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Somatic DNA Damages in Risk Factors for Coronary Artery Disease: Modifiable and Non-Modifiable

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Key Words:

CAD, Somatic DNA Damages, Risk Factors, Modifiable, Non-Modifiable

Abstract:

The most prevalent cause of death among people in the United States is coronary artery disease (CAD), sometimes known as heart disease. Although widespread, it is entirely avoidable. Early screening, diagnosis, and treatment of coronary artery disease (CAD) and its risk factors are all possible. The goal is to investigate both the modifiable and non-modifiable somatic DNA damage factors that are associated with CAD risk.

1. Introduction:

Coronary artery disease, often known as CAD, is a complicated condition that may be caused by a combination of environmental and hereditary risk factors. Damage to the somatic copy of a gene may result in mutations and changes in gene expression, both of which can contribute to the development and progression of coronary artery disease [1]. This is a significant factor in the pathogenesis of CAD.

There are risk factors for CAD that can be modified, as well as risk factors that cannot be modified, that may cause somatic DNA damage. Age, gender, and a person's genetic predisposition are examples of elements that cannot be changed. For instance, some genetic variations have been linked to an elevated risk of CAD and may impact DNA repair pathways [2]. These findings suggest that these variants have a role in the disease.

Tobacco use, obesity, insufficient physical exercise, a poor diet, and exposure to environmental contaminants are all modifiable risk factors for coronary artery disease (CAD) that may lead to somatic DNA damage. It is widely known that smoking is a risk factor for coronary artery disease (CAD), and it is also known to cause somatic DNA damage via the creation of reactive oxygen species (ROS) and the development of DNA adducts. The formation of reactive oxygen species (ROS) and inflammation are two more ways that obesity and a lack of physical exercise might contribute to somatic DNA damage [3].

Inadequate nutrition, especially diets that are heavy in saturated fats, may also contribute to somatic DNA damage via the generation of reactive oxygen species (ROS) and the buildup of products of lipid peroxidation. Oxidative stress and the production of DNA adducts are two mechanisms that may contribute to somatic DNA damage [4]. Other environmental pollutants, such as air pollution and heavy metals, can also contribute to somatic DNA damage.

In coronary artery disease (CAD), somatic DNA damage may be caused by a number of causes, including those that can be modified, those that cannot be modified, hereditary factors, and epigenetic factors. Examples of genetic polymorphisms that may contribute to defective DNA repair systems and an increased risk of DNA damage include variations in genes that are responsible for DNA repair. Alterations in gene expression brought on by epigenetic alterations, such as DNA methylation, may also contribute to the development of coronary artery disease [5].

Overall, somatic DNA damage is a significant contribution to coronary artery disease (CAD), and the risk factors that may contribute to this damage include both those that can be modified and those that cannot be modified. It is possible to lower the risk of coronary artery disease (CAD) and improve outcomes

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for those who already have the illness by reducing their exposure to modifiable risk factors and addressing genetic and epigenetic variables [5].

DNA damage

The "inflammatory response to injury" hypothesis is the most prominent theory concerning the pathophysiological mechanisms of atherosclerotic plaque formation. This hypothesis asserts that the proliferation of smooth muscle cells (SMC) is an inflammatory-fibroproliferative reaction to various insults to the artery wall [6]. On the other hand, there is evidence to support the hypothesis that modifications at the DNA level may play a substantial role in the pathogenesis of the illness. In light of these observations, a notion referred to as the "monoclonal" hypothesis of atherosclerosis has been proposed. According to this theory, the first step in the development of atherosclerosis is a mutation that changes a single, isolated smooth muscle cell into the progenitor of a proliferative clone, similar to the way that carcinogenesis works [7].

When transfected into 3T3 cells, DNA samples isolated from smooth muscle cells had the capacity to change into different cell types; the altered cells were able to cause tumours to develop in nude mice. In addition, the p53 protein, which has the ability to inhibit the growth of tumours, is found to have abnormally accumulated in the smooth cells of some individuals who have had coronary angioplasty, leading to an increase in the proliferation of myocells that is known as restenosis [7].

