

Plasma Pentraxin3 (PTX3) as a Marker of Non Alcoholic Fatty Liver Disease (NAFLD) in Obese Children

Thesis

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وَأَنْزَلَ اللَّهُ عَلَيْكَ
الْكِتَابَ وَالْحِكْمَةَ
وَعَلَّمَكَ مَا لَمْ تَكُنْ
تَعْلَمُ وَكَانَ فَضْلُ اللَّهِ
عَلَيْكَ عَظِيمًا

صدق الله العظيم

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LIST OF ABBREVIATIONS

Abbrev.	Meaning
11 β HSD1	: 11 Beta hydroxysteroid dehydrogenase 1
ALT	: Alanine aminotransferase
ASH	: Alcoholic steatohepatitis
AST	: Aspartate aminotransferase
AUROC	: Area under the receiver operating characteristic
BP	: Blood pressure
BMI	: Body mass index
CF	: Cystic fibrosis
CHC	: Chronic hepatitis C
CK-18	: Cytokeratin 18
CRN	: Clinical research network
CRP	: C-reactive protein
CT	: Computed tomography
CVD	: Cardiovascular disease
DBP	: Diastolic blood pressure
DM	: Diabetes mellitus
DNL	: De novo lipogenesis
ELISA	: Enzyme linked sandwich immunoassay
ER Stress	: Endoplasmic reticulum stress
FA	: Fatty liver
FFA	: Free fatty acids
GGT	: Gamma glutamyl transferase
G/I Ratio	: Glucose/ insulin ratio
GSH-Px	: Glutathione peroxidase

Abbrev.	Meaning
HBV	: Hepatitis B virus
HCC	: Hepatocellular carcinoma
HCV	: Hepatitis C virus
HMG COA	: 3-Hydroxy-3 methyglutaryl coenzyme A
HOMA-IR	: Homeostasis model assessment of insulin resistance
HSCs	: Hepatic stellate cells
IFL	: Isolated fatty liver
IKK β	: Inhibitor of nuclear factor kappa-b kinase subunit beta.
IL-6	: Interleukin-6
IL-8	: Interleukin-8
INR	: International normalizing ratio
IR	: Insulin resistance
IRS	: Insulin receptors
ISAK	: International Society for the Advancement of Kinanthropometry
LDL	: Low density lipoprotein
LFTS	: Liver function tests
LPS	: Lipopolysaccharide
mg/dl	: Milligram per deciliter
mm	: Millimeter
mm.Hg	: Millimeter mercury
MR	: Magnetic resonance
MRI	: Magnetic resonance imaging
MRS	: Magnetic resonance spectroscopy
NAFLD	: Non alcoholic fatty liver disease
NAS	: NAFLD activity score

Abbrev.	Meaning
NASH	: Nonalcoholic steatohepatitis
NF-KB	: Nuclear factor kappa B
NHANES	: National Health and Nutrition Examination Survey
NHBPEP	: National High Blood Pressure Education Program
NHMRC	: National Health and Medical Research Council
OSA	: Obstructive sleep apnea
PCOS	: Polycystic ovarian syndrome
PPAR	: Peroxisome proliferative activated receptor
ROC	: Receiver Operating Characteristic
ROS	: Reactive oxygen species
SAP	: Serum amyloid component
SBP	: Systolic blood pressure
SD	: Standard deviation
SDS	: Sudden death syndrome
SREBP	: Sterol regulatory element binding protein
TC	: Total cholesterol
TG	: Triglycerides
TGF- β	: Tissue growth factor-beta
THV	: Terminal hepatic venule
TNF- α	: Tumor necrosis factor alpha
TPS	: Tissue polypeptide specific antigen
U/L	: Unit/liter
U/S	: Ultrasonography
UDCA	: Urosdeoxycholic acid
VLDL	: Very low density lipoproteins
W/H	: Waist to hip ratio
Wt.	: Weight

INTRODUCTION

Obesity is the most relevant risk factor for NAFLD in children and several studies have described the prevalence and risk factors of NAFLD in these populations (**Fraser, 2007**).

Obese children with waist circumference or above the 90th percentile are at higher risk for dyslipidemia and insulin resistance than obese children with normal waist circumference. These results inductance that routine waist circumference evaluation in obese children may help clinicians identify which obese children are at greater risk of diabetes and other cardiovascular disease (**Bassali et al., 2009**).

Nonalcoholic fatty liver disease (NAFLD) is the most common cause of liver disease in the preadolescent and adolescent age groups in the United States (**Patton et al., 2008**).

The development of NAFLD in children requires the coexistence of multiple factors. Among the numerous risk factors, many are similar to risk factors that have been identified in the adult population, including obesity, visceral adiposity, insulin resistance, and presence of other features of the metabolic syndrome. Other risk factors, such as race, ethnicity, sex, and distribution and progression of pubertal development, are exclusive to pediatric NAFLD (**Alis, 2009**).

The majority of patients with NAFLD and NASH are asymptomatic with mild, incidental elevation of aminotransferases. No specific symptoms can distinguish NAFLD or NASH from other types of liver disease. The diagnosis of NAFLD requires the exclusion of other specific etiologies of liver disease and excessive alcohol consumption. The majority of patients have 1 or more risk factors for metabolic syndrome, such as type 2 diabetes, obesity or hyperlipidemia. When symptoms occur, the most common complaint is fatigue and occasionally right upper quadrant abdominal discomfort (**Rafiq, 2009**).

In this context, early identification of patients with nonalcoholic steatohepatitis prior to the onset of advanced fibrosis would be helpful in guiding aggressive intervention. Liver biopsy remains the gold standard for obtaining an accurate diagnosis of nonalcoholic steatohepatitis, as well as for differentiating this condition from simple steatosis. Unfortunately, biopsy is a costly and invasive diagnostic procedure (**Wieckowska et al., 2008**). Pentraxin 3 (PTX3) is produced by a variety of tissues and cells and in particular by innate immunity cells in response to proinflammatory signals and endothelial cells (**Mantovani et al., 2006**).

Because of this extrahepatic synthesis and in contrast to CRP, PTX3 levels are believed to be a true independent indicator of disease activity produced at sites of inflammation (**Fazzini et al., 2001**)