# ASSESSMENT OF IMPACT OF HEPATOCELLULAR CARCINOMA ON HEALTH RELATED QUALITY OF LIFE

#### Thesis

Submitted for Partial Fulfillment of Master Degree in **Tropical Medicine** 

By

Hisham Ali Ahmed

M.B.B.CH Faculty of Medicine Al-Azhar University

Supervised By

#### **Professor Doctor Hassan Hamdy**

Professor of Tropical Medicine Faculty of medicine - Ain Shams University

#### **Doctor Eman Mahmoud Fathy Barakat**

Assistant Professor of Tropical Medicine Faculty of medicine - Ain Shams University

#### **Doctor Runia Fouad El Folly**

Lecturer of Tropical Medicine Faculty of medicine - Ain Shams University

> Faculty of Medicine Ain Shams University **2011**

# تقييم تأثير سرطان الكبد الأولي على الكفاءة الكفاءة الصحية للحياة

رسالة مقدمة توطئة للحصول على درجة الماجستير في طب المناطق الحارة

مقدمه من طبيب/ هشام على أحمد بكالوريوس الطب والجراحة جامعة الأزهر

تحت إشراف أد/ حسن حمدى أستاذ طب المناطق الحارة كلية الطب - جامعة عين شمس

# أ.د.م/ إيـمان محمود فتحـى بركات

أستاذ مساعد طب المناطق الحارة كلية الطب - جامعة عين شمس

د/ رنيا فواد الفولى مدرس طب المناطق الحارة كلية الطب - جامعة عين شمس كلية الطب جامعة عين شمس ٢٠١١

#### **SUMMARY**

HCC has a great and potentially adverse impact on physical health and psychological well-being, and breaks the pattern of a patient's life. In addition to medical treatment and physical factors, psychosocial variables also play an important role in determining *HRQoL*.

Because HCC has its specific etiologies, epidemiology, clinical problems, treatments, and disease progression, generic plus disease-specific measures are essential to provide a comprehensive picture of *HRQoL*.

Compromised *HRQoL* has been shown in patients with liver disease including cirrhosis. *HRQoL* increasingly is considered an important end point in cancer clinical trials and clinical care, along with the traditional end points such as tumor response rate. *HRQoL* concerns in patients with HCC include generic domains, such as physical symptoms and psychological issues.

**To our knowledge**, none of the available Egyptian studies had assessed the effect of HCC on the health-related quality of life (*HRQoL*).

The aim of the current study was to assess the effect of hepatocellular carcinoma on the health-related quality of life (HRQoL), as well as to assess the effect of locoregional





#### After giving all thanks to **ALLAH**

I would like to express my most profound gratitude and extreme appreciation to **Professor Dr. Hassan Hamdy**, Professor of Tropical Medicine, Faculty of Medicine, Ain-Shams University for dedicating so much of his precious time and effort to help me complete this work.

I would like to express my great thanks to Dr. Eman Mahmoud Fathy Barakat, Assistant Professor of Tropical Medicine, Faculty of Medicine, Ain-Shams University, for her kind advice, support, continuous help and cooperation through the whole work.

I would like to express my great thanks to Dr. Runia Fouad El Folly, Lecturer of Tropical Medicine, Faculty of Medicine, Ain-Shams University, who freely gave her time, effort and experience along with continuous quidance through out this work.

Great thanks to Hepatoma Group.

Hisham Ali Ahmed

# **LIST OF CONTENTS**

Title	Page No.
List of Tables	I
List of Figures	III
List of Abbreviations	IV
Introduction	1
Aim of the work	4
Review of Literature	
Hepatocellular carcinoma in egypt	5
Diagnosis of hepatocellular carcinoma	13
Treatment of hepatocellular carcinoma	22
HRQOL in HCC	43
Patients and methods	51
Results	65
Discussion	91
Summary	104
Conclusions	108
Recommendations	109
References	110
Arabic summary	

