Emerging genetic profile of type 2 diabetes mellitus patients and controls in south western Nigeria: Catalyst for sustainable development

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Abstract

***Backgroun*d:** In sub-Saharan Africa, Type 2 diabetes care is greatly hampered by huge financial burden causing poor accessibility to healthcare. This study determined the genetic and environmental factors with potentials of attaining Goals 3 and 17 of the Sustainable Development Goals (SDGs) in Nigeria.
Methodology: This study was a case-control study. A multistage sampling technique was employed in the selection of 1500 patients with T2DM and 1500 controls in South Western Nigeria. Biophysical measurements and Glycaemic biomarkers were assessed for all respondents. Odds Ratio (OR) was determined with a level of significance was set at P<0.05
Results: The prevalence of Type 2 DM was 5%. However rural communities had older subjects with T2DM as compared with urban communities P<0.01. Glycaemic biomarkers and biophysical profiles were age and sex-related p<0.05 in both rural and urban communities. Transcription Factor 7 like 2 (TCF7L2) was found to be genetic marker of T2DM.
Conclusion: Transcription Factor 7 like 2 gene is a genetic marker of T2DM in Nigeria, which forms a framework for achieving goals 3 and 17 of the SDGs

Profil génétique émergent des patients et contrôles du diabète de type 2 dans le sud-ouest du Nigéria : catalyseur du développement durable

Résumé
Contexte de l'étude : En Afrique subsaharienne, les soins du diabète de type 2 sont grandement entravés par un énorme fardeau financier entraînant une mauvaise accessibilité aux soins de santé. Cette étude a déterminé les facteurs génétiques et environnementaux susceptibles d'atteindre les objectifs 3 et 17 des objectifs de développement durable (ODD) au Nigéria.
Méthode de l'étude: Cette étude était une étude cas-témoins. Une technique d'échantillonnage à plusieurs étapes a été utilisée pour la sélection de 1 500 patients atteints de DT2 et de 1 500 témoins dans le sud-ouest du Nigéria. Les mesures biophysiques et les biomarqueurs glycémiques ont été évalués pour tous les répondants. Le rapport de cotes (OR) a été déterminé avec un niveau de signification fixé à P <0,05.
Résultat de l'étude : La prévalence du diabète de type 2 était de 5 %. Cependant, les communautés rurales comptaient des sujets plus âgés atteints de DT2 par rapport aux communautés urbaines P <0,01. Les biomarqueurs glycémiques et les profils biophysiques étaient liés à l'âge et au sexe, p <0,05 dans les communautés rurales et urbaines. Le facteur de transcription 7 comme 2 (TCF7L2) s'est avéré être un marqueur génétique du DT2.
Conclusion : Le gène du facteur de transcription 7, comme le gène 2, est un marqueur génétique du DT2 au Nigéria, qui constitue un cadre pour atteindre les objectifs 3 et 17 des ODD.

INTRODUCTION

Type 2 Diabetes (T2DM) is a public health problem with genetic, dietary, and environmental interaction with targets to improve population health as seen with the Sustainable Development Goals (SDGs) (1). It is reported by the International Diabetes Federation (IDF) that there were 382 million people living with diabetes worldwide in 2013, and this figure is anticipated to rise to 592 million by 2035(2). Over the last three decades, the incidence of T2D and related complications has rapidly increased worldwide (3). T2D is a complex metabolic disorder that is caused by multiple factors (4). Classic genetic analyses performed in family and twin studies have clearly shown that up to 70% of the variance in T2D susceptibility in the population is explained by genetic factors (5). Individuals with T2D-affected siblings have a two to three-fold increased risk of developing T2D compared with the general population (6). The majority of diabetics reside in low- and middle-income nations, where rapid changes in lifestyle have increased the diabetes prevalence, cardiovascular diseases, and cancer, and these countries are expected to had the highest rate of diabetes occurrence in the next 20 years. About 615 million people have been estimated to be affected by year 2045 of which the sub-Sahara will account for 15.5 million people by then. The prevalence of the disease in Nigeria was 4.3% in 2016, about 5.5% in 2018 and projected to be 6.3% in 2020 (4).

