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Study of oxidant stress among Children with nonalcoholic Fatty liver disease

Thesis

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✍ Mostafa Mohammed Ahmed

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List of Abbreviations

NAFLD	**:**	Nonalcoholic fatty liver disease.
NASH	**:**	Nonalcoholic steatohepatitis.
CDC	**:**	Centers for disease control and prevention.
BMI	**:**	Body mass index.
IOTF	**:**	International Obesity Task Force.
WHR	**:**	Waist-to-hip ratio.
HOMA-IR	**:**	Homeostasis model of insulin resistance.
PCOS	**:**	Polycystic ovary syndrome.
HDL	**:**	High-density lipoprotein.
ALT	**:**	Alanine aminotransferase.
NHANES III	**:**	American National Health and Examination Survey, cycle III.
AST	**:**	Aspartate aminotransferase.
ALP	**:**	Alkaline phosphatase.
GGT	**:**	Gamma-glutamyl-transpeptidase.
US	**:**	Ultrasonography.
CT	**:**	Computerized tomographic scan.
MRI	**:**	Magnetic resonance imaging.

MRS	**:**	Magnetic resonance spectroscopy.
HTGC	**:**	Hepatic triglyceride content.
CRN	**:**	Clinical Research Network.
UDCA	**:**	Ursodeoxycholic acid.
SOD	**:**	Superoxide Dismutase enzyme.
NO-	**:**	Nitric oxide.
ROS	**:**	Reactive oxygen species.
RNS	**:**	Reactive nitrogen species.
TBARS	**:**	Thiobarbituric acid reactive substance.
LDL	**:**	Low density lipoprotein.
AMP	**:**	Adenosine monophosphate.
PPV	**:**	Positive predictive value.

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Introduction

Non alcoholic fatty liver disease (NAFLD) is emerging as an important cause of chronic liver disease with a spectrum ranging from asymptomatic transaminsemia to life - threaten complications of cirrhosis and hepato cellular carcinoma **(Madan et al, 2004).**

A number of evidences mainly derived from animal studies suggest the role of oxidative stress in producing liver injury in NAFLD.

Increased levels of reactive oxygen species and products of lipid peroxidant have been demonstrated in this condition **(Yang et al, 2000).**

Patients with (NAFLD) exhibit increased levels of hepatic cytochrome p 450 - 2E1 and thiobarbituric acid reactants, which are markers of lipid peroxidation **(Weltman et al, 1998).**

Furthermore, biochemical and histological improvement has been demonstrated in patients with NAFLD who have been treated with antioxidants **(Harrison et al, 2003).**

The Aim of the study

We conducted this study to look for relative levels of circulating lipid peroxidant products and to demonstrate any correlation with biochemical parameters, among patients with NAFLD.

Nonalcoholic fatty liver disease

Definition

Nonalcoholic fatty liver disease **(NAFLD)** is the most common form of chronic liver disease in both children and adults and threatens to become a serious public health problem **(Angulo, 2002; Wieckowska et al., 2005)**. NAFLD encompasses a wide spectrum of conditions associated with over accumulation of fat in the liver ranging from fatty liver or NAFL (nonalcoholic fatty liver) to steatohepatitis or NASH (nonalcoholic steatohepatitis) to advanced fibrosis and cirrhosis **(Angulo, 2002)**.

Nonalcoholic fatty liver disease refers to the accumulation of fat, mainly triglycerides, in hepatocytes so that it exceeds 5% of the liver weight. Primary NAFLD results from insulin resistance and thus frequently occurs as part of the metabolic changes that accompany obesity, type 2 diabetes and dyslipidemia. However, it is important to exclude secondary causes of steatosis. Nonalcoholic

fatty liver disease is by definition not alcohol-induced. Alcohol abuse, hepatotoxic medications and other liver conditions should be ruled out. However, given the high prevalence of obesity, diabetes and dyslipidemia in the general population, NAFLD often coexists with liver diseases of other etiology **(Powell, 2005)**.

Although NAFL, which is the most common form of NAFLD, appears to follow a benign nonprogressive clinical course, NASH is a potentially serious condition because as many as 25% of these patients may progress to cirrhosis and experience complications of portal hypertension, liver failure, and hepatocellular carcinoma **(Ekstedt et al., 2006)**.

Nonalcoholic fatty liver disease represents a spectrum of disease ranging from simple steatosis, which is considered relatively benign, to NASH and to NAFLD-associated cirrhosis and end-stage liver disease. NAFLD has become a common cause of liver transplant. It also has been identified as an important risk factor for development of primary liver cancer, mostly due to NAFLD-associated cirrhosis **(Bullock et al., 2004).**

Nonalcoholic fatty liver disease **(NAFLD)** represents a continuous spectrum of liver disease that to

some degree shares the histologic features of large-droplet (macrovesicular) fat accumulation in hepatocytes. By definition, the cause of disease is not acute or chronic alcohol ingestion; however, the peculiar negative name for this condition emanates from its histologic similarity in adults to alcoholic liver disease. The histologic disorders comprising NAFLD range from simple steatosis through nonalcoholic steatohepatitis **(NASH)**, in which there is steatosis along with inflammation and fibrosis, to cirrhosis in which fat accumulation may be less obvious. Although certain genetic/metabolic diseases and hepatotoxic drugs can cause liver damage resembling NAFLD. The term NAFLD should be reserved for a metabolic disorder affecting the liver that is a consequence of abnormal insulin action, namely hyperinsulinemia associated with insulin resistance. This disease is proving to be highly prevalent in adults and children. Undoubtedly the increased prevalence of NAFLD reflects the worldwide increase in obesity, which is reaching epidemic proportions. The long-term course of NAFLD remains unknown **(Diana et al., 2006)**.