A STUDY OF RISK FACTORS OF HEPATOCELLULAR CARCINOMA AMONG EGYPTIAN PATIENTS

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AFB1	: Aflatoxin B1
AFM1	: Aflatoxin M1
AFP	: Alpha fetoprotein
AFP L3	: Lens culinaris agglutinin A reactive AFP
AFP P4+P5	: Erythroagglutinating phytoheamagglutinin reactive AFP
Alpha-1-AT	: Alpha one antitrypsin
ALT	: Alanine aminotransferase
APC	: Adenomatous polyposis coli
AST	: Aspartate aminotransferase
BCLC	: Barcelona Clinic Liver Cancer
bFGF	: Basic fibroblast growth factor
BRCA2	: Breast cancer 2
CA	: Cancer Antigen
CAH	: Chronic active hepatitis
CD	: Cluster of differentiation
CDC	: Center for Control of Diseases and prevention
CGH	: Comparative genomic hybridization
CLD	: Chronic liver disease
CLIP	: Cancer of the Liver Italian Program
CMV	: Cytomegalovirus
COX	: Cyclooxygenase
CRP	: C - reactive protein
CT	: Computed Tomography
CTA	: CT arteriography
CTAP	: CT arterio – portography
DCP	: Desgamma-carboxy prothrombin
DNA	: Deoxy Ribonucleic Acid
EASL	: European Association for the Study of the Liver
EBV	: Epstein Barr Virus
EGFR	: Epidermal growth factor receptor
Fas	: Factor of apoptotic signal
FHL	: Focal hepatic lesion
FLC	: Fibrolamellar carcinoma
5-FU	: 5-Fluorouracil

HB	: Hepatoblastoma
HBcAg	: Hepatitis B core antigen
HBcAb	: Hepatitis B core antibody
HBeAg	: Hepatitis B e antigen
HBeAb	: Hepatitis B e antibody
HBsAb	: Hepatitis B surface antibody
HBsAg	: Hepatitis B surface antigen
HBV	: Hepatitis B Virus
HCB	: Hexachlorobenzene
HCC	: Hepatocellular carcinoma
HCH	: Hexachlorocyclohexane
HCV	: Hepatitis C Virus
HDV	: Hepatitis D Virus
HE	: Heptachlor Epoxide
HFG	: Hemochromatosis familial gene
HG-DN	: High grade dysplastic nodule
hTERT	: Human telomerase reverse transcriptase
IARC	: International Agency for Research on Cancer
IFN	: Interferon
IGF	: Insulin like growth factor
IGFBP–3	: Insulin like growth factor binding protein-3
IGF2R	: Insulin like growth factor 2 receptor
IRS	: Insulin receptor substrate
IVC	: Inferior vena cava
JIS	: Japan Integrated Score
LDLT	: Living donor liver transplantation
LG-DN	: Low grade dysplastic nodule
M6P	: Mannose-6-phosphate
MRI	: Magnetic resonance imaging
MRN	: Macroregenerative nodule
mRNA	: Messenger Ribonucleic acid
MSSH	: Metabolic syndrome steatohepatitis
NAFLD	: Non Alcoholic Fatty Liver Disease
NASH	: Non Alcoholic steatohepatitis

NCI	: National Cancer Institute
NCL	: Non cirrhotic liver
NF KB	: Nuclear factor Kappa B
OR	: Odds Ratio
PAI	: Percutaneous acetic acid injection
PBC	: Primary biliary cirrhosis
PCBs	: Polychlorinated biphenyls
PCR	: Polymerase chain reaction
PEI	: Percutaneous ethanol injection
PHT	: Portal hypertension
PIVKA II	: Protein induced by vitamin K absence or antagonism II
PMCT	: Percutaneous microwave coagulation therapy
RAR	: Retinoic acid receptor
RB	: Retinoblastoma
RCT	: Randomized Controlled Trial
RFA	: Radiofrequency ablation
ROS	: Reactive oxygen species
RNA	: Ribonucleic acid
SIGN	: Safe injection global network
SLIDE	: S, stage; Li, liver damage; De, Desgamma carboxy Prothrombin
TACE	: Transcatheter arterial chemoembolization
TAE	: Transcatheter arterial embolization
THI	: Tissue harmonic imaging
TGF	: Transforming growth factor
TNF	: Tumor necrosis factor
TNM	: Tumour, node, metastasis
UK	: United Kingdom .
UNOS	: United Network of Organ Sharing
U/S	: Ultrasonography
USA	: United States of America
VEGF	: Vascular endothelial growth factor
WHO	: World Health Organization
Y	: Yittrium

