Jurnal Ilmiah Mahasiswa Kedokteran Universitas Airlangga

JUXTA: Jurnal Ilmiah Mahasiswa Kedokteran Universitas Airlangga
2023 January, XIV (01)

ORIGINAL ARTICLE

Profiles of Clinical and Liver Function Test of Hepatitis B and C Patients with Liver Cirrhosis

Andreas Novaldi Watang[1], Aryati Aryati[2,3*], Ulfa Kholili[4]

[1]Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia.
[2]Department of Clinical Pathology, Faculty of Medicine, Universitas Airlangga/Dr. Soetomo General Academic Hospital, Surabaya, Indonesia.
[3]Indonesian Society of Clinical Pathology and Laboratory Medicine, Jakarta, Indonesia.
[4]Department of Internal Medicine, Faculty of Medicine, Universitas Airlangga/Dr. Soetomo General Academic Hospital, Surabaya, Indonesia.

ABSTRACT

Introduction: Liver cirrhosis is a degenerative liver disease that ranks 14th as a global problem and has a high prevalence rate. This study aimed to determine the clinical and laboratory profile of inpatients with liver cirrhosis.

Methods: Medical record data of liver cirrhosis patients at Dr. Soetomo General Academic Hospital, Surabaya, in 2018-2019, were used in this cross-sectional descriptive observational study. The results were analyzed statistically to determine the different profiles between patients with liver cirrhosis caused by hepatitis B and C.

Results: 112 subjects in this study had liver cirrhosis caused by hepatitis B or C. The majority of cirrhotic patients were males over 40 years old. Melena was the most frequent complaint, and abdominal enlargement and hepatitis B virus (HBV) infection were the most common causes. Liver function tests in hepatitis B and C patients respectively showed albumin results of 2.73 g/dL (± 0.54); 2.75 g/dL (± 0.61), prothrombin time was 14.75 seconds (10.80-49.40); 14.9 seconds (11.1-19.1), direct bilirubin 1.17 mg/dL (0.9-17.05); 0.82 mg/dL (0.12-8.43), total bilirubin 2.18 mg/dL (0.28-24.9); 1.58 mg/dL (0.38-9.7), AST 50.5 U/L (16-826); 48.5 U/L (31-545), ALT 51.5 U/L (8-869); 38.5 (12-127). Subjects with hepatitis B and C had a median length of stay of 7.00 days, with an overall mean of 7.16 days. There was no significant difference in the results between patients with liver cirrhosis due to hepatitis B and C.

Conclusion: There was no significant difference between patients with liver cirrhosis caused by hepatitis B and C.

* Correspondence: aryati@fk.unair.ac.id

JUXTA: Jurnal Ilmiah Mahasiswa Kedokteran Universitas Airlangga
p-ISSN: 1907-3623; e-ISSN: 2684-9453
DOI: 10.20473/juxta.V14I12023.30-35

ARTICLE INFO

Article history:

Received 3-11-2022

Received in revised form 8-12-2022

Accepted 11-12-2022

Available online 10-01-2023

Keywords:
Liver cirrhosis,
Hepatitis,
Hepatitis B,
Hepatitis C.

Cite this as:
Watang AN, Aryati A, Kholili U. Profiles of Clinical and Liver Function Test of Hepatitis B and C Patients with Liver Cirrhosis. *JUXTA J Ilm Mhs Kedokt Univ Airlangga* 2023; 14: 30–35.

Introduction

Liver cirrhosis is a progressive chronic liver disease characterized as regenerative nodules surrounded by fibrous bands in response to chronic liver injury, leading to portal hypertension and end-stage liver disease.[1] Various lesion can damage the liver, including viral infections, toxins, hereditary conditions, or autoimmune processes. After a prolonged injury, most of the liver tissue becomes fibrous, leading to loss of function and progression of cirrhosis.[2] In developed countries, the most common causes of cirrhosis are hepatitis C virus (HCV), alcoholic liver disease, and non-alcoholic steatohepatitis (NASH). Meanwhile, hepatitis B virus (HBV) and HCV are the most common causes in developing countries.[2]

