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Evaluation of Atherogenic Index of Plasma and Lipid Ratios in Patients with Head and Neck Squamous Cell Carcinoma in North Indian Study Group

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Abstract: Cancers have become a leading cause of morbidity and mortality in today's world. With time the incidence of cancers is rapidly rising. Head and neck carcinomas pose real threat being very aggressive in their course and also poor prognosis adds on to their occurrence. India have real issue of being containing nearly one third of HNSCC patients. Betel nut chewing, smoking, poor oral hygiene and viral infections like HPV are major factors behind HNSCC. Many markers and factors are being studied for better understanding of management of these patients. In this study thirty patients diagnosed with HNSCC were enrolled. They were studied with routine biochemical markers and interleukin-6 also. On studying their lipid profile, different lipid ratios and atherogenic index of plasma (AIP) were found to be on higher side in advanced treatment group. AIP and these ratios can be used as biomarkers providing useful information about risk stratification and severity in HNSCC patients. More research is warranted in about AIP and the lipid ratios in HNSCC patients to make these markers more useful in these patients.

Introduction

Cancer continues to be one of the primary causes of mortality worldwide, presenting a growing challenge to global health systems. As reported by the International Agency for Research on Cancer (IARC), nearly 20 million new cancer cases were identified globally in 2022, and around 9.7 million individuals died due to this disease[1]. With the aging population and rising prevalence of lifestyle-related risk factors—such as tobacco consumption, poor dietary habits,

and environmental carcinogens—these figures are projected to surpass 35 million new cases annually by 2050[1].

Among the many other cancer types, head and neck squamous cell carcinoma (HNSCC) is particularly significant due to its aggressive clinical course and unfavourable or poor prognosis. Arising from the squamous epithelial lining of mucosal surfaces including the oral cavity, pharynx, and larynx, HNSCC represents the seventh most common malignancy worldwide, accounting for approximately 660,000 new cases and over 325,000 deaths each year[2,3].

India unfortunately carries a disproportionate large share of this global pevalence, contributing to nearly one-third of global HNSCC cases[4]. Data from Indian population-based cancer registries indicate that head and neck malignancies account for around 25.7% of cancers in males and 7.7% in females. This indicates its major prevalence among males[5].The age-adjusted incidence is roughly 21 per 100,000 men and 6 per 100,000 women, with Northeast India reporting the highest rates, exceeding 31 per 100,000 in men[5].

Multiple well-established risk factors contribute to the pathogenesis of HNSCC. The use of tobacco tops as main cause, both in smoked and smokeless forms, which is linked to nearly 80% of cases in India[6]. The combination of alcohol and tobacco further amplifies the carcinogenic effect[6]. Other contributing factors include betel nut (areca) chewing, poor dental hygiene, micronutrient deficiencies, and infections with oncogenic viruses like human papillomavirus (HPV) and Epstein–Barr virus (EBV)[7]. Among these HPV subtype 16 has been increasingly associated with oropharyngeal cancers, especially among younger adults[7]. Indian studies report HPV positivity in HNSCC ranging from 7% to 78%, a variation attributed to differences in diagnostic modalities employed[7].

In recent years, attention has also turned to the metabolic alterations associated with cancer, including changes in lipid metabolism. The lipid profile, comprising total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), and triglycerides (TG), is increasingly being investigated as a non-invasive biomarker in various cancers. Abnormal lipid metabolism in cancer is linked to membrane synthesis, energy storage, and signalling functions essential for tumor proliferation and metastasis. Furthermore, lipid-derived ratios, such as TC/HDL, LDL/HDL, and TG/HDL, have demonstrated prognostic value in several malignancies[8]. One particularly promising indicator is the Atherogenic Index of Plasma (AIP), calculated as log(TG/HDL), which reflects the balance between protective and atherogenic lipoproteins. Elevated AIP has been associated not only with cardiovascular disease but also with systemic inflammation and metabolic syndrome—conditions that share a pathophysiological basis with carcinogenesis[9]. Several studies have reported that higher AIP values correlate with increased cancer risk, tumor aggressiveness, and poorer outcomes[10,11], suggesting that lipid parameters and AIP could serve as cost-effective adjuncts in cancer risk stratification and prognosis assessment. **Aim**: To study lipid ratios and atherogenic index of plasma in patients with head and neck squamous cell carcinoma

Materials and Methods

For the study, 30 newly diagnosed patients with HNSCC and 30 age and sex matched healthy individuals were enrolled after informed consent. Detailed history, clinical examination, radiological and histopathological examination was done for establishing diagnosis. Staging was done according to the American Joint Committee on Cancer (AJCC) 2010 criteria[12]. Written informed consent from the patient was collected to participate in the study.

Inclusion Criteria: Newly diagnosed histopathologically proven adult patients with HNSCC before starting any treatment irrespective of age, sex and staging of the disease.

