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REVIEW

Predisposition of Obesity through Genetic and Non-Genetic Risk Factors

Alice Jayapradha Cheekurthy*

Department of Biochemistry, Maris Stella College (Autonomous), Vijayawada-8, Andhra Pradesh, India

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ABSTRACT

Globally there is an increase in the number of people affected by obesity. This has increased the count of individuals to double, triple, and even quadruple. Obesity is a complex disease that has a genetic, behavioural, socioeconomic, and environmental effect. This raises morbidity and mortality in obesity. It is an important predisposition for diabetes as well as the current pandemic COVID-19. The rationale of this case-control observational study is to identify obese individuals among the diabetic and non-diabetic population. The study includes non - genetic factors like lipid profiles with genetic factors in form of SNP as a predisposition factor. The amplified portion of the ADIPOQ gene sequence revealed the presence of SNPs rs2241767 in 46.3% population and showed increased lipid profile values. It can be concluded that these are important predisposing factors for obesity.

1. Introduction

1.1 Obesity

Obesity is a complex metabolic disorder in which there is an excessive amount of body fat [1]. It is an important predisposing factor for other health problems like diabetes and hypertension and vice versa [2]. Many of the diabetics were found to be suffering from a complication of obesity. The non-diabetic obese people are at high risk for diabetes. This rise in the prevalence of obesity is due to economic growth, industrialization, mechanized transport, urbanization. as defined by WHO Overweight and obesity abnormal accumulation of fat that poses a health risk. A body mass index (BMI) over 25 is considered overweight, and over 30 is obese [2]. With each year passing by over 4 million people are dying. It has increased the global burden of disease in individuals as well as the healthcare systems now and in the future also.

1.2 Type 2 Diabetes Mellitus

It is a condition when the body not able to use the insulin produced by the pancreas [2]. Type 2 Diabetes mellitus is common in adults and accounts for around 90% of all diabetes cases. It is known to lead to increased risks for infections. Patients with diabetes are more likely to experience severe complications from COVID-19, and those with poorly-controlled blood sugar are even at higher risk of death. Diabetes if not controlled can lead to complications like obesity.

**Corresponding Author:*
Alice Jayapradha Cheekurthy,
Department of Biochemistry, Maris Stella College (Autonomous), Vijayawada-8, Andhra Pradesh, India;
Email: alicejaya@gmail.com

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1.3 ADIPOQ

Adiponectin gene, responsible for the major adipocyte secretory protein is located on chromosome 3q27. It plays an important role in the metabolism of fat and the regulation of glucose. Insulin sensitivity in muscle and liver and thereby regulates energy homeostasis and glucose tolerance. Obesity and diabetes are associated with low circulating levels of adiponectin [3,4]. The Single Nucleotide Polymorphisms in ADPOQ are responsible for obesity [5].

2. Materials and methodology

2.1 Sample Collection

Following the protocol, the left-over peripheral blood samples were collected from 200 diabetes subjects in EDTA and non-EDTA vials from the subjects visiting the diagnostic center. They were driven for testing of Blood sugars and Lipid profile either with self-interest or prescribed by the doctor.

2.2 Selection of Polymorphism

We limited our selection of genetic variants with SNPs rs2241767 [6]. in ADIPOQ.to the previously reported Single nucleotide polymorphisms in recent epidemiological studies.

2.3 Selection of Biochemical Parameters

Triglycerides, High-Density Lipoprotein (HDL), low-density lipoprotein (LDL), and Very low-density lipoproteins (VLDL) are the different types of cholesterol present in the blood. The abnormalities in the plasma and blood levels of lipids are proved to be the best predictors of obesity. Obesity can affectively change lipid profile values from normal to be hypercholesterolemia, hypertriglyceridemia can lead to cardiovascular events [7-10].

2.4 Methodology

Only 180 (90 cases and 90 controls) were selected for the study and of which only 51 Samples were processed for genetic study. Extraction and purification of DNA were done using modified Sambrook et al. protocol [11-13]. ADIPOQ genes with the specified target region of SNP associated with obesity were amplified using Polymerase chain reaction. The PCR amplified products were qualitatively checked on 1.2% agarose gel electrophoresis [14] and were visualized in a transilluminator after staining with ethidium bromide. These amplicons were then subjected to sequencing by the Sanger sequencing method [15]. The sequenced portions of the genes were checked for the consistency of reported mutations of ADIPOQ genes in our samples.

