

## Apo lipoprotein A-1 polymorphism Association with Coronary Artery Plaque Progression in Type 2 Diabetic Patients

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### Abstract

Type 2 diabetes mellitus (T2DM) is one of the most common diseases with a high incidence and prevalence throughout the world. The prevalence of type 2 diabetes is rising at an alarming rate due to increase in life expectancy, obesity, physical inactivity and adoption of sedentary lifestyles. This study aimed to investigate the association of APOA1 polymorphism (-75 G/A and +83 C/T) with dyslipidemias, to assess the association of Apolipoprotein A1 gene polymorphism and coronary artery disease in type 2 diabetic patients and also aimed to study the susceptibility to CAD among Egyptian patients with T2DM. The subjects of the study were enrolled as thirty six (36) as a control group, thirty six (36) known to be T2DM without any cardiovascular complications and thirty six (36) known to be T2DM with coronary artery disease. The greater part about them were subjected with careful historical backdrop taking, finish clinical examination, research center investigations including (FPS, 2hr postprandial blood glucose, HbA1C Furthermore finish lipid profile) What's more coronary angiography to diabetic patients confounded with coronary supply route infection. We discovered that, no critical Contrast of the circulation for each genotype or alleles the middle of control assembly and diabetic one assembly Be that as both (CT & TT) genotypes and t alleles were a greater amount dispersed in the confounded diabetic bunch thereabouts we camwood Think as of them as a hazard figure to lowlife Previously, kind 2 diabetic patients. Both ga Furthermore AA genotypes Also An allele of APOA1 G-75A were altogether higher done controls over both T2DM Assemblies (without or for CAD).

**Keywords:** APOA1, Genotypes, Obesity and T2DM.

### 1. Introduction

Kind 2 diabetes mellitus (T2DM) is a standout amongst the The greater part regular ailments with a secondary occurrence Furthermore predominance for those universe. Those pervasiveness of sort 2 diabetes is climbing toward an disturbing rate because of build done term expectancy, obesity, physical inertia Furthermore selection about inactive lifestyles. Over Creating countries, the amount of kin for diabetes will expansion by 150 % in the following 25 a considerable length of time. Egypt may be in the universe 8th put As far as diabetes occurrence [1]. Apolipoprotein A1 (apoA1) may be those real Apolipoprotein constituent of the high-definition TV (HDL) Also is included over opposite cholesterol transport. Dependent upon now, a few single-nucleotide polymorphisms (SNPs) have been recognized in the APOA1 gene placed on the in length arm about chromosome 11. A regular G-to-A move placed -75 build pairs (bp) upstream from those interpretation begin site of the APOA1 gene need been examined extensively. In turn polymorphism site might have been identifier in the main intron of the APOA1 gene that includes move about C-to-T at +83 bp that need Additionally been demonstrated will influence hdl What's more apoA1 levels [2]. The A large portion incessant deadly mishap muddling from claiming T2DM is CAD, representing About 60 % from claiming passages Around T2DM patients [3]. Patients for T2DM would laid open to An two-four fold higher danger for Creating lowlife over those all populace. Thus, it is about essential significance in T2DM management with determine the factors that predispose these patients on create lowlife.

Done fact, better seeing of the pathogenesis for CVD Also T2DM may be of extraordinary interest to right on

time prediction Also ID number of at-risk patients and to better clinical administration. Therefore, the point of the current examine might have been with research those Acquaintanceship about APOA1 polymorphism (-75 G/A Furthermore +83 C/T) with dyslipidemias Furthermore powerlessness with lowlife "around egyptian patients with T2DM.

### 2. Subjects and methods

This consider might have been conveyed crazy during those inward drug divisions Also therapeutic natural chemistry Department; employees from claiming Medicine, Benha school. Thirty six solid incline subjects were selected Concerning illustration control aggregation.

Situation group: this assembly included 36 patients with T2DM analysis agreeing ada 2016; fasting plasma glucose levels of  $\geq 126$  mg/dL (7.0 mmol/L) alternately 2-h postprandial plasma glucose levels about  $\geq 200$  mg/dL (11.1 mmol/L). The selected patients were review examination Furthermore separated under two bunches as stated by coronary angiography results: diabetic cardiovascular patients (n=18) Furthermore 18 diabetic patients without lowlife. Those coronary angiography might have been completed at cardiology division from claiming Benha school healing centers.

#### 2.1 specialized foul plan

##### 2.1.1 webpage for study

The ponder might have been directed over offices for inner Medicine, outpatient facility Furthermore Biochemistry, staff from claiming medicine, Benha school.

### 2. 1. 2 test size

As stated by certainty interim 95%, force 80%. APOA1 35%. Chances proportion 3. 6. So, test span 108: 36 clinched alongside each gathering.

