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Tafaul-Al-Ahsa Cancer Foundation Wins EXCELLENCE AWARD for Cancer Awareness Initiatives at Gulf Cancer Awareness Week 2024

The Gulf Oncology Society meeting resulted in fruitful outcomes, with young doctors showing keen enthusiasm for assuming leadership roles and implementing impactful initiatives.

The Official Journal of the Gulf Federation For Cancer Control

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Epidemiological, Diagnostic and Therapeutic Aspects of Hepatocellular Carcinoma in Morocco: A Case Series and Review of Literature

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Abstract

Introduction: Hepatocellular carcinoma (HCC) is the most common primary liver tumor. It is considered a global public health problem given its incidence and high mortality rate. Epidemiological studies on hepatocellular carcinoma in our Moroccan and North African contexts are rare. Hence, our study aims to determine the epidemiological, clinical, paraclinical, etiological and therapeutic aspects of this pathology in our context.

Materials and methods: We conducted a descriptive retrospective study on patients with HCC treated by the Hepato–gastroenterology department of the university hospital of Mohammed VI in Marrakech over a period of 7 years spread between 01/01/2015 and 31/12/2021. The epidemiological characteristics, diagnostic methods and therapeutic management of HCC in these patients have been described and analyzed.

Results: 100 patients with HCC were identified and included in our study. The average age was 63.3 ± 12.63 years with a male predominance. The predominant etiology was cirrhosis (87% of cases) then viral hepatitis C (35%) and B (27%) and of unknown origin in 29% of cases. HCC revealed cirrhosis in 41% and was diagnosed during cirrhosis surveillance in 36% of cases. The functional signs were dominated by abdominal pain (68%), deterioration of general condition (58%) and abdominal distension (43%). Alfa–fetoprotein was elevated in 73% of cases and was above 400ng/ml in 41% of cases. The diagnosis was mainly radiological in 92% and histological in 8% of cases. The radiological aspects of HCC were dominated by mononodular form (58%), a right lobar location (80%), a diameter greater than 5 cm (58%), a typical vascular aspect (86%) with portal thrombosis in 24% and metastases in 36% of cases, especially in lymph nodes. The majority of cirrhosis in our series was classified as Child–Pugh stage B (46%) at the time of diagnosis and most patients had an advanced stage of HCC with 31% at BCLC C and 28% at BCLC D. 72% of patients received palliative treatment, and only 6% received curative treatment. At the end of the study, 48% of patients had died with an overall survival of 6.5 months.

Conclusion: Our study achieved its main objective by providing a snapshot of HCC in our context and confirmed that HCC remains with poor prognosis since its diagnosis is often late, limiting the therapeutic choices with a very short median survival. It also noted that the viral etiology remains the main cause of HCC in our population. Therefore, prevention remains the best therapeutic approach against HCC and the need for a national or at least a regional HCC registry in our country is essential in order to develop targeted preventive measures adapted to our context and to improve the diagnostic and therapeutic approaches for our patients.

Keywords: Hepatocellular carcinoma – Liver cancer – Epidemiology – Observational study – Morocco

Introduction:

Hepatocellular carcinoma is the most common primary liver tumor, accounting for more than 80% of cases[1]. According to GLOBOCAN 2020 estimates, it is the sixth most commonly diagnosed cancer and the third leading cause of cancer deaths worldwide [2]. In 2020, its incidence was estimated at 905,700 newly diagnosed cases and its mortality at 830,200 globally[2].

Cirrhosis is the main risk factor for HCC since it most often occurs in the cirrhotic liver [1,3–5]. Advanced age, male gender, viral B and C infections and aflatoxins are also major

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risk factors for HCC[1,3,5]. However, other factors such as type 2 diabetes and metabolic syndrome are increasingly implicated in its pathogenesis [1,3,5]. Unlike other solid tumours, its diagnosis is often non–invasive in the case of cirrhosis and is based on imaging data. Histological confirmation is only necessary if the radiological aspect is atypical and in non–cirrhotic patients[1,4,6]. The ideal curative treatment is liver transplantation as it treats not only the tumor but also the underlying cirrhosis[4,7,8]. However, its indications are limited given the organ shortage as well as its frequent contraindications. Surgical resection is even less indicated since most patients consult at an advanced stage of the disease. Thus, other percutaneous curative treatments have been proposed allowing either chemical or thermal ablation of nodules such as radiofrequency and microwave ablation. For advanced HCC, palliative treatment is based either on intra–arterial therapies such as chemoembolization or radioembolization, or on systemic therapy with a tyrosine kinase inhibitor.

After several years of therapeutic stagnation, the advent of immunotherapy and especially immunological checkpoint inhibitors (ICI) has revolutionized the management of advanced HCCs [9,10].

Epidemiological studies on HCC in our context are rare. The BRIDGE study[11] which is considered the largest descriptive study of HCC in the world did not include African countries in its data, and even the largest multicenter African study [12] did not include neither Morocco nor other North African countries, which makes studies like ours important in order to understand the epidemiological, diagnostic and therapeutic profile of HCC in our context. Through this study, we aim to describe the epidemiological, clinical, paraclinical and therapeutic characteristics of HCC in the hepato–gastroenterology department of the University hospital of Mohammed VI of Marrakech in comparison with the literature data.

Patients and methods:

Design and subjects:

We conducted a descriptive study on patients with HCC treated by the Hepato–gastroenterology department of the university hospital of Mohammed VI in Marrakech over a period of 7 years spread between 1st January 2015 and 31st December 2021.

The study's main objective is to describe the epidemiological profile, the etiological factors, the diagnostic methods as well as the management of HCC patients by comparing the results of our service with the literature data.

Inclusion criteria:

- Patients with confirmed diagnosis of HCC either histological (on a liver biopsy or on an operating specimen) or a typical radiological appearance with epidemiological and clinico–biological context in favor of HCC in accordance with AASLD, EASL or comparable local guidelines.
- Patients cared for in the hepato–gastroenterology department of the university hospital Mohammed VI of Marrakech
- For the literature review component, the PubMed database was searched using a combination of MESH terms related to HCC. The MESH terms used were "hepatocellular carcinoma", "hepatocarcinoma", "Observational study" AND "hepatocellular carcinoma", "Observational study" AND "hepatocarcinoma". Studies published between 2010 and 2023 were included. All publications enrolled were in English (except for one in Spanish and another one in French). Data on patient demographics, clinical findings, management and outcomes were extracted. The bibliographies of all included studies were revealed to find other eligible cases.