About 300 million people worldwide have chronic HBV infection, and 170 million by HCV. It is estimated that chronic HBV and HCV infection causes 57% of cases of liver cirrhosis in the world.[3] Globally, one-third of the world's population is infected with hepatitis B, 5% become chronic carriers, and a quarter of these develop cirrhosis and liver carcinoma.[4] 20%-30% of people who develop a chronic infection due to hepatitis C will develop cirrhosis of the liver within 15-25 years.[5] In Indonesia, in 2007, according to the Basic Health Research of Indonesia, the prevalence of active hepatitis B cases was 9.4%, and in 2013 it decreased to 7.1%. Therefore, Indonesia is a moderate-high hepatitis B endemic area.[6] Unlike Indonesia, in Europe, the prevalence of chronic hepatitis due to HBV is 0.5%-0.7%, and HCV is around 0.13%-3.26%.[7]

The prevalence of liver cirrhosis worldwide is estimated at 100 (range 25-100)/100,000 population, but it varies by country and region.[8] Liver cirrhosis ranks 14th as adults' most common cause of death worldwide.[9] Each year, one million people die from chronic hepatitis B and/or C infection, mostly caused by end-liver stage disease, including liver cirrhosis, hepatocellular carcinoma, or liver failure.[10] In Europe, the annual mortality from liver cirrhosis is 170,000.[7] The mortality rate caused by liver cirrhosis and carcinoma in Asia and Africa is estimated from 500,000 to 1.2 million per year.[11] According to the World Health Organization (WHO), about 170 million people were infected with liver cirrhosis. This figure covers about 3% of the entire human population worldwide, and each year, new infections of liver cirrhosis increase by 3-4 million people.[12]

The incidence of liver disease cases in Indonesia is very high. About 20 million Indonesians suffer from chronic liver disease. This figure calculates the prevalence of patients with hepatitis B infection in Indonesia, around 5%-10%, and hepatitis C, around 2%-3%. In the course of the disease, 20%-40% of people with chronic liver disease will develop liver cirrhosis in about 15 years, depending on how long a person has had chronic hepatitis.[12] According to reports from government-based general hospitals in Indonesia, the average prevalence of liver cirrhosis is 3.5% of all patients treated in Internal Medicine wards.[13]

The high morbidity and mortality rates of liver cirrhosis due to hepatitis B and C underlie this study. Things examined in this study were differences in patient profiles in the form of age, sex, and education of patients with liver cirrhosis due to hepatitis B and C, as well as differences in clinical features, liver function, complications, and length of stay of patients with liver cirrhosis due to hepatitis B and C. This study aimed to determine the clinical and laboratory profile of inpatients with liver cirrhosis at Dr. Soetomo General Academic Hospital, Surabaya, in 2018-2019.

Methods

Medical record data of liver cirrhosis patients at Dr. Soetomo General Academic Hospital, Surabaya, in 20,18-2019 were used in this cross-sectional descriptive observational study. The inclusion criteria were inpatient medical record data from patients diagnosed with liver cirrhosis due to hepatitis B and/or C from 1 January 2018-31 December 2019. Missing or incomplete medical record data were excluded. The variables in this study were patient characteristics, including age, gender, recent education, complaints, liver function test, degree of severity using Child-Pugh score, and records of length of stay. Input research data used Ms. Excel and then statistically processed using SPSS. This study had received ethical clearance from Ethical Committee for Health Research Dr. Soetomo General Academic Hospital, Surabaya.

Results

From the medical records department Dr. Soetomo General Academic Hospital, Surabaya, 131 hepatitis B and C patients who experienced liver cirrhosis were obtained. Of these, the data of 19 patients were excluded. There were 12 patients whose medical record data could not be found in the medical records department Dr. Soetomo General Academic Hospital, Surabaya. A total of 7 patients did not have sufficient complete data to be diagnosed with liver cirrhosis and/or had hepatitis B and C. Therefore, the included study sample was 112 patients.

