Relation of Lactobacilli Acidophilus to Non-Alcoholic Fatty Liver in A Sample of Egyptian Population

Thesis

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By

Kamal Mohie El-din Selim

M.B.B.Ch.

Under Supervision of

Prof. Dr. Magda Shokry Mohamed

Professor of Internal Medicine, And Endocrinology
Faculty of Medicine- Ain Shams University

Prof. Dr. Yara Mohamed Eid

Professor of Internal Medicine, And Endocrinology
Faculty of Medicine- Ain Shams University

Dr. Nagwa Roshdy Mohamed

Lecturer of Internal Medicine, And Endocrinology
Faculty of Medicine- Ain Shams University

Faculty of Medicine
Ain Shams University
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List of Abbreviations

Abb.	Full term
AASLD	American association for the study of liver disease
ACG	American college of gastroenterology
AGA	American gastroenterological association
AHA	American Heart Association
ALP	Alkaline phosphatase level
ALT	Alanine transaminase
ANA	Antinuclear antibodies
ARBs	Angiotensin II receptor blockers
ASMA	Anti smooth muscle antibody
AST	Aspartate aminotransferase
BMI	Body mass index
CAP	Controlled attenuation parameter
CBC	Complete blood count
CDAD	Clostridium Difficile Associated Diarrhea
CT	Computed tomography
CUS	Conventional ultrasonography
CVD	Cardiovascular diseases
DM	Diabetes Mellitus
FGF15	Fibroblast grown factor 15
FIB-4	Fibrosis-4 Index
FLI	Fatty Liver Index
FMF	Familial Mediterranean Fever
FXR	Farnesoid X receptor
GF	Germ free
GGT	Gamma glutamyl transferase

Abb.	Full term
GWAS	Genome wide association studies
HBV	Hepatitis B virus
HCC	Hepatocellular carcinoma
HCV	Hepatitis C virus
HDL-C	High-density lipoprotein cholesterol
HFD	High fat diet
HIS	Hepatic Steatosis Index
IBD	Inflammatory bowel disease
IgA	Immunoglobulin A
IHTG	Intrahepatic triglyceride
IR	Insulin resistance
LC	Liver cirrhosis
LPS	Lipopolysaccharide
LSM	Liver stiffness measurement
MCDD	Methionine-choline deficient diet
MetSyn	Metabolic syndrome
MRE	Magnetic resonance elastography
MRI-PDFF	Magnetic resonance imaging proton density fat fraction
MRS	Magnetic resonance spectroscopy
NAFLD	Non-alcoholic fatty liver
NASH	Non-alcoholic steatohepatitis
NFS	NAFLD Fibrosis Score
NHLBI	National Heart, Lung, and Blood Institute
NLRs	NOD-like receptors
PEMT	Phosphatidylethanolamine N-methyltransferase
PH	Portal hypertension

Abb.	Full term
SCFAs	Short chain fatty acids
SPEP	Serum protein electrophoresis
TIBC	Total iron binding capacity
TG	Triglyceride
TLRs	Toll-like receptors
TNF-α	Tumour necrosis factor alpha
TPN	Total parentral nutrition
VCTE	Vibration-controlled transient elastography
VLDL	Very low-density lipoprotein
VRE	Vancomycin resistant enteorococci

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Relation of Lactobacilli Acidophilus to Non-Alcoholic Fatty Liver in A Sample of Egyptian Population

Abstract

Background: The gut microbiota and its characterization have become a major research area in biomedicine. Some recent studies have suggested that they play a fundamental role in some metabolic diseases like obesity, cardiovascular diseases and non alcoholic fatty liver.

Aim of Work: To detect possible relation of lactobacilli Acidophilus to non-alcoholic fatty liver disease in a sample of Egyptian population, as a preliminary approach to future treatment with probiotics, prebiotics or diet modulation.

Methodology: The study included 60 patients divided into three groups; 20 obese subjects with non-alcoholic fatty liver (NAFLD), 20 lean subjects with non-alcoholic fatty liver (NAFLD) and 20 healthy subjects as control group lean without fatty liver.

Results: The results of this study showed: **(1)** No statistically significant difference among the study groups regarding stool Lactobacillus Acidophilus positive/negative results. **(2)** Significantly higher serum ALT & AST among NAFLD obese patients when compared to healthy control individuals. **(3)** Significantly higher total Cholesterol, triglycerides and LDL among NAFLD obese patients when compared to healthy control individuals. **(4)** Significantly higher HDL among healthy control individuals when compared with NAFLD obese and NAFLD lean groups. **(5)** Significantly higher FBG, 2hrsPPBG and HbA1c among NAFLD obese patients when compared to healthy control individuals. **(6)** Significant negative correlation between the cycle threshold PCR of lactobacillus acidophilus and serum liver enzymes ALT & AST in the control group. As the concentration of lactobacillus acidophilus increases, the ALT & AST tended to increase among the control group.

