

# Is Induction of Anomalies in Lymphocytes of the Residents of High Background Radiation Areas Associated with Increased Cancer Risk?

Mortazavi S. M. J.<sup>1,2</sup>, Mortazavi Gh.<sup>2</sup>, Mortazavi S. A. R.<sup>3</sup>, Paknahad M.<sup>4,5\*</sup>

## ABSTRACT

Man has been exposed to different levels of natural background radiation since the creation of human life. There are inhabited areas around the world with extraordinary levels of natural background radiation. The level of natural radiation in these areas is up to two orders of magnitude higher than other places. Areas such as Yangjiang, China; Guarapari, Brazil; and Kerala, India are among the areas with high levels of natural radiation. Ramsar a coastal city in North Iran has some inhabited areas with the highest known levels of background radiation around the world. People who live in high background radiation areas (HBRAs) such as Ramsar do not record any detrimental biological effects. While some cytogenetic studies conducted in HBRAs have shown increased frequencies of unstable chromosome aberration, other investigations failed to find a significant difference. This short review is an attempt to verify if induction of chromosomal anomalies in the lymphocytes of the residents of high background radiation areas is associated with increased cancer risk.

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## Keywords

Human Lymphocytes, High Background Radiation Areas, Natural Radiation, Cancer Risk

## Introduction

Humans are immersed in an ocean of natural background radiation. Some basic factors such as altitude and the concentration of radionuclides in the Earth's crust determine the level of background exposure in each place. Interestingly, there are inhabited areas around the world with extraordinary levels of natural background radiation (up to two orders of magnitude higher than other places). These extraordinary high levels of background radiation have been reported to be due to high concentration of some radionuclides in the soil or water streams or due to above-the-normal concentrations of indoor radon and its decay products. Although the level of background radiation in areas such as Yangjiang, China; Guarapari, Brazil; and Kerala, India is extraordinarily high, Ramsar, a coastal city in North Iran, has some inhabited areas with the highest known levels of background radiation around the world. It is worth noting that people have lived for many generations in high background radiation areas (HBRAs) such as

<sup>1</sup>Professor of Medical Physics, Medical Physics Department, School of Medicine, Shiraz University of Medical Sciences, Shiraz, Iran

<sup>2</sup>Ionizing and Non-ionizing Radiation Protection Research Center (INIR-PRC), Shiraz University of Medical Sciences, Shiraz, Iran

<sup>3</sup>Student of Research Committee, School of Medicine, Shiraz University of Medical Sciences, Shiraz, Iran

<sup>4</sup>Oral and Dental Disease Research Center, School of Dentistry, Shiraz University of Medical Sciences, Shiraz, Iran

<sup>5</sup>Assistant Professor of Oral and Maxillofacial Radiology, School of Dentistry, Shiraz University of Medical Sciences, Shiraz, Iran

\*Corresponding author: M. Paknahad, D.Ds Oral and Maxillofacial Radiology Department, Shiraz Dental School, Ghasrodasht Street, Shiraz, Iran.  
E-mail: paknahadmaryam@yahoo.com

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Kelara (35 mSv/y) and Ramsar (260 mSv/y) [1] without any recorded detrimental biological effects. Indoor levels of Rn-222 in some houses in Ramsar are as high as 31,000 Bq/m<sup>3</sup>, resulting in mean internal exposures up to 71 mSv/y [2]. It is well documented that Ramsar, has inhabited areas with the highest recorded levels of background radiation on Earth [3]. The health effects of exposure to above-the-normal levels of natural ionizing radiation in HBRAs of Ramsar [4-10] including the first reports on the induction of adaptive response (AR) in the residents of these areas [11, 12] have been previously reported by our team. Some evidence shows that that exposure to high levels of natural background radiation can induce adaptive phenomena in microorganisms which make them better cope with the lethal effects of even antibiotics [13].

