

بِسْمِ اللّٰهِ الرَّحْمٰنِ الرَّحِیْمِ

وَعَلَّمَ آدَمَ الْأَسْمَاءَ كُلَّهَا ثُمَّ عَرَضَهُمْ عَلَى الْمَلَائِكَةِ فَقَالَ أَنْبِئُونِي بِأَسْمَاءِ هَؤُلَاءِ  
إِنْ كُنْتُمْ صَادِقِينَ (31) قَالُوا سُبْحَانَكَ لَا عِلْمَ لَنَا إِلَّا مَا عَلَّمْتَنَا إِنَّكَ أَنْتَ الْعَلِيمُ  
الْحَكِيمُ (32)

سورة البقرة

## **Dedication**

I would like to dedicate my work to all of my family and friends, starting with the first person I have known in this world my mother (Fatima) and the man that taught me how to be a good mother inspired me and gave me the opportunity to be where I am today and advised me by his experience to achieving this work to my wonderful father (Ibrahim).

To the people that I have lived most of my life with them, my amazing brothers and sisters whose supporting me, and my beloved sons (Osama and Ahmed).

I also dedicate this thesis to my many friends who have supported me throughout the process. I will always appreciate all they have done.

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## **Abstract**

This study is a case-control hospital-based study conducted from December 2016 to November 2020 in Khartoum State in Sudan.

This study aimed to assessment of fat mass and obesity-associated gene (rs9939609) single nucleotide polymorphism in susceptibility to metabolic syndrome in Sudanese patients.

Two hundred fifteen Sudanese patients diagnosed with metabolic syndrome according to international diabetes federation (IDF) criteria at three different hospitals (Zinam Diabetic Centre, Gaber-Aboeliz, and Rebate Teaching Hospital), age range 37-84 years old. And two hundred fifteen healthy individuals were considered as a control group, age and sex were matched in both groups.

Ethical approval for this study was obtained by Ethical Committee of Ministry of Health, after approving from Scientific Committee of the College of Medical Laboratory Science at Sudan University of Science and Technology, written informed consent was obtained from all study subjects.

Waist circumference, BMI, and blood pressure were measured. Blood samples were analyzed for sd-LDL using the ELISA technique, lipids and fasting blood glucose were measured by Mindray automation, blood genomic DNA was extracted using kits, and genotyped for single nucleotide polymorphisms (rs 9939609) of FTO gene by polymerase chain reaction (PCR-RFLP) analysis. Whole DNA sequencing was done by using HiSeq Macrogen Company (Korea).

Data were computed and analyzed by using SPSS version 21 and bioinformatics tools.

The results of the study showed that there were significantly increased Waist circumference, total cholesterol, triglyceride, LDL-C, fasting blood glucose, Systolic, Diastolic blood pressure, and decreased HDL-C in

patients compared to control with *P*-value (0.000). An insignificant difference was found in sd-LDL in the case compared to control with *P*-value (0.209).

The heterozygous and homozygous mutants a risk factor for metabolic syndrome in our population, with *P*-value (0.000, 0.017) and OR (5.191, 2.297) respectively. The result also showed significantly increased distribution of mutant A allele in metabolic syndrome patients compared to the T allele in healthy individuals.

The FTO (rs9939609) gene polymorphism showed an insignificant association between FTO gene polymorphism and study variable (age, sex, dietary habits, and physical activity), moreover, a significant association was found between the FTO gene and BMI with *P*-value (0.017), on the other hand, significantly increased total cholesterol and dietary intake in AT/AA Genotypes compared to TT genotype.

Insignificant difference in metabolic syndrome components between males and females except in BMI significantly increased in females compared to males with *P*-value (0.016).

In conclusion, the FTO (rs 9939609) gene is considered as a risk factor for metabolic syndrome in Sudanese patients.

## الخلاصة

أجريت هذه الدراسة التحليلية في الفترة مابين ديسمبر 2016 إلى نوفمبر 2020 لتقييم صورة تعدد إشكال النيوكيلوتيد المفردة (رس 9939609) في الجين المتعلق بكتلة الدهون والبدانة لقابلية متلازمة التمثيل الغذائي في ولاية الخرطوم 215 0 شخص من مرضاء متلازمة التمثيل الغذائي تمه تشخيصهم عن طريق منظمة الاتحاد الدولي لسكري، تم جمعهم كمجموعة اختبار من مستشفيات مختلفه (مركز جابر أبو العز لسكري، مركز زنام لسكري ومستشفى الرباط التعليمي) بولاية الخرطوم . تتراوح أعمار المرضى 37-84 وتم جمع 215 من الأشخاص الأصحاء بنفس أعمار المرضاء من نفس النوع من النساء والرجال كمجموعة مكافئه ضابطة . تم أخذ موافقة الدراسة من وزارة الصحة، وبعد اجازة خطة البحث من كلية المختبرات الطبية لجامعة السودان، وتم اخذ موافقة المرضاء الذين لهم الرغبة للمشاركة في هذه الدراسة. تم قياس محيط الخصر، ومؤشر كتلة الجسم وقياس ضغط الدم .ومن ثم تم أخذ عينات من الدم من كلا المجموعتين (مجموعة الاختبار والمجموعة الضابطة) تم قياس sd-LDL عن طريق جهاز الاليزا، والدهون وجلكوز الدم الصائم عن طريق جهاز مندرى، كما تم استخلاص الحمض النووي باستخدام طريقة الكتس لأداء تقنية تفاعل البلمره المتسلسل لتضاعف الحمض النووي واستخدام تقنية طول قطعة تعدد الإشكال للتعرف علي النمط الجيني . كما تم حساب البيانات وتحليلها بواسطة برنامج الحزمة الاحصائية للعلوم الاجتماعية (SPSS النسخة 21).