The age distribution of hepatitis B patients with liver cirrhosis shows the age range of 51-60 years old was the largest with 32 people (28.58%), and hepatitis C patients with the age range of 41-50 years old was the largest with 14 people (12.50%) (Table 1).

The proportion of cirrhosis infected with chronic hepatitis B was relatively higher in males with a male:female ratio = 3.5:1 compared to cirrhosis infected with chronic hepatitis C with a ratio of 2:1 (Table 1).

Based on data collection of hospitalized patients, the most recent education of hepatitis B and/or C patients who experienced liver cirrhosis was high school graduates, namely 69 people with a percentage of 61.61%. The least number of graduates was a diploma with a percentage of 0.89% (Table 1).

Based on medical record data, various complaints were obtained. The most complaints that patients with liver cirrhosis felt due to hepatitis B was stomach enlargement (26 patients), and due to hepatitis C was

melena (14 patients). There were no significant differences between the complaints felt by patients with liver cirrhosis due to hepatitis B and C. However, the complaints of hematemesis were found to be significant (Table 2).

Table 1. Age, gender, and education distribution of hepatitis B and C patients with liver cirrhosis at Dr. Soetomo General Academic Hospital, Surabaya, in 2018-2019

Variable	Group	Liver cirrhosis with hepatitis B	Liver cirrhosis with hepatitis C	Total
Age	<20	0	0	0 (0.00%)
	20-30	2	0	2 (1.78%)
	31-40	4	2	6 (5.36%)
	41-50	25	14	39 (34.82%)
	51-60	32	5	37 (33.04%)
	>60	19	9	28 (25.00%)
Gender	Male	64	18	82 (73.21%)
	Female	20	10	30 (26.79%)
Education	Elementary school	17		15,18%
	Junior high school	8		7,14%
	Senior high school	69		61,61%
	Diploma	1		0,89%
	Bachelor	8		7,14%
	Other	9		8,04%

Source: Research data, processed

Table 2. Complaints of hepatitis B and C patients with liver cirrhosis at Dr. Soetomo General Academic Hospital, Surabaya, in 2018-2019

Complaint	Liver cirrhosis with hepatitis B (n = 82)	Liver cirrhosis with hepatitis C (n = 30)	p-value
Melena	25	14	0.111
Enlarged stomach	26	5	0.115
Hematemesis	12	12	0.004
Lethargic	18	5	0.540
Stomach pain	15	4	0.536
Difficulty breathing	9	5	0.420
Nausea	10	1	0.163
Vomiting	8	0	0.076
Loss of consciousness	5	2	0.912
Fever	3	1	0.935

Source: Research data, processed

Table 3 shows the results of albumin liver function tests in hepatitis B patients with liver cirrhosis obtained a mean result of 2.73 g/dL (± 0.54) with one missing data (1.22%), and in hepatitis C patients the mean result was 2.75 g/dL (± 0.61). This result difference was not significant.

Table 3. Results of liver function test of albumin, prothrombin time, direct bilirubin, total bilirubin, AST, and ALT of hepatitis B and C Patients with liver cirrhosis at Dr. Soetomo General Academic Hospital, Surabaya, in 2018-2019

Liver function test	Liver cirrhosis with hepatitis B (n = 82)	Liver cirrhosis with hepatitis C (n = 30)	p-value
Albumin (g/dL)	2.73 (± 0.54)	2.75 (± 0.61)	0.908
Prothrombin Time (Second)	14.75(10.8–49.4)	14.9 (11.1–19.1)	0.984
Direct bilirubin (mg/dL)	1.17 (0.9–17.05)	0.82 (0.12–8.43)	0.778
Total bilirubin (mg/dL)	2.18 (0.28–24.9)	1.58 (0.38–9.7)	0.781
AST (U/L)	50.5 (16–826)	48.5 (31–545)	0.429
ALT (U/L)	51.5 (8–869)	38.5 (12–127)	0.094

