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Research Article

Apolipoprotein C3 C1100T and C3238G Polymorphisms and Cardiovascular Disease Risk among Obese Type 2 Diabetics in Southwestern Nigeria.

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ABSTRACT

Obesity is associated with cardiovascular disease (CVD) risk and type 2 diabetes mellitus (T2DM). Apolipoprotein (APO) C3 C3238G and C1100T gene polymorphisms are risk factors for CVD but their relationship with obesity and T2DM in Black Africans has not been fully elucidated. Association of these gene polymorphisms with hypertension and dyslipidemia among obese type 2 diabetics in a Southwest Nigerian population was assessed.One hundred and thirty-eight (138) non-obese diabetics, 107 obese diabetics, 100 obese non-diabetics and 100 control subjects attending metabolic clinic in Osun State Nigeria were enrolled. Anthropometric parameters were measured. Fasting blood sugar (FBS), lipid profile and APOC3 protein were estimated using standard lab procedures. APOC3 gene polymorphisms were analyzed by polymerase chain reaction - restriction fragment length polymorphism. Data were analyzed and significant level set at $p<0.05$. APOC3238G G allele was associated with higher risk of hypertension (OR=2.39, 95%CI=1.03-5.53; p=0.042) in obese diabetics compared to other groups. Highest frequency for hypertension was observed among obese diabetics expressing CC than CG and GG genotypes. GG genotype was associated with dyslipidemia in obese diabetic subjects exhibiting APO C3 C3238G single nucleotide polymorphism (SNP). Homozygous CC genotype showed highest frequency (χ^2: 25.515, $p<0.05$) than other genotypes and was associated with increased atherogenic indices among obese diabetic subjects expressing APO C3 C1100T SNP. APOC3 C1100T gene and polymorphic alleles of the G variant of APOC3 C3238G gene were associated with dyslipidemia and hypertension in obese T2DM individuals, thereby contributing to increased risk of CVD among the studied population.

Keywords: apolipoprotein C3 polymorphism, cardiovascular disease, Nigerian

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INTRODUCTION

Obesity, defined as excessive fat accumulation (WHO, 2012) is caused by multiple factors which can be genetic and cultural. These include a chronic imbalance of energy intake and expenditure (Iloh *et al*., 2011), sedentary lifestyle and endocrine disorders (Mercado-Gonzales *et al*., 2019). Obesity increases the risk of morbidity from hypertension, dyslipidemia, type 2 diabetes, coronary heart disease and stroke (Xavier, 2009). Obesity-associated changes in lipid transport precede insulin resistance and development of atherosclerotic cardiovascular disease and T2DM (Hwang, 2012).

The prevalence of obesity in West Africa is estimated to be 10% (Abubakari, 2008) while in Nigeria the prevalence of obesity and diabetes ranges from 3% and 22.2% respectively (Innocent *et al*.,2013). ApoC3 is mainly synthesized in the liver and to some extent in the intestines (Raposo *et al.*, 2015) and plays a key role in lipid metabolism, proinflammatory and atherogenic processes (Hiukka *et al.*, 2009).

Experimental evidence suggested that proteins related to plasma lipoprotein transport, such as apolipoprotein C may play a role in obesity (Li *et al*, 2014). ApoC3 is an inhibitor of lipoprotein lipase (LPL) impairing the uptake of lipoprotein remnants by the liver. Mutations in the gene encoding APOC3 are associated with low triglyceride levels and decreased

CVD risk while overexpression of APOC3 is associated with hypertriglyceridaemia (Boren J *et al*, 2020).

Apolipoprotein C3 is involved in transport and clearance of chylomicron remnants, very-low-density lipoprotein (VLDL) and HDL from the bloodstream thus emerging as a target linking hypertriglyceridaemia with CVD. (Wulff *et al*, 2018). In addition, a strong positive correlation of ApoC3 with TG concentration has been reported in human and animal studies (Kohan, 2015). Two common single nucleotide polymorphisms, 1100 C/T and 3238 C/G, have been identified in the APOC3 gene. Case control studies have suggested that the APOC3 C3238G genotype is a risk factor for dyslipidemia, hypertension, cardiovascular disorder and coronary artery disease (CAD) in obese Asian populations (Jo G *et al*, 2018; Cui F *et al*, 2014). Obesity and overweight were assumed to be a problem of high-income countries, however, an increasing unfavorable trend especially in sub-Saharan African region categorized as low and medium income countries poses a grave challenge (WHO, 2016). Therefore, the association of APOC3 C3238G and C1100T gene polymorphisms in the development of obesity as well as hypertension and other cardiovascular disease risk factors in type 2 diabetic subjects of Nigerian origin was investigated in the present study.

