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ORIGINAL ARTICLE

Regulation of p53 in Benign and Malignant lesions

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ABSTRACT
The goal of this research was to assess the extent of P53 overexpression in pre-malignant and malignant oral lesions to that of the standard oral mucous membrane. The present study has been classified into three groups. The grouped samples were subsequently immune-histochemically examined for P53 protein expression using an indirect 1mmunoenzyme LSAB technique. To improve the sensitivity of diagnosis of instances that may proceed to cancer, P53 immuno-histochemical analysis should be used in combination with histology criteria.
Keywords: *leukoplakia, immunohistochemistry,tobacco mucous membrane, gene expression.*

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INTRODUCTION

Squamous cell carcinoma is the country's sixth utmost cancer type, accounting for 5.5 percent of all cancers [1]. Every year, over 500,000 new instances of oral cancer are detected worldwide, with three-quarters of these occurrences occurring in the developing nation, including around 65,000 cases in sub-continent [2,3]. Oral cancer is the world's most prevalent cancer, and it is the third most frequent disease in India [4].Tobacco and alcohol intake have been firmly confirmed as the main causes of intra-oral chemicals in the worldwide situation contributing to oral and oropharyngeal cancers, according to epidemiological, clinical, and laboratory evidence [5]. Tobacco consumption can also induce leukoplakia and erythroplakia, two main clinically recognized precancerous lesions [6]. Oral submucous fibrosis, which is predominantly connected with the chewing of areca nuts, has been predictable as a precancerous disease in India and numerous other Southeast Asian nations [7]. In India, cigarettes account for less than one-fifth (19%) of total tobacco use. The remaining is smoked in a dry form, such as mishiri and smoking gum. Areca nuts are utilized as areca nuts in their natural state. 'Panmasala' isanother areca nut recipes that are ready to eat right away [8].

Oral carcinogenesis is a multi-stage process that comprises the stages of start, development, and promotion. The most significant and crucial event of the chemical carcinogenes is the interaction between suspected carcinogens [9-10]. Tumors are caused by genetic damage that disrupts the normal regulatory pathways that govern basic cellular processes. Tumor suppressor genes (TSG) are genes that slow or stop cell cycle development, hence limiting tumour growth [11]. TSG produces a substance that inhibits the expression or activity of genes involved in cell growth and proliferation [12]. The loss of activity of the p53 tumour suppressor gene is linked to nearly all human malignancies, demonstrating that p53 plays a key role in cancer genesis. P53 is a tumour suppressor protein produced by the p53 gene [13]. Loss of P53 function results in a loss of cell cycle regulation and the accumulation of damage-induced mutations, which leads to cell malignancy [14]. P53 deactivation occurs when the p53 gene is mutated or when the P53 protein is stabilized by binding to other molecules such as MDM2 [15]. P53 expression in mouth cancers and premalignancies has been widely researched [16]. Cigarette smoking was connected to p53 alterations at nonendogenous mutation sites, according to preliminary findings. The purpose of this research is to demonstrate the presence of P53 in inducing apoptosis using immunohistochemistry (OSCC).

MATERIAL AND METHODS

A number of eighty formalin (FO)fixed, paraffin (PA) embedded cases were examined. At a specified hospital, fixed tissue samples from the oral cavity were taken from the Pathology Department. These were then sorted into two groups: baseline and research. The control sample comprised of 10 oral cavity samples that were FO fixed, PA embedded, and histo-pathologically identified as normal oral mucous membrane. Oral leukoplakia and oral squamous cell carcinoma were histopathologically identified in the study sample of 70 formalin fixed, paraffin embedded tissues. To perform a comparison between the two groups, a similar quantity of cases were chosen in the study group, namely 35 out of 69 oral leukoplakia cases and 35 out of 52 oral squamous carcinoma cases. A thorough clinical history was gathered.The control sample consisted of 10 oral cavity samples that were FO fixed, PA embedded, and histopathologically identified as normal healthy oral mucosa. The control sample ranged in age from 23 to 46 years old. The research group comprised of 70 oral cavity samples that were histopathologically identified as carcinoma after being formalin fixed and paraffin embedded. The research group ranges in age from 28 to 91 years old.The samples were further categorized into two sub-groups:

Group I - Oral leukoplakia tissue samples that have been histopathologically diagnosed, FO-fixed, and PA-embedded

Group II - The study included 35 samples that had been histopathologically identified, FO-fixed, and PA-embedded.

