Computer tomography findings among adult patients with suspected hepatocellular carcinoma at Muhimbili national hospital

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COMPUTER TOMOGRAPHY FINDINGS AMONG ADULT PATIENTS WITH SUSPECTED HEPATOCELLULAR CARCINOMA AT MUHIMBILI NATIONAL HOSPITAL

By

William Ndosi

A Dissertation Submitted in (partial) Fulfillment of the Requirement for the Degree of Master of Science (Radiology and Imaging) of the

Muhimbili University of Health and Allied Sciences
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CERTIFICATION

The undersigned certifies that he has read and hereby recommends for acceptance by Muhimbili University of Health and Allied Sciences **a** dissertation entitled: **"Computer tomography findings among adult patients with suspected hepatocellular carcinoma at Muhimbili National Hospital**" in (partial) fulfillment of the requirement for the degree of Master of Medicine (Radiology) of Muhimbili University of Health and Allied Sciences

_____

Dr. M. Balowa

(Supervisor)

_____

Date

DECLARATION AND COPYRIGHT

I**, William Ndosi,** declare that this **dissertation** is my own original work and that it has not been presented and will not be presented to any other university for a similar or any other degree award.

Signature…….. **Date**……..

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DEDICATION

This dissertation is dedicated to

My father Dr. Bethuel N. Ndosi for his everlasting encouragement and support,

My treasured mother Mrs. Gladness H. Ndosi for her wonderful care and concern,

And to My loving brothers Christopher and Humphrey Ndosi for their tireless support

ABSTRACT

Background: Liver cancers account for 6% of the worlds cancer incidence, 9% of the global cancer mortality burden and the second most common cause of death due to cancer worldwide. Of the primary hepatic malignancies, HCC accounts for 80% of cases. HCC primarily affects males more than females. HCC is mostly associated with chronic liver disease or cirrhosis. There is classical HCC and its variants.

Objectives: To determine the role of CT radiological patterns in the management of adult patients with clinically diagnosed hepatic mass at MNH from December 2015 - March 2016.

Methodology: Patients with clinically diagnosed hepatic mass who underwent abdominal CT scan examination were included in the study. The images were examined and reported by the principal investigator together with a Radiologist. The report was issued after reaching a consensus.

Results: A total of seventy four (74) patients were involved in this study. HCC was seen in twenty seven (36.0 %) patients. HCC was non-significantly associated with males (45.00% vs. 26.47%, p-value= 0.099) and in patients 60 years and below (47.62% vs. 32.08% %, p-value= 0.216). Radiological features of HCC included a shrunken liver (18.52% vs. 2.13%, p-value= 0.013) and nodular liver appearance (33.33% vs. 0%, p-value= 0.000) in HCC. Heterogeneous mass attenuation (33.33% vs. 12.77%, p-value= 0.034), irregular mass margins (74.07% vs. 55.32%, p-value= 0.109), complex mass properties (40.74% vs. 70.21%, p-value= 0.013) with mainly solid content predominance (66.67% vs. 29.79%, p-value= 0.002). Post contrast images showed HCC with heterogeneous enhancement pattern to be 33.33% vs. 8.51% (p-value= 0.007), ascites (48.15% vs. 19.15% p-value= 0.009) and less likely para-aortic lymph nodes (7.41% vs. 17.02% p-value= 0.244).

Conclusion: HCC is well described by non-contrasted and contrasted abdominal CT scan examinations. HCC was mainly affecting males and patients aged 60 years and below. HCC mainly presents with a shrunken liver, nodular liver outline, heterogeneously attenuating

complex masses with irregular outline, predominantly solid with heterogeneous enhancement, peripheral fat stranding, ascites and less likely para-aortic lymphadenopathy.

Recommendations: It is recommended a larger sample size to be used in future studies.

TABLE OF CONTENTS

CERTIFICATION i
DECLARATION AND COPYRIGHT ii
ACKNOWLEDGEMENTS iii
DEDICATION iv
ABSTRACT v
TABLE OF CONTENTS vii
LIST OF TABLES ix
LIST OF ABBREVIATIONS x
CHAPTER ONE 1
1.0 INTRODUCTION 1
1.1 Background 1
1.2 Literature review 3
1.3 Problem Statement 4
1.4 Rationale 5
1.5 Objectives 6
1.5.1 Broad Objective 6
1.5.2 Specific objectives 6
CHAPTER TWO 7
2.0 MATERIALS AND METHODS 7
2.1 Study design 7
2.2 Study population and study area 7
2.3 Inclusion criteria 7
2.4 Exclusion criteria 7
2.5 Sampling procedures 8
2.6 Sampling and Sample size 8
2.7 Ethical issues 8
2.8 Data collection procedure: 9
2.8.1Questionnaires and CT scan findings recording form. 9

2.9 Study variables 9
2.9.2 Independent variable 9
2.10 Data analysis plan 9
CHAPTER THREE 10
3.0 RESULTS 10
CHAPTER FOUR 15
4.0 DISCUSSION 15
CHAPTER FIVE 18
5.0 CONCLUSION AND RECOMMENDATION 18
5.1 Conclusion 18
5.2 Recommendations 18
5.3 Limitations 18
REFERENCES 19
APPENDICES 24
Appendix I: Questionnaire English Version 24