### Chromosome Aberration

Although some cytogenetic studies conducted in HBRAs of Ramsar have shown increased frequencies of unstable chromosome aberration [14], other studies were unable to find any statistically significant difference in the frequency of chromosome aberration in lymphocytes of HBRAs and normal background radiation areas (NBRAs) [11, 15]. Increased frequency of chromosome aberrations (dicentric and rings) in HBRA of Southern China, an area with three to five times higher levels of background radiation compared to that of the control area has been previously reported. However, they could not detect any significant increase in the frequency of translocations in HBRA [16]. However, researchers found a positive correlation between the rates of dicentric and ring chromosomes and age in HBRAs of China, while a similar relationship was not detectable in control areas. This study showed that the frequency of dicentric and rings increased linearly over lifetime due to exposure to chronic background radiation [17]. Very similar to the findings of Ramsar, Chinese researchers also could not detect any

increase in the frequency of translocation in the residents of HBRAs [18]. It has been reported that in Southern China, the level of chromosome aberrations induced by exposure to above-the-normal levels of natural radiation is not as important as those induced by other mutagenic factors such as smoking [19, 20]. In this light, it seems that metabolic factors or mutagenic agents (other than ionizing radiation) in HBRAs of China play a more important role in the induction of chromosome aberrations than ionizing radiation [21]. Therefore, it can be argued that the induction of stable type chromosome aberrations in HBRAs of China is more affected by the chemical mutagens and metabolic factors than high background radiation [22]. Another study conducted on the frequencies of chromosomal aberration and karyotype anomalies in the newborns from HBRAs of Kelara could not reveal any difference with the levels found in NBRAs [23]. In China, Zhang *et al.* also reported that the above-the-normal levels of natural radiation possibly play a less significant role than smoking in the induction of stable type chromosome aberrations (translocations and inversions). In spite of this, some reports indicate that the frequencies of both stable and unstable chromosome aberrations (dicentric and rings) in the residents of HBRAs were higher than control areas [24].

It has also been reported that elevated level of background radiation in Kerala coast was not associated with any significant effect on the telomere length of newborns [25]. Indian scientists also found that exposure to high levels of natural radiation could not affect telomere length in adult population residing in HBRAs of Kerala coast [26]. In an experiment performed on the spontaneous rates of DNA double strand breaks (DSBs) in peripheral blood mononuclear cells of the residents of HBRAs of Kelara and a NBRA, it was shown that the dose rate of 5.0 mGy/year could be a possible threshold dose for the induction of DSBs by in-vivo chronic low-dose radiation

exposure [27].

### Micronuclei Assay

It is generally believed that higher levels of environmental radiation are always equal to higher rates of micronuclei (MN). Furthermore, experiments performed later on the induction of micronuclei either in Ramsar [28] and Kerala [29, 30] could not reveal any statistically significant difference between the overall frequency of MN in HBRAs and the normal background radiation areas. In another study, it was suggested that elevated level of naturally occurring radiation in Kerala has no significant effect on the induction of micronuclei frequency among the newborns [31].

### Comet Assay

Mohammadi et al. in their study performed in 2006 showed that the rates of induced DNA damage and repair were significantly higher in the mononuclear cells of the resident of HBRAs compared to those of NBRAs [28]. In another study, it was found that spontaneous level of DNA damage and the induced DNA damage in all challenging doses in high natural background radiation areas of Ramsar were considerably higher than control groups [32]. In a similar pattern, the inhabitants of Tamil Nadu, India HBRAs showed significant risk of genetic damage that was confirmed by the alkaline comet assay. In this study, a significant rise in comet tail frequency was observed in the residents of HBRAs compared to controls. However, due to significant role of some major confounding factors, the authors conclude that exposure to elevated levels of background radiation by itself does not pose any significant risk of genetic damage [33].

### Cancer Incidence

Although in some areas, high levels of background radiation have been linked to increased frequency of chromosome aberrations in the circulating lymphocytes of the residents; the carcinogenic effect of these levels of natu-

