International Journal on Science and Technology (IJSAT)
E-ISSN: 2229-7677 ● Website: www.ijsat.org ● Email: editor@ijsat.org

Effects of Environmental Degradation on Genetic Integrity

Dr. Naadir Kamal[1], Azra Kamal[2], Md. Matloob Raza Khan[3]

[1]Assistant Professor, Dr. C.V. Raman University, Vaishali, Bihar, [2,3] Assistant Director, Forensic Science Laboratory, Home (Police) Department, Bihar, Patna, India.

Abstract

Gene-environment interactions play a crucial role in determining susceptibility to various diseases, as genetic variations influence individual responses to environmental factors. This paper explores how exposure to ozone, air pollution, pesticides, and ionizing radiation affects human health by altering gene expression and inducing genetic damage. Ozone exposure is linked to respiratory diseases such as asthma and COPD, with genetic polymorphisms in oxidative stress and inflammatory genes modifying individual risk. Fine particulate air pollution (PM2.5) has been associated with an increased risk of Autism Spectrum Disorder (ASD), particularly in genetically predisposed individuals. Pesticides contribute to genetic hazards by disrupting detoxification mechanisms, leading to DNA damage and increased risk of neurological disorders such as Parkinson's disease. The effects of radiation exposure on genomes have been extensively studied in both human and plant populations exposed to nuclear disasters, medical radiation, and environmental contamination. Ionizing radiation exposure results in genomic instability, mutations, and increased cancer risks, as observed in populations affected by nuclear accidents. Cytogenetic biomonitoring studies have demonstrated the significance of chromosomal aberrations, micronuclei formation, and sister chromatid exchanges as biomarkers of genetic damage due to environmental pollutants. The National Center for Toxicogenomics (NCT) aims to enhance understanding of environmental toxicology through genomic technologies. Given the growing impact of environmental pollutants on genetic health, multidisciplinary research in environmental genomics is essential for developing protective measures, early detection methods, and effective policy interventions to mitigate genetic hazards.

Keywords: Gene-environment interactions, genomic instability, chromosomal aberrations, genetic hazards and environmental contamination.

1.Introduction

1.1 Gene-Environment Interaction

Most diseases arise from a complex interplay between an individual's genetic composition and their exposure to environmental factors such as ozone, pesticides, air pollution, dust mites, radiations and more. Variations in genetic factors lead to differences in how individuals respond to the same environmental agent. Consequently, some individuals have a lower risk of developing a disease from environmental exposure, while others are significantly more susceptible. The genome (genes) and the epigenome (chemical modifications of DNA and chromatin) work together to determine the phenotype, whether it

manifests as health or disease. The epigenome mediates the effect of the environment on our genes by translating the unique programs into gene expression patterns, turning gene expression "on" or "off" with physiological or pathological consequences. Exposure to environmental chemicals like heavy metals can alter gene expression, increasing the likelihood of cancer development.

1.2 Ozone response and oxidative stress genes

Ozone (O3) is a gaseous air pollutant formed when sunlight interacts with hydrocarbons and nitrogen oxides emitted from vehicle exhaust. Higher outdoor ozone levels have been linked to a greater risk of hospital admissions for asthma and Chronic Obstructive Pulmonary Disease (COPD), as well as increased mortality among asthma patients and the general population. Ozone exposure can lead to modifications in respiratory symptoms, lung function, biomarkers, and asthma risk due to polymorphisms in oxidative stress genes such as NQO1, GSTM1, and GSTP1. Variations in inflammatory genes like TNF affect lung function responses to ozone and influence how different ozone levels contribute to asthma development. Polymorphisms in oxidative stress genes (GSTM1, GSTP1) impact the body's response to combined exposures to ragweed pollen and diesel exhaust particles.

