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Characteristics of patients with Hepatitis B and C at Dr. Moewardi General Hospital in Surakarta, Indonesia

Benedictus Aditya Satya Laksana Adji[1], Triyanta Yuli Pramana[2], Tri Nugraha Susilawati[3*]

[1]Faculty of Medicine, Universitas Sebelas Maret, Surakarta, Indonesia, [2]Department of Internal Medicine, Dr. Moewardi Hospital/ Faculty of Medicine, Universitas Sebelas Maret, Surakarta, Indonesia, [3]Department of Microbiology, Faculty of Medicine, Universitas Sebelas Maret, Surakarta, Indonesia

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ABSTRACT

Hepatitis B virus (HBV) and hepatitis C virus (HCV) infections remain a significant health burden in the world, which is mainly attributed to patients who develop chronic hepatitis, liver cirrhosis, and hepatocellular carcinoma (HCC). The epidemiology of hepatitis B and C in Surakarta, Central Java Province, Indonesia has never been reported. This study aimed to investigate the demographic, clinical, and laboratory characteristics of patients with hepatitis B and C who were admitted to Dr. Moewardi General Hospital, Surakarta in 2019. The medical records of patients with hepatitis B (n=94) and hepatitis C (n=75) were examined, and the data were analyzed using the chi-square and Mann-Whitney tests. The patients with hepatitis C were generally older, more likely to develop jaundice and ascites, and had higher levels of serum urea, creatinine, AST, and total bilirubin compared to those with hepatitis B. In conclusion, patients with HCV infection had worse clinical presentation and laboratory profiles than those with HBV infection. However, further research is needed on a wider scale to confirm this result.

ABSTRAK

Infeksi virus hepatitis B (HBV) dan C (HCV) masih merupakan beban kesehatan yang signifikan bagi dunia terutama pada pasien yang penyakitnya berkembang menjadi hepatitis kronis, sirosis hati, dan karsinoma hepatoseluler (HCC). Epidemiologi hepatitis B dan C di Surakarta, Provinsi Jawa Tengah, Indonesia belum pernah dilaporkan sebelumnya. Penelitian ini bertujuan untuk menganalisis karakteristik demografrik, klinik, dan laboratorik dari pasien hepatitis B dan C yang dirawat inap di RS Dr. Moewardi pada tahun 2019. Data diperoleh dari rekam medis pasien dengan hepatitis B (n=94) dan hepatitis C (n=75) dan dianalisis menggunakan uji *chi-square* dan uji Mann Whitney. Pada pasien dengan hepatitis C ditemukan rerata usia yang lebih tua, jumlah kasus dengan ikterik dan ascites yang lebih banyak, serta kadar ureum, kreatinin, SGOT dan bilirubin total di serum yang lebih tinggi dibandingkan pada pasien dengan hepatitis B. Berdasarkan hasil penelitian tersebut, dapat disimpulkan bahwa infeksi HCV berhubungan dengan derajat penyakit yang lebih berat dibandingkan infeksi HBV. Namun demikian, perlu penelitian lebih lanjut dalam skala yang lebih luas untuk mengkonfirmasi hasil ini.

Keywords:
hepatitis B;
hepatitis C;
HBV;
HCV;
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*corresponding author: tri.susilawati@staff.uns.ac.id

INTRODUCTION

Hepatitis B virus (HBV) and hepatitis C virus (HCV) infections are common in the world. It is estimated that there are 2 billion people have been infected by HBV and currently 257 million people live with chronic HBV infection.[1] Meanwhile, there are 71 million people infected with HCV in the world and 2.3 million people of them are co-infected with HIV.[2] Altogether, hepatitis B and C had caused 1.2 million deaths as a result of acute and chronic infections and their complications.[3]

The prevalence of HBV is classified as moderate to high in Indonesia, ranging from 2.5% to 10% of the general population, depending on which region of the country.[4] In Central Java Province, for instance, the prevalence of HBV infection is moderate; i.e., 6-7% of the population. Fortunately, Indonesia has a fairly low prevalence rate of anti HCV antibodies; i.e., around 0.8%. Thus, it can be estimated that the prevalence of HCV infection is much lower than that of HBV.[5]

Hepatitis B and C are a global health burden since these diseases may develop into more severe liver diseases, such as chronic hepatitis, cirrhosis of the liver, hepatocellular carcinoma (HCC), and liver failure. Each spectrum of the disease has its characteristics that can serve to assess disease progression.[6]