LIST OF TABLES

Table 1: Frequency table of imaging diagnosis among patients with suspected HCC undergoing abdominal computed tomography at MNH……...10

Table 2: Sociodemographic characteristics among patients with suspected HCC undergoing abdominal computed tomography at MNH……..10

Table 3a: Abdominal CT findings among patients with suspected HCC: liver size, liver surface, liver attenuation and mass attenuation……11

Table 3b: Abdominal CT findings among patients with suspected HCC: liver size, liver surface, liver attenuation and mass attenuation……12

Table 3c: Abdominal CT findings among patients with suspected HCC: mass margins, mass properties, content predominance and contrast enhancement…13

Table 3d: Abdominal CT findings among patients with suspected HCC: Calcification, peripheral fat stranding, ascites and lymphadenopathy……..14

LIST OF ABBREVIATIONS

MNH - Muhimbili National Hospital

US - Ultrasound

CT - Computed Tomography

HCC - Hepatocellular carcinoma/ Hepatoma

MRI - Magnetic Resonance Imaging

MDCT - Multidetector - row computed tomography

MUHAS - Muhimbili University of Health and Allied Sciences

TShs - Tanzania shillings

UECT - Un-enhanced computed tomography

CECT - Contrast-enhanced computed tomography

HU - Hounsfield units

CLD - Chronic liver disease

BMI - Body mass index

α-FP - Alpha-fetoprotein

CHAPTER ONE

1.0 INTRODUCTION

1.1 Background

Liver cancers account for 6% of the worlds cancer incidence, 9% of the global cancer mortality burden and the second most common cause of death due to cancer worldwide (1). Metastases is the most common tumor type seen in the liver (1). Of the primary hepatic malignancies, hepatocellular carcinoma (HCC) accounts for 80% of cases(1,2).

HCC primarily affects males more than females, with the ratios averaging between 2:1 to 4:1(1–3). Female predilection is very rare and is seen in the fibrolamellar subtype of HCC. A study done (4) found the male to female ratio to be 9:14 and another study (5) found a female predilection of 51.5% vs. 26.3%(4,5)

HCC is generally seen in the adult population (6) with peak ages in high-risk African populations tending to range between 60 to 65 years in males and then decline, and 65 to 70 years in females with a decline in cases beyond that age group (2). Some studies have shown the incidence of HCC to be inversely proportional to the age peak in a particular region i.e. a younger age peak is seen in areas with a high incidence of HCC and older age peak in a low incidence area(7,8).

HCC is mostly associated with chronic liver disease or cirrhosis (9)(10), mainly(78%) caused by viral hepatitis (HBV, 53%; HCV, 25%, respectively) (6)(10). Other known risk factors for contracting HCC include increased BMI, diabetes, iron overload syndromes, alcohol use, tobacco use, contraceptive use, aflatoxin exposure and betel quid chewing (11).

The liver undergoes several functional and structural changes before reaching the stage of cirrhosis(12). These changes include hepatic steatosis as the initial reversible stage and is a response of hepatocytes to chronic injury, mostly seen in alcohol-induced cirrhosis (12). In this condition there is diffuse fatty infiltration of the liver which presents as an average hepatic attenuation of at least 10 HU less than splenic attenuation on unenhanced CT (12)(13). The

presence of normal course vascular structures within the fatty infiltration is vital in differentiating this condition from liver tumors (12). If not managed properly, the disease may progress into chronic irreversible liver disease with further structural deformity and functional disarray.

Hepatic nodular lesions may evolve and these may be categorized as regenerative nodules, dysplastic nodules and finally HCC(12)(14).

Rarely HCC may develop in the non-cirrhotic liver, although some degree of fibrosis is seen(15). In general, the patients are younger and there is a single or dominant mass in 72% - 82% of cases (15). The mass is usually large (mean diameter of 12 cm) and commonly has a scar (15). The central scar demonstrates delayed enhancement in 25% of cases in delayed/equilibrium phase images on CT hepatic contrast imaging protocol (15). These features are similar to fibrolamellar HCC. In contrast to fibrolamellar HCC, HCC in the non-cirrhotic liver usually has a male predilection and elevated serum tumor markers i.e. α-FP levels greater than 200 ng/mL (15)(16)(17). In addition, calcifications and lymphadenopathy is rarely seen in HCC in the non-cirrhotic liver while it is rather common (40% - 68% and 50% - 70% respectively) in fibrolamellar HCC(15).

1.2 Literature review

CT radiologic features of HCC

Since HCC is associated with liver cirrhosis, it is important to note some of the features of cirrhosis which may be present in the setting of HCC. The CT radiologic features of cirrhosis include a shrunken (mostly affecting the right lobe and associated with a normal or hypertrophied caudal and left lobe) liver(13,18). Although this is the most common presentation, HCC with enlarged livers was reported in 7 cases amongst 31 patients in a study done (19) for the detection of HCC during a clinical follow-up in patients with chronic liver disease. A study done (20) revealed the presence of HCC in normal sized livers in all 68 patients involved in the study. The occurrence of HCC in normal sized and enlarged livers may be attributable to the fact that HCC may also present in the non-cirrhotic liver (19,20).

Another common feature seen in patients with HCC associated with liver cirrhosis is a nodular liver outline or parenchymal nodules (13)(18). Hepatocellular carcinoma (HCC) in the setting of a smooth liver outline may be seen in the non-cirrhotic liver(21).