Exclusion criteria:

- Patients with uncertain diagnosis of HCC
- Patients diagnosed with HCC before the 1st of January 2015 and after the 31st of December 2021
- Patients diagnosed with other primary liver cancers such as cholangiocarcinoma or liver metastases
- Patients of non–Moroccan nationality
- Pregnant women and children (age<15 years)
- Files that are incomplete or not found
- In terms of our literature review, we excluded comments, editorials, other study types without clinical data from patients, unavailable articles and studies with insufficient data. Also, studies published prior to 2010 and/or including children or pregnant women were excluded.

Data collection:

The demographic, diagnostic and therapeutic data as well as the follow–up of the patients were collected from the medical files as well as the computerized archives of our hepato–gastroenterology department.

Some therapeutic and follow–up data for our patients were collected by telephonic follow–up as well as from

the archives of oncology and general surgery departments of our university hospital.

Data analysis:

The exploitation of the data was based on a pre–established sheet while respecting the anonymity and confidentiality of the patients.

The analysis focused on descriptive data. Quantitative data were presented by means, medians, standard deviations and intervals. Qualitative data was presented by numbers, frequencies and percentages.

Data entry and analysis was performed using EXCEL 2016 software.

Limitations of the study:

The retrospective nature of our study imposes some challenges such as the lack of some information in the medical records. Most of the patients were lost to sight after the therapeutic indication was made and were unreachable by telephone contact during the realization of this work.

Ethical Considerations:

The rules of ethics relating to the respect of confidentiality and the protection of patient–specific data were respected during the realization of this work.

Results:

Over a period of seven years, our department numbered 246 hospitalizations with the diagnoses of "HCC", "Hepatic nodule", "Nodular liver" including 113 patients with confirmed diagnoses of HCC. Only 100 files were admitted according to our inclusion/exclusion criteria.

The average age in our study population was 63.3 years with a standard deviation of 12.63 and extremes ranging from 17 to 87 years. The majority of our patients (84%) were between 50 and 80 years old. The male/female ratio was 1.5 with 60% men and 40% women.

In our series, 6% of patients had no known risk factors. A total of 87% of our patients had cirrhosis at the time of the diagnosis of HCC and 13% of patients had a non–cirrhotic liver, of which 3% had chronic viral liver disease: two cases of HBV and one case of HCV. Cirrhosis was secondary to viral hepatitis C in 39% of the cases, to viral hepatitis B in 29% and of unknown etiology in 22% of cases. The other etiologies are summarized in Table 1.

17% of patients were chronic alcoholic and smokers, 1% chronic alcoholic only and 10% were chronic smokers only. Diabetes mellitus (DT2) was present in 17% of our cases while hypertension (HTN) was noted in 20%. 33% of our patients had a high body mass index (BMI >25 kg/m²), of which 20% were overweight (BMI between 25 and 30) and 11% were obese (BMI >30). None of our patients had a history of dyslipidemia. In total, 13% of patients had an association of DT2 and obesity/overweight and 8% an association of DT2, hypertension and obesity/overweight. Among our patients, 85% had risk factors for viral transmission, 6% had a notion of medicinal plants consumption and 2% a history of unlabeled jaundice. Regarding risk factors for viral transmission, informal dental care was present in 73% of cases followed by fire points in 31% of cases. Other comorbidities are shown in Table 1.

HCC in our series was indicative of an unknown cirrhosis in 41% of our cases, diagnosed during surveillance of known cirrhosis in 36%, due to a cirrhotic decompensation in 9% of cases and due to other symptoms in 14% of cases. 71% of our patients were symptomatic at the time of diagnosis; Abdominal pain was the predominant symptom (68%), especially in the right hypochondrium, followed by deterioration of general condition (58%), abdominal distension (43%) and then jaundice (25%). Other symptoms are detailed in Table 1.

The predominant physical signs were abdominal tenderness in 68% of our cases, hepatomegaly in 51%, ascites in 45%, signs of portal hypertension: splenomegaly (SPM) in 37% and collateral venous circulation (CVC) in 27%, as well as jaundice which was present in 25% of our series. Troisier's ganglion was palpable in 2 patients of our series. Other physical signs are mentioned in Table 1.

As to biological findings, AFP was elevated in 73% of our cases. It was greater than 400 in 41% and in the range of 200–400 ng/ml in 9% of cases. The average AFP level in our series was 5487.9 (+/– 15362) with extremes ranging from 0.4 to 100,000 ng/ml. Some of our patients had, in addition to the elevation of AFP, an elevation of other tumour markers, especially CA19.9 (14%) and CA125 (7%). Liver function was normal in 22% of our patients. Cholestasis with cytolysis was objectified in 44%, while isolated cholestasis in 19% of cases, and isolated cytolysis in 15% of cases. Hyperbilirubinemia was noted in 69% of our cases and was above 30 mg/l in 16%. Hypoalbuminemia was noted in 80% of cases and the TP was less than 50% in 20% of cases. No data available on factor V in our series.

As for radiological findings, abdominal ultrasound was the first–line examination in 71% of cases. It required additional cross–sectional imaging in all but one of the cases. Abdominal CT angiography was the reference examination performed in 87% of cases. MRI was performed in 49% of cases complementary to an ultrasound and/or a CT.

