ORIGINAL ARTICLE

Profile of Patients of Hepatocellular Carcinoma in The Internal Medicine Inpatient Room at Dr. Soetomo General Academic Hospital

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ABSTRACT

Introduction: Primary liver cancer is the sixth most frequently diagnosed cancer and the third leading cause of cancer death worldwide in 2020, with approximately 906,000 new cases and 830,000 deaths. Primary liver cancer includes hepatocellular carcinoma (HCC), with a percentage of 75%-85% of cases. The poor prognosis of HCC is mainly related to late diagnosis.
Methods: This research is a descriptive study with a cross-sectional study. Data retrieval is taken from secondary data in the form of medical record data. The sampling technique used was the total sampling technique.
Results: The number of HCC patients in the Internal Medicine Inpatient Room at Dr. Soetomo General Academic Hospital for 1 January 2017–31 December 2019 who met the inclusion and exclusion criteria was 60. The male sex had the highest number of 43 patients (71.7%), with the highest age group being 50-59 years old.
Conclusion: Profile of HCC patients in the Internal Medicine Inpatient Room at Dr. Soetomo General Academic Hospital in the 2017-2019, dominated by male patients aged 50-59 years, the most risk factors were HBsAg positive, upnormal liver function, positive tumor markers, and had BCLC stage C.

Keywords: Cancer, Hepatocellular carcinoma, BCLC

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INTRODUCTION

Primary liver cancer is the sixth most frequently diagnosed cancer and the third leading cause of cancer death worldwide in 2020, with approximately 906,000 new cases and 830,000 deaths (Sung et al., 2021). In Indonesia, liver cancer is the fifth-highest cancer in both sexes and the third highest in males, with 21,392 new cases (5.4%) and 16,412 new cases (9%), respectively. Primary liver cancer includes hepatocellular carcinoma (HCC) with a percentage of 75%-85% of cases and intrahepatic cholangiocarcinoma with a percentage of 10%-15% of cases, as well as other rare types (Sung et al., 2021).

The most common cause of HCC worldwide is hepatitis B virus (HBV) which accounts for about 50% (Bodzin, 2015). HBV is the main cause of HCC in most of Asia and Africa, while hepatitis C virus (VHC) is the main etiology of HCC in the United States, Europe, Japan, and South America (Axley et al., 2017). The development of HCC is started by liver injury involving inflammation leading to hepatocyte necrosis and regeneration. This chronic liver disease successively transitions to fibrosis, cirrhosis, and HCC (Suresh et al., 2020). The diagnosis of HCC consisted of the patient's history, physical examination, imaging (ultrasonic, MRI, or CT scan, which showed the presence of a liver mass typical for HCC), and an increase in serum AFP (Anggraini, 2019).

HCC is a significant cause of morbidity and mortality. This leads to an unfavorable prognosis with aggressive cancer growth and a high recurrence rate (Siddiqui et al., 2018). Relatively 5-year survival after diagnosis of HCC is universally below 20% and ranges from 7-9% in Asia to 19% in Western countries (Laube et al., 2020). The clinical condition of the disease at the time of diagnosis often decides the prognosis and survival rate of HCC patients (Jaka et al., 2014). The poor prognosis of HCC is mostly related to the delay in diagnosis (Ayoub et al., 2019). HCC can develop unnoticed in patients with moderately good liver function and go undetected from early diagnosis because of indistinct complaints and uncertain symptoms. In developing countries with limited surveillance resources, this will cause the diagnosis of HCC is usually delayed (Dimitroulis et al., 2017). Insufficient use of treatment and/or delay in treatment has also been described as a potential cause of poor cancer outcomes (Singal et al., 2013).

HCC is one of the cancers that not only has high case and mortality rates but also has a poor prognosis. Therefore, to improve preventive efforts, it is necessary to conduct research related to the profile of HCC patients. This research was held in Dr. Soetomo General Academic Hospital Surabaya, East Java.

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METHODS

This research is a descriptive study with a cross-sectional study. Data retrieval is taken from secondary data in the form of medical record data. The sampling technique used was the total sampling technique. The sample in this study was patients treated in the Internal Medicine Inpatient Room at Dr. Soetomo General Academic Hospital who met the inclusion and exclusion criteria. The inclusion criteria of this study were patients who were treated in the Internal Medicine Inpatient Room, Dr. Soetomo General Academic Hospital, for the period January 1, 2017–December 31, 2019, with the diagnosis code International Statistical Classification of Disease (ICD) X C22.0 and aged over 18 years. The exclusion criteria for this study were patients with incomplete medical record data. The data that met the inclusion and exclusion criteria were then processed using the SPSS program. Categorical data are presented in the form of frequency and percentage tables. Numerical data are presented with mean ± SD and median.

