An Estimation of some DNA Repair Genes Polymorphisms APE1, XRCC1, and RAD18) in X-Ray Technicians

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Abstract
The current study dealt with detection of some DNA repair genes polymorphisms in individuals worked in the X-ray department in Al-Sadr hospital city in Al-Najaf province. In this study, about 20 X-ray workers who worked in the Najaf province from 15/2/ 2023 to 15/3/ 2023, participated. Thirty people in the control group appeared to be in good condition. the present study was suggested, three DNA repair genes with common SNPs were enrolled, including X-ray repair cross-complementing group 1 (XRCC1) Arg399Gln (28152) G>A, apurinic /apyrimidinic endonuclease 1(APE1) Asp148Glu (rs3136820), and RAD18 Arg302Gln (rs373572), The data analysis showed significant association (p =0.002) of RAD18 genotyping with workers, AA was more frequented in workers than control while GG didn't appear in cases. A significant association of XRCC1 (AG) with workers (p= 0.005), AA didn't appear in cases and GG was low frequented in cases than in control. Non-significant associations of APE1 (p= 0.2978, p =0.174) with case. Belong to work time, all genes included (RAD 18, XRCC1, and APE1) were non-significant affected by work time, at p-value of RAD 18 genotypes (p 0.581), XRCC1 (p =0.194) and APE1 (p= 0.891). The time of x-ray exposure was divided into less than 6 hours and more than 6 hours, with a Non-significant association of RAD18 (p =0.191), XRCC1(p= 0.662), and APE1 (p =0.576) with the time of exposure, the work duration also divided to two classes (more than 10 years and less than 10 years), non-significant associations were observed, RAD 18 (P= 0.888), XRCC1 (p= 0.319) and APE1 (p= 0.496). The present results concluded that there were significant associations between RAD18 Arg302Gln (rs373572),(AA)polymorphism was frequented in workers than control and XRCC1 Arg399Gln (28152) G>A with x-ray workers and non-significant association with APE1 Asp148Glu (rs3136820), on the other hand, the time, number of exposure and work period didn't associate with repair genes.

Keywords: DNA repair genes, polymorphisms, APE1, XRCC1, RAD18, X-ray technicians.

Introduction

The electromagnetic radiation used in medical applications is X-ray produced artificially outside of a nucleus, with lower energy than γ-ray (Introduction to Radiation, 2012). The mechanism of action of Ionizing radiation is ionized atoms throw eliminate an electron from their orbits to form ions with a positive charge and negative charge of the free electron (Introduction to Radiation, 2012), several factors impact the harmful activities of ionizing radiation on living cells included dose rate, dose amount, gender, age, and target types, On the other hand, there was direct and indirect interaction, the direct interaction resulted from interact the ionizing radiation with critical goals directly like DNA molecules. the indirect interaction caused by interact ionized radiation with water in the cell, to form both ions and free radicals (Cember *et al.*, 2008). Radiological health, Health physics, or radiological engineering are terms utilized in public health fields like the engineering of environmental health that deals with ionizing and nonionizing radiation using in safely to prevent any radiation biological impacts on humans. The health physicist is contributed to the safety aspects in the design of processes, tools, and facilities using sources of radiation and radioactive waste safe disposal,

so the radiation exposure should be lowered and will at all times have acceptable limits; it should be kept the environment and personnel under constant conditions to ascertain that these designs are effective indeed (Waller *et al*., 2015). If control tests are observed to be ineffective or if they break down, the health physicist should be able to estimate the level of hazard and make some guides regarding remedial action (Cember *et al*., 2008). All tissues and cells in the body of human do not have the same radio sensitivity; several of them are radio resistance while others are radiosensitive (Shafiee *et al*., 2016) Hematopoiesis is one of the vital radiosensitive systems to radiation. It was considered that peripheral blood count is appropriate to use as a biomarker to evaluate ionizing radiation damage (Rozgaj *et al*., 1999).