PREPARATION OF SLIDES

The histopathologically detected oral carcinoma PA wax blocks were chosen. A rotary microtome, LEICA, was used to cut them into 3-5 thin tissue slices. Hematoxylin and Eosin staining, and P53 staining, were used on these slides. P53-stained slides were examined under a light-microscope at a magnification of 400x. The study groups were properly analysed, and 100 cells were counted in total. The cells considered are then counted among the 100 cells. The presence of Pp53 protein was verified by a brown precipitate visible within the nucleus. The p53 positive study-samples were then graded on a 4-point scale depending on the cell's percentage that stained positive for P53. The findings were then statistically examined using the Chi-square (x2) test of significance. A probability of <0.05 was regarded as significant in this test.

RESULTS

The p53 gene is upregulated in inducing apoptosis and oral squamous cell, as according our results. Eighty histologically identified, FO fixed, PA embedded tissue specimens were taken and split into different clusters: control and research. The control group comprised of ten FO-fixed, PA-embedded samples of normal oral mucous membrane that were histopathologically identified as such.7/35 (20%) of the samples in Group I tested positive for P53, but none of the samples in the control study-group tested positive for P53. But none of the samples in the control group tested positive for P53. Because the p value was 0.197, the result was not significant. P53 was found in 7/35 (20%) samples from group I and 12/35 (34.29%) samples from group II. Six samples from group II showed 3+ staining, but none of the ones from group I did. The statistical significance was determined by the p value of 0.025.P53 appeared as a dark stain within the nucleus in all of the research groups. However, the stain's pattern of expression differed amongst the groups. [Figure 1A-D]. P53 staining was found in the basal and proximal suprabasal levels in Group I. Group II - The P53 brown stain was widespread, affecting all layers of the organ. The intensity of the stain differed across the two research groups as well. P53 staining is less strong in Group I. P53 staining is more strong in Group II.

DISCUSSION

The most mutual molecular mechanisms in human malignancies are mutations in the p53 gene [17]. The P53 gene is found on 17thchromosome and expresses the P53 protein, involved in a number of important functions in the cell, and is influenced by a variety of stress signals, along with DNA damage and inflammation. In reaction to DNA damage, the P53 protein causes cell cycle arrest in the G1 phase, allowing for DNA repair or the control of death if the damage is irreversible [18-20]. Be a result, the p53 gene is referred to as a tumour suppressor gene. 80 histopathologically identified, FO-fixed, PA-embedded tissue studies were evaluated in this investigation. These samples were divided into two groups: control and study. Ten normal samples made up the control group. This revealed that in the case of oral carcinoma, a greater fraction of cells possess mutant or stabilised p53 protein [21-24]. This aligns with the findings of the following studies: According to Balaraman *et al* [16], when cells develop a more malignant character, p53 expression increases gradually. p53 staining was more intense in dysplasia specimens than in hyperplasia specimens, and it was even more intense in OSCC specimens than in dysplasia [25-27]. From hyperplasia through dysplasia to OSCC, 28 percent of those with positive P53

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express10n progressed [28, 29]. There was also a variation in p53 expression patterns across the research groups.