Definition of risk factors for Diabetes Mellitus (5)(6)(7):

In Hypertension measures an average of three measurements was used at a cutoff of ≥140/90 mmHg, a history of hypertension, or the use of antihypertensive drugs was considered to be signs of hypertension. A self-reported history of hypertension, antihypertensive drug usage, or an average blood pressure reading of 140/90 mmHg or higher was used to define hypertension in controls (7). According to the National Cholesterol Education Program (NCEP) 2021 guidelines or use of a statin before the commencement of a stroke, dyslipidemia can be referred to as TC 5.2mmol/L, HDL-C 1.03mmol/l for men and 1.30 mmol/l for women, TG 1.7mmol/l, or LDL-C 3.4mmol/l. The LDL/HDL ratio was dichotomized using the lowest two tertiles (1.97 and 1.98-2.95) and the highest tertile (2.96) as normal versus high LDL/HDL ratio, respectively, based on the distribution of the LDL/HDL ratio in the current investigation (8). Cardiomyopathy, heart failure, ischemic heart disease, and rheumatic heart disease were used to characterize cardiac disease based on past or present diagnoses (8).

Obesity

We measured body mass index (BMI) and waist-to-hip ratio (WHR). Men and women were given cutoffs for waist circumference of 94 cm and 80 cm, respectively. Men and women were given cutoffs for WHR of 0.90 and 0.85, respectively. If a person frequently engaged in moderate activity (such as walking, cycling, or gardening) or intense exercise (such as jogging, football, or vigorous swimming) for four hours or more each week, they were considered to be physically active. Dietary history included consuming meat, fish, green leafy vegetables, salt on the table, nuts, sweets, and other locally common food items on a frequent basis. Regular consumption was outlined as consumption on a daily, weekly, or at least monthly basis as opposed to none in a month (8).

Alcohol consumption (or drinking) was divided into two categories: low drinkers (1-2 drinks per day for females and 1-3 drinks per day for males) and high drinkers (>2 drinks per day for females and >3 drinks per day for males), Current users of alcohol (users of any form of alcoholic drinks) were classified as either current users or never/former drinkers (8). A current smoker is someone who has smoked tobacco at any point in the previous 12 months, and never or a former smoker is someone who has never smoked (8).

Psychosocial stress included indicators of stress at home or at work (such as irritation, anxiety, or trouble sleeping) as well as life events that occurred in the two weeks before the study (8).

The definition of a family history of cardiovascular risk/diseases was based on the participant's self-reported family history of any hypertension, diabetes, dyslipidemia, stroke, cardiac disease, or obesity (7).

Since several studies have revealed that 75% of diabetics also have hypertension, co-morbidities are known to exist in some patients. In this study, environmental and genetic factors associated with type 2 diabetes in South Western Nigeria are investigated, as well as factors associated with diabetes complications.

METHODOLOGY

Study Population

1500 participants attending the Endocrinology Clinics of LAUTECH Teaching Hospitals (both in Osogbo and Ogbomoso), Osun

State Hospital Management Board, Asubiaro, Osogbo, Osun State and Bowen University Teaching Hospital, Ogbomoso, Oyo State southwestern Nigeria and diagnosed with T2DM were recruited in this study. Diagnosis by the attending physician was based on the International Diabetes Association IDF Criteria (7,8) These include: fasting plasma glucose level > 126mg/dL or 2 hours postprandial glucose level > 200mg/dL during a 75g oral glucose tolerance test HbA1c .> 6.5% and self-reported history of diabetes.

1500 apparently healthy age-matched recruited from communities in Osun and Oyo States participated as controls. These underwent health examinations and were confirmed not to have DM, cardiovascular disease, pregnancy, or on any lipid-lowering regimen.

