Research Article

Association of polymorphisms of xeroderma pigmentosum complementation group D gene with cervical cancer in Maharashtrian population: A case-control study

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ABSTRACT

Background: Maharashtrian population is at the risk of cervical cancer (CC) and is not subjected to investigate the cancer susceptibility in association with genetic determinants. **Objectives:** This study was aimed to evaluate the association of single nucleotide polymorphisms (SNPs) in DNA repair gene xeroderma pigmentosum complementation group D (XPD) with CC risk from rural Maharashtra. **Materials and Methods:** We used polymerase chain reaction and-restriction fragment length polymorphism to analyze SNPs in XPD gene from 350 patients with CC and 400 age and sex-matched disease-free controls. **Results:** The results indicated no significant difference in the genotype distribution between CC patients and controls for the XPD gene at codon 156 of exon 6 and codon 751 of exon 23, but the results showed that allele frequencies of XPD Asn 312 of codon 312 of exon 10 (odds ratio = 0.31; 95% confidence intervals = [0.16–0.63]; P = <0.001) genotype showed negative association with CC risk. **Conclusion:** This study indicated the role of XPD (cd312) in modifying genetic susceptibility of an individual to CC in Maharashtrian patients.

KEY WORDS: Cervical Cancer; Genetic Polymorphism; Xeroderma Pigmentosum Complementation Group D; Polymerase Chain Reaction and Restriction Fragment Length Polymorphism

INTRODUCTION

Cervical cancer (CC) is a leading health problem worldwide, particularly a serious burden in developing countries including India. Over the past few years, it was observed that millions of women are diagnosed with CC, and thousands of deaths have been reported every year due to this deadly disease from different parts of India. It is universally concerned that the etiologic factors involved in cervical carcinogenesis could be either a combination of reproductive factors such as sexual habits like age at intercourse, sexual partners, multiple pregnancies, tobacco and drinking habits, use of oral contraceptives or infection with human papillomavirus (HPV), or other sexually transmitted diseases. Although the impact of such etiologic risk factors related to CC development, only small portion of women develops CC which suggests that other endogenic factors such as genetic determinants may also contribute to the development of CC. Identification of such genetic determinants associated with CC may contribute to understand mechanisms behind the development of cancer. The exogenous risk factors such as tobacco, alcohol or infection with oncogenic HPV cause the formation of deoxyribonucleic acid (DNA) lesions. Till now, more than 100 molecules in several DNA repair mechanisms have been reported which helps in

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the maintenance of individual's genomic integrity and genetic stability. Base excision repair (BER), nucleotide excision repair (NER), double strand repair, and DNA mismatch repair are the four major pathways involved in DNA repair mechanism.

Xeroderma pigmentosum complementation group D (XPD) is a major component of the NER pathway which involved in recognition and repair of a variety of bulky DNA lesions such as pyrimidine dimmers or other chemical or photo adducts.[1] Genetic polymorphisms in the NER pathway genes have been associated with individual's susceptibility to develop cancer. Number of such polymorphisms in DNA repair genes has been frequently studied and some of them were evidenced to be concerned with cancer risk with significance. XPD is highly polymorphic gene and about 17 single nucleotide polymorphisms (SNPs) have been reported in this gene, of which six were found in exons and 11 in introns which occurred in codons 156 (rs238406), 312 (rs1799793), and 751(rs13181) are common.[2] Earlier studies investigated the association of polymorphisms of XPD and head and neck,[3,4] oesophagus,[5] lung,[6,7] and breast cancer,[8] but some of the studies produced contradictory or an inconclusive results which found no involvement of XPD genotypes in breast cancer.[9,10] Similarly, studies were carried out on polymorphisms of XPD and its association with various cancers including bladder,[11] prostate,[12,13] breast,[8] and lung cancer[14] in Indian population. Some of the studies from Indian population produced insignificant results showing a negative association of XPD polymorphisms with prostate,[15] lung,[16] and gastric cancer risk.[17] Few studies have also investigated the probable association between the risk of CC and polymorphisms in XPD but previous interpretations were inconsistent in terms of their role in CC susceptibility.[18,19]