A heterogeneous attenuation pattern of the liver on UECT is also associated with cirrhosis and consequently HCC. This represents the presence of fatty infiltration, fibrosis and hepatic parenchymal nodules or masses(18)(22).

Ascites is a secondary feature which further cements the diagnosis of cirrhosis(23). Hepatocellular carcinoma (HCC) in the absence of ascites is seen in non-cirrhotic livers or non-alcoholic fatty liver disease(24).

In general HCC may present either as a nodule or a mass. These tumors tend to be highly vascularised. The mass itself mostly appears as a hypoattenuating or mixed attenuating mass on UECT with irregular outlines/margins, and shows early arterial phase hyperenhancement compared to liver parenchyma with subsequent hypoenhancement compared to liver parenchyma in the portal-venous and delayed phase images i.e. washout appearance (25,26). The mixed attenuation pattern corresponds to central necrosis or hemorrhage seen in large HCC masses (16).

1.3 Problem Statement

HCC remains one of the most common cancers in the world and a leading cause of morbidity and mortality globally. In 2003 the International Agency for Research in Cancer (IARC) registry reported the relative (proportional) frequencies of HCC to be 29.7/100 000 persons/year in East Africa. Tanzania was registered to have 8.8/ 100 000 persons/year for males and 4.1/100 000 persons/year for females respectively(27).

Histopathology is the definitive diagnostic tool. Performing a histopathological examination requires multiple resources which are limited in the setup of the study area. As an adjunct diagnostic examination, CT aides greatly in the management of HCC. CT scan examination of the abdomen provides superior resolution of different tissues within the abdomen including the liver. The role of CT scan evaluation in the diagnosis of HCC is invaluable to the radiologist and eventually the management of the patient.

Due to cost and availability, the examination is unfortunately not done frequently enough and most patients who require an abdominal CT examination to aid further and accurate diagnosis do not undergo the examination in Tanzania. Furthermore, there are delays in performing the examination because other cheaper and more easily available diagnostic modalities such as US are used first.

MNH is Tanzania's largest referral hospital and performs, roughly, between 8 - 12 abdominal CT scans per day. Due to the above mentioned limitations, a study such as this has not been done at MNH or in Dar es salaam region in general. The study aims to provide useful information in the radiological features of HCC amongst adult patients with hepatic masses and clinically suspected HCC.

1.4 Rationale

Abdominal CT scan examination is an ideal radiological modality in imaging the liver in search of hepatic lesions, particularly masses such as HCC. With its ever increasing resolution capabilities and shortening scan times, abdominal CT scan examination is, and will, continue to be a vital tool to the radiologist and the medical team in general in diagnosing HCC masses.

Although the examination can only be done in a few centers in Tanzania, it is important that the interpretation of the few examinations done and images provided are well understood. This not only applies to the Radiologist, who is the primary interpreter, but also to the entire medical team involved in the management of patients with HCC.

As it is the first of its kind in the Dar es salaam region, this study aims at providing a platform for the basic interpretation of radiological features of HCC masses in adult patients at MNH. With the continuing improvement of CT technology and its availability in Dar es salaam, Tanzania, it also serves as a "stepping stone" for further studies to venture into. Furthermore the information from this study will help identify a foundation for some of the radiological features seen in patients with HCC masses at MNH. In addition, it will also help to highlight on the shortcomings of CT radiological patterns in the management of patients with clinically suspected HCC at MNH.

1.5 Objectives

1.5.1 Broad Objective

To determine the computer tomography findings among adult patients with suspected HCC at Muhimbili National Hospital from December 2015 - March 2016.

1.5.2 Specific objectives

1. To determine the socio-demographic characteristics of adult patients who presented with suspected HCC at Muhimbili National Hospital from December 2015 - March 2016.

2. To determine the CT imaging findings among adult patients presenting with suspected HCC at Muhimbili National Hospital from December 2015 - March 2016.

CHAPTER TWO

2.0 MATERIALS AND METHODS

2.1 Study design

This is a hospital based cross-sectional descriptive study conducted at MNH from December 2015 - March 2016.

2.2 Study population and study area

The study population includes all adult patients with suspected HCC who underwent abdominal CT scan investigation at MNH from December 2015 - March 2016.

MNH is the largest referral and teaching hospital in Tanzania, located in Dar es Salaam city. It receives referred patients from all referral hospitals of the country, as well as patients from various hospitals in Dar-Es-Salaam, its surrounding regions and sometimes self-referred as well as emergency cases.

The Radiology and Imaging department of Muhimbili National Hospital is well equipped. It has almost all imaging modalities in place. These include Radiography units, ultrasound, Radiofluoroscopy, CT and MRI. Others include mammography and dental radiography.

There are 8 diagnostic Radiologists and 28 Radiographers, together with other supporting staff including nurses and attendants.

2.3 Inclusion criteria

All patients who underwent abdominal CT scan investigation with suspected HCC at MNH from December 2015- March 2016.

2.4 Exclusion criteria

All patients who are not suspected of HCC who were subjected to abdominal CT scan investigation at MNH from December 2015- March 2016 were excluded.

2.5 Sampling procedures

The sampling procedure used in the study is convenience sampling with the representative participants being those patients with suspected HCC who underwent abdominal CT scan from December 2015 - March 2016.

