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Association of aberrant expressions of ATM, γH2AX and p53 proteins with the prognosis and development of gallbladder cancer: A cohort study

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Abstract

Gallbladder cancer (GBC) frequency and mortality renders it one of the most frequent leading diseases due to leakage of methyl isocyanate (MIC) among the population that survived in the tragedy taken place at Bhopal, India in 1984. Despite the considerable progress in understanding the molecular pathology of carcinogenesis of GBC are hitherto unknown that necessitate to take a step forward for the better understanding of the mechanism at molecular level. Based on these facts, the study had aimed for the purpose of assessing ATM, γH2AX and p53 expression through immuno histo-fluorescence using spectral bioimaging. A total of 92 surgically resected cases of the gallbladder cancer were used. Out of these 31 patients were men, and 61 were women. Age range 16–85 yrs, mean age 45.83 ± 1.50 yrs) with 70 adenocarcinoma (13 well differentiated, 48 moderately differentiated and 09 poorly differentiated), 10 adenosquamous carcinoma and 12 gallbladder adenoma were examined. Of the 92 samples, 64%, 55% and 81% showed positivity for ATM, γH2AX and p53 expression respectively in moderately differentiated adenocarcinomas suggesting the prevalence and invasiveness of the disease in the MIC exposed population. However, the high rate of p53 expression suggests its major role in GBC. In conclusions, the data of this study signify the extent of DNA damage that has occurred due to the toxic exposure to MIC and expression of DNA repair factors viz., ATM, γ-H2AX and p53 phosphorylation states are indirectly promoting genomic instability and appear to be the major factors involved in the carcinogenesis of gallbladder. Therefore, these could be valuable biomarker for the early detection of the disease.