11-15(3.5%) of teeth were filled, respectively. In addition, in 6% of healthy people, all teeth were filled. Percentages of tooth extraction, decayed teeth, bleeding, inflamed, and or surgieried gums in both cancer and healthy groups are also given in Table 3. Odds ratios (95 % confidence intervals) in cancer and healthy groups were indicated in Table-3. All of the odd ratio and confidence intervals in this

Table 1. Distribution of oral and dental scores in cancer and healthy groups.

Statistic	Count	Mean	Middle	SD	Skewness	Confidence Interval	Lower Limit	Upper Limit
Cancer	201	26.8		11.4	0.02	42	5	47
Healthy	199	34.2	39	13.7	-0.22	40	10	50

Oral health in cancer patients and healthy people

Eur J Transl Myol 32 (4): 10672, 2022 doi: 10.4081/ejtm.2022.10672

Table 2. Frequency of oral health criteria in cancer and healthy groups.

	Cancer	Healthy
	Frequency (%)	Frequency (%)
Use of toothbrush per day:	No	19 (10)
	One time	53 (27)
	More than 2 time	118 (59)
	No answer	9 (4)
Dental kinds:	Denture	14 (7)
	Natural	185 (93)
Filled teeth:	0-1	122 (61)
	2-3	52 (26)
	4-10	7 (3.5)
	11-15	7 (3.5)
	All of tooth	11 (6)
Extracted tooth:	0-2	151 (76)
	3-4	21 (11)
	5-10	5 (2)
	More than 11	22 (11)
Decayed tooth:	0-2	151 (76)
	3-4	21 (11)
	5-10	5 (2)
	More than 11	8 (4)
	No answer	14 (7)
Gums health:	Healthy	173 (87)
	Hemorrhagic	19 (10)
	Inflamed	5 (2)
	Surgeried	2 (1)
	Total	199 (100)

study were meaningful in cancer and controls, which indicates that all of the criteria could be considered as a risk factor in cancer induction in humans.

Discussion

Despite the many advances that have been made in the diagnosis and treatment of cancer, there is still no consensus among scientists on the etiologies of cancer, which is increasing in mortality and morbidity all over the world.²¹⁻²⁵ For this reason, prevention, diagnosis and treatment methods are confusing. There is also no definitive treatment for all types of cancer. Therefore, in this study, the history and scores of oral health in cancer and healthy individuals was studied retrospectively in a cross-sectional study to show that microbial contamination in human life might be important in cancer. In fact, we hypothesized that the oral health score could be an indirect indicator of the contamination of people with various microbes in their early life that in turn can induce cancer in later years.

As we know, the majority of deadly cancers, including oral, tracheal, bronchus, colorectal, prostate, lung, and stomach cancers,²³⁻²⁵ occurs in anatomical sites, which are full of microbial normal floor, or easily exposed to external transient pathogens. This fact, suggests that scientists should have attention and focus on dynamic activities of microbes in emergence of cancer instead of classic proposed risk factors. Even in this regard, it can be noted that the prevalence of some cancers has been greatly reduced after the use of microbial vaccines. As an example, human cancers in liver, oral and cervical have been severely reduced by vaccination against HBV, and HPV viruses.²⁵ Also there is a huge repertoire of blood or mucosal microbes even in healthy people and thousands of known carcinogenic, and metabolism deteriorating antigens released from normal microbiota and pathogens, which should be considered in cancer induction in future studies.¹⁶ Oral hygiene may reflect systemic diseases,²⁶ and most cancer patients have

Table 3. Odds ratios (95 % confidence intervals) for cancer risk in relation to oral health-related criteria in comparison with healthy group.

