"Molecular Characterization And Its Association To Ap Endonuclease-1 (Ape1) And X-Ray Cross-Complementing Group 1 (Xrcc1), As A Dna Repair Protein From Patients With The Risk Of Age-Related Cataract At A Tertiary Care Centre, Uttar Pradesh"

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Abstract

Introduction: Age-related cataract is the leading cause of blindness in the world. (AP)-endonuclease APE1 and the X-ray cross-complementing group 1 (XRCC1) are the key enzymes taking part in the repair of DNA damage. The association of X-ray cross-complementing group 1 (XRCC1) and AP endonuclease-1 (APE1) plays a critical role as polymorphisms of DNA repair genes decreasing the ability to repair DNA damage, leaving human body a greatly increased susceptibility to cancer or age-related diseases.

Aim and objective: To study the Molecular characterization and its Association to AP endonuclease-1 (APE) and X-ray cross-complementing group 1 (XRCC1), as a DNA Repair protein from patients with the risk of age-related cataract at a Tertiary Care Centre, Uttar Pradesh.

Material and methods: This was a case control study carried out in the Department of Anatomy & Department of Ophthalmology of RMCH&RC for a period of 2 year i.e., June 2020 to June 2022. A total of 500 clinical suspected cases were included in our study in which 250 patients were confirmed as cataract positive patients whereas 250 were the Controls. The Demographic profiles of the cases were recorded after duly obtaining consent. The 5ml of venous blood was collected in Ethylene diamine tetraacetic acid tubes.
DNA was extracted by using Qiagen DNA Extraction kit as per manufactures guidelines. The AP endonuclease-1 (APE) and X-ray cross-complementing group 1 (XRCC1) gene was detected by the conventional PCR.

Results: In the present study the maximum number of cases were reported in the Females as compared to the Males with the maximum age group of 51-60 years being affected the most. The Expression of (AP) –endonuclease (APE1) gene was more 68.4 % as compared to X-ray cross-complementing group 1 (XRCC1) with 62.8 %. The increase expression indicates the presence of these genes in the DNA repair damage.

Conclusion: The Expression of (AP)-endonuclease (APE1) gene was more 68.4% as compared to X-ray cross-complementing group 1 (XRCC1) with 62.8%. The increase expression indicates the presence of these genes in the DNA repair damage. So, there should be early screening and its molecular detection of the DNA repair gene, which will help the clinician in the early diagnosis as well as early treatment of the cataract.

Keywords: Association, APE1, XRCC1, Molecular characterization, DNA, PCR

INTRODUCTION:

Cataract is the opacity of the natural human lens, which may be resulted from congenital, developmental and acquired causes. It has been singled for nearly half of the blind population, is one of the most common causes of visual impairment in the world [1]. Most cataracts arise because of ageing of the crystalline lens, as new lens fibres continue to be laid down in the crystalline lens, but thou existing ones are not replaced [2]. With ageing, there is a gradual accumulation of yellow-brown pigment within the lens, which reduces light transmission [3].

WHO estimates, that cataract is the main cause of blindness globally accounting 47.8% which translates to 17.7million. Every year, an extra 1-2 million people go blind. Every five seconds one person in our world goes blind, and a child goes blind every minute [4].

The prevalence of cataract is higher in females than males in the developed and developing countries. In developing countries, cataract occurs at an earlier age [5].

The risk factors like diabetes mellitus, high myopia, occupational exposure to metal work, atopic dermatitis, and smoking are responsible for presenile cataract [6]. The steroid use, alcohol use, cigarette smoking, and exposure to sunlight were also identified [7]. Despite the public health significance of cataract in India, there are few reports on the risk factors for age related cataract from India [8].

X-ray cross-complementing group 1 (XRCC1) and AP endonuclease-1 (APE1), a DNA repair protein involved in single-strand breaks (SSBs) and BER pathway, has been reported to be responsible for the efficient repair of DNA damage caused by active oxygen, ionization, and alkylating agents is mainly responsible for cataract in patients [9]. The association of XRCC1 and APE1 plays a critical role in the elevated susceptibility to age-related cataracts revealing that this mutation was also regarded as one of the potential mechanisms increasing the risk of age-related cataracts.