MATERIALS AND METHODS

Study design: This was a hospital based case control study involving patients diagnosed with type 2 diabetes mellitus attending diabetic clinic and receiving treatment at the Family Health Clinics of Osun State University Teaching Hospital and State Specialist Hospital Asubiaro Osogbo, Osun state, Nigeria. Duration of the study was between October 2018 to March 2021.

Type 2 diabetes mellitus was diagnosed by the attending physician based on the American Diabetes Association Criteria. These include: fasting plasma glucose $\geq$ 126mg/dL, random blood glucose $\geq$ 200 mg/dL and laboratory confirmatory report of glycated haemoglobin (ADA, 2014).

Control subjects were confirmed to be free of diabetes based on the fasting plasma glucose levels using well calibrated glucometer (Accu-Check with glucometer strips). All subjects completed structured questionnaire which captured their demographic information, medical history and lifestyle habits. Obese subjects defined by BMI $\geq$ 30Kg/m^2 and met diagnostic criteria for type II diabetes were included while individuals with history of hepatitis, fibrosis and chronic alcoholics were excluded from the study**.**

Sample size calculation: The sample size was determined using Leslie Fisher's formula for estimating single proportions and minimum sample size as follows:

$$n = \frac{z^2pq}{d^2}$$

where n = minimum sample size required in population greater than 10,000

- *Z = Standard normal variate for 95 % confidence level, (Z = 1.96)*
- *d = acceptable difference; using 5 % (d = 0.05)*
- *q = 1 – p*
- *p= prevalence rate (4.9%)*

Subject Grouping: The study participants were categorized into: (i). One hundred and thirty-eight non-obese diabetics (ii). One hundred and seven obese diabetics (iii**)** One hundred obese non-diabetics (positive controls). (iv) One hundred non-obese non-diabetes (negative controls)

Ethical Consideration: All the participants were informed of the purpose of the research and their consent sought and obtained. Ethical clearance was obtained from the research ethical review committee of the State Hospital Asubiaro Osogbo, Osun State (HREC/27/04/2015/SSHO/42).

Sample collection: Eight ml peripheral venous blood was collected from each participant. 2ml of blood was dispensed into tubes containing fluoride oxalate, 5ml into EDTA tubes whiles the rest was dispensed into plain tubes. The tubes were then placed in a centrifuge (eppendorf 5425) and spun at 3000 x g for 10 minutes to obtain the plasma. Plasma glucose was measured immediately and the plasma for the measurement of other biochemical variables were stored in the freezer at -80°C until analysis.

Biochemical /laboratory measurements: Weight and height were measured in subjects wearing light clothing and without shoes. Body weight was measured in kg using mechanical weighing scale (Beurer GmbH, Germany). Height was measured to the nearest 1 cm using Stature Meter (SJRGILAC) and later converted to meter (m). Waist circumference (WC) was measured midway between the lowest rib and the iliac crest and hip circumference (HC) at the level of the greater trochanters with legs close together, using a non-stretchable measuring tape by an average of three measurements nearest to 0.05 inch. The waist-hip ratio (WHR) equals WC divided by HC (Agarwal *et al*., 2012). Sphygmomanometer and stethoscope were used to measure the blood diastolic and systolic pressures of the subjects twice at sitting position during a ten minutes interval. An average of the readings was recorded in millimetres of mercury (mmHg). Pre-hypertension was defined as systolic reading of 120mmHg -139mmHg and diastolic (80-89 mmHg) while a systolic reading ≥140mmHg and diastolic ≥90 mmHg) was considered hypertensive (Bruce, 2023)

The BMI was computed using the standard formula:

BMI= weight (kg)/ height (m^2)

DNA extraction: Genomic DNA was isolated from the whole blood using DNA extraction kit. Determination of DNA purity and concentration was done spectrophotometrically at 260nm and 280nm respectively. Amplification of the *APOC3* 1100 C/T andC3238G promoter gene polymorphism was done by Polymerase Chain Reaction (PCR).