1.3 Fine particulate air pollution linked with increased autism risk

Particulate matter (PM) is a mixture of solid and liquid particles whose deposition within the lung is determined by diameter. PM10 are coarse, ''thoracic'' particles ,10 mm in diameter, PM2.5 are fine, ''respirable'' particles ,2.5 mm and ultrafine particles are ,100 nm. According to a new study from Harvard School of Public Health (HSPH). The greater the exposure, the greater the risk, researchers found. It was the first U.S.-wide study exploring the link between airborne particulate matter and autism. The researchers explored the association between autism and exposure to $PM_{2.5.}$ Little association was found between air pollution from larger-sized particles ($PM_{10\text{-}2.5}$) and autism. Air pollution are one of the environmental factors researchers believe may be associated with Autism Spectrum Disorder (ASD). In 2013 the American Psychiatric Association updated the criteria for diagnosing ASD in the fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5)(1).It represents a heterogeneous group of disorders that causes impairment in social interaction, as well as the presence of repetitive, restricted behaviours and interests. According to the Centres for Disease Control and Prevention, ASD affects roughly 1 in 68 children. Autism affects people for their entire lives, and often comes with other conditions, such as epilepsy, sleep disturbances, and gastrointestinal problems.

1.4 Health Impacts Linked to Pesticides Exposure:

Exposure to pesticides can range from mild skin irritation to birth defects, tumors, genetic changes, blood and nerve disorders, endocrine disruption, and even coma or death. The Natural Resource Defense Council has collected data which recorded higher incidence of childhood leukemia, brain cancer and birth defects due to early exposure to pesticides. Pesticides have been considered potential chemical mutagens: experimental data revealed that various agrochemical ingredients possess mutagenic properties inducing mutations, chromosomal alterations or DNA damage. Genetic damage associated with pesticides occurs in human populations subject to high exposure levels due to intensive use, misuse or failure of control measures. Studies using DNA –based methods also indicate that certain chemicals disrupt gene expression and this may follow on to generations that are not exposed to pesticides through epigenetic inheritance. This means that negative impact of pesticide usage can be extremely long term, even after the substance has been out lawed.

1.5 Effect of Ionizing Radiation:

Radiation exposure has significant consequences on genomic integrity, leading to mutations, chromosomal abnormalities, and increased disease susceptibility. Ionizing radiation, in particular, causes direct DNA damage through double-strand breaks (DSBs), oxidative stress, and disruption of cellular repair mechanisms. The effects of radiation exposure on genomes have been extensively studied in both human and plant populations exposed to nuclear disasters, medical radiation, and environmental contamination. Exposure to ionizing radiation can influence plant growth and development in various ways. Low doses may have stimulatory effects, while moderate levels can increasingly hinder vegetative growth. At high radiation levels, plants experience significant reductions in reproductive success and overall yield. The 1986 Chernobyl Nuclear Power Plant (ChNPP) accident released extremely high levels of acute ionizing radiation, causing severe damage or death to Scots pine (Pinus sylvestris) trees in the surrounding areas. The affected trees were removed and buried, with new plantations established a few years later. More than three decades after the ChNPP accident, the elevated levels of ionising radiation of ≥11 μ Gy h 1 (annual dose ≥ 98 mGy) cause substantial DNA damage and (sub)cellular effects in young Scots pine trees(2) .Recent research on Chernobyl liquidators has found some evidence of an increased risk of leukemia and other blood-related cancers. There are also indications of a higher likelihood of developing cataracts and potential links to an increased risk of cardiovascular diseases, even after exposure to low doses and low-dose-rate radiation(3).

2.Discussion

2.1 Genomics of ozone exposure

Polymorphisms in two metabolising enzymes have been associated with the effects of ozone exposure in human studies: an enzyme that produces hydroquinones that may react with ozone to reactive oxygen species (NAD(P)H:quinone oxidoreductase 1, NQO1), and a detoxification enzyme that reduces oxidative stress (glutathione-S-transferase M1, GSTM1) (4). When ozone is inhaled, it reacts with substrates in the epithelial lining fluid (eg, hydroquinones, formed from quinones by the enzyme NQO1), to produce reactive oxygen species, which are potentially damaging to the lung.A polymorphism is present in the NQO1 gene in exon 6, leading to a substitution at amino acid 187 of proline to serine. The proline form of the NQO1enzyme is resistant to degradation, making it more active than the serine form. With increased NQO1 enzyme activity, there is more reaction with ozone and greater build-up of reactive oxygen species. If there is also a deletion of the GSTM1 gene(null genotype), leading to impaired detoxification of reactive oxygen species, then this combination of polymorphisms (high production of reactive oxygen species and impaired detoxification) confers a high risk of oxidative stress from ozone.

