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Review on studies in high background radiation areas (HBRAs) of various parts of the world

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Abstract

The present paper reviews the studies of populations living in high background radiation areas (HBRA). Past studies have shown that high background radiation has been repeatedly shown to increase the frequency of chromosome aberrations in the circulating lymphocytes of exposed persons, but its carcinogenic effect is still unproven. A further area of research is whether long term exposure to background radiation cause DNA damage, which was evaluated by determination of the frequency of micronucleus formation and it was suggested that a challenging dose rendered the cells of those who live in HBRAs less susceptible to damage compared to the control group in normal background radiation area (NBRA). It has also been reported that higher level of apoptosis was observed after the challenging dose in the HBRA group. It was also remarkable that after introducing a challenging dose, the major part of the damage induced in the HBRA groups, were repaired indicating the improved repair ability within them, which was detected using comet assay. In addition, studies have found significant differences in certain immunological parameters suggestive of an active immune surveillance there and hematological parameters and various other parameter studies was not significant between those in high and normal background radiation area. All these studies could be related to the induction of an adaptive response in the individuals of HBRA.

Keywords: High background radiation area; Chromosomal aberrations, Challenging dose, Adaptive response.

1. Introduction

There are certain regions in the world, where the background radiation is high due to the local geological controls and geochemical effects and cause increased levels of terrestrial radiation (UNSCEAR, 1993, 2000). Very High Background Radiation Areas (HBRAs) are found at Guarapari, coastal region of Espirito Santo and the Morro Do Forro in Minas Gerais in Brazil (Cullen, 1997; Penna Franca, 1977; Bennett, 1997; Paschoa, 2000); Yangjiang in China (Wei et al., 1993; Wei and Sugahara, 2000); Southwest coast of India (Sunta et al., 1982; Sunta, 1993; Mishra,1993; Paul et al.,1998); Ramsar and Mahallat in Iran (Sohrabi,1993; Ghiassi-nejad et al.,2002); in the United States and Canada (NCRP, 1987), and in some other countries (UNSCEAR, 2000). The sources of these high background radiations are the monazite sand deposits in the first three cases, while the radium in soil/water and the radon in air are responsible for the radiation at Ramsar in Iran. In India, there are quite a few monazite sand bearing placer deposits causing natural HBRAs along its long coastline (UNSCEAR, 2000). Ullal in Karnataka (Radhakrishna et al., 1993), Kalpakkam (Kannan et al., 2002) in Tamilnadu, coastal parts of Tamilnadu and Kerala state and the Southwestern coast of India are known for HBRAs (Mishra, 1993; Sunta, 1993). In these HBRAs the radiation levels of the local inhabitants are similar to or above those of people employed in the nuclear industries or radiation medicine. Some of these areas have been under study

for many years in order to determine the risks and effects of long term, natural radiation exposure (Sohrabi, 1998). Past studies have shown that a high level of natural background radiation does not have a lethal effect on the individuals living for a long time there. In fact data on the effects of high level radiation on several parameters in the inhabitants of HBRAs are very much limited.

Radiobiological studies in HBRAs have provided the opportunity to directly observe the effects of long time radiation on human beings there.

Table 1. Mean and maximum annual natural terrestrial radiation doses to the inhabitants of some areas around the world.

Country	Area	Approximate population	Absorbed Dose rate in air[a] ($nGy\ h^{-1}$)
Brazil	Guarapari	73 000	90-170 (street) 90-90 000 (beaches)
Iran	Ramsar[b] Mahallat	2 000	70-17 000 800-4000
India	Karunagappally	400 000	200-4 000
China	Yangjiang	80 000	370 (average)

a includes cosmic and terrestrial radiation.
b it should be noted that the monazite sand beaches at Guarapari in Brazil have a higher dose rate, but these areas are uninhabited. Therefore it can be claimed that Ramsar has the highest level of natural radioactivity studied so far.
Source: UNSCEAR 2000.