Primer for APOC3 1100 C/T rs4520
Forward 5′-AGA GGC CGA TCC ACC CCA CTC AGC C-3′
Reverse 5′-GGC GGT CTT GGT GGC GTG CTT CAG G-3′

Primer for APOC3 3238 C/Grs5128
Forward: 5′-CAT GGT TGC CTA CAG AGG AGT-3′
Reverse: 5′-TGA CCT TCC GCA CAA AGC TGT-3′

PCR- restriction fragment length polymorphism (PCR-RFLP) assay was employed to assess the *APOC3* gene polymorphisms as previously described (Waterworth *et al.*, 1999)

Estimation of plasma glucose was done by Oxidase-Peroxidase method, glycated heamoglobin (Hba1c) was estimated using Biosystems Hemoglobin A1C Reagent and lipid profile determined by analytical procedure.

Statistical analysis:

IBM SPSS version 25.0 software package and graph pad prism 5.0 were used to determine the means, standard deviation, correlations and one-way analysis of variance (ANOVA) among study groups. Allelic frequencies were estimated by gene-counting method. The sample-size dependent standard error of alleles was calculated in terms of 95% confidence interval (CI) of the estimates. Chi-square goodness-of-fit was used to verify the agreement of the observed genotype frequencies with those expected ones (Hardy-Weinberg equilibrium) in various study groups. Contingency table approach (Fisher's RxC test) was used to determine if there is significant differences in allele frequencies among all subjects. P<0.05 was considered as level of significance.

RESULTS

A larger proportion of all subjects (64.7%) were between 31-50 years with female preponderance (76.6%). From Table 1 the mean body mass index, systolic blood pressure, diastolic blood pressure and waist hip ratio were higher among obese diabetic subjects compared to the other groups (p<0.05). The highest mean values of cardiac risk ratio and atherogenic coefficient (p>0.05) was recorded in obese diabetics compared to other subjects (Table 2).

Pearson Chi square analysis results of genotype and allele frequencies of APOC3 C3238G and C1100T polymorphisms among the study subjects were presented in Table 3. The frequency of homologous CC genotype was highest among obese diabetics compared to GG and CG genotypes. Distribution of G allele (APOC3 C3238G) showed highest frequency among obese diabetics.

The genotypic and allelic frequencies of APO C3 C3238G polymorphism and risk of hypertension among all participants were presented in table 4. Highest frequency for pre-hypertension was seen in CC genotypes of all groups while the highest frequency for occurrence of hypertension was observed among obese diabetics expressing CC compared to CG ad GG genotypes . The G allele of APOC3 C3238G genotype was significantly associated with higher risk of hypertension among obese diabetic subjects when compared with other groups. There were no significant association recorded for APO C3 C1100T polymorphism and risk of hypertension among participants (Table not shown).

Table 1:
Anthropometric parameters among the study subjects (mean±SD)

Subject/ parameters	Obese diabetic (n=107)	Non obese diabetic (n=138)	Obese non-diabetic (n=100)	Non obese non-diabetic (n=100)	P
Age	45.69±1.17	40.94±0.97	41.96±1.24	43.14±1.10	0.015*
BMI (kg/m^2)	34.06±0.29	24.13±0.19	33.22±0.25	23.59±0.28	0.000*
SBP (mmHg)	142.48±2.69	125.82±1.69	133.58±2.27	128.61±2.46	0.000*
DBP(mmHg)	84.80±1.19	81.72±0.93	85.46±1.01	77.20±0.89	0.000*
WC(cm)	98.52±0.86	79.72±0.64	93.86±0.71	76.78±0.91	0.000*
HC (cm)	108.08±0.86	87.27±0.64	105.42±0.71	89.34±0.91	0.000*
WHR	0.91±0.00	0.91±0.00	0.89±0.00	0.86±0.00	0.000*

* Significant at the 0.05 level (2-tailed)

BW = Body Weight; BMI = Body mass index; SBP = Systolic blood pressure; DBP = Diastolic blood pressure; WC =Waist Circumference; HC = Height Circumference; WHR= Waist Hip Ratio