أظهرت نتائج الدراسة أن هناك أهمية في زيادة محيط الخصر، والكلوسترول، والدهون الثلاثية، والبروتين الصغير (LDL-C)، وجلكوز الدم، وزيادة ضغط الدم ونقصي البروتين مرتفع الكثافة (HDL-C) مقارنة مع المجموعة الضابطة القيمة الاحتمالية (0.000)، كما لا يوجد هناك فرق ذو دلالة احصائية في البروتين الصغير مرتفع الكثافة (sd-LDL) بين مجموعة الاختبار والمجموعة الضابطة القيمة الاحتمالية (0.297).

اشارت الدراسه ان الطفرات متغايرة الزيجوت والطفرات متماثلة اللواقح عامل خطر لمتلازمة التمثيل الغذائي القيمة الاحتمالية (0.017 و 0.000) علي التوالي. كما اثبتت الدراسه ان الأليل المتنحي للصورة المتعددة الجينية (رس 9939609) لجين السمنه والبدانه يزيد في الاشخاص المرضاء مقارنة مع الاصحاء 0

اظهرت نتائج الدراسة ان تعدد الاشكال الجيني (رس 9939609) لجين كتلة الدهون والبدانه مرتبط ارتباطا ضئيلا بي متغيرات الدراسة (العمر، الجنس، العادات الغذائية والنشاط البدني) عند

المرضاء. كما يوجد علاقة ذات دلالة احصائية بين تعدد الاشكال الجيني (رس9939609 ) لجين كتلة الدهون والبدانه وموشر كتلة الجسم القيمة الاحتمالية (0.017). من ناحيه اخري توجد هناك زياده كبيره معنويه في الكوليسترول الكلي والمتناول الغذائي في متغاير الزيجوت ومتمائل الزيجوت عند المرضي مقارنة بالافراد الاصحاء. كما يوجد اختلاف طفيف في مكونات متلازمة التمثيل الغذائي بين الاناث والذكور لكن توجد أهمية ذات دلالة احصائية لزيادة مؤشر كتلة الجسم عند الاناث مقارنة مع الذكور القيمة الاحتمالية (0.016).

ختاما أثبتت نتائج الدراسة أن وجود الأليل المتنحي للصورة المتعددة المنفرده (رس9939609) في كتلة جين الدهون والبدانه يمثل عامل خطر لمرضي متلازمة الايض في السودان .

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## List of Abbreviation

Abbreviation	Full name
BMI	Body Mass Index
BMR	Basal Metabolic Rate
BP	Blood Pressure
cAMP	cyclic Adenosine Mono phosphate
CE	Cholesterol Esters
CETP	Cholesterol Ester Transfer protein
CHE	Cholesteryl Esterase
CHO	Cholesterol Oxidase
DNA	Deoxyribonucleic Acid
EDTA	Ethylene Diamine Tetra Acetate
ELISA	Enzyme Linked Immunosorbent assay
ESC	European Society of Science
ESH	European Society of Hypertension
FBG	Fasting Blood Glucose
FFA	Free Fatty Acids
GLUT4	Glucose Uptake Transport 4
GWAS	Genome Wide Association studies
H <sub>2</sub> O <sub>2</sub>	Hydrogen Peroxide
HDL-C	High Density Lipoprotein Cholesterol
HMG-CO	Hydroxyl Methyl Glutaryl Coenzyme A
HSL	Hormone Sensitive Lipase
IDF	International Diabetes Federation
IGT	Impaired Glucose Tolerance
IR	Insulin Resistance
IRS	Insulin Resistance Substrate
ISBN	International Standard Book Number

LDL-C	Low Density Lipoprotein Cholesterol
LP	Lipoprotein
MHO	Metabolic Health Obese
MTOR	Mammalian Target of Rapamycin
NCEP	National Cholesterol Education Program
NDSR	National Diabetes Statistics Report
NEFA	Non Esterified Fatty Acid
NHNES	National Health and Nutrition Examination
O <sub>2</sub>	Oxygen
OD	Optical Density
PA	Physical Activity
PAMELA	Pressioni Arteriose Monitorate E loro Association
PCR	Polymerase Chain Reaction
PI3K	Phosphatidyl Inositol -3-Kinase
PKC	Protein Kinase C
POD	Peroxidase
RFLP	Restriction Fragment Length polymorphism
S6KI	S 6 Kinase bete 1
SdLDL	Small dense Low density lipoprotein
SNP	Single Nucleotide Polymorphism
SREBPs	Sterol Regulatory Element Binding Proteins
T2DM	Type 2 Diabetes Mellitus
TG	Triglyceride
UTR	UN Translated Region
VLDL	Very Low Density Lipoprotein
WHO	World Health Organization