To the best of our knowledge, studies on SNPs in XPD and their association with CC risk in Indian population are missing. Therefore, we hypothesized that the polymorphisms in three sites of XPD gene (Arg156Arg, Asp312Asn, and Lys751Gln) might contribute to etiology of CC. To test this hypothesis, we proposed a hospital based case–control study to investigate the SNPs in XPD and their association with risk of CC in Maharashtrian population. We genotyped these three polymorphisms; (A) XPD C22541A at codon 156 of the exon 6, (B) XPD G23592A at codon 312 in the exon 10, and (C) XPD A35931C at codon 751 in the exon 23 from 350 patients with CC and 400 controls to evaluate their association with CC development in a population from Southwestern Maharashtra region of India.

MATERIALS AND METHODS

Study Subjects

A total of 350 newly diagnosed CC patients and 400 healthy, cancer-free, age-matched females as controls were included in this study. All cases ranged in age from 20 to 80 years (mean ± standard deviation [SD]) (48.67 ± 13.78) were recruited immediately after being diagnosed during the year 2014–2017.

Place of Study

This study was conducted in Krishna Institute of Medical Sciences "Deemed to be University" from Southwestern Maharashtra of India.

Selection of Cases and Controls

Incidence cases of CC were identified using colposcopy at Department of Obstetrics and Gynecology of the Krishna Hospital and Medical Research Centre (KH and MRC) and cell cytology at Department of Pathology of Krishna Institute of Medical Sciences. Controls were randomly selected from a group of women visiting to KH and MRC for blood donation and other purposes.

Inclusion and Exclusion Criteria

Relatives of cases with prior history of cancer were excluded from the study. All 100% of cases and controls agreed to provide a blood sample included.

Genomic DNA Isolation from Whole Blood

Genomic DNA was extracted from 5 ml of blood using blood genomic DNA extraction and purification Kit (Invitrogen Life Technologies).

Genotyping Assays

Genotyping assay was performed by polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP). Oligonucleotides used to amplify the polymorphic sites of interest were: (A) XPD C22541A at codon 156 of the exon 6(rs238406), (B) XPD G23592A at codon 312 in the exon 10 (rs1799793), and (C) XPD A35931C at codon 751 in the exon 23(rs13181). The primers selected to amplify the specific SNPs of interest were; Forward 5'- TGG AGT GCT ATG GCA CGA TCT CT -3'; Reverse 5'-5'- CCA TGG GCA TCA AAT TCC TGG GA -3' for codon 156; Forward 5'-CTG TTG GTG GGT GCC CGT ATC TGT TGG TCT-3', Reverse 5′-TAA TAT CGG GGC TCA CCC TGC AGC ACT TCC T- 3' for codon 312, and Forward 5'- GCC CGC TCT GGA TTA TAC G -3'; Reverse 5'- CTA TCA TCT CCT GGC CCC C -3' for codon 751. The PCR amplifications were performed in separate reactions of 20 micro liter (μL) reaction volumes containing 0.2 μg of genomic DNA, 10 picomoles of each above mentioned primers, 200 μm each dNTPs, 10 mili molar (mM) Tris-HCl (pH 9.0), 50 mM KCl 1.5 mM MgCl2, and 1 unit of Taq DNA polymerase (GeNei, Merck Biosciences). The amplification with different PCR conditions was carried out in a thermal cycler (Eppendorf). The conditions for PCR of XPD codon 156 of 644 bp (denaturation at 95°C–5 min, 30 cycles of 95°C–30 s, 60°C–30 s, 72°C–30 s,

Table 1: Distribution of selected demographic variables of CC cases and healthy controls