2.6 Sampling and Sample size

All adult patients with suspected HCC and subjected to abdominal CT scan with the eventual diagnosis of a hepatic mass/es from December 2015 -March 2016 were included in the study.

The sample size is calculated from the formula $n=Z^2P(1-P)/E^2$ where

n= sample size,

Z = (1.96)

P = prevalence = 4.6%. This is the prevalence of HCC due to aflatoxin globally(28)

95% confidence interval was used.

E = error margin 5%

Therefore $n= \frac{(1.96)^2 \times 0.046\ (1 - 0.046)}{(0.05)^2}$

n = 67 + 7 (10% 0f 67) , so the sample size in this study is 74 patients

2.7 Ethical issues

Ethical clearance to conduct the study was obtained from Muhimbili University (MUHAS) ethical committee. Before data collection, permission to conduct the study at MNH Radiology department was obtained from the MNH relevant authority. The information recorded in the questionnaire and clinical forms were used for study purposes and not otherwise.

2.8 Data collection procedure:

2.8.1Questionnaires and CT scan findings recording form.

The questionnaires were filled in by the investigator and were used to collect socio-demographic information such as age, sex, symptoms and radiological patterns/findings. These were filled in at the time of reporting abdominal CT scan reports. In addition abdominal CT scan reports were used to classify the findings which aided in planning management.

2.9 Study variables

2.9.1 Dependent variable

The dependent variable in the study was an adult patient with clinically suspected HCC who underwent an abdominal CT scan investigation at MNH.

2.9.2 Independent variable

The independent variable in the study is the role of CT radiological features in the diagnosis of adult patients with clinically suspected HCC at MNH.

2.10 Data analysis plan

The study used a descriptive data analysis plan involving univariate analysis describing the distribution, central tendency and dispersion of the data. The data collected from the questionnaires was scored in the following way using SPSS version 16.0 program:

1. Type of mass (according to whether the mass enhances or not, respectively):

I. Cystic: 1
II. Solid: 2
III. Complex:3

2. Lymph node involvement associated with hepatic masses:

I. Present: 1
II. Absent: 2

CHAPTER THREE

3.0 RESULTS

Table 1: Frequency table of imaging diagnosis among patients with suspected HCC undergoing abdominal computed tomography at MNH

Diagnosis	Frequency	Percent
HCC	27	36.5
Metastasis	30	40.5
Lymphoma	4	5.4
Simple cyst	10	13.5
Hepatic abscess	2	2.7
Polycystic liver	1	1.4
Total	74	100.0

A total of seventy four (74) patients were involved in this study. 36.0 % of the patients were found to have HCC (Table 1).

Table 2: Sociodemographic characteristics among patients with suspected HCC undergoing abdominal computed tomography at MNH

	HCC				
	Yes	**No**			
Age	**N= 27**	**N= 47**	**N= 74**	**X^2**	**p-value**
Below 60 years	10 (47.62%)	11 (52.38%)	21 (28.38%)	1.568	0.216
60 years and above	17 (32.08%)	36 (67.92%)	53 (71.62%)		
Sex	**N= 27**	**N= 47**	**N= 74**	**X^2**	**p-value**
Male	18 (45.00%)	22 (55.00%)	40 (54.05%)	2.723	0.099
Female	9 (26.47%)	25 (73.53%)	34 (45.95%)		

Male gender was non-significantly lesser associated with patients with HCC (p-value= 0.216)(Table 2).

HCC, in the adults, was found to be non-significantly lesser associated with patients 60 years and below (p-value= 0.099)(Table 2).

Table 3a: Abdominal CT findings among patients with suspected HCC: liver size, liver surface, liver attenuation and mass attenuation

	HCC				
	Yes	**No**	**Total**		
Shrunken liver	**N=27**	**N=47**	**N=74**	**X^2**	**p-value**
Yes	5 (18.52%)	1 (2.13%)	6 (8.11%)	6.184	0.013
No	22 (81.48%)	46 (97.87%)	68 (91.89%)		
Enlarged liver	**N=27**	**N=47**	**N=74**	**X^2**	**p-value**
Yes	20 (74.07%)	27 (57.45%)	47 (63.51%)	2.046	0.153
No	7 (25.93%)	20 (42.55%)	27 (26.49%)		
Nodular Liver surface	**N=27**	**N=47**	**N=74**	**X^2**	**p-value**
Yes	9 (33.33%)	0 (0%)	9 (12.16%)	17.836	0.000
No	18 (66.67%)	47 (100%)	65 (87.84%)		
Heterogeneous liver attenuation	**N=27**	**N=47**	**N=74**	**X^2**	**p-value**
Yes	1 (3.70%)	0 (0.0%)	1 (1.35%)	1.765	0.184
No	26 (96.30%)	47 (100%)	73 (98.65%)		
Normal liver attenuation	**N=27**	**N=47**	**N=74**	**X^2**	**p-value**
Yes	21 (77.78%)	47 (100%)	68 (91.89%)	11.366	0.001
No	6 (22.22%)	0 (0%)	6 (8.11%)		

Table 3b: Abdominal CT findings among patients with suspected HCC: liver size, liver surface, liver attenuation and mass attenuation

	HCC				
	Yes	**No**	**Total**		
Hypoattenuating liver	**N=27**	**N=47**	**N=74**	**X^2**	**p-value**
Yes	5 (18.52%)	0 (0.0%)	5 (6.76%)	9.334	0.002
No	22 (81.48%)	47 (100%)	69 (93.24%)		
Heterogeneous mass attenuation	**N=27**	**N=47**	**N=74**	**X^2**	**p-value**
Yes	9 (33.33%)	6 (12.77%)	15 (20.27%)	4.489	0.034
No	18 (66.67%)	41 (87.23%)	59 (79.73%)		

A significant association between shrunken liver and HCC was seen (18.52 % vs. 2.13%; p-value= 0.013) (Table 3a).