Therefore, the present study is undertaken to study the Molecular characterization and its Association to AP endonuclease-1 (APE1) and X-ray cross-complementing group 1 (XRCC1), as a DNA Repair protein from patients with the risk of age-related cataract at a Tertiary Care Centre, Uttar Pradesh".

MATERIAL AND METHODS:

This was a case control study carried out in the Department of Anatomy & Department of Ophthalmology of RMCH&RC for a period of 2 year i.e., June 2020 to June 2022. A total of 500 clinical suspected cases was included in the study in which 250 patients was confirmed as cataract positive patients whereas 250 were the Controls. Ethical clearance was duly obtained from the Institutional Ethical Committee of (RMCH&RC). **Inclusion and Exclusion criteria** - Patients affected with cataract and those who were ready to give their consent were included whereas patients suffering from any immunocompromised disease, patients with type1 diabetes mellitus, those with any thyroid disorder, tuberculosis and cancer, pregnant and lactating females were excluded from the study.

The Demographic profiles of the cases were recorded after duly obtaining consent. The 5ml of the venous blood was collected in Ethylene diamine tetraacetic acid tubes and transported into the Laboratory immediately after the collection for further Analysis. In case of any delay the samples was stored at 4ºC and then proceeded for the DNA Extraction.

The XRCC1 and APE1 a DNA repair protein involved in single-strand breaks (SSBs) and BER pathway, have been reported to be responsible for the efficient repair of DNA damage caused by active oxygen, ionization, and alkylating agents is mainly responsible for cataract in patients.

The DNA extraction was carried out using **Qiagen DNA Extraction** Kit and the Convencial PCR was done for the detection of APE1 and XRCC1 gene as per manufactures guidelines, where the confirmation of the gene of interest was studied.

GENOTYPIC METHOD:

The Molecular Detection of DNA extraction was done to detect the presence of XRCC1 and APE1 gene in clinically positive cataract positive patients with the history like personal and demographic data, reason for visit or presenting complaint, past eye history, general medical history, family eye history and allergy history along with examinations like slit lamp examination and applanation tonometry test were recorded.

DNA Extraction: For the detection of XRCC1 and APE1 gene, chromosomal DNA from the clinical positive cataract patients was done. DNA extraction was carried out using a commercial available the DNA Extraction kit (Qiagen DNA Extraction Kit) as indicated by manufacturer's instructions.

Molecular characterization polymorphism of APE1 and XRCC1 gene among the Senile cataract patients was performed.

Fig 1: DNA extraction Kit

Fig 2: DNA Extraction Reagents

The primers for APE1 and XRCC1 for the detection of gene of interest was designed and confirmed by NCBI. The Primers was obtained from "**Saha gene'** and was reconstituted with sterile double distilled water based according to the manufacturer's instruction.

Fig 3: Primers for APE1 and XRCC1 gene

Fig 4: Primers for XRCC1 Gene

Fig 5: Primers for APE 1 Gene

The DNA fragments was amplified by PCR. The condition required for amplification mentioned below [10].

Gene	Primer sequence	Length (bp)	Cycling Conditions
APE1	Forward- 5-CCTAACCCGAGCACAAAGAAG-3	352bp	The PCR condItions were 94°C for 3 minutes, followed by 35 cycles of 94°C for 30 seconds, 60°C for 30 seconds, 72°C for 30 seconds, and a final extension step at 72°C for 10 minutes. [10]
	Reverse 5-CGAGCCAACTCTGTGCCTTAC-3		

Table No. 1: Primers for APE1 Gene Polymorphism

Gene	Primer sequence (5' to 3')	Length (bp)	Cycling Conditions
XRCC1	Forward- 5-ACCTAACTGGCATCTTCACTTCTG-3	278bp	The PCR conditions were 94°C for 4 minutes, followed by 40 cycles of 94°C for 30 seconds, 60°C for 30 seconds, 72°C for 30 seconds, and a final extension step at 72°C for 10 minutes. [10]
	Reverse 5-TAGTCTGCTGGCTCTGGGCT-3		