Variable	Cases *n*=350	Controls *n*=400	*P*-value based on χ^2
Age (mean±SD) years	48.67±13.78	46.37±13.90	0.03
	***n* (%)**	***n* (%)**	
≤50	215 (61.40)	284 (71.00)	
51–60	59 (16.90)	69 (17.20)	
61–70	57 (16.30)	34 (08.50)	
>70	19 (5.40)	13 (03.20)	
Tobacco smoking status			<0.001
Tobacco users	189 (54.00)	113 (28.20)	
Tobacco no users	161 (46.00)	287 (71.80)	
Age at first pregnancy (years)			<0.001
15–20	276 (78.90)	181 (45.25)	
21–25	73 (20.90)	178 (44.50)	
26–30	00 (0.00)	36 (9.00)	
31–35	01 (0.20)	05 (01.25)	
Diet			0.59
Vegetarian	97 (27.70)	118 (29.50)	
Mixed	253 (72.30)	282 (70.50)	
Education			<0.001
High School	139 (39.71)	108 (27.00)	
High School graduate (12 years)	24 (06.86)	49 (12.25)	
College/graduate	43 (12.29)	129 (32.25)	
No school	144 (41.14)	114 (28.50)	
Economic status			<0.001
Poor	198 (56.58)	132 (33.00)	
Middle	97 (27.71)	161 (40.25)	
Rich	55 (15.71)	107 (26.75)	
Family history of cancer			<0.001
Yes	62 (17.71)	10 (02.50)	
No	288 (82.29)	390 (97.50)	

SD: Standard deviation

and final extension at 72°C–10 min), XPD codon 312 of 751bp, 95°C–5 min, 35 cycles of 95°C–30 s, 62°C–45 s, 72°C–30 s, 72°C–10 min, and XPD codon 751 of 436 bp (95°C–5 min, 30 cycles of 95°C–30 s, 55°C–30 s, 72°C–45 s, and 72°C–10 min). After confirmation of the amplification of specific fragments by agarose gel electrophoresis, each PCR products were allowed for restriction digestion with specific restriction enzymes (Fermentas, Thermo Fisher Scientific USA) at 37°C. 2 units of TfiI, StyI, and PstI restriction endonucleases were used, respectively, for digestion of 644, 751, and 436 bp of exon 6, 10, and 23 of XPD gene. The restriction digested PCR products were resolved on 2.0% agarose gels, documented with transilluminator system (BioRad Laboratories).

Statistical Analysis

The association between the XPD genotypes and risk of CC development were studied using odds ratio (OR). Both the univariate and multivariate logistic regression analyses were employed to calculate the adjusted ORs and 95% confidence intervals (CIs) with adjustment of variables to determine the CC risk associated with genotypes. The differences in the distribution between cases and controls were tested using the Chi-square test.

Ethics and Biosafety

Ethics approval for the use of human subjects in research by Institutional Ethics and Biosafety Committee of Krishna Institute of Medical Sciences "Deemed to be University."

RESULTS

A total of 350 patients and 400 cancer-free controls were included in the study. The characteristics of the study participants are summarized in Table 1. The mean ± SD age of cases and controls was 48.67 ± 13.78 (median: 50 and

range 25–75) and controls 46.37 ± 13.90 (median: 33.5 and range 24–75) years, respectively.

Association between SNPs of XPD Gene and Risk of CC

We have analyzed the distribution and association between the previously described polymorphisms of cd156 (silent nucleotide substitution), cd312 and cd751 (non-conservative amino acid substitutions) in XPD gene of rural Maharashtrian population. The distribution of XPD genotypes and the concordance of the polymorphisms in patients with CC and controls are presented in Table 2.

Analysis of the XPD C22541A codon 156 exon 6

The association of XPD genotypes and CC risk is shown in Table 2. The frequency of wild-type *XPD 22541*CC homozygotes was 31.43% in patients and 36.25% in controls whereas the variant XPD22541A allele was lower in the cases (15.71%) than in the controls (17.50%). The frequency of *XPD22541 CA* heterozygotes was 52.86% in cases and 46.25% in controls [Table 2]. Thus, the C→A polymorphisms in exon 6 do not result in change at codon 156 in cases as well as controls.