Study	Country	Number	Sex ratio	Age	Etiology (%)	Comorbidities	Clinical symptoms (%)	AFP (ng/l)	Radiological findings (%)	Prognostic factors (%)	Treatment (%)	Survival (%)
Our study	Morocco (Marrakech)	100	1.5	63.3	Cirrhosis 87% Non cirrhotic10% HCV 35 HBV 27 Unknown 29 HBV+C 3 PBC 2 NASH 2 AIH 1 Overlap Sd 1	None 6 Smoking + Alcohol 17 Smoking 10 Alcohol 1 DT2+HTN 11 HTN 9 T2D 6 Overweight 20 Obesity 11 RFVH 85 Jaundice 2 COPD 1 Cardiopathy 2% Other tumours 2	None 29 Abdominal pain 68 AGS 58 Abdominal distension 43 Jaundice 25 GI bleeding 8 Diarrhea 3 Abdominal mass 2 Vomiting 2	<10 (27%) 10–400 (32%) >400 (41%)	Location : Right lobe (80%) Left lobe (12%) Bilobar (8%) Number : Mononodular (57%) 2–3 nodules (14%) Multinodular (29%) Diameter : <2cm (14%) 2–5 cm (28%) >5cm (58%) Typical vascular kinetics (86%) Ascites (31%) Dilated PV (17%) SPM (27%) PVT (24%) Metastasis : ADP (23%) Lung (16%) Adrenal gland (2%) Bone (2%) Peritoneal (1%)	OMS: 0 23% 1 29% 2 33% 3 10% 4 5% CTP: A 39% B 46% C16% Okuda: I 31% II 46% III 23% BCLC: A 16% B 21 % C 28% D 25%	RFA 3 LR 3 TACE 29 Sorafenib 5 Symptomatic treatment (38%) Lost to follow–up 22%	48 deaths 15 alive 37 lost to follow–up
Firwana et al.(14)	Morocco (Rabat)	440	1.7:1	63.3	Cirrhosis 100% HCV 69.7 HBV 15.2 Alcohol 0.9 Unknown 13.8%	None 43 RFVH 29.5 Jaundice 7.2 Smoking 21 Alcohol 10 T2D 9.5 HTN 8.8 Asthma 3.4 Pulmonary TBK 3.4	None 61.3 Abdominal pain 25, Jaundice 5.2, Asthenia 2.7, GI bleeding 2.2, Ascites 1.8, Other (pruritus, AGS) 1.5	>400 (17.5%)	HPM 42.7 Liver atrophy 5.2 1 nodule 50.6 2 nodules 26.1 3 nodules 10.6 > 3 nodules 12.5 SPM 24.3 Ascites 23.1 Dilated PV 12.9 Dilated splenic vein 7 ADP 2.2	CTP: A 66.1 B 27.4 C 6.4	RFA 9.7 LR 13.1 LT 0.2 PAI 17.9 AAI 2.5 Symptomatic 33.8	————
Bahri et al.(15)	Tunisia, Morocco, Algeria	164	1.5	62	Cirrhosis 65,8 Non cirrhotic 15,2 HCV 60 HBV 17.9 Unknown 22	T2D 18 Alcohol 17.6 Other (NM)	NM	NM	NM	NM	NM	NM

Study	Country	Number	Sex ratio	Age	Etiology (%)	Comorbidities	Clinical symptoms (%)	AFP (ng/l)	Radiological findings (%)	Prognostic factors (%)	Treatment (%)	Survival (%)
Pratic et al.(24)	Maroc (Marrakech)	76	1.7	59	Cirrhosis 72.3 Healthy liver 25 Chronic Hepatitis B or C 2.5 HCV 18,2 HBV 12,7 HCV+ alcohol 1,8 Alcohol 9,1 PBC 1,8 NASH 1,8 Unknown 54,5	NM	Abdominal pain 75 AGS 50 Jaundice 14,5 HPM 55,2 Ascites 39,4 SPM 19,7 Signs of HCI 13	>200 (81.4%)	Multinodular (> 2 nodules) 60,5 1 nodule 22,3 Infiltrating 6,6 Diameter : 1–14 cm Typical vascular kinetics 54,5 PVT 23,6 Metastasis : ADP 19,7 Bone 6,5 Peritoneum 25	CTP: A 20 B 31 C 38,1 Unknown 10,9 Okuda : I 18,1 II 32,7 III 38,2 Unknown 10,9 BCLC : A 13,1 B 10,5 C 21 D 50 Unknown 5,4	LT 1.3 LR 3.9 RFA 9.2 Sorafenib (+SBRT in one case) Symptomatic52,6 Lost to follow–up 6,7	Death 26.3
Musunuri et al.(25)	India	339	10,3	62.8	Cirrhotic 73.2 Non cirrhotic 26.8 Unknown 51.3 Alcohol 19.4 HBV 17.4 HCV 5.8 Alcohol + HBV 3.2 Alcohol + HCV 1.1 HBV+C 0.5 Others (Wilson disease, AIH, GSD) 0.8	T2D 44.2 HTA 32.4 HIV 0.9 ischemic cardiopathy 8.5 hypothyroidism 2.9 CVA 3.8 CKD 3.2 COPD 3.5	None 16.81 Abdominal pain 24.4 Ascites 24.1 Anorexia 20 Weight loss 17.9 Fatigue 10.9 GI bleed 6.4 Jaundice 6.1 Abdominal mass 1.7 Other 2.9	Normal (27.4%) 10–400 (24%) >400 (49%)	Location of tumor Right lobe 51.2 Left lobe 16.3 Bilobar 32.3 Number of lesions Single 33.4 Two 11.4 Multiple 55 Size of the lesion < 2 cm 5.7 2–5 cm 33.7 5 cm 60.6 Macrovascular thrombosis 45.7 PVT 67.5 Infradiaphramatic thrombosis 25.9 Supradiaphragmatic thrombosis 6.4 Tumor thrombosis 17.6 Metastasis 22.1	CTP: A 41 B 45.4 C 13.6 BCLC: 0 1.7 A 10.3 B 25.4 C 48.8 D 13.6 Okuda: I 17.7 II 62.8 III 19.5	Curative 13.6 LR 6 (+TACE prior to resection in 4 cases) RFA 7.1 LT 0.4 TARE 0.4 TACE 13.2 Palliative SBRT 1.1 palliative radiotherapy to vertebral metastasis 0.4 Sorafenib 54.1 Symptomatic 21.9	NM

