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Assessing cancer mortality in high natural background radiation areas: a systematic review

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Abstract

Introduction: Low background radiation levels are constantly around us, but generally there are some high natural background radiation areas (HNBRAs) in the world including Ramsar in Iran, Guarapari in Brazil, Kerala in India, Arkaroola in Australia, and Yangjiang in China. The present study aims to explore the relationship between living in HNBRAs and cancer mortality rate.

Materials and Methods: A perfect search was conducted in Google Scholar, Scopus, PubMed, and databases and articles with the key terms "High natural background radiation", "cancer prevalence in HNBRAs", " natural radiation" and " mortality" using MeSH.

Results: The results of this study are based on articles published in national and international journals, dissertations, and reference sites. In a total of 156 documents, 33 (21.15%) were selected. Many epidemiological and experimental studies demonstrated that at low natural background radiation doses, cancer incidence is not proportionally related to living in HNBRAs, while even beneficial effects are often observed at low natural background radiation doses. It is evident that chronic radiation exposure is not only less harmful per unit dose than acute radiation but can also induce cellular responses such that adaptation phenomena appear. Thus, some researchers have reported a direct relationship between HNBR and cancer mortality, and some others have found no relationship between the two variables.

Conclusion: More recent studies have highlighted the absence of any direct connection between high natural background radiation and the prevalence of cancer in people living in HNBRAs. Some studies have suggested that low natural background radiation is not only harmless but may be beneficial to health through adaptations, while others believe that even the smallest doses of radiation are harmful.

Keywords: Cancer, Natural radiation, High natural background radiation areas, Ramsar, Mortality

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Introduction

Radiation refers to the release or transfer of energy in the form of waves or particles that can penetrate matter and humans. Radiations are divided into two groups of ionizing and non-ionizing rays according to their effects on matter (1). Radioactive materials exist throughout nature and can be detected in soil, rock, water, air, and plants (2). These materials enter the body by inhalation or swallowing (1). In addition to exposure from inside the body, humans are also externally affected by radioactive materials outside the body and space (cosmic radiation) (3). The average natural radiation rate is about 2.4 Millie Sievert (mSv) per year (4). This amount is four times the global average rate of artificial radioactivity, which was about 0.6 mSv per year in 2008 (2). In some rich countries, the frequent use of medical imaging leads to higher average rates of artificial radioactivity compared to the natural radioactivity rate (5). In Europe, natural radioactivity ranges from 2 mSv per year in England to more than 7 mSv per year for some groups in Finland (6) some areas contain doses or amounts higher than the national average. In general, places with high natural background radiation include Ramsar in Iran, Guarapari in Brazil, Kerala in India, Arkaroola in Australia, and Yangjiang in China (5, 7). The problem of high background radiation in the world has been attracting the attention of researchers for a long time (8). The history of radiobiology shows that the biological effect of relatively high radiation doses was recognized only shortly after the discovery of X-rays and radioactivity, but the effects of low radiation doses on human health are still unknown and are the focus of many investigations (9). There is controversy over whether low radiation rates pose a significant health risk. On one hand, the linear no-threshold model (LNT) assumes that even the smallest amounts of radiation are harmful (10) and, on the other hand, it argues that exposure to low-level radiation is not only harmless (11), but may also benefit health through adaptation (12-15).

According to the United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR, 2000), the coastal city of Ramsar has the highest level of background radiation among all residential areas in the world (16). For example, the average natural radiation rate is about 13 mSv per year in Kerala and about 240 mSv per year in Ramsar (17). The use of laboratory animals in medical sciences has led to progress in the prevention and treatment of diseases so that they are used to study many incurable human diseases such as heart failure and stroke (18, 19). Hence, high natural background radiation in Ramsar has motivated researchers to conduct many experiments on the effects of these radiations on vital parameters in animal and human samples (20, 21). Surprisingly, the maximum annual dose allowed for radiation technologists (radiographers) is 20 mSv per year, and following the recommendation of the International Commission on Radiological Protection (ICRP), to prevent the possible effects of radiation such as cancer and genetic diseases, the annual dose for ordinary people should be less than 1 mSv (22). A comparison of natural background radiation doses in different regions of the world shows the radiation rate in Ramsar is about 90 times the dose that forced the evacuation of 200,000 residents in the areas contaminated by the Chernobyl disaster in 1986 (23). Simple scientific estimates have shown more physical and health problems in all residents of high natural background radiation areas (HNBRAs) in Ramsar with radiation exposure of a maximum of 240 mSv per year compared to normal people with an average radiation rate of 1 mSv per year (24-26). However, previous studies in the literature have reported inconsistent results (27). To this end, the present study aimed to investigate the cancer mortality rate in people living in high natural background radiation areas (HNBRAs) and to find out whether there is a relationship between living in these areas and cancer deaths.