Study Design

This study was a case-control study carried out in Southwestern Nigeria from 2015-to 2018

Sample size determination

The sample size for Genetic studies was determined using QUANTO version 1.2.4 software (7,8). This was validated with the genetic calculator. A sample size of 3000 people was sufficient to calculate the prevalence of diabetes in the population with a 95% confidence interval (CI) of less than 1%. Based on 1500 cases and 1500 controls, logistic regression studies with diabetes as an outcome had more than 80% power to identify odds ratios (ORs) as low as 1.2 for exposure prevalences equal to 30%. The same power can be used to identify ORs below 1.2 for exposure prevalences higher than 30%. Additionally, the study will have more than 80% power to identify ORs of at least 1.5 for exposure prevalences as low as 5%. With this sample size, we have more than 80% power, employing a genome-wide statistical threshold, to investigate genetic variations that account for 0.5% of the variation in a relevant characteristic.

Sampling Technique

A multistage sampling technique was employed in the selection of 1500 patients with T2DM and 1500 controls in Southwestern Nigeria

Study Instruments

Patients with Type 2 DM and control subjects were interviewed at the time of recruitment in order to obtain their demographic information with the aid of a questionnaire. Both groups underwent health examinations and were confirmed to be diabetic or not

Pretesting of Research Instrument

Research instruments were all tested in State Hospitals Akure and Ondo and UNIMED Teaching Hospital Ondo State

Data Collection and Management

Blood Collection: Overnight fasting blood samples (5ml) was collected from all subjects via venipuncture of an antecubital vein. 3ml was dispensed into Na2-EDTA containing test tubes (final concentration 1mg/ml) and 2ml into fluoride oxalate bottles for the estimation of fasting plasma glucose. Samples were centrifuged at 1000rpm for 15min using Uniscope Laboratory Centrifuge (Model 5m112 Surgifriend Medics, England) at room temperature to separate whole blood from plasma. Plasma harvested from EDTA tubes was used for total cholesterol, triglyceride, and HDL-Cholesterol estimations

Anthropometric indices and plasma lipid profile: Anthropometric indices measurement included weight in light clothing with shoes off using analogue bathroom scale, and height using a stadiometer. BMI was computed as weight (kg)/height (m^2). Plasma total cholesterol, triglycerides, high-density lipoprotein were quantified using enzymatic kits (Boehringer Mannheim, Mannheim, Germany) and low-density lipoprotein estimated as previously described. DNA extraction and PCR procedure DNA was isolated using Isolate II Genomic DNA kit, BIOLINE according to the manufacturer's instructions (11).

The sequencing was conducted at the Molecular laboratory at the Ladoke Akintola University of Technology. The design of primer for SNP rs7903146 TCF7L2 gene identification was done by primary design software. SNP was identified by the reverse and forward primers. Each primer ware tested with Genious and Primer Blast software from NCBI to identify the suitability of primer. The mixed composition of PCR reaction includes DNA template, MgCl2, buffers, and primer to determine the success of the PCR reaction. The isolated DNA was amplified using the Mix PCR PureTaq Ready-To-Go PCR Beads (RTG) from GE Healthcare (11).

Analysis of sequencing and bioinformatics results from TCF7L2 gene variants in Southwestern Nigeria was carried out qualitatively. The qualitative phase of analysis

included: analysis of kontig to determine the good or bad quality of sequences of DNA bases resulting from sequencing. Kontig analysis was done using Genious software. Blast analysis was used to determine the validity of the results of sequencing of the research object species. Blast analysis was done using the Blast program at NCBI. Alignment was used to determine single nucleotide polymorphism between DNA base sequences as sequenced with SNP rs7903146 TCF7L2. Alignment was done using the software. Genotyping of the G and/or A alleles at position - 1082 in IL-10 promoter region was performed by amplification refractory mutation system [ARMS] PCR as previously described [20]. Allele A was subjected to amplification using the Forward Sense Primer FSP-A (5' -AAC ACT ACT AAG GCT TCT TTG GGT A-3'). Similarly, allele G was amplified employing the primer FSP-G (5'-AAC ACT ACT AAG GCT TCT TTG GGT G -3'). In order to ensure the integrity of the experimental setup, internal control primers [5' TGC CAA GTG GAG CAC CCA A 3' and 5' TGC CAA GTG GAG CAC CCA A 3'] were utilized for amplifying a 700-bp fragment in each reaction (8). The amplified PCR products (161bp) were separated by electrophoresis stained with ethidium bromide on a 1.5% agarose gel and visualized under ultraviolet light. For verification of molecular analysis results, some of the samples were tested twice (11).