Source: Research data, processed

Table 3 shows the results of liver function tests in hepatitis B and C patients with liver cirrhosis at Dr. Soetomo General Academic Hospital, Surabaya, in 2018-2019. In liver cirrhosis patients due to hepatitis B, the results obtained prothrombin time with a median of 14.75 seconds (10.80-49.40), and eight patients (9.76%) did not have prothrombin time examination data. The median for direct bilirubin was 1.17 mg/dL (0.9-17.05), and total bilirubin was 2.18 mg/dL (0.28–24.9), with the number of patients without data of direct and total bilirubin examination was seven patients (8.54%). The median of aspartate aminotransferase (AST) was 50.5 U/L (16-826), and alanine aminotransferase (ALT) examination obtained a median of 51.5 U/L (8-869). One patient (1.22%) did not have examination data for AST and ALT. In hepatitis C patients, prothrombin time results were obtained with a median of 14.9 seconds (11.1-19.1). Six patients (20%) did not have prothrombin time examination data. The median for direct bilirubin was 0.82 mg/dL (0.12-8.43), and the total bilirubin was 1.58 mg/dL (0.38–9.7), with the number of patients without data of direct and total bilirubin examination was 6 patients (20%). The median of AST was 48.5 U/L (31-545), and the ALT examination obtained a median of 38.5 U/L (12-127). One patient (3.33%) did not have examination data for AST and ALT. From the results of statistical tests, there was no significant

difference between liver function tests of hepatitis B and C patients with liver cirrhosis.

Table 4. Complications of hepatitis B and C patients with liver cirrhosis at Dr. Soetomo General Academic Hospital, Surabaya, in 2018-2019

Complication	Liver cirrhosis with hepatitis B (n = 82)	Liver cirrhosis with hepatitis C (n = 30)	Total
Hematemesis	25	14	0.004
Melena	12	12	0.111
Ascites	13	6	0.605
Hepatic Encephalopathy	5	2	0.912
Lung Effusion	9	5	0.420

Source: Research data, processed

Table 4 shows that the complications that occurred in patients with liver cirrhosis were various. In this study, most complications in patients with liver cirrhosis due to hepatitis B and C are hematemesis. There was no significant difference between complications of hepatitis B and C patients with liver cirrhosis.

Table 5. Complications of hepatitis B and C patients with liver cirrhosis at Dr. Soetomo General Academic Hospital, Surabaya, in 2018-2019

Child-Pugh	Liver cirrhosis with hepatitis B (n = 82)	Liver cirrhosis with hepatitis C (n = 30)	p-value
A	12	3	0.524
B	31	17	0.074
C	36	9	0.184

Source: Research data, processed

Table 5 shows the severity of Child-Pugh in patients with liver cirrhosis due to hepatitis B was Child-Pugh C with a total of 36 patients, and the most due to hepatitis C was Child-Pugh B as many as 17 patients. There was no significant difference between liver cirrhosis caused by hepatitis B and C. The Child-Pugh severity of 4 patients (3.57%) could not be determined.

Table 6. Length of stay of hepatitis B and C patients with liver cirrhosis at Dr. Soetomo General Academic Hospital, Surabaya, in 2018-2019

Length of Stay	Median (Min-Max)	p-value
Liver cirrhosis with hepatitis B	7.00 (2.00–20.00)	0.653
Liver cirrhosis with hepatitis C	7.00 (2.00–14.00)	

Source: Research data, processed

Table 6 shows the median results were 7.00 days (2.00-20.00) in patients with liver cirrhosis due to hepatitis B and 7.00 days (2.00-14.00) caused by hepatitis C. The mean length of stay was 7.16 days. The difference in length of stay between patients with liver cirrhosis caused by hepatitis B and C was insignificant.