Materials and Methods

This study is one of the systematic reviews with the aim of investigating the cancer mortality rate in people living with HNBRAs until December 30, 2017. The research was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-analyses guidelines (PRISMA) (28).

One of the inclusion criteria for entering the research was a quantitative study mentioning the mortality rate due to cancer in HNBRAs. The exclusion criteria of this research were: not mentioning the mortality rate caused by cancer in HNBRAs, lack of relation between the study and the research topic, qualitative articles, and articles with repetitive topics.

A perfect search was conducted using the Persian keywords and English synonymous in international databases including MEDLINE, Google Scholar, Scopus, PubMed, and databases and articles with the key terms "High natural background radiation", "The mortality rate due to cancer in high natural background radiation areas", "natural radiation" and "mortality" using MeSH and Boolean operators such as "AND", "OR" and "NO" were searched published by 11/30/2022 and a number of articles related to prevalence of cancer in residents of high natural background radiation areas were selected. The search databases were to accomplish searches with high sensitivity (Highly Sensitive Searching) and also the search was achieved by a senior researcher and expert in the field of searching databases. The entire process of research including, search, selection of contents, typicality valuation of studies, and data gathering was accomplished independently by two researchers to evade publication bias, and the third researcher was performing the final assessment in the event of a conflict. After the search, EndNoteTM software was used to reveal duplicates. Also, manual searching was done by reviewing the reference list of suitable articles.

Results

In a systematic comprehensive search, 156 articles relevant were found on the above-mentioned database published by 11/30/2022. After the checking Items found, 62 of them were eliminated via investigating titles and their abstracts and 94 were eligible for evaluation of their full-text.

Afterward, articles that lacked inclusion criteria or studies that had incomplete information or had exclusion criteria were excluded from this research. Eventually, 28 (21.15%) remaining documents were selected in this systematic review. The characteristics of a number of studies used in the present study are given in Table 1.

Table 1. The characteristics of the studies included in the present study.

Name	Year	Location	Result
BEIR VII (1,2)	1990, 2006	Generally	The number of radiation-initiated cancers is exceptionally little compared with the number of actually happening cancers making location of this overabundance exceptionally troublesome.
Gianferrart et al. (29)	1962	Piemonte, Italy	Mortality rates from other causes as well as cancer are higher in HBR than in NBR.
Mortazavi et al. (30)	2005	Ramsar, Iran	Appeared that the frequency of lung cancer in individuals living in Ramsar is lower than Also lymphocytes within the control bunch. experienced a compromise, and their reaction to rehashed high-dose radiation was lower.
David Elroei et al. (31)	2021	United States	Appeared a critical diminishment within the mortality rate from cancers in both men and women.
Hendry et al. (32)	2009	Guarapari, Brazil; Kerala, India; Ramsar, Iran; Yangjiang, China	These considers illustrated no expanded dangers within the HNBR ranges compared to control/reference populaces. The later ponder in Yangjiang, China, appeared a noteworthy abundance of non-cancer mortality. In Iran, as it were chromatid-type variations (not particular for radiation) were found to be enhanced.