During the development of HBV and HCV infection, many metabolic processes are disturbed and these can be detected in the physical examination as well as the results of laboratory investigation. The clinical manifestations of the disease that are associated with impaired liver function include jaundice of the skin and sclera, dark urine, and ascites. A blood test is often necessary to evaluate the disease progression by monitoring the increased levels of serum glutamic pyruvic transaminase (SGPT) and serum glutamic oxaloacetic transaminase (SGOT).[7] The differences in clinical manifestations as well as laboratory profiles among patients with hepatitis B and hepatitis C may provide important information for monitoring disease progression as well as predicting the outcomes. Some knowledge of the local disease burden is important to develop an effective strategy for infection control and management of hepatitis B and C. This study aimed to describe the epidemiology of hepatitis B and hepatitis C in Surakarta, Central Java Province, Indonesia. Furthermore, the clinical and laboratory characteristics of the patients would be further evaluated.

MATERIALS AND METHODS

Design and subjects

It was an analytic observational study with a cross-sectional design, conducted from January to March 2020. Data were collected from patients who had the diagnosis of hepatitis B or hepatitis C and were admitted to Dr. Moewardi Hospital, Surakarta in 2019. Dr. Moewardi General Hospital is the main referral hospital in Central Java Province, Indonesia. The hospital is well equipped with a clinic of gastroenterohepatology and endoscopy facilities. The diagnosis of hepatitis B was confirmed by HBsAg serology whereas hepatitis C was confirmed by the presence of anti-HCV antibody and HCV RNA.

Procedure

As the initial search of the records, we employed the international classification of diseases 10 (ICD-10) Verison 2019 and the search codes were B18.1 for “chronic viral hepatitis B without delta-agent” and B18.2 “for chronic viral hepatitis C”. After the medical records were collected, the records of patients who had comorbidities that could affect liver function were excluded; such as those with a history of alcohol consumption and those taking hepatotoxic drugs. Records with incomplete data were also excluded as well as those with

HBV and HCV coinfection. The search enabled researchers to identify patients with HBV or HCV-associated cirrhosis and hepatocellular carcinoma and automatically excluded hepatitis D infection. The data collected include demographic characteristics (i.e., patients' age, gender, and address), the presence of clinical manifestations (i.e., jaundice, nausea, vomiting, abdominal pain, ascites, dark urine, and oedema), and the results of laboratory investigation (i.e., the levels of serum SGPT, SGOT, urea, creatinine, and total bilirubin.

Statistical analysis

Data were analyzed using the IBM SPSS software version 22.0 (IBM Corp., Armonk, NY, USA). The differences between groups were analyzed by using the chi-square test and the Mann-Whitney test and the results were considered statistically significant if the p-value is less than 0.05 ($p<0.05$).

RESULTS

A total of 94 cases of hepatitis B and 75 cases of hepatitis C who were treated at Dr. Moewardi Hospital during the period of 2019 were evaluated. TABLE 1 shows that on average, patients with hepatitis C were older than those with hepatitis B. Patients with hepatitis B were mostly from Karanganyar district whilst hepatitis C cases were more prevalent in Surakarta district. Both hepatitis B and C sufferers were male predominant, accounting for around two-thirds of the total cases. TABLE 2 shows that patients with hepatitis C had a higher incidence of jaundice, dark urine, and ascites compared to those with hepatitis B.

TABLE 1. Demographic characteristics of patients with Hepatitis B (n=94) and C (n=75) at Dr. Moewardi General Hospital

Variable	Hepatitis B [n (%)]	Hepatitis C [n (%)]	p
Age (mean±SD years)	49.79±13.30	58.91±14.05	0.000*
• 21-30	8 (8.5)	2 (2.7)	
• 31-40	12 (12.8)	9 (12.0)	
• 41-50	27 (28.7)	7 (9.3)	
• 51-60	31 (33.0)	22 (29.3)	
• 61-70	8 (8.5)	16 (21.3)	
• >70	8 (8.5)	19 (25.3)	
Address			
• Surakarta	12 (12.8)	22 (29.3)	
• Sragen	19 (20.2)	8 (10.7)	
• Karanganyar	25 (26.6)	12 (16.0)	
• Sukoharjo	13 (13.8)	13 (17.3)	
• Wonogiri	4 (4.3)	6 (8.0)	0.79
• Boyolali	7 (7.4)	6 (8.0)	
• Klaten	1 (1.1)	2 (2.7)	
• Yogyakarta	2 (2.1)	2 (2.7)	
• East Java	11 (11.7)	4 (5.3)	
Sex			
• Male	62 (66.0)	49 (65.3)	0.932
• Female	32 (34.0)	26 (34.7)	

