بسم الله الرحمن الرحيم

تم رفع هذه الرسالة بواسطة / سلوي محمود عقل

بقسم التوثيق الإلكتروني بمركز الشبكات وتكنولوجيا المعلومات دون أدنى مسئولية عن محتوى هذه الرسالة.

ملاحظات:
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Correlation between Primary Knee Osteoarthritis and Metabolic Syndrome among Egyptian Patients

Thesis

Submitted for Partial fulfillment of Master Degree in Internal Medicine

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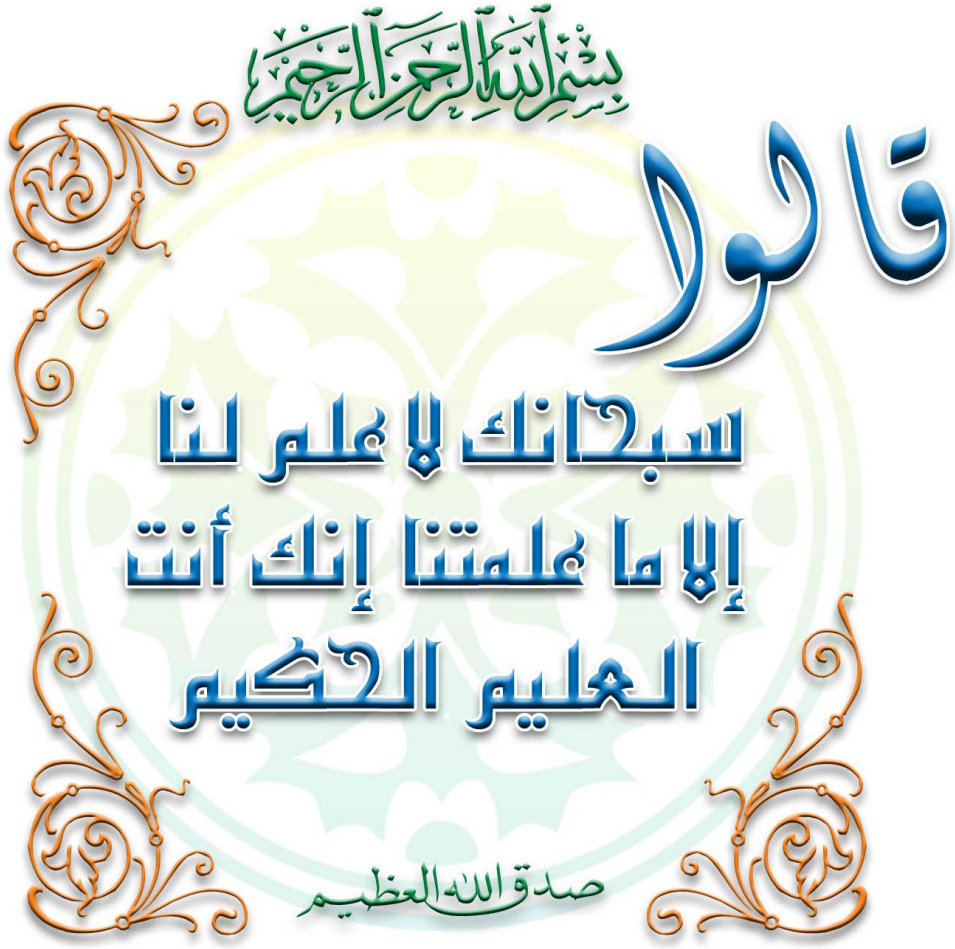
2021



سورة البقرة الآية: ٣٢

Acknowledgment

First and foremost, I feel always indebted to **ALLAH,**
the Most Kind and Most Merciful.