Microsatellite sequences have been used to acquire important information that demonstrates particular molecular abnormalities in atherosclerotic lesions. Microsatellites are comprised of small DNA sequences that are very repetitive and are prone to replication mistakes, namely frame shift mutations [8]. Defective repair of mismatched bases is responsible for an elevated mutation rate and extensive microsatellite instability in a subset of malignancies, primarily sporadic human tumours. This phenomenon occurs in a small percentage of cases of cancer. It is likely that a cell clone that has microsatellite instability would gain a proliferative advantage, which will ultimately result in the expansion of smooth muscle cells that are unique to the atherosclerotic plaque. It is interesting to observe that microsatellite sequences were altered in atherosclerotic tissues from the same individuals [9], but not in normal vascular tissues. According to the findings, there is a consistent pattern of mutation in the microsatellite sequence that can be found in atherosclerotic plaque obtained from a variety of people as well as from experimental animals.

In populations that were exposed to arsenic and dioxin, there was a discernible rise in the death rate caused by cancer, in addition to an increase in the mortality rate caused by diseases connected to atherosclerosis. According to the findings of epidemiological research, some carcinogenic agents, such as vinyl chloride monomer (VCM) and industrial combustion effluents containing polycyclic aromatic hydrocarbons (PAHs), do in fact have an atherogenic impact. Lastly, a history of past exposure to ionising radiation seems to be associated with an increased risk of severe plaque development that is both premature and localised in the irradiated region [10]. Assuming that atherosclerotic and neoplastic lesions have similar pathogenetic mechanisms, it is reasonable to anticipate that at least some well-known mutagenic agents will exert atherogenic as well as carcinogenic effects, and that populations that are at a high risk for cancer may show an increased incidence of atherosclerosis-related diseases.

Atherosclerosis and cancer share a number of molecular markers and gene-regulating mechanisms that have been linked to the genesis and progression of the illness. It would seem that the development of these persistent disorders takes place in stages, with genetic, dietary, psychosocial, environmental, and viral variables all having an impact on their manifestations. In addition, both laboratory and clinical research on atherosclerosis and cancer have shown that the clotting system is affected by similar pathological pathways in both diseases. Furthermore, emerging novel therapeutic strategies have similarly targeted both atherosclerosis and cancer. These strategies include reducing oxidative stress, inhibiting chemokine, cytokine, and growth factor cell signal transmit, down-regulating excess matrix digestion, inactivating nuclear factor- B (NF- B) signal pathway, interfering with cell cycle regulation, and applying radiation treatment for controlling the expansion and invasion of both atherosclerosis and cancer [10].

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These data, when taken as a whole, lend credence to the hypothesis that atherogenesis is linked to mutagenesis and carcinogenesis.

2. Methodology

The primary goals of the research were to determine whether or not there were any somatic DNA damages related with non-modifiable and modifiable risk variables among patients with coronary artery disease (CAD), as well as to locate novel biomarkers for the early diagnosis of CAD. Following receipt of ethical approval from the institutional ethics committee, the framework for a case control research was selected. The interview method was used to collect information from all of the research respondents as well as the control subjects. This information included their demographic records, family history, and disease-related records in accordance with the questionnaire. Anthropometric data such as height, weight, and belly circumference were collected in order to calculate the body mass index and determine whether or not the subject was obese. Under sterile conditions, venous blood samples (both aliquots with and without anti-coagulant) were obtained and processed in a laboratory for the purpose of determining the extent of DNA damage, performing biochemical estimations, and conducting molecular analysis using conventional procedures. Documentation and analysis of the observations and findings were carried out using the statistical programme SPSS version 22.