Measurement of outcome variables. Independent variables were the existence of the polymorphism rs7903146 TCF7L2 and socio-demographic variables, while the dependent variable is the prevalence of T2DM in cases and non-diabetic patients.

Statistical analyses

Statistical analyses were performed using SAS (version 9.4) and R statistical program (version 3.4.2). Frequencies were presented as percentages, continuous variables as Mean and standard deviation. ANOVA was employed to compare groups, $\chi 2$ test to examine differences in age and other variables between the subjects. The frequencies of alleles and genotypes of the whole group or subgroups of patients were compared using binary logistic regression. Odds ratio and 95% CI were employed to measure the strength of association between Genetic variants, SNP rs7903146 TCF7L2, IL-10 polymorphisms and the T2DM risk under the comparisons of heterozygote and homozygote. The level of significant for combined OR was set at $p<0.05$

Ethical Considerations

The Study protocol was approved by the Ethical Committees of both Ladoke Akintola University (LAUTECH) Teaching Hospital, Ogbomoso. (with Reference n Number: LTH/OGB/EC/2015/083), Oyo State and LAUTECH College of Health Sciences, Osogbo, Osun State(with Reference Number LAU/CHS/DEAN/ETHICAL/.052). Informed consent was sought for and obtained from all participants.

Limitation of the study

Although the recruitment of incident/prevalent cases could introduce potential bias when assessing the association between behavioral, environmental, or biological determinants of T2D and its complications, it is clear that large scale studies can provide important insights into the impact of relevant risk factors of T2D.

RESULTS

Among all 3000 subjects recruited, 1890 (63%) resided in urban, 690 (23%) in semi-urban, and 420 (14%) in rural settings. Comparing cases with controls, 1143 (76.2%) versus 336 (22.4%) had hypertension,1239 (82.6%) versus 849 (56.6%) had dyslipidaemia; 330 (22.0%) versus number (22.6%) had obesity; 783 (52.2%) versus 330 (22.2%) had positive family history and 45 (3%) versus 15 (1%) were current cigarette smokers ($p<0{\cdot}0001$ for all comparisons). Waist-to-hip ratio ($p<0{\cdot}0001$), but not BMI ($p=0{\cdot}64$), was significantly higher among patients with T2DM than controls (table 1). Furthermore, patients with T2DM were more likely to consume sugar ($p<0{\cdot}0001$), consume meat ($p<0{\cdot}0001$), whole grains ($p=0{\cdot}01$) and add salt at the table ($p<0{\cdot}0001$), on a regular basis, but less likely to consume green leafy vegetables regularly ($p<0{\cdot}0001$) compared with controls (table 1).
Hypertension, dyslipidaemia, stress, and low consumption of green leafy vegetables were associated with T2DM regardless of age cutoff. Positive family history was significantly more associated with T2DM in people younger than 40 years, whereas consumption of sugar, regular meat consumption, current cigarette smoking, and addition of table salt, were significantly associated with T2DM patients in those 40 years and older (table 1). T2DM patients had the highest frequency of IL 10 -1082A/C genotype (58.3%) while -1082AC frequency was highest (63.1%) in non-diabetics. Non- significant associations between IL 10 -1082 gene polymorphism and T2DM risk (for AA genotype:

p = 0.95; for AA genotype, p = 0.38) were recorded. Fasting plasma glucose, 2hours post-prandial, total cholesterol and triglyceride were all significantly elevated in IL 10 -1082C/C than AC and AA genotypes in T2DM subjects ($p<0.001$). Expression of A allele was higher in controls than T2DM patients. Table 2 and 3. A possible association between the IL-10 1082AC genotype and risk of diabetes mellitus may be seen Nigerian population.

