

**THE VALUE OF HUMAN GLUTATHIONE S-
TRANSFERASES IN EARLY DETECTION OF
CYSTIC FIBROSIS RELATED LIVER DISEASE**

Thesis

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Dedication

To the soul of my father,
to whom, I loved too much

To my mother, god saves her
and gives her health and
strength.

To my sister for her
encouragement.

To my husband for his
continuous support, patience
and understanding

To my lovely two kids.

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For all those who were
Teaching and Backing me to
reach Such a Stage of Education
and Knowledge

Abstract

Objective: Cystic fibrosis (CF) is a genetic disease that typically produces symptoms of malnutrition and chronic respiratory infections and remains the most common life threatening autosomal recessive disorder in white population, with a frequency of about 1 in 2500 live births. For a long time, CF was thought to be a rarity among Arabs. Recently, case reports from several Arab countries have been published, sue. CF is caused by mutations in a single gene on the long arm of chromosome 7 encoding a protein called the CF transmembrane regulator (CFTR). The defect in CFTR leads to pathological changes in all organs with mucous secretory glands, e.g. airways, pancrease, gut, biliary tract, vas deferens and sweat glands. With increase life expectancy in patients with CF, liver manifestations complicating the clinical course of the disease have emerged as a significant medical issue and it is now considered the third leading cause of death in patients with CF. Besides improved survival, increased recognition of liver disease (LD) also has been fastened by substantial changes in follow up modalities our time, including more frequently resorting to laboratory determinations and ultrasonography. Children with CF are predisposed to liver disease because of the lack of a functional CFTR protein on the biliary epithelium. The characteristic hepatic histological lesion in CF is focal biliary fibrosis. It is probably due to the focal nature of the damage that the clinical signs arc few and overall hepatic function is preserved until the late stages. The prompt recognition of CF liver disease is now important because of the potential beneficial effects of treatment with ursodeoxycholic acid and the need to design trials of its prophylactic use.

Methods: In our study, we aimed to investigate the early evaluation of clinical, biochemical (mainly serum level of GST) and ultrasonographic features of liver disease in a group of children with CF and comparing them with 2 groups (hepatic group and controls). In a recent study as regard biochemical investigation, it was found that human glutathione- S- transferases (hGST) which are cytosolic detoxification enzyme accounting for about 3% of the cytoplasmic proteins in hepatocytes showed some rise indicating early liver damage. As regard ultrasonography, it was found that abnormal echogenicity was often found in the absence of biochemical and/or clinical disease. It was concluded that periodic ultrasonographic examination could be an early indicator of disease.

Results: As regard the serum level of GST enzyme (normal value about 2000-3000 U/L), the results revealed a highly significant difference between controls and (hepatic + CF) groups. As regard the ultrasonographic changes among three groups, the results revealed a highly significant difference between controls and Hepatic + CF) groups. From these results we can confirm that GST is a sensitive value in early detection of liver affection in general with no specificity to CF patients.

Conclusion: serum GST with US scan of liver seem to be sensitive markers than transaminases for detection of liver affection in general with no specificity to CF patients, so we can use both of them to detect early liver affection in general included CFLD.

Key words:

(CF- CFTR- CFLD- Biliary fibrosis – GST- U/S)

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List of Abbreviations

ΔF508	Delta F 508
ABPA	Allergic bronchopulmonary aspergillosis
ACC	Acetylcysteine
ALT	Alanine aminotransferase
AST	Aspartate aminotransferase
ATP	Adenosine triphosphate
C-AMP	Adenosine monophosphate
CF	Cystic fibrosis
CFAA	Cystic fibrosis associated arthritis
CFLD or	Cystic fibrosis related liver disease
CFRLD	
CFRDM	Cystic fibrosis related diabetes mellitus
CFTR	Transmembrane conductance regulator
CL	Chloride
CO₂	Carbon dioxide
CPX	8-cyclopentyl-1,3-Dipropyl xanthin
CT	Computed tomography scan
CVS	Chorionic villus sampling
d	Day
DHLA	Dihydrolipoic Acid
DIOS	Distal intestinal obstruction syndrome
DKA	Diabetic ketoacidosis
DNA	Dinuclutide aminotransferase
DNase	Deoxy libonuclease
EC	Enteric coated

EEG	Electroencephalogram
ENac	Epithelial sodium channel
ERCP	Endoscopic retrograde cholangiopathy
FEV1	Forced expiratory volume in first second
FO2	Oxygen flow
FVC	Functional vital capacity
G6PD	Glucose -6-phosphate dehydrogenase
GGT	4-glutamyltransferase
GOR	Gastroesophageal reflux
GSSG	Glutathione disulfide
GST	Glutathione –s-transferase
hGST	Human glutathione-s-transferase
HPOA	Hypertrophic pulmonary osteoarthropathy
HRCT	High resolution CT
IL	Interleukin
IRT	Immunoreactive trypsin
IU	International unit
IV	Intravenous
IVIG	Intravenous immunoglobulins
K	Potassium
LD	Liver disease
m	Month
MC	Mucous clearance
MRCP	Magnetic resonance cholangiopancreatography
Na	Sodium
NAL	Nacystelyn
NSAID	Non steroidal anti-inflammatory drugs

PD	Potential difference
PEM	Protein energy malnutrition
PET	Pancreatic enzyme therapy
Ph	Ph value
PHT	Portal hypertension
PI	Pancreatic insufficiency
PKA	Protein kinase A
PS	Pancreatic sufficiency
Ps.A	Pseudo monas aeruginosa
RDA	Recommended daily allowance
rhTrx	Recombinant human thioredoxin
RNA	Ribonucleotide aminotransferase
RV	Residual volume
SaO₂	Oxygen saturation
SLPI	Secretory leukoprotease Inhibitor
TIPSS	Transjugular intrahepatic porto-systemic shunts
TLC	Total lung capacity
TNF	Tumor necrosis factor
TRL	Threonine, arginine, leucine
TrX	Thioredoxin
U.S	United state
U/S	Ultrasonography
UDCA	Ursodeoxy cholic acid
yr	Years
α-1AT	Alpha-1 antitrypsin

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