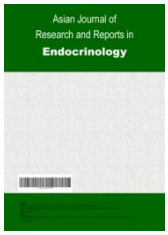

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Obesity and Type 2 Diabetes Markers and Their Association with Fat-mass and Obesity-associated Gene (FTO) Variants in Some Selected Ethnic Populations in Niger Delta, Nigeria

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Authors' contributions

This work was carried out in collaboration among all authors. Authors NOE and HB designed the study. Authors NOE and EON wrote the literature review, while authors HB and IE carried out the statistical analysis and author NOE wrote the first draft of the manuscript and carried out the laboratory analysis. All authors read and approved the final manuscript.

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ABSTRACT

Aim: To assess the levels of some glycemic parameters and their association with fat-mass and obesity-associated gene (FTO) variants in some selected ethnic populations in Niger Delta, Nigeria.
Study Design: Case-controlled observational study.
Place and Duration of Study: Federal Medical Centre, Asaba, Delta State and Safety Molecular Pathology Laboratory, Enugu, Nigeria, between March 2020 and February 2022.
Methodology: The association between sixteen (16) Single Nucleotide Polymorphisms in the FTO gene and some biomarkers of obesity and type 2 diabetes (fasting blood glucose, HbA1c, adiponectin, insulin, C-peptide, Homeostatic model assessment (HOMA) of β-cell function and insulin resistance (HOMA-IR) and body mass index) was studied in ninety-eight (98) type 2 diabetes (T2D) subjects (78 cases and 20 controls) from four different tribes in the Niger Delta region, Nigeria. Multistage sampling method was employed in the subject selection. The subjects were first separated into two groups – new cases (less than a year of diagnosis as Diabetic) and old cases (one year & above). Equal number of samples was then randomly collected from each of

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the cluster groups. 10mls of blood was collected into EDTA and plain bottles for the assay of the above-named markers, and were assayed using spectrophotometric and ELISA methods. The data were analyzed using GraphPad Prism, version 8.0.2 and p values less than *.05* were considered statistically significant.

Results: Significant association between rs9939609 variant genotype (A) allele of FTO gene with BMI (*p<.01*), HOMA-IR (*p<.01*), and Insulin (*p<.01*) were observed in obese subjects, but only BMI (*p<.01*) with obese and T2D subjects combined. The results also found a moderate to strong correlation between variants rs201041270 (GA/AA) with adiponectin (*p<.05*) and with Insulin (*p<.05*), rs531215275 (CA/AA), mild with C-peptide *p<.05*), rs1410999299 (AG/GG) with C-peptide (*p<.05*), rs145884431 (GA/GG) with HbA1c (*p<.05*), rs146138389 (CT/CC) with insulin (*p<.05*) and rs886052102 (AG/AA) with FBS (*p<.05*) and strongly with HbA1c (*p<.01*).

Conclusion: Knowledge of the dominant SNPs that are consistent with some specific biomarkers in some ethnic groups, may provide platform for prevention of its expression through informed wise choice of lifestyle change and proper dieting.

Keywords: Diabetes; obesity; FTO gene variants; Niger Delta; Nigeria.

1. INTRODUCTION

Obesity and type 2 diabetes (T2D) are complex diseases that affect people all over the world. As a result, identifying the risk factors for obesity and T2D is critical, as its incidence continues to rise in many countries [1]. Obesity and cardiovascular risk factors were shown to be more prevalent in Nigerian studies [2]. As a result, Nigeria is not immune to the epidemic. Obesity is a metabolic illness induced by a high-calorie diet and/or malnutrition, which leads to an increase in abnormal body fat accumulation and increases the risk of a variety of chronic diseases, including T2D, cardiovascular disease, and cancer [3]. Obesity is a complex disorder influenced by both environmental and hereditary factors, and it serves as a catalyst for a number of other diseases [4]. Obesity is a complicated condition with a variety of heritable and behavioural characteristics, and it is a leading cause of type 2 diabetes (T2D). Obesity and T2D are currently epidemics in China and around the world, posing a huge public health threat. Overweight and obesity are responsible for approximately 58 percent of T2D worldwide [5]. The most common type of diabetes is type 2 diabetes mellitus (T2DM), which accounts for more than 90% of all diabetes occurrences globally [6]. Polymorphisms in the fat-mass and obesity-associated gene (FTO) have been linked to obesity in a number of studies [7,8], and obesity is a significant risk factor for type 2 diabetes (T2D) [9]. Environmental/lifestyle factors such as physical activity, time spent sitting, and calorie intake, according to Oyeyemi et al. [10], may be a significant modulator and/or mediator in the link between FTO rs9939609 and BMI in Nigeria. While numerous studies have found that the relationship between FTO mutations and the risk of T2D remains significant after adjusting for BMI, a surrogate measure of obesity, others have been unable to substantiate this conclusion [5]. The BMI assessed at the time of enrolment, i.e., current BMI, which was collected a considerable time after the diagnosis of T2D, was employed for the analyses in numerous studies exploring this issue [9]. Although we have made significant progress in our understanding of the genetics of T2D, there is still much to learn about the disease's aetiology. More than 40 loci associated with T2D or glycemic traits have been reported and reproduced, only a minor part of the genetic component of the disease has been explained, and the causative variants and affected genes are unknown for many of the loci [11]. Several studies have demonstrated that polymorphisms within the fat-mass and obesity associated gene (FTO) are associated with type 2 diabetes (T2D). However, it is unclear if the FTO locus' effects on T2D susceptibility are independent of fat-mass increases [12]. In white European adults and children, common variations of the FTO (fat mass and obesity associated) gene were found to be substantially linked with BMI, obesity, and type 2 diabetes [13]. The association with type 2 diabetes was entirely explained by the association with BMI. The link of FTO polymorphisms with type 2 diabetes and BMI has been independently identified in numerous white European populations (Dina et al. 2007), while the results in Asians are mixed, which could be due to different study methodologies, insufficient sample sizes, or ethnic differences [14]. The most prevalent biomarker for diagnosing prediabetes and diabetes is HbA1c. It is formed when glucose binds to the amino-terminal group of the