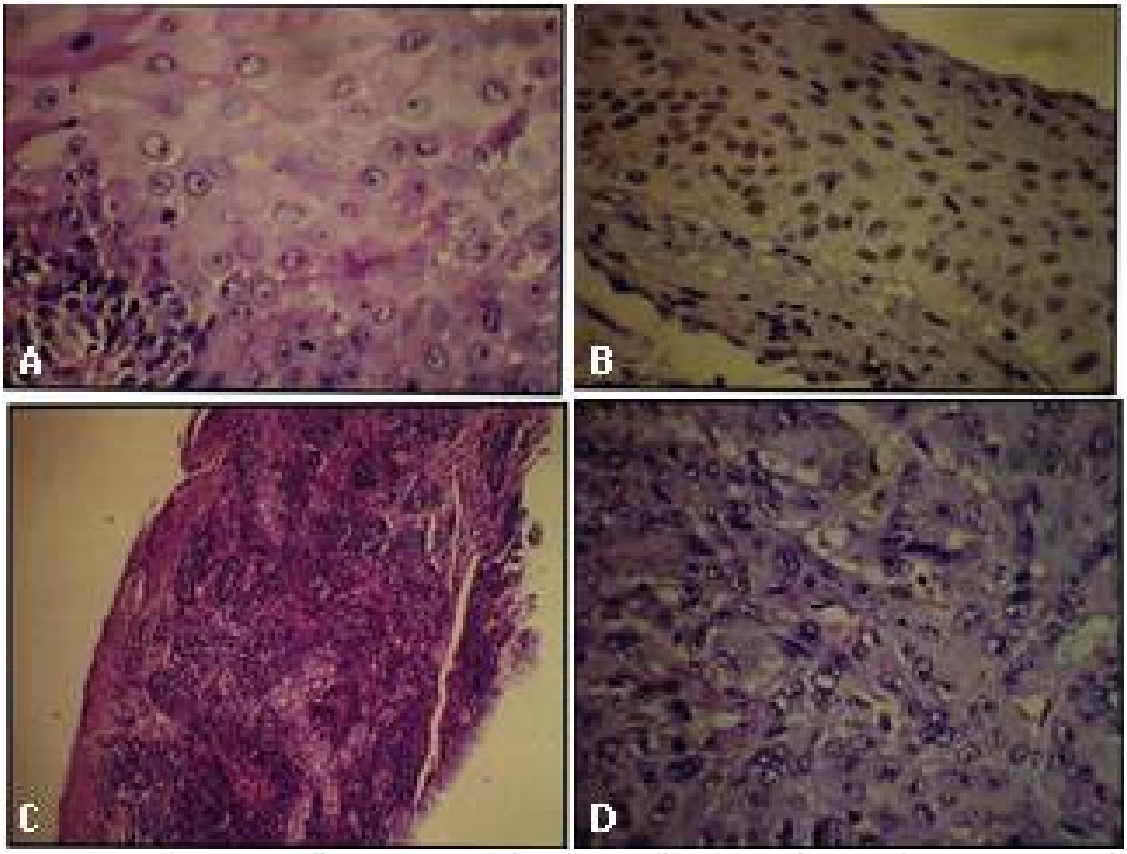

Figure 1. A. Oral squamous cell carcinoma; B. Oral squamous cell carcinoma showing p53 expression; C. Oral squamous cell carcinoma- H & Ex 100; D.H & E of Oral squamous cell carcinoma.

CONCLUSION

One of the most prevalent occurrences in oral carcinogenesis is the expression of the P53 protein. The p53 is expressed in a number of ways in premalignancies and oral squamous cell carcinoma. Variations in aetiology and ethnic background, as well as differences in immunohistochemical techniques used, can explain the disparity in the frequency of tumours expressing the protein.p53 protein was found to be positive in a large percentage of samples in this investigation. Immunohistochemistry-detected P53 protein might be one of the most important biomarker. In oral squamous cell carcinoma, the pattern of p53 expression was different, with diffuse staining.This means that p53 protein accumulates throughout time when normal cells transform into dysplastic lesions, and then into invasive cancer. As a result, it's possible that P53 may be used as a tumour marker. P53 protein expression may aid in assessing prognosis and play a crucial protagonist in cancer therapy for the cure of oral squamous cell carcinoma. Careful systematic studies with a larger sample size, on the other hand, might aid in determining the role of P53 protein in oral carcinogenesis.

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