RESULTS

Table 1 General Characteristics of HCC Patients

	Characteristic	N (%)
GENDER	Male	43 (71.7)
	Female	17 (28.3)
AGE	20-29 years	2 (3.3)
	30-39 years	8 (13.3)
	40-49 years	13 (21.7)
	50-59 years	19 (31.7)
	60-69 years	10 (16.7)
	70-79 years	5 (8.3)
	80-89 years	2 (3.3)
	>90 years	1 (1.7)
EDUCATION	Primary school	11 (18.3)
	Junior high school	4 (6.7)
	Senior high school	39 (65)
	College	3 (5)
	Others	3 (5)
PROFESSION	Government employees	9 (15)
	Private employees	24 (40)
	Entrepreneur	9 (15)
	Farmer	5 (8.3)
	Housewife	10 (16.7)
	Indonesian security personnel or police	1 (1.7)
	Doesn't work	2 (3.3)

Table 2 Spesific Characteristic of HCC Patients

	Characteristic	N (%)	Mean±SD	Median
RISK FACTOR	HbsAg positive	43 (71.7)		
	Anti HCV positive	8 (13.3)		
	HbsAg negative and anti HCV negative	8 (13.3)		
	HbsAg positive and anti HCV positive	1 (1.7)		
LABORATORIUM FINDING	Hemoglobin (g/dL)		10.71±2.95	11.05
	Leukosit (/uL)		11,931.13±5,804.25	11,175
	Trombosit (/uL)		323,783.33±161,549.5	314,000
	Albumin (g/dL)		3.02±0.56	3.1
	SGOT (U/L)		310.2±277.73	203
	SGPT (U/L)		120.33±185.24	62.5
	Bilirubin total (mg/dL)		6.04±7.58	3.28
	AFP			
	<20 ng/mL	8 (13.3)		
	20-400 ng/mL	4 (6.7)		
	>400 ng/mL	25 (41.7)		
	Unknown	23 (38.3)		
RADIOLOGICAL FINDING	Presence of nodules	60 (100)		
	Ascites	12 (20)		
	Hepatomegaly	9 (15)		
	Splenomegaly	10 (16.7)		
	Liver cirrhosis	6 (10)		
	Thrombus vena porta	5 (8.3)		
	Kolesistisis	2 (3.3)		
	Kolelitiasis	1 (1.7)		
BCLC	BCLC A	4 (6.7)		
	BCLC B	9 (15)		
	BCLC C	27 (45)		
	BCLC D	20 (33.3)		
THERAPY	Symptomatic	52 (86.7)		
	TACE	8 (13.3)		
	Sorafenib	1 (1.7)		
CLINICAL OUTCOME	Alive	40 (66.7)		
	Dead	20 (33.3)		
CAUSE OF DEATH	Acute liver failure	4 (20)		
	Septic shock	9 (45)		
	Cardiovascular event	3 (15)		
	Respiratory failure	4 (20)		
	No description	2 (10)		

DISCUSSION

The number of HCC patients in the Internal Medicine Inpatient Room at Dr. Soetomo General Academic Hospital for the period 1 January 2017–31 December 2019 who met this study's inclusion and exclusion criteria was 60. The patient profile is divided based on two characteristics, namely general characteristics and specific characteristics. The general characteristics of patients consist of gender, age, education, and occupation. Patient-specific characteristics consisted of risk factors, laboratory findings, radiological findings, HCC stage, therapy, clinical outcomes, and cause of death. Laboratory findings consist of hemoglobin, leukocytes, platelets, albumin, SGOT, SGPT, total bilirubin, and AFP. Radiological findings were obtained from the

abdominal ultrasound examination and CT scan results.