Discussion

In this study, the highest age range prevalence of hepatitis B and C patients with liver cirrhosis was 41-50 years old, followed by 51-60 years old, with numbers and percentages that were not much different. One study showed that most cirrhosis due to HBV and HCV was over 40.[14] In addition, a study conducted at Prof. Dr. R. D. Kandou Hospital Manado showed that the most liver cirrhosis was experienced in the age range 51-60 years old.[15] Another study conducted at Dr. M. Djamil General Hospital Padang showed that most liver cirrhosis was in the age range 51-60 years old.[16] A study of age and ethnicity in patients with liver cirrhosis at Parkland Memorial Hospital, Texas, found that the median age of patients with hepatitis B and C cirrhosis was 50 years old or older.[14]

In this study, most hepatitis B and C patients with liver cirrhosis were males. This is in accordance with other studies that male patients have a greater number than females.[17] In addition, other studies also stated that males have a mortality tendency of two times greater than females due to liver disease and cirrhosis.[18] This is supported by the fact that 78% of subjects with liver cirrhosis were males and 22% were females.[19] In India, patients with chronic liver disease showed a proportion of 80% males and 20% females.[20]

This study shows that hepatitis B and C patients with liver cirrhosis were mostly high school graduates. This is consistent with other studies that showed patients with high school education had the largest percentage (68.7%).[21] A study at Dr. Sardjito General Hospital Yogyakarta showed that secondary education (junior high school–senior high school) was the largest at 43.3%.[22]

The most common cause of liver cirrhosis in studies is the hepatitis B virus. In western countries, alcohol is the main cause of liver cirrhosis.[23] In addition to Europe, cases of non-alcoholic fatty liver disease are found in about 2%-44% of the general population.[7] Meanwhile, in Indonesia, hepatitis B and C viruses are the main causes of liver cirrhosis. Other studies conducted at Prof. Dr. R. D. Kandou Hospital Manado and Dr. Cipto Mangunkusumo Hospital Jakarta showed that the most cause of liver cirrhosis is the hepatitis B virus.[15,24]

The results of medical record data in this study showed that the most patient complaints were an enlarged abdomen in hepatitis B and melena in hepatitis C. In one study, most complaints were in the form of ascites and abdominal distension, while in another study were in the form of hematemesis and abdominal obstruction.[15,21] In Atatürk University, Faculty of Medicine, Gastroenterology Clinic and Polyclinic, Turkey, studies on the highest frequency of complications of liver cirrhosis were ascites

(83%), hematemesis (56%), and others. This difference in clinical manifestations occurred due to the wide variety of clinical symptoms in patients with liver cirrhosis.[25]

Liver function tests which usually perform on patients with liver cirrhosis can show a mild to moderate increase in AST and ALT and a disturbance in the production of serum albumin and coagulation factors. This impaired liver function can increase the prothrombin time and direct and total bilirubin levels.[2] This is consistent with what was found in this study.

The severity of Child-Pugh's liver cirrhosis in this study showed that Child-Pugh C and B were the most in patients with cirrhosis due to hepatitis B and C, respectively. A study by Lovena, *et al*. (2017) and Prakoeswa, *et al*. (2015) showed that the highest degree of liver cirrhosis severity was Child-Pugh C.[16,21] There were differences between those studies and this study in the form of the number of samples used. Lovena, *et al*. (2017) used 304 people, and Prakoeswa, *et al*. (2015) used 163 people.[16,21] Another study related to the relationship between liver cirrhosis and esophageal varices found that most patients with esophageal varices had a Child-Pugh B degree of 53.85%.[26] Meanwhile, this study used 112 people. Those studies showed that patients who came and were hospitalized in health facilities had a moderate to a high degree of severity.

The length of stay of patients with hepatitis B and C who experienced liver cirrhosis at Dr. Soetomo General Academic Hospital, Surabaya, in 2018-2019 had a median value of 7.00 days (2.00-20.00) and 7.00 days (2.00-14.00), respectively with an overall mean of 7.16 days. This differs from previous studies by Abidzah (2019) and Stiphany (2012), with a mean hospitalization of nine days and 9.31 days.[27,28] This difference can be caused by factors of the type of complications and the source of financing.[27] A study conducted in 2011 at some hospitals in California, Florida, Massachusetts, Mississippi, New York, and Washington found that the highest length of stay was in the range of 5-13 days (39.5%), followed by 2-4 days (39.2%).[29] This study showed that patients with maximum hospitalization had >1 complication with a high degree of severity.