Table No. 2: Primers for XRCC1 Gene Polymorphism

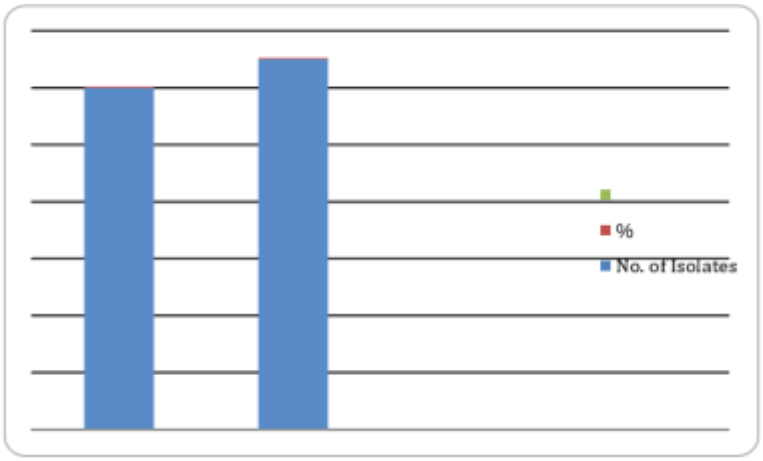
The PCR for the detection of XRCC1 and APE1 gene was done and then run on the Electrophoresis unit which was further seen under the Gel documentation system.

RESULTS

A total of 500 clinical patients were included in the study in which 250 patients was confirmed as cataract positive and 250 were the control group. The 5ml of the venous blood was collected in Ethylene diamine tetraacetic acid tubes. All patients from OPD, positive for Cataract was included in this study. The Age, Gender and Residence distribution etc was recorded, which is illustrated in the Table below.

S. No.	Gender	Frequency	Percentage
1	Male	120	48 %
2	Female	130	52 %

Table No. 3- Genderwise distribution of Number of Patients with Cataract



Graph No. 1: Genderwise distribution of Number of Patients with Cataract

Males was found with 48% and Females with 52% which stated the dominancy of Females to be more in the present study.

S. No.	Diseases	Male	Female	Total (n=500)
1	Cataract	120	130	250
2	Glaucoma	05	04	09
3	Chalazion	10	04	14
4	Refraction Error	35	41	76
5	Pterygium	01	01	02
6	Presbyopia	04	08	12
7	Stye	03	03	06
8	Concretion	01	00	01
9	Squint	04	12	16
10	ARMD	08	06	14
11	Foreign Body	07	05	12
12	Corneal Ulcer	04	07	11
13	Corneal Opacity	02	03	05
14	MGD	02	01	03
15	Entropion	01	01	02
16	Ectropion	02	00	02
17	Primary Angle Closure Glaucoma	02	06	08
18	Esotropia	01	02	03
19	Chronic dacryocystitis	02	04	06
20	Nonproliferative Diabetic Retinopathy	07	02	09
21	Other diseases	20	19	39
		241	259	500

Table No. 4: Diseasewise Distribution of patients

Out of the total number of disease there were 250 patients affected with cataract and other 250 with other disease such as Glaucoma, Chalazion,, Refraction Error etc.

S. No.	Age	Male	Female	Total	Percentage
1.	30-40	01	04	05	2%
2.	41-50	12	24	36	14.4%
3	**51-60**	**47**	**60**	**107**	**42.8%**
4.	**61-70**	**37**	**31**	**68**	**27.2%**
5.	71-80	17	13	30	12%
6.	81-90	03	00	03	1.2%
7.	91-100	00	01	01	0.4%
		117	**133**	**250**	**100%**

Table No. 5: Age wise Distribution of Cataract patients

The maximum number of cases was reported in the age group of 51-60 years of age followed by 61-70 years and the minimum in the age group of 30-40 years and 81-90 years. It was also noted that there was no cases found in the age above or 91 years.

S. No.	Residence	No. of Patients (n= 250)	Percentage
1	Kanpur	190	76 %
2	Other then Kanpur	60	24 %

Table No. 6: Residence wise Distribution of Cataract patients

It was observed that the maximum number of cases was reported from the Kanpur region with 76% rate.

