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Review Article

Exploring the Role of Medical Geology and Diet as Non-Genetic Factors in Cancer Resistance in Ramsar, Northern Iran: A Review

Hassan Bahrami[1], Pouya Zohdparast[2], AmirAli Fallah[3], Hassan Vafapour[4], Alireza Mortazavi[5], Seyed Mohammad Javad Mortazavi[3,4*], Seyed Jalil Masoumi[6*]

1. Independent Health/Nutrition Researcher, Tehran, Iran
2. Petroleum Engineering, Institute of Petroleum Engineering, University of Tehran, Tehran, Iran
3. Department of Medical Physics and Engineering, School of Medicine, Shiraz University of Medical Sciences, Shiraz, Iran
4. Ionizing and Non-Ionizing Radiation Protection Research Center (INIRPRC), Shiraz University of Medical Sciences, Shiraz, Iran
5. MVLS College, The University of Glasgow, Glasgow, Scotland, UK
6. Nutrition Research Center, Department of Clinical Nutrition, School of Nutrition and Food Sciences, Shiraz University of Medical Sciences, Shiraz, Iran

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*Corresponding author:
Seyed Jalil Masoumim MD, MPH, PhD;
Department of Clinical Nutrition, School of Nutrition and Food Sciences, Shiraz University of Medical Sciences, Shiraz, Iran.
Email: masoumi7415@gmail.com
Seyed Mohammad Javad Mortazavi, PhD;
Ionizing and Non-Ionizing Radiation Protection Research Center,Shiraz University of Medical Sciences, Shiraz, Iran.
Email: mmortazavi@sums.ac.ir
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ABSTRACT

This article explores the notably low cancer incidence among the indigenous population in Ramsar, Iran, an area with the world's highest levels of natural background radiation. The elevated radium concentrations in sedimentary rocks, hot springs, and indoor air provide a unique environment for studying radiation exposure and adaptation. Beyond genetic factors, this study hypothesized that the predominantly plant-based diet of Ramsar residents that is rich in raw vegetables, fruits, nuts, and garlic; plays a significant role in mitigating cancer risks. This manuscript synthesized existing evidences on diet's protective role against cancer, contrasting it with the impact of acidogenic diets high in processed foods and animal proteins, as observed in Hungary. The findings highlighted how lifestyle and diet could modify the health impacts of environmental stressors.

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Introduction

Natural sources of radioactivity, including uranium, radium, and radon, are widespread in the environment and contribute significantly to human radiation exposure. These naturally occurring radioactive materials (NORMs) account for approximately 82% of total human radiation exposures (1, 2). Uranium and thorium decay the series of radionuclides that are found in various geological formations, rocks, soils, and building materials (2, 3). The distribution of these radioactive elements is influenced by geochemical processes and environmental factors (3). Human activities, such as the use of phosphate fertilizers were shown to redistribute large amounts of uranium and radium throughout the environment (4). Additionally, waste gypsum piles from fertilizer production are significant sources of radon emissions (4). Understanding the distribution and behavior of these natural radioactive materials is crucial for assessing potential radiological impacts and managing human exposure to background radiation (2). Human exposure to these elements is heightened in areas near uranium deposits, extraction sites, or regions with unique geochemical characteristics. Ramsar, Iran, is a notable example of such a region, where sedimentary rocks contain radium concentrations up to a million times higher than typical levels (5, 6).

It was shown that high background radiation areas (HBRAs) in Ramsar have provided insights into the effects of chronic low-dose radiation exposure. Residents of these HBRAs receive annual radiation doses of up to 260 mSv, significantly exceeding recommended limits (5, 7). Cytogenetic studies have shown no significant differences in chromosomal abnormalities between HBRA inhabitants and those in areas with normal background radiation, and HBRA residents even display reduced chromosomal damage when exposed to high-dose radiation (5, 8, 9). Preliminary investigations suggested no detrimental health effects among HBRA populations (10, 11). However, due to small sample sizes, further research is needed to draw definitive conclusions about cancer risks (7). An animal study indicated that short-term exposure to extremely high levels of natural radiation in Ramsar did not induce oxidative stress (12). These findings challenge the linear no-threshold model and suggest potential adaptive responses to chronic low-dose radiation exposure.

Mortazavi's studies on high background radiation areas, particularly in Ramsar, have significant implications for environmental health. These studies challenge traditional views on radiation exposure and its health impacts, suggesting the potential protective effects against cancer in high-radiation environments. These researches conducted in Ramsar provided a unique perspective on the biological effects of chronic radiation exposure, which could influence public health policies and radiation safety standards (5, 12, 13). So this study determined the non-genetic factors of cancer resistance among Ramsar residents in relation to medical geology and the diet searching the available data sources.

Medical Geology of HBRAs in Ramsar

Ramsar is located in northern Iran and is renowned as a HBRA due to its elevated natural radiation levels, primarily attributed to the presence of radioactive elements in its sedimentary rocks. This region provides a unique setting to study the health implications of long-term exposure to high levels of natural radiation. The high radiation levels in Ramsar are mainly due to the presence of radium, a decay product of uranium, in the local sedimentary rocks. These radium concentrations are significantly higher than typical global levels, leading to an increased radiation exposure through various pathways, including soil, water, and air. Radon gas, a decay product of radium, is a significant contributor to indoor radiation exposure in the region (14). Despite the high radiation background, studies have suggested that the residents of Ramsar do not exhibit the expected negative health effects, such as increased cancer rates. This phenomenon has sparked interest in the concept of an "adaptive response," where low doses of radiation might enhance cellular resistance to damage from higher doses. However, the mechanisms behind this are not fully understood and require further investigation.

