EVALUATION SIGNIFCANCE OF INTERLEUKIN-6 IN DIAGNOSIS AND PROGNOSIS OF HEPATOCELLULAR CARCINOMA

THESIS

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In internal medicine

By

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قَالُوا سُبْحَانَكَ
لَا عِلْمَ لَنَا
إِلَّا مَا عَلَّمْتَنَا
إِنَّكَ أَنتَ
الْعَلِيمُ الْحَكِيمُ
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LIST OF ABBREVIATIONS

AASLD	American Association For The Study of Liver disease
AFP	Alpha-fetoprotein
AFP-L3	Lectin-bound alpha-fetoprotein
AFBI	Aflatoxin BI
AJCC	American Joint Committee on Cancer
aGVHD	Acute graft-versus-host disease
ALT	Alanine aminotransferase.
ALP	Alkaline phosphatase
AMA	Anti-mitochondrial Antibody.
ANA	Antinuclear antibody.
ANF	Antinuclear factor.
Anti-LKM1	Antibody to Liver-kidney microsomes.
AST	Aspartate aminotransferase.
α_1-AT	α_1-Antitrypsin.
ALF	Alpha L Fucosidase.
AFU	Alpha-L-fucosidase
AJCC	American Joint committee on cancer
BUN	Blood urea nitrogen.
BCLC	Barcelona clinic liver cancer.
BCDF	B-cell differentiating factor.
BCGF	B-cell growth factor
BSF	B-cell stimulating factor
BMT	Bone marrow transplantation
BDNF	Brain-derived neurotophic factor
CEA	Carcinoembryoic Antigen.
CEUS	Contrast enhanced ultrasound
CKs	Ckemokines.
CHB	Chronic Hepatitis B
CLD	Chronic liver disease.
CNTE	Ciliary neurotrophic factor.
Cr	Creatinine.
CT	Computed tomography.
CLIP	Cancer of the liver Italian program.
CCC	Cholangiocarcinoma

D.bilirubin.	Direct bilirubin.
DCP	Des gamma carboxy prothrombin.
DNA	Deoxy-ribo nucleic acid.
DUS	Doppler ultrasound.
EGF	Epidermal growth factor.
ELISA	Enzyme linked immunosorbont assay.
Epo	Erythropoietin.
ESR	Erythrocyte sedimentation rate.
EUS	Endoscopic ultrasound.
FGF	Fibroblast growth factor.
FNH	Focal nodular hyperplasia.
FDG	fluoro-2-deoxy-D-glucose
FDA	Food and Drug administration.
GGT	Gamma glutamyl-transferase.
γ-globulin	Gamma globulin.
G-CSF	Granulocyte colony stimulating factor.
GM-CSF	Granulocyte-macrophage colony stimulating factor.
HbsAg	Hepatitis B surface antigen.
HBV	Hepatitis B virus.
HBIG	Hepatitis B immunoglobulin.
HDV	Hepatitis D virus.
HCV	Hepatitis C virus.
HCV Ab	Hepatitis C virus antibody.
HFL	Hepatic focal lesion.
HCC	Hepatocellular carcinoma.
HAI	Histology Activity Index.
HFE	Hereditary Hemochromatosis Gene
HIV	Human immunodeficiency virus
HSC	Hepatic stellate cell.
HSF	Hepatocyte-stimulating factor
H-ALP	HCC specific alkaline phosphatase
HLA	Human leucocyte antigen.
HRT	Hormonal replacement therapy
IFN	Interferon
IGIE	Interferon-gamma inducing factor.
IGF	Insulin-like growth factor.