Study	Country	Number	Sex ratio	Age	Etiology (%)	Comorbidities	Clinical symptoms (%)	AFP (ng/l)	Radiological findings (%)	Prognostic factors (%)	Treatment (%)	Survival (%)
Mansoor et al.(26)	Pakistan	278	2.23	60	Cirrhosis 100% No risk factors 5.4 HCV 54 HCV+DM 29 HBV+/−DM 6 HBV+C+/−DM 1.8 Alcohol +/− DM 3.6	NM	NM	<300 (64%) <= 300 (33.8%) Unknown (2.2%)	Unifocal 50.4 Multifocal 49.6 Size : <3 cm 16.2 3–5 cm 42.8 >5cm 41	CTP: A 84 B 11.5 C 4.3 BCLC: A 34.2 B 51.8 C 9.7 D 4.3	LR 2.2 Ablation (RFA, PEI) 4.3 TACE 65.1 TACE + Other (LR, RFA, PEI, Sorafenib) 8.3 Sorafenib 5 Symptomatic 15.1	NM
Gouttéet al.(16)	France	31,927	4	68	Cirrhosis (73.4) Alcohol 44 HCV 8 HBV 2.8 Mixed etiology 8.7 Unknown 36.4	Cardiopathy 16,5 T2D 32,4 Obesity 10 HTN 39,4	NM	NM	NM	NM	Curative treatment 22.8 LT 3.8 LR 11.2 Ablation 7.8 Palliative treatment: TACE 12.0 Chemotherapy 8.1 Symptomatic 57	NM
Rosa et al. (17)	France	782	6.7	67	Cirrhosis 86 Alcohol 72 HCV 15 HBV 9	NM	NM	NM	Mononodular 36 2–3 nodules 20 Multinodular 30 Infiltrative 14 PVT 27 Metastases 13	CTP: A 46 B 36 C 18	Curative 26 LT 7 LR 10 RFA 9 Palliative 35 TACE 14 Sorafenib 17 Symptomatic 39	Death 37.8
Schütte et al. (18)	Germany	650	4	65.7	Cirrhosis 80.7 Alcohol 52.2 HCV 13.7 HBV 3.6 NASH 5.9 Other 2.3 >1 risk factor 10 No data 12.2	T2D 52 Obesity 66.1	NM	<5 (15.5%) 5–200 (43.8%) >200 (40.7%)	Mononodular 39.7 Multinodular 60.3 PVT 29.7 Metastasis 24: ADP 10.15 Lung 7.38 Bone 4.46 Adrenal gland 3.08 Peritoneum 1.54	CTP: A 57.14 B 30.86 C 8.76 Unknown 3.24 BCLC: A 15.8 B 30 C 45.5 D 8.62	Curative : LR 13.23 LT 1.08 RFA 1.23 PEI 3.69. Palliative : TACE 22.92 Brachytherapy 9.08 SIR 3.54 Chemotherapy 3.38 Sorafenib 7.69 Other systemic therapies 18.15	NM

Study	Country	Number	Sex ratio	Age	Etiology (%)	Comorbidities	Clinical symptoms (%)	AFP (ng/l)	Radiological findings (%)	Prognostic factors (%)	Treatment (%)	Survival (%)
Farah et al. (19)	South America (Brazil, Argentina, Colombia, Peru, Ecuador and Chile)	339	1.56	67	Cirrhosis 80 Non–Cirrhotic 20 NASH 37 HCV 21 HBV 12 Alcohol 17 Other 6 None 7	T2D 57	NM	NM	NM	BCLC A 43 B 33 C 13 D 11	Curative treatment 28 LR 13 LT 6 RFA 7 PEI 2 Palliative treatment: TACE/TARE 27 Systemic therapy 12 Symptomatic 17 None 10	Death 52
De lope et al. (20)	Spain	686	4.5	67	Cirrhosis 87 Chronic hepatopathy 9 Healthy liver 4 Alcohol 35,4 HCV 29,7 Alcohol + HCV 14,7 NASH 5,9 HBV 3,8 Other 10,5	T2D 37 HTN 44.8 Dyslipidémia 12.7 Overweight/Obesity 69.9 HIV 1.9 Other tumors 17.4 Family history of CHC 2.7	None 58.1	<20 (59.7%) 20–400 (23.9%) >400 (16.4%)	Mononodular <2cm 14.7 Unique 2–5 cm 31.1 Unique >5cm 10 2–3 nodules 11.5 Multinodular 32.6 Vascular invasion 17.8 Métastases 8	CTP: A 62.9 B 29.3 C 7.1 BCLC: 0 10,9 A 42,9 B 19,4 C 15,5 D 11,2	Curative : LT 10 LR 11.2 Ablation 22 (RFA 13.7 PEI 2.47 MWA 2.18) TACE 22.7 Sorafenib 10.5 Y90 1.5	NM
Turcano et al. (27)	Moldova	139	1.9	59	Cirrhosis 82.9 HCV 55.3 HBV 36.1 HVD 18.5 HBV+C 13.6 HBV+C+D 7.2	Alcohol 53.6 Smoking 30 T2D 46.1 Overweight 34.7 Familial tumors 14.8 Previous personal tumors 12.2 RFVH : IVDU 9.8 Tatoos 12.7 Transfusion 46 Sex–transmitted infection 2.3	Abdominal pain 98 Weight loss 87.6 Encephalopathy 75 GI bleeding 26.7 Ascites 86.6 Digestive tract ulcers and inflammation 20.5	Normal 23.3 10–300 30.8 >300 45.8	Multinodular 35.5 PVT 58.7 Lymph nodes 79.3 Metastases 83.7	CTP: A 13.2 B 42.4 C 44.3	LT 3 LR 41.5 Chemotherapy 38.4 None 16.9	NM