Analysis of the XPD G23592A codon 312 exon 10

Table 2 showed the distribution of genotypes and frequency of G23592A polymorphisms in patients with CC and controls. The G>A polymorphism in codon 312 of the exon 10 results in Asp>Asn substitution. The frequency of *XPD 23592GG* homozygotes was 85.43% in cases and 49.50% in controls whereas *23592AA* homozygote was 03.71% in cases and 06.75% in controls. The frequency of *23592GA* heterozygotes was 10.86% in cases and 43.75% in controls [Table 2]. Compared to *23592GG* genotype, the variant genotype *23592AA* genotype was negatively associated with CC risk (OR = 0.31; 95% CI = [0.16–0.63]; P = 0.001). The 23592 variants XPD gene are extremely lower and do not contribute to the CC risk in the population of Maharashtra.

Analysis of the XPD A35931C codon 751 exon23

The PCR of XPD codon 751 produced in the product of 436 bp. The PCR amplified products when digested with PstI, yielded wild-type (*35931A*) alleles of 290, 146 bp fragments, and the polymorphic (C) allele produces three fragments of 227, 146, and 63 bp [Figure 1]. The A→C polymorphism in exon 23 at nucleotide position 35931 gives rise to the amino acid substitution Lys→Gln in the codon 751. Table 2 displays the distribution of genotypes and frequency of alleles of the A35931C polymorphisms in patients with CC and controls. The frequency of the XPD 35931C allele in cases was higher (6.28%) than the controls (8.00%).

Association of age at cancer occurrence, tobacco status, and age at first pregnancy with CC risk

The association between XPD and the risk of CC was further examined after stratification of confounding factors such as age, age at first pregnancy and tobacco chewing status. In Maharashtrian patients, the age of CC beginning is 30 years, considerably lesser than reported in other reports. To assess the relationship of analyzed polymorphisms with the age at occurrence of CC, we grouped the patients as ≤50 (n = 95) or >50 (n = 75) years of age and compared with age-matched controls which surprisingly showed that the XPD cd 312 (OR = 0.24; CI = 0.12–0.46); $P < 0.0001$) displayed negative risk of CC at the age below 50. Furthermore, the association of CC with first delivery age was reviewed in this study which showed that 15–20 years age of first delivery, considerably associated with increased CC risk. The distribution of genotype polymorphisms along with the statistical analysis is shown in Table 3.

Table 2: The genotype frequencies of XPD gene variants in untreated CC patients and controls

Gene	Genotype	Cases (n=350) (%)	Control n=400 (%)	OR (95% CI)	P value	Adjusted OR (95% CI)	P value
XPD Arg156Arg codon 156 Ex-6 C22541Ars238406	CC/CC	110 (31.43)	145 (36.25)	1		1	
	CC/AA	185 (52.86)	185 (46.25)	1.31 (0.95–1.81)	0.09	1.32 (0.95–1.84)	0.95
	AA/AA	55 (15.71)	70 (17.50)	1.03 (0.67–1.59)	0.87	1.06 (0.67–1.67)	0.78
	CC/AA+AA/AA	240 (68.57)	255 (63.75)	1.24 (0.91–1.68)	0.16	1.27 (0.93–1.74)	0.12
XPD Asp312Asn codon312 Ex-10 G23591A rs1799793	GG/GG	299 (85.43)	198 (49.50)	1		1	
	GG/AA	38 (10.86)	175 (43.75)	0.14 (0.09–0.21)	0.0001*	0.42 (0.28–0.65)	0.001
	AA/AA	13 (3.71)	27 (6.75)	0.31 (0.16–0.63)	0.001*	0.23 (0.12–0.45)	0.001
	GG/AA+AA/AA	51 (14.57)	202 (50.50)	0.16 (0.11–0.23)	0.0001*	0.35 (0.24–0.51)	0.001
XPD Lys751Gln codon751 Ex-23 A35931C rs13181	AA/AA	155 (44.29)	187 (46.75)	1		1	
	AA/CC	173 (49.43)	181 (45.25)	1.15 (0.85–1.55)	0.34	1.09 (0.80–1.50)	0.56
	CC/CC	22 (6.28)	32 (8.00)	0.82 (0.46–1.48)	0.52	0.82 (0.44–1.50)	0.52
	AA/CC+CC/CC	195 (55.14)	213 (53.25)	1.10 (0.82–1.47)	0.49	1.08 (0.80–1.46)	0.59

