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Article

Assessment Outcomes Effect of Apolipoprotein E4 Allele on Cardiovascular Diseases

Firas Hameed Abd Alsafi[1]

1. M.B.Ch.B., CABM. Med., FICMS. Cardio, Ministry of Health, Baghdad Medical office Al-Karkh, Ibn Al-Bitar Center for Cardiac Surgery, Adult Cardiology Department, Baghdad, Iraq

* Correspondence: Firasalsafi@gmail.com

Abstract: The apolipoprotein E4 allele is a genetic risk factor that has a negative impact on the quality of life of people with cardiovascular disease. Our current study aimed to evaluate the effect of apolipoprotein E4 allele in cardiovascular patients (n=85). A total of 85 elderly patients with cardiovascular disease were enrolled in the study, which was conducted at hospitals in Baghdad, Iraq, between 18 January 2022 and 27 October 2023. Comprehensive cardiovascular examinations were performed on each patient, including blood pressure, heart rate, and other vital sign measurements. APOE genotype analysis was conducted to evaluate the impact on the patients. Additionally, questionnaires were administered to assess the quality of life of patients with cardiovascular disease. In terms of clinical outcomes, chest pain was identified as the most prevalent symptom among patients, with a total of 38 cases. Additionally, the E3/E4 genotype of the APOE gene was observed in 41.18% of patients, which was associated with an increase in serum lipid-lipoprotein levels in terms of SBP (145.39 ± 27.46) mmHg and DBP (87.89 ± The mean values for the variables were as follows: glucose (3.11 ± 1.12) mg/dL, triglycerides (224 ± 46.25) mg/dL, LDL-C (167.29 ± 12.92) mg/dL, and HDL-C (14.82 ± 3.82) mg/dL. The adverse findings revealed that 23 cases involved heart attacks, and 30 cases involved strokes. Patients with CVD who carried the apolipoprotein E4 allele exhibited negative impacts on their quality of life, as evidenced by the following scores: physical functioning (46.38 ± 14.26), energy/fatigue (53.25 ± 12.29), and emotional problems (62.10 ± 10.29). In general, patients with the apolipoprotein E4 allele exhibit elevated levels of lipid profiles, which signify an elevated risk of severe complications in patients with cardiovascular disease.

Keywords: Apolipoprotein E4 Allele, Cardiovascular diseases, Elderly patients

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1. Introduction

Cardiovascular disease (CVD) causes 34.3% of the fatalities in the United States, totaling around 831,000 deaths. Approximately 75 million people had hypertension, over 18 million experienced coronary heart disease (CHD), as well as 6.4 million had been diagnosed in cerebrovascular accidents (strokes) [1 – 4]. Events and diagnoses primarily occur in adults aged 65 years and beyond, while the incidence for coronary artery disease and stroke is significantly raised, in fourfold, compared to those aged 18 to 64 years [5]. The projected expenses related to the treatment of cardiac, cerebrovascular, and hypertensive disorders among heart-aged Medicare enrollees in 2013 exceed $50,000 per person [6, 7].

According to the official data from the National Center of Health Statistics, the percentage of the population aged over 65 living with these illnesses in the United States decreased by nearly 20% from 2010 to 2014 [8]. It is likely that mortality from cardiovascular diseases for people in these risk factors is merely postponed, resulting in a future increase in CVD morbidity among the population over eighty years old, as those who would have

succumbed are sustained with the illness, thereby exacerbating the burden of chronic CVD complications [9 – 12]. The management and prevention for cardiovascular disease (CVD) associated risks have advanced, and these medications are more accessible than ever.

In 2003 and 2004, 24 million Americans were prescribed statin medications, with incidence having notably higher among individuals aged 75 and older exhibiting higher lower-density lipoprotein cholesterol (LDL-C) levels than among those aged 20 to 39 years [13 – 15]. The act of cigarette smoking is a behavior observed in individuals, with a gradual decline in prevalence. Between 2006 and 2008, 23 percent of individuals over 18 years old were current smokers, while the prevalence was nearly 40% among those aged over 65 years [16, 17]. Individuals possessing the APOE4 allele may exhibit a higher level in low-density lipoprotein (LDL) cholesterol, commonly referred to as 'bad' cholesterol, in their bloodstream. Elevated LDL cholesterol levels can lead to atherosclerosis, mostly caused by arterial constriction due to plaque deposition, so obstructing blood flow from the heart as well as essential organs. Apolipoprotein E is essential for chylomicron production in conjunction with VLDLs and HDL and is involved in lipid metabolism, transport, and digestion [18]. APOE, conversely, is polymorphic and has three prevalent alleles: epsilon 2 (ε2), epsilon 3 (ε3), and epsilon 4 (ε4), along with six distinct genotypes derived from these alleles. In several investigations, APOE polymorphism appeared to influence individuals with cardiovascular disease [19, 20].