I'd like to express my respectful thanks and profound gratitude to **Prof. Dr. Amina Badreldin Abdelaziz,** *Professor of Internal Medicine and Rheumatology, Faculty of Medicine, Ain Shams University for her keen guidance, kind supervision, valuable advice and continuous encouragement, which made possible the completion of this work.*

I am also delighted to express my deepest gratitude and thanks to **Ass. Prof. Dr. Nashwa ALy Morshedi,** *Assistant Professor of Internal Medicine and Rheumatology, Faculty of Medicine, Ain Shams University, for her kind care, continuous supervision, valuable instructions, constant help and great assistance throughout this work.*

I am deeply thankful to **Dr. Sara Farid Samaan,** *Lecturer of Internal Medicine and Rheumatology, Faculty of Medicine, Ain Shams University, for her great help, active participation and guidance.*

Sabreen Abdelkader Mahmoud

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List of Abbreviations

Abb.	Full term
AC	Articular cartilage
ACEIs	Angiotensin receptor blockers and converting enzyme inhibitors
ACL	Anterior Cruciate Ligament
ADAMTS	A disintegrin and metalloproteinase with thrombospondin motifs
ALT	Alanine aminotransferase
AMPK	AMP-activated protein kinase
AP	Anteroposterior
AST	Aspartate aminotransferase
BA	Betamethasone Acetate
BMI	Body mass index
BML	Bone marrow lesions
BSP	Beta-methasone Sodium Phosphate
CAD	Coronary artery disease
CBC	Complete blood count
CCL5	Chemokine ligand 5
COX-2	Cyclooxygenase-2
CR	Conventional Radiology
CRP	C-reactive protein
CS	Corticoids
CVD	Cardiovascular diseases
DM	Diabetes mellitus
DMM	Destabilization of the medial meniscus
DNA	Deoxyribonucleic acid
DPP	Diabetes Prevention Program
DPP4	Dipeptidyl peptidase 4
ECM	Extracellular matrix

List of Abbreviations Cont...

Abb.	Full term
EGIR	European Group for the Study of Insulin Resistance 1999
ESCEO	Economic Aspects of Osteoporosis and Osteoarthritis
ESR	Erythrocyte sedimentation rate
FDA	Food and Drug Administration
FFAs	Free fatty acids
FGFs	Fibroblast growth factors
GAG	Glycosaminoglycan
GHSR-1a	GH secretagogue receptor 1a
GLP-1	Glucagon-like-peptide 1
GLUT-1	Glucose transporters
HAQ	Health assessment questionnaire
HAQ-DI	Health Assessment Questionnaire-Disability Index
HDL	High-density lipoprotein
HIF2α	Hypoxia-inducible factor 2 α (),
HLA	Human leukocyte antigen
HMW	High molecular weight
HOMA-IR	Homeostasis Model Assessment-Insulin Resistance
HPLC	High-performance liquid chromatography
IDF	International Diabetes Federation
IGFs	Insulin-like growth factors
IGT	Impaired glucose tolerance
IL	Interleukin
IPFP	Infrapatellar fat pad
IR	Immediate Release

List of Abbreviations Cont...

Abb.	Full term
IRS	Insulin receptor substrate
K–L	Kellgren and Lawrence
KOA	Knee OA
LAR	Leptin/adiponectin ratio
LDL	Low-density lipoprotein
LKB4	Leukotrienes
MA	Methylprednisolone Acetate
MCP-1	Monocyte chemoattractant protein 1
MetS	Metabolic syndrome
MMP	Matrix metalloproteinases
MRC	Mitochondrial electron transport chain
MRI	Magnetic Reasonant Imaging
MT	Meniscal tear
MTP	Metatarsophalangeal
NAFLD	Non-alcoholic fatty liver disease
NAMPT	Nicotinamide phosphoribosyltransferase
NCEP	National Cholesterol Education Program
ncRNA	Non-coding RNA
NFκB	Nuclear factor kappa B
NGF	Nerve growth factor
NHANES	National Health and Nutrition Examination Survey
NO	Nitric oxide
NOS2	Nitric oxide synthase
NPY	Neuropeptide Y
NSAIDs	Non-steroidal anti-inflammatory drugs
OA	Osteoarthritis
OxLDL	Oxidized LDL

List of Abbreviations Cont...