No significant association between enlarged liver size and HCC (74.07 % vs. 57.45%; p-value= 0.153) (Table 3a).

A significant association was seen in cases with a nodular liver surface and HCC (33.33 % vs. 0.0%; p-value= 0.000) (Table 3a).

No significant association was seen between a heterogeneous liver attenuation and HCC (3.70% vs. 0%; p-value= 0.184) (Table 3a)..

Normal liver attenuation was significantly lesser associated with HCC (77.78% vs. 100%; p-value= 0.001) (Table 3a).

A hypoattenuating liver was found to be significantly associated with HCC (18.52% vs. 0%; p-value= 0.002) (Table 3b).

A heterogeneous mass attenuation was significantly associated with HCC, (33.33% vs. 12.77%; p-value= 0.034) (Table 3b).

Table 3c: Abdominal CT findings among patients with suspected HCC: mass margins, mass properties, content predominance and contrast enhancement

	HCC				
	Yes	**No**	**Total**	**X^2**	**p-value**
Irregular mass margins	**N=27**	**N=47**	**N=74**		
Yes	20 (74.07%)	26 (55.32%)	46 (62.16%)	2.565	0.109
No	7 (25.93%)	21 (44.68%)	28 (37.84%)		
Complex Mass properties	**N=27**	**N=47**	**N=74**	**X^2**	**p-value**
Yes	11 (40.74%)	33 (70.21%)	44 (59.46%)	6.179	0.013
No	16 (53.3%)	14 (29.79%)	30 (40.5%)		
Solid content predominance	**N=27**	**N=47**	**N=74**	**X^2**	**p-value**
Yes	18 (66.67%)	14 (29.79%)	32 (43.24%)	9.503	0.002
No	9 (33.33%)	33 (70.21%)	42 (56.76%)		
Heterogeneous contrast enhancement	**N=27**	**N=47**	**N=74**		
Yes	9 (33.33%)	4 (8.51%)	10 (13.5%)	7.297	0.007
No	18 (66.67%)	43 (91.49%)	64 (86.49%)		

Irregular mass margins was found to be non-significantly associated with HCC (74.07% vs. 55.32%; p-value= 0.109) (Table 3c).

Complex hepatic masses were significantly lesser associated with HCC (40.74% vs. 70.21%; p-value= 0.013) (Table 3c).

Solid content predominance of the mass was significantly associated with HCC (66.67% vs. 29.79%; p-value= 0.002) (Table 3c).

Heterogeneous mass enhancement post-contrast administration had no significant association with HCC (33.33% v 8.51%)(p-value= 0.007)(Table 3c).

Table 3d: Abdominal CT findings among patients with suspected HCC: Calcification, peripheral fat stranding, ascites and lymphadenopathy

	HCC				
	Yes	**No**	**Total**	**X^2**	**p-value**
Calcification	**N=27**	**N=47**	**N=74**		
Present	0 (0.0%)	1 (2.13%)	1 (1.4%)	0.582	0.445
Absent	27 (100%)	46 (97.87%)	73 (98.6%)		
Ascites	**N=27**	**N=47**	**N=74**		
Present	13 (48.15%)	9 (19.15%)	22 (29.7%)	6.903	0.009
Absent	14 (51.85%)	38 (80.85%)	52 (70.3%)		
Lymphadenopathy	**N=27**	**N=47**	**N=74**		
Present	2 (7.41%)	8 (17.02%)	10 (13.5%)	1.356	0.244
Absent	25 (92.59%)	39 (82.98%)	64 (86.5%)		

Calcification was non-significantly lesser associated with HCC (0% vs 2.13%; p-value= 0.445) (Table 3d).

Ascites was not significantly associated with HCC(48.15% vs. 19.15%; p-value= 0.009) (Table 3d).

Lymphadenopathy was non-significantly lesser associated with HCC(7.41% vs. 17.02%; p-value= 0.244)(Table 3d).

CHAPTER FOUR

4.0 DISCUSSION

The gender distribution for HCC seen in the study i.e. male patients were more affected in comparison to female patients is consistent with another study done which showed on average the male: female ratio to be between 2:1 and 4:1(2). Another study also found a male predilection with HCC(29).

The age group found to be non-significantly associated with HCC i.e. 60 years and younger population, is noted in studies done which accredited the increasing emergence of HCC in younger adult populations to the hepatitis B and C virus or HBV & HBC and a general increase in other risk factors(2)(6).

There is a strong correlation between HCC and chronic liver disease including cirrhosis. In non-Asian populations, the people most likely to develop HCC are those with hepatic cirrhosis(18). The features of liver cirrhosis investigated in this study included liver size, surface/outline and attenuation with respect to the liver and additional features included the presence or absence of ascites.