*Indicates significant OR (P<0.001), P value determined based on χ^2, XPD: Xeroderma pigmentosum complementation group D, OR: Odds ratio, CI: Confidence interval, CC: Cervical cancer

DISCUSSION

This study was proposed to investigate the relationship between reported SNPs of XPD and the elevated risk for CC particularly in the parts of western Maharashtra. We determined the genotypic frequency of polymorphisms of (A) XPD C22541A at codon 156 of the exon 6, (B) XPD G23592A at codon 312 in the exon 10, and (C) XPD A35931C at codon 751 in the exon23. The frequency of allele of the XPD polymorphisms at 22541 (C-A), 23592 (G-A), and 35931 (A-C) did not show much variation with the CC risk in the western Maharashtrian population. We found a negative association of SNPs of XPD codon 312 at Asp 312 Asn polymorphism with CC risk.

Earlier few researchers reported reduced DNA repair capacity due to 312Asn genotypes for various cancers including bladder,[20] prostate,[13] and lung cancer.[14] Furthermore, the Lys751Gln T > G, rs13181 SNP at codon 751 of exon 23 of XPD causes a non-synonymous substitution which had been studied for its role in the susceptibility of various cancers.[5,6,8,21] Although a number of polymorphisms reported in codons 156, 312, and 751 of exon 6, 10, and 23 which are common in XPD gene,[2] we did not find any report stating association of XPD codon 156 with the development of any cancer type. In our study, the frequency of Asn allele XPD 312 was 0.03 that of XPD 156 allele Arg was 0.15 and that frequency of XPD 751 allele Gln was 0.06 which were to some extent different from other reports. The investigations into the relationship between polymorphisms in XPD gene and susceptibility to cancer have not yet produced consistent results in different populations. Number of studies highlighted the role of XPD polymorphisms in cancer susceptibility including, lung,[5] prostate,[12] breast,[8] and head and neck cancer[3,4] among different ethnic populations, whereas other studies failed to find positive association of XPD polymorphism in the head and neck cancer[22] or breast carcinoma.[9,10] Furthermore, few studies from Northern and Southern India have reported the SNPs in the XPD in relation to a variety of cancer risks including bladder,[11] lung,[14] prostate,[13] and breast cancer[8] whereas some studies showed negative association of SNPs of codon 312 and codon 751 in the XPD gene with development of prostate,[15] lung,[16] and gastric cancer.[17] Thus, these earlier interpretations suggested that SNPs (rs238406, rs1799793, and rs13181) of XPD may or may not involve in cancer susceptibility, but our earlier studies showed positive evidence for XPD gene at position 23592 of codon 312 of exon 10 polymorphism associated with the risk of breast cancer[23] and polymorphism in BER pathway gene associated with head and neck cancer risk.[24]

However, there were no reports available on the relationship between SNPs of NER pathway genes including XPD and their susceptibility to CC in Maharashtra where the prevalence of CC cases is high. Therefore, we investigated the development of CC and association of polymorphisms in XPD gene from Maharashtrian population which showed negative association XPD gene (SNP rs1799793) at codon 312 in the exon 10 which may play a role in cervical carcinogenesis in Maharashtrian women. Such type of analysis will enhance our skill to categorize susceptible individuals for cervical carcinogenesis in the studied population. Although the study is first in the medical literature to investigate and to show the association of polymorphism in XPD and CC occurrence, it showed similar outcome as mentioned in the above studies.