In general studies, there were no differences in the research variables tested between patients with liver cirrhosis caused by hepatitis B and C.

Strength and Limitations

This study provides new insights and developments regarding the profile of liver cirrhosis due to hepatitis B and C. This study did not include data on other etiology of cirrhosis, such as non-viral causes, and only took samples of hospitalized patients.

Conclusion

The distribution of liver cirrhosis patients due to hepatitis B and C was mostly males older than 40 years old and high school graduates. The most common cause of liver cirrhosis was hepatitis B. The results of the liver function test show a decrease in liver function. Most complaints were abdominal enlargement and melena in hepatitis B and C patients, respectively. In general studies, there were no differences in the research variables tested between patients with liver cirrhosis caused by hepatitis B and C.

Acknowledgments

Thanks to the academic supervisor, medical record officer, and Ms. Stephanie who participated in this research work.

Conflict of Interest

The authors declared there is no conflict of interest.

Funding

This study was self-funded by the authors.

Ethical Clearance

This study had received ethical clearance from Ethical Committee for Health Research Dr. Soetomo General Academic Hospital, Surabaya (no. 1907/KEPK/III/2020) on 23 March 2020.

References

1. Yuwono B, Maimunah U, Widodo B. The Association between The Degree of Liver Cirrhosis Severity and Zinc Serum Level. *Current Internal Medicine Research and Practice Surabaya Journal* 2020; 1: 5. [Journal]
2. Sharma B, John S. *Hepatic Cirrhosis*, http://www.ncbi.nlm.nih.gov/pubmed/16255293 (2022).
3. Lin J. Virus-Related Liver Cirrhosis: Molecular Basis and Therapeutic Options. *World J Gastroenterol* 2014; 20: 6457. [PubMed]
4. Jefferies M, Rauff B, Rashid H, *et al*. Update on Global Epidemiology of Viral Hepatitis and Preventive Strategies. *World J Clin Cases* 2018; 6: 589–599. [PubMed]
5. Toshikuni N. Hepatitis C-Related Liver Cirrhosis - Strategies for the Prevention of Hepatic Decompensation, Hepatocarcinogenesis, and Mortality. *World J Gastroenterol* 2014; 20: 2876. [PubMed]
6. Muljono DH. Epidemiology of Hepatitis B and C in Republic of Indonesia. *Euroasian J hepato-gastroenterology* 2017; 7: 55–59. [PubMed]
7. Blachier M, Leleu H, Peck-Radosavljevic M, *et al*. The Burden of Liver Disease in Europe: A Review of Available Epidemiological Data. *J Hepatol* 2013; 58: 593–608. [PubMed] [ScienceDirect]
8. Garcia-Tsao G. Cirrhosis and Its Sequelae. In: *Goldman's Cecil Medicine*. Elsevier, pp. 999–1007.
9. Tsochatzis EA, Bosch J, Burroughs AK. Liver Cirrhosis. *Lancet* 2014; 383: 1749–1761. [ScienceDirect]
10. Guan R, Lui HF. Treatment of Hepatitis B in Decompensated Liver Cirrhosis. *Int J Hepatol* 2011; 2011: 1–11. [PubMed]
11. E. Blum H. Hepatitis B: Diagnosis and Management. *AIMS Med Sci* 2021; 8: 1–10. [Journal]
12. Alfiani E. *Asuhan Keperawatan Pada Tn.S dengan Sirosis Hepatis di Ruang Cempaka BRSUD Sukoharjo*. Muhammadiyah Surakarta,