Study	Country	Number	Sex ratio	Age	Etiology (%)	Comorbidities	Clinical symptoms (%)	AFP (ng/l)	Radiological findings (%)	Prognostic factors (%)	Treatment (%)	Survival (%)
Fenoglio et al. (28)	Italy	256	2.45	70	Cirrhosis 91.4 Chronic hepatopathy 7 Healthy liver 1.56 HCV 52.3 Alcohol 18.7 HBV 8.2 HBV+C 3.1 HBV+Alcohol 2.3 HCV+Alcohol 3.5 PBC1.6 AIH 0.8 HH 1.2 Unknown 8.2	T2D 8.2	NM	> 100 (23%) > 200 (28.9%) Unknown in the rest of cases	Mononodular, 47.7 Paucifocal 21.4 Multifocal 24.3 Massive 6.6 Portal thrombosis (11.3%) Ascites 26.6 Metastases 7.4	CTP: A 62.1 B 32.4 C 5.5 BCLC 0 7.4 A 34.7 B 42.6 C 10.6 D 4.7	Curative (33.6%) LT 0.8 LR 5.46 PEI 1.95, RFA 25.39 Palliative: TACE 41 SIRT 1.56 Chemotherapy 5.47 None 26.95	Deaths 67.2
Wang et al. (29)	China	2887	4.5	57.7	Cirrhosis 82.8% HBV 77.5 Other: NM	NM	NM	<400 (73.7%) >400 (26.3%)	Number: 1 (61.5) 2 (7.2) ≥3 (31.3) Tumor size (cm): <=5 (47.1) >5 (52.9) PVT (25.2)	CTP: A 56.9 B 35.1 C 8 BCLC A 21.4 B 40 C 30.5 D 8.1	Surgical treatment (14.1) RFA/MCA (3.3) Surgical treatment +TACE (17.2) TACE (39.3) Symptomatic (26.1)	NM
Yang et al. (12)	Cameroon Egypt, Ethiopia, Ghana, Ivory Coast, Nigeria, Sudan, Tanzania, and Uganda	2566	2.7	58 in Egypt 46 in Others	Cirrhosis In Egypt (100) In others: (66) In Egypt: HCV 84 HBV 1 HBV+C2 Alcohol 0 Unknown 12 In others: HCV 6 HBV 55 HBV+C3 Alcohol 13 Unknown 22	NM	NM	NM	Multinodular 59.5 Vascular invasion 12.8 Metastases 10.8	CTP: In Egypt: A 36 B 62 C 2 In others: A 7 B 66 C 27 BCLC: In Egypt: A–B 31 C 62 D 7 In others: A–B 5 C 23 D 72	In Egypt: LT <1 LR 2 RFA 32 TACE 36 Sorafenib 5 In others: LT 0 LR <1 RFA 0 TACE <1 Sorafenib 1	NM

Study	Country	Number	Sex ratio	Age	Etiology (%)	Comorbidities	Clinical symptoms (%)	AFP (ng/l)	Radiological findings (%)	Prognostic factors (%)	Treatment (%)	Survival (%)
Sweed et al. (21)	Egypt	530	5.16	58	Cirrhosis 74.9 Chronic hepatitis 23.6 Normal 1.5 HCV (90.6) HBV (1.1) HCV/HBV (0.6) Non–viral (7.7)	Bilharzial infection (1.2) History of another malignancy (1.2)	NM	>=20 (60%) >=200 (27%) >=400 (17.3%)	Mononodular (67.7) Multinodular (32.3) Metastatic 3.2	NM	NM	Deaths 49.5
Ekinci et al. (30)	Turkey	545	4.68	59.5	Cirrhosis 87.5 Chronic hepatopathy 10.2 Healthy liver 2.3 HBV 52.6 HCV 22 HVD 6.7 HBV+C 1.8 Cryptogenic 7.1 Alcohol 3.85 NAFLD 1.83 AIH 0.9 HH 0.18	NM	NM	>100 (44.2%)	Mononodular 61 Multinodular 35 Diffuse 3.9 Macrovascular invasion 6.8 Metastasis 4.8	CTP: A 45.3 B 25.7 C 16.5 BCLC: 0 2.6 A 27.9 B 19.2 C 21.1 D 29.2	Curative: LR (5) LT (10.3) RFA (2.2) PEI/AAI (0.9) Palliative: None (43.7) TACE (31.5) Y90 radioembolization (3.5) Sorafenib (2.9)	NM
Hassan–Kadle et al. (32)	Somalia	268	2,8	52.6	Cirrhosis 26.3 Non cirrhosis 70.6 HCV 15 HBV 41 HCV/HBV1 Non–viral 43	T2D 4.5 Malaria 11.6 TBK 11.6 HIV 5.6	NM	NM	Number : Mononodular 16.1 Multinodular 16.9 Size (cm): <5 (46.26) 5–10 (14.17) >10 (36.71) Tumor distribution Unilobular 87.6 Bilobular 12.4 PVT 15.4	CTP: A 73.6 B 17.2 C 9	NM	NM

Study	Country	Number	Sex ratio	Age	Etiology (%)	Comorbidities	Clinical symptoms (%)	AFP (ng/l)	Radiological findings (%)	Prognostic factors (%)	Treatment (%)	Survival (%)
Tachi et al. (22)	Ghana	198	2	45.2	Cirrhosis 7.7 HBV 71.7 HCV 8.5 HIV 7.4	Alcohol 39.2 Smoking 6.7	Abdominal pain (74.2) Weight loss (75.8) Anorexia (45.4) Abdominal distention (42.8) Jaundice (44.9) Pedal swelling (30.4) Abdominal mass (21.7) Fever (8.8) GI bleeding (8.2)	>10 (81.6%) >165.3 (52%)	Mononodular 22.7 Multinodular 40.2 Ascites 21.1	NM	Analgesia 54.1 Sorafenib 1.5 MWA 0.3	NM
Diallo et al. (23)	Senegal	229	6.6	47.4	Cirrhosis 71.3% HBV only 53.3 HCV 1.3 HBV+ HCV 0.9 HBV+HIV 0.9 HBV+ Alcohol 5.7 HBV+T2D 4.8 HBV + obesity 3.9 Alcohol 3.9 AIH 0.4 Obesity 3.9 Unknown 20.9	Familial chronic HBV 3.9 Familial history of liver disease 5.2 Chronic HBV 4.4 T2D 8.3 Alcohol 9.6 Smoking 23.6 Overweight 4.8	Abdominal pain 91.7 HPM 74.2 Jaundice 62.9 Oedema 41.9 Ascites 33.2 CVC 16.2 SPM 12.7 HE 4.8	Normal (12.2%) 10–400 (19.6%) >400 (68.1%)	Nodular HCC 68.2 Mnonodular 33 2–3 nodules 9 Multinodular 26.2 Infiltrative 10.6 PVT 40.8 Metastass: pulmonary (8.7) spinal and bone (1.7) peritoneal carcinosis (1.7)	CTP: A 15.8 B 59.6 C 24.6 BCLC: A 3.5 B 1.8 C 43.2 D 51.5	Curative 5.2: LR 2.6 RFA 0.4 PEI 1.7 Palliative : TACE 3.1 Symptomatic 91.7	Deaths 38%
Shaaban et al. (36)	Kuwait	111	5.53	61.8	HCV 40.5 HBV 8.1 Alcohol 2.7 T2D 30.6 Unknown 18.1	NM	NM	< 400 63.4%) > 400 (23.3%) Unknown (13.3%)	Mononodular 32.4 Multinodular 61.2 Unknown 6.4 Metastasis: Lymph Node (21.6) Lung (9.9) Bone (6.3) Skin (1.1%) Unknown (7.3) Vascular invasion (23.4)	CTP: A 25 B 44 C 20 Unknown 11	Curative: LR 8.3 RFA 8.1 Palliative: No treatment 65 Sorafenib 35 TACE 12.6	NM