ral radiation is not proven yet [34]. The link between different levels of natural radiation and cancer morbidity and mortality has been addressed in some countries. The findings of these studies are controversial. While studies conducted in Italy [35] and Poland showed a positive association, studies performed in India [36] and Ireland [37] failed to show any significant relationship. In Ramsar, a slight increase was found in cancer mortality and morbidity among female residents of HBRAs. However, the observed differences for both mortality ratios and incidence ratios were not statistically significant [38]. Nevertheless, Mortazavi et al. showed a negative correlation between radon concentration and frequency of lung cancer in eight districts of Ramsar with different levels of radon [39]. In China, Tao et al. could not reveal any increased cancer risk associated with high levels of natural radiation in HBRA of Yangjiang [40]. An earlier study also showed that the mortality from all cancers and those from leukemia, breast and lung cancers (which are more likely radiation-induced) was not higher in the residents of HBRAs of China compared to that of the control areas. The authors concluded that their findings were in line with this assumption that lower mortality from cancer in the HBRAs is a hormetic effect induced by exposure to a 3 fold higher dose rate of background radiation in those areas [24]. The mortality of all cancers in HBRA was generally lower than that of the control area; however, the differences were not statistically significant. In contrast with the predictions of LNT, cancer mortality studies performed in HBRAs of Yangjiang demonstrate that the cumulative natural radiation dose was not linked to cancer mortality [41, 42].

Indian researchers also were not able to detect excess cancer risk from exposure to terrestrial gamma radiation in HBRAs of Kerala. Furthermore, no association was found between the rate of leukemia and exposure to high levels of natural radiation in these areas [43]. In contrast with these reports, in Brazil,

it was reported that the cancer mortality for Poços de Caldas and Guarapari was higher than the expected levels (compared with their respective reference population). However, cancer mortality in Araxá was lower than expected levels [44]. We have previously reported that the residents of HBRAs are possibly among the people whose genetic makeup has made them resistant, at least to some extent, to the detrimental effects of low levels of ionizing radiation [45]. Recent advances in developing simple mathematical models for prediction of radon concentration in homes located in HBRAs of Ramsar as well as models which can predict the levels of tumor markers [46] help scientist better evaluate the cancer risk in HBRAs.

## Conclusion

While some cytogenetic studies performed in HBRAs have shown increased frequencies of unstable chromosome aberration, the majority of studies performed so far failed to find statistically significant differences. In spite of the reports which indicate a link between the levels of background radiation and increased frequency of chromosome aberrations in the circulating lymphocytes of the residents of HBRAs, the carcinogenic effect of the elevated levels of natural radiation is not proven yet. In this review, we tried to verify if induction of anomalies in the lymphocytes of the residents of high background radiation areas was associated with increased cancer risk. Altogether, we believe that as the residents of HBRAs and their ancestors have been exposed to extraordinary high levels of natural background radiation over many generations, if these levels of ionizing radiation were detrimental to their health, causing genetic abnormalities or an increased risk of cancer, it should be evident in these inhabitants. However, due to the limitations of the studies conducted on the residents of HBRAs, these findings should be interpreted with caution.

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## Conflict of Interest

None

## References

1. Sutou S. A message to Fukushima: nothing to fear but fear itself. *Genes Environ.* 2016;**38**:12. doi.org/10.1186/s41021-016-0039-7. PubMed PMID: 27350831. PubMed PMCID: 4918197.
2. Sohrabi M. World high background natural radiation areas: Need to protect public from radiation exposure. *Radiation Measurements.* 2013;**50**:166-71. doi.org/10.1016/j.radmeas.2012.03.011.
3. Mortazavi S, Niroomand-Rad A, Roshan-Shomal P, Razavi-Toosi S, Mossayeb-Zadeh M, Moghadam M. Does short-term exposure to elevated levels of natural gamma radiation in Ramsar cause oxidative stress? *Int J Appl Basic Med Res.* 2014;**4**:72-6. doi.org/10.4103/2229-516X.136778. PubMed PMID: 25143879. PubMed PMCID: 4137645.
4. Mortazavi S, Niroomand-Rad A, Mozdarani H, Roshan-Shomal P, Razavi-Toosi S, Zarghani H. Short-term exposure to high levels of natural external gamma radiation does not induce survival adaptive response. *Int J Radiat Res.* 2012;**10**:165-70.
5. Mortazavi S, Ghiassi-Nejad M, Rezaiean M, editors. Cancer risk due to exposure to high levels of natural radon in the inhabitants of Ramsar, Iran. International Congress Series; 2005: Elsevier.
6. Mortazavi S, Abbasi A, Asadi R, Hemmati A, editors. The need for considering social, economic, and psychological factors in warning the general public from the possible risks due to residing in HLNRA. International Congress Series; 2005: Elsevier.
7. Mortazavi S, Karam P. Apparent lack of radiation susceptibility among residents of the high background radiation area in Ramsar, Iran: can we relax our standards? *Radioactivity in the Environment.* 2005;**7**:1141-7. doi.org/10.1016/S1569-4860(04)07140-2.
8. Taeb S, Mortazavi S, Ghaderi A, Mozdarani H, de Almeida C, Kardan M, et al. Alterations of PSA, CA15. 3, CA125, Cyfra21-1, CEA, CA19. 9, AFP and Tag72 tumor markers in human blood serum due to long term exposure to high levels of natural background radiation in Ramsar, Iran. *Int J Radiat*