The base excision repair system is a major mechanism for correcting base lesions, like oxidative alteration, that started with a glycosylase-dependent detection and damaged base removal from the DNA strand to form an apurinic/apyrimidinic site. later, the APE1 protein cleave phosphor-diester bonds in the DNA double helix from the apurinic/apyrimidinic site, which leads to a nucleotide gap and the 3'OH free end (Whitaker *et al.*, 2017). Later the gap was ligated by other proteins, like DNA ligase IIIα (Lig IIIα), XRCC1, DNA-dependent protein kinase, poly (ADP-ribose) polymerase 1, and a catalytic subunit (Bauer *et al*., 2011). The other type of repair system is *RAD18*, it's an integral protein have a RING finger domain. Also, it has the activity of ubiquitin-ligating enzyme (E3) (Joazeiro *et al*., 2000) and is vital to proliferating cell nuclear antigen ubiquitination. Monoubiquitinated PCNA enhances translesion synthesis and recruits translesion synthesis polymerases to the DNA lesions sites (Huang *et al.*, 2009)

Methodology

Sample collection and study subjects: a case-control study was conducted in the DNA lab at Babylon University. 20 X-ray employees were enrolled in the current study from different x-ray centers in Najaf province, and 30 individuals were as a control group healthy. as the collection of samples began from February 2023 to March 2023. The patient and control groups were aged 24–46 . Blood and data were collected from each subject with ethical approval belonging to the ministry of higher education and scientific research, and the approval of the two study groups. data collected from cases were (age, duration of work, and period of work).

DNA isolation and detection of polymorphism: the DNA was isolated from each sample by favorgen instruction, then detected purity and concentration, and three DNA repair genes were studied (table 1).

Table (1). The primers sets of three genes used in the present study

Gene (SNPs)	Sequences	TM	Products Size	References
APE1 Asp148Glu (rs3136820)	F1:5′CCTACGGCATAGGTGAG ACC	60	The G 167 bp, T 236 bp, and 360 bp common band	Ito *et al*., (2004)
	R1:5′-TCCTGATCATGCTCCTCC-3'			
	F2:5′TCTGTTTCATTTCTATAG GCGAT			
	R2:5′-GTCAATTTCTTCATGTGC CA			
XRCC1 Arg399Gln (28152) G>A	F2 5′TCCCTGCGCCGCTGCAGTT TCT	59	The G (399Arg) 447 bp, A (399Gln) 222	Ito *et al*., (2004)

	R1-TGGCGTGTGAGGCCTTACCTCC F2, TCGGCGGCTGCCCTCCCA R2 AGCCCTCTGTGACCTCCCAGGC		bp and 630bp common band	
The RAD-18 Arg302Gln (rs373572)	F1:5'-ATACCCATCACCCATCTT C R1, GTCTTCTCTATATTTTCGATTTCTT F2,TTAACAGCTGCTGAAATAGTCG R2,CTGAAATAGCCCATTAACATACA	60	Gln 146 pb , and 106 bp Arg. A 206 bp common band	Das *et al.*, (2018)

Electrophoresis: the XRCC1, RAD18, and APE1 amplification products were visualized by horizontal agarose electrophoresis using (agarose gel 1%, 75 V, 25 mA for 50 min) with ethidium bromide stain. Bands were detected in comparison with a DNA ladder (100 bp-1000 bp) under UV light using (vilber) photo documentation.

Data analysis: the workers were classified according to work time into two groups (less than 6 hours and more than 6 hours), according to exposure to X-ray time (less than 6 hours and more than 4 times), according to exposure to X-ray number (less than 6 hours and more than 4 times) and according to work duration (less than 10 years and more than 10 years). The allele frequency is represented as a percentage, significantly calculated by an odd ratio CI 95%, at a p-value less (than 0.05).