### 2. 1. 3 Incorporation criteria

Egyptian participants, Age: 30-80 years, sufficient hepatic, renal Furthermore respiratory works.

### 2. 1. 4 avoidance criteria

Patients with sort 1 DM, vicinity for liver or kidney disease, Thyroid, immune system alternately whatever animated incendiary diseases, Patients for liquor admission complex Also Patients getting corticosteroid pills.

### 2. 2 Operational design

The event – control study, steps and the subjects will be arranged under 3 groups: Aggregation 1: control group: period What's more sex-matched aggregation for negative family history of diabetes, obesity, hypertension and coronary supply route infection.

Assembly 2: Patients for sort 2 dm without lowlife.

Assembly 3: Patients for sort 2 dm Furthermore lowlife.

### 2. 3 Managerial design

#### 2. 3. 1 Moral consideration

A composed educated assent will be made from those patients for demonstration of the procedure, workable dangers.

#### 2. 3. 2 The greater part subjects about this study were subjected of the following

cautious history taking, careful clinical examination, schedule research center investigations, investigate investigations: -Detection of Apo lipoprotein A1 polymorphism Eventually Tom's perusing multiplex intensification recalcitrant change framework PCR (Multi-ARMS PCR).

Schedule Investigations Including: Finish blood picture, 2- liver capacity tests, 3-Renal work tests, 4-fasting Also post prandial plasma glucose Furthermore 5-fasting lipid profile.

Research examination Eventually Tom's perusing dna Extraction: Every last one of fill in might have been conveyed out in the atomic science lab in the restorative natural chemistry Branch. Every last one of reagents were Exceedingly purified explanatory PCR-materials. Every last one of tubes, tips pipettes utilized for dna extraction were DNase, rnase spare tubes with Abstain from tainting bought from Gentra (Minnapolis. USA).

### 3. Results

APOA1 G-75A polymorphism has 2 allele (G & A) and 3 genotypes (GG & AA) as homozygote genotypes and (GA) as heterozygote genotype. There were statistically significant higher distribution of A allele, GA and AA genotypes (p- value <0.05) in control group than diabetic non ischemic group. APOA1 C+83T: This gene polymorphism has 2 allele (C & T) and 3 genotypes (CC & TT) as homozygote genotypes and (CT). There was non-significant difference as regard the distribution of alleles or genotypes between control and diabetic non ischemic group Table (1).

Regarding distribution of APOA1 G-75A polymorphism : There were statistically significant ( p-value <0.05) higher distribution of A allele, GA and AA genotypes in control group than diabetic ischemic group so they are protective. Regarding distribution of APOA1 C+83T polymorphism: There were statistically significant (p- value <0.05) higher distribution of T allele and (CT&TT) genotypes in diabetic ischemic group than control group Table (2).

There was non-significant statistically impact (p-value >0.05) to any genotype of APOA1 G-75A polymorphism on blood pressure and anthropometric measurements among diabetic ischemic patients Table (3).

There was non-significant impact to any genotype of APOA1 C 83 T polymorphism on BMI and waist circumference among diabetic ischemic patients. There were significant statistically impact of (CT & TT) genotypes of APOA1 C 83 T polymorphism on SBP and DBP among diabetic ischemic patients Table (4).

There were non-significant impact (p- value >0.05) to any genotype of APOA1 C 83 T polymorphism on lipid profile among diabetic ischemic patients Fig (1).

**Table (1)** Distribution of Apolipoprotein A1 polymorphism genotypes and allele frequencies in healthy control group and diabetic ischemic patients.

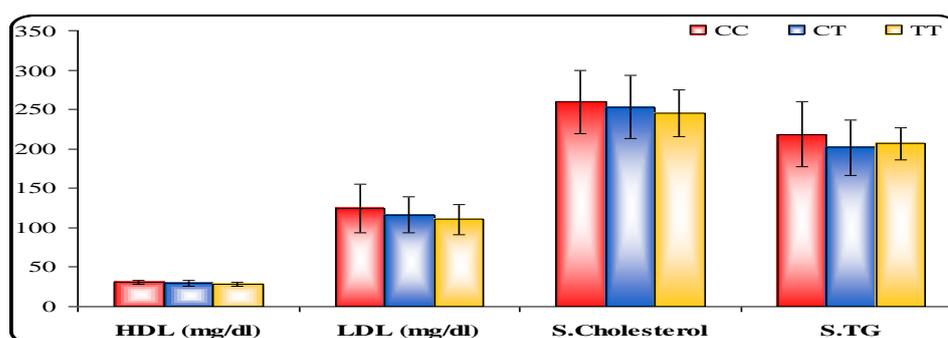
		Controls n=18		Diabetic with CVD n=18		OR(95%CI)	P
APOA1 G-75A	GG	11	(30.5)	27	(75)		
	GA	20	(55.6)	8	(22.2)	0.16(0.06-0.48)	0.001**
	AA	5	(13.9)	1	(2.8)	0.08(0.01-0.78)	0.011*
	G allele	42	(58.3)	62	(86.1)		
	A allele	30	(41.7)	10	(13.9)	0.23(0.10-0.51)	<0.001**
APOA1 C+83T	CC	23	(63.9)	11	(30.6)		
	CT	13	(36.1)	17	(47.2)	2.7(0.99-7.57)	0.05*
	TT	0	(0)	8	(22.2)	1.7(1.17-2.53)	0.001**
	C allele	59	(81.9)	39	(54.2)		
	T allele	13	(18.1)	33	(45.8)	3.8(1.79-8.20)	<0.001**