2. Cytogenetic studies

2.1 Chromosomal aberrations

The study of chromosomal aberration frequency in peripheral blood lymphocytes is a sensitive assay for detecting exposure to radiation (Chen & Wei, 1991). Cytogenetic analysis performed by conventional G-banding technique revealed that chromatid breaks in the HBRA group were higher than those in the control group from NBRA. When individual chromosomes were compared separately; it was found that the breaks of chromosomes 2, 8 and 9 were higher. It was interestingly found that the higher frequencies of aberrations were found in the older age group and it was not found statistically significant, the possibility of an age effect was suggested (Ghiassi-Nejad et al., 2004). Several groups have reported that the frequencies of unstable aberrations (dicentrics and rings) were significantly higher in the HBRA whereas those of stable aberrations (translocations and inversions) were not; in comparison with their respective control groups from NBRAs. It was considered that the increase of dicentrics and rings was mainly attributable to the increase in the cumulative dose. The cumulative dose increases with the age of an individual living there (Hayata et al., 1999). It was also reported that cultured lymphocytes of the residents of HBRAs when exposed to a challenging dose, showed fewer chromatid aberrations than those of the control group from NBRAs (Ghiassi-Nejad et al, 2001). But cytogenetic studies on newborns from both high and normal background radiation area revealed that the frequencies of chromosomal aberration and karyotype anomalies were very similar (Ramachandran et al., 2012). There is a recent report of the low frequency of double strand breaks in peripheral blood mononuclear cells of individuals from high level natural radiation areas of Karunagappally in Kerala (Jain et al, 2016).

2.2. Telomere length

Telomere ends protect the human genome from a variety of environmental exposures including ionizing radiation. So far using cell lines, few *in vitro* experiments have shown telomere length variation in response to ionizing radiation. But in *in vivo* studies, the natural background radiation has no significant effect on telomere length among the adult population residing in HBRA. This could been indication of better repair capacity of HBRA individuals at telomeric ends (Das et al., 2009).

2.3. Micronuclei and Apoptosis Studies

Micronuclei and apoptotic cell death are biological indicators for the assessment of radiosensitivity. A study was carried out in which some blood samples from both HBRAs and NBRAs were exposed to a challenge dose to induce radiogenic chromosomal abnormalities; the result of the studies clearly indicates that priming irradiation with low chronic doses in the HBRAs induce the cells less susceptible to the challenging dose. In HBRA group, smaller number of micronuclei and higher level of apoptosis was observed after the challenging dose than the respective control group from NBRA. This would be the result of increased resistance to radiation stress and a more rigorous checkpoint at cell division. The results of micronuclei and apoptosis suggest that an adaptive response might be induced in people in areas with high background radiation. Adaptive response can lead to a reduction of initial damage evoked by the challenging dose; influence the progression of the cell cycle and the incensement of apoptosis (Mohammadi et al., 2006).

2.4. Comet Assay Studies

Comet assay has shown to be both sensitive and rapid in the detection of breaks in the DNA-strands of individual cells.It was remarkable that the spontaneous level of DNA damage in inhabitants of HBRA was significantly higher than that of the inhabitants in NBRAs. After introducing challenging dose, more damage was induced in the inhabitants of HBRA indicating more susceptible site to break and/or more alkaline labile sites were present in the lymphocytes of individuals in HBRAs. Moreover the rate of DNA repair was more pronounced in the inhabitants of HBRA; which was revealed after two hours of incubation following the challenging dose (Mohammadi et al., 2006)

3. Hematological studies

Long term exposure to radiation did not affect the haematological parameters in the individuals there. The counts of white blood cells (WBC), lymphocy tes, monocytes, granulocytes and erythrocytes (red blood cells); measurements of hemoglobin, hematocrit, mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), red cell distribution width (RDW), platelet and mean platelet volume (MPV) showed not any significant difference between the inhabitants in HBRAs and NBRAs (Ghiassi-Nejad et al., 2002).

4. Immunological studies

Reports about the immune status of the inhabitants of the HNBR showed that high doses of natural radiation are not immunosuppressive. Cell-mediated immunity examination revealed that there was a tendency of strengthening of immune functions among the HBRA inhabitants (Liu et al., 1987). Studies showed that concentrations of immunoglobulin M (IgM), immuno globulin A (IgA) and immunoglobulin G (IgG) were in the normal ranges for the HBRA and NBRA groups, however, HBRA group had slightly higher serum IgG than the NBRA groups but the difference was not significant. But the level of total serum immunoglobulin E (IgE) was significantly increased in the HBRA group. The C3 and C4 complement system were in the normal ranges for both groups (Ghiassi-Nejad et al., 2002). Another study on the immune status of the inhabitants of the HBRA revealed that there was a definite increase in reactivity of T lymphocytes to PHA, a slight increase in the percentage of T lymphocytes and a tendancy towards enhancement of unscheduled DNA synthesis in peripheral blood lymphocytes (Liu et al., 1987).

Immunological studies also suggests that the total serum antioxidant level in the exposed people was significantly lower than the control group of NBRA, this may be because of shift from a Type I response characterized by intense phagocytic activity to Type II immunity which is characterized by high antibody titers. Type I response generate more free radicals than Type II response, in addition to the free radicals generated as a result of high environmental radiation, so that to adapt the high radiation environment, shift to Type II response made the serum antioxidant level lower in the exposed group (Attar et al; 2007).