Abb.	Full term
PGE2	Prostaglandin E2
PKC	Protein Kinase C
PMN	Polymorphonuclear
PON-1	Paraoxonase-1
PRP	Platelet rich plasma
PUFAs	Polyunsaturated fatty acids
RAS	Renin-angiotensin system
RF	Rheumatoid Factor
ROS	Reactive oxygen species
SFA	Saturated fatty acids
SGLT2	Sodium-glucose co-transporter 2
T2DM	Type 2 diabetes mellitus
TA	Triamcinolone Acetate
TGFβ	Transforming growth factor-β
TGs	Triglycerides
TH	Triamcinolone Hexacetonide
TNF	Tumor Necrosis Factor
TNF-α	Tumor necrosis factor alpha
US	Ultrasound
VEGF	Vascular Endothelial Growth Factor
VLDL	Very-low-density lipoprotein
WBC	White Blood Cell
WC	Waist circumference
WHO	World Health Organization
WOMAC	Western Ontario and McMaster Universities Osteoarthritis Index

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INTRODUCTION

Osteoarthritis (OA) is a chronic, debilitating joint disease characterized by degenerative changes in the bones, cartilage, menisci, ligaments, and synovial tissues and is therefore considered a disease of the whole joint ***(Wick et al., 2014).***

Metabolic syndrome is defined as presence of any three components out of five, i.e., high waist circumference (in males ≥ 94 cm, in females ≥ 80 cm),Raised triglycerides: ≥150 mg/dl (1.7 mmol/l) or history of specific treatment for this lipid abnormality, low HDL (< 40 mg/dl (1.03 mmol/l) in males and < 50 mg/dl (1.29 mmol/l) in females or lipid-lowering medication), hypertension (≥130/85 mmHg or treatment for hypertension), Raised Fasting plasma gluocose: (≥ 100 mg/dl or previously diagnosed type 2 DM ***(Alberti et al., 2009).***

Knee is the largest synovial joint in humans; it is composed by osseous structures (distal femur, proximal tibia, and patella), cartilage (meniscus and hyaline cartilage), ligaments and a synovial membrane. The latter is in charge of the production of the synovial fluid, which provides lubrication and nutrients to the avascular cartilage ***(Sharma et al., 2017).***

Metabolic syndrome may affect the occurrence of OA through low-grade inflammation, by altering the microvasculature of subchondral bone, or by causing neuromuscular impairment ***(Richards et al., 2016).***

Metabolites characteristics including energy metabolism and lipid and carbohydrate metabolism in the OA patients' synovial tissue cultures were significantly decreased compared with those with little or no evidence of the disease ***(Zhang et al., 2015).***

Recent epidemiological and clinical data have highlighted that a metabolic syndrome (MetS) rather than obesity itself has the greatest impact on the initiation and severity of OA ***(Haugen et al., 2011).***

Beyond the role of common pathogenic mechanisms for metabolic diseases and osteoarthritis (i.e., low-grade inflammation and oxidative stress), metabolic diseases have a direct systemic effect on joints. In addition to the impact of weight, obesity-associated inflammation is associated with osteoarthritis severity and may modulate osteoarthritis progression ***(Courties et al., 2017).***

In OA, the synovial fluid has been found to contain multiple inflammatory mediators including plasma proteins (C-reactive protein, proposed as a marker for development and progression of OA), prostaglandins (PGE2), leukotrienes (LKB4), cytokines (TNF, IL1β, IL6, IL15, IL17, IL18, IL21), growth factors (TGFβ, FGFs, VEGF, NGF), nitric oxide, and complement components ***(Robinson et al., 2016).***

The role of inflammation is not well-understood and there is an ongoing debate to determine if the inflammatory reaction triggers the OA changes, or instead, the inflammation is secondary to the OA changes ***(Ayhan et al., 2014).***