**Table (2)** show the impact of the different genotypes of APOA1 G-75A polymorphism on clinical and anthropometric parameters in diabetic ischemic patients.

	APOA1 G-75A (n=18) ,(Mean± SD)					
	GG (N=13)	GA (N=4)	AA (N=1)	P1	P2	P3
<b>SBP (mm/hg)</b>	139.3±15.2	147.5±14.9	150.0±0.0	0.187	0.343	0.820
<b>DBP (mm/hg)</b>	99.3±13.4	107.5±12.8	100.0±0.0	0.134	0.943	0.944
<b>BMI</b>	23.5±1.9	24.4±1.9	22.2±0.0	0.247	0.359	0.126
<b>waist circumference (cm)</b>	80.9±8.8	82.1±9.8	83.0±0.0	0.743	0.747	0.900

**Table (3)** show the impact of the different genotypes of APOA1 C+83T polymorphism on clinical and anthropometric measurements in diabetic ischemic patients.

	APOA1 C+83T (n=18) ,(Mean± SD)					
	CC (N=13)	CT (N=4)	TT (N=1)	P1	P2	P3
<b>SBP (mm/hg)</b>	133.6±15.7	142.4±13.9	150.0±13.1	0.125	0.019*	0.221
<b>DBP (mm/hg)</b>	93.6±15.7	102.4±13.9	108.8±13.6	0.127	0.031*	0.308
<b>BMI</b>	23.6±1.9	23.5±2.0	23.9±2.1	0.904	0.706	0.605
<b>waist circumference (cm)</b>	83.7±9.8	78.5±7.8	83.6±8.7	0.134	0.980	0.184



**Fig (1)** Show the impact of the different genotypes of APOA1 C+83T polymorphism on lipid profile in diabetic ischemic patients.

#### 4. Discussion

To fact, finer seeing of the pathogenesis from claiming CVD Also T2DM is about great enthusiasm for punctual prediction What's more ID number of at-risk patients Furthermore for superior clinical oversaw economy. Therefore, those point alternately the present investigation might have been with examine those cooperation for APOA1 polymorphism (-75 G/A What's more +83 C/T) with dyslipidemias and defenselessness with lowlife Around egyptian patients with T2DM.

So as to superior explain the lowlife hazard factors, we further subgrouping our T2DM patients as stated by bring about shortages about coronary angiography to T2DM without lowlife Also T2DM with lowlife. Around T2DM patients, lowlife subgroup needed altogether more span from claiming dm Furthermore higher values for systolic and in addition diastolic Circulatory strain contrasted with T2DM patients without lowlife. Furthermore, diabetic patients required altogether bring down qualities from claiming waist circumduction What's more hdl contrasted with control one assembly.

In understanding for our results, [4] found non- huge connection the middle of corpulence What's more improvement from claiming lowlife "around sort 2 diabetic patients [4].

The The greater part vital finding from claiming our consider that, APOA1 G-75A might have been that ga Furthermore AA genotypes What's more a allele for APOA1 G-75A were essentially higher clinched alongside controls over T2DM without lowlife cases. Thus, the hazard of T2DM might have been altogether bring down Around patients carrying ga & AA genotypes over the individuals carrying GG genotype.

An pilot consider in An north indian number proposed that APOA1 polymorphisms (-75 G/A Also +83 C/T) might be defenselessness to myocardial localized necrosis [5]. Moreover, An brazilian elderly associate demonstrated that APOA1 polymorphisms (-75 G/A Furthermore +83 C/T) Might a chance to be Concerning illustration danger figures to hypertension Also Weight [6].