Study	Country	Number	Sex ratio	Age	Etiology (%)	Comorbidities	Clinical symptoms (%)	AFP (ng/l)	Radiological findings (%)	Prognostic factors (%)	Treatment (%)	Survival (%)
Shaker et al. (35)	Egypt	1313	3.72	56	Cirrhosis 100% HCV (91.32) HBV (2.51) HBV+ HCV (2.67) Non viral (3.5)	Transfusion (20.3) Surgery (46.1) Schistosomial IV therapy (66.9)	Asymptomatic (50) Abdominal pain (66.3) Weight loss (43.6) Fever (18.8) Haematemesis (14) Fatigability (62.4) Bleeding (48.3) HE (7.5) Jaundice (26.3) LLO (49) Ascites (35.8)	<20 (32.9%) 20–400 (36.4%) >400 (30.6%)	Number Mononodular (61.5) 2–3 lesions (20.5) >3 lesions (18.1) PVT : 81.6	CTP: A (39.5) B (44.2) C (16.3) BCLC A (47.83) B (24.6) C (11.3) D (16.2)	NM	NM
Elmoghazy et al. (37)	Qatar	180	5	58.8	Cirrhosis 100 % HCV (60) HBV (23.3) HCV/ HBV (3.9) HCV/ HBV/HDV (0.6) Alcohol (2.8) Cryptogenic (9.4)	T2D (38) HTA (32) coronary artery disease (4)	NM	NM	Mononodular(46) Multinodular (54) PVT (29.4) Metastasis (26): Abdominal sites (51) thoracic (27.7) Bone (14.9) Unusual sites (6.4)	CTP: A (42.2) B (45.6) C (12.2) Performance 0 (39.4) 1 (20) 2 (15) 3 (8.3) 4 (2.8)	NM	NM
Al–Naamani et al. (34)	Oman	284	2.1	61	Cirrhosis (79.9) Non cirrhotic (20.1%) HCV (35) HBV (32.3) Alcohol (7) Cryptogenic (0.7) Unknown (25)	NM	NM	<200 (50.8%) 200–400 (5.4%) >400 (43.8%)	Number: Mononodular (48.5) 2–3 nodules (13) Multinodular (24.8) Diffuse (13.7) Size (cm): <2 (13.7) 2–5 (38.4) >5 (31.9) Diffuse lesions (16)	CTP: A (34.1) B (36.8) C (29.2)	LR (4.9) LR+ RFA (0.7) LR+ TACE (0.4) LR+ LT (0.7) LR + Sorafenib (0.7) RFA alone (5.6) RFA+TACE (1.8) RFA+ TACE +sorafenib (0.7) RFA+ sorafenib (1.1) TACE alone (10.9) TACE+ sorafenib (7) TACE+ LT (0.4) LT+ TACE+ sorafenib (0.7) LR+ RFA+ TACE +sorafenib (0.4) LT alone (0.7) Sorafenib alone (11.6) LT+ sorafenib (0.7) None (51.1)	NM

Table 1: Information of our series in comparison with the reported series

Abbreviations : HCV : hepatitic viral C infection, HBV : hepatitis viral B infection, PBC : primary biliary cholangitis, NASH : non–alcoholic steatohepatitis, AIH : Autoimmune hepatitis, DT2 : Type 2 diabetes, HTN : Hypertension, RFVH : Risk factors for viral hepatopathy, COPD : chronic obstructive pulmonary disease, AGS : Alteration of general status, GI bleeding : gastrointestinal bleeding, PV: portal vein, SPM: splenomegaly, PVT :portal vein thrombosis, ADP: adenopathy, CTP : Child–Turcot–Pugh score, RFA, radiofrequency ablation, LR: Liver resection, TACE, transarteriel chemoembolization, CVA : cerebrovascular accident, CKD : Chronic kidney disease,

The HCCs in our series were most often of right lobar location (80%), mononodular (57%) or multinodular (29%), and often of size greater than 5cm (58%) with an average size of 7 cm (0.7–19 cm)

The appearance of HCC on ultrasound was often isoechoic (48% of cases), on spontaneous contrast CT was mainly hypodense in 55% of cases and isodense in 40% of cases, while on MRI was most often hypointense in T1 in 59% of cases and hyperintense in T2 in 71% of cases. The vascular aspect was typical of HCC in 86% of cases and atypical in 13%; Atypical features were either non–specific enhancement or no enhancement. Portal thrombosis was detected in 24% of cases and locoregional lymphadenopathies in 23%. Other radiological features are detailed in Table 1.

Histological confirmation was only necessary in 8% of cases and was performed by ultrasound–guided liver biopsy in all cases. The histological grade of HCC in our series was dominated by grade 1 (well differentiated) in five cases followed by grade 2 (moderately differentiated) in three cases and was unspecified in two cases. The underlying liver was healthy in six cases and cirrhotic in four cases.

In 92% of our cases, the diagnosis of HCC was based on a set of epidemiological, clinical, biological and radiological arguments according to the recommendations of the European Association for the Study of the Liver (EASL). The diagnosis was made by CT in 48% of cases, by MRI in 43% of cases and by abdominal ultrasound alone in one case. Histological evidence was only necessary for diagnosis in eight of our cases.

In terms of prognostic assessment, at diagnosis, 33% of cases had a moderate deterioration of general condition with an OMS 2 and most cases had a score of Child–Pugh B followed by A in 46% and 39%, respectively. The majority were classified Okuda II (46%) and most were classified as BCLC C and D in 28 and 25% of cases, respectively. Intermediate–stage disease BCLC B was noted in 21% and early–stage disease BCLC A In 16% of cases.

Distant metastasis were present in 36% of cases at the diagnosis. The most frequent sites were lymph nodes (23%) and thoracic (16%). Other sites included bones (2%), adrenal glands (2%) and peritoneum (1%).