Based on the results of table 1, most gender was treated in the Internal Medicine Inpatient Room at Dr. Soetomo General Academic Hospital because of HCC is male with 43 patients (71.7%). Similar results were also found by Puri et al. (2021) and Rahmawati et al. (2019) that the male sex is more dominant by 82.5% and 74.9%, respectively. In the Asia Pacific region (especially North and South Korea, Indonesia, and Vietnam), the rate of liver cancer in men is more than 4 times that in women (Zhu et al., 2016). The age group of 50-59 years is the age group that is mostly treated in the Internal Medicine Inpatient Room at Dr. Soetomo General Academic Hospital because of HCC, with a total of 19 patients (31.7%). The average age of the patients being treated was 52.8 years. These results are not much different from the research found by Jasirwan et al. (2019) that HCC patients have an average age of 56 years and 55 years, respectively. The global age distribution of liver cancer cases is related to the predominant viral hepatitis in the underlying population and the age at which it was infected (Mittal, 2013). In some parts of Asia and most African countries, HCC is generally diagnosed in the 30-60 year age range (Yang et al., 2019). In resource-rich countries, the age at diagnosis of HCC from these countries ranges from the early 60s to the mid-70s (Kew, 2014).

High school is the education most patients take in the Internal Medicine Inpatient Room at Dr. Soetomo General Academic Hospital because of HCC with 39 patients (65%). The same thing happened in the research of Yehia et al. (2020) that 49.2% of HCC patients had reached the secondary level of education. However, Turati et al. (2013) research stated that patients with HCC who reached the level of education for 12 years were the lowest at 14 (8%). Private employees are the occupations that are owned mainly by patients who are treated in the Internal Medicine Inpatient Room at Dr. Soetomo General Academic Hospital because of the HCC with 24 patients (40%). This result is different from the research of Purba and Rey (2018) at Haji Adam Malik Hospital Medan, where most jobs held by HCC patients are entrepreneurs (27.5%).

Risk factors for HCC patients were divided based on the serologic results of hepatitis B and hepatitis C, namely HBsAg and anti-HCV. Based on table 2, HBsAg positive is the most common risk factor for HCC patients in the Internal Medicine Inpatient Room at Dr. Soetomo General Academic Hospital because of HCC with 43 patients (71.7%). Purba and Rey (2018) also found that HBV was the most common risk factor for HCC patients (47.3%). Different levels of exposure to HCC risk factors are assumed to be the cause of the variation in the distribution of the disease. In developing countries, the main risk factors for HCC are chronic HBV infection and exposed by aflatoxins. In contrast, the main risk factors in developed countries are liver cirrhosis because of HCV infection and alcohol abuse (Magnussen and Parsi, 2013). HBV infection is one of the most common infections in humans, with about 2 billion people worldwide infected or have been infected with this virus. HBV is believed to be second only to tobacco smoking as an environmental carcinogen exposed to humans, causing about 55% of all liver cancers globally (Kew, 2014).

Hemoglobin levels in patients treated in the Internal Medicine Inpatient Room due to HCC had an average ± SD and median values of 10.71 ± 2.95 and 11.05, indicating a decrease in hemoglobin. The same thing happened in the study of Kumar (2008), where the average value of hemoglobin decreased. The cohort study by Finkelmeier et al. (2014) showed that the level of anemia correlated with the severity of liver insufficiency, stage, and prognosis of HCC patients. Hemoglobin levels below 13 g/dl are associated with higher mortality and shorter overall survival.

The leukocyte levels in the patients had mean ± SD and median values of 11,931.13 ± 5,804.25 and 11,175 which indicated an increase in leukocytes. Elevated white blood cell counts have been related to varied diseases such as cardiovascular disease, infections, diabetes, metabolic syndrome, nonalcoholic fatty liver disease, conditions associated with insulin resistance, and chronic low-grade inflammation (Chung et al., 2016). Platelet levels in patients had an average ± SD and median values of 323,783.33 ± 161,549.5 and 314,000, which indicated normal platelet levels. The same thing happened in the research of Rahmawati et al. (2019) and Abdelmoez et al. (2019), which showed normal platelet levels in HCC patients. Platelets are closely associated with the occurrence and development of liver diseases, such as hepatocellular carcinoma, non-alcoholic fatty liver disease, viral hepatitis, acute-chronic liver failure, and autoimmune hepatitis (Chen et al., 2020).

Albumin levels in patients treated in the Internal Medicine Inpatient Room due to hepatocellular carcinoma at Dr. Soetomo General Academic Hospital had a mean value of ± SD and a median of 3.02 ± 0.56 and 3.1, which indicated a decrease in albumin. According to research conducted by Bağırsakçı et al. (2017), patients with low albumin levels had worse liver function and significantly more aggressive tumors than patients with normal albumin. They discovered that high albumin concentrations inhibit the growth of HCC cells in the culture medium in each cell type.