S. No.	Gender	Smokers	Smokers (%)	Nonsmokers	Nonsmokers (%)
1.	Male (120)	37	30.83%	83	69.16 %
2.	Female (130)	18	13.84%	112	86.15 %

Table No.7: Smokers and Nonsmokers among Cataract patients

Gender	Smokers	Smokers %	Nonsmokers	Nonsmokers %
Male (119)	30	25.21 %	89	74.79 %
Female (131)	13	9.9 %	118	90.1 %

Table No.8: Smokers and Nonsmokers in Control patients

It was also noted that the no. of cases of smokers was more in Males (30.83) as compared to the Females (13.84%). In the control group the rate of Male smokers was more with 25.21%.

S. No.	Gender	Alcohol drinkers	Alcohol drinkers (%)	Non Alcohol drinkers	Non Alcohol drinkers (%)
1.	**Male (120)**	30	25 %	90	75 %
2.	**Female (130)**	6	4.6 %	124	95.3 %

Table No. 9: Alcohol Drinkers and Non Alcohol drinkers in Cataract patients

Gender	Alcohol drinkers	Alcohol drinkers %	Non Alcohol drinkers	Non Alcohol drinkers %
Male (119)	16	13.4 %	103	86.6 %
Female (131)	5	3.8 %	126	96.2 %

Table No. 10: Alcohol Drinkers and Non Alcohol drinkers in Control patients

In the current study it was observed that the ratio of Alcohol drinkers was more as compared to the Non alcoholic drinkers (75%) with Males (25%) dietry habits been affected more as compared to the Females (4.6%) . It was also noted that the Male alcohol drinkers was more 13.4% as compared to the female (3.8%) in the control group.
The DNA was extracted and seen under the Gel Documentation system after the run on the Electrophosesis.

Fig No. 6: The Extracted DNA for the XRCC1 gene

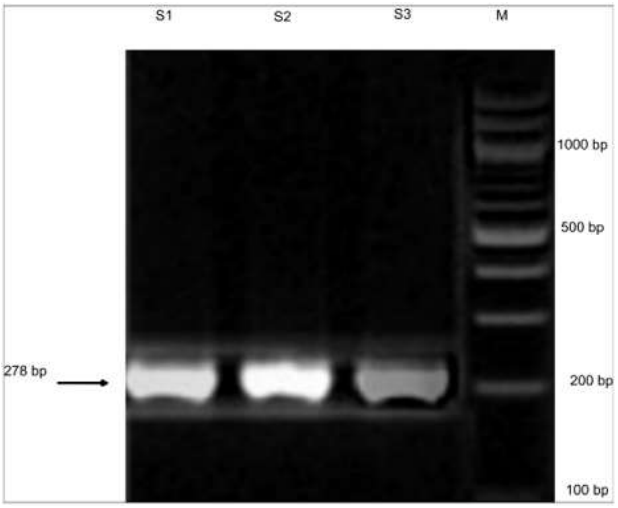


Fig No. 7: Amplified DNA with PCR for XRCC1 gene with patient suffering from cataract. Lane M is DNA ladder; Lane S1 and S3 is sample positive for XRCC1 gene (278bp); Lane S2 is the positive control for XRCC1 gene

Gender	Expressed	Expressed %	Non Expressed	Non Expressed %
Male (120)	74	61.67 %	46	38.33 %
Female (130)	83	63.85 %	47	36.15 %

Table No. 11: Genderwise XRCC1 gene in Cataract patients

Expressed	Expressed %	Non Expressed	Non Expressed %
157	62.8 %	93	37.2 %

Table No. 12: Genderwise XRCC1 gene in Cataract patients

Gender	Expressed	Expressed %	Non Expressed	Non Expressed %
Male (119)	35	29.41 %	84	70.59 %
Female (131)	41	31.30 %	90	68.70 %

Table No. 13: Genderwise XRCC1 gene in Control patients

Expressed	Expressed %	Non Expressed	Non Expressed %
76	30.4 %	174	69.6 %

Table No. 14: XRCC1 gene in Control patients (250)

			Group		Total	Chi Sq	P value
			Control	Cases			
XRCC1	Not Expressed	Frequency	174	93	267	52.732	<0.01*
		%	69.6%	37.2%	53.4%		
	Expresses	Frequency	76	157	233		
		%	30.4%	62.8%	46.6%		
Total		Frequency	250	250	500		
		%	100.0%	100.0%	100.0%		

Table No. 15: XRCC1 gene Expression

In the study it was observed that XRCC1 gene was slightly more affected in Females (63.8%) than with Males (61.6%). Whereas, the expression of XRCC1 was 62.8% and 37.2% was not expressed and it was stastically significant.
In the control group also the Females expression for XRCC1 gene was more with 31.3% and Males being 29.4%. The expression for XRCC1 gene was 30.4% and Non expressed were 69.6% in the control group.