Those fascinating result about our investigation might have been the protective impact for ga and AA genotypes and An allele from claiming APOA1 G-75A. Against improvement of lowlife. In regards APOA1 C+83T, our comes about uncovered that tt What's more ct genotypes What's more t allele about APOA1 C+83T were altogether higher Previously, T2DM with lowlife cases over control (TT 22. 2% vs. 0%; CT: 47. 2% vs. 36. 1%; t allele: 45. 8% vs. 18. 1%, respectively). Those hazard about lowlife were fundamentally higher "around patients carrying ct & tt genotypes over the individuals carrying cc genotype (OR (95%CI): 2. 7(0. 99-7. 57),. Cons similarly, reports about [7] shown that those people for the APOA1 -75 An allele were liable will need an easier danger about lowlife Concerning illustration an aftereffect about its impact on higher serum focuses about ApoA1 What's more HDL-C. Extra investigations are required on affirm this finding [7].

Also, comparative outcomes were depicted in [8] contemplate they tracks those conveyance of different genotypes of APOA1 g 75 An polymorphism over diabetic patients with past myocardial localized necrosis.

Similarly as an outcome for our studies, we concentrated on the effect of APOA1 G-75A Furthermore C+83T genes polymorphism with respect to clinical, anthropometric Also lab aspects of T2DM without lowlife bunches. Obviously, our discoveries uncovered non- noteworthy contrasts between APOA1 G-75A Also C+83T genotypes or alleles.

On investigation led by [6] the dissemination about t allele What's more (CT&TT) genotypes may be additional in the diabetic assembly muddled with lowlife Along these lines they need aid hazard figure to coronary ischemia Around diabetic patients. [9]. Interestingly, our discoveries uncovered non- critical contrasts the middle of APOA1 C+83T genotypes or alleles dissemination Concerning illustration see pulse levels , glycemic control What's more lipid profile.

Comparable effects affirmed Eventually Tom's perusing [9] who discovered no critical impact of variant genotypes of APOA1 c 83 tonal pulse Also anthropometric estimations "around diabetic patients. [9]. In understanding for our study, [10] who found no critical impact about variant genotypes from claiming APOA1 c 83 t polymorphism once blood glucose level over diabetic non-complicated patients. [10]. On the other side, [9] recognized that t allele assume part done poor controlling about blood glucose level. There would even now vague effects viewing cooperation between APOA1 -75 a allele and plasma lipids [9].

## 5. Conclusion

Our results revealed that both GA and AA genotypes and A allele of APOA1 G-75A were significantly higher in controls than both T2DM groups (without or with CAD) Thus, the individuals with GA and AA genotypes and A allele were likely to have a lower risk of T2DM and CAD as a result of its effect on HDL-C. Regarding APOA1 C+83T, TT and CT genotypes and T allele of APOA1 C+83T were significantly higher in T2DM with CAD cases than control thus they can be considered arisk factor for CAD among T2DM patients.

## References

- [1] Norbert Freinkel, *Diabetes Care* , Vol. 41, 2018.
- [2] D. Mozaffarian, EJ. Benjamin, AS. Go, *Heart disease and stroke statistics--2015 update: a report from the American Heart Association. Circulation*, Vol.131, PP.29-322, 2015.
- [3] Y.M. Park, R. Kashyap, *Insulin promotes macrophage foam cell formation: potential implications in diabetes-related atherosclerosis. Lab Invest*, Vol.92, PP.1171, 2012.
- [4] K. William, A. B. Gregory, K. K. Lester, *The Relationship between Body Mass Index and the Severity of Coronary Artery Disease in Patients Referred for Coronary Angiography . Cardiology Research and Practice*, Article ID, Vol. 5481671, PP.10, 2017.
- [5] R. Dawar, A. Gurtoo, R. Singh, *Apolipoprotein A1 gene polymorphism (G-75A and C+83T) in patients with myocardial infarction: A pilot study in a North Indian population. Am J Clin Pathol*, Vol.134(2), PP.249-255, 2010.
- [6] Y. Chen, J. Rollins, B. Paigen, *Genetic and genomic insights into the molecular basis of atherosclerosis. Cell Metab*, Vol.6, PP.164, 2007.
- [7] B. Liao, K. Cheng, S. Dong, *Effect of apolipoprotein A1 genetic polymorphisms on lipid profiles and the risk of coronary artery disease. Diagnostic pathology*, Vol. 10(1), PP.102, 2015.
- [8] E. Angotti, E. Mele, F. Costanzo, *A polymorphism (GA transition) in the -78 position of the apolipoprotein A-I promoter increases transcription efficiency*, Vol.26, PP.17371-17374, 1994.
- [9] Z. Yangchun, H. Dayi, Y. Xinchun, *Relationship among apolipoprotein A1 gene polymorphism, lipid levels and coronary atherosclerosis disease. Chin Med J (Engl)*, Vol.116, PP.665-668, 2003.
- [10] K. Bora , MS. Pathak, P. Borah, *Association of the Apolipoprotein A-I gene polymorphisms with cardiovascular disease risk factors and atherogenic indices in patients from assam, Northeast India. Balkan J.,Medical Genetics*, Vol.52, PP.65-58,2017.