Numerous correlations between T2D and the gene transcription factor 7-like 2 (TCF7L2), specifically the intronic SNP rs7903146 in numerous ethnic groups, have been documented across different population. Genetic associations between Transcription Factor 7 Like 2 rs7903146 **candidate** genes for T2D include ZRANB3 is an African –specific type 2 diabetes loci although In people of African descent, several potential genes for T2D and related features have been studied. (**Table 4)**

DISCUSSION

Every year, there is increasing in the incidence of Type 2 diabetes (T2D) in Africa including Nigeria.T2DM is now a public health and developmental issue affecting billions of the world's populations, especially in Sub Saharan Africa and Low- and Middle-income countries (LMICs.) The SDGs Goals 3, 5, 17 has indicators targeted at slowing the pace of the global Health problem. The rising incidence of Type 2 Diabetes around the world is largely due to the obesity pandemic.However, not everyone who is fat develops diabetes, a robust familial background significantly contributes to the susceptibility of an individual towards developing diabetes (14, 15,16).

Key risk factors such as hypertension, prediabetes, dyslipidaemia, stress, and little or poor consumption of green leafy vegetable consumption were associated with T2DM. Obesity, physical inactivity, regular meat intake, salt intake, and cardiac diseases were associated with T2DM (16, 17) Emerging determinants of T2DM include an overlap with. Hypertension, dyslipidaemia, and low consumption of green leafy vegetables were independently associated withT2DM in South Western Nigeria. However, obesity, stress, regular meat consumption, and regular sugar consumption were significantly associated with T2DM occurrence among Nigerians, whereas cardiac diseases, physical inactivity, current cigarette smoking, and salt consumption have added their effect on the burden of the public problem (16,17).

Data from this study revealed that IL-10 -1082AA genotype has the highest frequency but was not significantly associated with increased risk of T2DM compared to AC or CC genotypes. A possible association between the IL-10 1082AC genotype and risk of diabetes mellitus was suggested in Nigerian (16, 17).

Genetic variants of T2DM include genotype markers such that a higher percentage of AA homozygotes was generally low in the studied population, nevertheless the expression of A allele was higher in controls than DM patients., AA genotype had significantly higher values of FPG, 2HPP, TC and LDL-C respectively than the CC homozygotes Similarly, plasma 2HPP value increased in AC heterozygote compared to AA genotype(16, 17) Numerous correlations with T2D were found for the gene transcription factor 7-like 2 (TCF7L2), specifically the intronic SNP rs7903146 in a variety of ethnic groupings and population types. (16, 17, 18,19)

ZRANB3 is an African –specific type 2 diabetes loci although in populations of African heritage, multiple potential genes for T2D and related characteristics have been studied (18).
Recent studies on Mobile phone ownership and willingness to receive mHealth services among patients with diabetes mellitus in South-West, Nigeria (23) should that mobile phone ownership can be used to improve adherence to medications for diabetes will lead to better outcomes of treatment and prevent complications

Pharmacist-led intervention in treatment non-adherence and associated direct costs of management among ambulatory patients with type 2 diabetes in southwestern Nigeria (24) also suggested that to improve the treatment of T2DM financial costs must be cut down to assist the patients and Public in Nigeria. Our understanding of the genetic basis of T2DM has been increased by the identification of multiple genomic loci that were not previously connected to the pathobiology of these disorders.

Nigerians and other African groups, however, have not been sufficiently represented in these international genomic initiatives. To enhance clinical and public health in Africa.. Awareness creation of diabetes mellitus amongst undergraduates in a Nigerian University (25) was carried out and this can be replicated amongst Artisans, Military, Paramilitary institutions as well as market outreaches as only a third of Nigerian population are aware of their Diabetes Status