- Res. 2014;**12**:133-8.
9. Mortazavi S, Mozdarani H. Is it time to shed some light on the black box of health policies regarding the inhabitants of the high background radiation areas of Ramsar. *Int J Radiat Res.* 2012;**10**:111-6.
  10. Mortazavi S, Mozdarani H. Non-linear phenomena in biological findings of the residents of high background radiation areas of Ramsar. *International Journal of Radiation Research.* 2013;**11**:3-9.
  11. Ghiassi-nejad M, Mortazavi SM, Cameron JR, Niroomand-rad A, Karam PA. Very high background radiation areas of Ramsar, Iran: preliminary biological studies. *Health Phys.* 2002;**82**:87-93. doi.org/10.1097/00004032-200201000-00011. PubMed PMID: 11769138.
  12. Mortazavi S, Shabestani-Monfared A, Ghiassi-Nejad M, Mozdarani H, editors. Radioadaptive responses induced in lymphocytes of the inhabitants in Ramsar, Iran. International Congress Series; 2005: Elsevier.
  13. Mortazavi SMJ, Zarei S, Taheri M, Tajbakhsh S, Mortazavi SA, Ranjbar S, et al. Sensitivity to Antibiotics of Bacteria Exposed to Gamma Radiation Emitted from Hot Soils of the High Background Radiation Areas of Ramsar, Northern Iran. *Int J Occup Environ Med.* 2017;**8**:80-4. doi.org/10.15171/ijoem.2017.958. PubMed PMID: 28432369.
  14. Ghiassi-Nejad M, Zakeri F, Assaei RG, Kariminia A. Long-term immune and cytogenetic effects of high level natural radiation on Ramsar inhabitants in Iran. *J Environ Radioact.* 2004;**74**:107-16. doi.org/10.1016/j.jenvrad.2003.12.001. PubMed PMID: 15063540.
  15. Fazeli T, Assaei RG, Sohrabi M, Haydari A, Varzegar R, Zakeri F, et al. Cytogenetic studies of inhabitants of a high natural radiation area of Ramsar, Iran. Vienna: IAEA; 1990. p. 459-464.
  16. Hayata I, Wang C, Zhang W, Chen D, Minamihisamatsu M, Morishima H, et al. Effect of high-level natural radiation on chromosomes of residents in southern China. *Cytogenet Genome Res.* 2004;**104**:237-9. doi.org/10.1159/000077496. PubMed PMID: 15162045.
  17. Jiang T, Hayata I, Wang C, Nakai S, Yao S, Yuan Y, et al. Dose-effect relationship of dicentric and ring chromosomes in lymphocytes of individuals living in the high background radiation areas in China. *J Radiat Res.* 2000;**41**:63-8. doi.org/10.1269/jrr.41.S63. PubMed PMID: 11142213.
  18. Hayata I, Wang C-Y, Zhang W, Minamihisamatsu M, Chen D-Q, Morishima H, et al., editors. Chromosome translocation in residents of high background radiation area in China. International Congress Series; 2002: Elsevier.