haemoglobin component. Rather than glucose levels at a particular time point, HbA1c shows chronic glycemia. HbA1c ≥6.5% (48 mmol/mol) for diabetes and 5.7–6.4% (39–46 mmol/mol) for prediabetes are the current ADA criteria [15]. HbA1c values above 7% are linked to an increased risk of morbidity and mortality. Higher HbA1c levels were similarly linked to an increased risk of CVD, cancer, and all-cause death in the Norfolk prospective trial [16]. Adiponectin, a protein generated from adipose tissue, has insulin sensitising, anti-inflammatory, and anti-atherogenic effects, and is a predictor of diabetes [17]. In diabetes preventive trials, lower levels of adiponectin have been linked to increased IR and obesity, while greater levels have been linked to lifestyle intervention groups [17]. Adiponectin's link to diabetes risk appears to be visible considerably earlier in the disease's progression; specifically, reduced adiponectin levels were found a decade before diabetes was diagnosed, particularly in men [17]. The connecting peptide, also known as the C-peptide, is a short 31-amino-acid polypeptide that joins the A-chain of insulin to the B-chain of proinsulin. The component of proinsulin that is cleaved prior to co-secretion with insulin by pancreatic beta cells is known as C-peptide. C-peptide is a widely used indicator of beta cell activity in the pancreas. It is created in equimolar levels to endogenous insulin, but it is excreted at a faster rate and over a longer period of time [18]. As a guide to beta cell activity, C-peptide testing is preferred to insulin testing. This is due to the fact that c-peptide degrades more slowly in the body than insulin (half-life of 20–30 minutes versus 3–5 minutes for insulin), allowing for a more consistent test window of fluctuating beta cell activity. The first description of the homeostatic model assessment (HOMA) of β-cell function and insulin resistance (IR) was in 1985 [19]. The approach is used to evaluate β-cell function and IR using basal glucose, insulin, or C-peptide concentrations. From fasting plasma insulin and glucose concentrations, the HOMA model is used to calculate insulin sensitivity and β-cell function [19]. In the baseline state, the connection between glucose and insulin reflects a balance between hepatic glucose output and insulin secretion, which is maintained by a feedback loop between both the liver and the -cells [20]. The model's predictions are based on experimental data from people and animals. In HOMA modelling of both β-cell function and IR, C-peptide, an indicator of insulin production, can be used. The model's notion is that insulin sensitivity (percent S) is a function of glucose metabolism driven by insulin action [20]. C-peptide is a reliable measure of insulin secretion but not of insulin action, and the model's concept is that insulin sensitivity (percent S) is a function of glucose metabolism motivated by insulin action. The employment of two tests to measure β-cell function and insulin sensitivity, C-peptide and insulin, respectively, lowers bias. The goal of this study was to look at the levels of various glycemic markers and their relationship to fat-mass and obesity-associated gene (FTO) variations in some ethnic groups in Nigeria's Niger Delta.

2. MATERIALS AND METHODS

2.1 Study Area

The study was carried out in Niger Delta region of Nigeria, with Federal Medical Centre, Asaba serving as the major point of the sample collection and some analysis. Some samples were also collected at Agbor & Bomadi. The Igbo participants were drawn from the Igbos of Delta State, Rivers State and Imo State; the Ijaw participants were drawn from the Ijaws of Delta State, Bayelsa State and Rivers State.

Nigeria's Niger Delta region, once known as the Oil Rivers, is a highly populated region and a major palm oil producer. It was renamed the Niger Coast Protectorate after its expansion. The Niger Delta, which runs parallel to the Gulf of Guinea on the Atlantic Ocean in Nigeria, was originally made up of the present-day Bayelsa, Rivers, and Delta states, but is now made up of nine coastal states. According to the federal government of Nigeria's current definition, the delta covers roughly 70,000 km2 and accounts for nearly 7% of the country's landmass. The Niger Delta comprises of level low lying muggy landscape that is befuddled by wandering and anastomosing streams, waterways and brooks [21].

Asaba, the capital city of Delta State, Nigeria is situated within geographical co-ordinates 6°11′52.23″N6°43′42.48″E. It is situated on a terrace of the lower Niger River, overlooking the point where the Anambra River flows into it. Beyond the river banks, on the high plains which are far more extensive than the river basins, secondary forest vegetation flourishes.

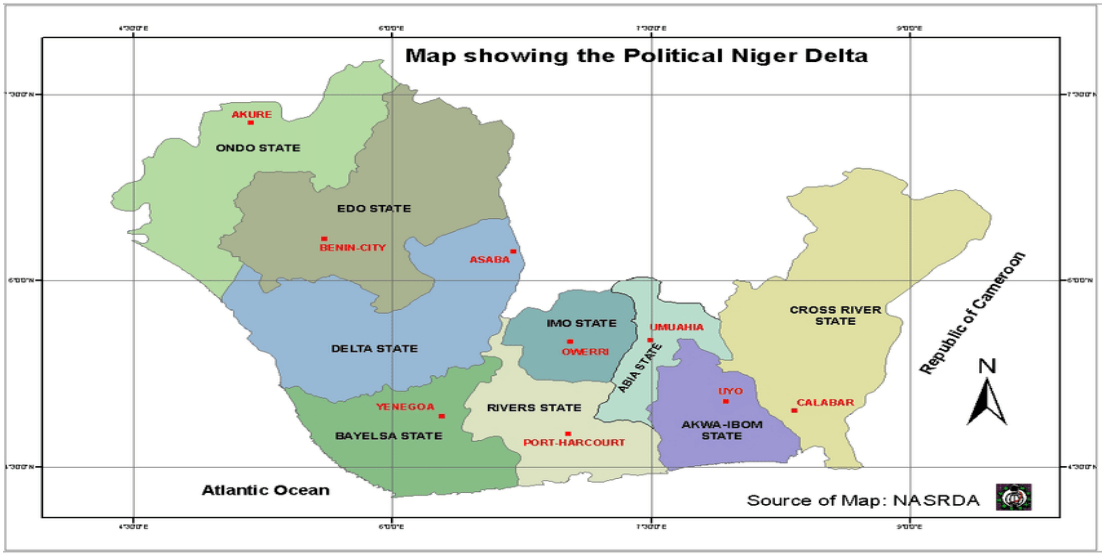

Fig. 1. Political Map of the Niger Delta Area

2.2 Research Design

This is a case-controlled observational study involving the association between FTO gene allele variants and HbA1c, Fasting blood glucose, Insulin, C-Peptides, Adiponectin and HOMA-IR in obese/T2D subjects from selected ethnic groups in Niger Delta, Nigeria. The bio-data and medical history of the subjects was obtained using questionnaire, measuring their weight with a calibrated weighing scale, height and waist circumference.