Hormone level studies demonstrated a decreased level of dehydroepiandrosterone (DHEA) and increased level of cortisol in the elderly HBRA group, might be due to higher cumulative doses and low levels of DHEA can be correlated to their increased Immunoglobulin E (Ig E) levels as already noted (Zakeri et al; 2005).

The comparison of CD4/CD8 ratio among high and normal background radiation area revealed that the absolute counts of CD4+ and CD8+ and CD4+/CD8+ ratio was not significantly different between the groups.(Borzoueisileh S et al; 2011). A significant increase of CD69 expression on CD4+ T LYM was found in the HBRA group (Zakeri et al; 2005).

5. Cancer studies

The induction of cancer appears to be the most important effect of low-dose ionizing radiation to occur in an exposed population (Stewart 1992). Ionizing radiation has sufficient energy to change the structure of molecules including DNA, within the cells of the human body. Some of these molecular changes are so complex that it may be difficult for the body's repair mechanism to mend them correctly, which results in cancer or other health effects. However, the induction of cancer by radiation is only detectable by statistical means; that is, the cancer of any given person cannot be attributed, with certainity to radiation, as opposed to some other causes (Shahbazi-Gahrouei, 2003). In the United States, Jagger (1998) showed a clear negative correlation of natural background radiation with overall cancer death. In HBRA of Yangjiang in China (Tao et al.1999) results showed that an increased cancer risk associated with the high levels of natural radiation was not found. The possibility of skin and thyroid cancers and leukemia is high due to the high levels of the natural background radiation in the Chaharmahal and Bakhtiari province (Shahbazi-Gahrouei, 2003). The cancer incidence study in Karunagappally, India, showed no HBR-related excess of malignant tumors (Nair RRK et al 2009). Based on a detailed analysis of the possible association between exposures to natural background radiation and childhood leukaemia, (Little et al.,2009) estimated that natural radiation could account for around 15–20% of cases in Great Britain. All these studies indicate that the correlation between cancer incidence and radiation is doubtful. Although the difference in the cancer mortality rates for the HBRA and NBRA are not significant, the findings are compatible with the assumption that the lower mortality from cancer in the HBRA is the result of the hormetic effects of the three-fold higher dose rate of background radiation in that areas. This assumption requires further study (Chen &Wei, 1991).

5.1. Thyroid cancer studies

It is well established that ionizing radiation causes thyroid cancer and nodules. Although the prevalence of mild diffuse goiter was higher in the high background radiation region, perhaps related to a low dietary intake of iodine,studies suggest that continuous exposure to low level radiation throughout life is unlikely to appreciably increase the risk of thyroid cancer (Z Wanget al, 1990).

6. Respiratory disease studies

A preliminary study held in Ramsar investigated the impact of high natural radiation on the respiratory system on the students living there compared with students in normal background radiation levels. It was found that some allergic symptoms such as rhinitis and weakness and fatigue, shedding tear and number of times catching a cold during a year are shown in high level in HBRA students, while there were no differences in bacterial respiratory diseases between the children of both groups (Emem Verdizadeh, 2000).

7. Radioadaptive response

The term radioadaptive response, first reported by Olivieri et al. in 1984.It is a biological defence mechanism in which low-dose ionizing radiation elicits cellular resistance to the genotoxic effects of subsequent irradiation. Preliminary studies suggests that prolonged exposure to very high levels of radiation could lead to the induction of radioresistance among exposed individuals, which has interesting implications for the phenomenon of radioresistance in living organism has long been a matter of interest for scientists. It may be possible that genetic alterations have occurred over the span of many generations to induce the radioresistance noted in all these studies. The cellular manifestation of radioadaptation have been verified by the decrease in the number of cells with micronuclei, increase in apoptotic cell death and overall increase in the repair of radiation induced breaks.

8. Conclusions

Considering many studies comprehensively, the conclusions are as follows; long term exposure to radiation has no lethal effect on the individuals there and the frequency of chromosomal aberrations (breaks, dicentrics, rings) in the circulating lymphocytes is high, while its carcinogenic effects are still unproven (Nair RRK et al, 2009). The high background radiation environment has no significant effect on telomere length and has no significant differences in haematological parameters but there will be changes in immune system suggestive of higher radiosensitivity of activated cells. In addition, residents in HBRAs have shown to be more prone to DNA damage and thus possess more pronounced DNA repair system. Briefly, the low micronuclei level, higher number of apoptotic cells and enhanced DNA repair following the challenging dose exposure, could be related to the induction of an adaptive

response in the exposed groups. Based on the results obtained from the studies on high background radiation areas, it has been suggested that radio adaptive response may have implications in radiation risk assessment (Mortazavi, 2002) and radiation protection (Karam et al, 2002). These studies contribute greatly to our advancing knowledge about the effect of radiation doses on the individuals there.

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