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Status of some minerals and impact of promoter hypermethylation of DAP-K gene in gastric carcinoma patients of Kashmir valley

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Gastric cancer is the fourth most common cancer and the second leading cause of worldwide cancer-related deaths, with a wide variation in incidence rates across different geographical areas. The current view of cancer is that a malignancy arises from a transformation of the genetic material of a normal cell, followed by successive mutations and by chain of alterations in genes such as DNA repair genes, oncogenes, Tumor suppressor genes such as DAP-K and others. Minerals are necessary to the functions of several transcriptional factors, proteins that recognize certain DNA sequences and control. The present work was a case control study and its aim was to ascertain the role of minerals and promoter hypermethylation of CpG islands of DAP-K gene in astric cancer patients among the Kashmiri population. Serum was extracted from all the samples and mineral estimation was done by AAS from serum, DNA was also extracted and was modified using bisulphite modification kit. Methylation-specific PCR was used for the analysis of the promoter hypermethylation status of DAP-K gene. The epigenetic analysis revealed that unlike other high risk regions, Kashmiri population has a different promoter hypermethylation profile of DAP-K gene and has different mineral profile. In our study mean serum copper levels were significantly different for the two genders ($p<0.05$), while as no significant differences were observed for iron and zinc levels. In methylation-specific PCR, the methylation status of the promoter region of DAP-K gene was as 67.50% (27/40) of the gastric cancer tissues that showed methylated DAP-K promoter and 32.50% (13/40) of the cases however showed unmethylated DAP-K promoter. Almost all 85% (17/20) of the histopathologically confirmed normal tissues showed unmethylated DAP-K promoter except only in 3 cases where DAP-K promoter was found to be methylated. The association of promoter hypermethylation with gastric cancer was evaluated by $\chi 2$ (Chi square) test and was found to be significant (P=0.0006). Occurrence of DAP-K methylation was found to be unequally distributed in males and females with more frequency in males than in females but the difference was not statistically significant (P=0.7635, Odds ratio=1.368 and 95% C.I=0.4197 to 4.456). When the frequency of DAP-K promoter methylation was compared with clinical staging of the disease, DAP-K promoter methylation was found to be certainly higher in Stage III/IV (85.71%) compared to stage I/II (57.69%) but the difference was not statistically significant (P=0.0673). These results suggest that DAP-K aberrant promoter hypermethylation in Kashmiri population contributes to the process of carcinogenesis in Gastric cancer and is reportedly one of the commonest epigenetic changes in the development of Gastric cancer.

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