2.3 Sample Size

A total of 98 subjects enrolled for this study. Sample size calculated based on the method of Allain et al. [22].

2.4 Sampling Method

Multistage sampling method was employed in the subject selection. The subjects were first separated into two groups – new cases (less than a year of diagnosis as Diabetic) and old cases (one year & above). Equal number of samples was then randomly collected from each of the cluster groups.

2.5 Selection Criteria

2.5.1 Inclusion criteria

Individuals who are purebred of the selected tribes in Niger Delta, aged at least 21 years diagnosed with T2D for at least one year. Controls: Individuals who are from the selected tribes with no history of diabetes, and a fasting blood glucose of less than 6.5mmol/l. The cluster groups were considered also.

2.5.2 Exclusion criteria

Individuals not of the selected tribes, those who are not purebred from the selected tribes, those who are critically ill subjects and female participants who are pregnancy.

2.6 Sample Collection and Analysis

2.6.1 Sample collection

Ten millilitres (10ml) of blood were randomly collected from 19-20 subjects from each of the selected tribes following the sampling methodology described earlier and 20 control made of 5 non-diabetic, non-obese subjects from each of the selected tribes. This was after completing the questionnaire and signing the consent form. Their body weight in kilogram, height in meter and waist circumference in centimeter was also measured and recorded. Order of dispensing and volume of the blood sample: 4.0ml into vacutainer type plain tubes, 4.0ml into vacutainer type EDTA K_3 (1^{st} Tube) & 2.0ml into vacutainer type EDTA K_3 (2^{nd} Tube) and fluoride oxalate tube for glucose analysis. All the tubes were appropriately labelled. The sample in the plain tube was allowed to retract, then centrifuged at 3000rpm. The serum was separated into two cryotubes (one for ELISA

assays- Adiponectin, Insulin, C-Peptide), labelled and stored at -15°C to -20°C. The second EDTA tube for Glycated haemoglobin was stored at 2-8°C and analysis done within two days of sample collection. The fasting blood glucose was performed immediately.

2.6.2 Sample Analysis

2.6.2.1 Fasting Blood Glucose (FBG)

FBS was performed using glucose oxidase method with kit from Randox Laboratories, UK.

2.6.2.2 Glycosylated Haemoglobin (HbA1c)

Quantitative determination of glycosylated Haemoglobin in blood was done using the modified Ion Exchange Resin method with kit from INTECO Diagnostics, UK [23].

2.6.2.3 Serum Insulin (Bio-Inteco ELISA Kit)

ELISA method was used to assay for Insulin, a quantitative test is based on a solid phase enzyme-linked immunosorbent assay.

2.6.2.3 Serum C-Peptide (Bio-Inteco ELISA Kit)

ELISA method was used to assay for C-peptide which is based on a solid phase enzyme-linked immunosorbent assay

2.6.2.3 Adiponectin (Bioassay ELISA Kit)

ELISA method was used to assay for Adinopectin.

2.6.2.4 Homeostatic Model Assessment for Insulin Resistance (HOMA-IR)

HOMA-IR index was calculated by using following formula: Fasting Insulin (mU/L) × Fasting Glucose (mmol/L)/22.5 [19].

Healthy Range; 0.5 – 1.4

2.6.2.5 Genomic DNA Extraction

Genomic DNA extractions of the samples was performed using Geneaid DNA Mini Kit (Blood/Cultured Cell).

2.6.2.6 Genotyping of SNPs

Genotyping of SNPs of the *FTO* gene was performed with the Illumina next-generation sequencing (NGS) using NextSeq 2000 Sequencing System. Purity and concentration of isolated DNA was determined by UV/VIS spectrophotometer NanoDrop ND-1000.

2.7 Statistical Analysis

The data were analyzed using GraphPad Prism, version 8.0.2, (California, USA). Quantitative variables were expressed as Mean (X) ± standard deviation (SD). One-Way Analysis of Variance (ANOVA) and students' statistical t-test were the inferential statistics used to observe the differences mean values, while Tukey's Post Hoc analysis was also done to observe the differences within different sub-classes. Linear regression and Pearson's correlation was carried out to determine the association between variables and statistical significance was set at $p<0.05$.

3. RESULTS AND DISCUSSION

This study (Table 1) observed a significant difference in the values obtained between the control and case in all the tribes in the FBS ($p<.01$), HbA1c ($p<.01$), Insulin ($p<.01$, HOMA-IR ($p<.01$) and BMI ($p<.01$), but none in Adiponectin ($p>.05$) and C-Peptide ($p>.05$). There were no differences between the FBS of the cases in the different tribes, but there was a difference in the HbA1c between the Urhobor/Isoko group and those of the Igbo group. This difference may not be unconnected to issue of management, as HbA1c measures blood glucose over a period of three months and is a better marker for monitoring treatment. HbA1c reflects chronic exposure to glucose, it is particularly useful for lifestyle modification counselling [24]. Also, there were differences between the Ijaw tribe (lower values) and the others in terms of HOMA-IR (Table 1). This suggests there could be a lower risk of insulin resistance with the Ijaw diabetics than the other tribes. The Urhobo/Isoko showed higher levels of insulin resistance. HOMA-IR analysis allowed assessment of inherent B-cell function and insulin sensitivity and could characterize the pathophysiology in those with abnormal glucose tolerance [20]. A higher BMI values was observed among the Urhobor/Isoko and Ika group suggesting a higher prevalence of obesity (Table 1). Energy balance due to type of food consumption and physical activity may play a role here. Obesity is the result of a positive energy balance, whereby energy intake exceeds expenditure, resulting in the storage of energy, primarily as lipids in white adipocytes. Energy

balance is modulated by food consumption and physical activity [25]. The World Health Organization (WHO) defines overweight as a body mass index of >25kg/m^2 and obesity as BMI of >30kg/m^2 the WHO has reported that, globally, overweight and obesity represent the fifth leading risk for death; furthermore, 44% of the Diabetes burden 23% of the ischemic heart disease burden, and 7-41% of certain cancer burdens are related to overweight and obesity [26]. Obesity is a major risk factor for type 2 diabetes [5] and an independent risk factor for diabetes and either BMI or waist-to-hip has been commonly used as a surrogate measures of adiposity [12,27]. The pattern seen with C-Peptide is not unexpected as C-Peptide is a useful tool in the classification and differention of diabetes into type 1, type 2 and MODY. It is also associated with duration of disease as well as age of diagnosis [28].