2.2 Air pollution: risk factor for Autism Spectrum Disorder (ASD)

Exposure to air pollution contributes to the risk of Autism Spectrum Disorder (5).Most common recurrent cytogenetic abnormalities in ASD involve duplications and deletions of the maternally derived chromosome 15 (6).Work supported by NIEHS indicates that early-life exposure to air pollution is a risk factor for autism. A 2014 study pointed to a likely gene-environment interaction. Children whose genetic makeup causes them to be more susceptible to the health effects of high levels of air pollution showed the highest risk for autism.

2.3 Genetic hazard due to intensive use of pesticides.

P-glycoprotein (P-gp) is encoded by the human multidrug resistance protein 1 (MDR) 1 gene(7).It play a critical role in the detoxification of pesticide. It acts as an epithelial barrier and performs as excretory functions in various normal human tissues. It can extrude lipophilic compounds including chemotherapeutic agents and pesticides to the extracellular space by the ATP-dependent efflux transport mechanism. Alterations in P-gp expression and function potentially depend on structural variations of the MDR1 gene. Study conducted by Schinkel etal ;1994 found that constructed mdr1a-disrupted mice had increased toxicity by the pesticides due to its decreased elimination than normal mdr1a mice(8) .Human MDR1 is located on chromosome 7q21.1, and many single nucleotide polymorphisms (SNPs) within this gene have been identified- The two common synonymous SNPs are C3435T (rs1045642), located in exon 26 at position 3435, and C1236T (rs1128503), located in exon 12 at position 1236 . The other frequent nonsynonymous SNP is G2677T/A (rs2032582), which is located in exon 22 at position 2677. This polymorphism could change the amino acid from alanine (Ala) to Serine (Ser) or threonine (Thr) and result in the lower P-gp expression .Another important MDR1 SNP is T-129C (rs3213619). This polymorphism is located in the promoter region, and it has been established that -129C allele has a decreased P-gp expression .Chun-Chieh Chen etal ; 2014 found that pesticide exposed individuals with susceptible MDR1 -129 genotypes may experience increased risk of DNA damage(9). Lee etal; 2004 ,observed that the MDR1 C3435T, C1236T, and G2677T/A genetic polymorphisms were significantly associated with a higher risk of developing Parkinson's disease (10).

2.4 Radiation exposure effects on genomes:

Long-term radiation exposure has been observed in plant species, particularly in regions affected by nuclear accidents such as Chernobyl and Fukushima. Scots pine (Pinus sylvestris) populations in the Chernobyl Exclusion Zone exhibit increased mutation rates, genomic instability, and developmental abnormalities due to chronic exposure to ionizing radiation (11). Exposure to radioactive iodine-131 (^{131}I) from the Chernobyl disaster increased the risk of thyroid cancer. This isotope emits radiation that can break chemical bonds in DNA, and when the body attempts to repair the damage, mutations may occur. Exposure to ionizing radiation can induce single-strand breaks (SSBs), double-strand breaks (DSBs), and oxidative base modifications, all of which contribute to genomic instability. DSBs are particularly hazardous because they can lead to chromosomal rearrangements, deletions, and mutations if not properly repaired (12). The repair of such damage is primarily mediated by non-homologous end joining (NHEJ) and homologous recombination (HR), but errors in these processes can result in mutations or carcinogenesis (13).Radiation exposure is associated with chromosomal aberrations (CAs), including translocations, deletions, and aneuploidy, which increase the risk of cancers such as leukemia and solid tumors (14). For example, survivors of the Hiroshima and Nagasaki atomic bombings exhibited higher frequencies of chromosomal rearrangements, which were linked to increased cancer incidence (15).In addition to direct genetic mutations, radiation exposure can induce epigenetic changes such as DNA methylation alterations and histone modifications, leading to gene expression dysregulation (16). These changes can be inherited by subsequent generations, contributing to transgenerational genomic instability.