http://eprints.ums.ac.id/2953/ (2008).
13. PPHI (Perhimpunan Peneliti Hati Indonesia). Sirosis hati. *PPHI*. [WebPage]
14. Sajja KC, Mohan DP, Rockey DC. Age and Ethnicity in Cirrhosis. *J Investig Med* 2014; 62: 920–926. [PubMed]
15. Patasik YZ, Waleleng BJ, Wantania F. Profil Pasien Sirosis Hati yang Dirawat Inap di RSUP Prof. Dr. R. D. Kandou Manado Periode Agustus 2012 – Agustus 2014. *e-CliniC*; 3. Epub ahead of print 11 February 2015. DOI: 10.35790/ecl.3.1.2015.6841. [Journal]
16. Lovena A, Miro S, Efrida E. Karakteristik Pasien Sirosis Hepatis di RSUP Dr. M. Djamil Padang. *J Kesehat Andalas* 2017; 6: 5. [Journal]
17. Dass E, Patel M, Patel S, *et al*. A Prospective Study of Liver Cirrhosis: An Overview, Prevalence, Clinical Manifestation & Investigations in Patients Admitted to the Medicine Ward in a Rural Teaching Hospital. *Int J Sci Res*; 7. Epub ahead of print 2018. DOI: 10.36106/ijsr. [Journal]
18. Guy J, Peters MG. Liver Disease in Women: The Influence of Gender on Epidemiology, Natural History, and Patient Outcomes. *Gastroenterol Hepatol (N Y)* 2013; 9: 633–9. [PubMed]
19. Nallagangula KS. Correlative Study of Hyaluronic Acid and YKL-40 with Conventional Markers for Cirrhosis of Liver. Epub ahead of print 2018. DOI: http://dx.doi.org/10.24966/GHR-. [PubMed]
20. Grewal U, Walia G, Bakshi R, *et al*. Hepatitis B and C Viruses, their coinfection and correlations in chronic liver disease patients: A tertiary care hospital study. *Int J Appl Basic Med Res* 2018; 8: 204. [PubMed]
21. Prakoeswa CA. *Profil Pasien Sirosis Hepatis yang Rawat Inap di Bagian Penyakit Dalam RSUD Dr. Soetomo Surabaya Tahun 2015*. Universitas Airlangga, https://repository.unair.ac.id/66267/ (2015).
22. Manik N, Wahyono D. *Evaluasi Kualitas Hidup pada Penderita Sirosis Hati di Instalasi Rawat Jalan Rsup Dr. Sardjito Yogyakarta*. Universitas Gajah Mada, http://etd.repository.ugm.ac.id/penelitian/detail/52016 (2011).
23. Sudoyo AW, Setiyohadi B, Alwi I, *et al*. *Buku Ajar Ilmu Penyakit Dalam*. Jakarta, http://pustaka.poltekkes-pdg.ac.id/index.php?p=show_detail&id=1281 (2006).
24. Kalista KF, Lesmana CRA, Sulaiman AS, *et al*. Profil Klinis Pasien Sirosis Hati dengan Varises Esofagus yang Menjalani Ligasi Varises Esofagus di Rumah Sakit Dr. Cipto Mangunkusumo. *J Penyakit Dalam Indones* 2019; 6: 36. [Garuda]
25. Topdagi O, Okcu N, Bilen N. The Frequency of Complications and the Etiology of Disease in Patients with Liver Cirrhosis in Erzurum. *Eurasian J Med* 2014; 46: 110–114. [PubMed]
26. Medisika HD, Boedi SP, Ichsan PG. Correlation between the Severity of Liver Cirrhosis with Esophageal Varices in RSUD Dr Soetomo Surabaya. *Current Internal Medicine Research and Practice Surabaya Journal* 2022; 3: 36–39. [Journal]
27. Marpaung S. Karakteristik Penderita Sirosis Hati Rawat Inap di Rsud Dr Pirngadi Medan Tahun 2010-2011. *Gizi, Kesehat Reproduksi dan Epidemiol*; 1, https://jurnal.usu.ac.id/index.php/gkre/article/view/375 (2012).
28. Abidzah A. *Karakteristik Penderita Sirosis Hati yang Dirawat Inap di Rumah Sakit Umum Haji Medan Tahun 2016-2018*, http://repositori.usu.ac.id/handle/123456789/20905 (2019).
29. Tapper EB, Halbert B, Mellinger J. Rates of and Reasons for Hospital Readmissions in Patients With Cirrhosis: A Multistate Population-based Cohort Study. *Clin Gastroenterol Hepatol* 2016; 14: 1181-1188.e2. [PubMed]