ABSTRACT:

Background : The development of hepatocellular carcinoma is a multistep process and the result of an accumulation of risks. Many factors may therefore contribute to the final common pathway of HCC. Our aim was to determine the risk factors for the development of hepatocellular carcinoma so that we will be able in future to put a strategy to prevent HCC in Egypt.

Patients and methods : This study was conducted on sixty cases of HCC as well as thirty patients with liver cirrhosis and another thirty healthy subjects without evidence of chronic liver disease. They were clinically assessed and investigated (Laboratory including complete blood count, liver biochemical profile, viral markers, alpha fetoprotein, anti Schistosomal antibody and serum aflatoxin, and imaging that was mainly by abdominal ultrasonography).

Results: HCV had a high prevalence among HCC cases while HBV had a declining role. Aflatoxin showed a significant role in pathogenesis of this malignancy. HCC commonly presented in males, farmers, heavy smokers and was associated with high incidence of unsafe water supply and exposure to pesticides. The majority of HCC cases (65%) had a single major risk factor, and few cases (8.3%) developed HCC on top of non cirrhotic liver.

Conclusion: HCC is multifactorial with interaction of major risk factors like HCV and aflatoxin, minor risk factors like exposure to pesticides and heavy smoking in pathogenesis of this malignancy. HBV infection, which is one of the major risk factors, was found to have a declining role in hepatocarcinogenesis in this work. Also, HCC may occur on top of non cirrhotic liver certainly with viral hepatitis.

Key words: Hepatocellular carcinoma – risk factors – HBV – HCV – cirrhosis – Aflatoxin – pesticides.

بسم الله الرحمن الرحيم

" يرفعِ اللهُ الذينَ آمنوُا منكم و الذينَ أوتوا العلمَ درجاتٍ "

سورة المجادلة – أية 11

Introduction

HCC is the fourth most common cancer worldwide **(Marrero, 2003)** and affects more than 500000 people globally annually (**Parkin, 2001).** The yearly incidence comprises between 2.5 and 7% of patients with liver cirrhosis (**Montalto et al, 2002).** Concerning the five year mortality, it exceeds 95% (**Parkin, 2001)** , that is why it was reported that the annual mortality rate from the tumor is virtually the same as its annual incidence (**Kew, 2002A)**. The incidence of HCC is rising and is expected to continue to rise over the next 15 years (**Marrero, 2003).** This is due to the large pool of persons infected with HCV, HBV or both in whom the cancer is in the latency period (**El Serag and Mason, 1999).**

The highest incidences occur in eastern and southeastern Asia, some of the western pacific islands, sub Saharan Africa. Intermediate incidences are found in eastern and southeastern Europe, the Carribean, central America and western Asia. HCC is uncommon in the remaining countries (**Kew, 2002A)**.

In Egypt, it was reported that 5% of cirrhotic patients will develop HCC **(Zakareya , 1996)**. The annual report of the cancer registry of metropolitan Cairo (1976-1980) had shown rising incidence of primary hepatic malignancy from 1.5% – 2% of total cancers **(Sherif and Ibrahim, 1987)**. The frequency of HCC cases attending National Cancer Institute (NCI) steadily increased from 1993 up to 1997 during which relative frequency reached 3.8% of all solid tumors**(Mohamed et al, 2000)**. This is