Effect of exposure-age on chromosomal rearrangements in methyl isocyanate (MIC) gas exposed survivors

Methyl isocyanate (MIC) gas disaster appeared one of the world's worst industrial disasters by claiming a huge toll of human lives instantly and as its aftermath effect. Besides respiratory, ophthalmic and psychological disorders, stress leukogram, including anemia, leucopenia, thrombocytopenia, etc. were reported in MIC-exposed survivors. However, exposure-index or exposure-response could not be measured or thought of immediately due mainly to attention required for medical management of the victims. Since chemical-induced DNA-lesions are S-dependent and survival of T-lymphocytes was apparent, late expression of MIC-exposure on survivors' immune status was likely of causing genetic aberration, which could further lead to genetic instability and cancer. Variable extent of chromosome aberrations (46 chromosomes in the human genome hold genes, which control the structure and function of one individual, and get inherited as 50% from each parent) was reported in exposed survivors and experimental systems, including depression of cell cycle and bone marrow-cellularity.

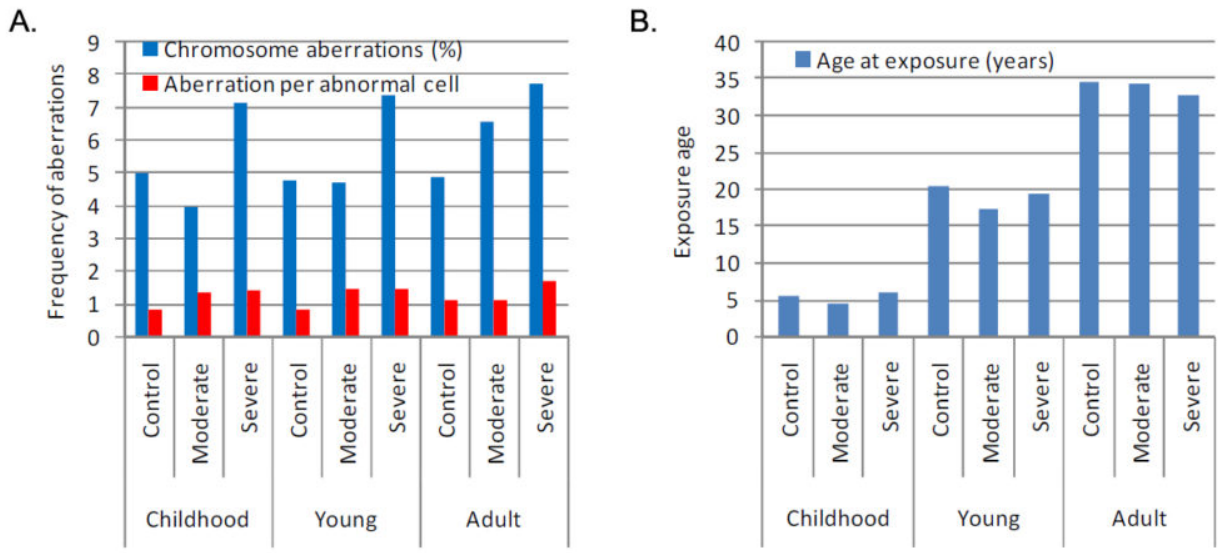

Fig. 1. Exposure age (A) and chromosome aberrations (B) in MIC-exposed survivors 30 years later

MIC-exposed survivors are three more decades older than before. Aging itself has deleterious effects on human health, especially in acquisition of somatic mutations leading to onset of malignancies. Therefore, impact of aging against the background exposure to MIC was measured as the acquisition of spontaneous chromosome aberrations and chromosomal rearrangements in peripheral blood cells of the exposed population 30-years post disaster. Numerical and structural abnormalities, including trisomy 8/X, monosomy 7/X, deletion, inversion, translocations, fragile

sites, markers and minutes, etc. were observed in one or two cells, whereas complex rearrangements with ?3 aberrations indicated genetic instability. Clonal abnormality (?2 cells with similar abnormality) with trisomy 8, monosomy/deletion in 7 and loss of Y chromosome in peripheral lymphocytes was noticed in few elderly individuals; however, its association could not be linked to their bone marrow-cytogenetics.

Among the present study population, 24%, 44% and 32% of childhood, young and adult groups respectively got exposed at 5.4 years, 25 years and 35 years of mean age, and all of them advanced 30+ years during the present study. Age-related but insignificant (due mainly to wide dispersion of aberration-frequencies and inter-individual variation) increase in aberrations was noticed in unexposed and exposed population. However, aberration frequency was significantly higher in the severely exposed adults compared to moderately exposed and unexposed population of the same age group (Fig.1). Exposure at childhood, young and adult age to moderate and severe extent revealed enhanced aberration frequency per abnormal cell. However, collectively, interaction between age and MIC-exposure on the incidence of chromosome aberration was not significant. Nevertheless, confounding effects of multiple biological and non-biological factors might have contribution on varying response to individualized aging. However, existence of stable rearrangements and few clonal aberrations, particularly in the elderly age group, poses the necessity of mutational screening with a view to tracking down the emergence of ‘founder mutations’ of cancers of various organs and preventing the burden of geriatric diseases as a whole. It is noteworthy that the MIC-exposed population is semi- or illiterate, occupied as day labourers and living below the poverty line. Lack of awareness of health and hygiene prevails in their living environment, and ignorance about the risk of future health may invite multiples of chronic diseases, especially tuberculosis, against a backdrop of impaired respiratory system due to MIC-exposure.

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