The dietary habits of Ramsar residents that are rich in antioxidants from fruits and vegetables, may play a role in mitigating the effects of radiation-induced oxidative stress (15). Additionally, comparative studies with other high-radiation areas, such as Guarapari in Brazil and Yangjiang in China, are essential to understand the uniqueness of Ramsar's health outcomes (16-19). The reliability of studies conducted in Ramsar is influenced by factors such as sample size and study design. Meta-analyses and reviews that aggregate data from multiple studies can provide more robust conclusions. Genetic factors, including potential adaptations to radiation, are also a critical area of research, potentially involving genome-wide association studies (GWAS). In summary, the medical geology of Ramsar offers a complex interplay of geological, biological, and environmental factors. Systematic research, considering geological sources, health studies, dietary influences, and genetic adaptations, is essential to fully comprehend the implications of high background radiation on human health. This knowledge could have far-reaching effects on radiation safety standards and space exploration strategies.

Protective Effects against Cancer

Cancer is still a significant health issue in the developing countries and is likely to rise in future (20). It can affect all body organs including brain (21), oral cavity (22), esophagus (23), stomach (24), colon (25), breast (26), lung (27), prostate (28), bladder (29), etc.

Mortazavi *et al.*'s studies on mice exposed to high levels of natural radiation in Ramsar found that higher radiation exposure did not correlate with increased cancer growth. Instead, mice in the highest radiation group showed reduced tumor size and progression, along with higher survival rates, suggesting a protective effect against melanoma progression (12, 13). Also in mouse and rat, when animals were irradiated with 10 Gy ^{60}CO for all the body area, acute radiation syndrome occurred (30-32). The concept of radiation adaptive response, as discussed by Bugała and Fornalski, supports these findings. Their research indicated a reduction in chromosomal aberrations, cancer incidence, and mortality in high background radiation areas, suggesting an adaptive biological response to chronic radiation (33).

Adaptive Response in Human Populations

Studies on Ramsar residents using micronucleus assays have shown significant differences in chromosomal damage between residents of high radiation areas and control groups. An adaptive response to radiation was noticed in residents showing less chromosomal damages when compared to controls after radiation exposure (34). The adaptive response is further supported by the observation that the frequency of chromosomal aberrations was correlated with individual radiosensitivity that indicates a complex interaction between radiation exposure and biological adaptation (33).

Broader Implications for Space Missions

The chronic exposure to high-linear energy transfer (LET) radiation in Ramsar was considered analogous to conditions in space, providing insights into potential radiobiological hazards for manned space missions. This research highlighted the importance of studying human populations in high radiation areas to better understand the long-term effects of radiation exposure (35). The potential benefits of high background radiation reveal that it is crucial to consider the variability in individual responses to radiation and the need for further researches to fully understand the mechanisms behind these adaptive responses. The implications for environmental health are profound, as they challenge existing radiation safety paradigms and suggest a need for reevaluation of current standards (36, 37).

Given these considerations, although high radiation exposure is typically associated with increased cancer risk, indigenous Ramsar residents exhibited a paradoxically low incidence of cancers, particularly lung and colorectal types. This phenomenon may result from a combination of genetic adaptations and lifestyle factors. This article investigated the potential protective role of Ramsar's predominantly plant-based diet in mitigating cancer risks, contrasting these findings with dietary and environmental conditions in other high-radiation areas, such as Hungary searching the available data sources.

Dietary Factors and Cancer Resistance

Cells require optimal conditions, including appropriate pH, oxygenation, and nutrient availability, to maintain normal function (38). Unfavorable environments can trigger cellular stress, leading to mutations and potentially cancer (39). The diet of Ramsar residents is consisted of raw garlic, fresh vegetables, fruits, nuts, and seeds that is rich in antioxidants and can support cellular resilience (40). In contrast, diets high in acidogenic foods, such as processed red meats, sugary drinks, and refined carbohydrates, are linked to higher cancer risks (41-43).

Research Supports

Regular consumption of raw garlic can reduce lung cancer risk by modulating inflammation and oxidative stress (44). Plant-based diets can improve metabolic homeostasis and reduce the likelihood of carcinogenesis (45). Antioxidant-rich foods can help maintain cellular health, creating conditions less conducive to cancer development (46).

Comparative Analysis: Ramsar vs. Hungary

Hungary's population exhibits high age-standardized rates of lung and colorectal cancers (47, 48). Factors contributing to this include Diets characterized by high animal protein and low fruit and vegetable intake (49) and exposure to heavy metals and radiation from natural and industrial sources (50). These findings contrast sharply with Ramsar, where residents consume a balanced, nutrient-dense diet. The observed disparities underscore the interplay between diet, environmental exposures, and cancer risk.

Radiation and Adaptation

Ramsar's indigenous residents have adapted over generations to high radiation levels. It was shown that long-term exposure may enhance cellular repair mechanisms and immune responses and reduce cancer susceptibility. Dietary factors can likely play a complementary role by minimizing oxidative stress and supporting DNA repair too (5, 8, 9, 12, 14, 34, 35).

Conclusion

The low cancer rates among Ramsar's indigenous population highlight the potential synergy between genetic adaptations and lifestyle factors, particularly diet. A predominantly plant-based diet, rich in antioxidants, appears to enhance resilience against radiation-induced stress and carcinogenesis. Conversely, populations with diets high in acidogenic foods, such as Hungary, demonstrated higher cancer rates under similar environmental conditions. These findings underscore the importance of dietary interventions in mitigating cancer risks in high-radiation environments. Future research should focus on integrating dietary studies with genetic and environmental analyses to develop holistic cancer prevention strategies.

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Authors' Contribution

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Conflict of Interest

None declared.

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