*Statistically significant ($p<0.05$)

TABLE 2. Clinical characteristics of patients with Hepatitis B (n=94) and C (n=75) at Dr. Moewardi General Hospital

Variable	Hepatitis B [n (%)]	Hepatitis C [n (%)]	p
Jaundice	25 (26.6)	34 (45.3)	0.011*
Nausea	33 (35.1)	37 (49.3)	0.062
Vomiting	33 (35.1)	22 (29.3)	0.426
Abdominal pain	54 (57.4)	34 (45.3)	0.117
Ascites	18 (19.1)	26 (34.7)	0.022*
Dark urine	2 (2.1)	10 (13.3)	0.005*
Oedema	4 (4.3)	4 (5.3)	0.743

*Statistically significant (p <0.05).

The results of laboratory investigations were shown in TABLE 3. Patients with hepatitis C had significantly higher levels of serum urea, creatinine, SGOT, and total bilirubin. In contrast, the levels of hemoglobin, hematocrit, thrombocyte, and erythrocyte in hepatitis B cases were significantly higher than that in hepatitis C.

TABLE 3. Laboratory characteristics of patients with Hepatitis B (n=94) and C (n=75) at Dr. Moewardi General Hospital

Variabel	Hepatitis B	Hepatitis C	p
Urea (mg/dL)	40.84±46.41	71.36±74.82	0.000*
Creatinine (U/L)	1.49±3.07	2.34±4.18	0.023*
SGPT (U/L)	64.35±84.43	60.49±59.46	0.499
SGOT (U/L)	86.03±101.55	115.33±118.95	0.036*
De Ritis Ratio	1.67±1.29	1.98±1.21	0.006*
• <1	25	8	0.009*
• >1	69	67	
Total bilirubin (mg/dL)	2.45±4.77	5.53±10.25	0.001*
Hemoglobin (g/dL)	13.47±15.98	10.10±2.51	0.000*
Hematocrit (%)	35.92±8.52	30.47±8.21	0.000*
Leucocyte (10^3/uL)	7.59±5.56	8.69±7.62	0.528
Thrombocyte (10^3/uL)	193.96±99.78	168.99±127.87	0.009*
Erythrocyte (million/uL)	4.10±1.02	3.42±0.86	0.000*

*Statistically significant (p <0.05)

We calculated the De Ritis ratio; i.e., the ratio between the serum levels of SGPT and SGOT (SGPT/SGOT). Most patients in this study had the De Ritis ratio with a value of >1, indicating chronic infection that leads to cirrhosis.[8] We found that hepatitis C patients had a significantly higher mean of De Ritis ratio than those with hepatitis B.

DISCUSSION

HBV and HCV infection may develop into a chronic infection and severe

complication such as liver cirrhosis and HCC.[5,6] The clinical manifestations of hepatitis B and C can be different depending on the phase of the disease and the viral respective characteristics.[7] In this study, we analyzed demographic, clinical, and laboratory characteristics of patients who had been admitted to a tertiary hospital in Indonesia with hepatitis B and C, irrespective of the stage of the disease.

We found that the sufferers of hepatitis B and hepatitis C were male predominant. This phenomenon is likely due to hormonal differences between males and females. It is important to note that the liver is a sexually dimorphic organ that expresses androgen and estrogen receptors. In hepatitis B, androgen can increase serum HBsAg levels whereas an increase in estrogen will reduce serum HBV DNA levels. Hepatitis B viral protein, the HBx protein, can increase the activity of androgen receptors, causing the development of more progressive HBV in males.[9] In hepatitis C, a previous study has reported that women tend to have a spontaneous clearance of HCV.[10]

Patients with hepatitis C are on average older than those with hepatitis B. This may be attributed to two factors: the virus' mode of transmission and the pathogenesis of the disease. Most HCV infections occur in adults, mainly acquired during blood transfusions or associated with risky lifestyles. In contrast, HBV infection is mostly transmitted vertically so that infection is initiated at an early ages.[11]