Conclusion: In this study we tried to find the relation between Lactobacillus Acidophilus and NAFLD, it included links related to serum ALT & AST in the control group, which are considered as surrogate markers of hepatic steatosis. It is still premature to put facts from this study, yet preliminary data suggest that Lactobacillus Acidophilus is correlated with ALT & AST. Experimental studies suggest that modulation of gut microbiota may be effective towards prevention and management of NAFLD and further investigations can lead to the use of these new opportunities.

Recommendation: Further studies with bigger sample size and more diverse population are needed to examine the relationship between Non alcoholic fatty liver, total plasma Cholesterol and LDL and the gut microbiome Lactobacillus Acidophilus.

Keyword: Gut microbiota, Non alcoholic fatty liver, Obesity.

Introduction

Non-alcoholic fatty liver (NAFLD) is defined by pathologic accumulation of fat in the liver and is regarded the most common liver disease worldwide, with an estimated prevalence of around 25-30% **(Ampuero et al., 2016).**

While NAFLD is generally a symptomatic, NAFLD patients feature an increased risk for development of other manifestations of the metabolic syndrome and accompanying complications such as cardiovascular diseases **(Corey et al., 2016).**

Non -alcoholic fatty liver, ranges from simple steatosis to inflammatory non-alcoholic steatohepatitis (NASH), with or without fibrosis, which frequently progress to life threatening disorders such as cirrhosis and hepatocellular carcinoma (HCC) **(Smagris et al., 2015).**

The relation between the gut microbiota and human health is being increasingly recognized. The normal gut microbiota has specific function in host nutrient metabolism, xenobiotic and drug metabolism, maintenance of structural integrity of the gut mucosal barrier, immunomodulation, and protection against pathogens **(Lagier et al., 2015).**

Gut microbiome represents a significant environmental factor contributing to non-alcoholic fatty liver development and its progression into non-alcoholic steatohepatitis **(Mouzaki et al., 2013).**

Several mechanisms have been suggested for the microbiome role in NAFLD and its complications; These include microbiome-induced regulation of gut barrier and inflammatory responses and metabolites produced or modified by the microbiota such as short-chain fatty acids, bile acids, and ethanol.

Microbiota populations are compositionally dynamic, and its changes in microbial population structure can occur under multiple environmental, immune, and nutritional circumstances **(Rooks and Garrett, 2016).**

There are only a limited number of studies that have examined microbiota composition in patient with simple steatosis or non-alcoholic steatohepatitis, and these have very dissimilar results **(Boursier et al., 2016).**

Also published data conducted upon Egyptian population included only one study that was conducted in diabetics with steatosis **(Abu Shanab, 2008).**

Aim of the Work

The aim of this work is to detect possible relation of lactobacillus acidophilus to non-alcoholic fatty liver disease in a sample of Egyptian population.

Non Alcoholic Fatty Liver

Fatty liver is the accumulation of triglycerides and the other fats in the liver cells. The amount of fatty acid in the liver depends on the balance between the processes of delivery and removal. In some patients, fatty liver may be accompanied by hepatic inflammation and liver cell death (steatohepatitis) **(Larter et al., 2008).**

Potential pathophysiological mechanisms for fatty liver include the following:-

- Decreased mitochondrial fatty acid beta-oxidation.
- Increased endogenous fatty acid synthesis or enhanced delivery of fatty acids to the liver.
- Deficient incorporation or export of triglycerides as very low-density lipoprotein (VLDL) **(Guy et al., 2012).**

No single pathway of cause and effect has been found. However, some studies show higher levels of activation of Hedgehog pathways (a signaling pathway that transmits information to embryonic cells required for proper cell differentiation. Different parts of the embryo have different concentrations of hedgehog signaling proteins. Activation of hedgehog pathway in the adult has been implicated in development of some diseases and cancers in various

organs) in patients with the most advanced fatty liver disease **(Guy et al., 2012).**

It was reported that in non-alcoholic fatty liver disease (NAFLD), a pro-coagulant imbalance processes from steatosis to metabolic cirrhosis, which may be caused by an increase in factor VIII and a reduction in protein C. The investigators speculated that this imbalance could play a role in the risk for cardiovascular disease and liver fibrosis, conditions commonly associated with NAFLD **(Tripodi et al., 2014)**.

Stages of non alcoholic fatty liver:

NAFLD develops in 4 main stages.

Most people will only ever develop the first stage, usually without realising it. In a small number of cases, it can progress and eventually lead to liver damage if not detected and managed. The main stages of NAFLD are:

1. **Simple fatty liver (steatosis)**- a largely harmless build-up of fat in the liver cells that may only be diagnosed during tests carried out for another reason.
2. **Non-alcoholic steatohepatitis (NASH)**- a more serious form of NAFLD, where the liver has become inflamed.