CONCLUSION

Our results showed that the XPD gene at position 23592 of codon 312 of exon 10 polymorphism negatively associated with the risk of CC. This analysis of correlation of DNA

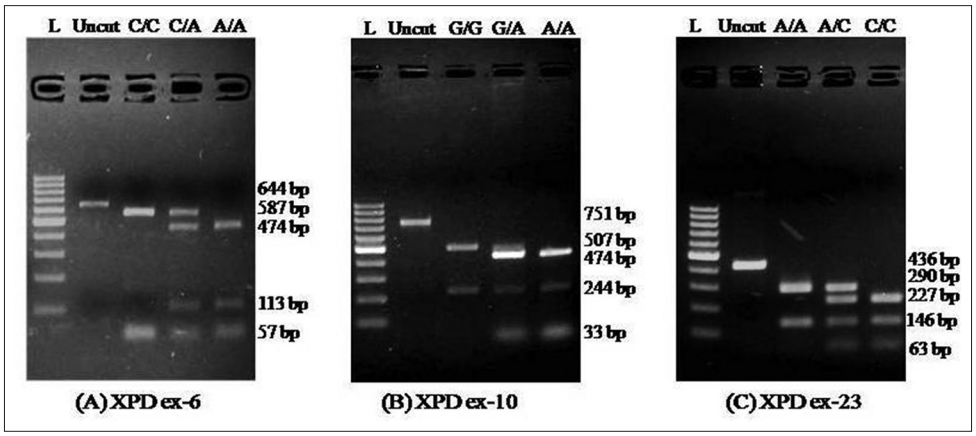

Figure 1: Representative agarose gel image showing nucleotide polymorphism by polymerase chain reaction (PCR) restriction fragment length polymorphism of (a) xeroderma pigmentosum complementation group D (XPD) C22541A at codon 156 of the exon 6 (lane 1: 100bp DNA ladder, lane 2: Uncut PCR product, lane 3: Wild-type allele, lane 4: Heterozygote, and lane 5: Variant allele), (b) XPD G23592A at codon 312 in the exon 10 (Lane 1: 100bp DNA ladder, lane 2: Uncut PCR product, lane 3: Asp/Asp genotype lane 4: Asp/Asn genotype, and lane 5: Cys/Cys genotype), and (c) XPD A35931C at codon 751 in the exon 23 (lane 1: 100bp DNA ladder, lane 2: Uncut PCR product, lane 3: Lys/Lys genotype lane 4: Lys/Gln genotype, and lane 5: Gln/Gln genotype)

Table 3: Stratification analysis of the demographic factors including age, tobacco smoking, age at first pregnancy, and distribution of genotypes of the XPD gene in the patients with CC and the control group from population of Maharashtra

