Assessing the Oral Flora Changes Pre-operatively, Post-operatively and Post Radiotherapy in Patients Having Oral Squamous Cell Carcinoma

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Authors' contributions

This work was carried out in collaboration between both authors. Both authors read and approved the final manuscript.

Study Protocol

ABSTRACT

Background: The occurrence of oral malignancies like oral squamous cell carcinoma has an effect on the microbiota present in the oral cavity. It is observed that radiotherapy exposures can also lead to disturbances within the oral microbiota.

Objectives: To assess the oral microbiota in patients having oral malignancy and in normal healthy individuals, and compare them to evaluate the changes associated with oral malignancies and their treatment.

Methodology: The study will be conducted in the Oral & Maxillofacial Surgery Department at SharadPawar Dental College, DMIMS, Sawangi(Wardha). The study comprises of 50 Participants who will participate in the study after agreeing to an informed consent.

Results: Athorough investigation of the biological behaviour of the microflorawas considered necessary to understand their exact specific roles in the process of carcinogenesis, which can be achieved by isolating the specific associated strains and their consequent profiling using various sequencing methods.

Conclusion: There can be a definite relationship between the prevalence of oral malignancies and their consequent changes in the oral microbiota.

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1. INTRODUCTION

The oral tissues and structures have a heterogenous nature, providing a diverse and distinctive ecological habitat to the micro organisms which are distributed in various niches of the saliva, teeth, mucosal surface and tongue [1].

Oral microbiome, as per definition, is the collective genome of microorganisms that are harbored within the oral cavity [2]. The complexity of the oral microbiota is enhanced due to the reason that the only part in the body where the mineralized hard tissues are naturally exposed to the external environment, is the mouth [1].

Researches in oral cancers, mainly oral squamous cell carcinoma(OSCC), have gained momentum in the recent past and a better understanding of the etiopathogenesis is the need for early diagnosis and better management [1].

Two types of bacteria, namely aerobes and anaerobes, collectively lead to the formation of multi species communities which are known as Biofilms, capable of resisting changes in their environment [2]. Oral cancer, primarily oral squamous cell carcinoma, is known to be arising from host genetics as well as environmental factors, tobacco, betel quid chewing, alcohol and HPV(Human Papilloma Virus) infection [3,4].

In recent times, the human oral microbiome is considered a new potential bio-marker reservoir for OCC & OPC [5]. Many reports show a few selected species in tumor tissues, such as Pseudomonas aeruginosa and *Fusobacterium nucleatum* are associated with OSCC. Other reports show five genera(bacillus, enterococcus, parvimonas, pepto streptococcus and slackia) showed differences between patients with epithelial precursor lesions and OSCC [5].

Thus, the characterization of changes in oral microbiota could help shed some light on assessing the prophylactic drug therapy in such patients, with a better accuracy.

In patients having oral malignancies, there is a gradual and significant change in the physical and physiological status of the tissues of the oral cavity. There is also a subsequent change in the patients overall habits, mental state, dietary habits, lifestyle and other associated aspects. Once the patient begins treatment, there is also a significant change in the status of the oral cavity and its associated structures because of treatment procedures, administration of drugs, dietary inhibitions, radiotherapy etc. All these events lead to changes in the overall condition of the oral cavity and the microbiota associated with it.

As a consequence and in conjunction to all these changes there is a subsequent modification in the nature and composition of the oral flora in terms of their numbers, diversity, behaviour and effects upon the individual.

The present study is focused at understanding these changes and their effects upon the oral microbiota and how these changes affect the overall prognosis and condition of the individual in terms of before and after treatment and radiotherapy exposures.

2. OBJECTIVES

To assess the oral microbiota in patients having oral malignancy and in normal healthy individuals, and compare them to evaluate the changes associated with oral malignancies and their treatment.

3. METHODS

The study will be conducted in the Oral & Maxillofacial Surgery Department at SharadPawar Dental College, DMIMS, Sawangi (Wardha). The study comprises of 50 Participants who will participate in the study after agreeing to an informed consent. The Patients will be selected by applying the following Inclusion and Exclusion criteria-

3.1 Inclusion Criteria

Patients with malignant conditions, particularly OSCC, in the age group of 30-60 years.

3.2 Exclusion Criteria

Patients having any other systemic conditions which require a routine and scheduled intake of drugs/medications.

Out of the total subjects, 25 will be of the study group (having OSCC or other oral malignant condition).

And 25 will be of the control group (not having any anomaly or any deleterious habits such as smoking, alcohol consumption, tobacco chewing etc.).

Tissue swabs from the buccal mucosa, vestibule and hard palate will be collected from all the subjects, with a prior informed consent.

The tissue swab for patients with malignancy, will be collected at three stages:

1. Pre- treatment
2. Post-treatment before discharge
3. After radiotherapy/radiation exposure.

After this, the obtained specimens will be cultured, sensitivity tests will be performed and the results will be compared.Swabs will be examined for the microbiota and compared between that of the control group and the study group. After this, data tabulation will be done to formulate the results.

4. EXPECTED RESULTS

Since during the course of development and progression of OSCC as a disease entity many changes take place such as dietary, physiological , microbiological etc and all these changes are inter-related and influence each other in many ways during disease development, during treatment and during exposure to external influences such as drugs, x-rays etc, a link or correlation can be expected between the disease as a whole, the disease process and with factors in various stages of disease and its management such as before treatment, after treatment and after radiographic exposure. Such correlations form the basis of this study and appropriate results can be seen.

