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List of Abbreviations

ALT: Alanine transaminase.

AST: Aspartate transaminase.

Asp: Aspartate

BMI: Body mass index.

BUN: Blood urea nitrogen.

CBC: Complete blood count.

CK18: Cytokeratin 18 Fragments

CT: Computerized Tomography

FBS: Fasting blood sugar

HBV: Hepatitis B virus.

HBA1C: hemoglobin A 1 C (Glycohemaglobin)

HCC: Hepatocellular carcinoma.

HCV: Hepatitis C virus.

HELLP: **H**emolysis, **E**levated **L**iver enzymes, **L**ow **P**latelet count

HTN: Hypertension.

HU: Hounsfield unit

IDDM: Insulin dependent Diabetes Mellitus.

List of Abbreviations (Cont.)

INR: International normalized ratio.

kDa: atomic mass unit = kilo dalton

LDL: Low density lipoprotein.

MAB: Monoclonal antibodies

MR: Magnetic Resonance.

NAFL: Nonalcoholic Fatty Liver

NAFLD: Nonalcoholic Fatty Liver Disease

NAS: NAFLD Activity Score

NASH: Nonalcoholic Steatohepatitis

PIVENS: Pioglitazone versus Vitamin E versus Placebo for the Treatment of Non-diabetic patients with Nonalcoholic steatohepatitis

PT: Prothrombin time.

PTT: Partial thromboplastin time.

SD: Standard deviation.

T2DM: Type 2 Diabetes Mellitus

TG: Triglycerides

U/S: Ultrasound

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Role of cytokeratin 18 in early detection of liver fibrosis in patients of nonalcoholic steatohepatitis in comparison with liver biopsy

Thesis
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دور الكراتين الخلوى 18 في الكشف المبكر عن تليف الكبد في المرضى الذين يعانون من ألتهاب الكبد الدهنى الغير كحولي بالمقارنة مع عينة الكبد

رسالة
المقدمة للحصول على ماجستير طب الباطنة العامة

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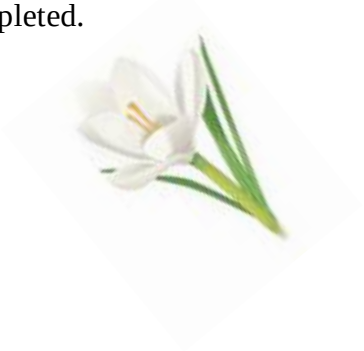

سورة البقرة الآية: ٣٢

Introduction

Fatty liver is the accumulation of triglycerides and 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. NAFLD encompasses a wide spectrum of conditions associated with over accumulation of fat in the liver ranging from nonalcoholic fatty liver disease (NAFLD) or simple steatosis to nonalcoholic steatohepatitis (NASH) and cirrhosis. ***(Bacon et al., 2004)***

Although Nonalcoholic fatty liver disease (NAFLD) typically follows a benign non progressive clinical course, NASH is a potentially serious condition; as many as 25% of patients may progress to cirrhosis and experience complications of portal hypertension, liver failure, and hepato-cellular carcinoma. (***Larter et al., 2006)***

NAFLD is the most common form of chronic liver disease in both children and adults and threatens to become a serious public health problem. The prevalence of NAFLD and NASH are higher than previously estimated among predominantly middle-aged patients. Although all ethnicities

are affected and patients have varying degrees of insulin sensitivity, Diabetic patients appear to be at the greatest risk for both NAFLD and NASH. ***(Browning et al., 2004)***

Other causes of NASH include obesity, metabolic syndrome, Wilson's disease, celiac disease high cholesterol and high triglycerides, rapid weight loss and malnutrition, some medications such as tamoxifen, amiodarone and methotrexate. ***(Pagano et al., 2002)***

At present, the available noninvasive tests to distinguish NASH from NAFLD include clinical signs and symptoms, routine laboratory and radiological imaging tests, and combinations of clinical and blood test results. Unfortunately, these tests are of limited use, and liver biopsy remains the only reliable way of diagnosing NASH and grading the severity of liver damage therefore, an urgent need to develop and validate a simple, reproducible, noninvasive test that both accurately distinguishes NASH from NAFLD and determines the stage and grade of the disease ***(Sanyal, 2002)***

Hepatocyte apoptosis, a highly organized and genetically controlled form of cell death, may play an important role in liver injury and disease progression in NAFLD. Increase in hepatocyte cell death by apoptosis is typically present in

humans with NASH as well as animal models of NASH but absent in those with NAFLD. A central consequence of the apoptotic process is the activation of the effector caspases (mainly caspase-3), which cleave a number of different substrates inside the cell—including cytokeratin 18 (CK-18), the major intermediate filament protein in the liver—resulting in the characteristic morphologic changes of apoptosis. ***(Guicciardi et al., 2005)***

It was recently demonstrated that plasma cytokeratin 18 (CK-18) fragment levels correlate with the magnitude of hepatocyte apoptosis and independently predict the presence of NASH. Determination of CK-18 fragments in the blood predicts histological NASH and severity of disease in a large, diverse population of patients with biopsy-proven NAFLD, supporting the potential usefulness of this test in clinical practice. ***(Linder et al., 2009)***

Aim of the Work

Evaluation of the role of cytokeratin 18 in early detection of liver fibrosis in patients of nonalcoholic steatohepatitis in comparison with liver biopsy