Gene	Genotype	Demographic factors							
		Age (cases/control)		Tobacco status (cases/control)			Age at first pregnancy (cases/control)		
		≤50 *n*=216/286	>50 *n*=134/114	Users *n*=189/113	Non-users *n*=161/287	15–20 *n*=277/183	21–5 *n*=72/178	26–30 *n*=0/34	31–35 *n*=1/5
XPD Arg156Arg codon 156 Ex-6 C22541A rs238406	CC/CC	70/98	40/47	61/44	49/101	87/66	23/63	0/13	0/3
	CC/AA+AA/AA	146/188	94/67	128/69	112/186	190/117	49/115	0/21	1/2
	OR (95% CI)	1.08 (0.74–1.58)	1.64 (0.97–2.78)	1.33 (0.82–2.17)	1.24 (0.8–1.87)	1.23 (0.83–1.82)	1.16 (0.65–2.09)	0.62 (0.01–33.55)	4.2 (0.11–151.9)
	P value	0.66	0.06	0.24	0.30	0.29	0.60	0.81	0.43
XPD Asp312Asn codon312 Ex-10 G23591A rs1799793	GG/GG	181/125	118/73	168/73	131/125	240/57	59/112	0/25	0/4
	GG/AA+AA/AA	35/161	16/41	21/40	30/162	37/126	13/66	0/9	1/1
	OR (95% CI)	0.15 (0.09–0.23)	0.24 (0.12–0.46)	0.22 (0.12–0.41)	0.17 (0.11–0.28)	0.06 (0.04–0.11)	0.37 (0.19–0.73)	2.68 (0.05–145.11)	9.0 (0.22–362.5)
	P value	0.0001	0.0001	0.0001	0.0001	0.0001	0.004	0.62	0.24
XPD Lys751Gln codon751 Ex-23 A35931C rs13181	AA/AA	88/143	67/44	90/51	65/136	128/74	27/86	0/25	0/2
	AA/CC+CC/CC	128/143	67/70	99/62	96/151	149/109	45/92	0/9	1/3
	OR (95% CI)	1.45 (1.01–2.07)	0.62 (0.37–1.04)	0.90 (0.56–1.44)	1.33 (0.89–1.96)	0.79 (0.54–1.15)	1.55 (0.88–2.72)	56.36 (3.00–100.10)	2.14 (0.05–77.54)
	P value	0.03	0.07	0.67	0.15	0.22	0.12	0.007	0.67

OR: Odds ratio, CI: Confidence interval, CC: Cervical cancer, XPD: Xeroderma pigmentosum complementation group D

repair genes and CC may provide a deeper insight into the genetic factors to CC risk in the unexplored population. Furthermore, this study is the first of its kind to report the combined effect of SNPs of the XPD gene on the risk of CC in Maharashtrian population.