A shrunken liver was found to be significantly associated with HCC. This is in-keeping with other studies which found a statistical significance between a shrunken liver and HCC (13) (18). An enlarged liver was not significantly associated with HCC although other studies done showed a significant association between enlarged livers and HCC in the non-cirrhotic liver setting(19) (20). The significant association seen in these studies may be attributed to the fact that the patients involved in these studies all had HCC in a non-cirrhotic liver.

A nodular liver surface was significantly associated with HCC and is in keeping with a study which found that, a nodular liver surface was significantly associated with HCC(23). Another study revealed a smooth liver surface to be significantly associated with HCC in the non-cirrhotic liver(21).

A hypoattenuating liver was found to be significantly associated with HCC and is in keeping with a study done which found a significant association between HCC and a hypoattenuating liver(30).

A normal liver attenuation was found to be less significantly associated with HCC which is contrary to other studies which found a significant association with heterogenous liver attenuation and HCC and non-significant association between HCC and normal liver attenuation(18)(22). A heterogenous liver attenuation was non-significantly associated with HCC in this study. The presence of a heterogeneous liver attenuation in HCC is attributable to the presence of fatty infiltration, fibrosis and hepatic parenchymal nodules or masses(18)(22). The difference in association seen may be attributable to the fact that both these studies, involved patients already diagnosed with HCC(18)(22).

Ascites was non-significantly associated with HCC and is contrary to other studies which found the presence of ascites to be significantly associated with HCC and seen in roughly 50% of cases at time of presentation(12,23,31–35).

Regional lymph-node involvement was seen with a frequency of less than 10% in this study and is contrary in comparison to a study done which found a frequency between regional lymph-node involvement and HCC being more than 30% (35). This discrepancy may be attributed to the fact that the study only analysed patients with extra-hepatic metastases of HCC whereas the present study was focused more on radiological features of adult patients with clinically suspected HCC.

Calcification was non-significantly lesser associated with HCC. According to a study done, calcification was reported in 15%-25% of malignant hepatocellular neoplasm's assessed with CT(36). It must be noted,however, that in the study, all patients had some form of liver calcification (36).

Heterogeneous mass attenuation and complex mass property were significantly associated with HCC on pre-contrast administered images. A solid content predominance of the masses

and a heterogeneous mass enhancement pattern post IV contrast administration were also found to be significantly associated with HCC.

Irregular mass margins on post-contrast administration images were non-significantly associated with HCC. Other studies done, reported a significant association between HCC and an irregular mass margin (37–39). The difference noted may be due to the fact that in the other studies MRI was the diagnostic modality used instead of CT (37–39).

CHAPTER FIVE

5.0 CONCLUSION AND RECOMMENDATION

5.1 Conclusion

The relation of HCC to gender in the study showed an expected outcome with the majority of cases involved in the study being male. The male: female ratio of 3:1 seen in the study is within the average ratio of HCC epidemiological presentation. The increase in the incidence of HCC in the older age group is in keeping with literature on the epidemiology of HCC especially in areas of high incidence.

Various ailments associated with HCC were identified/documented. These ailments included ascites, and regional lymph node involvement. Calcification was absent and not seen in a single case. Ascites was common and associated with roughly a half of all HCC cases. Lymph node involvement was also relatively rare.

The liver was shrunken with a nodular outline in the majority of cases. Most cases involved in the study had a heterogeneously attenuating mass pattern on pre-contrast images, irregular margined masses with a predominantly solid mass property and heterogenously enhancing pattern post IV contrast administration.

5.2 Recommendations

The following are the recommendations from the study:

1. Biopsy histology results to be considered in future studies in correlation with radiological patterns observed to confirm or change the diagnosis.
2. Larger sample size to be used in future studies.

5.3 Limitations

The study had 2 limitations. The following are the limitations experienced in the study:

1. Few patients were involved in the study.
2. Hospital based study and so the results cannot be generalised to general population.

REFERENCES

1. Bernard W, Christopher PW. World cancer report 2014. international agency for research on cancer. World Health Organization, Lyon, France. 2014.

2. El–Serag HB, Rudolph KL. Hepatocellular carcinoma: epidemiology and molecular carcinogenesis. Gastroenterology. 2007 Jun 30;132(7):2557-76.

3. Ryder SD. Guidelines for the diagnosis and treatment of hepatocellular carcinoma (HCC) in adults. Gut. 2003 May 1;52(suppl 3):iii1-8.

4. El-Serag HB, Davila JA. Is fibrolamellar carcinoma different from hepatocellular carcinoma? A US population-based study. Hepatology. 2004 Mar 1;39(3):798-803.

5. Farhi DC, Shikes RH, Murari PJ, Silverberg SG. Hepatocellular carcinoma in young people. Cancer. 1983 Oct 15;52(8):1516-25.

6. Jemal A, Center MM, DeSantis C, Ward EM. Global patterns of cancer incidence and mortality rates and trends. Cancer Epidemiology and Prevention Biomarkers. 2010 Aug 1;19(8):1893-907.

7. LEONG TY, LEONG AS. Epidemiology and carcinogenesis of hepatocellular carcinoma. Hpb. 2005 Mar 1;7(1):5-15.

8. El-Serag HB, Davila JA, Petersen NJ, McGlynn KA. The continuing increase in the incidence of hepatocellular carcinoma in the United States: an update. Annals of internal medicine. 2003 Nov 18;139(10):817-23.