This work found a significant correlation between rs9939609 variant genotype of FTO gene with metabolic traits indices in obese against non-obese (Tables 16 and 17) by the attendant increases in BMI ($p<.01$), HOMA-IR ($p<.05$), and Insulin ($p<.01$) values with the carriers of the risk allele (A) in the obese subjects, but more strongly and only with BMI ($p<.01$) for with obese and T2D subjects combined (Table 16). This may be suggesting that the effect of rs9939609 with T2D in Niger Delta population could be obesity mediated and not independently. This is in line with the findings among African-American in the ARIC Study conducted by Chauhan et al. [29] in north Indian population and by Yang et al. [30] in a multiple population involving East Asia, South Asia, North America and North African, but concurrent and independent association with both obesity and T2D was observed by Yajnik et al. 2008 in South Asian Indians, Li et al. [14] in South Asia and Sabarneh et al. [6] in Palestine. However, Hennig et al. [31] and Apalasamy et al. [26] found no association among Malaysian Malays and the mostly lean homogenous Mandinka Gambians. A genome-wide associated study confirmed that rs9939609 variant located within the first intron of the FTO gene predisposes European population to diabetes through an effect on body mass index (BMI) [32]. Variants in the fat mass and obesity-associated gene FTO have been identified as the most powerful common genetic risk factors for obesity and type 2 diabetes. The first connection of an FTO variant with obesity and T2D was found in a European population with variant rs9939609 [32]. Since then, a genetic link between rs9939609 and obesity and T2D has been established in a Korean population [33]. Indians [29]. African ancestry & African - American [34], Palestine [6] and some other studies have also shown that the association of FTO variants with obesity or T2D is not ethnic dependent [5]. In a pilot study conducted in Nigeria in 2017, Oyeyemi et al. [10] analyzed SNP rs9939609 of the FTO gene in a group of people with obesity and control. Individual with the FTO risk allele (A) had significantly high obesity risk factors (BMI, WC etc.) and this was also in tandem with some earlier studies [35]. This study is in agreement with their findings, thus suggesting an association between FTO rs9939609 and obesity. However, a 2009 study did not find any influence by FTO gene variation on measures of body mass in Gambians living a traditional lifestyle. They were described as lean population. According to Henning et al. 2009, any influence of FTO genotype on body mass may be of minimal consequence in a thin community with little excess food available, compared to similar ethnic cultures with abundant food.

The study (Tables 3, 4, 5, 6, 7, 8, 9 & 10) found correlation between variants rs201041270 (GA/AA) with adiponectin ($p<.05$) and with Insulin ($p<.05$), rs531215275 (CA/AA), mild with C-peptide ($p<.05$), rs146056272 (TC/CC) with creatinine ($p<.01$), rs1410999299 (AG/GG) with C-peptide ($p<.05$), rs145884431 (GA/GG) with HbA1c ($p<.05$) & MDRD ($p<.05$), rs146138389 (CT/CC) with insulin ($p<.05$) and rs886052102 (AG/AA) with FBS ($p<.05$) & strongly with HbA1c ($p<.01$). Adiponectin is an independent predictor of diabetes because it has insulin sensitising, anti-inflammatory, and anti-atherogenic characteristics. The most prevalent biomarker for diagnosing prediabetes and diabetes is HbA1c. Rather than glucose levels at a particular time point, HbA1c shows chronic glycemia. C-peptide is a widely used indicator of beta cell activity in the pancreas. It is created in equimolar levels to endogenous insulin, but it is excreted at a faster rate and over a longer period of time [18].

Table 1. One-Way ANOVA Results of Mean±SD of Fasting Blood Glucose**, Insulin Resistance and Related Biochemical Parameters of Subjects of Niger Delta Tribes with FTO gene variations**

Parameters	Ijaw	Urhobo	Ika	Igbo	Control	Fvalue	pvalue	Remark
FBS (mmol/L)	9.05 ± 3.15[a]	7.67 ± 3.45[a]	7.03± 3.20[a]	9.05 ± 3.04[a]	4.92 ± 0.66[b]	7.037	<0.0001	S
HbA1c (%)	9.02 ± 1.44[a]	8.03 ± 1.75[ac]	8.96± 1.49[a]	10.08±2.05[ad]	6.57 ± 0.99[b]	13.77	<0.0001	S
Adiponectin (mg/L)	6.11 ± 2.15	5.43 ± 1.73	5.72 ± 1.32	7.46 ± 1.85	10.30 ± 2.72	0.948	0.4399	NS
Insulin (uIU/ml)	6.19 ± 5.0[a]	17.66±4.79[bc]	14.92±8.93[bc]	15.60±7.21[bc]	8.96 ± 5.06[ad]	11.46	<0.0001	S
C-Peptide ng/ml	1.06 ± 0.87	0.88 ± 0.74	1.41 ± 1.72	1.08 ± 0.75	0.89 ± 0.56	0.918	0.4564	NS
HOMA-IR	2.56 ± 3.07[a]	5.96 ± 2.95[bc]	4.66 ± 3.87[ac]	5.17 ± 1.99[bc]	1.97 ± 1.09[ad]	7.719	<0.0001	S
BMI	24.25 ±4.48[a]	30.25 ± 6.67[b]	30.28± 5.89[b]	27.77 ± 5.05[a]	28.27± 5.31[a]	3.969	0.0051	S

PostHoc (Tukey's):

Within same row, values with different superscripts (a, b), (c, d) differ significantly when various tribes were compared against each other. S=Significant, NS=Not Significant At p<0.05.

Abbreviations: *BMI=Body Mass Index, FBS=Fasting Blood glucose, HbA1c= Glycated Haemoglobin, HOMA-IR=Insulin Resistance*

Table 2. Comparative Results of Mean ± SD of Fasting Blood Glucose, Insulin Resistance and Related Biochemical Parameters of Subjects of Niger Delta Tribes with FTO gene Variations on Special Diet

Parameters	No special diet	Special diet	T value	P value	Remark
FBS (mmol/L)	8.46 ± 3.63	7.87 ± 2.84	0.800	0.426	NS
HbA1c (%)	8.94 ± 1.79	9.119 ± 1.891	0.431	0.667	NS
Adiponectin(mg/L)	5.56 ± 7.06	6.94 ± 10.78	0.690	0.491	NS
Insulin (uIU/ml)	13.13 ± 6.979	14.15 ± 9.02	0.572	0.568	NS
C-Peptide ng/ml	1.05 ± 0.95	1.19 ± 1.07	0.558	0.578	NS
HOMA-IR	4.95 ± 3.95	4.14 ± 2.04	1.120	0.266	NS
BMI	28.46 ± 6.67	27.73 ± 5.17	0.539	0.590	NS

S=Significant, NS=Not Significant At p<0.05.