Table 2:
Biochemical parameters among the study subjects (mean±SD)

Groups/ parameters	Obese diabetic (n=107)	Non obese diabetic (n=138)	Obese non-diabetic (n=100)	Non obese non-diabetic (n=100)	P
TC (mmol/l)	5.36±0.09	4.94±0.07	4.99±0.10	4.32±0.08	0.566
TG (mmol/l)	1.62±0.05	1.61±0.03	1.13±0.06	0.82±0.06	0.913
HDL-C (mmol/L)	0.94±0.02	1.18±0.02	1.15±0.03	1.08±0.03	0.369
LDL-C (mmol/L)	3.69±0.08	3.03±0.06	3.32±0.10	2.87±0.08	0.711
LDL:HDL	4.24±0.15	2.72±0.09	3.09±0.13	2.91±0.12	0.715
AIP	0.24±0.02	0.14±0.01	0.04±0.02	0.19±0.03	0. 358
CRR	6.12±0.19	4.37±0.10	4.56±0.14	4.30±0.14	0.000*
Non HDL	4.42±0.08	3.76±0.07	3.83±0.10	3.24±0.08	0.373
Atherogenic Coefficient	5.12±0.19	3.37±0.10	3.56±0.14	3.30±0.14	0.035*
HbA1c mmol/l	9.51±0.15	7.33±0.17	6.70±0.22	5.68±0.21	0.000*
FBS	9.55±0.13	9.20±0.13	5.41±0.09	5.25±0.12	0.000*

* Significant at the 0.05 level (2-tailed)

TC = Total Cholesterol; TG = Triglycerol; HDL-C = High Density Lipoprotein Cholesterol; LDL-C= Low Density Lipoprotein Cholesterol; AIP = Atherogenic index of plasma; CRR = Cardiac risk ratio

Table 3:
Genotypic and allelic distribution of APOC3 C3238G and APOC3 C1100T polymorphisms in all subjects

Gene	Variant	NOD n=85	NOND n=76	OND n-60	OD n=107	χ^2
APO C3 C3238G	CC	58(68.2%)	65(85.5%)	20(33.3%)	74(69.1%)	25.515*
	CG	15(17.7%)	12(15.8%)	25(41.7%)	21(19.6%)	
	GG	12(14.1%)	9(11.8%)	15(25.0%)	12(20.0%)	
	G	21(7.7%)	11(4.0%)	20(7.3%)	33(12.0%)	23.032*
	C	67(24.5%)	57(20.8%)	25(9.1%)	95(34.7%)	2.282
APO C3 C1100T	CC	47(55.3%)	51(67.1%)	21(35.0%)	64(23.4%)	13.116*
	CT	23(27.1%)	14(18.4%)	22(36.7%)	28(10.2%)	
	TT	15(17.6%)	11(14.5%)	17(28.3%)	15(5.5%)	
	C	64(23.4%)	55(20.1%)	23(8.4%)	92(33.6%)	3.061
	T	12(4.4%)	6(2.2%)	7(2.6%)	15(5.5%)	3.455

**significant<0.05*

Table 4:
Genotype and allele frequencies of APO C3 C3238G polymorphism and risk of hypertension among all subjects

Subjects	Genotype/ Allele	Pre -hypertensive (n=68)	Hypertensive (n=107)	p-value	OR (95% CI)
NOD	CC	15(19.7%)	11(14.5%)	0.481	1.0 (Reference)
	CG	5(6.6%)	4(5.3%)	0.376	0.50(0.11-2.32)
	GG	1(1.3%)	3(3.9%)	1.000	1.00(0.16-6.25)
NOND	CC	15(24.6%)	14(23.0%)	0.666	1.0 (Reference)
	CG	3(4.9%)	0(0.0%)	0.368	0.39(0.05-3.04)
	GG	0(0.0%)	2(3.3%)	0.999	0.00(0.00-0.00)
OND	CC	4(13.3%)	2(6.7%)	0.457	1.0 (Reference)
	CG	3(10.0%)	9(30.0%)	0.828	0.89(0.31-2.56)
	GG	0(0.0%)	4(13.3%)	0.331	0.56(0.17-1.80)
OD	CC	13(12.1%)	45(42.1%)	0.089	1.0 (Reference)
	CG	3(2.8%)	7(6.5%)	0.482	1.55(0.46-5.28)
	GG	6(5.6%)	6(5.6%)	0.349	0.50(0.12-2.13)
NOD	G	6(7.9%)	7(9.2%)	0.226	0.50(0.16-1.54)
NOND	G	3(4.9%)	2(3.3%)	0.507	1.75(0.34-9.13)
OND	G	3(10.0%)	13(43.3%)	0.431	1.32(0.66-2.63)
OD	G	9(8.4%)	13(12.1%)	0.042*	2.39(1.03-5.53)
NOD	C	20(26.3%)	15(19.7%)	0.472	1.73(0.39-7.77)
NOND	C	18(29.5%)	14(23.0%)	0.283	3.07(0.40-23.87)
OND	C	7(23.3%)	11(36.7%)	0.625	1.29(0.46-3.62)
OD	C	16(15.0%)	52(48.6%)	0.757	0.83(0.25-2.75)