Exclusion Criteria: Patients suffering from any other chronic disease, on any medication/ supplements and lactating and pregnant females.

Complete hemogram were done using standard automated technique using standard kits. The serum levels of glucose, urea, creatinine, uric acid, lipid profile, calcium, phosphorus, aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase, total protein and albumin/globulin ratio were analyzed on auto-analyzer (Randox Suzuka, United Kingdom, model no. 6L7WD5J) using kits. Serum IL-6 levels were analyzed by enzyme linked immuno sorbent assay (ELISA) method.[13] The data was compiled and analyzed using appropriate statistical methods.

Results

The mean age of patients with head and neck squamous cell carcinoma (HNSCC) was 54.63 ± 8.07 years, whereas in the control group, it was 53.37 ± 9.12 years. The mean weight of the cases was 52.07 ± 7.6 kg, while that of the controls was 56.9 ± 10.6 kg. The average height among cases was 1.69 ± 0.06 metres, and among controls, it was 1.68 ± 0.04 metres. The mean Body Mass Index (BMI) in the cases was 19.13 ± 2.87, compared to 20.07 ± 3.36 in the control group. Out of the 30 HNSCC cases, 29 patients (97%) were male and only one (3%) was female. The control group had the same gender distribution.

Among cases, carcinoma of the larynx was the most common site (11 cases; 36.7%), followed by carcinoma of the oropharynx (10 cases; 33%), carcinoma of the base of the tongue (6 cases; 20%), and carcinoma of the tonsil (3 cases; 10%). With respect to clinical symptoms, 8 patients (26.7%) had difficulty in swallowing, while another 8 (26.7%) reported hoarseness of voice. Twelve patients (40%) complained of pain in the throat region, and only 2 cases (6%) presented with neck swelling. Regarding personal habits, 28 cases (93.3%) were smokers and 2 (6.7%) were non-smokers. Tobacco chewing was reported in 25 patients (83.3%) while 5 (16.6%) did not use tobacco. Notably, 15 patients (50%) were both alcohol users and smokers. Alcohol consumption was reported in 20 cases (66.7%) and 10 were non alcoholic (33.3%).

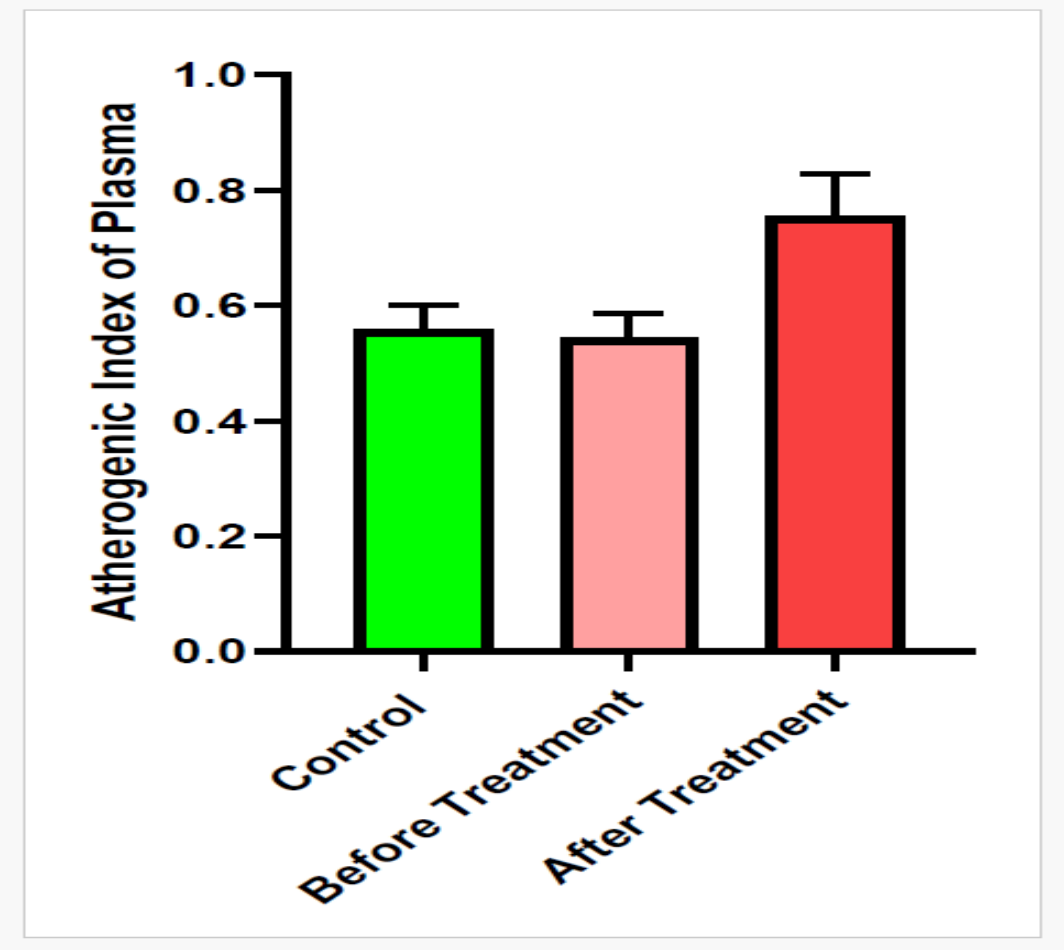
Staging was done as per the American Joint Committee on Cancer (AJCC) 2010 criteria. Eleven patients (36.7%) presented in stage IV and 19 (63%) in stage III. None of the patients presented in the early stages (I and II). Karnofsky Performance Status (KPS) was assessed in all patients. Fifteen patients (50%) had a KPS of 80, and the remaining 15 (50%) had a score of 70.