Results

The results of the present study illustrated that the mean age was (36.90±10.42) years, the mean exposure time was (3.95±2.85) years, and the duration of work was (9.80±8.78) years. Here we detect some DNA repair genes polymorphisms in individuals who worked in the X-ray department in Al-Sadr hospital city in Al-Najaf province. The results showed APE1 gene appeared in GT, TT genotypes, RAD18 gene polymorphism with AA and AG genotypes, and XRCC1 genotypes with (GA and GG genotypes in cases (figure 1).

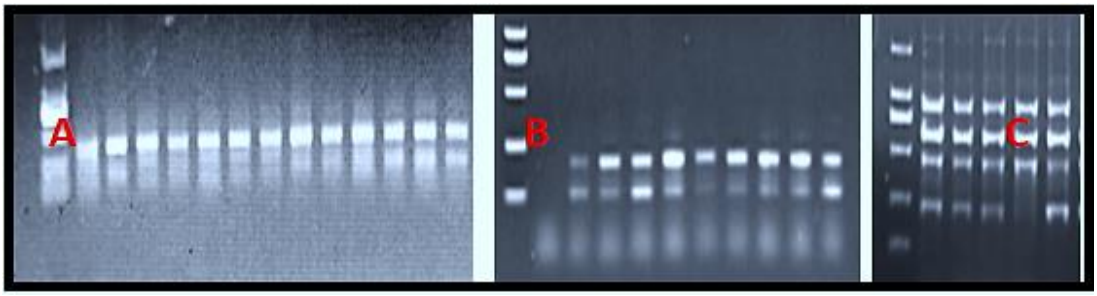

Figure.(1) The electrophoresis pattern of DNA repair genes polymorphism, A; APE1 gene with (GT, TT) genotypes, B; RAD18 gene polymorphism with (AA) genotype, C; XRCC1 genotypes with (GA, AA, and GG) genotypes. DNA ladder (100bp-1kb).

The distribution of genotyping is clarified in the table (2), the data analysis showed a significant association (p =0.002) of RAD18 genotyping with workers (AA) more frequently in workers

than control while GG didn't appear in cases. A significant association of XRCC1 (AG) with workers (p= 0.005), AA didn't appear in cases and GG low frequent in cases than in control. Non-significant associations of APE1 (p= 0.298, p= 0.174). Belong to work time, all genes included (RAD 18, XRCC1, and APE1) were non-significant affected by work time, the p-value of RAD 18 genotypes (p= 0.581), XRCC1 (p=0.194) and APE1(p= 0.891) table (3). The time of x-ray exposure was divided into less than 6 hours and more than 6 hours, with a Non-significant association of RAD18 (p= 0.191), XRCC1(p =0.662), and APE1 (p= 0.5759) with a time of exposure (table 4). the repair system genes polymorphisms distribution according to exposure to X-ray number showed non-significant relations, RAD18 (p= 0.948), XRCC1 (p=0.942), and APE1 (p=0.891) table (5). The work duration was also divided into two classes (more than 10 years and less than 10 years), and non-significant associations were observed, RAD 18 (p= 0.888), XRCC1 (p= 0.319), and APE1 (p =0.496) table (6).

Table (2) the distribution of repair genes polymorphisms in study groups (odd ratio, CI95%, P value less than 0.05)

Genotyping RAD 18	Patients	Control	Odd ratio CI	P value
AG	7 (35%)	28(93.33%)	26.000	0.002
AA	13 (65%)	2(6.66%)	4.733 - 142.838	
GG	0	0		
				XRCC1
AG	18 (90%)	14(46%)	10.286	0.0050
GG	2(10%)	13(43.33%)	2.020 - 52.365	
AA	0	3(10%)	0.771	0.876
			0.0297 - 20.017	
				APE 1
GT	14 (70%)	16(53.33%)	0.528	0.298
GG	0	5(16.66%)	0.158 - 1.759	
TT	6(30%)	8(26.66%)	8.412	0.174
			0.391 -181.198	

Table (3). The repair system genes polymorphisms distribution according to work time