3. Results

A mean CBMN frequency of 12.5 ±0.9 was reported for 200 of the subjects who participated in the study, while a mean CBMN frequency of 10.2 ±0.6 was observed for 100 of the subjects who served as controls. This indicates that the mean CBMN frequency was higher among the subjects who participated in the study than it was among the control subjects (Table & Figure 1) (300 subjects were enrolled in the study).

Table 1: Distribution o f Mean CBMN frequency between study andcontrol groups

Group	Study subjects	Control subjects
Mean CBMN frequency	12.5±0.9	10.2±0.6.

Values are mean ±SD

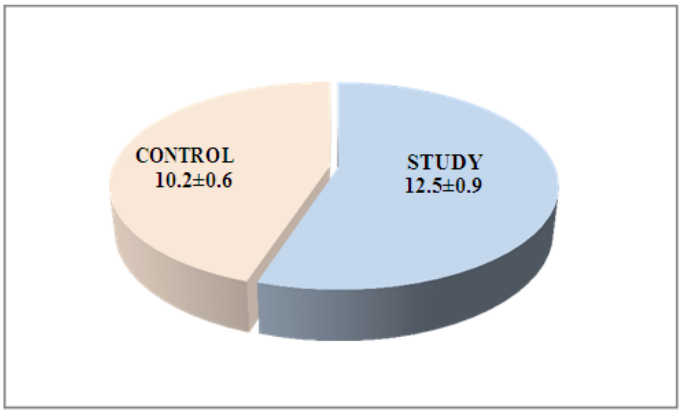

Figure 1: Distribution o f Mean CBMN frequency among study andcontrol subjects

In terms of ADMA, the study group had a higher mean value (137±27.4) compared to the control group's (58.5±17.9); in terms of CERK, the study group had a higher mean value (179.5±54.2) compared to the control group's (44.5±20.0); and when looking at Lp-PLA2, the study group had a higher mean value (391±2.1) (Table 2; Figure 2).

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Table 2: Distribution of ADMA, CERK & Lp-PLA2 (Emerging risk markers) among study and control group

Category		ADMA (ng/mL)	CERK (pg/mL)	Lp-PLA2 (ng/mL)
Study	**Mean**	137.8	179.5	39.6
	SD	27.4	54.2	12.1
Control	**Mean**	58.5	44.5	17.7
	SD	17.9	20	2.5

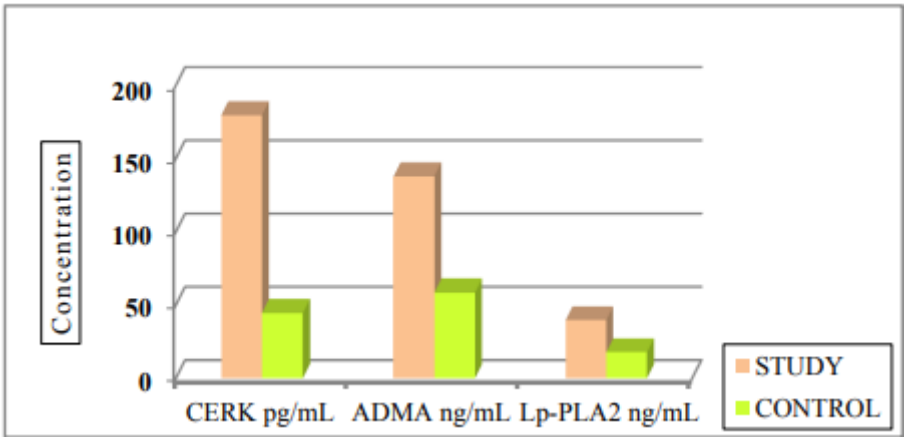

Figure 2: Emerging risk markers Distribution among study and control groups

Obesity, diabetes in the family, hypertension, and dyslipidemia were all significantly different between the study participants and controls ($p<0.05$; Table 3; Figure 3).