2. Patients and Methods

2.1. Study Design Patients

Cross-sectional research was performed to assess the impact on the apolipoprotein E4 allele in individuals with cardiovascular disease. Eighty-five individuals were enrolled who completed comprehensive demographic and biochemical assessments conducted by physicians. Patient data were gathered from hospitals in Baghdad, Iraq, from the 18th of January, 2022, until October 27, 2023, with a follow-up duration of one year. This study encompassed exclusion criteria that involved individuals under 50 years of age and those with a history of myocardial infarctions or significant surgical procedures. All patient data were evaluated and documented using the statistical program SPSS, version 22.0.

2.2. Demographic Data

Our study documented demographic and fundamental data at the time of diagnosis for patients, encompassing age, gender, body mass index, and smoking status, in addition to prevalent symptoms that elucidated the historical dissemination of indicators among patients, specifically (chest pain, shortness of breath, fatigue, and palpitations).

2.3. Patient Data Collection and Analysis

Data was collected for people aged 50 to 65 years. DNA samples were acquired from the participants of the program, which assessed their food patterns, daily behaviors, and genotypes. The genotypes associated with the apolipoprotein E4 (APOE) gene have been determined, with three genotype forms in APOE*E4 carriers (E2/E4, E3/E4, E4/E4) being established.

In addition, genetic familial history, medical history, and data regarding lifestyle behaviors were extracted from clinical records. Additional clinical data and biochemical information were acquired from laboratory tests that measured blood lipid levels and systolic (SBP) as well as diastolic (DBP) blood pressures. Dyslipidaemia is identified when any of the following criteria are met: (i) Serum low-density lipoprotein cholesterol (LDL-

C) exceeds 130 mg/dL; (ii) serum triglycerides (TG) exceed 150 mg/dL; (iii) serum total cholesterol levels (TC) exceed 200 mg/dL; (iv) serum high-density lipoprotein cholesterol (HDL-C) is less than 40 mg/dL.

Hypertension is defined as a systolic blood pressure above 140 mmHg and a diastolic pressure over 90 mmHg. Diabetes is diagnosed in an individual with a fasting blood sugar level of 6.11 mmol/L or above. Exclusion criteria were malignant neoplasms, hepatic disorders, and autoimmune conditions. The exclusion criteria were renal illness, hepatic disease, endocrine disorders, metabolic disorders, and autoimmune diseases.

Additionally, our study discovered the issues arising from the adverse effects of the apolipoprotein E4 allele on individuals with cardiovascular disorders, specifically in relation to heart attack, stroke, heart failure, along with peripheral arterial disease. Furthermore, our study evaluated patients' quality of life utilizing the SF-36 Health Survey scale. The SF-36 Health Survey is a widely utilized tool for assessing health-related aspects of life. The survey comprises thirty-six questions and assesses seven distinct dimensions of health, scored on a scale from 0 to 100, with higher scores indicating superior quality of life. The dimensions include physical well-being, psychological function, emotional issues, energy/fatigue, social functioning, pain, as well as general health perception.

3. Results

Table 1. Demographic features of participants

Features		**Participants (n = 85)**	**Percentage (%)**
Age			
	50 – 55	35	41.18%
	56 – 60	24	28.24%
	61 – 65	26	30.59%
Sex			
	Male	51	60.0%
	Female	34	40.0%
BMI (kg/m2)			
	Underweight	12	14.12%
	Normal weight	4	4.71%
	Overweight	23	27.06%
	Obesity	46	54.12%
Smoking			
	Smokers	39	45.88%
	Non – smokers	46	54.12%

Poor diet			
	Yes	67	78.82%
	No	18	21.18%
Comorbidities			
	Hypertension	67	78.82%
	Dyslipidemia	62	72.94%
	Diabetes	30	35.29%
	Heart failure	14	16.47%
	Kidney disease	27	31.76%
	Coronary heart disease	20	23.53%
ASA classification			
	I	14	16.47%
	II	16	18.82%
	III	38	44.71%
	IV	17	20.0%
Education status			
	Primary	18	21.18%
	Secondary	32	37.65%
	University/post–graduated	35	41.18%
Monthly income, $			
	< 500	17	20.0%
	501 – 800	26	30.59%
	> 800	42	49.41%