Genotyping RAD 18	More than 6 hours	Less than 6 hours	Odd ratio	P value
AG	3(15%)	4(20%)	21.000	0.058
AA	0	13(65%)	0.900 - 489.789	
				XRCC1
AG	2(10%)	16(80%)	8.000	0.194
GG	1(5%)	1(5%)	0.347 - 184.375	
				APE 1
GT	2(10%)	12(60%)	1.2000	0.893
TT	1(5%)	5(25%)	0.088 - 16.440	

Table (4). The repair system genes polymorphisms distribution according to exposure to X-ray time

Genotyping RAD 18	More than 6 hours	Less than 6 hours	Odd ratio	P value
AG	3(15%)	4(20%)	4.125	0.191
AA	2(10%)	11(55%)	0.493 - 34.500	
				XRCC1
AG	5(25%)	13(65%)	0.4909	0.662
GG	0	2(10%)	0.020 - 11.974	
				APE 1
GT	3(15%)	11(55%)	1.8333	0.576
TT	2(10%)	4(20%)	0.219 - 15.334	

Table (5). The repair system genes polymorphisms distribution according to exposure to X-ray number

Genotyping RAD 18	More than 4 times	Less than 4 times	Odd ratio	P value
AG	1(5%)	6(30%)	0.917	0.948
AA	2(10%)	11(55%)	0.068 - 12.323	
				XRCC1
AG	3(15%)	15(75%)	0.886	0.942
GG	0	2(10%)	0.034 - 22.853	
APE 1				
GT	2(10%)	12(60%)	1.2000	0.891
TT	1(5%)	5(25%)	0.088 - 16.440	

Table (6). The repair system genes polymorphisms distribution according to work duration

Genotyping RAD 18	More than 10 years	Less than 10 years	Odd ratio	P value
AG	3(15%)	4(20%)	0.875	0.888
AA	6(30%)	7(35%)	0.137 - 5.576	
				XRCC1
AG	9(45%)	9(45%)	0.200	0.319
GG	0	2(10%)	0.008 -4.746	
				APE 1
GT	7(35%)	7(35%)	0.500	0.496
TT	2(10%)	4(20%)	0.068 - 3.675	

Discussion

The ionizing radiation utilized in medical applications has increased in the last decade, therefore the technician's number of X-rays also increased, Iraq the technicians work without any protection tools and the multiple exposures to low levels of x-ray may be implicated in different cell mechanisms declined, the association of IR and DNA damage has been documented in different reports, IR stimulates a variety of DNA damage by direct or indirect impacts through ionization events generated by ROS, as well as mammalian cells exposure to of gamma or photon radiation (1 Gy) lead to 1000 single-strand breaks, 150 DNA-protein cross-links, 500 damaged bases, and 40 double strand breaks (Dahm-Daphi & Dikomey, 1996). Eileen *et al.*, (2012) postulated that some genetic association studies of IR impacts have

focused on the detection of many SNPs in candidate genes, like the control of cell cycle and DNA repair genes that are well studied according to the critical role in genome integrity maintained and particular relevance in situations where exposure is too low levels of radiation that increased in the oxidative stress levels.

Redon *et al.*, (2010) and Aparicio *et al.*, 2014) illustrated that Ionizing radiation causes Double-strand DNA breaks directly, in addition to base damages that are indirectly induced. These effects may be because of stimulation ROS by radiation that is indirectly implicated in DNA lesions, like apurinic/apyrimidinic (abasic) sites, single strand breaks, modifications in sugar moiety, and deaminated adducted bases. When DNA is damaged, this damage happened in different DNA sites that may be illustrated in the results of the current study, however; the cell repair machinery is triggered and arrests the cell cycle at specific control checkpoints to repair DNA lesions and arrested the cycle. On the other hand, the intrinsic radiosensitivity of tumor cells is strongly stimulated by the cell's Double Strand Break repair capability (Mladenov_*et al.*,_2013). The accumulation of DNA damage leads to induction disease if the repair activity was low, thus the x-ray worker should be avoided these harmful effects by using personal protective equipment and also using the repair genes polymorphism estimation as a preliminary test before work in the x-ray field to avoid the bad output of these employees.