Yamaoka et al. (33)	2004	Okayama, Japan	The result shows us that the small dose of radon has healing effects and can be used as a treatment.
Thompson et al. (34)	2008	Case - Control Study	lung In their studies, they found a link between cancer and radon exposure.
Fornalski et al. (35)	2011	Poland	The results indicate that in different doses, the relation can be seen as increasing, decreasing and hormesis effects.
Denton et al. (36)	2013	Guam, USA	Data shows that residents of areas with higher radon levels are more resistant to lung cancer than their counterparts.
Wei et al. (37)	2000	Yangjiang, China	The results of the human body's adaptive response test show that long-term exposure to high background radiation causes lymphocytes to show less sensitivity in laboratory conditions.
Hauri et al. (38)	2013	Switzerland	The gotten comes about did not appear a relationship between indoor radon and children's cancer. There was no prove of direct exposure–response affiliations for any of the results.
Jaikrishan et al. (39)	2013	Kerala, India	Appeared no coordinate relationship between radiation levels in HNBRs and cancer mortality. Moreover, did not influence stillbirths and major intrinsic mutations in newborn children.
Kumar et al. (40)	2012	Kerala, India	The DNA harm of those who lived within the HNBR region diminished with age, whereas the DNA harm of the reference bunch expanded with age.

Discussion

There is no place on the earth without natural ionizing background radiation. This background radiation is now much lower than when our planet was formed. This clearly shows that organisms living in the same environment for a long time evolve to adapt to this radiation dose (41). Many studies conducted in this field have not shown that background radiation has caused an acute or latent disease such as cancer (41). Numerous epidemiological and experimental studies demonstrated that at low natural background radiation doses, cancer incidence is not proportionally related to living in HNBRAs, while even beneficial effects are often observed at low natural background radiation doses (42). Moreover, it is evident that chronic radiation exposure is not only less harmful per unit dose than acute radiation but can also induce cellular responses leading to adaptation phenomena (43-45).

A review study by Aliyu and Ramli on studies addressing life in HNBR areas has critically received extensive attention (45). The authors concluded that the number of epidemiological studies may not be sufficient to rule out the effect of increased radiation in HNBRAs. For instance, cytogenic studies on biological systems have shown some chromosomal aberrations in people living in HNBRAs (46). However, most of the reviewed studies have not found any relationship between cancer mortality and reduced life expectancy. Moreover, Mortazavi et al, showed that the incidence of lung cancer in people living in Ramsar is lower than in the control group (30). Interestingly, Ghiassi-Nejad et al, found the presence of an adaptation response in people living in HNBRAs (47).

As stated earlier, existing regulations on radiation protection rely heavily on the LNT model, which predicts that any dose of ionizing radiation, however small, carries a certain risk of harm to health, particularly cancer (48). This hypothesis has its origin in the wrong behavior of several influential scientists in the world (49).

The data presented by Gianferrart et al, on cancer mortality in HNBRAs and natural background radiation areas (NBRAs) show that mortality is related to the difference in internal and external radiation and the effects of radiation are more obvious due to increased cumulative dose at the age of 61 to 80 years (29).

It is not reasonable to confirm the relationship between cancer incidence and natural radiation based on the results reported by Gianferrart et al (29). However, some studies have shown that natural sources of small doses of radiation can increase the probability of developing cancer (50).. In contrast, Elroei et al, showed a significant reduction in the mortality rate from lung and bronchial, pancreatic, colon, and rectal cancers in both men and women living in HNBRAs and were stated that can even have useful health effects in humans (31).

According to the study by Gianferrart et al, significant reductions were observed for brain cancer and bladder cancer only in men. Besides, there is a clear tendency for liver and bile duct cancer (29). In contrast, no significant effects were observed for leukemia, kidney, pelvic, and stomach cancers nor gender-specific cancers (cervical, ovarian, breast, and prostate) for either men or women (29).

Natural background radiation levels on the earth vary significantly, even by a factor of two. The magnitude of the radiation level varies from place to place with a global average annual effective dose of about 2.5 mS (32). Jagger showed that in NBR areas, the radiation rates at lower altitudes are lower than at higher altitudes (13). Besides, a comparison of low and high areas in terms of cancer rates showed lower cancer rates in high altitudes (51).

However, in some places (e.g., Ramsar in Iran), the radiation levels increase several times (30, 32, 45). Thus, areas with dose rates higher than about 10 mSv per year are commonly called HNBRAs (30, 32, 45). The results obtained so far are still speculative and it is not possible to say how big the uncertainties are, nor is it clear whether the observed chromosomal aberrations are correlated with cancer incidence and/or mortality (41). This article further emphasized the relationship between dose level, dose rate, and cancer mortality in groups of individuals living in HNBRAs (46). Moreover, since most of the previous studies emphasized a linear relationship, ellipse analysis was performed in this study to investigate this relationship (31).