OR = Odds ratio; CI =95% Confidence Interval

Table 5:
Plasma lipid profile and APO C3 concentrations in different Genotypes of subjects with APO C3 C3238G polymorphism

Group/Genotype		**TC (mmol/l)**	**TG (mmol/l)**	**HDL-C (mmol/L)**	**LDL-C (mmol/L)**	**AIP**	**CRR**	**Non HDL**	**APO C3 (mg/dL)**
NOD (n=138)	CC (n=94)	5.06±0.10	1.61±0.04	1.21±0.03	3.11±0.09	0.13±0.02	4.39±0.17	3.84±0.09	9.35±0.25
	CG (n=24)	4.92±0.40	1.90±0.06	1.06±0.07	2.99±0.34	0.26±0.04	4.67±0.24	3.86±0.35	10.15±0.55
	GG (n=20)	4.63±0.17	1.55±0.06	1.32±0.06	2.60±0.22	0.07±0.03	3.58±0.23	3.31±0.21	11.63±0.99
NOND (n=100)	CC (n=72)	4.37±0.13	0.75±0.04	1.03±0.04	3.00±0.12	0.17±0.04	4.54±0.22	3.34±0.13	8.99±0.24
	CG (n=16)	4.06±0.33	0.36±0.07	1.22±0.07	2.68±0.37	0.59±0.11	3.48±0.44	2.84±0.39	7.37±0.39
	GG (n=12)	4.63±0.16	0.54±0.04	1.05±0.03	3.33±0.20	0.29±0.02	4.44±0.25	3.58±0.18	7.33±0.63
OND (n=100)	CC (n=33)	4.84±0.09	0.84±0.05	1.07±0.09	3.39±0.13	0.10±0.02	4.90±0.52	3.77±0.11	7.54±1.00
	CG (n=42)	5.02±0.21	0.92±0.07	1.05±0.07	3.55±0.20	0.06±0.03	5.14±0.42	3.97±0.22	9.28±0.99
	GG (n=25)	4.55±0.34	1.77±0.51	1.62±0.27	2.13±0.35	0.01±0.18	3.21±0.61	2.94±0.54	9.60±0.93
OD (n=107)	CC (n=64)	5.26±0.11	1.60±0.05	0.91±0.03	3.63±0.09	0.26±0.02	6.29±0.24	4.35±0.09	11.31±0.42
	CG (n=21)	5.54±0.23	1.73±0.15	1.03±0.03	3.73±0.21	0.21±0.03	5.47±0.27	4.52±0.22	10.97±0.69
	GG (n=22)	5.63±0.11	1.54±0.08	0.97±0.06	3.96±0.09	0.21±0.05	6.17±0.58	4.66±0.09	11.73±0.48
P		0.000	0.000	0.002	0.000	0.000	0.001	0.000	0.001

Table 6:
Plasma lipid profile and APO C3 concentrations in different genotypes of subjects with APO C3 C1100T polymorphism