Fig No. 8: DNA seen under gel documentation system for the APE1 gene

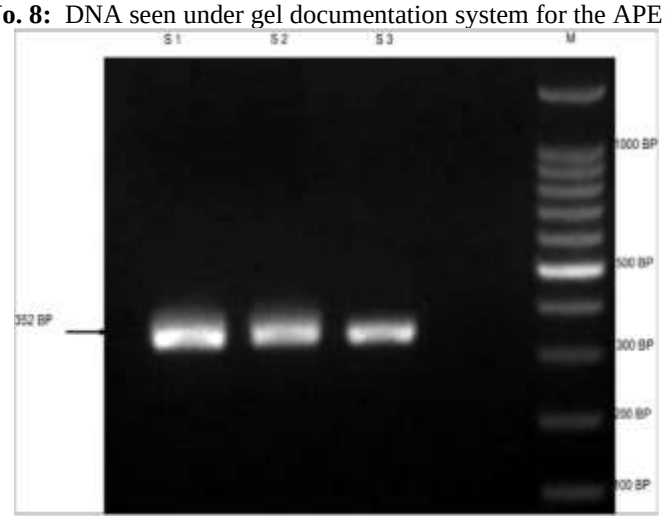


Fig No. 9: Amplified DNA with PCR for APE1 gene with patient suffering from cataract. Lane M is the DNA ladder; Lane S2 and S3 is sample positive for APE1 gene (352bp); Lane S1 is the positive control for APE1 gene and Lane B is the Sample Negative for APE1 gene

Gender	Expressed	Expressed %	Non Expressed	Non Expressed %
Male (120)	80	66.67 %	40	33.33 %
Female (130)	91	70 %	39	30 %

Table No. 16: Genderwise APE1 gene in Cataract patients

Expressed	Expressed %	Non Expressed	Non Expressed %
171	68.4 %	79	31.6 %

Table No. 17: Genderwise APE1 gene in Cataract patients

Gender	Expressed	Expressed %	Non Expressed	Non Expressed %
Male (119)	34	28.57 %	85	71.43 %
Female (131)	45	34.35 %	86	65.65 %

Table No.18: Genderwise APE1 gene in Control patients

Expressed	Expressed %	Non Expressed	Non Expressed %
79	31.6 %	171	68.4 %

Table No. 19: APE1 gene in Control patients (250)

			Group		Total	Chi Sq	P value
			Control	Cases			
APE1	Not Expressed	Frequency	171	79	250	67.712	<0.01**
		%	68.4%	31.6%	50.0%		
	Expressed	Frequency	79	171	250		
		%	31.6%	68.4%	50.0%		
Total		Frequency	250	250	500		
		%	100.0%	100.0%	100.0%		

Table No. 20: APE1 gene Expression

In this study it was observed that Expression of APE1 gene was more in Females (70%) as compared to the Males (66.6%). In the control group the Expression of APE1 gene was 31.6% and that of Non expressed was 68.4%.

In the study it was also observed that APE1 gene was the most expressed with 68.4% followed by XRCC1 with 62.8%. Thus early screening and detection of APE1 and XRCC1 genetic polymorphisms may be useful for identifying age-related cataract patients at an early stage.

DISCUSSION

Cataract is the opacity of the natural human lens, which may be resulted from congenital, developmental and acquired causes and one of the most common causes of visual impairment in the world cause of nearly half of the blind population. It is a vision impairing disease that occurs due to aging, and mainly affects elderly patients or people above the age of 50 [1].