The lipid ratios and Atherogenic Index of Plasma (AIP) findings are presented in the table. The graph illustrates the comparative mean ± SD of AIP between the two groups.

Parameter	**Mean**	**SD**
AIP (Group A)	0.54	0.22
AIP (Group B)	0.75	0.40
AIP (Group C)	0.55	0.23
HDL-TC (Group A)	135.26	39.26
HDL-TC (Group B)	120.03	32.04

HDL-TC (Group C)	96.93	34.10
LDL/HDL-c (Group A)	2.93	0.96
LDL/HDL-c (Group B)	3.61	3.91
LDL/HDL-c (Group C)	2.42	0.82
TG/HDL-c (Group A)	3.91	1.81
TG/HDL-c (Group B)	17.13	62.84
TG/HDL-c (Group C)	4.09	1.92
TC/HDL-c (Group A)	4.91	2.14
TC/HDL-c (Group B)	6.43	7.71
TC/HDL-c (Group C)	4.25	0.92

Table: Showing the lipid ratios and Atherogenic Index of Plasma



Graph: Showing the Atherogenic Index of Plasma in three groups

Discussion

In the present study, analysis of lipid profiles and derived ratios such as AIP, HDL/TC, LDL/HDL-c, TG/HDL-c, and TC/HDL-c in patients with HNSCC revealed notable differences across clinical groups. Group B exhibited the highest mean AIP value (0.75 ± 0.40) compared to Groups A and C. AIP, a logarithmic function of TG/HDL-c, is considered a strong indicator of plasma atherogenicity and a predictor of cardiovascular risk, but recent evidence suggests

its potential role in cancer pathophysiology, possibly due to lipid peroxidation and inflammation[14],[15].

The significantly elevated TG/HDL-c ratio in Group B (17.13 ± 62.84) compared to Groups A and C supports the hypothesis that triglyceride-rich lipoproteins may contribute to cancer progression by altering membrane lipid rafts and affecting cell signalling[16]. Similarly, increased LDL/HDL-c and TC/HDL-c ratios in Group B point to a more dysregulated lipid metabolism in these patients. These indices are increasingly recognized as markers not only of cardiovascular disease but also of poor prognosis in malignancies, including HNSCC[17].

The inverse relationship observed in HDL/TC ratios in Group C (96.93 ± 34.10) as compared to Group A (135.26 ± 39.26) reflects a decrease in protective high-density lipoprotein (HDL) levels. HDL plays a known role in modulating oxidative stress and inflammation, mechanisms crucial to tumorigenesis[18]. The lowest HDL-TC ratio in Group C could indicate enhanced oxidative stress in advanced disease stages, as also suggested by similar findings in other cancers[19].

Atherogenic Index of Plasma (AIP) has gained attention as a reliable marker for lipid abnormalities that may reflect systemic inflammation and oxidative imbalance, both crucial contributors to tumor initiation and progression[20]. The elevated AIP in Group B patients further supports the association between altered lipid metabolism and cancer aggressiveness. Moreover, some studies report that high AIP correlates with increased expression of fatty acid synthesis-related enzymes in tumors[21].

The variations in lipid ratios among the groups in this study emphasize the utility of these parameters as potential biomarkers for risk stratification and disease severity in HNSCC patients. Given that traditional markers like BMI and weight are often non-specific, biochemical parameters such as AIP, LDL/HDL-c, and TG/HDL-c may offer greater clinical utility for monitoring metabolic health in cancer patients

Conclusion

The present study highlights significant alterations in lipid profiles and derived indices among HNSCC patients, particularly elevated AIP, TG/HDL-c, and LDL/HDL-c ratios in more advanced clinical groups. These findings suggest that atherogenic lipid parameters, especially AIP, may serve as accessible and cost-effective biomarkers for assessing disease severity, metabolic status, and possibly cancer progression in HNSCC patients. Further research is warranted to validate these associations and explore their prognostic implications.

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