9. Seeff LB. Introduction: The burden of hepatocellular carcinoma. Gastroenterology. 2004 Nov 1;127(5):S1-4.

10. Tsukuma H, Hiyama T, Tanaka S, Nakao M, Yabuuchi T, Kitamura T, Nakanishi K, Fujimoto I, Inoue A, Yamazaki H, Kawashima T. Risk factors for hepatocellular carcinoma among patients with chronic liver disease. New England journal of

medicine. 1993 Jun 24;328(25):1797-801.

11. Blonski W, Kotlyar DS, Forde KA. Non-viral causes of hepatocellular carcinoma. World journal of gastroenterology: WJG. 2010 Aug 7;16(29):3603.

12. Sangster GP, Previgliano CH, Nader M, Chwoschtschinsky E, Heldmann MG. MDCT imaging findings of liver cirrhosis: spectrum of hepatic and extrahepatic abdominal complications. HPB Surgery. 2013 Aug 6;2013.

13. Mergo PJ, Ros PR, Buetow PC, Buck JL. Diffuse disease of the liver: radiologic-pathologic correlation. Radiographics. 1994 Nov;14(6):1291-307.

14. Wanless IR. Terminology of nodular hepatocellular lesions. Hepatology. 1995 Sep 1;22(3):983-93.

15. Vilgrain V, Paradis V, Menu Y, Mortele KJ, Terris B, Ros PR. Primary Hepatic Malignant Neoplasms: Radiologic-Pathologic Correlations. InRadiologic-Pathologic Correlations from Head to Toe 2005 (pp. 367-389). Springer Berlin Heidelberg.

16. Chung YE, Park MS, Park YN, Lee HJ, Seok JY, Yu JS, Kim MJ. Hepatocellular carcinoma variants: radiologic-pathologic correlation. American Journal of Roentgenology. 2009 Jul;193(1):W7-13.

17. Colli A, Fraquelli M, Conte D. Alpha-fetoprotein and hepatocellular carcinoma. The American journal of gastroenterology. 2006 Aug 1;101(8):1939.

18. Oliver 3rd JH, Baron RL, Federle MP, Rockette Jr HE. Detecting hepatocellular carcinoma: value of unenhanced or arterial phase CT imaging or both used in conjunction with conventional portal venous phase contrast-enhanced CT imaging. AJR. American journal of roentgenology. 1996 Jul;167(1):71-7.

19. Kubo Y, Okuda K, Musha H, Nakashima T. Detection of hepatocellular carcinoma during a clinical follow-up of chronic liver disease. Gastroenterology. 1978 Mar 1;74(3):578-82.

20. Bismuth H, Chiche L, Castaing D. Surgical treatment of hepatocellular carcinomas in noncirrhotic liver: experience with 68 liver resections. World journal of surgery. 1995 Jan 1;19(1):35-41.

21. Gaddikeri S, McNeeley MF, Wang CL, Bhargava P, Dighe MK, Yeh MM, Dubinsky TJ, Kolokythas O, Lalwani N. Hepatocellular carcinoma in the noncirrhotic liver. American Journal of Roentgenology. 2014 Jul;203(1):W34-47.

22. Shapiro RS, Katz R, Mendelson DS, Halton KP, Schwartz ME, Miller CM. Detection of hepatocellular carcinoma in cirrhotic patients: sensitivity of CT and ultrasonography. Journal of ultrasound in medicine. 1996 Jul 1;15(7):497-502.

23. Brancatelli G, Federle MP, Ambrosini R, Lagalla R, Carriero A, Midiri M, Vilgrain V. Cirrhosis: CT and MR imaging evaluation. European journal of radiology. 2007 Jan 31;61(1):57-69.

24. Guzman G, Brunt EM, Petrovic LM, Chejfec G, Layden TJ, Cotler SJ. Does nonalcoholic fatty liver disease predispose patients to hepatocellular carcinoma in the absence of cirrhosis?. Archives of pathology & laboratory medicine. 2008 Nov;132(11):1761-6.

25. Baron RL, Brancatelli G. Computed tomographic imaging of hepatocellular carcinoma. Gastroenterology. 2004 Nov 30;127(5):S133-43.

26. Giorgio A, Ferraioli G, Tarantino L, de Stefano G, Scala V, Scarano F, Coppola C, Del Viscovo L. Contrast-enhanced sonographic appearance of hepatocellular carcinoma in patients with cirrhosis: comparison with contrast-enhanced helical CT appearance. American Journal of Roentgenology. 2004 Nov;183(5):1319-26.

27. Kew MC. Epidemiology of hepatocellular carcinoma in sub-Saharan Africa. Ann Hepatol. 2013 Mar 1;12(2):173-82.

28. Liu Y, Wu F. Global burden of aflatoxin-induced hepatocellular carcinoma: a risk assessment. Environmental health perspectives. 2010 Jun;118(6):818.

29. Bosh FX. Hepatocellular carcinoma in the world: Epidemiological questions. Etiology, pathology, and treatment of hepatocellular carcinoma in North America. 1991:35-4.

30. Iannaccone R, Piacentini F, Murakami T, Paradis V, Belghiti J, Hori M, Kim T, Durand F, Wakasa K, Monden M, Nakamura H. Hepatocellular carcinoma in patients with nonalcoholic fatty liver disease: helical CT and MR imaging findings with clinical-pathologic comparison. Radiology. 2007 May;243(2):422-30.