Table 3: Physiological characteristics Distribution and Odds ratio among study and control groups

Physiological	Characters	FH of	Diabetics	FH of	Hypertension	FH of	Dyslipidemia	Obesity	
		Yes	No	Yes	No	Yes	No	Yes	No
Study	**N**	90	110	118	82	129	71	69	131
	%	45	55	59	41	64.5	35.5	34.5	65.5
Control	**N**	13	87	17	83	19	81	19	81
	%	13	87	17	83	19	81	19	81

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P		0	0	0	0.005
95% CI for OR	**OR**	5.47	7.03	7.75	2.45
	L	2.8	3.8	4.3	1.2
	U	10.4	12.7	13.8	4

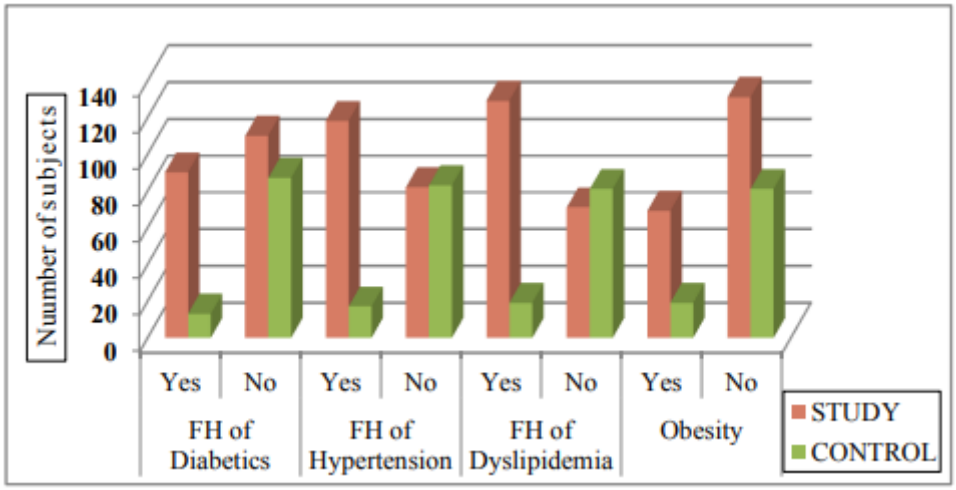

Figure 3: Distribution of physiological characteristics among studyand control groups

Anthropometric measures (waist circumference, weight, and body mass index) and metabolic measures (age, parity, and fasting plasma glucose) showed statistical significance between the study subjects and the controls at p0.05 in the t-test for continuous variables in demographic and physiological characteristics (Figure 4 and Table 4).

Table 4: Demographic and physiological charactersTest by t-test among study and control groups

Category		**Demographic characters**			**Physiological characters**		
Variables		Age	Birth Order	Abdominal Circumference(cm)	Height (m)	Weight (Kg)	BMI (Kg/m^2)
Study	**Mean**	48.2	3.14	94.1	1.584	67	26.8
	SD	5.1	5.3	16.5	0.11	11.5	4.6
Control	**Mean**	47.5	2.87	81.5	1.584	57.9	23.1

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	SD	6.6	6.1	17.7	0.086	8	2.6
T		1.07	1.18	6.14	0.028	7.141	7.574
P		0.286	0.118	**<0.001**	0.978	**<0.001**	**<0.001**