Table 2. Distribution of symptoms at patients with CVD

Symptoms	**N = 85**	**Percentage %**
Chest pain	38	44.71%
Shortness of breath	20	23.53%
Fatigue	13	15.29%

Palpitations	14	16.47%

Table 3. Determine the genotype of the APOE gene in patients

Genotype	**N = 85**	**Percentage %**
E2/E4	24	28.24%
E3/E4	35	41.18%
E4/E4	26	30.59%

Table 4. Serum lipid-lipoprotein levels of participants

Data	**CVD outcomes**
SBP (mmHg)	145.39 ± 27.46
DBP (mmHg)	87.89 ± 12.77
Glucose (mg/dL)	3.11 ± 1.12
Triglyceride (mg/dL)	224 ± 46.25
TC (mg/dL)	203 ± 17.37
LDL-C (mg/dL)	167.29 ± 12.92
HDL-C (mg/dL)	14.82 ± 3.82
Apo-A1, g/L	1.76 ± 0.26
Apo-B, g/L	0.98 ± 0.24

Table 5. Distribution of complications related to E4 on patients with CVD

Complications	***N = 85***	***%***
Heart attack	23	27.06%
Stroke	30	35.29%
Heart failure	20	23.53%
Peripheral artery disease	12	14.12%

Table 6. Assessment of quality of life at participants with CVD

Items	SF-36 Health Survey
Physical functioning	46.38 ± 14.26
Psychological function	67.45 ± 16.44
Emotional problems	62.10 ± 10.29
Energy/fatigue	53.25 ± 12.29
Social functioning	63.05 ± 10.50
Pain	65.37 ± 9.63
General health perception	62.17 ± 6.07

4. Discussion

APOE is a pivotal gene related to cardiovascular disease [21]. The current study investigated the relationship among APOE polymorphisms and cardiovascular disease, as well as the corresponding lipid levels. Previous studies [22, 23, 24] have shown the predictive capacity for the APOE ε4 allele regarding cardiovascular risk across diverse populations. The ε4 allele also influences the risk in CAD (coronary artery disease) among Italy patients. In CAD patients, the prevalence of CAD progression differed related to different APOE genotypes, with 81% having ε4, 58% E3/4, along with 53% E2/4 or E4/4 [25].

In the same vein, our research identified that the genetic variations of APOE E3/4 and E4/4 had a tendency of raising the probability of developing CVD among the patients. The presence of such genotypes also resulted in an increased incidence of cardiovascular diseases, in addition to levels of lipids such as TC and LDL-C. However, the ε4 allele does not appear to modify CVD risk according to previous studies.

The E3/E4 genotype is the most prevalent, even though the ε4 allele is considered as the main risk factor for cardiovascular disease (CVD) [26, 27, 28]. Our study showed a significant association between the E3/E4 genotype and cardiovascular disease in people, in accordance with other research findings. A logistic regression research, following correcting both age, sex, as well as smoking, revealed that the ε4 allele was associated with greater cardiovascular disease risk.

In people with cardiovascular disease, HDL, triglyceride, and LDL levels were shown to be higher in ε4 carriers in comparison with ε4 non-carriers. Patients with ε4 genotype and cardiovascular disease had significantly lower levels of HDL and ApoA1 [29, 30, 31, 32]. The correlation among the E4 risk allele and lipid profiles is clinically contentious. Elevated total cholesterol, as well as LDL cholesterol blood levels, have been previously documented in the community of Japanese ε4 allele carriers.

Nonetheless, there was no association between the APOE polymorphisms in the population of Tunisia and other lipid profiles such as HDL-C [33, 34]. In the Germany study [35], women with cardiovascular disease and the ε4 allele demonstrated elevated LDLC and decreased HDL-C, indicating there may be a gender factor in the effect of the APOE polymorphism.

5. Conclusion

It has been found that the ApoE4 variety of apolipoprotein E is related to an increased susceptibility to cardiovascular illnesses as well as difficulties experienced by patients suffering from these illnesses, which this study we have conducted indicates that subjects with the ApoE4 genotype would likely suffer from severe cardiovascular catastrophes that include but are not limited to, heart attack and stroke, heart failure as well as peripheral vascular diseases, which would lower the quality of life of these individuals, where it is significant for individuals bearing the ApoE4 allele to take note of their cardiovascular health in order to boost their general well-being.

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