DNA repair enzyme X-ray repair cross-complementing-1 and (AP)-endonuclease (APE1) gene plays an important role in continuously monitor chromosomes to correct damaged nucleotide residues generated by exposure to carcinogens and cytotoxic compounds. Studies have confirmed that polymorphisms of DNA repair genes decreased their ability to repair DNA damage, leaving human body a greatly increased susceptibility to cancer or age-related diseases [11]. Base excision repair (BER) is of great importance in DNA excision repair pathway as XRCC1 is the key enzymes in base excision repair pathway [12], repair protein involved in single-strand breaks (SSBs) and BER pathway, has been reported to be responsible for the efficient repair of DNA damage caused by active oxygen, ionization, and alkylating agents is mainly responsible for cataract in patients [13].

In the present it was found that the Females (52%) were affected more as compared to the Males (48%). It was also observed that the gene expression was also higher in the females compared to males. The expression of XRCC1 gene was slightly more affected in Females (63.8%) than with Males (61.6%), whereas the expression of APE1 gene was more in Females (70%) as compared to the Males (66.6%). This study was in support with the study performed by the other authors where the rate of females was higher [14]. The study by S. Deepanjana was also parallel to our study where the females were affected more than males [15].

In the present study maximum number of cases was reported in the age group of 51-60 years of age followed by 61-70 years and the minimum in the age group of 30-40 years and and 81-90 years. This finding was similar to the other study where the maximum number of cases was recorded in the age group of 51-60 years [14,15].

In the current study the presence of XRCC1 and APE1 gene as a DNA repair gene was detected. This finding was parallel to many other studies where XRCC1 and APE1 genes was detected in senile cataract patients [16,17] . The DNA damage of lens epithelial cells may be the primary cause of lens opacity. DNA repair efficacy affected by genetic defect, which is associated with age related cataract (ARC) [18].

It is noteworthy that XRCC1 was demonstrated to be implicated in single-strand breaks and the BER pathway, which is one of the most important pathways involved in the repair of oxidative and UV-related DNA damage [19,13] . However, the variants of XRCC1 may contribute to disturbing single-base damage repair and single-strand DNA breaks resulting from endogenous oxidative radiation and inflammatory DNA damaging processes [20]. The APE1 gene, which encodes a majority of AP endonucleases in human body, is located on chromosome 14q11.2. The protein fills a vital role in handling endogenous DNA damage that, when left unrepaired, triggers apoptotic cell death [21].

The XRCC1 and APE1 gene may have a strong association with the ability to repair that could potentially influence many age-related diseases including cancers, atherosclerosis, and eye problems such as glaucoma, age-related macular degeneration, and pterygium [22]. More importantly, genetic polymorphisms of XRCC1 have also been frequently documented in many human age-related cataract cases [23]. In this regard, it states that the genetic polymorphisms of XRCC1 may be related to the development and progression of age-related cataract.

It has been well accepted that oxidative stress plays a critical role in the pathogenesis of senile cataract. Therefore the XRCC1 and the APE1 gene genetic polymorphisms may be useful for identifying age-related cataract patients at an early stage [24]

CONCLUSION

X-ray cross-complementing group 1 (XRCC1) and AP endonuclease-1 (APE1) plays a critical role in the elevated susceptibility to age-related cataracts revealing that this mutation was also regarded as one of the potential mechanisms increasing the risk of age-related cataracts. Thus early screening and detection of XRCC1 and APE1 genetic polymorphisms is useful for identifying age-related cataract patients at an early stage.

REFERENCES:

1. Klein BE, Klein R, Lee KE, Danforth LG. Drug use and five year incidence of age-related cataracts. The Beaver Dam Eye Study Ophthalmology. 2001; 108:1670–4.
2. Solberg Y, Rosner M, Belkin M. The association between cigarette smoking and ocular diseases Surv Ophthalmol. 1998; 42:535–47.
3. Klein BE, Klein R, Lee KE, Meuer SM. Socioeconomic and lifestyle factors and the 10-year incidence of age-related cataracts Am J Ophthalmol. 2003; 136:506–12.
4. Thylefors B, Negrel AD, Pararajasegaram R, Dadzie KY. Global data on blindness. Bull World Health Organ 1995;73: 115-21.
5. Nirmalan PK, Krishnadas R, Ramakrishnan R, et al. Lens opacities in a rural population of southern India. The Aravind Comprehensive Eye Study. Invest Ophthalmol Vis Sci 2003;44:4639–43.
6. Cumming RG, Mitchell P, Smith W. Diet and cataract: The Blue Mountains eye study. Ophthalmology. 2000;107:450–6.
7. Rahman A, Yahya K, Shaikh A, Fasih U, Zuberi BF. Risk factors associated with pre-senile cataract. Pak J Med Sci. 2011;27:145–8.
8. Vasudevan M, Premnath G. A prospective observational study to analyze the causes and types of pre senile cataract in South Indian patients. J Evol Med Dent Sci. 2014; 3:12308–15.
9. K.W. CaldecottXRCC1 and DNA strand break repair. DNARepair. 2003; 2:9:955-969.
10. Chen Wang, Qiaohong Lai and Jun Hu. Senile cataract and genetic polymorphisms of APE1, XRCC1 and OGG1. Int J Clin Exp Pathol. 2015; 8(12):16036-16045.
11. Dianov GL, Sleeth KM, Dianova, II and Allinson SL. Repair of abasic sites in DNA. Mutat Res. 2003;531: 157-163.

12. Langie SA, Kowalczyk P Sabine, Tomaszewski B , Vasilaki A , Maas L, MoonenEetal. Redox and epigenetic regulation of the APE1 gene in the hippocampus of piglets: The effect of early life exposures. DNA Repair (Amst). 2014; 18: 52-62.
13. Kulkarni A, Wilson DM.. The involvement of DNA-damage and -repair defects in neurological dysfunction. Am J Hum Genet. 2008; 82:539–66.
14. Research: Gender differences in blindness, cataract blindness and cataract surgical coverage in India: a systematic review and meta-analysis doi 10.1136/bjophthalmol-2018-313562. Journal: British Journal of Ophthalmology
15. S. Deepanjana. Cataract Blindness In India Much More Prevalent In Women Than Men, Finds. Medical Dialogues. 2019; 7:10
16. Unal M, Güven M, Batar B, Ozaydin A, Sarici A, Devranoğlu K. Polymorphisms of DNA repair genes XPD and XRCC1 and risk of cataract development. Exp Eye Res. 2007; 85(3):328-34.
17. Wang C, Lai Q,Zang S, Hu J. Senile cataract and genetic polymorphisms of ape1, xrcc1 and ogg1. International journal of clinical and experimental pathology. 2015; 8(12): 16036-16045.
18. Zha Xu, Liang G, Zhang Y, Linkun Ma, Siquan Zhu, Xueying Zhao. The relationship of DNA repair gene XPD, XRCC1, OGG1, APE1, and WRN polymorphism with the risk of age-related cataract in Hani people from Mojiang region in Yunnan. Int J Clin Exp Med. 2016; 9(5):8706-8712.
19. Xin-Xin Chi, You-Yu Liu, Su-Ning Shi, Zhuang Cong, Yu-Qing Liang, Hui-Jun Zhang.XRCC1 and XPD genetic polymorphisms and susceptibility to age-related cataract: A meta-analysis. 2015; 21:335-346.
20. Luo YF, Wang BB, Zhou Z, Ding XC, Hu SS, Zhou GK, Ma X, Qi YH. Polymorphisms of the DNA repair genes XPD and XRCC1 and the risk of age-related cataract development in Han Chinese. Curr Eye Res. 2011; 36:632–6.
21. Fung H and Demple B. A vital role for Ape1/Ref1 protein in repairing spontaneous DNA damage in human cells. Mol Cell. 2005; 17: 463-470.
22. Zhang Y, Zhang L, Song Z, Sun DL, Liu HR, Fu SB, Liu DR, Liu P. Genetic polymorphisms in DNA repair genes OGG1, APE1, XRCC1, and XPD and the risk of age-related cataract. Ophthalmology. 2012; 119:900–6.
23. Padma G, Mamata M, Reddy KR, Padma T. Polymorphisms in two DNA repair genes (XPD and XRCC1)–association with age related cataracts. Mol Vis. 2011;17:127–33.
24. Cui YH Jing CX, Pan HW. Association of blood antioxidants and vitamins with risk of age-related cataract: a meta-analysis of observational studies. Am J Clin Nutr. 2013; 98:778–86