On the other hand, the results show that the age were non significant changes agree with (Asma et al 2023) the time and number of exposure and the work period didn't affect APE1 and XRCC, RAD18, polymorphisms of X-ray repair cross complementing group 1 (XRCC1) and X-ray repair cross complementing group 3 (XRCC3) have been studied extensively(Sorour et al 2013).but it's associated with workers in x-ray fields, this should be taken into consideration when working in this field and for used protective tools to avoid disease incidence.

Moreover, Exposure to IR found to be involved in cancer etiology (Ron, 1998), and lesions stimulated by IR are repaired by base excision repair and homologous recombination repair (Demple and Harrison, 1994; Wallace, 1994; Lindahl, 2000; Brenneman *et al.*, 2000), the Hypersensitivity to IR may stimulate from somatic mutations of repair genes, polymorphisms of base excision repair genes like *APE1* and *XRCC1* and a low level of protein expression secondary to other cellular dysfunction. Jennifer *et al.*, (2001) suggested that the substitution variants of amino acid in base excision repair genes are correlated with a mitotic delay in response to IR. Since the hypersensitivity to IR inheritance and deficient repair of IR-induced lesions may serve as markers for low-penetrant predisposition genes in the tumor, Jennifer et al., (2001) reported linked between SNPs of two DNA repair genes and IR sensitivity, the structural alterations of *APE1* and *XRCC1* proteins may have functional significance. First, the *APE1* 148 Glu variant allele has a small but non-significant impact on endonuclease and DNA binding activity (Hadi *et al.*, 2000) and this didn't agree with the present study, we need a further investigation about this employee in Iraq.

Conclusion

The present results concluded that there were significant associations between (AA)genotype RAD18 more frequently in workers than control while GG didn't appear in cases and this study revealed significant association of XRCC1(AG) with x-ray workers, while (AA) didn't appear in case . Non-significant association with APE1, on the other hand, the time, number of exposure, and work period didn't associate with repair genes.