  19. Wang C, Zhang W, Minamihisamatsu M, Morishima H, Yuan Y, Jiang T, et al., editors. Chromosome study in high background radiation area in Southern China. International Congress Series; 2005: Elsevier.
  20. Zhang W, Wang C, Chen D, Minamihisamatsu M, Morishima H, Yuan Y, et al. Effect of smoking on chromosomes compared with that of radiation in the residents of a high-background radiation area in China. *J Radiat Res.* 2004;**45**:441-6. doi.org/10.1269/jrr.45.441. PubMed PMID: 15613790.
  21. Hayata I, Wang C, Zhang W, Chen D, Minamihisamatsu M, Morishima H, et al. Chromosome translocation in residents of the high background radiation areas in southern China. *J Radiat Res.* 2000;**41 Suppl**:69-74. doi.org/10.1269/jrr.41.S69. PubMed PMID: 11142214.
  22. Zhang W, Wang C, Chen D, Minamihisamatsu M, Morishima H, Yuan Y, et al. Imperceptible effect of radiation based on stable type chromosome aberrations accumulated in the lymphocytes of residents in the high background radiation area in China. *J Radiat Res.* 2003;**44**:69-74. doi.org/10.1269/jrr.44.69. PubMed PMID: 12841602.
  23. Ramachandran EN, Karuppasamy CV, Cheriyan VD, Soren DC, Das B, Anilkumar V, et al. Cytogenetic studies on newborns from high and normal level natural radiation areas of Kerala in southwest coast of India. *Int J Radiat Biol.* 2013;**89**:259-67. doi.org/10.3109/09553002.2013.747014. PubMed PMID: 23134065.
  24. Chen D, Wei L. Chromosome aberration, cancer mortality and hormetic phenomena among inhabitants in areas of high background radiation in China. *J Radiat Res.* 1991;**32 Suppl 2**:46-53. doi.org/10.1269/jrr.32.SUPPLEMENT2\_46. PubMed PMID: 1823366.
  25. Das B, Saini D, Seshadri M. No evidence of telomere length attrition in newborns from high level natural background radiation areas in Kerala coast, south west India. *Int J Radiat Biol.* 2012;**88**:642-7. doi.org/10.3109/09553002.2012.699135. PubMed PMID: 22668000.
  26. Das B, Saini D, Seshadri M. Telomere length in human adults and high level natural background radiation. *PLoS One.* 2009;**4**:e8440. doi.org/10.1371/journal.pone.0008440. PubMed PMID: 20037654. PubMed PMCID: 2793520.
  27. Jain V, Kumar PR, Koya PK, Jaikrishan G, Das B. Lack of increased DNA double-strand breaks in peripheral blood mononuclear cells of individuals from high level natural radiation areas of Kerala coast in India. *Mutat Res.* 2016;**788**:50-7. doi.

