بسم الله الرحمن الرحيم

MONA MAGHRABY

شبكة المعلومات الجامعية

التوثيق الالكتروني والميكروفيلم

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جامعة عين شمس

التوثيق الإلكتروني والميكروفيلم

قسم

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علي هذه الأقراص المدمجة قد أعدت دون أية تغيرات

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MONA MAGHRABY

Evaluation of Reduced Glutathione Plasma Level in Type 2 Diabetic Patients with Fatty Liver

Thesis

Submitted for the Partial Fulfillment of
Master's Degree in Clinical Nutrition

By

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Dalia Abdelwahab

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List of Abbreviations

Abb.	Full term
AGES	*Advanced glycation end products*
ALT	*Alanine aminotransferase*
AOPP	*Advanced oxidant protein products*
AST	*Aspartate aminotransferase*
BMI	*Body mass index*
CAT	*Catalase*
CM	*Centimeters*
CMRS	*Chylomicrons remnants*
CMS	*Chylomicrons*
CRP	*C-Reactive Protein*
ELISA	*Enzyme-linked immunosorbent assay*
FFAS	*Free Fatty acids*
FFQ	*Food-fréquence questionnaire*
GGT	*Gamma-glutamyl transférase*
GSH	*Reduced glutathione*
GSR	*Glutathione reductase*
GSSG	*Oxidized glutathione*
H1-MRS	*Proton magnetic resonance spectroscopy*
HBA1C%	*Glycosylated hemoglobin*
HCC	*Hepatocellular carcinoma*
IDF	*International diabetes federation*
IL10	*Interleukin-10*
IL6	*Interleukin-6*
KG	*Kilogram*
LFT	*Liver function tests*
LPS	*Lipopolysaccharides*
MDA	*Malondialdehyde*
Mit	*Mitochondria*
NAC	*N-acetylcysteine*
NADPH	*Nicotinamide adenosine dinucleotide phosphate*
NAFL	*Non-alcoholic fatty liver*

List of Abbreviations **cont...**

Abb.	Full term
NAFLD	*Non-alcoholic fatty liver disease*
NAS	*NAFLD activity score*
NASH	*Non-alcoholic steatohepatitis*
NO	*Nitrogen oxide*
OGTT	*Oral glucose tolerance test*
PBS	*Phosphate Buffered Saline*
PKC	*Protein kinase c*
PM10	*Particulate matter 10*
P-VALUE	*Probability that statistics results get by chance*
r	*Correlation coefficient*
ROS	*Reactive oxygen species*
SAM	*S-adenosyl-l-methionine*
SBP	*Systolic blood pressure*
SD	*Standard deviation*
SPSS	*Statistical package for social science*
T2DM	*Type 2 diabetes*
TG	*Triglycerides*
TMB	*3,3',5,5'-Tetramethylbenzidine*
TNF alpha	*Tumor Necrosis Factor alpha*
T-TEST	*Student t-test*
U	*Mann-Whitney u test*
VLDLS	*Very-low-density lipoproteins*
WC	*Waist circumference*
WHR	*Waist: hip ratio*
µg	*Microgram*
µL	*Microlitre*
µmoL	*Micromole*
µM	*Micromolar*

INTRODUCTION

Diabetes Mellitus is a group of metabolic diseases characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both. The chronic hyperglycemia of diabetes is associated with long-term damage, dysfunction, and failure of different organs, especially the eyes, kidneys, nerves, heart, and blood vessels ***(Dennedy et al., 2015).***

Type 2 diabetes (T2DM) and its complications represent a major worldwide public health challenge, with high-rate morbidity and mortality ***(Narayan, 2016).*** Type 2 diabetes, previously referred to as "non-insulin-dependent diabetes" or "adult-onset diabetes," accounts for 90–95% of all diabetes. This form encompasses individuals who have relative (rather than absolute) insulin deficiency and have peripheral insulin resistance ***(Herman et al., 2017).*** In several developing countries, many of type 2 diabetic patients exhibit poor glycemic control which represents a major problem ***(Ferguson et al., 2013).*** Chronic hyperglycemia leads to oxidative stress that often associated with the development of microvascular diabetic complications and increases the risk of diabetic macrovascular disease ***(Bigagli & Lodovici, 2019).*** Hyperglycemia-induced cellular damage through several mechanisms including oxidative stress (i.e. increased superoxide production), increased advanced glycation end

products formation, polyol pathway activity and protein kinase C activation ***(Whiting et al., 2008)***.

Fatty liver is a clinical condition characterized by accumulation of lipids within hepatocytes so when hepatic fat content exceeding 5% of the liver weight this considered as fatty liver ***(El-Serag et al., 2004)***. It is commonly related to various components of metabolic syndrome including obesity, diabetes mellitus, and dyslipidemia ***(Kumar et al., 2020).*** Non-alcoholic fatty liver disease (NAFLD) has a great focus worldwide, as it is expected to affect 75% of patients with type2 diabetes mellitus (T2DM) ***(Adams et al., 2017).*** According to some studies, up to 30% of patients with NAFLD progress to non-alcoholic steatohepatitis (NASH) and further to liver cirrhosis and hepatocellular carcinoma (HCC) ***(Lee et al., 2021).***

Glutathione is a major intracellular antioxidant and plays a key role in reducing the effects of oxidative stress ***(Wu et al., 2004).*** Glutathione is a tripeptide that plays an essential role in serious physiological processes affecting the maintenance of redox balance, reduction of oxidative stress and enhancement of metabolic detoxification ***(Minich & Brown, 2019)***. Several research reported that erythrocyte reduced glutathione (GSH) concentration is decreased in patients with type 2 diabetes. However, the exact mechanisms accountable for glutathione deficiency in type 2 diabetes have not been fully well-known ***(Lutchmansingh et al., 2018).*** It is seeming that enhancing dietary intake of glutathione precursors, co-factors, and whole

foods could improve health by optimizing glutathione status in our body. These dietary sources include lean protein sources, brassica vegetables, polyphenol-rich fruits and vegetables, herbs and spices, green tea, and omega-3 fatty acid rich-foods such as fish ***(Minich & Brown, 2019).***

AIM OF THE WORK

The aim of this study is to assess reduced glutathione plasma level then evaluate its correlation with the dietary factors, fasting blood glucose levels, HBA1c and lipid profile in type 2 diabetic patients with fatty liver.