# **LIST OF TABLES**

Tab. No.	Title	Page No.
Tables in the I	<u>Review of Literature</u>	
Table (I):	HCC screening is recommended in high risk patients	14
Table (II):	Okuda staging variables.	54
Table (III):	BCLC staging system:	54
Table (IV):	Performance status score (PS) of World Health Organization	55
Table (V):	Child Turcotte Pugh scoring system	58
<u>Tables in the Results</u>		
<b>Table (1):</b>	Demographic characteristics of the two studied groups:	66
<b>Table (2):</b>	Clinical Symptoms & Signs of the two studied groups:	67
<b>Table (3):</b>	Laboratory data of HCC Group and Control Group:	68
<b>Table (4):</b>	Clinical classification of HCC Group and Control Group:	69
<b>Table (5):</b>	Clinical staging of HCC Groups:	70
<b>Table (6):</b>	Assessment of the results of Group I and Group II after intervention:	71
<b>Table (7):</b>	Laboratory data of Group I before and after intervention:	72
<b>Table (8):</b>	Health-related quality of life of Group I (before intervention) and control group:	73
<b>Table (9):</b>	Health-related quality of life of Group I (after intervention) and control group:	74
<b>Table (10):</b>	Health-related quality of life of Group I before and after intervention:	75

# LIST OF TABLES (Cont...)

Tab. No.	Title	Page No.
<b>Table</b> (11):	Laboratory data of Group II before and after intervention	77
<b>Table (12):</b>	Health-related quality of life of Group II (before intervention) and control group:	78
<b>Table (13):</b>	Health-related quality of life of Group II (after intervention) and control group:	79
<b>Table (14):</b>	Health-related quality of life of Group II before and after intervention:	80
<b>Table (15):</b>	Health-related quality of life of Group I and Group II before intervention:	82
<b>Table (16):</b>	Health-related quality of life f Group I and Group II after intervention:	83
<b>Table (17):</b>	Significant correlation between items of Health-related quality of life and other parameters:	85
<b>Table</b> (18):	Comparison between complete & incomplete response after radiofrequency	87
<b>Table (19):</b>	Comparison between complete & incomplete response after chemoembolization	89

# **LIST OF FIGURES**

Fig. No.	Title	Page No.
Figures in the	Review of Literature	
Figure (I):	The suggested Egyptian Guideline diagnostic after detection of a hepatic nodule by ultrasound	21
Figure (II):	Algorithm for staging and treating patients diagnosed as having HCC based on Barcelona clinic liver cancer guidelines	24
Figure (III):	AASLD practical guideline for management of HCC	
Figure (IV):	The BCLC staging system for HCC. M, metastasis classification; N, node classification; PS, performance status; RFA, radiofrequency ablation; TACE, transarterial chemoembolization	53
Figures in the	<u>Results</u>	
Figure (1):	Demographic characteristics of the two studied groups	66
Figure (2):	Clinical classification of HCC Group and Control Group.	69
Figure (3):	Scoring Systems of HCC Groups	70
Figure (4):	Assessment of the response of Group I and Group II after intervention	71
Figure (5):	Health-related quality of life of Group I before and after intervention	76
Figure (6):	Health-related quality of life of Group II before and after intervention	81
<b>Figure (7):</b>	Health-related quality of life of Group I and Group II after intervention	84
Figure (8):	Comparison between complete & incomplete response after Radiofrequency Ablation	
Figure (9):	Comparison between complete & incomplete response after Trans-arterial Chemoembolization.	

# **LIST OF ABBREVIATIONS**

Abbrev	Full term
AASLD	American Association For The Study of Liver disease
AFP	Alpha Feto Protein
BCLC	Barcelona Clinic Liver Cancer
CLD	Chronic liver disease
CLDQ	Chronic Liver Disease Questionnaire
CT	Computerized Tomography
DNA	Deoxy Ribo Nucleic Acid
EASL	European Association for the Study of the Liver
HBV	Hepatitis B virus
HCC	Hepatocellular carcinoma
HCV	Hepatitis C virus
HQLQ	Hepatitis Quality of Life Questionnaire
HRQoL	Health-related quality of life
LDQOL	Liver Disease Quality Of Life
MECC	Middle East Cancer Consortium
MRI	Magnetic resonance imaging
OLT	Orthotopic liver transplantation
PAT	Parenteral antischistosomal treatment
PDGFR-β	Platelet-derived growth factor receptor beta
PEI	Percutaneous ethanol injection
PEIT	Percutaneous ethanol injection therapy
RCT	Randomized controlled trial
RFA	Radiofrequency ablation
SF-36	Short Form-36
TACE	Transcatheter arterial chemoembolization
TAE	Trans-Arterial Embolization
TOCE	Transarterial oil-based chemoembolization
UCSF	University of California at San Francisco
US	Ultrasonography
VEGF	Vascular endothelial growth factor
<b>VEGFRs</b>	Vascular endothelial growth factor receptors

### **INTRODUCTION**

The main goals of the health care system for patients with chronic diseases are to prevent additional ill health and to facilitate a life without compromised activities of daily living. An important part of treatment is to improve Health-related quality of life (HRQoL) and to support the ability to cope with stressors related to disease (*Mittermaier et al.*, 2004).