References

1- Introduction to Radiation, Minister of Public Works and Government Services Canada (PWGSC), Published by the Canadian Nuclear Safety Commission. 2012. [Google Scholar]
2- Cember H, Johnson TE. Introduction to Health Physics. 4th ed. New York: McGraw-Hill Education; 2008. [Google Scholar]
3- Shafiee M, Hoseinnezhad E, Vafapour H, Borzoueisileh S, Ghorbani M, Rashidfar R. Hematological findings in medical professionals involved at intraoperative fluoroscopy. *Global Journal of Health Science*. 2016;8:232. [Google Scholar]
4- Rozgaj R, Kašuba V, Šentija K, Prlić I. Radiation-induced chromosomal aberrations and haematological alterations in hospital workers. *Occup Med*. 1999;49:353–60. [PubMed] [Google Scholar].
5- Whitaker, A.M.; Schaich, M.A.; Smith, M.R.; Flynn, T.S.; Freudenthal, B.D. Base excision repair of oxidative DNA damage: From mechanism to disease. Front. Biosci. (Landmark Ed.) 2017, 22, 1493–1522. [Google Scholar] [CrossRef][Green Version].
6- Bauer, M.; Goldstein, M.; Christmann, M.; Becker, H.; Heylmann, D.; Kaina, B. Human monocytes are severely impaired in base and DNA double-strand break repair that renders them vulnerable to oxidative stress. Proc. Natl. Acad. Sci. USA 2011, 108, 21105–21110. [Google Scholar] [CrossRef][Green Version].
7- Joazeiro CA, Weissman AM. RING finger proteins: mediators of ubiquitin ligase activity. Cell 2000; 102: 549–52. [PubMed] [Google Scholar]
8- Huang J, Huen MS, Kim H, Leung CC, Glover JN, Yu X, et al. RAD18 transmits DNA damage signalling to elicit homologous recombination repair. Nat Cell Biol 2009; 11: 592–603. [PMC free article] [PubMed] [Google Scholar].
9- Ito H, Matsuo K, Hamajima N, Mitsudomi T, Sugiura T, Saito T, Yasue T, Lee KM, Kang D, Yoo KY, Sato S, Ueda R, Tajima K. Gene-environment interactions between the smoking habit and polymorphisms in the DNA repair genes, APE1 Asp148Glu and XRCC1 Arg399Gln, in Japanese lung cancer risk. Carcinogenesis. 2004 Aug;25(8):1395-401. doi: 10.1093/carcin/bgh153. Epub 2004 Mar 25. PMID: 15044328.
10- Das S, Purkayastha S, Roy H, Sinha A, Choudhury Y. Polymorphisms in DNA repair genes increase the risk for type 2 diabetes mellitus and hypertension. Biomol Concepts. 2018 Jun 9;9(1):80-93. doi: 10.1515/bmc-2018-0008. PMID: 29886452.
11- Hussain, M. A., Dawod , K. M., Khether, A. A . (2021). Gene Action, Heterosis and Combining Ability in Maize Hybrids B- Using Line x Tester Analysis. Kufa Journal for Agricultural Sciences, 13(2), 30–40. Retrieved from https://journal.uokufa.edu.iq/index.php/kjas/article/view/3653
12- J. Dahm-Daphi, E. Dikomey Rejoining of DNA double-strand breaks in X-irradiated CHO cells studied by constant- and graded-field gel electrophoresis Int. J. Radiat. Biol., 69 (1996), pp. 615-621
13- Eileen Pernot, Janet Hall, Sarah Baatout, Mohammed Abderrafi Benotmane, Eric Blanchardon, Simon Bouffler, Houssein El Saghire, Maria Gomolka, Anne Guertler, Mats Harms-Ringdahl, Penny Jeggo, Michaela Kreuzer, Dominique Laurier, Carita Lindholm, Radhia Mkacher, Roel Quintens, Kai Rothkamm, Laure Sabatier, Soile Tapio, Florent de Vathaire, Elisabeth Cardis, Ionizing radiation biomarkers for potential use in epidemiological studies, Mutation Research/Reviews in Mutation Research, Volume 751, Issue 2, 2012, Pages 258-286.
14- Rafaat, J. G. (2022). Effect of pit and plastic bag methods and some additives on chemical composition of grass-legume mixture silages. Kufa Journal for Agricultural Sciences, 14(1), 11–20. https://doi.org/10.36077/kjas/2022/140102
15- Tahmasebi, A., Nasrollahi, F. (2022). Comparison of DNA extraction methods from Halocnemum strabilaceum (Amaranthaceae). Journal of Wildlife and Biodiversity, 7(1), 81–97. https://doi.org/10.5281/zenodo.6498963

16- Tahmasebi, A. ., Nasrollahi, F. . (2022). Comparison of DNA extraction methods from Halocnemum strabilaceum (Amaranthaceae). Journal of Wildlife and Biodiversity, 7(1), 81–97. https://doi.org/10.5281/zenodo.6498963

17- Jeza, G. T., & Bekele, A. (2023). Seasonal distribution model of African elephants (Loxodonta africana) under a changing environment and land use in Omo National Park, Ethiopia. Journal of Wildlife and Biodiversity, 7(3), 96–117. https://doi.org/10.5281/zenodo.7783039

18- Redon CE, Nakamura AJ, Zhang Y-W, Ji JJ, Bonner WM, Kinders RJ, Parchment RE, Doroshow JH, Pommier Y. Histone gammaH2AX and poly(ADP-ribose) as clinical pharmacodynamic biomarkers. Clin Cancer Res. 2010;16:4532–4542. [PMC free article] [PubMed] [Google Scholar].

