The present study was conducted in the Department of Biochemistry, Jawaharlal Nehru Medical College, AMU, Aligarh during the period November, 2004 to March 2007. The study comprised of patients of oral cancer attending the Otorhinolaryngology (E.N.T) O.P.D. or outdoors admitted to their wards. The salient features of the present study are as follows:-

The present study comprised of 100 oral cancer patients and 150 control subjects. Biopsy specimens were taken from 60 oral cancer patients and 10 controls. Blood samples were collected from all the subjects.

The purpose of the present study was to evaluate the expression of p53 and Cyclin D1 in tobacco and betel quid chewers of northern India. We further aimed to evaluate the association of hOGG1 Ser^{326}Cys, XRCCI Arg^{280}His, CYP2E1 Dra1 and CYP2E1 Rsal polymorphisms with risk of oral cancer in tobacco and betel quid chewers.

The 60 oral cancer biopsy samples were further divided into well differentiated, moderately differentiated and poorly differentiated squamous cell carcinomas on basis of degree of differentiation. Well differentiated SCC was found to be the commonest, 34 cases (56.66%) followed by moderately differentiated SCC, 18 cases (30%) and poorly differentiated SCC, 08 cases (13.33%).

- The cases belonged to age group of 25-100 years while the controls belonged to age group of 0-100 years.
• There were 75 males (75%) and 25 females (25%) in the cases while 115 males (76.66%) and 35 females (23.33%) in the controls.

• The mean age of male and female patients was 58 and 53 years respectively while mean age of male and female controls was 56 & 54 years respectively.

• There was definite male preponderance with a male to female ratio of 3: 1 in cases and 3.28:1 in controls.

• Most cases (68.97%) presented with some complaint within first 6 months of the start of the lesion.

• Maximum number of patients complained of dysphagia (80 cases) followed by pain in the lesion (50 cases), burning in the mouth & throat (45 cases) and pain during swallowing (29 cases).

• Tobacco and betel quid chewing was found to be very important risk factor for development of oral cancer by chi square test \( \chi^2 = 135.226, p=0.00 \).

• Maximum cases, 45 (45%) were having malignancy of buccal mucosa, followed by tongue, 22 cases (22%) and floor of mouth, 17 cases (17%) respectively. Other malignancies were less common like lip (6%), hard palate (5%) and gingivia 3%.

• Histopathology revealed squamous cell carcinomas in all oral cancer biopsy specimens.

Protein Expression

Sixty biopsies of oral cancer patients with tobacco and betel quid chewing habit and 10 normal biopsies were immunohistochemically evaluated for p53 and cyclin D1 expression and the results were expressed as positive cases (%) and positivity.

p53 Expression

• p53 immunostaining was positive in 39 (65%) cases of oral cancer with a p53 positivity of 26.46±23.90 (mean±SD) while there was no detectable p53 expression in controls.
- The percentage of positive cases as well as p53 positivity showed an increase as the grade of differentiation advanced. Significant association was found between p53 positivity and degree of differentiation of tumors \((p=0.029)\).

- A significant difference in p53 positivity was noted on comparing well differentiated \((20.0, \pm 19.32)\) and poorly differentiated \((47.5, \pm 31.38)\) OSCC, \(p=0.001\).

- p53 expression was more frequently seen in gingiva \((100\%)\), floor of mouth \((71\%)\), tongue \((70\%)\) and buccal mucosa \(64.5\%)\) and less in sites like hard palate \((50\%)\) and retro molar region \((50\%)\).

- There was no association between p53 expression and primary site of cancer \((p=0.964)\) in tobacco and betel quid chewers from northern India.

**Cyclin D1 Expression:**

- Cyclin D1 immunostaining was positive in 35 cases of oral cancer with a Cyclin D1 positivity of \(22.16\pm22.18\) \((\text{mean } \pm \text{SD})\) while there was no detectable Cyclin D1 expression in controls.

- The percentage of positive cases as well as Cyclin D1 positivity showed an increase as the grade of differentiation advanced.

- No significant association was found between Cyclin D1 positivity and degree of differentiation of tumors \((p=0.138)\).

- A significant difference in Cyclin D1 positivity was observed \((p=0.043)\) on comparing well differentiated \((16.61 \pm 17.89)\) and poorly differentiated \((37.0\pm32.51)\) OSCC, as well as between well differentiated \((16.61 \pm 17.89)\) and moderately differentiate OSCC \((24.38\pm21.93)\), \(p=0.002\). Similarly significant difference in Cyclin D1 positivity was observed on comparing moderately differentiated \((24.38\pm21.93)\) and poorly differentiated \((37.0\pm32.51)\) OSCC, \(p=0.043\).

- Cyclin D1 expression was more frequently seen in hard palate \((75\%)\), buccal mucosa \((67\%)\) and lip \((60\%)\) while expression of Cyclin D1 was less in sites like gingiva \((0\%)\), tongue \((40\%)\) and floor of mouth \((43\%)\).

- There was no association between Cyclin D1 expression and primary site of oral cancer \((p=0.528)\) in tobacco and betel quid chewers of northern India.
Genetic Susceptibility

One hundred blood samples of oral cancer patients with tobacco and betel quid chewing habit and 150 controls were evaluated by PCR-RFLP to study association of XRCCI Arg^{280}His, hOGGI Ser^{326}Cys, CYP2E1 Dral and CYP2E1 Rsal polymorphisms with oral cancer risk.

XRCCI Arg^{280}His polymorphism

- XRCCI Arg^{280}His Polymorphism was found to be associated significantly with risk of oral cancer in tobacco and betel quid chewers (p=.015).
- The individuals with variant genotypes (Arg/His, His/His) were at increased risk of oral cancer (OR= 1.63, 95% CI=1.1—2.413) as compared to individuals having wild type homozygous genotype (Arg/Arg).

hOGGI Ser^{326}Cys polymorphism

- hOGGI Ser^{326}Cys polymorphism was found to be significantly associated with the risk of oral cancer in tobacco and betel quid chewers (p=0.00).
- The individuals with the variant genotype (Ser/Cys or Cys/Cys) were at increased risk of oral cancer as compared to individuals having wild type genotype Ser/Ser (OR= 2.3, 95%CI= 1.5-3.61).

CYP2E1 Rsal Polymorphism

- CYP2E1 Rsal polymorphism was found to be significantly associated with the risk of oral cancer in tobacco and betel quid chewers (p=.001).
- The individuals with the variant genotype (C/C or A/C) were at increased risk of oral cancer as compared to individuals having wild type genotype A/A (OR= 2.0, 95% CI= 1.3-2.9).
CYP2E1 Dral Polymorphism

- CYP2E1 Dral polymorphism was found to be significantly associated with the risk of oral cancer in tobacco and betel quid chewers (p=0.049)

- The individuals with the variant genotype (D/C or C/C) were at increased risk of oral cancer as compared to individuals having wild type genotype D/D (OR= 1.37, 95% CI = 0.9-1.89).

Thus XRCCI Arg^{280}His, hOGGI Ser^{126}Cys, CYP2E1 Rsal and CYP2E1 Dral polymorphisms were associated with increased risk of oral cancer in tobacco and betel quid chewers in northern India.