		GROUP		OR	95% CI	
		Cancer	healthy		Upper	Lower
Dental kind	dentures	84	14	9.49	17.48	5.15
	natural	117	185	1:00		
Tooth brushing per day	2<	17	118	1.00		
	1	66	53	8.6	16.1	4.6
	not use	94	19	34.3	69.7	16.9
Filled Tooth	0-1	46	122	1.0		
	2-3	53	52	2.7	4.5	1.6
	4-10	24	7	9.1	22.5	3.7
	11-15	16	7	6.1	15.7	2.3
	All of tooth	62	11	14.9	30.9	7.2
Extracted Tooth	0-2	38	151	1.0		
	3-4	47	21	8.9	16.6	4.8
	5-10	10	5	7.9	24.6	2.6
	More than 11	106	22	19.1	34.2	10.7
Decayed Tooth	0-2	81	151	1.0		
	3-4	39	21	3.5	6.3	1.9
	5-10	7	5	2.6	8.5	0.8
	More than 11	9	8	2.1	5.6	0.8
	No Answer	65	14	8.7	16.4	4.6
Gums Health	Healthy	128	173	1.0		
	Hemorrhagic	33	19	2.3	4.3	1.3
	Inflamed	33	5	8.9	23.5	3.4
	Surgeried	7	2	4.7	23.2	1.0
Total		201	199			

lower oral hygiene before diagnosis,²⁷⁻²⁹ increasing the risk of highly deadly odontogenic infections as well as mucositis during cytotoxic treatments.³⁰⁻³¹ In fact, it is the microbial population that affects and determines the oral cavity health, and recently role of the microbiota have been discussed in producing many of the important non-infectious diseases. Mouth health and microbial diversity may have a critical role in immunity development and inducing many of the abnormalities because of antigenic repertoire delivering to the immune system. Oral hygiene is neglecting in high percent of people,¹² causing many complications, including periodontitis, dental loss, and in turn oral and colon cancers, and other complicate diseases such as cardiovascular disease, and preterm birth.^{5,7-9,11,16-19, 32-34} In this regard, relationships between oral health such as dental loss and periodontitis with oral, lung, upper gastrointestinal, and pancreas cancers have been

reported in different studies.^{5,8-9,14,35} For example, presence of periodontal pathogen *Porphyromonas gingivalis* was evaluated and proposed as a predictor of death in orodigestive tract cancers.¹⁷ In a study by Tongzhang, tooth loss has been reported as a strong risk factor of oral cancer, odds ratio (OR) in cases with 15 – 32 tooth loss in comparison with no dental loss was calculated 5.3 for men and 7.3 for women's, respectively. In this study also a relation between cancer risk and brushing was reported in cases don't using of daily teeth brushing in comparison with groups having no signs of oral related health problems.³⁶ In other prospective cohort study, 0-10 tooth loss has meaningful relation with pancreas cancer.³⁷ and local activation of carcinogens by oral microbes or release of pro-inflammatory mediators have been proposed for relationship between cancer inductions by oral microbiota in organs other than oral cavity.¹⁰ In this

study, regardless of the type of cancer, oral health in a number of healthy and cancer patients was investigated. Frequency and odd ratios of pairwise comparison of different criteria in this study including toothbrush, dental kinds, filled, extracted, and decayed teeth, and gums health in cancer and healthy groups in Table 2 and Table 3 indicates that all of them were significantly different, which shows the importance of oral health and possibly the role of cocktails of microbes living in the mouth of patients in the development of cancer, although this level of studies cannot directly attribute the cause of cancer to microbes. However, as a more important factor than other known risk factors should be considered in future studies.

In conclusion, this study shows that a previous history of lower oral health is associated with cancer, indicating the important role of microbes, or molecules released from them and their risks on the immune system and ultimately the incidence of cancer. Role of microbial interactions with our body in cancer induction is very complicated and higher statistical evidence is needed before concluding that in the majority of cancers microbial antigens have an important inducing role that needs to be elucidated in the future.

List of acronyms

HBV - Hepatitis B

HIV - Human immunodeficiency virus

HPV - Human Papillomavirus

OR - odds ratio

Contributions of Authors

HHZ contributed in the conception of the work, conducting the study, revising the draft. RP And HHZ contributed in analysis, or interpretation of data, drafting the work and revising it critically for important intellectual content. RP contributed in draft and critical revision for important intellectual content. MHZ contributed substantially to conception, design and drafting the work. All authors read and approved the final edited typescript.

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Conflict of Interest

The authors declare no conflict of interests.

Ethical Publication Statement

We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

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Oral health in cancer patients and healthy people

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