Public Health Implications of the study

T2DM, which is brought on by the interplay of environmental, behavioral, and genetic factors. The rising incidence of Type 2 DM around the world is partly due to the obesity epidemic. But not everyone who is obese gets diabetes, and having a good family history is a significant risk factor for diabetes (19). In Nigeria and Sub-Saharan Africa, Policies have to be put in place to stem the tide of T2DM epidemic and obesity. Researches in Genomics in Nigeria and Africa have strategically helped determine environmental determinants of T2DM(20),Genetic determinants of T2DM; the intronic SNP rs7903146ZRANB3(18,19,22) using strong partnerships for sustainable development. African Governments and researchers on the continent can support join initiates to improve population health. Moving research from bench side to the clinics and then the communities take several years, sometimes 22 years reference. Understanding the double burden of diseases can help put short and middle - term plans to reduce the burden of T2DM on the continent. The Nigeria Medical Community can build statistical and machine learning models that integrate genetic and genomic data to prioritize variants, genes, and cell types, and to decode the causal functional architecture underlying heritable complex diseases — including Type 2 Diabetes, Hypertension, Stroke, others NCDs

CONCLUSION

Increasing age, places of residence, Positive family history Genetic marker of T2DM such as Transcription Factor 7 like 2 and ZRANB3 genes is a genetic marker of T2DM in Nigeria can be evaluated in larger studies with larger sample size To improve public health in Nigeria and globally knowledge of major risk factors such as hypertension, dyslipidaemia, stress, and unhealthy diet including obesity, physical inactivity, regular meat intake, salt intake, and cardiac diseases with positive family history were associated with T2DM Interventions can be prioritized to include adopting health lifestyles, prevention onset of complications of T2DM and improve drug adherence for Diabetes on medications

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Conflict of interest: We declare that there is no potential conflict of interest.

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Table 1: Emerging Characteristics of respondent with Diabetes as Health outcome

Characteristics		Diabetic status: Non Diabetic controls (n=1500)	Diabetic status: Diabetes Cases (n=1500)	*P*-value
State				
	Osun	486 (32.4)	458 (30.5)	
	Oyo	1014 (67.6)	1042 (69.5)	
Sex				
	Female	783 (52.2)	783 (52.2)	
	Male	717 (47.8)	717 (47.8)	
Age (years), *mean* ± *SD*	<40years	756 (50.4)	747(49.8)	0.783
	=40years	744 (49.6)	753 (50.2)	
Education				
	None	354 (23.6)	300 (20.0)	<0.001
	Primary school	375 (25.0)	303 (20.2)	
	Secondary school and above	771 (51.4)	897 (59.8)	
Monthly Income				
	< 100USD	932(62.8)	711 (47.4)	<0.001
	= 100USD	558(37.2)	789 (52.6)	
Family History				
	Alcohol Use (Yes)	345 (23.0)	374 (24.9)	0.079
	Family history of CVD	360 (24.0)	465 (36.1)	<0.001
	Family history of T2DM	330 (22.2)	783 (52.2)	<0.001
	Family history of HTN	486 (32.4)	576 (38.4)	0.007
	Family history of Dsylipidemia	324 (21.6)	429 (28.6)	0.076
	Physical inactivity	39 (2.6)	66 (4.4)	<0.001
Adding Salt				
	Never	1371 (91.4)	1401 (93.4)	<0.001
	Very Often	108 (8.6)	99 (6.6)	
Green leafy vegetable				
	None	432 (28.8)	411 (27.4)	<0.001
	Some	1068 (71.2)	1089 (72.6)	
Sugar Consumption				
	None	1053 (70.4)	1059 (70.6)	<0.001
	Some	447 (29.6)	441 (29.4)	
Meat Consumption				
	None	363 (24.2)	375 (25.0)	<0.001
	Some	1137 (75.8)	1125 (75.0)	
Anthropometric measurements	WHR, *mean* ± *SD*	0.91±0.08	0.94±0.08	<0.001
	WHR = 0.90 (males) & 0.85 (females)	1056 (70.4)	1263 (84.2)	<0.001
	BMI (kg/m^2), *mean* ± *SD*	26.31±5.74	26.83±5.34	<0.001
	BMI = 30kg/m^2	339 (22.6)	330 (22.0)	0.001
Blood pressure & Lipid profiles				
	SBP (mmHg), *mean* ± *SD*	137.37±24.44	158.80±31.06	<0.001
	DBP (mmHg), *mean* ± *SD*	83.03±14.40	95.45±18.32	<0.001
	Hypertension (Yes)	336 (22.4)	1143 (76.2)	<0.001
	Dyslipidemia, (Yes)	849 (56.6)	1239 (82.6)	<0.001
Fasting glucose				
	Normal ; =126	1464 (97.6)	1044 (69.6)	**<0.001**
	High; >126	36(2.4)	454 (30.4)	**<0.001**
	Mean ± SD	88.2±15.3	124.0±51.2	**<0.001**