Hendry et al, reviewed the results of HNBR radiation studies and the cancer risk of populations living in HNBRAs (Guarapari in Brazil, Kerala in India, Ramsar in Iran, and Yangjiang in China) to estimate the potential health risks at low doses (32). It is worth noting that low doses of radon can even have healing effects, as discussed by Yamaoka et al (33). As no statistically significant evidence of harmful effects of doses has been observed, a review of case-control studies indicated no clear association between high-level radon exposure and lung cancer in miners (30).

Hendry et al, have provided convincing evidence of the relationship between long-term exposure to radiation and the occurrence of disease in a certain dose range (32). Moreover, they have reasonably argued that "many countries that have HNBRAs lack health statistics, especially cancer prevalence statistics (32). An analysis of 28 reports on lung cancer, possibly caused by radon , shows that the published data have large gaps and are scattered (52). For instance, there are no clear findings for a radon concentration of 800 Bq/m^3 (Becquerel per cubic meter) (52). These statistical findings of radon contradict the conclusions drawn by UNSCEAR highlighting the high radiation risk, even at a radon concentration of 100 Bq/m3 (53). Ecological studies have been often performed on large and widely reported cohorts, and our knowledge of the health effects of ionizing radiation is largely based on such studies(54). For example, Cohen’s controversial analysis of the risk of radon shows a reduction in lung cancer (55). The incidence of cancer with increasing radon exposure was later confirmed in case-control studies by Thompson et al (34). Additional ecological studies have analyzed the risk of cancer caused by natural radiation in China (Wei et al) , Guam (Denton et.al) , Poland (Fornalski et al) (35), the United States and Switzerland (Hauri et al) (35-38). Another recent case-control study conducted by Jaikrishan et al in 2013 (39) did not show a direct relationship between radiation levels in HNBRs and cancer mortality. Moreover, HNBR radiation levels in Kerala, India, did not affect stillbirths and major congenital malformations in infants (56).

The often-stated adaptation theory assumes that people living in HNBRAs have adapted to the radiation levels in the area (44). Previous increases in natural radiation levels, assuming to be correct, indicate that radiation protection recommendations can consider the radiation level in a given environment as the best reference level (32, 45). Feinendegen et al and Scott et al, have focused on mechanisms that are not yet fully understood and do not involve adaptive protection as far as regulators of radiation protection are concerned (52, 57). On the other hand, Mortazavi et al, showed that lymphocytes from individuals residing in the HNBR area of Ramsar underwent a compromise, and their response to repeated high-dose radiation was lower (30). The results of another study conducted by Kumar et al, in the HNBR area of Kerala, India, showed that the incidence of DNA damage per person decreased with age, while in the control population, the incidence of DNA damage, as expected, increased with age (40). Finally, the lack of any correlation between living in HNBRs and cancer deaths in biophysical studies can be attributed only to this adaptive protection (adaptive response effect) (52, 57), as a general basis for radiation hormesis. The elliptic analysis is more effective than linear analysis in describing the data with functions containing several different components (58).

Conclusions

Cancer mortality risks from low doses, like high background radiation exposures, appear to be absent or much lower than effects commonly assumed, especially when assessed by epidemiological methods alone. However, the current epidemiological and experimental data do not favor low-induced doses. Following the findings of the present study, the claim that exposure to HNBR rates leads to cancer is unjustified and misleading. The results of the Bayesian analysis, as presented in this paper and applied to the available data for HNBR regions, indicated that cancer mortality decreases in proportion to dose. However, these results could not lead to any positive correlation between cancer mortality and radiation doses. Therefore, if hormesis, i.e. benefits outweighing harm, is not proven, it can still be argued that there must be a minimum threshold dose for cancer, where benefits and harms balance each other.

Author contribution

All the authors met the standard writing criteria based on the recommendations of the International Committee of Medical Journal Editors and all contributed equally to the writing of the work.

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Conflict of interest

The authors declare no competing interests.

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