Group/Genotype		TC (mmol/L)	TG (mmol/L)	HDL-C (mmol/L)	LDL-C (mmol/L)	LDL:HDL	AIP	CRR	Non HDL	APO 3 (mg/dl)
NOD (n=138)	CC	4.96±0.10	1.60±0.04	1.26±0.04	2.98±0.09	2.75±0.15	0.13±0.02	4.39±0.17	3.84±0.09	9.76±0.35
	CT	4.91±0.26	1.76±0.06	1.12±0.05	2.99±0.22	2.81±0.21	0.26±0.04	4.67±0.24	3.86±0.35	9.72±0.36
	TT	5.17±0.29	1.65±0.11	1.13±0.08	3.29±0.22	2.04±0.22	0.07±0.03	3.58±0.23	3.31±0.21	9.72±0.64
NOND (n=100)	CC	4.24±0.13	0.72±0.05	1.03±0.04	2.89±0.12	3.15±0.18	0.17±0.04	4.54±0.22	3.34±0.13	8.69±0.25
	CT	4.55±0.14	0.54±0.03	1.18±0.13	3.13±0.26	2.34±0.41	0.59±0.11	3.48±0.44	2.84±0.39	8.71±0.75
	TT	4.91±0.44	0.72±0.14	1.08±0.03	3.50±0.37	3.20±0.26	0.29±0.02	4.44±0.25	3.58±0.18	8.66±0.51
OND (n=100)	CC	4.47±0.14	1.09±0.20	1.36±0.15	2.62±0.25	3.53±0.50	0.10±0.02	4.90±0.52	3.77±0.11	7.92±0.78
	CT	5.23±0.22	1.11±0.19	1.09±0.08	3.63±0.21	3.73±0.41	0.06±0.03	5.14±0.42	3.97±0.22	9.05±1.09
	TT	4.95±0.11	0.83±0.10	0.94±0.09	3.63±0.09	1.60±0.42	0.01±0.18	3.21±0.61	2.94±0.54	9.57±1.54
OD (n=107)	CC	5.38±0.12	1.64±0.06	0.95±0.03	3.68±0.10	4.37±0.19	0.26±0.02	6.29±0.24	4.35±0.09	11.41±0.40
	CT	5.26±0.17	1.63±0.11	0.93±0.04	3.59±0.16	3.71±0.26	0.21±0.03	5.47±0.27	4.52±0.22	10.42±0.77
	TT	5.44±0.22	1.47±0.07	0.89±0.06	3.89±0.19	4.38±0.46	0.21±0.05	6.17±0.58	4.66±0.09	12.40±0.48
P		0.001	0.000	0.000	0.001	0.000	0.000	0.002	0.000	0.000

The levels of plasma LDL-C, LDL:HDL, Non HDL and APO C3 were significantly higher in the GG genotype compared to the CC homozygote and CG heterozygote among obese diabetic subjects exhibiting APO C3 C3238G SNP. Obese diabetic subjects with the CC genotype had higher AIP and CRR (p <0.05) values than CG and GG genotypes. These findings persisted in the overall sample, mean values of TG among homozygote GG showed a significant reduction among obese diabetic subjects when compared to homozygote CC and GG . Decreased TG, LDL:HDL, AIP, non HDL was seen among the Non obese diabetics with homozygote GG compared to homozygote CC and heterozygote CG (p<0.05) (Table 5).

Table 6 presents the association of APO C3 C1100T SNP and cardiovascular disease risk factors among the participants. Serum TG, HDL-C, AIP and CRR were increased among obese diabetic subjects with CC genotype compared to homozgous TT and heterozygote TC (P<0.05) while a significant increase in mean of TC, non HDL and APO CIII were recorded in homozygote TT than homozygote CC and heterozygote CT respectively.

DISCUSSION

Diabetic dyslipidemia is characterized by hypertriglyceridemia and accumulation of remnant particles, apoC3 may aggravate the hypertriglyceridemia by impairing the lipolysis of triglyceride-rich lipoproteins including very low density lipoproteins (VLDL) (Jo *et al*, 2018). In this study APOC3 level was increased among obese diabetic subjects supporting the assertion that apoC3 might contribute to an increased risk of dyslipidemia related coronary artery disease (CAD) (Wulff, 2018). .