Table 2: Genotypes in T2DM patients (mean±SD) in South West Nigeria

Genotypes in T2DM subjects (mean±SD) in South West Nigeria				
Parameters/ Genotypes	CC (n=150)	AC (n=450)	AA (n=900)	P-value
Age (years)	51.67±3.71	47.42±1.77	50.32±1.22	0.438
FPG(mg/dl)	125.0±7.51	132.3±2.42	150.79±5.76	0.001*
2HPP(mg/ dl)	235.5±5.29	229.7±3.51	258.3±8.53	0.001*
HbA1c(%)	6.6±0.11	6.7±0.12	6.8±0.14	0.001*
BMI (kg/m2)	21.07±0.91	25.98±0.85	25.11±0.61	0.007*
TC (mg/dl)	138.3±7.54	172.8±5.03	191.3±7.78	0.001*
TG (mg/dl)	117.6±18.26	108.8±7.84	131.46±13.17	0.193
HDL-C (mg/dl)	34.33±2.33	40.13±0.83	42.68±1.11	0.001*
LDL-C (mg/dl)	80.67±1.86	110.8±4.13	123.46±6.25	0.001*
DBP (mmHg	88.0±2.52	112.8±5.58	103.79±4.69	0.338
SBP (mmHg)	136.33±8.41	116.4±5.38	119.68±4.54	0.319

Table 3: Genotypes in Community controls subjects (mean±SD) in South West Nigeria

Genotypes in community controls from the communities (mean±SD) In South West Nigeria				
Parameters/ Genotypes	**CC (n=150)**	**AC (n=750)**	**AA (n=600)**	**P-val**
Age (years)	54.25±2.46	45.07±1.48	49.25±2.25	0.038*
FPG(mg/dl)	83.0±2.48	84.55±2.68	86.50±3.68	0.835
2HPP(mg/ dl)	90.25±3.04	90.10±2.44	100.50±3.96	0.001*
HbA1c(%)	5.9±0.12	6.0±0.16	6.2±0.19	0.001*
BMI (kg/m2)	22.78±1.49	22.09±0.48	22.37±0.73	0.859
TC (mg/dl)	166.0±18.01	147.76±6.40	150.83±8.16	0.000*
TG (mg/dl)	96.75±4.09	89.14±3.61	95.0±4.27	0.193
HDL-C (mg/dl)	38.25±2.25	37.45±1.43	42.75±1.74	0.058
LDL-C (mg/dl)	108.25±15.98	92.41±5.09	88.83±6.7	0.001*
DBP (mmHg	84.0±2.04	82.17±0.55	87.67±3.75	0.225
SBP (mmHg)	117.50±2.02	117.59±0.71	114.58±4.16	0.677

Table 4: Genetic variants in patients with T2DM in South west Nigeria

Chromosome	BP	SNPs	Gene	P-val
10	114758349	rs7903146	TCF7L2	0.001*
10	114754071	rs34872471	TCF7L2	0.06
10	114754784	rs35198068	TCF7L2	0.06
12	66289518	rs138066904	HMGA2	0.08
2	136064024	2:136064024	ZRANB3	0.001*
2	136019729	rs1465146591	ZRANB3	0.001*
10	114754088	rs7901695	TCF7L2	0.001*
10	114756041	rs4506565	TCF7L2	0.001*
10	114747860	rs386418874`	TCF7L2	0.001*
10	114754601	rs59326375	TCF7L2	0.001*
10	136226838	2:136226838	Leptin receptor gene	0.01
10	44062728	rs116050569	Leptin	0.01
10	114755496	rs116050569	TNF	0.08
10	44071333	rs531496714	FTO	0.01

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