Therapeutic decisions in our cases were made in multidisciplinary consultation meetings (RCPs) following the recommendations of the EASL They took into consideration the characteristics of the patient, of the tumour and of the underlying liver. Thus, 72% of our patients received palliative treatment while only 6% received curative treatment and 22% of patients were lost to follow–up.

In terms of palliative treatment, 29% of cases received chemoembolization (TACE), 5% received Sorafenib while 38% received only symptomatic treatment. In terms of curative treatment, three cases received radiofrequency (RFA) and the other three surgical resections.

The overall survival in our series was 6.5 months with extremes ranging from one week to 6 years. 48% of patients had died at the time our study took place, 46% of them within a year of HCC diagnosis.

Discussion:

According to the 2020 GLOBOCAN estimates, HCC is the sixth most diagnosed cancer and the third leading cause of cancer deaths in the world, with an estimated incidence of 905,700 and an estimated mortality of 830,200 in 2020[2]. These numbers are expected to increase by 55% between 2020 and 2040 with an estimated 1.4 million new cases in 2040[2]. In Morocco, HCC was ranked the 13th most common cancer and the ninth cause of cancer death with an estimated incidence of 1,311 cases in 2020 [13]. In the absence of a national cancer registry, these estimates were based on the cancer registries of Casablanca and Rabat. No register is available in the city of Marrakech nor in the southern region of Morocco, hence the interest of descriptive studies such as ours.

In Table 1, we describe epidemiological, clinical, paraclinical findings and offered treatments in our series in comparison with the findings of the other literature series. The average age in our series was 63.3 years which is consistent with the results of the study by Firwana et al. from Rabat and the study by Bahri et al. including the three Maghreb countries (Morocco, Tunisia and Algeria) reporting mean ages of 63.3 and 62, respectively[14,15]. It is also consistent with the averages reported in areas of medium and low incidence such as Europe and North America ranging from 63 to 68 years[3,4,11,16–20]. In Africa, it varies significantly between Egypt where it is 58 years and Sub–Saharan Africa where it is younger at around 45 years[12,21–23]. We noted a male predominance in our patients with a sex ratio of 1.5. This is close to the ratios reported in Morocco and other Maghreb countries of 1.7 and 1.53, respectively[14,15]. While, the ratios reported in other regions of the world are even higher varying from 2 to 5[3,12,18,19,22,24–26].

Cirrhosis is the main risk factor for HCC since it develops in more than 90% of cases on a cirrhotic liver[3–5]. Cirrhosis was present in 87% of our patients which corresponds to the literature data[3,15–20,27–30]. The etiologies of cirrhosis in our series were dominated by viral hepatitis C and B. This agrees with the data of Firwana et al. and Bahri et al. [14,15] HVC is also the main etiology of cirrhosis in Egypt, the United States, Pakistan and Italy where it is responsible

for more than 50% of cases[2,3,11,12,21,26,28,31]. However, HVB remains the main etiology of cirrhosis in the world and mainly in Sub–Saharan Africa, Asia and in some countries of the Middle East as reported by the series of Yang et al., Diallo et al and Ekinci et al[2,3,11,12,22,23,29,31,32]. In the European series of Goutté et al., Rosa et al. and Schütte et al., alcoholism was the main etiology of cirrhosis[16–18].

Of our patients, 18% were chronic alcoholics. This agrees with the data from the Moroccan and North African studies[14,15]. However, it is a lower rate compared to the European and North American studies where alcoholism is the first and the second cause of HCC[16,18,20,27,28]. Also, 27% of our patients were chronic smokers, which agrees with the literature data[14,23,27]. 17% of our cases were type 2 diabetics, this agrees with the series of Bahri et al. which reports a rate of 18% [15] but other European and North American series report higher rates (Table 1). 11% of our patients had obesity, which is comparable to the series of Goutté et al. [16] but is lower compared to the series of De Lope et al. and Turcanu et al [20,27].

Regarding the circumstances of the diagnosis, only a third of the HCCs in our series were diagnosed during surveillance. This percentage is less than that of the series of Firwana et al. but more important than those of the series of Vaz et al., Musunuri et al. and Turcanu et al.[14,25,27,33]. Also, in the majority of cases (41%) the diagnosis of HCC was indicative of an unknown underlying cirrhosis. Musunuri et al. reported a similar proportion of 46% of cases in India and Vaz et al. 30% in Switzerland[25,33]. In symptomatic patients, abdominal pain was the most common reason for consultation in our series. This agrees with the literature data (Table 1). In our series, abdominal tenderness was the predominant physical sign in 68% of cases followed by deterioration of general condition in 8%, HPM in 51% and ascites in 45%. This corresponds to the data of other series (Table 1).

Paraclinically, 41% of our patients had an AFP level above 400. This corresponds to data from the series of Musunuri et al., Turcanu et al., Al Naamani et al.[25,27,34]. However, 27% of our patients had a normal level of AFP, this also corresponds to the data of other series (Table 1).

As for the radiological data, the most frequent location of HCC in our series was the right hepatic lobe in 80% of cases. This corresponds to the data of the other series[18,25,35]. The most common form of HCC in our series was mononodular in 57% of cases followed by the multinodular form in 29% of cases. This also corresponds to the literature data (Table1), except for the series of Musunuri et al. and Schütte et al. where the multinodular form was the most frequent[18,25]. The majority of nodules in our series had a diameter greater than 5 cm, with an average of 7 cm. This corresponds to the literature data[18,23,25,26,29]. This highlights that the majority of HCCs were diagnosed at an advanced stage. Portal veinous thrombosis was present in 24% of our patients which corresponds to data from the series of Wang et al[29]. However, higher percentages are reported in the literature ranging from 30 to 46% (Table1).

In terms of histology, the majority of HCCs (5%) in our series were WHO grade 1 (well differentiated). This does not correspond to the data of the other series where grade 2 was the most predominant[18,21,35].

Following the recommendations of the European Association for the study of the liver, the diagnosis of HCC in our series was non–invasive and radiological in 92% of cases before a typical aspect and classic vascular kinetics of HCC. This corresponds to the literature data except for the study by Schütte et al. [18] where the diagnosis was histological in 77% and radiological in 23% of cases (Table 1). The main diagnostic mean was CT in our series (48%) followed by MRI (43%). This corresponds to the data of the other series [19,20,23,26–28,30,34,36,37] except for that of Tachi et al. where the diagnosis of HCC was confirmed by ultrasound in 71% of cases[22]. The authors explain this by the cost and unavailability of other imaging techniques in their country.