Abbreviations: *BMI=Body Mass Index, FBS=Fasting Blood glucose HbA1c= Glycated Haemoglobin, HOMA-IR=Insulin Resistance*

Table 3. Association of FTO rs73609956 variant with glycemic parameters of Obese|T2D in Niger Delta tribes using Dominant Model

Parameters	TT	TA/AA	GLR, P value	PC, p value	T-test, p value
FBS (mmol/L)	8.16 ± 3.34	8.93 ± 1.69	0.6877	0.6877	0.6957
HbA1c (%)	9.03 ± 1.85	8.73 ± 1.33	0.3831	0.3831	0.7833
Adiponectin(mg/L)	6.32 ± 9.04	2.77 ± 0.45	0.6154	0.6154	0.5013
Insulin (uIU/ml)	13.72 ± 7.93	10.37 ± 8.72	0.3353	0.3353	0.4762
C-Peptide ng/ml	1.09 ± 1.10	1.53 ± 1.00	0.2601	0.2601	0.4973
HOMA-IR	4.59 ± 3.24	4.33 ± 4.15	0.4044	0.4044	0.8911
BMI	28.18 ± 6.00	27.00 ± 7.65	0.2073	0.2073	0.7416

GLR=General Linear Regression, PC=Pearson's Correlation, t-test=students' statistical test, p @ <0.05. T= Wild (Dominant), A=Polymorphic.

Table 4. Association of FTO rs116753298 variant with glycemic parameters of Obese|T2D in Niger Delta tribes using Dominant Model

Parameter	CC	CT/TT	GLR, P value	PC, p value	t-test, p value
FBS (mmol/L)	8.24 ± 3.34	6.56 ± 1.54	0.6416	0.6416	0.2683
HbA1c (%)	9.06 ± 1.83	8.82 ± 1.99	0.7034	0.7034	0.7792
Adiponectin(mg/L)	6.40 ± 9.22	3.46 ± 0.537	0.9084	0.9084	0.4802
Insulin (uIU/ml)	13.69 ± 7.90	11.72 ± 9.76	0.7036	0.7036	0.5969
C-Peptide ng/ml	1.13 ± 1.11	1.01 ± 1.00	0.5305	0.5305	0.8043
HOMA-IR	4.63 ± 3.27	3.08 ± 2.41	0.7816	0.7816	0.3017
BMI	28.46 ± 5.96	25.06 ± 5.70	0.4830	0.4830	0.2195

GLR=General Linear Regression, PC=Pearson's Correlation, t-test=students' statistical test, p @ <0.05. C= Wild (Dominant), T=Polymorphic.

Table 5. Association of FTO rs201041270 variant with glycemic parameters of Obese|T2D in Niger Delta tribes using Dominant Model

Parameter	GG	GA/AA	GLR, P value	PC, p value	t-test, p value
FBS (mmol/L)	8.16 ± 3.32	8.57 ± 3.16	0.9356	0.9356	0.7768
HbA1c (%)	8.98 ± 1.85	9.43 ± 1.45	0.5156	0.5156	0.5699
Adiponectin(mg/L)	6.31 ± 4.12	4.55 ± 2.67	**0.0198**	**0.0198**	0.6432
Insulin (uIU/ml)	13.58 ± 8.01	13.72 ± 7.32	**0.0464**	**0.0464**	0.9678
C-Peptide ng/ml	1.12 ± 1.11	0.95 ± 0.90	0.0034	0.0034	0.7146
HOMA-IR	4.57 ± 3.29	4.80 ± 2.91	0.2005	0.2005	0.8688
BMI	28.28 ± 6.12	26.35 ± 4.44	0.0943	0.0943	0.4536

GLR=General Linear Regression, PC=Pearson's Correlation, t-test=students' statistical test, p @ <0.05. G= Wild (Dominant), A=Polymorphic.

Table 6. Association of FTO rs531215275 variant with glycemic parameters of Obese|T2D in Niger Delta tribes using Dominant Model

Parameter	CC	CA/AA	GLR, P value	PC, p value	t-test, p value
FBS (mmol/L)	8.29 ± 3.36	7.21 ± 2.52	0.9747	0.9747	0.4129
HbA1c (%)	8.99 ± 1.83	9.27 ± 1.91	0.8983	0.8983	0.7237
Adiponectin(mg/L)	6.30 ± 5.20	4.88 ± 3.90	0.2171	0.2171	0.6891
Insulin (uIU/ml)	13.58 ± 7.97	13.64 ± 7.98	0.2718	0.2718	0.9854
C-Peptide ng/ml	1.03 ± 1.01	1.93 ± 1.62	0.6985	0.6985	**0.0374**
HOMA-IR	4.64 ± 3.34	3.97 ± 1.92	0.0502	0.0502	0.6023
BMI	27.98 ± 6.12	29.71 ± 4.87	0.4372	0.4372	0.4703

GLR=General Linear Regression, PC=Pearson's Correlation, t-test=students' statistical test, p @ <0.05. C= Wild (Dominant), A=Polymorphic.