Table 1.

GENE	Ref. sequence	Reported SNP	Amplicon	% positive
ADIPOQ	rs2241767	G/T	186853309-186853804	46.3%

2.5 Analysis of Biochemical Parameters

The mean of the lipid profile characteristics were found to be total cholesterol =176.8 ± 50.3 mg/dl; triglycerides =198.1 ± 87.7 mg/dl; HDL=42.5 ± 4.7 mg /dl and LDL=86.4 ± 25.8 mg/dl, VLDL=41.8 ± 20.7. The lipid ratios like total cholesterol/HDL=4.16 ± 10.7 cholesterol and the LDL cholesterol/HDL cholesterol ratio 2.0 ± 5.48. Table 2 shown below gives the list of the lipid profile characteristics of T2DM cases and Controls.

Table 2. Lipid Profile Characteristics

Parmeter	T2DM Cases Mean±SD	Controls Mean±SD	Normal Range	*p*=value
Total Cholesterol	176.8±50.3	163±51.7	130-250	0.09
Triglycerides	198.1±87.7	141±56.9	50-150	0.1
HDL	42.5±4.7	43.2±5.9	35-70	0.05
LDL	86.4±25.8	44.0+28.6	Upto140	0.09
VLDL	41.8±20.7	28.6±13.6	10-40	0.09

2.6 Analysis of Variation

The SNP rs2241767 is present in T2DM 19 cases. The nucleotide is changed from G→T but there the corresponding amino acid change showing the risk for obesity.

3. Discussion and Result

Excessive energy intake followed by lack of sufficient physical activity leads to increased morbidity and mortality [16.17] is observed in obese people, It has become an economic burden on self as well as for the healthcare system [18-20]. Both genetic and non-genetic factors contribute to the increasing prevalence of obesity [21].

Significant associations between overweight and gene polymorphisms of ADIPOQ were found in the diabetic subjects of our case-control observational study. The insulin resistance also causes reduced retention of free