REFERENCES

1. Chen JZ, Kadlubar FF. A new clue to glaucoma pathogenesis. Am J Med 2003;114:697-8.
2. Benhamou S, Sarasin A. ERCC2/XPD gene polymorphisms and lung cancer: A HuGE review. Am J Epidemiol 2005;161:1-4.
3. Kietthubthew S, Sriplung H, Au WW, Ishida T. Polymorphism in DNA repair genes and oral squamous cell carcinoma in Thailand. Int J Hyg Environ Health 2006;209:21-9.
4. Wang Y, Spitz MR, Lee JJ, Huang M, Lippman SM, Wu X, *et al*. Nucleotide excision repair pathway genes and oral premalignant lesions. Clin Cancer Res 2007;13:3753-8.
5. Yuan L, Cui D, Zhao EJ, Jia CZ, Wang LD, Lu WQ, *et al*. XPD lys751Gln polymorphism and esophageal cancer risk: A meta-analysis involving 2288 cases and 4096 controls. World J Gastroenterol 2011;17:2343-8.
6. Zhan P, Wang Q, Wei SZ, Wang J, Qian Q, Yu LK, *et al.* ERCC2/XPD lys751Gln and asp312Asn gene polymorphism and lung cancer risk: A meta-analysis involving 22 case-control studies. J Thorac Oncol 2010;5:1337-45.
7. Pramanik S, Devi S, Chowdhary S, Surendran ST, Krishnamurthi K, Chakrabarti T, *et al*. DNA repair gene polymorphisms at XRCC1, XRCC3, XPD, and OGG1 loci in Maharashtrian population of central India. Chemosphere 2011;82:941-6.
8. Samson M, Singh SS, Rama R, Sridevi V, Rajkumar T. XPD lys751Gln increases the risk of breast cancer. Oncol Lett 2011;2:155-9.
9. Romanowicz-Makowska H, Sobczuk A, Smolarz B, Fiks T, Kulig A. XPD lys751Gln polymorphism analysis in women with sporadic breast cancer. Pol J Pathol 2007;58:245-9.
10. Shore RE, Zeleniuch-Jacquotte A, Currie D, Mohrenweiser H, Afanasyeva Y, Koenig KL, *et al.* Polymorphisms in XPC and ERCC2 genes, smoking and breast cancer risk. Int J Cancer 2008;122:2101-5.
11. Sobti RC, Kaur S, Sharma VL, Singh SK, Hosseini SA, Kler R, *et al.* Susceptibility of XPD and RAD51 genetic variants to carcinoma of urinary bladder in North Indian population. DNA Cell Biol 2012;31:199-210.
12. Sobti RC, Berhane N, Melese S, Mahdi SA, Gupta L, Thakur H, *et al.* Impact of XPD gene polymorphism on risk of prostate cancer on North Indian population. Mol Cell Biochem 2012;362:263-8.
13. Mittal RD, Mandal RK. Genetic variation in nucleotide excision repair pathway genes influence prostate and bladder cancer susceptibility in North Indian population. Indian J Hum Genet 2012;18:47-55.
14. Lawania S, Singh N, Behera D, Sharma S. Xeroderma pigmentosum complementation group D polymorphism toward lung cancer susceptibility survival and response in patients treated with platinum chemotherapy. Future Oncol 2017;13:2645-65.
15. Tabrez ZS, Vijayalakshmi PS, Venkataramanan SS. Prostate cancer: Role of XRCC1 and XPD gene polymorphisms in South Indian patients. Ind J Urol 2008;24:pS8-S8.
16. Saikia BJ, Phukan RK, Sharma SK, Sekhon GS, Mahanta J. Interaction of XRCC1 and XPD gene polymorphisms with lifestyle and environmental factors regarding susceptibility to lung cancer in a high incidence population in North East India. Asian Pac J Cancer Prev 2014;15:1993-9.
17. Nissar B, Kadla SA, Khan NS, Shah IA, Majid M, Afshan F, *et al*. DNA repair gene XRCC1 and XPD polymorphisms and gastric cancer risk: A case-control study outcome from Kashmir, India. Anal Cell Pathol 2018;3806514:8.
18. He X, Ye F, Zhang J, Cheng Q, Shen J, Chen H. Susceptibility of XRCC3, XPD and XPG genetic variants to cervical carcinoma. Pathobiology 2008;75:356-63.
19. Yilmaz E, Celik O, Celik E, Turkcuoglu I, Simsek Y, Karaer A, *et al.* XPD and XRCC1 gene polymorphism in patients with normal and abnormal cervical cytology by pap smear. Eur Rev Med Pharmacol Sci 2012;16:1713-8.
20. Gangwar R, Ahirwar D, Mandhani A, Mittal RD. Influence of XPD and APE1 DNA repair gene polymorphism on bladder cancer susceptibility in North India. Urology 2009;73:675-80.
21. Mitra AK, Singh N, Garg VK, Chaturvedi R, Sharma M, Rath SK, *et al*. Statistically significant association of the single nucleotide polymorphism (SNP) rs13181 (ERCC2) with predisposition to squamous cell carcinomas of the head and neck (SCCHN) and breast cancer in the North Indian population. J Exp Clin Cancer Res 2009;28:104.
22. Bau DT, Tsai MH, Huang CY, Lee CC, Tseng HC, Lo YL, *et al.* Relationship between polymorphisms of nucleotide excision repair genes and oral cancer risk in Taiwan: Evidence for modification of smoking habit. Chin J Physiol 2007;50:294-300.
23. Datkhile KD, Bhosale SJ, Patil MN, Kakade SV. Genetic polymorphisms of DNA repair gene (XPD) and breast cancer risk in a hospital based case-control study from Maharashtra. Int J Health Sci Res 2017;7:290-8.
24. Datkhile KD, Patil MN, Khamkar TS, Vhaval RD, Durgawale PP, Chougule PG, *et al*. Geneic polymorphisms in DNA repair genes (hOGG1 & APE1) and their association with oral cancer susceptibility in rural Indian population: A hospital based case-control study. Int J Med Sci Public Health 2017;6:23-8.

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