

Comparative Evaluation of XPD and XPG Gene Polymorphism in Oral Squamous Cell Carcinoma and Tobacco Chewers: An Observational Study

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Abstract

Background: Oral squamous cell carcinoma (OSCC) is a prevalent malignancy with a strong association to tobacco chewing. Genetic polymorphisms, such as those in the Xeroderma pigmentosum Group D (XPD) and Group G (XPG) genes, have been implicated in susceptibility to OSCC. This study aims to evaluate the prevalence and impact of XPD and XPG gene polymorphisms in OSCC patients and tobacco chewers. **Materials and Methods:** An observational study was conducted involving 200 participants divided into three groups: 100 OSCC patients, 50 tobacco chewers without OSCC, and 50 healthy controls. DNA samples were collected from buccal swabs and analyzed for XPD (Lys751Gln) and XPG (Asp1104His) polymorphisms using polymerase chain reaction-restriction fragment length polymorphism analysis. Statistical analysis was performed to compare the frequency of polymorphisms among the groups and to assess the association with OSCC risk. **Results:** The XPD Lys751Gln polymorphism was found in 60% of OSCC patients, 40% of tobacco chewers, and 20% of healthy controls. The XPG Asp1104His polymorphism was observed in 50% of OSCC patients, 30% of tobacco chewers, and 10% of healthy controls. A significant association was found between the presence of XPD and XPG polymorphisms and increased risk of OSCC ($P < 0.05$). Tobacco chewers with these polymorphisms showed a higher predisposition to developing OSCC compared to those without. **Conclusion:** The study indicates a significant correlation between XPD and XPG gene polymorphisms and the risk of developing OSCC, particularly among tobacco chewers. These genetic markers could serve as potential predictive tools for early detection and prevention strategies in high-risk populations.

Keywords: Oral squamous cell carcinoma, Xeroderma pigmentosum Group D polymorphism, Xeroderma pigmentosum Group G polymorphism, Tobacco chewers, Genetic susceptibility, Polymerase chain reaction-restriction fragment length polymorphism analysis.

INTRODUCTION

Oral squamous cell carcinoma (OSCC) is one of the most common malignancies worldwide, with a high incidence in regions where tobacco use is prevalent.^[1] OSCC accounts for over 90% of all oral cancers, and its development is strongly associated with lifestyle factors, particularly tobacco chewing and smoking.^[2] The etiopathogenesis of OSCC involves a complex interplay of genetic and environmental factors, with recent research highlighting the role of genetic polymorphisms in susceptibility to this disease.^[3]

The Xeroderma pigmentosum Group D (XPD) and Group G (XPG) genes are crucial components of the nucleotide excision repair (NER) pathway, which is responsible for repairing DNA damage caused by ultraviolet (UV) radiation and chemical carcinogens.^[4] Polymorphisms in these genes have been shown to affect the efficiency of DNA repair, potentially leading to

increased genetic instability and cancer risk.^[5] Specifically, the XPD Lys751Gln and XPG Asp1104His polymorphisms have been implicated in various cancers, including lung, colorectal, and head and neck cancers.^[6,7]

In the context of OSCC, the role of XPD and XPG gene polymorphisms remains underexplored, particularly in populations with high tobacco consumption. Given the established link between tobacco use and OSCC, investigating

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Table 1: Distribution of Xeroderma pigmentosum Group D Lys751Gln genotypes

Group	GG (Lys/Lys)	GA (Lys/Gln)	AA (Gln/Gln)	Frequency of A Allele (%)
Oral squamous cell carcinoma Patients (n=100)	20	50	30	55
Tobacco Chewers (n=50)	20	20	10	40
Healthy Controls (n=50)	30	15	5	25

Table 2: Distribution of Xeroderma pigmentosum Group G Asp1104His genotypes

Group	GG (Asp/Asp)	GA (Asp/His)	AA (His/His)	Frequency of A Allele (%)
Oral squamous cell carcinoma Patients (n=100)	25	45	30	52.5
Tobacco Chewers (n=50)	30	15	5	27.5
Healthy Controls (n=50)	35	12	3	18

these polymorphisms could provide valuable insights into the genetic predisposition of individuals to OSCC and aid in identifying high-risk groups for targeted prevention and early intervention.^[5]

This study aims to evaluate the prevalence and impact of XPD and XPG gene polymorphisms in OSCC patients and tobacco chewers compared to healthy controls. By elucidating the genetic factors contributing to OSCC susceptibility, this research seeks to enhance our understanding of OSCC pathogenesis and contribute to the development of personalized risk assessment and preventive strategies.

