Association between Insulin Resistance and Gastro-esophageal Reflux Disease

Thesis

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بِسْمِ اللّهِ الرّحمَنِ الرّحيمِ

(...رَبِّ أَوزعنِي أَن أَشكُرَ نِعمَتَكَ الّتِي أَنْعَمْتَ عَلَيَّ و عَلى والِدَيَّ

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Mohamed Mahmoud Mohamed Said

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List of Abbreviations

ACE : Angiotensin converting enzyme
ACh : Acetylcholine
AHA : American Heart Association
AMPK : AMP-activated protein kinase
ARBs : Angiotensin receptor blockers
ATP : Adenosine triphosphate
baPWV : Brachial-ankle pulse wave velocity
BMI : Body mass index
BP : Blood pressure
CGIT : Combined glucose-insulin test
CGMS : Continuous glucose monitoring system
CGRP : Calcitonin gene-related peptide
CHD : Coronary heart disease
COPD : Chronic obstructive pulmonary disease
cRDQ : Core Reflux Disease Questionnaire
CRP : C-reactive protein
DBP : Diastoli blood pressure
DGER : Duodenogastroesophageal reflux
DMN : Dorsal motor nucleus
EE : Erosive esophagitis
EGD : Esophagogastroduodenoscopy
ERD : Erosive reflux disease
ENOS : Endothelial nitric oxide synthase
ER : Endoplasmic Reticulum
FAs : Fatty acids
FBI : Fasting blood suger
FBS : Fasting blood insulin
FDA : Food and Drug Administration
FSIVGTT : Frequently sampled IV glucose tolerance tests
GEJ : Gastroesophageal junction
GERD : Gastroesophageal refux disease
GLP-1 : Glucagon-like peptide-1

List of Abbreviations *(Cont...)*

GPR120 : G-protein coupled receptor 120
H.Pylori : Helicobacter pylori
H2RAs : Histamine 2 receptor antagonists
HDL : High density lipoprotein
HGD : High-grade dysplasia
HOMA : Homeostatic model assessment
HPA : Hypothalamus pituitary axis
IDF : International Diabetes Federation
IHS : International Health Services
IL-1 : Interleukin-1
IM : Intestinal Metaplasia
IR : Insulin resistance
IRAS : Insulin Resistance Atherosclerosis Study
IRS : Insulin receptor substrate
ISI : Insulin sensitivity index
IST : Insulin sensitivity test
LA : Los Angeles
LDL : Low density lipoprotein
LES : Lower esophageal sphincter
LGD : Low-grade dysplasia
MODY : Maturity Onset diabetes of the Young
MS : Metabolic syndrome
NAFLD : Nonalcoholic fatty liver disease
NCEPATP : National Cholesterol Education Programme Adult Treatment Panel
NERD : Nonerosive disease
NO : Nitric oxide
NTS : Nucleus tractus solitarius
OGTT : Oral glucose tolerance test
OSA : Obstructive sleep apnea
PAI-1 : Plasminogen activator inhibitor-1
PCOS : Poly Cystic Ovarian Syndrome
PPID : Pituitary pars intermedia dysfunction

List of Abbreviations *(Cont...)*

PPIs : Proton pump inhibitors
PTH : Parathyroid hormone
QOL : Quality of life
SBP : Systolic blood pressure
SCJ : Squamocolumnar junction
SD : Standard deviation
SHBG : Sex-hormone binding globulin
SP : Substance P
SPSS : Statistical Program for Social Science
T2DM : Type 2 diabetes
TG : Triglycerides
TC : Total cholesterol
TLESRs : Transient lower esophageal sphincter relaxations
TNF : Tumor necrosis factor
UA : Uric acid
UES : Upper esophageal sphincter
US : United State
VIP : Vasoactive intestinal peptide
WHO : World Health Organization
11β-HSD1 : 11β-Hydroxysteroid Dehydrogenase Type 1

Introduction

Gastroesophageal refux disease (GERD) is defined as an abnormal reflux of gastric contents into the esophagus at least once a week, leading to symptoms such as heartburn and/or acid regurgitation, and/or esophageal mucosal damage, which may also provoke long-term complications, such as Barrett's esophagus ***(Lerardi et al.,2010).***

Metabolic syndrome, which includes interrelated risk factors for cardiovascular disease and diabetes, is a common disorder that threatens public health in many countries ***(Alberti et al., 2009).*** Recent studies have identified that insulin resistance (IR), a principal component of metabolic syndrome, as well as related metabolic abnormalities, plays a role in carcinogenesis ***(Chen et al., 2008).***

In addition, the various metabolic syndrome components increase the risk of several non cardiovascular diseases, such as non-alcoholic fatty liver disease, polycystic ovary syndrome, obstructive sleep apnoea ***(Eckel et al., 2005),*** and GERD ***(Chung et al., 2008).*** GERD is known not only to affect the quality of patients' lives but may also increase the risk of oesophageal adenocarcinoma ***(Lee et al., 2009).***

Unfortunately, GERD is becoming increasingly prevalent in Asia, where it is currently estimated to affect more than 10% of the population ***(Goh, 2011).*** Identification of risk factors for