Table 7. Association of FTO rs146056278 variant with glycemic parameters of Obese|T2D in Niger Delta tribes using Dominant Model

Parameter	TT	TC/CC	GLR, P value	PC, p value	t-test, p value
FBS (mmol/L)	8.17 ± 3.32	8.95 ± 2.61	TFP	TFP	0.7456
HbA1c (%)	9.01 ± 1.82	9.60 ± 2.82	TFP	TFP	0.6537
Adiponectin(mg/L)	6.27 ± 8.99	2.75 ± 0.63	TFP	TFP	0.5838
Insulin (uIU/ml)	13.45 ± 7.97	18.90 ± 1.41	TFP	TFP	0.3404
C-Peptide ng/ml	1.09 ± 1.09	1.50 ± 1.56	TFP	TFP	0.6121
HOMA-IR	4.51 ± 3.25	7.45 ± 1.63	TFP	TFP	0.2087
BMI	28.17 ± 6.09	26.75 ± 0.78	TFP	TFP	0.7441

GLR=General Linear Regression, PC=Pearson's Correlation, t-test=students' statistical test, p @ <0.05. C= Wild (Dominant), A=Polymorphic. TFP=Too few pairs available for analysis

Table 8. Association of FTO rs1410999299 variant with glycemic parameters of Obese|T2D in Niger Delta tribes using Dominant Model

Parameters	AA	AG/GG	GLR, P value	PC, p value	t-test, p value
FBS (mmol/L)	8.21 ± 3.35	7.92 ± 2.59	0.5280	0.5280	0.8480
HbA1c (%)	9.09 ± 1.83	8.02 ± 1.70	0.7144	0.7144	0.2088
Adiponectin(mg/L)	6.37 ± 5.15	3.38 ± 1.28	0.7367	0.7367	0.4704
Insulin (uIU/ml)	13.63 ± 7.9	12.96 ± 8.33	0.1962	0.1962	0.8557
C-Peptide ng/ml	1.12 ± 1.10	0.92 ± 1.02	**0.0360**	**0.0360**	0.6934
HOMA-IR	4.60 ± 3.28	4.36 ± 3.03	0.2214	0.2214	0.8726
BMI	28.33 ± 6.08	25.16 ± 4.35	0.2256	0.2256	0.2562

GLR=General Linear Regression, PC=Pearson's Correlation, t-test=students' statistical test, p @ <0.05. A= Wild (Dominant), G=Polymorphic.

Table 9. Association of FTO rs79206939 variant with glycemic parameters of Obese|T2D in Niger Delta tribes using Dominant Model

Parameters	GG	AG/AA	GLR, P value	PC, p value	t-test, p value
FBS (mmol/L)	8.17 ± 3.32	8.62 ± 2.99	0.9794	0.9794	0.7915
HbA1c (%)	9.01 ± 1.86	9.22 ± 1.25	0.5349	0.5349	0.8211
Adiponectin(mg/L)	6.37 ± 9.09	2.67 ± 0.49	0.1119	0.1119	0.4220
Insulin (uIU/ml)	13.64 ± 7.95	12.68 ± 8.50	0.2789	0.2789	0.8144
C-Peptide (ng/ml)	1.10 ± 1.10	1.27 ± 1.04	0.9197	0.9197	0.7577
HOMA-IR	4.60 ± 3.27	4.35 ± 2.95	0.4687	0.4687	0.8818

GLR=General Linear Regression, PC=Pearson's Correlation, t-test=students' statistical test, p @ <0.05. G= Wild (Dominant), A=Polymorphic.

Table 10. Association of FTO rs145884431 variant with glycemic parameters of Obese|T2D in Niger Delta tribes using Dominant Model

Parameter	AA	GA/GG	GLR, P value	PC, p value	t-test, p value
FBS (mmol/L)	8.12 ± 3.17	8.92 ± 4.66	0.8147	0.8147	0.5418
HbA1c (%)	8.989 ± 1.859	9.35 ± 1.59	**0.0117**	**0.0117**	0.6146
Adiponectin(mg/L)	6.48 ± 4.26	3.05 ± 0.72	0.5419	0.5419	0.3337
Insulin (uIU/ml)	13.47 ± 7.93	14.80 ± 8.27	0.4525	0.4525	0.6751
C-Peptide ng/ml	1.12 ± 1.12	1.01 ± 0.82	0.8606	0.8606	0.8130
HOMA-IR	4.64 ± 3.37	4.01 ± 1.40	0.3465	0.3465	0.6278
BMI	28.35 ± 6.10	25.90 ± 4.83	0.9480	0.9480	0.3067

GLR=General Linear Regression, PC=Pearson's Correlation, t-test=students' statistical test, p @ <0.05. A= Wild (Dominant), G=Polymorphic.

Table 11a. Association of FTO rs61743972 variant with glycemic parameters of Obese|T2D in Niger Delta tribes using Dominant Model

Parameters	AA	GA/GG	GLR, P value	PC, p value	t-test, p value
FBS (mmol/L)	8.27 ± 3.32	6.98 ± 2.77	0.1159	0.1159	0.3977
HbA1c (%)	9.01 ± 1.86	9.08 ± 1.26	0.8689	0.8689	0.9415
Adiponectin (mg/L)	6.39 ± 4.15	2.94 ± 0.26	0.4790	0.4790	0.4034
Insulin (uIU/ml)	13.29 ± 7.47	18.08 ± 13.44	0.3931	0.3931	0.1925
C-Peptide ng/ml	1.14 ± 1.11	0.58 ± 0.44	0.6987	0.6987	0.2677
HOMA-IR	4.58 ± 3.31	4.580 ± 2.183	0.3139	0.3139	0.9958
BMI	28.07 ± 6.11	29.12 ± 4.75	0.5710	0.5710	0.7075

GLR=General Linear Regression, PC=Pearson's Correlation, t-test=students' statistical test, p @ <0.05. A= Wild (Dominant), G=Polymorphic.

Table 11b. Association of FTO rs2014496428 variant with glycemic parameters of Obese|T2D in Niger Delta tribes using Dominant Model

Parameter	TT	CT/CC	GLR, P value	PC, p value	t-test, p value
FBS (mmol/L)	8.27 ± 3.23	7.23 ± 4.21	0.5465	0.5465	0.4605
HbA1c (%)	9.08 ± 1.84	8.21 ± 1.58	0.7557	0.7557	0.2658
Adiponectin(mg/L)	6.26 ± 4.14	5.11 ± 3.34	0.9163	0.9163	0.7624
Insulin (uIU/ml)	12.97 ± 7.37	21.25 ± 11.0	0.1275	0.1275	0.0129
C-Peptide ng/ml	1.13 ± 1.11	0.83 ± 0.92	0.5643	0.5643	0.5254
HOMA-IR	4.45 ± 3.14	6.21 ± 4.32	0.9375	0.9375	0.2032
BMI	28.22 ± 6.18	27.03 ± 3.43	0.7618	0.7618	0.6442

GLR=General Linear Regression, PC=Pearson's Correlation, t-test=students' statistical test, p @ <0.05. T= Wild (Dominant), C=Polymorphic.