The SGOT and SGPT level inpatients had a mean value of ±SD and a median of 310.2 ± 277.73 and 120.33 ± 185.24, respectively. This shows an increase in the value of SGOT and SGPT. An increase in SGOT and SGPT also occurred in the study of Aljumah et al. (2016) and Akkiz et al. (2017). Patients with higher SGOT/SGPT levels have a poorer prognosis than patients with lower SGOT/SGPT levels, and SGOT/SGPT is a risk factor for overall survival in primary liver cancer patients (Zhang et al., 2019).Total bilirubin levels in inpatients had a mean value of ± SD and a median of 6.04 ± 7.58 and 3.28 mg/dL, indicating an increase in total bilirubin. Similar results also occurred in the study of Akkiz et al. (2017), which revealed an increase in bilirubin. Carr et al. (2014) research show a relationship between bilirubin levels and the aggressiveness index of liver cancer. HCC patients with abnormal bilirubin levels have a worse prognosis, increased incidence of portal vein thrombosis, tumor multifocality, and higher AFP levels.

AFP level >400 ng/mL is the AFP level mainly owned by HCC patients treated in the Internal Medicine Inpatient Room at Dr. Soetomo General Academic Hospital with 25 patients (41.7%). The same thing happened in the study of Kumar (2008), that AFP >400 was the highest level found in HCC patients. The group with the highest AFP level (>400) had a larger tumor size than AFP <20 and AFP 20-400. At AFP >400, significantly more micro and macrovascular invasion were found in HCC patients (Chan et al., 2019).

The presence of nodules was the most common radiological finding in the majority of HCC patients who were treated in the Internal Medicine Inpatient Room at Dr. Soetomo General Academic Hospital with 60 patients (100%). Based on the study of Nowicki et al. (2017), the most common form of HCC encountered is a solitary tumor with a diameter greater than 20 mm. Still, HCC may also present as a multifocal lesion or diffuse disease. HCC stages

are classified based on Barcelona Clinic Liver Disease (BCLC). BCLC C is the most common HCC stage found in HCC patients treated in the Internal Medicine Inpatient Room at Dr. Soetomo General Academic Hospital, with a total of 27 patients (45%). This is different from Puri et al. (2021) study that most KHS patients have BCLC stage B. BCLC stage C in patients with cancer-related symptoms (symptomatic tumors, ECOG 1-2), macrovascular invasion (either segmental or portal invasion) or extrahepatic spread (lymph node involvement or metastases) bear a poor prognosis, with expected median survival times of 6–8 months, or 25% at one year (European Association for the Study of the Liver, 2018).

Symptomatic therapy is the most widely given therapy to HCC patients in the Internal Medicine Inpatient Room at Dr. Soetomo General Academic Hospital, with 52 patients (86.7%). Hasan et al. (2020) research stated that the most commonly found therapy is supportive therapy (65.8%). If detected very early, HCC is curable with an excellent long-term prognosis. The main treatment options are surgical resection or liver transplantation if the patient is a suitable transplant candidate. However, in most HCC patients, cancer is detected at an advanced stage where surgical treatment is no longer an option (Ogunwobi et al., 2019). Live clinic outcomes are the most common clinical outcome in patients admitted to the Internal Medicine Inpatient Room Dr. Soetomo General Academic Hospital because of HCC, with a total of 40 patients (66.7%). At the same time, 20 patients (33.3%) died. Of the 26 patients who died, the leading cause of death was a septic shock in 9 patients (45%). In contrast to the study of Jaka et al. (2014), which stated that 66 patients died in the hospital, giving a mortality rate of 46.5%, with liver failure being the most common cause of death for 34 patients (55.5%).

CONCLUSION

Profile of HCC patients in the Internal Medicine Inpatient Room at Dr. Soetomo General Academic Hospital in the 2017-2019, dominated by male patients aged 50-59 years, the most risk factors were HBsAg positive, upnormal liver function, positive tumor markers, and had BCLC stage C.

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CONFLICT OF INTEREST

The authors declare there is no conflict of interest.

ETHICS CONSIDERATION

This research was ethically cleared and approved by Ethical Committee for Health research of Dr Soetomo General Academic Hospital certificate number 0398/101/4/XI/2020.

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AUTHOR CONTRIBUTION

All author have contributed to all procss in this research, including preparation, data gathering and analysis, drafting and approval for publication of this manuscript.

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