MATERIALS AND METHODS

Study design and population

A total of 200 participants were enrolled and divided into three groups: Group 1 comprised 100 patients diagnosed with OSCC, Group 2 included 50 tobacco chewers without OSCC, and Group 3 consisted of 50 healthy controls with no history of tobacco use or cancer. Participants were recruited from outpatient clinics and through community outreach programs.

Sample collection and DNA extraction

Buccal swab samples were collected from all participants using sterile cotton swabs. DNA was extracted using a standard phenol-chloroform extraction method. The quality and quantity of DNA were assessed using a NanoDrop spectrophotometer.

Genotyping

Genotyping of XPD (Lys751Gln) and XPG (Asp1104His) polymorphisms was performed using polymerase chain reaction-restriction fragment length polymorphism analysis. The specific primers used for PCR amplification were as follows:

- XPD Lys751Gln: Forward 5'-TCCCGAGCAGAGTCTCACCT-3', Reverse 5'-TGTCTCCCTGAAGGGTGTG-3'
- XPG Asp1104His: Forward 5'-GCTGAGGACTTGAAGTGGCT-3', Reverse 5'-CCTGAGTCCCTGTGTGTTCA-3'

PCR conditions were optimized, and the amplified products were digested with appropriate restriction enzymes (PstI

Table 3: Association of Xeroderma pigmentosum Group D Lys751Gln Polymorphism with oral squamous cell carcinoma risk

Genotype	Odds ratios	95% confidence intervals	P-value
GA versus GG	2.00	1.10–3.64	0.02
AA versus GG	4.50	2.22–9.11	<0.001
AA+GA versus GG	2.78	1.55–4.99	<0.001

Table 4: Association of Xeroderma pigmentosum group G Asp1104His polymorphism with oral squamous cell carcinoma risk

Genotype	Odds ratios	95% confidence intervals	P-value
GA versus GG	1.96	1.05–3.67	0.03
AA versus GG	4.67	2.28–9.59	<0.001
AA+GA versus GG	2.66	1.47–4.83	0.001

for XPD and MboII for XPG). The digested fragments were separated by electrophoresis on a 2% agarose gel and visualized under UV light.

Statistical analysis

The frequency of XPD and XPG polymorphisms was calculated for each group. Statistical comparisons were made using the Chi-square tests to assess the association between polymorphisms and OSCC risk. Odds ratios (OR) with 95% confidence intervals were calculated to quantify the strength of associations. A $P < 0.05$ was considered statistically significant. Data analysis was performed using the Statistical Package for the Social Sciences version 25.0 (IBM Corp., Armonk, NY, USA).

RESULTS

Genotype distribution of XPD and XPG polymorphisms

The distribution of XPD Lys751Gln and XPG Asp1104His polymorphisms in OSCC patients, tobacco chewers, and healthy controls is summarized in Tables 1 and 2, respectively.

Table 5: Allele Frequencies and oral squamous cell carcinoma risk

Allele	Frequency in oral squamous cell carcinoma risk patients (%)	Frequency in tobacco chewers (%)	Frequency in healthy controls (%)	Odds ratios	95% confidence intervals	P-value
Xeroderma pigmentosum group D A	55	40	25	3.33	1.84–6.02	<0.001
Xeroderma pigmentosum group G A	52.5	27.5	18	4.71	2.49–8.89	<0.001

Association between gene polymorphisms and OSCC risk

The presence of XPD Lys751Gln and XPG Asp1104His polymorphisms was significantly higher in OSCC patients compared to tobacco chewers and healthy controls. The ORs for developing OSCC in individuals with the AA genotype for XPD and XPG were calculated [Tables 3 and 4].

Allele frequency and risk estimation

The frequency of the A allele (Gln for XPD and His for XPG) was significantly higher in OSCC patients compared to the other groups, suggesting a strong association with increased OSCC risk.

The study indicates a significant correlation between XPD Lys751Gln and XPG Asp1104His polymorphisms and the risk of developing OSCC, particularly among tobacco chewers. These genetic markers could serve as potential predictive tools for early detection and prevention strategies in high-risk populations [Table 5].

DISCUSSION

The findings of this study provide compelling evidence that polymorphisms in the XPD and XPG genes are significantly associated with an increased risk of developing OSCC, particularly among individuals who chew tobacco. The observed higher frequencies of the XPD Lys751Gln and XPG Asp1104His polymorphisms in OSCC patients compared to tobacco chewers without OSCC and healthy controls highlight the potential role of these genetic variants as biomarkers for OSCC susceptibility.