2.5 Cytogenetic Biomonitoring Studies

Genetic damage at the chromosomal level entails an alteration in either chromosome number or chromosome structure, and such alterations can be measured as Chromosomal Aberrations (CA), Micro Nuclei (MN) frequency and Sister-Chromatid Exchanges (SCE) analysis (17).A review of the literature

dealing with genotoxicity in human groups exposed to pesticides showed a large number of studies employing CA test, SCE analysis and MN assay . A Chomosomal Aberrations (CA) is a missing of extra or irregular portion of chromosomal DNA . Increased levels of CA have been associated with increased cancer risk. Micronuclei are acentric chromosomal fragments or whole chromosomes left behind during mitotic cellular division and appear in the cytoplasm of interphase cells as small additional nuclei. Micronuclei assays reflect chromosomal aberrations rapidly they are extremely useful for quick assessment of chromosomal damage. Sister Chromatids Exchanges (SCE) analysis was also adopted as an indicator of genotoxicity. The modulation of SCE by DNA precursors raises the possibility that DNA changes are responsible for the induction of SCE and mutations in mammalian cells. High levels of SCE and MN frequency have been observed in persons at higher cancer risk due to environmental exposure to a wide variety of carcinogens.

2.6 The National Center for Toxicogenomics: Using New Technologies to Inform Mechanistic Toxicology

National Institute of Environmental Health Sciences (NIEHS) has created the National Center for Toxicogenomics (NCT). This center's mission is to promote the evolution and coordinated use of gene expression technologies and to apply them to the assessment of toxicologic effects in humans (18.)It has established a new program that will apply powerful new techniques for studying gene and protein activity in order to identify unknown toxic substances more quickly and help treat people at the greatest risk for diseases caused by environmental pollutants or toxicants .The primary goal of this center's is to provide a worldwide reference system of genome-wide gene expression data and to develop a knowledge base of chemical effects in biological systems. Such a knowledge base will also, as a secondary goal, provide a profound understanding of the mechanisms by which stressor-induced injury occurs. This center's also using new technologies i.e Genomics-based tools enable the evaluation of gene-environment interactions and facilitate the identification of gene expression changes in response to toxicants. Microarray technology and next-generation sequencing (NGS) allow for genome-wide expression profiling, providing insight into molecular pathways affected by environmental exposures (19). These technologies help identify early biomarkers of toxicity, offering predictive models for human health risks.

3. Conclusion

Our genome is a huge field to be slowly unraveled. It is an unfinished work, drawn as we discover every gene, every interaction, every feature unraveled. We are rapidly advancing our work, but much remains to be drawn. Data on the occurrence of pollution-related illnesses among defined populations in developing countries are scanty. Genetic hazard related to environmental degradation needs educational programs in order to implement protection measure. There is a need to develop a more sensitive method to highlight early DNA damages in the exposed individuals. Protecting plant communities in ecosystems contaminated by radionuclides requires implementing strategies that reduce radiation exposure and foster ecological restoration. Understanding radiation-induced genomic damage is crucial for developing protective measures, including radioprotective agents, improved medical imaging protocols, and radiation shielding technologies. Further research in radiation genomics is necessary to identify biomarkers for radiation exposure and susceptibility. Thus a broad range of multidisciplinary studies is required in environmental genomics.

