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Research Article

Outcomes of hepatocellular carcinoma among patients receiving systemic therapy

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Abstract

Background: Hepatocellular carcinoma (HCC) is a prevalent and highly lethal form of cancer that has shown significant progress in treatment modalities in recent times. The Systemic therapy for HCC has changed since the introduction of the molecular targeted agent sorafenib in 2007.. This study aimed at assessment of the outcome of patients with HCC receiving systemic therapy for three months. **Methods:** This prospective observational study was conducted among HCC Patients who attending the outpatient clinic at Hepatology and gastroenterology Minia University Hospital from January 2023 to December 2023. 110 patients diagnosed with HCC who were categorized as BCLC B-C and underwent systemic therapy were included in the study. **Results:** mean age of HCC patients was 45.5 ± 15.8., About 77% were male, 69% were rural residents and 91% were HCV positive, all patients were child score type A and 98% were in sorafenib. There is statistically significant difference in number of focal lesion before and after treatment. (p value <0.05) as 32% of HCC patients had multiple focal lesion before treatment and become 22.7% after treatment. Regarding outcome of HCC patients within 3 months of follow up, about 14.5% died after 3 months and also 14.5 stopped treatment due to complication and the remaining 71% continued treatment. Regarding course of disease, about 47% had progressive course, 23.5% had regressive course while only 29% had stationary course. **Conclusions:** individuals who have been diagnosed with advanced stage hepatocellular carcinoma (HCC) experience positive outcomes from sorafenib.

Keywords: hepatocellular carcinoma**,** Sorafenib, Survival, outcome

Introduction

Liver cancer ranks as the sixth most prevalent form of cancer globally[1]. Hepatocellular carcinoma (HCC) is frequently associated with cirrhosis caused by hepatitis B or C[2].

Nevertheless, the overall long-term outlook for HCC remains unsatisfactory as a result of its significant heterogeneity and frequent recurrence. Hence, there is a pressing requirement for reliable predictors that can reliably evaluate the prognosis of HCC patients receiving systemic therapy [3]. The approval for the use of Sorafenib (Nexavar®) in HCC was granted in 2007. Sorafenib is a multikinase inhibitor that is taken orally [4]. It blocks the activity of several tyrosine kinases found on the surface of cells, including as vascular endothelial growth factor receptor (VEGFR)-1, VEGFR-2, VEGFR-3, and platelet-derived growth factor receptor. These kinases play a role in the signaling, growth, formation of blood vessels, and programmed cell death in tumor cells.

In laboratory conditions, sorafenib hinders the growth of HCC cells and triggers their programmed cell death. It also inhibits the growth of tumors, reduces the formation of new blood vessels within tumors, and induces programmed cell death in tumor cells in animal models of HCC[5].

Sorafenib is currently recognized as the established systemic treatment for HCC in

patients with well-preserved liver function (Child-Pugh class A) and advanced stage HCC (BCL-C), which is defined by the presence of portal invasion and/or extrahepatic dissemination while maintaining normal liver function[6].

Aim of the study:

1- assessment of the outcome of HCC patients receiving systemic therapy who attend hepatology outpatient clinic at Minia University Hospital

2- follow up HCC patients after receiving systemic therapy by liver function tests and copmlete blood count and alphafeto protein level before and after the treatment

3- Follow up radiological findings before and after 3 months of systemic therapy

Patients and Methods

This prospective observational study was conducted to HCC Patients attending the hepatology outpatient clinic at Hepatology and Gastroenterology Minia University Hospital.

The study included 110 HCC patients (BCLC B-C) and received systemic therapy during the period of January 2023 to December 2023.

The following information was collected from the clinic medical record system for all HCC patients participated in the study. Patient characteristics included gender, age, history hypertension and diabetes mellitus. Clinical parameters as HCV, and HBV serological status, performance status, Barcelona Clinic Liver Cancer (BCLC) stage were collected.

Liver function tests including levels of ALT, AST, total bilirubin (TBIL), albumin, and prothrombin time (PT), Tumor-related features as serum AFP level, tumor size, number of focal lesions, size, portal vein thrombosis and distant metastasis) were recorded.