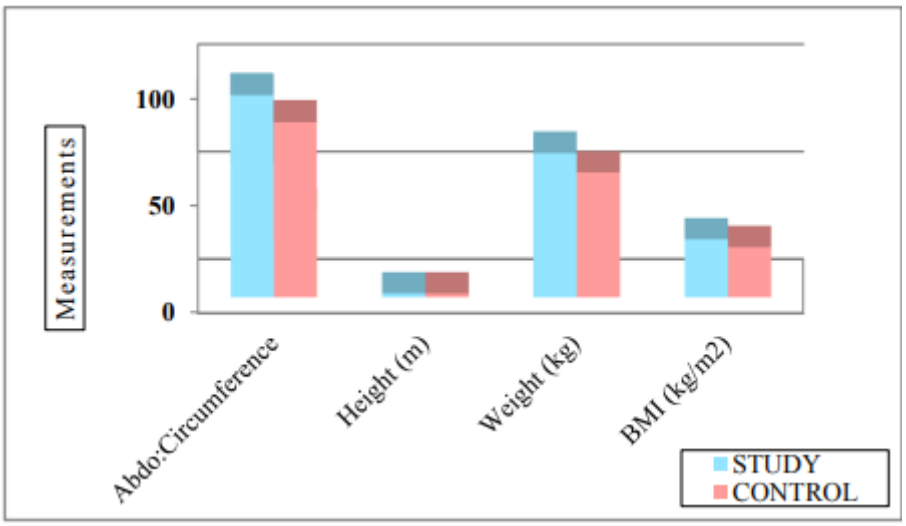

Figure 4: Among study and control group t-test for demographicand physiological characters

Coronary artery disease was associated with elevated levels of modifiable biochemical parameters such as fasting blood sugar (FBS), total cholesterol (TC), low-density lipoprotein (LDL), and triglycerides (TG) and decreased levels of high-density lipoprotein (HDL) (Table 5; Figure 5).

Table 5: Fasting blood sugar and lipid parameters amongstudy and control group by t-test

FBS & Lipid parameters		**Fasting Blood Sugar (mg/dL)**	**Total Cholesterol (mg/dL)**	**High Density Lipoprotein (mg/dL)**	**Low Density Lipoprotein (mg/dL)**	**Triglycerides (mg/dL)**
Study	Mean	144.6	213.8	33.7	156.6	197.1
	SD	70.6	43.2	7.1	54.3	44.2
Control	Mean	96.9	161.6	48.1	110.9	120.9
	SD	18.5	30.1	8.3	15.6	23.9
T		6.64	10.83	-15.57	8.24	16.11
P		**<0.001**	**<0.001**	**<0.001**	**<0.001**	**<0.001**

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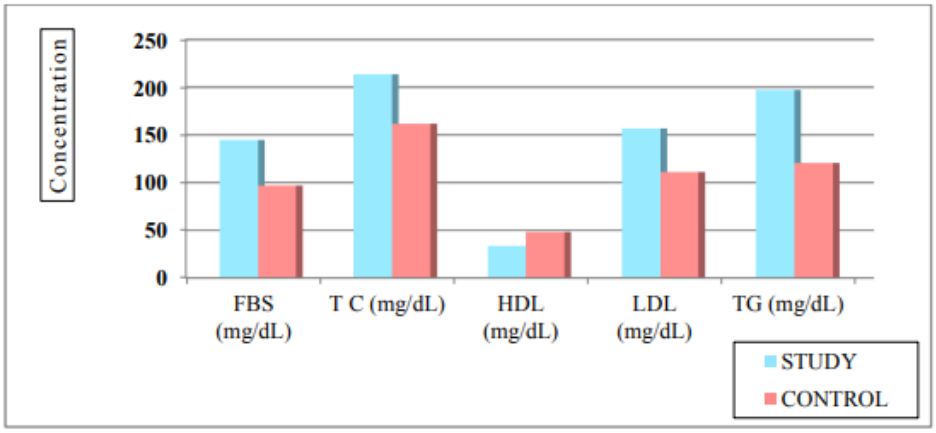

Figure 5: Comparison of FBS and lipids parameters among study andcontrol groups

4. Conclusion:

According to the findings of this research, coronary artery disease (CAD) is directly linked to hypertension, diabetes mellitus, obesity, hypertriglyceridemia, high LDL-C, high levels of urea, creatinine, hsCRP, fibrinogen, T3, and TSH, as well as a lower level of HDL-C and antioxidants.

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