31. Zahir ST, Aalipour E, Vakili M, Gane MD. CLINICOPATHOLOGICAL FEATURES OF LIVER TUMOURS: A TEN-YEAR STUDY. Journal of Ayub Medical College Abbottabad. 2015 Dec 15;27(4):775-9.

32. Redvanly RD, Nelson RC, Stieber AC, Dodd 3rd GD. Imaging in the preoperative evaluation of adult liver-transplant candidates: goals, merits of various procedures, and recommendations. AJR. American journal of roentgenology. 1995 Mar;164(3):611-7.

33. Bruix J, Sherman M. Management of hepatocellular carcinoma: an update. Hepatology. 2011 Mar 1;53(3):1020-2.

34. Tyrrel RT, Montemayor KA, Bernardino ME. CT density of mesenteric, retroperitoneal, and subcutaneous fat in cirrhotic patients: comparison with control subjects. AJR. American journal of roentgenology. 1990 Jul;155(1):73-5.

35. Uchino K, Tateishi R, Shiina S, Kanda M, Masuzaki R, Kondo Y, Goto T, Omata M, Yoshida H, Koike K. Hepatocellular carcinoma with extrahepatic metastasis. Cancer. 2011 Oct 1;117(19):4475-83.

36. Stoupis C, Taylor HM, Paley MR, Buetow PC, Marre S, Baer HU, Vock P, Ros PR. The Rocky liver: radiologic-pathologic correlation of calcified hepatic masses. Radiographics. 1998 May;18(3):675-85.

37. Kanematsu M, Semelka RC, Leonardou P, Mastropasqua M, Lee JK. Hepatocellular carcinoma of diffuse type: MR imaging findings and clinical manifestations. Journal of Magnetic Resonance Imaging. 2003 Aug 1;18(2):189-95.

38. Halıloğlu N, Özkavukcu E, Erden A, Erden İ. MR imaging in diffuse-type hepatocellular carcinoma with synchronous portal vein thrombi. The Turkish journal of gastroenterology: the official journal of Turkish Society of Gastroenterology. 2011;22(2):158-64.

39. Park YS, Lee CH, Kim BH, Lee J, Choi JW, Kim KA, Ahn JH, Park CM. Using Gd-EOB-DTPA-enhanced 3-T MRI for the differentiation of infiltrative hepatocellular carcinoma and focal confluent fibrosis in liver cirrhosis. Magnetic resonance imaging. 2013 Sep 30;31(7):1137-42.

APPENDICES

Appendix I: Questionnaire English Version

RECORDING FORM FOR DERMOGRAPHIC DATA AND SYMPTOMS ASSOCIATED WITH THE ABDOMEN

ID No. ..... Date: _____/_____/2014/15

I. Socio-demographic details

i. Gender

1.) Male [ ] 2.) Female [ ]

II. Date of Birth (year): .....

III. Symptoms:

- Abdominal swelling 1. Yes 2. No
- Losing weight without trying 1. Yes 2. No
- Loss of appetite 1. Yes 2. No
- Upper abdominal pain 1. Yes 2. No
- Nausea and vomiting 1. Yes 2. No
- General weakness and fatigue 1. Yes 2. No
- Abdominal swelling 1. Yes 2. No
- Yellow discoloration of your skin and the whites of your eyes (jaundice) 1. Yes 2. No
- White, chalky stools 1. Yes 2. No
- Melena 1. Yes 2. No
- Hematemesis 1. Yes 2. No
- Other: .....

IV. General imaging findings:

1. Presence of hepatic mass 1. Yes 2. No
2. Presence of lymph nodes (para-aortic) 1. Yes 2. No
3. Ascites 1. Yes 2. No

V. Liver:

A. Size (cms) .....

1. Enlarged 2. Normal size 3. Shrunken

B. Surface

25.

26.

1. Smooth 2. Nodular

C. Characteristics of the mass:

1. Homogeneity: a. Homogenous b. Heterogeneous
2. Margins: a. Smooth b. Irregular
3. Properties of the mass a. Solid b. Cystic
4. Complexity: a. Simple b. Complex (if complex go to no.3).
5. Content predominance: a. Solid b. Cystic
6. Attenuation: a. Hypo b. Iso c. Hyper
7. Enhancement: a. Enhancing b. Non-enhancing c. Mixed
8. Presence of calcification: a. Yes b. No
9. Vascular encasement: a. Yes b. No
10. Vascular invasion: a. Yes b. No
11. Peripheral soft tissue stranding: a. Yes b. No

D. The most likely diagnosis:

1. Hepatoma a. Yes b. No
2. Hemangioma a. Yes b. No
3. Hepatic adenoma a. Yes b. No
4. Focal Nodular Hyperplasia (FNH) a. Yes b. No
5. Metastasis a. Yes b. No
6. Liver cirrhosis a. Yes b. No
7. Simple hepatic cyst a. Yes b. No
8. Hydatid cyst a. Yes b. No
9. Hepatic abscess a. Yes b. No
10. Liver cirrhosis a. Yes b. No
11. Biliary cystic tumor a. Yes b. No
12. Hepatic metastasis a. Yes b. No
13. Fibrolamellar Carcinoma (FLC) a. Yes b. No
14. Cholangiocarcinoma a. Yes b. No
15. Primary hepatic leiomyosarcoma a. Yes b. No

Other .....