Child-Pugh score incorporates variables of ascites, hepatic encephalopathy, total bilirubin, albumin, and INR of the patient. The total of the scoring system is further classified into Child-Pugh A (5–6 points in total), Child-Pugh B (7–9 points in total), and Child-Pugh C (10–15 points in total). The classification of liver cirrhosis based on this scoring can determine the probability of mortality rate of cirrhosis patients, with class A, B, and C having 10%, 30%, and 70–80% mortality rate respectively.

Follow up

Patients who were registered had a systematic follow-up after a period of 3 months. The patients got regular follow-up using blood AFP testing and contrast-enhanced CT scans every 3 months. The main measure of interest in this study was the Overall Survival. The survival status of patients was verified by death records or by making telephone inquiries to the patients or their family. The overall survival was determined by measuring the time from the initiation of systemic medication to the occurrence of death, with the length being measured in months.

Ethical consideration:

The study received approval from the ethical committee of the Faculty of Medicine, Minia University. The participants or their legal representatives were notified of the objective of the study and its potential outcomes, while ensuring the confidentiality of the data.

Statistical Analysis

The data was gathered, arranged, and analyzed statistically using SPSS 26 for Windows (SPSS Inc., Chicago, IL, USA).

The data was subjected to normality testing using the Shapiro-Wilk test. The qualitative data were represented using frequency and relative percentages. The McNemar's test was utilized to evaluate the discrepancy between categorical variables before and after the intervention.

The quantitative data were displayed as the mean ± standard deviation (SD), median, and range for both parametric and non-parametric data.

All statistical comparisons were conducted using a two-tailed test and considered significant. A P-value ≤ 0.05 shows a significant difference, a p <0.001 indicates a highly significant difference, while a P >0.05 indicates a non-significant difference.

Results

Mean age of HCC patients was 45.5 ± 15.8 with 88% above 60 years , about 77% were males and 23% were females with male to female ratio 3.4:1, also about 69% were rural residents and 91% were HCV positive , all patients were child score type A and 98% were in sorafenib and about 54% had performance

score (Table 1). There is statistically significant difference in number of focal lesion before and after treatment. (p value <0.05) as 32% of HCC

patients had multiple focal lesion before treatment. and become 22.7% after treatment. with significant reduction in number of patients with multiple focal lesion. Non-significant difference (p value>0.05) was found regarding presence of Portal venous thrombosis before and after treatment, as about 36.6% had PVT before treatment and 39% had PVT after treatment. Regarding size of focal lesion no significant difference was found and number of patients who had metastasis was 11 cases (10%) (Table 2). As shown in table 3, mean hemoglobin level among the studied cases was13.2±50.8, mean leucocyte and platelet count(10^9/L**)** was 6.4 ±2.1 & 145 ±45.8.and total number of patients had Alpha feto-protein more than 400 ng/ml was 60 cases who represented 54.5% of total cases with median 175 and interquartile range was 14-1100.

Regarding outcome of HCC patients within 3 months of follow up, about 14.5% died after 3 months and also 14.5 stopped treatment due to complication and the remaining 71% continued treatment. Regarding course of disease, about 47% had progressive course, 23.5% had regressive course while only 29% had stationary course (Table 4).

Table (1): baseline characteristics of the studied cases

Baseline characteristics (N=110)		Descriptive statistics
Age	**Mean ± SD** **Median (Range)**	45.5 ± 15.8 43 (18:76)
Age group	**>60 years** **<60 years**	97(88.2%) 13(11.8%)
Residence	**Rural** **Urban**	76(69%) 34(31%)
Sex	**Male** **Female**	85(77.3%) 25(22.7%)
HCV	**Yes** **No**	100(90.9%) 10(9.1%)
Comorbid disease	**DM** **Hypertension** **Other**	8(7.3%) 8(7.3%) 1(0.9%)
Child score	**Child A** **Child B**	110(100%) 0 (0%)
Type of systemic therapy	**Sorafenib** **Regorafenib**	108(98%) 2(2%)
Performance	**0** **1**	51(46.4%) 59(53.6%)

Table (2): Radiological finding of the studied cases

Radiological finding	Before traetment	After treatment	P value
No. of focal lesion Solitary Multiple	 74(67.3%) 36(32.7%)	 85(77.3%) 25(22.7%)	 0.001*
Presence of Portal venous thrombosis	40(36.4%)	43(39%)	0.25
Size of focal lesion <3 cm ≥3 cm	 7(6.4%) 103(93.6%)	 7(6.4%) 103(93.6%)	 ____
Presence of metastasis	11(10%)		