A previous study reported that atherogenic indices are valuable predictors of CVD risk (Pereira *et al*., 2012). The traditional serum lipid profile was limited in predicting CVD risk for those at the lower and the higher end of the spectrum. Data from this study revealed a pro-atherogenic tendency of C allele of the apoC3 C1100T SNPs reflecting a propensity for cardiovascular disease risk. Plasma LDL-C, LDL: HDL, Non HDL and APO C3 concentrations were increased in obese diabetic subjects expressing the GG genotype of apoC3 C1100T SNP while CC genotype non- obese diabetics had highest AIP and CRR values respectively. A critical connection of obesity, diabetes mellitus and dyslipidemia might be linked to the development of insulin resistance in peripheral tissues resulting in an enhanced hepatic flux of fatty acids from dietary sources, intravascular lipolysis and from adipose tissue resistant to the antilipolytic effects of insulin (Klop *et al.*, 2002).

A lower value of body mass index observed among obese non diabetic as compared to obese diabetic subjects. This findings is in line with that of Jerant (2015) who reported increase in body mass index among overweight and obese diabetic subject in a study on Body mass index and health status in diabetic and non diabetic individual and also in agreement with another study confirming that the vast majority of patients with T2DM are overweight or obese, and that obese people are at the highest risk of developing T2DM (Hamer, 2013).

A significant association was observed between the G allele and hypertension as well as CC genotypes and pre-hypertension among obese diabetics expressing *APOC3* C3238 G SNP. Although the exact mechanism by which *APOC3* C3238 G contribute to an increased incidence of hypertension is still unclear, it was widely hypothesized that this could be as a result of its effect on altered lipid metabolism that is strongly associated with cardiovascular disease risk (Sarwar, 2007). A previous study also reported that individuals with pre-hypertension are at higher risk of developing hypercholesterolemia, obesity and diabetes than those with optimal blood pressure (Bruce, 2023).

In this study, the mean systolic blood pressure was significantly higher while the mean diastolic pressure was found to be lower in obese diabetic subject compared to obese non diabetics. This observation agrees with a similar finding associating diastolic and systolic dysfunction with obesity (Kearns, 2014) and at variance with another (Alla *et al*, 2014) that reported an increase in the mean diastolic blood pressure in obese diabetics compared to obese non diabetic subjects. Discrepancies in the report of previous and present observations on blood pressure measurements could be due to lifestyle of the subjects such as inadequate exercise or dietary habit.

In conclusion, findings of this study showed that *APOC3* C1100T and G variant alleles of *APOC3* C3238G gene were associated with dyslipidemia, hypertension and altered anthropometric parameters thus suggesting that *APOC3* C3238G and *APOC3* C1100T contribute to an increased risk of cardiovascular risk. Further studies are important to verify these results and to test the concept that apoC-III synthesis may be an attractive therapeutic target to reduce the residual risk, particularly in obese subjects with type 2 diabetes with abnormal triglyceride metabolism.

A limitation of this study is that potential selection bias might have occurred, because this is a hospital-based case control study and the subjects may not be representative of the general population

REFERENCES

Abubakari A., Lauder W., Agyemang C., Jones M., Kirk A. (2008): Prevalence and time trends in obesity among adult West African population: a meta analysis. Obesity reviews. 9(4):297-311.

Alla L., Dov G., Marina S. (2014): Normal weight diabetic patients versus obese diabetics: relation of overall and abdominal adiposity to vascular health. Cardiovascular Diabetology. vol 13, Article no 141.

American Diabetes Association. (2014): Diagnosis and classification of diabetes mellitus Diabetes Care. 37(Suppl. 1): S81-S90.

Boren J., Packard C.J., Taskinen M. (2020): The roles of APOCIII on metabolism of triglceride-rich lipoproteins in humans. Front Endocrinol (Lausanne). 11:474. Doi:10.3389/fendo.2020.00474.

Bruce D.F. (2018): Prehypertension: Are you at risk? Hypertension/ High blood pressure guide. March 2018. Reviewed by C. Dertsartassian. www.webmd.com

Cui F, Li K, Li Y, Zhang X, An C. (2014): apolipoproteinC3 genetic polymorphisms are associated with lipids and Coronary Artery Disease in Chinese population. Lipids Health Dis. 13:170.

Hamer M., Bostock S., Hackett R. (2013): Objectively assessed sedentary time and type 2 diabetes mellitus: a case-control study. Diabetologia. 56(12):2761-2.

Hiukka A., Stahlman M., Petterson C., Adiels M., Teneberg S. (2009): ApoCIII enriched LDL in Type 2 diabetes displays altered lipid composition, increased susceptibility for sphingomelinase. Diabetes . 2018-2026.