References

1. American Psychiatric Association. (2013). Diagnostic and statistical manual of mental disorders (5th ed.). Arlington, VA: American Psychiatric Publishing.
2. Line Nybakkena,b,*,1, YeonKyeong Leeb,c,f,1, Dag A. Bredea,b, Melissa H. Mageroyd, Ole Christian Linda,b, Brit Salbua,b, Valery Kashparovb,e, Jorunn E. Olsenb,c(2023). Long term effects of ionising radiation in the Chernobyl Exclusion zone on DNA integrity and chemical defence systems of Scots pine (Pinus sylvestris)ScienceoftheTotalEnvironment904166844.
3. E. Cardis1 and M. Hatch2 (2011)The Chernobyl accident — an epidemiological perspective; Clin Oncol (R Coll Radiol). 2011 May ; 23(4): 251–260. doi:10.1016/j.clon.2011.01.510.
4. A Yang, K M Fong,P V Zimmerman,S T Holgate,J W Holloway(2008) .Genetic susceptibility to the respiratory effects of air pollution ;63:555–563.
5. Autism and the Environment, (2014), National Institutes of Health, U.S. Department of Health and Human Services,www.niehs.nih.gov.
6. Richard J. Schroer, Mary C. Phelan, Ron C. Michaelis, Eric C. Crawford, Steven A. Skinner,Michael Cuccaro, Richard J. Simensen, Janet Bishop, Cindy Skinner, Don Fender and Roger E. Stevenson,(1998). Autism and Maternally Derived Aberrations of Chromosome 15q ,American Journal of Medical Genetics 76:327–336.
7. C.C.Chen, C.H. Huang, M.T. M. Wu, C.H.Chou, C.C. Huang, T.Y. Tseng, F.Y Chang, Y.T. Li, C.C. Tsai, T.S. Wang, and R.H.Wong , (2014), Multidrug Resistance 1 Gene Variants, Pesticide Exposure, and Increased Risk of DNA Damage, BioMed Research International.,9.
8. Schinkel, A. H., Smit, J. J. M., van Tellingen, O., Beijnen, J. H., Wagenaar, E., van Deemter, L., ... & Borst, P. (1994). Disruption of the mouse mdr1a P-glycoprotein gene leads to a deficiency in the blood-brain barrier and increased sensitivity to drugs. Cell, 77(4), 491-502. https://doi.org/10.1016/0092-8674(94)90212-7.
9. Chen, C.-C., Huang, C.-H., Wu, M.-T. M., Chou, C.-H., Lin, Y.-J., Tsai, C.-H., & Ko, Y.-C. (2014). Multidrug Resistance 1 Gene Variants, Pesticide Exposure, and Increased Risk of DNA Damage. BioMed Research International, 2014, Article ID 965729.
10. C G L Lee, K Tang, Y B Cheung, L P Wong, C Tan, H Shen, Y Zhao, R Pavanni, E J D Lee, M-C Wong, S S Chong, E K Tan .. J Med Genet (2004) MDR1, the blood–brain barrier transporter, is associated with Parkinson's disease in ethnic Chinese;41: e60 .
11. Møller, A. P., & Mousseau, T. A. (2013). Low-dose radiation, Chernobyl, and wild organism health. Annual Review of Ecology, Evolution, and Systematics, 44, 329-348.
12. Jeggo, P., Lobrich, M., & Stewart, G. (2011). DNA repair, genome stability and cancer: A historical perspective. Nature Reviews Cancer, 11(5), 336-346.
13. Little, J. B. (2003). Genomic instability and radiation. Journal of Radiation Research, 44(4), 335-344.
14. Müller, W. U., & Durante, M. (2001). Chromosomal aberrations and radiation-induced cancer. Mutation Research, 477(1-2), 91-102.
15. Preston, D. L., Shimizu, Y., Pierce, D. A., Suyama, A., & Mabuchi, K. (2007). Studies of mortality of atomic bomb survivors. Radiation Research, 168(1), 1-64.
16. Barcellos-Hoff, M. H., & Nguyen, D. H. (2009). Radiation carcinogenesis and epigenetics: How does exposure drive risk? Nature Reviews Cancer, 9(9), 696-707.

17. C. Bolognesi. (2003), Genotoxicity of pesticides: A review of human biomonitoring studies, Mutat Res., (543),251–272.
18. National Center for Toxicogenomics, New NIH Center at National Institute of Environmental Health Sciences, Environmental Health Perspectives ,Editorial, volume 110 | number 1 | january 2002.
19. Nuwaysir, E. F., Bittner, M., Trent, J., Barrett, J. C., & Afshari, C. A. (1999). Microarrays and toxicology: The advent of toxicogenomics. Molecular Carcinogenesis, 24(3), 153-159.