- mean significant at p value <0.05*

Table (3): Baseline laboratory investigation of the studied patients

laboratory investigation	Overall patients

	(No =110)
Hb (gm/L) (Mean± SD)	13.2±50.8
Leukocyte [10^9/L) (Mean± SD)	6.4 ±2.1
PLT (10^9/L) (Mean± SD)	145 ±45.8
ALT (U/L) **(**Mean± SD)	37 (22–64)
AST (U/L) (median, IQR)	41 (31–58)
Albumin (g/L) (mean± SD)	3.5±4.1
Bilirubin (g/L) (median, IQR)	2.8 (2.3–7.8)
INR (Mean± SD)	1.2±7.5
AFP (ng/ml) (median,IQR)	175 (14 -1100)
AFP (ng/m) n(%) <400(ng/ml) >400(ng/ml)	50(45.5%) 60(54.5%)

Table (4): outcome of HCC patients receiving systemic therapy

Outcome and course of HCC patients (N=110)	Frequency and percentage
Outcome	
Death after 3 months	16(14.5%)
Stop treatment due to complication	16(14.5%)
Continue treatment	78(71%)
Course	
Progressive	52(47.3%)
Regressive	26(23.6%)
Stationary	32(29.1%)

Discussion

Hepatocellular carcinoma (HCC) is a prevalent and highly lethal form of cancer that has shown significant progress in treatment modalities in recent times. Enhanced comprehension of the tumor's inherent progression and the establishment of staging systems, like the BCLC (Barcelona Clinic Liver Cancer) system, which classify patients according to tumor size, liver diseases, and functional status, have led to more precise prognosis forecasts and more appropriate treatment approaches.

In the present study the mean age of HCC patients was 45.5 ± 15.8, about 77.3% were male and 22.7% were female with male to female ratio 3.4:1, also about 69% were rural residents and 90% were HCV positive. The patients' characteristics were similar to Zhang et al.,[7] who found out of 414 patients, 332 (83.6%) were males and 82 (24.2%) were females. The median age of the patients was 56, 75% were rural residents, but the majority of the patients had HBV infection (75.8%).

In the present study there was a significant reduction in number of focal areas after the treatment compared to before treatment, as 32% of HCC patients had multiple focal lesions before treatment and become 22.7% after treatment. This result is in line with a prospective study conducted on 99 HCC patients treated with sorafenib reported absence of hepatic focal lesions after treatment versus presence before

treatment, it was found to be predictive of survival in univariate analysis [8].

The presence of portal venous thrombosis exhibited a non-significant difference before and after the treatment (36.4%, 39%) respectively with (p value>0.05) and the presence of metastasis was 25.5%. Jeong, et al [9] demonstrated that among 143 consecutive patients with unresectable HCC were treated with sorafenib, 30 patients with advanced HCC and PVTT (Vp3 or 4) were treated with sorafenib monotherapy, only 3 patients (10%) had a partial response regarding PVT with non-significant difference between before and after treatment (p-value.0.05).

Moreover, Zheng et al.,[10] confirmed the previous study with a prospective study condu-cted on 64 patients, patients were randomly assigned (1:1 ratio) to receive sorafenib (400 mg twice daily) plus 3cir-OFF HAIC (35 mg/m2 oxaliplatin [hours 0–2] followed by 600 mg/m2 5-fluorouracil [hours 2–24], days 1–3) with a standardized percutaneous port catheter system or sorafenib alone (400 mg twice daily) every 4 weeks, regarding sorafenib mono-therapy There was no significant heterogeneity of the findings between patients with Vp3 and those with Vp4 before and after the treatment (P=0.68 for heterogeneity). All previous studies confirmed our findings.

Conclusion

Presently, therapeutic interventions like as resection, transplantation, and ablation can improve the likelihood of survival in individuals diagnosed with early-stage HCC and offer the potential for a lasting remedy. Chemoembolization is effective in treating patients diagnosed with intermediate stage HCC. However, individuals who have been diagnosed with advanced stage hepatocellular carcinoma (HCC) experience positive outcomes from sorafenib, a medication that inhibits several kinases and has both antiangiogenic and antiproliferative properties.

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