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ADIPOQ_11    CTACACTGATATAAACTATATGAAGGCATTCATTATTAACTAAGGCCTAGACACAGGGA
ADIPOQ_24    CTACACTGATATAAACTATATGAAGGCATTCATTATTAACTAAGGCCTAGACACAGGGA
ADIPOQ_12    CTACACTGATATAAACTATATGAAGGCATTCATTATTAACTAAGGCCTAGACACAGGGA
ADIPOQ_9     CTACACTGATATAAACTATATGAAGGCATTCATTATTAACTAAGGCCTAGACACAGGGA
ADIPOQ_2     CTACACTGATATAAACTATATGAAGGCATTCATTATTAACTAAGGCCTAGACACAGGGA
ADIPOQ_14    CTACACTGATATAAACTATATGAAGGCATTCATTATTAACTAAGGCCTAGACACAGGGA
ADIPOQ_15    CTACACTGATATAAACTATATGAAGGCATTCATTATTAACTAAGGCCTAGACACAGGGA
ADIPOQ_22    CTACACTGATATAAACTATATGAAGGCATTCATTATTAACTAAGGCCTAGACACAGGGA
ADIPOQ_26    CTACACTGATATAAACTATATGAAGGCATTCATTATTAACTAAGGCCTAGACACAGGGA
ADIPOQ_27    CTACACTGATATAAACTATATGAAGGCATTCATTATTAACTAAGGCCTAGACACAGGGA
ADIPOQ_28    CTACACTGATATAAACTATATGAAGGCATTCATTATTAACTAAGGCCTAGACACAGGGA
ADIPOQ_30    CTACACTGATATAAACTATATGAAGGCATTCATTATTAACTAAGGCCTAGACACAGGGA
ADIPOQ_37    CTACACTGATATAAACTATATGAAGGCATTCATTATTAACTAAGGCCTAGACACAGGGA
ADIPOQ_40    CTACACTGATATAAACTATATGAAGGCATTCATTATTAACTAAGGCCTAGACACAGGGA
ADIPOQ_1     CTACACTGATATAAACTATATGAAGGCATTCATTATTAACTAAGGCCTAGACACAGGGA
ADIPOQ_36    CTACACTGATATAAACTATATGAAGTCATTCATTATTAACTAAGGCCTAGACACAGGGA
ADIPOQ_21    CTACACTGATATAAACTATATGAAGTCATTCATTATTAACTAAGGCCTAGACACAGGGA
ADIPOQ_8     CTACACTGATATAAACTATATGAAGTCATTCATTATTAACTAAGGCCTAGACACAGGGA
ADIPOQ_34    CTACACTGATATAAACTATATGAAGGCATTCATTATTAACTAAGGCCTAGACACAGGGA
ADIPOQ_19    CTACACTGATATAAACTATATGAAGGCATTCATTATTAACTAAGGCCTAGACACAGGGA
ADIPOQ_6     CTACACTGATATAAACTATATGAAGGCATTCATTATTAACTAAGGCCTAGACACAGGGA
ADIPOQ_38    CTACACTGATATAAACTATATGAAGTCATTCATTATTAACTAAGGCCTAGACACAGGGA
ADIPOQ_33    CTACACTGATATAAACTATATGAAGTCATTCATTATTAACTAAGGCCTAGACACAGGGA
ADIPOQ_23    CTACACTGATATAAACTATATGAAGTCATTCATTATTAACTAAGGCCTAGACACAGGGA
ADIPOQ_18    CTACACTGATATAAACTATATGAAGTCATTCATTATTAACTAAGGCCTAGACACAGGGA
ADIPOQ_10    CTACACTGATATAAACTATATGAAGTCATTCATTATTAACTAAGGCCTAGACACAGGGA
ADIPOQ_5     CTACACTGATATAAACTATATGAAGTCATTCATTATTAACTAAGGCCTAGACACAGGGA
ADIPOQ_39    CTACACTGATATAAACTATATGAAGTCATTCATTATTAACTAAGGCCTAGACACAGGGA
ADIPOQ_25    CTACACTGATATAAACTATATGAAGTCATTCATTATTAACTAAGGCCTAGACACAGGGA
ADIPOQ_13    CTACACTGATATAAACTATATGAAGTCATTCATTATTAACTAAGGCCTAGACACAGGGA
ADIPOQ_35    CTACACTGATATAAACTATATGAAGTCATTCATTATTAACTAAGGCCTAGACACAGGGA
ADIPOQ_31    CTACACTGATATAAACTATATGAAGTCATTCATTATTAACTAAGGCCTAGACACAGGGA
ADIPOQ_29    CTACACTGATATAAACTATATGAAGTCATTCATTATTAACTAAGGCCTAGACACAGGGA
ADIPOQ_20    CTACACTGATATAAACTATATGAAGTCATTCATTATTAACTAAGGCCTAGACACAGGGA
ADIPOQ_16    CTACACTGATATAAACTATATGAAGTCATTCATTATTAACTAAGGCCTAGACACAGGGA
ADIPOQ_7     CTACACTGATATAAACTATATGAAGTCATTCATTATTAACTAAGGCCTAGACACAGGGA
ADIPOQ_3     CTACACTGATATAAACTATATGAAGTCATTCATTATTAACTAAGGCCTAGACACAGGGA
ADIPOQ_32    CTACACTGATATAAACTATATGAAGGCATTCATTATTAACTAAGGCCTAGACACAGGGA
ADIPOQ_17    CTACACTGATATAAACTATATGAAGGCATTCATTATTAACTAAGGCCTAGACACAGGGA
ADIPOQ_4     CTACACTGATATAAACTATATGAAGGCATTCATTATTAACTAAGGCCTAGACACAGGGA
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fatty acids by the adipocytes [22]

A strong influence of biochemical parameters like Lipid profile was observed to show the relationship with obesity. The presence of the above ADIPOQ gene SNPs shows the susceptibility to obesity. The impaired lipid profile values are the important predisposing factors for obesity and responsible for Type 2 Diabetes and cardiovascular disease in normal subjects' controls and cases respectively.

4. Conclusion

Obesity is the result of Cumulative effects of both genetic components and biochemical parameters.

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