Table 11c. Association of FTO rs146138389 variant with glycemic parameters of Obese|T2D in Niger Delta tribes using Dominant Model

Parameters	TT	CT/CC	GLR, P value	PC, p value	t-test, p value
FBS (mmol/L)	8.22 ± 3.28	7.62 ± 4.11	0.6989	0.6989	0.7246
HbA1c (%)	9.09 ± 1.81	7.62 ± 1.74	0.8315	0.8315	0.1183
Adiponectin(mg/L)	6.35 ± 4.09	2.97 ± 0.55	0.0665	0.0665	0.4629
Insulin (uIU/ml)	13.16 ± 7.43	21.78 ± 13.3	0.8933	0.8933	**0.0332**
C-Peptide ng/ml	1.13 ± 1.10	1.23 ± 1.09	0.7707	0.7707	0.8292
HOMA-IR	4.51 ± 3.27	6.05 ± 2.46	0.5672	0.5672	0.3586
BMI	28.18 ± 6.05	27.18 ± 5.98	0.2558	0.2558	0.7459

GLR=General Linear Regression, PC=Pearson's Correlation, t-test=students' statistical test, p @ <0.05. T= Wild (Dominant), C=Polymorphic.

Table 12. Association of FTO rs886052102 variant glycemic parameters of Obese|T2D in Niger Delta tribes using Dominant Model

Parameters	GG	AG/AA	GLR, P value	PC, p value	t-test, p value
FBS (mmol/L)	8.19 ± 3.33	12.88 ± 9.36	0.4705	0.4705	0.0171
HbA1c (%)	9.00 ± 1.86	9.53 ± 0.66	**0.0054**	**0.0054**	0.6246
Adiponectin(mg/L)	6.31 ± 5.20	4.88 ± 4.09	0.3144	0.3144	0.8210
Insulin (uIU/ml)	13.48 ± 8.07	13.83 ± 7.64	0.3656	0.3656	0.9411
C-Peptide ng/ml	1.13 ± 1.10	0.50 ± 0.43	0.5935	0.5935	0.3298
HOMA-IR	4.58 ± 3.29	4.67 ± 2.08	0.1779	0.1779	0.9660
BMI	28.14 ± 6.10	28.03 ± 3.53	0.4078	0.4078	0.9767

GLR=General Linear Regression, PC=Pearson's Correlation, t-test=students' statistical test, p @ <0.05. G= Wild (Dominant), A=Polymorphic.

Table 13. Association of FTO rs14474317 variant with glycemic parameters of Obese|T2D in Niger Delta tribes using Dominant Model

Parameter	AA	GA/GG	GLR, P value	PC, p value	t-test, p value
FBS (mmol/L)	8.12 ± 3.17	9.57 ± 5.63	0.8129	0.8129	0.3943
HbA1c (%)	8.97 ± 1.82	10.05 ± 1.89	0.3839	0.3839	0.2516
Adiponectin(mg/L)	6.13 ± 5.04	7.15 ± 5.98	0.3144	0.3144	0.8250
Insulin (uIU/ml)	13.56 ± 7.93	14.08 ± 8.92	0.4732	0.4732	0.9010
C-Peptide ng/ml	1.14 ± 1.11	1.00 ± 0.87	0.3148	0.3148	0.8401
HOMA-IR	4.47 ± 2.91	6.87 ± 7.61	0.8315	0.8315	0.1494
BMI	28.38 ± 6.04	23.38 ± 2.78	0.1357	0.1357	0.1049

GLR=General Linear Regression, PC=Pearson's Correlation, t-test=students' statistical test, p @ <0.05. G= Wild (Dominant), A=Polymorphic.

Table 14. Association of FTO rs886052103 variant with glycemic parameters of Obese|T2D in Niger Delta tribes using Dominant Model

Parameter	TT	CT/CC	GLR, P value	PC, p value	t-test, p value
FBS (mmol/L)	8.16 ± 3.34	8.93 ± 1.69	0.6877	0.6877	0.6957
HbA1c (%)	9.03 ± 1.85	8.73 ± 1.33	0.3831	0.3831	0.7833
Adiponectin(mg/L)	6.33 ± 4.043	2.77 ± 0.45	0.6154	0.6154	0.5013
Insulin (uIU/ml)	13.72 ± 7.92	10.37 ± 8.72	0.3353	0.3353	0.4762
C-Peptide ng/ml	1.09 ± 1.01	1.53 ± 1.00	0.2601	0.2601	0.4973
HOMA-IR	4.597 ± 3.24	4.33 ± 4.15	0.4044	0.4044	0.8911
BMI	28.18 ± 6.00	27.00 ± 7.65	0.2073	0.2073	0.7416

GLR=General Linear Regression, PC=Pearson's Correlation, t-test=students' statistical test, p @ <0.05. T= Wild (Dominant), C=Polymorphic.

Table 15. Association of FTO rs8050136 variant with glycemic parameters of Obese|T2D in Niger Delta tribes using Dominant Model

Parameter	CC	AC/AA	GLR, P value	PC, p value	t-test, p value
FBS (mmol/L)	8.05 ± 3.22	8.84 ± 3.66	0.8330	0.8330	0.4227
HbA1c (%)	8.92 ± 1.89	9.47 ± 1.45	0.5257	0.5257	0.3143
Adiponectin(mg/L)	6.79 ± 4.67	3.27 ± 1.36	0.4334	0.4334	0.1803
Insulin (uIU/ml)	13.63 ± 7.97	13.39 ± 7.98	0.7729	0.7729	0.9162
C-Peptide (ng/ml)	1.09 ± 1.12	1.18 ± 0.98	0.3132	0.3132	0.7743
HOMA-IR	4.43 ± 2.78	5.32 ± 4.95	0.9604	0.9604	0.3550
BMI	27.60 ± 5.81	30.65 ± 6.53	0.1581	0.1581	0.0849

GLR=General Linear Regression, PC=Pearson's Correlation, t-test=students' statistical test, p @ <0.05. C= Wild (Dominant), A=Polymorphic.