Iloh G.A.N., Amadi A., Nwankwo B.O., Ugwu V.C. (2011): Obesity in adult Nigerians: A study of its pattern and common primary co-morbidities in a rural Mission General Hospital in Imo State, South-eastern Nigeria. Nigeria Journal of Clinical Practice. 14(2):212-218.

Innocent I.C., Abali C., Collins J., Ohagwu K.A., Imoh M.E. (2013): Prevalence of overweight and obesity in adult Nigerian- a systematic review. Diabetes. 43-47.

Jerant A., Bertakis K.D., Franks P. (2015): Body mass index and health status in diabetic and non-diabetic individuals. Nutr Diabetes. 27;5(4):e152. Doi:10.1038/nutd.2015.2.

Jo G., Kwak S., Kim J.Y., Lim H., Shin M. (2018): Association between genetic variant of apolipoproteinC3 and incident hypertension stratified by obesity in Korea. Nutrients 10(11):1595.

Kearns K., Dee A., Perry I. (2014): Chronic disease burden associated with overweight and obesity in Ireland: the effects of a small BMI reduction at population level. BMC Public Health 14, 143. Doi: 10.1186/1471-2458-14-143

Klop B, Elte JWF, Cabezas MC. (2013): Dyslipidemia in obesity: mechanisms and potential targets. Nutrients. 5(4), 1218-1240. 10.3390/nu5041218.

Kohan A.B. (2015): Apolipoprotein C-III: a potent modulator of hypertriglyceridemia and cardiovascular disease. Curr Opin Endocrinol Diabetes Obes.;22(2):119–25.

Li YH, Liu L (2014). Apolipoprotein E synthesized by adipocyte and apolipoprotein E carried on lipoproteins modulate adipocyte triglyceride content. Lipids Health Dis.;13(1):136.

Mercado-Gonzales S.I., Carpio-Rodríguez A.N., Carrillo-Larco R.M., Bernabé-Ortiz A. (2019): Sleep Duration and Risk of Obesity by Sex: Nine-Year Follow-Up of the Young Lives Study in Peru. Child Obes. 15(4):237-243. [PubMed]

Pereira T. Kelishandi R. (2012): Dyslipidemia and cardiovascular risk: lipid ratios as risk factors for cardiovascular disease. Dyslipidemia – From Prevention to Treatment. Rijeka. Croatia: InTech Europe. pp. 279–302.

Raposo H.F., Paiva A.A., Kato L.S. (2015): Apolipoprotein CIII overexpression exacerbates diet-induced obesity due to adipose tissue higher exogenous lipid uptake and retention and lower lipolysis rates. Nutr Metab (Lond) 12, 61 https://doi.org/10.1186/s12986-015-0058-6

Sarwar N, Danesh J, Eiriksdottir G, Sigurdsson G, Wareham N, Bingham S, Boekholdt S.M., Khaw K.T., Gudnason V. (2007): Triglycerides and the risk of coronary heart disease: 10, 158 incident cases among 262, 525 participants in 29 Western prospective studies. Circulation. 115: 450-458. 10.1161/circulationaha.106.637793

Waterworth DM, Ribalta J, Nicaud V, Dallongeville J, Humphries SE, Talmud P: (1999): ApoCIII gene variants modulate postprandial response to both glucose and fat tolerance tests. Circulation. 99: 1872-1877. 10.1161/01.CIR.99.14.1872

World Health Organization. (2012): Obesity: preventing and managing the global epidemic: report of a WHO consultation. World Health Organization; Geneva p. 253.

World Health Organization (2016). Obesity and overweight. Geneva: World Health Organization,.

Wulff A.B., Nordestgaard B.G., Tybjaerg-Hansen A. (2018): APOC3 Loss- of- function mutations, remnant cholesterol, low-density lipoprotein cholesterol and cardiovascular risk: Mediation and Meta-analyses of 137895 individuals. Arterioscler Thromb Vasc Biol. 38:660-668. Doi:10.1161/atvbaha.117.310473.

Xavier P. (2009): The Medical Risks of Obesity. Journal Postgrad Med. 121(6): 21–33.doi: 10.3810/pgm.2009.11.2074.