5. DISCUSSION

Oral squamous cell carcinoma is a fairly common malignant condition and affects individuals all over the globe. This condition is seen mostly associated with chronic cigarette or pipe smokers, tobacco chewers, alcoholics, individuals having excessive x-ray exposure, poor oral hygiene habits, immunodeficiency etc. A variety of factors play a dominant role in the development and progression of this condition.

Clinically, the changes brought about by this disease includes long standing ulcerations, isolated red-white lesions, pain, paresthesia, dysphagia etc. Microbiologically there are some significant changes in the nature, composition and behavior of the oral microbiota which in turn can lead to several related manifestations. Since cancer is a complicated disease, the affected individuals undergo heavy drug therapies, radiation therapies, diet modifications etc, there can be seen some associated changes due to these factors within the composition and behavior of certain aspects of the oral cavity such as physiological functioning, microflora changes and these changes can be assessed so as to predict or relate the development of the condition in terms of its rate, severity, location etc. There is a significant change seen before treatment, after treatment and after radiographic exposures in such patients in terms of their physiologic functioning and microflora.

PP Gaonkar et al and colleagues conducted a study to find and verify a possible link between oral microbial flora and oral cancer. They hypothesized that the oral microbial flora can have an associated role in oral cancer, however they assumed this role to be an indirect one. They studied the inter relationship between various factors such as oral microflora with alcohol and carcinogenesis, oral microflora, oral hygiene and carcinogenesis, oral microflora and cancers of sites other than the oral cavity and found that there is a possibility of a link between the development and prevalence of oral and non oral cancers with oral microflora. They concluded that with the presence or oral cancer, there is a shift in the oral microbiota from non-pathogenic resident microflora to non-resident pathogenic ones.

In the study conducted by Yenkai Lim et al, the possibility of oral microbiome being a new biomarker for oral and oro-pharyngeal cancers was discovered. According to this author, the more commonly used biomarkers include DNA, RNA and Proteins are not of much practical use in clinical aspect. The author discovered that the oral microbiota participates in the process of disease initiation and progression within the oral cavity as well at separate distant sites. They found that the presence of malignant conditions like oral squamous cell carcinoma affects the microbiota in the oral cavity both directly as well as indirectly in a significant way and concluded that the reliability and effectiveness of oral microbiota as a new biomarker can be

considered in cases of malignancies such as oral squamous cell carcinoma.

In the study conducted by Hongsen Zhao et al, an analysis was made to understand and unravel the connections between oral microfloradysbiosis and the presence of OSCC. Prevalence of certain bacteria and changes in bacterial community composition was analyzed and compared to normal oral flora.It was observed that the phylogenetic diversity in the microbiota of oral squamous cell carcinoma patients was found to be significantly greater in the surface of the lesion as compared to individuals without malignancies. They also found an increased bacterial complexity within the salivary samples and found that in patients having malignancy there was a remarkable drop in the richness and diversity of the oral bacterial species. They concluded the presence of an oral microbiotadysbiosis to be prevalent during the course of development and treatment of OSCC.

Naoki Fukuma et al conducted a study to analyse the performance of oral microbiome as a biomarker in predicting the occurence of oral cavity cancers and oro-pharyngeal cancers. The focus of the study was to check whether oral microbiome changes and reactions could predict the presence and development of oral cavity cancers and oro-pharyngeal cancers with accuracy and specificity.

It was observed that when the oral microflora profiles from disease free, healthy controls and cancer patients was compared, a significant, consistent and reliable pattern was observed describing the changes and features of the oral microbiome panel in predicting whether a normal or atrisk individual is going to develop oral and oro-pharyngeal cancer and the extent to which the disease will progress. It was concluded that the changes in oral microbiome as a biomarker are consistent and reliable to predict the occurrence and severity of oral and oro-pharyngeal cancers.

In the study conducted by Chia Yu Yang et al, a correlation between the community dynamics of oral microflora and staging of oral squamous cell carcinoma was assessed. In this study the main focus was to find out and relate the changes in specific bacterial species in terms of their numbers, behavior, localization etc, to the development and progression of various stages of oral squamous cell carcinoma. It was found that as the malignancy develops and starts to spread, there is a specific pattern of changes seen in the behavior and population of a few specific important bacterial species such as Fusobacterium, Streptococcus, Haemophilus, Porphyromonas etc. It was concluded that the development and progression of oral squamous cell carcinoma leads to changes in the pattern, composition and behavior of certain specific gram negative and gram positive bacterial groups and that these changes are in conjunction to each other. A number of studies reflected on different aspects of oral squamous cell carcinoma [6-18].

6. CONCLUSION

There can be a definite relationship between the prevalence of oral malignancies and their consequent changes in the oral microbiota.

CONSENT

As per international standard or university standard, Participants' written consent will be collected and preserved by the author(s).

ETHICAL APPROVAL

As per international standard or university standard written ethical approval will be collected and preserved by the author(s).

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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Peer-review history:
The peer review history for this paper can be accessed here:
https://www.sdiarticle5.com/review-history/81043