- org/10.1016/j.mrfmmm.2016.03.002. PubMed PMID: 27063255.
28. Mohammadi S, Taghavi-Dehaghani M, Gharaati MR, Masoomi R, Ghiassi-Nejad M. Adaptive response of blood lymphocytes of inhabitants residing in high background radiation areas of Ramsar-micronuclei, apoptosis and comet assays. *J Radiat Res.* 2006;**47**:279-85. doi.org/10.1269/jrr.0575. PubMed PMID: 16988494.
  29. Karuppasamy CV, Ramachandran EN, Kumar VA, Kumar PR, Koya PK, Jaikrishan G, et al. Peripheral blood lymphocyte micronucleus frequencies in men from areas of Kerala, India, with high vs normal levels of natural background ionizing radiation. *Mutat Res Genet Toxicol Environ Mutagen.* 2016;**800-801**:40-5. doi.org/10.1016/j.mrgentox.2016.03.005. PubMed PMID: 27085474.
  30. Das B. Genetic studies on human population residing in High Level Natural Radiation Areas of Kerala coast. *BARC News letter.* 2010:28-37.
  31. Das B, Karuppasamy CV. Spontaneous frequency of micronuclei among the newborns from high level natural radiation areas of Kerala in the southwest coast of India. *Int J Radiat Biol.* 2009;**85**:272-80. doi.org/10.1080/09553000902751462. PubMed PMID: 19296343.
  32. Masoomi JR, Mohammadi S, Amini M, Ghiassi-Nejad M. High background radiation areas of Ramsar in Iran: evaluation of DNA damage by alkaline single cell gel electrophoresis (SCGE). *J Environ Radioact.* 2006;**86**:176-86. doi.org/10.1016/j.jenvrad.2005.08.005. PubMed PMID: 16376699.
  33. Balachandar V, Kumar RK, Prakash V, Devi SM, Kumar BL, Manikantan P, et al. Evaluation of genetic alterations in inhabitants of a naturally high level background radiation and Kudankulam nuclear power project site in India. *Asian Pac J Cancer Prev.* 2011;**12**:35-41. PubMed PMID: 21517228.
  34. Nair RR, Rajan B, Akiba S, Jayalekshmi P, Nair MK, Gangadharan P, et al. Background radiation and cancer incidence in Kerala, India-Karanagappally cohort study. *Health Phys.* 2009;**96**:55-66. doi.org/10.1097/01.HP.0000327646.54923.11. PubMed PMID: 19066487.
  35. Gianferrari L, Serra A, Morganti G, Gualandri V, Bonino A. Mortality from cancer in an area of high background radiation. *Bull World Health Organ.* 1962;**26**:696-7. PubMed PMID: 13898293. PubMed PMCID: 2555782.
  36. Gopal-Ayengar A, Sundaram K, Mistry K, Sunta C. Evaluation of the long-term effects of high background radiation on selected population groups of the Kerala coast. and others; Bhabha Atomic Research Centre, Bombay (India), 1971.
  37. Allwright SP, Colgan PA, McAulay IR, Mullins E. Natural background radiation and cancer mortality in the Republic of Ireland. *Int J Epidemiol.* 1983;**12**:414-8. doi.org/10.1093/ije/12.4.414. PubMed PMID: 6654560.
  38. Mosavi-Jarrahi A, Mohagheghi M, Akiba S, Yazdizadeh B, Motamedi N, Monfared AS, editors. Mortality and morbidity from cancer in the population exposed to high level of natural radiation area in Ramsar, Iran. International Congress Series; 2005: Elsevier.
  39. Mortazavi S, Ghiassi-Nejad M, Rezaiean M, editors. Cancer risk due to exposure to high levels of natural radon in the inhabitants of Ramsar, Iran. International Congress Series; 2005: Elsevier.
  40. Tao Z, Zha Y, Akiba S, Sun Q, Zou J, Li J, et al. Cancer mortality in the high background radiation areas of Yangjiang, China during the period between 1979 and 1995. *J Radiat Res.* 2000;**41 Suppl**:31-41. doi.org/10.1269/jrr.41.S31. PubMed PMID: 11142210.
  41. Tao Z, Akiba S, Zha Y, Sun Q, Zou J, Li J, et al. Cancer and non-cancer mortality among Inhabitants in the high background radiation area of Yangjiang, China (1979-1998). *Health Phys.* 2012;**102**:173-81. doi.org/10.1097/HP.0b013e31822c7f1e. PubMed PMID: 22217590.
  42. Zou J, Tao Z, Sun Q, Akiba S, Zha Y, Sugahara T, et al., editors. Cancer and non-cancer epidemiological study in the high background radiation area of Yangjiang, China. International Congress Series; 2005: Elsevier.
  43. Nair RR, Rajan B, Akiba S, Jayalekshmi P, Nair MK, Gangadharan P, et al. Background radiation and cancer incidence in Kerala, India-Karanagappally cohort study. *Health Phys.* 2009;**96**:55-66. doi.org/10.1097/01.HP.0000327646.54923.11. PubMed PMID: 19066487.
  44. Veiga LH, Koifman S, editors. Pattern of cancer mortality in some Brazilian HBRA. International Congress Series; 2005: Elsevier.
  45. Mortazavi S, Mozdarani H. Can recent Berkeley findings help us to find a solution to the paradox of cancer incidence in high natural background radiation areas of Ramsar, Iran? *Iranian Journal of Radiation Research (IJRR)* . 2015;**13**(4):383-4.
  46. Mortazavi S, Zamani A, Tavakkoli-Golpayegani A, Taeb S. Development of a Preliminary Mathematical Model to Predict the Indoor Radon Concentration in Normal and High Background Radiation Areas of Ramsar. *Soft Computing Applications: Springer*; 2016. p. 373-7.