19- Hussain, M. A., Dawod, K. M., Khether, A. A. (2021). Gene Action, Heterosis and Combining Ability in Maize Hybrids A- Using Half Diallel Analysis. Kufa Journal for Agricultural Sciences, 13(2), 18–29. Retrieved from https://journal.uokufa.edu.iq/index.php/kjas/article/view/3652

20- N.A.A. Jasim, A.D.S. Wadi . (2023). Study of the Biodiversity of Fish in The Kufa River, Pollution and Community Health Effects, BioRes Scientia Publishers. 1(2):1-17. DOI: 10.59657/2993-5776.brs.23.009

21- Aparicio T, Baer R, Gautier J. DNA double-strand break repair pathway choice and cancer. DNA Repair. 2014;19:169–175. [PMC free article] [PubMed] [Google Scholar]

22- Mladenov E, Magin S, Soni A, Iliakis G. DNA double-strand break repair as determinant of cellular radiosensitivity to killing and target in radiation therapy. Front Oncol. 2013;3:1–18. [PMC free article] [PubMed] [Google Scholar].

23- Ron,E. (1998) Ionizing radiation and cancer risk: evidence from epidemiology. Radiat. Res., 150, S30–S41.

24- Zainab Mahdi Jasim Al-Saygh , Zahraa Sami Razzaq Najjar , Mona N. Al-Terehi . (2023). Association of Catalase Promoter Haplotype and Catalase Level in The X-Ray Employments., Journal Alharf., Issue. November, No. 19

25- Demple,B. and Harrison,L. (1994) Repair of oxidative damage to DNA: enzymology and biology. Annu. Rev. Biochem., 63, 915–948.

26- M. Boopathi, D. Khanna, P. Mohandass, P. Venkatraman, K. Kanakavel, C. Narmada and S.Vignesh. (2023). A dose volume histogram based correction factor for dosimetric comparison of radiotherapy treatment plans: preliminary study., Onkologia i Radioterapia., Volume 17, Issue 9, 2023

27- Nahdema A A Jasim ., Mohamed Abed Al-abass .2023. Isolation and Identification of Copepods Indivuals from Kufa River Molecular Diversity Study. International Journal of Medical Research. 2, 5 (Oct. 2023), 10–24., Available from: http://ijmr.online/index.php/ijmr/article/view/35

28- Wallace,S.S. (1994) DNA damages processed by base excision repair: biological consequences. Int. J. Radiat. Biol., 66, 579–589.

29- Lindahl,T. (2000) Suppression of spontaneous mutagenesis in human cells by DNA base excision–repair. Mutat. Res., 462, 129–135.

30- Brenneman,M.A., Weiss,A.E., Nickoloff,J.A. and Chen,D.J. (2000(XRCC3 is required for efficient repair of chromosome breaks by homologous recombination. Mutat. Res, .459,89-97.

31- Aparna, J., Pillai, P., & Ampili, M. (2021). Antibacterial Activity of Clerodendrum infortunatum L. AND Vanda spathulata (L.) Spreng. AGAINST Escherichia coli AND Klebsiella sp. Uttar Pradesh Journal of Zoology , 637-644.

32- Mattigatti, S., & Datkhile, K. (2021). Synthesis, characterization and application of green synthesized ag nps in endodontic therapy to reduce microbial biofilm. Uttar Pradesh Journal of Zoology,42(12), 25-30.

33- Jennifer J. Hu, Tasha R. Smith, Mark Steven Miller, Harvey W. Mohrenweiser, Andrea Golden, L.Douglas Case, Amino acid substitution variants of APE1 and XRCC1 genes associated with ionizing radiation sensitivity, Carcinogenesis, Volume 22, Issue 6, June 2001, Pages 917–922, https://doi.org/10.1093/carcin/22.6.917.

34- Hadi,M.Z., Coleman,M.A., Fidelis,K., Mohrenweiser,H.W. and Wilson III,D.M. (2000) Functional characterization of Ape1 variants identified in the human population. Nucleic Acids Res., 28, 3871–3879.

35- Waller EJ, van Maanen J. The role of the health physicist in nuclear security. Health Phys. 2015 Apr;108(4):468-76. doi: 10.1097/HP.0000000000000258. PMID: 25706142; PMCID: PMC4418781.