Table 16. Association of FTO rs9939609 variant glycemic parameters of Obese|T2D in Niger Delta tribes using Dominant Model

Parameter	TT	AT/AA	GLR, P value	PC, p value	t-test, p value
FBS (mmol/L)	8.42 ± 3.20	7.353 ± 3.595	0.4002	0.4002	0.2371
HbA1c (%)	9.11 ± 1.94	8.68 ± 1.33	0.4110	0.4110	0.4016
Adiponectin(mg/L)	5.79 ± 7.74	7.60 ± 12.48	0.9864	0.9864	0.4607
Insulin (uIU/ml)	13.34 ± 8.12	14.50 ± 7.30	0.9125	0.9125	0.5968
C-Peptide ng/ml	1.07 ± 1.01	1.24 ± 1.09	0.4138	0.4138	0.5777
HOMA-IR	4.54 ± 3.13	4.74 ± 3.74	0.8588	0.8588	0.8275
BMI	26.62 ± 5.03	33.74 ± 6.16	**0.0010**	**0.0010**	**<0.0001**

GLR=General Linear Regression, PC=Pearson's Correlation, t-test=students' statistical test, p @ <0.05. T= Wild (Dominant), A=Polymorphic.

Association of FTO Gene Variants with Metabolic and Lipid Parameters and Renal Indices of Obese in Niger Delta Tribes Using Dominant Model

Table 17. Association of FTO rs9939609 variant with glycemic parameters of Obese in Niger Delta tribes using Dominant Model

Parameters	TT (Obese)	TA/AA (Obese)	GLR, P value	PC, p value	T-test, p value
FBS (mmol/L)	8.17 ± 2.93	6.98 ± 3.42	0.0695	0.0695	0.2740
HbA1c (%)	8.83 ± 1.81	8.88 ± 1.38	0.4010	0.4010	0.9355
Adiponectin(mg/L)	6.05 ± 4.64	8.78 ± 4.15	0.4851	0.4851	0.4272
Insulin (uIU/ml)	12.22 ± 6.30	16.42 ± 5.73	**0.0031**	**0.0031**	**0.0541**
C-Peptide (ng/ml)	1.36 ± 1.47	1.27 ± 1.05	0.5141	0.5141	0.8483
HOMA-IR	4.28 ± 2.92	4.93 ± 2.59	**0.0199**	**0.0199**	0.5084
BMI	30.30 ± 5.50	36.22 ± 4.67	0.3666	0.3666	**0.0023**

GLR=General Linear Regression, PC=Pearson's Correlation, t-test=students' statistical test, p @ <0.05. T= Wild (Dominant), A=Polymorphic.

Table 18. Association of FTO rs531215275 variant with glycemic parameters of Obese in Niger Delta tribes using Dominant Model

Parameters	CC (Obese)	CA/AA (Obese)	GLR, P value	PC, p value	T-test, p value
FBS (mmol/L)	7.49 ± 2.88	6.63 ± 2.01	0.4903	0.4903	0.6265
HbA1c (%)	8.68 ± 1.55	9.07 ± 0.66	0.1836	0.1836	0.7061
Adiponectin(mg/L)	7.872 ± 13.96	3.13 ± 0.25	0.2682	0.2682	0.4664
Insulin (uIU/ml)	14.99 ± 5.480	16.23 ± 7.75	0.1846	0.1846	0.7196
C-Peptide (ng/ml)	1.23 ± 1.31	2.80 ± 1.80	0.4423	0.4423	0.0673
HOMA-IR	5.02 ± 2.89	4.50 ± 1.71	0.9354	0.9354	0.7625
BMI	33.71 ± 4.95	34.53 ± 1.43	0.3480	0.3480	0.7795

GLR=General Linear Regression, PC=Pearson's Correlation, t-test=students' statistical test, p @ <0.05. C= Wild (Dominant), A=Polymorphic.

With the significant association shown by these other variants discussed above with T2D markers such as adiponectin, C-peptide, HbA1c and fasting insulin without corresponding effect on BMI, we can infer that these variants genotype (rs201041270, rs531215275, rs1410999299, rs145884431, rs146138389 & rs886052102) (Tables 11, 12,13,14,15,16,17, 18 and 19) exercises their effect on T2D independent of BMI in the Niger Delta population, with rs886052102 having the strongest association. This finding is somewhat new and may by supporting the school of thought about ethnic/population context of the various FTO gene variants. This is consistent with results from other studies that suggest different FTO gene variants associated with T2D, obesity or T2D/obesity either together or differently in different ethnic or geographical populations [22]. Evidence of statistical interaction between race

Table 19. Association of FTO rs8050136 variant with glycemic parameters of Obese in Niger Delta tribes using Dominant Model

Parameters	CC (Obese)	CA/AA (Obese)	GLR, p value	PC, p value	T-test, p value
FBS (mmol/L)	7.388 ± 3.01	7.17 ± 2.01	0.6345	0.6345	0.8597
HbA1c (%)	8.48 ± 1.73	9.13 ± 1.53	0.3552	0.3552	0.3787
Adiponectin(mg/L)	8.54 ± 11.41	3.03 ± 0.80	0.4967	0.4967	0.2160
Insulin (uIU/ml)	14.93 ± 4.96	14.53 ± 7.9	0.5807	0.5807	0.8673
C-Peptide ng/ml	1.34 ± 1.45	1.500 ± 1.22	0.5770	0.5770	0.7849
HOMA-IR	5.01 ± 3.06	4.08 ± 1.33	0.6076	0.6076	0.4448
BMI	33.11 ± 4.44	35.57 ± 5.74	0.3784	0.3784	0.2299

GLR=General Linear Regression, PC=Pearson's Correlation, t-test=students' statistical test, p @ <0.05. C= Wild (Dominant), A=Polymorphic.

and the FTO polymorphism shown after combining African American and white participants further suggests that the influence of the FTO gene on diabetes susceptibility may be context dependent [27]. There is also the speculation of genetic architecture of diabetes differing in different ethnic group and variation in other genetic or environmental factors that contribute to the development of T2D may underlie in the apparent disparate effects of the FTO gene in different populations [27].

4. CONCLUSION

The study found a strong association between the variant genotype rs9939609 with obesity in Niger Delta tribes, but no significant independent association with T2D. The type 2 diabetes risk resulting from rs9939609 variant of the FTO gene in this region may be obesity mediated as evidenced by the increases observed in the BMI of the carriers of the risk allele (A). However, findings showed a significant association between some other variants with type 2 diabetes independent of body mass index, especially the rs886052102 and rs201041270 genotype variants.

DISCLAIMER

The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

CONSENT

All authors declare that 'written informed consent was obtained from the patient (or other approved parties) for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editorial office/Chief Editor/Editorial Board members of this journal.

ETHICAL APPROVAL

Ethical approval and permission were sought and obtained from the ethical committee of Federal Medical Centre, Asaba. Informed consent of the participants involved was also obtained using the consent form and anthropometric data was obtained via a questionnaire.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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