IL	Interlukin
ICGHN	International Consensus Group for Hepatocellular Neoplasia
IOUS	Intraoperative ultrasound.
IVC	Inferior vena cava
K	Potassium.
LCF	Liver cell failure.
LGDN	Low-grade dysplastic nodules
HGDN	high-grade dysplastic nodules
LIF	Leukemia inhibitory factor.
Na	Sodium.
NASH	Non-alcoholic Steatohepatitis
NK	Natural killer.
NS	Non structural.
NAFLD	Non-alcoholic fatty liver disease.
NT	Neurotrophin.
NGF	Nerve growth factor.
MCT	Microwave coagulation ablation.
M-CSF	Monocyte colony stimulating factor.
MDCT	multidetector CT
MELD	Model for End-stage Liver Disease
MIF	Migration inhibition factor.
MOIVC	Membranous obstruction of inferior vena cava.
MRI	Magnetic reasonant imaging.
OCP	Oral contraceptive pills.
PAI	Percutaneous acetic acid injection.
PAF	Platelet activating factor.
PCR	Polymerase chain reaction
P CEA	Polyclonal carcino-embryonic antigen.
PEI	Percutaneous ethanol injection
PET	Positron emission tomography
PIVKA-II	Protein induced by vitamin K absence or antagonist.
PUO	Pyrexia of unkown origin.
PTH	Parathyroid hormone.
PDGF	Platelet derived growth factor.
RIA	Radioimmuno essay
RNA	Ribo nucleic acid

ROS	Reactive oxygen species.
RFA	Radiofrequency ablation
SMA	Smooth Muscle Antibodies.
SCF	Stem cell factor.
TACE	Transarterial chemoembolization
TAE	Transarterial embolisation.
T. bilirubin	Total bilirubin.
TCGF	T-cell growth factor
TH	T helper
TPO	Thrombopoietin.
TNM	Tumor node metastasis.
TNF	Tissue necrosis factor.
TGF	Transforming growth factor
UCSF	University of California, San Francisco
UNOS	United Network for Organ Sharing
US	Ultrasound.
VIP	Vasoactive intestinal peptide.
VEGF	Vascular endothelium growth factor.

Introduction

Hepatocellular carcinoma (HCC) is the fifth most common cancer worldwide and chronic C virus (HCV) infection is a major cause of HCC in the United States, Southern European countries and Japan. ***(El-Serag and RudophL,2007).***The host immune responses to HCV are often not strong enough to completely clear the infection , resulting in chronic stimulation of antigen-specific immune response**,** hepatocyte damage is induced by the continued expression of cytokines and recruitment of activated inflammatory cells to the liver which is followed by hepatocyte regeneration , this persistent cycle of necro-inflamation and hepatocyte regeneration is thought to provide a mitogenic and mutagenic environment leading to HCC development ***(Elsharkawy and Mann , 2007).***

Interleukin-6(IL-6) is a multifunctional cytokine largely responsible for the hepatic response to infections or systemic inflammation .Serum IL-6 levels are elevated in patients with chronic liver inflammation including alcoholic hepatitis, hepatitis B, HCV infections and steatohepatitis. ***(Wieckowska et al, 2008).***

Serum IL-6 levels are reportedly higher in patients with HCC than in those without ***(Porta et al, 2008)***. In chronic hepatitis, IL-6 produced mainly by activated Kupffer cells, intensifies local inflammatory responses and induces compensatory hepatocyte proliferation, facilatiting malignant transformation of hepatocyte ***(Naugler and Karin 2008).***

Giannitrapani et al, 2002 have already reported that IL-6 could be a more sensitive marker in identifying HCCs than alpha fetoprotein which still remains the most commonly used marker for this cancer, even though its real utility for detecting HCC seem s to be limited especially in Europe, where the number of HCCs poorly expressing alpha fetoprotein seems to be increasing, probably reflecting a more differentiated phenotype. ***(Giannitrapani et al, 2002)***.

Porta et al, 2008 have reported that circulating IL-6 is significantly higher in HCC patients than in cirrhotic patients and IL-6 values were highest in patients with more advanced disease**.** This may of value in prognosis of hepatocellular carcinoma ***(Porta et al, 2008)***.

Aim of THE Work

To evaluate the significance of interleukin 6 in diagnosis of hepatocellular carcinoma in comparison to serum alpha fetoprotein and this may also of value in prognosis of hepatocellular carcinoma.