Pathogenically, there are differences in how HBV and HCV infection develop into HCC. HBV infection can develop into HCC in three ways: chronic necroinflammation, combining HBV DNA with hepatocyte DNA, and the influence of HBV proteins, such as HBx.[12] Chronic inflammation of hepatitis causes a continuous cycle of necrosis-inflammation-regeneration. This continuous proliferation of hepatocytes is likely to cause epigenetic changes, oncogenic mutations, and telomere shortening. The integration of viral DNA with hepatocyte DNA causes changes in the genetic structure of the host DNA thereby increasing the hepatocarcinogenesis process. HBx protein can alter the expression of growth-stimulating genes. This process causes an acceleration of tumor formation. HBx can accelerate tumor formation by promoting the proliferation of "altered cells". Furthermore, HBx acts as a cofactor in the hepatocarcinogenesis process.[13] In contrast with HBV, the development of HCC in HCV infection is mainly due to chronic inflammation. Moreover, HCV is an RNA virus so there is no merger between the virus and the host genome. This condition causes a longer process in developing HCC in HCV infection.[14,15]

The study of clinical characteristics shows that there are significant differences in the prevalence of ascites, dark urine, and jaundice among hepatitis B and C cases. It has been known that ascites can appear only in chronic hepatitis B and C while dark urine and jaundice usually appear in both acute and chronic hepatitis. Ascites develops as a result of portal hypertension in patients with cirrhosis of the liver whilst dark urine and jaundice are caused by hyperbilirubinemia.[16]

HBV and HCV infection causes damage to the hepatocytes which results in disruption of bilirubin excretion. Disruption excretion of bilirubin leads to retention of bilirubin in the blood resulting in jaundice. The conjugated bilirubin in the blood is finally excreted through urine causing dark-colored urine.[17] Our study found that patients with hepatitis C had a higher level of total bilirubin in their serum compared with those who had hepatitis B (p = 0.017).

Levels of serum urea and creatinine are indicators of kidney health and increased levels of urea and creatinine

are associated with kidney damage.[18] In this study, we found that the levels of serum urea and creatinine in hepatitis C were higher than that in hepatitis B (p <0.05), indicating a worse renal dysfunction in hepatitis C. Liver cirrhosis, which is more common in hepatitis C, can facilitate kidney damage due to portal hypertension.[19] In addition, chronic hepatitis C triggers an immune reaction that attacks the kidneys resulting in glomerulonephritis.[20] Treatment of hepatitis C may also decrease kidney function. Sofosbuvir is thought to have a nephrotoxic effect on the kidneys, although this opinion is still being debated.[21] Nevertheless, patients with kidney disease requiring hemodialysis can be the source of HBV and HCV transmission.[22] A previous study conducted in Yogyakarta, Indonesia found that the prevalence of HBV and HCV in hemodialysis patients was 24.2% and 83.2%, respectively. [23]

The study found that the levels of serum SGPT and SGOT, as well as total bilirubin, were higher in hepatitis C than those in hepatitis B, confirming the results of previous studies.[24,25] In particular, a significant increase in SGOT levels is associated with a higher degree of liver inflammation and damage among patients with hepatitis C. However, the exact mechanism by which HCV causes more damage to the liver is not known with certainty. On average, our study participants had the De Ritis ratio values of >1. An increase in the De Ritis ratio value of >1 is associated with the progression of fibrosis to cirrhosis although this assessment has poor sensitivity.[8] A combination of De Ritis ratio values with the results of a platelet count of <150.000/mm3 and prothrombin time test provides a better sensitivity in predicting the development of chirrosis.[26]

This study implies that public health measures should be taken to reduce the prevalence of hepatitis B and hepatitis C in Surakarta as well as to prevent further transmission of HBV and HCV in the population. In clinical practice, close monitoring should be carefully and regularly performed particularly for patients with HCV infection as it can rapidly deteriorate patients' health due to the disease itself and the medication. The results of liver and renal function tests can serve as key indicators in monitoring disease progression and evaluating therapy. In more-advanced laboratory settings, molecular studies should be performed to identify high-circulating viral genotypes in the community as well as genetic polymorphism of the patients. Such studies are important for portraying HBV and HCV molecular epidemiology as well as analyzing the complex correlation between the agent, host, disease, and therapeutic responses.

CONCLUSION

The patients with HCV infection are more often presenting with worse disease progression than those with HBV infection. Further research is needed on a broader scale to confirm this phenomenon.

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