Regarding the prognostic evaluation, the majority of patients in our series had a moderate deterioration in general condition with a WHO score of 2 in 33% of cases and of 1 in 29%. This corresponds to the literature data.

In our series, the majority of patients (46%) had a Child B score. This corresponds to the data from the series of Musunuri et al., of Shaaban et al., of Elmoghazy et al. and of Shaker et al.[25,35–37]. However, in other series, the Child A was predominant such as the series of Mansoor et al., of Schütte et al. and of Delope et al.[18,20,26]. Also, 46% of our patients were classified as Okuda II. This corresponds to the data of Musunuri et al. while in the series of Pratic et al. the majority had an Okuda III [24,25]. In our series, the majority of patients had an advanced or terminal stage of HCC at the time of diagnosis (59% of BCLC C and D) which signals a diagnostic delay in 59% of cases in our context. This agrees with the series of Pratic et al of Musunuri et al., of Schütte et al., of Diallo et al.[18,23–25] Other series have had different results; Stage B was the most frequent in the series of Mansoor et al., of Fenoglio et al. and of Wang et al.[26,28,29], while stage A was the most frequent in the series of Farah et al., DeLope et al. and Shaker et al.[19,20,35].

In terms of tumour extension, 36% of our cases had distant metastases at the time of diagnosis. Shaaban et al. reported a similar rate of 37.8%[36]. The other series had varying percentages from 4.8 to 84% of cases (Table

1). Lymph node metastases were the most common site in our series, followed by lung and then bone metastases. This corresponds to the literature data (Table 1).

The therapeutic decision before HCC must be made in RCPs. This decision must take into account the characteristics of the patient, the prognostic evaluation of the tumour and the underlying liver, as well as the local technical platforms. The indications in our study were based on the recommendations of the EASL of 2018[4].

The majority of our cases (72%), benefited from palliative treatment while only 6% received curative treatment. In other series, palliative treatment was the main treatment varying from 53 to 95% of cases (Table1). This can be explained by late diagnosis of patients with HCC who often present at advanced stages (BCLC C and D) inaccessible to curative treatment. In some countries like ours, this can also be linked to the lack of means limiting access to certain treatments.

As for the curative treatment, in our series, three cases received a resection and the three others RFA. None of our patients benefited from a liver transplant. In the literature, the most indicated curative treatment was surgical resection followed by RFA and liver transplantation (Table 1). Other percutaneous ablation techniques were rarely used, such as microwave ablation and percutaneous injection of alcohol or acetic acid. Palliative treatment in our series was most often symptomatic in 38% of cases, in the form of TACE in 29% of cases and Sorafenib in only 5%. This corresponds to the data of other series except those of Mansoor and aL and of Fenoglio et al. where TACE was the most common received treatment[26,28], and those of Musunuri et al, of Schutte et al and of Turcanu et al where systemic treatment with sorafenib was predominant[18,25,27] (Table 1).

Several series have reported therapeutic combinations of curative and palliative treatment such as surgical resection with sorafenib or with TACE as adjuvant or neo–adjuvant treatment (Table 1). However, in the literature, there are no clear recommendations on this subject.

Recommendations:

Before concluding, we would like to mention some important observations of our study.

The first observation to note is that viral etiology (C and B) remains predominant in our context, very probably linked to the high prevalence of viral transmission risk factors dominated by informal dental care and fire points, which reflects that these traditional practices are still present in our society and that awareness must be strengthened in this regard.

The second and most important observation is that almost half of the patients in our series (41%) had undiagnosed cirrhosis that was revealed by HCC. Which raises the question of how can 41 patients escape the diagnosis of cirrhosis long enough to develop HCC and emphasizes the value of screening for cirrhosis in patients with obvious risk factors;

The third observation is that no data on aflatoxins were available in our series, although several studies have suggested that it may have an important role in the burden of HCC in our country. Thus, further studies are needed to establish the prevalence of aflatoxins and their involvement in the risk of HCC in our context.

The fourth observation is that the majority of patients had tumours of more than 5 cm in diameter and 59% had advanced disease at the time of diagnosis. This signals a diagnostic delay and underlines the importance of strengthening HCC monitoring and screening protocols in cirrhotic patients and, as mentioned above, even non–cirrhotic patients but with obvious risk factors.

The fifth observation is that a third of our patients were diagnosed under surveillance (36% in total, and 78.2% of known cirrhotics). This reflects the effectiveness of our department's monitoring protocol. But, the late stage of the diagnosis calls for an optimization of this protocol.

The sixth observation is that 9% of HCCs were diagnosed following decompensation therefore each cirrhotic decompensation must lead to an exploration of the liver in search of a HCC.

The seventh observation is that no patient in our series had benefited from a liver transplant despite the indication due to the shortage of organs. Hence the importance of raising awareness about organ donation and the development of liver transplant programs in our country.

The eight observation is that the lack of means remains the greatest obstacle to access to healthcare as reported by relatives of patients after telephonic contact. In this regard, the latest establishment of obligatory health insurance in our country can improve access to healthcare and solve this problem.

Conclusion :

In conclusion, despite its many limitations, our study accomplished its main objective and gave us an overview of the epidemiological, clinical and paraclinical, etiological and therapeutic means of HCC in our context.

Moreover, our study confirms that HCC remains of poor prognosis; the majority of patients were only accessible to palliative treatment and almost half of the patients died at

the end of the study after a short average survival of 6.5 months, all treatments combined.

This highlights the importance of prevention which must be:

- Primary (by preventing HCC risk factors)
- Secondary (by preventing occurrence of HCC in patients with cirrhosis or other risk factors)
- and tertiary (by preventing tumour progression and/or recurrence)

All in all, a regional or national HCC registry will allow us to have a general overview of this pathology in our country and will help establish screening, diagnostic and follow–up protocols that are specific to our context in order to offer better care to our patients.

Data Availability:

The data supporting this case series are from previously reported studies and datasets, which have been cited. The patients's personal data are available from the corresponding author upon request and cannot be disclosed publicly due to the patient privacy policy of our institution.

Conflicts of Interest:

The authors declare that they have no conflicts of interest.

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