The concept HRQoL is subjective and multidimensional and incorporates physical, emotional, and social aspects of health perception and health functioning (*Larsson* et al., 2008). Standardized assessment of HRQoL preceding each consultation may potentially provide physicians with valuable information (*Gutteling et al.*, 2008).

Among patients with chronic liver disease, impairment in HRQoL has been reported. Hepatocellular carcinoma (HCC), one of the major sequelae of chronic liver diseases, is now increasing worldwide and the HRQoL of patients with HCC is an area of interest (*Kondo et al.*, 2007).

Owing to recent advances in diagnostic imaging and availability of tumor biomarkers specific to HCC, the cancer can now often be detected at an early stage (*Shiratori et al.*, 2001), where there are presumably no specific symptoms associated with HCC. The impact of these small HCC on HRQOL remains uncertain (*Kondo et al.*, 2007).

In the past two decades, percutaneous tumor ablation techniques, such as percutaneous ethanol injection therapy (PEIT) and radiofrequency ablation (RFA), have been accepted as effective and safe therapies for patients with small HCC who are not candidates for hepatic resection (*Shiina et al.*, 2005). These less-invasive therapies may be preferable from the viewpoint of patients' HRQoL, especially because of the high recurrence rate of HCC even after complete tumor removal, which requires repeated treatment of each recurrence (*Koike et al.*, 2000).

In medical practice, the preferences between different kinds of treatment or follow-up can be better investigated with the application of HRQoL. Furthermore, it can influence and aid the choice of therapeutic management for a specific disease, motivating the patient to take part in decisions that are in his/her own interest, through language that can be readily understood. In public health, these studies can favor better use of resources allocated to the health sector (*Carr and Higginson*, 2001).

Generic instruments are widely used, can be universally applied and allow comparisons of different diseases or populations. A generic instrument should be chosen when a healthy control group is used or when making a comparison with other diseases. Generic instruments, however, have a number of limitations, of which the most important is that they do not allow specific aspects of a disease to be studied (*Chen et al.*, 2005).

For this reason, Specific Instruments for assessing HRQoL are being increasingly developed and used. These instruments can be specific to a certain disease (e.g., diabetes, asthma or liver diseases), be applied to a particular population of patients (e.g., elderly patients) or be specific to a function (e.g., functional capacity or sexual function). Specific instruments are more comprehensive and capture all the possible changes that can occur during the course of a disease (*Strauss and Teixeira*, 2006).

They are also better able to detect improvements or deterioration related to aspects under investigation and have proved very useful in evaluating therapies in clinical trials. There are some questionnaires available regarding liver disease as Chronic Liver Disease Questionnaire (CLDQ) (*Gralnek et al.*, 2000). Liver Disease Quality Of Life (LDQOL) and Hepatitis Quality of Life Questionnaire (HQLQ) (*Strauss and Teixeira*, 2006).

The Short Form-36 (SF-36) health survey is a generic health status measurement consisting of 36 items in eight domains, which has demonstrated good reliability and validity in chronic disease populations, including patients with chronic liver diseases (*Kondo et al.*, 2007).

In clinical practice, HRQoL prediction from objective variables is necessary and may be useful. For that purpose, the relationship between subjective HRQoL scores and objective clinical variables, such as presence of ascites, status of HCC and laboratory data, should be analyzed further (*Kondo et al.*, 2007).

# **AIM OF THE WORK**

#### The aims of this study were to:

- 1- Assess the effect of hepatocellular carcinoma on the health-related quality of life (HRQoL).
- 2- Assess the effect of locoregional therapy of hepatocellular carcinoma on the health-related quality of life (HRQoL).