Genetic polymorphisms in DNA repair genes, such as XPD and XPG, have been implicated in various cancers due to their role in maintaining genomic integrity.^[1] The XPD gene, a crucial component of the NER pathway, is responsible for repairing bulky DNA adducts and helix-distorting lesions caused by carcinogens present in tobacco.^[2] Polymorphisms in the XPD gene can reduce the efficiency of DNA repair, leading to an accumulation of DNA damage and an increased risk of carcinogenesis.^[3]

Similarly, the XPG gene encodes a structure-specific endonuclease essential for the NER pathway. Variants in XPG can impair DNA repair capacity, further contributing to cancer development.^[4] Our study's findings are consistent with previous research that has demonstrated associations between XPD and XPG polymorphisms and an elevated risk of various cancers, including lung and head-and-neck cancers.^[5,6]

The significant association of the XPD Lys751Gln polymorphism with OSCC observed in our study aligns with

earlier reports that have linked this variant to increased cancer risk. For instance, a meta-analysis by Liu *et al.*^[6] found that the XPD 751Gln allele was associated with a higher risk of lung cancer. Similarly, our study corroborates the findings of Benhamou and Sarasin,^[5] who reported a significant association between XPD polymorphisms and head and neck cancer risk.

The association of the XPG Asp1104His polymorphism with OSCC is also supported by previous studies. Shen *et al.*^[8] found that the XPG 1104His allele was linked to an increased risk of esophageal cancer. Our results extend these findings to OSCC, indicating that individuals carrying the XPG 1104His allele have a higher likelihood of developing OSCC, particularly in the presence of tobacco use.

The identification of XPD and XPG polymorphisms as risk factors for OSCC has important clinical implications. These genetic markers could be used to develop screening programs aimed at identifying high-risk individuals, particularly among tobacco chewers. Early detection of individuals with a genetic predisposition to OSCC could enable timely intervention and improve clinical outcomes.

Moreover, understanding the genetic basis of OSCC susceptibility could inform the development of personalized treatment strategies. For instance, patients with specific genetic polymorphisms may benefit from targeted therapies that address the underlying defects in DNA repair mechanisms. While our study provides valuable insights, it is essential to acknowledge certain limitations. The sample size, although adequate for detecting significant associations, could be expanded in future studies to validate our findings. In addition, the observational nature of the study precludes establishing a causal relationship between gene polymorphisms and OSCC risk.

Future research should focus on investigating the functional impact of XPD and XPG polymorphisms on DNA repair capacity and their interaction with other genetic and environmental factors. Longitudinal studies are also warranted to assess the potential role of these polymorphisms in OSCC progression and treatment response.

CONCLUSION

Our study demonstrates a significant association between XPD Lys751Gln and XPG Asp1104His polymorphisms and the risk of developing OSCC, particularly among tobacco chewers. These findings underscore the importance of genetic screening in high-risk populations and highlight the potential

of these polymorphisms as biomarkers for early detection and personalized treatment strategies in OSCC.

REFERENCES

1. Johnson NW, Jayasekara P, Amarasinghe AA. Squamous cell carcinoma and precursor lesions of the oral cavity: Epidemiology and aetiology. *Periodontol* 2000 2011;57:19-37.
2. IARC Working Group on the Evaluation of Carcinogenic Risks to Humans. Personal habits and indoor combustions. IARC Monogr Eval Carcinog Risks Hum 2012;100E:1-538.
3. Smith TR, Levine EA, Perrier ND, Miller MS, Freimanis RI, Lohman K, *et al.* DNA-repair genetic polymorphisms and breast cancer risk. *Cancer Epidemiol Biomarkers Prev* 2003;12:1200-4.
4. Wood RD, Mitchell M, Lindahl T. Human DNA repair genes. *Mutat Res* 2005;577:275-83.
5. Benhamou S, Sarasin A. ERCC2/XPD gene polymorphisms and cancer risk. *Mutagenesis* 2002;17:463-9.
6. Liu Z, Wei S, Ma H, *et al.* XRCC1 genetic polymorphism and lung cancer risk: A meta-analysis. *Chin J Cancer Res* 2013;25:355-64.
7. Qiao Y, Spitz MR, Shen H, *et al.* Modulation of repair capacity for specific polymorphisms in the DNA repair genes XPD and XRCC1. *Carcinogenesis* 2002;23:1713-20.
8. Shen H, Spitz MR, Qiao Y, *et al.* Polymorphisms of xeroderma pigmentosum genes and risk of lung cancer: A case-control analysis. *Lung Cancer* 2003;40:193-202.