Challenges and Gaps in the Management of Chronic Hepatitis C Infection: Insight from A Tertiary Hospital in Indonesia

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ABSTRACT

Background: *Hepatitis C virus (HCV) infection remains a significant public health burden in Indonesia, affecting approximately 2.5 million people. The introduction of direct-acting antivirals (DAAs) has revolutionized HCV management by offering highly effective and well-tolerated treatment options. Since 2017, Indonesia has implemented an HCV cascade of care and a government-funded DAA program to support the World Health Organization (WHO) goal of HCV elimination by 2030. However, challenges in diagnostic accessibility and treatment follow-up continue to hamper progress. This study aims to evaluate the implementation of the HCV cascade of care at Dr. Kariadi General Hospital, Semarang, Indonesia.*

Methods: *A retrospective descriptive study was conducted at Dr. Kariadi General Hospital, which included data from patients who tested positive for anti-HCV antibodies between January 2019 and November 2024. HCV treatment was categorized into five stages: (1) positive anti-HCV antibody test, (2) HCV RNA test, (3) positive HCV RNA result, (4) treatment initiation, and (5) sustained virologic response 12 weeks post-treatment (SVR12). Data analysis was performed using SPSS Statistics version 26. Categorical variables were expressed as frequencies and percentages, and findings were presented as numbers and proportions across each stage of the care cascade.*

Results: *Among 317 patients with positive anti-HCV antibody results (55% men, 45% women; median age: 56 years), 280 (88%) underwent HCV RNA testing, and 213 (76%) were confirmed positive. Of these, 185 patients (87%) initiated treatment, 144 (78%) completed therapy, and 108 (75%) achieved SVR12.*

Conclusion: *This study shows that significant gaps remain at various stages of the HCV care cascade, particularly in confirmatory HCV RNA testing, treatment initiation, and post-treatment follow-up.*

Keywords: *Cascade of Care, Hepatitis C, Indonesia*

ABSTRAK

Latar Belakang: *Infeksi virus Hepatitis C (HCV) masih menjadi masalah kesehatan yang signifikan di Indonesia, dengan perkiraan 2,5 juta orang terinfeksi. Kemunculan terapi antivirus kerja langsung (DAA) telah meningkatkan luaran pengobatan secara signifikan, dengan tingkat kesembuhan yang tinggi. Sejak 2017, Indonesia telah menerapkan sistem perawatan berjenjang HCV dan menyediakan program terapi DAA gratis*

sebagai bagian dari target global WHO untuk eliminasi HCV pada tahun 2030. Namun, hambatan terkait aksesibilitas dan keterjangkauan tes dan pengobatan masih menjadi tantangan dalam upaya eliminasi. Penelitian ini bertujuan untuk mengevaluasi implementasi kaskade pengobatan HCV di RSUP Dr. Kariadi, Semarang, Indonesia.

***Metode:** Penelitian deskriptif retrospektif ini dilakukan di RSUP Dr. Kariadi dengan menganalisis data pasien dengan hasil antibodi anti-HCV positif pada periode Januari 2019–November 2024. Tahapan kaskade pengobatan dikategorikan menjadi lima tahap: (1) hasil anti-HCV positif, (2) pemeriksaan RNA HCV, (3) hasil RNA HCV positif, (4) inisiasi terapi, dan (5) pencapaian sustained virologic response 12 minggu setelah terapi (SVR12). Analisis data dilakukan menggunakan SPSS 26. Variabel kategorikal disajikan dalam bentuk frekuensi dan persentase, sementara hasil disajikan sebagai jumlah dan proporsi pada setiap kaskade pengobatan.*

***Hasil:** Dari 317 pasien dengan hasil anti-HCV positif (55% pria, 45% wanita; median usia 56 tahun), 280 (88%) menjalani tes RNA HCV, dan 213 (76%) terkonfirmasi positif. Terapi dimulai pada 185 pasien (87%), 144 (78%) menyelesaikan pengobatan, dan 108 pasien (75%) mencapai SVR12.*

***Kesimpulan:** Studi ini mengungkapkan adanya kesenjangan yang signifikan pada beberapa tahap kaskade pengobatan HCV, terutama dalam tes RNA HCV, inisiasi terapi, dan tindak lanjut pascaterapi.*

***Kata Kunci:** Hepatitis C, Indonesia, Kaskade pengobatan*

INTRODUCTION

Hepatitis C virus (HCV) infection remains a major global health problem, contributing significantly to morbidity and mortality. It is estimated that approximately 55–85% of individuals infected with HCV will develop chronic infection, which can progress to liver fibrosis and ultimately cirrhosis. Among those with cirrhosis, approximately 1–3% may develop hepatocellular carcinoma (HCC).[1,2] According to the World Health Organization (WHO), in 2022, approximately 50 million people were living with chronic hepatitis C virus (HCV) infection worldwide, with an estimated 1 million new infections annually and around 242,000 deaths, mainly due to cirrhosis and HCC.[3]

In addition to liver complications, HCV is also associated with a variety of comorbidities, including depression, diabetes mellitus, and chronic kidney disease.[1,4] The introduction of direct-acting antivirals (DAAs) in 2011 marked a significant shift in HCV management, replacing interferon-based therapy with treatments offering cure rates exceeding 95%. These therapeutic advances prompted intensive global efforts to reduce the burden of HCV. In response, the WHO launched the Global Health Sector Strategy for Viral Hepatitis (2016–2021), which aims to eliminate hepatitis as a public health threat by 2030. To achieve this goal, the WHO set an ambitious target of diagnosing 90% of infected individuals and treating at least 80% of them.[1,5,6]

In Indonesia, anti-HCV prevalence is estimated at 1% in the general population and may reach up to 90% among injecting drug users.[2,7] It is estimated that approximately 2.5 million people are living with HCV in the country. In contrast to the national downward trend in hepatitis B infections, HCV prevalence appears to be stable or increasing without targeted interventions.[6] As part of its commitment to the WHO elimination goal, the Indonesian government initiated a free DAA program in seven provinces in 2017, which was subsequently expanded to additional provinces between 2018 and 2019.[8] By 2021, the national treatment program had reached 19 provinces and involved 41 general hospitals.[9]

Despite these important achievements, significant gaps persist in the hepatitis C cascade of care. Dr. Kariadi General Hospital, as a tertiary referral and teaching hospital, serves as one of the key centers for HCV management and implementation of the national treatment program. Evaluating the cascade of care in this setting is therefore important to identify real-world gaps and inform strategies to improve HCV elimination efforts. This study aimed to evaluate the cascade of care for HCV patients at Dr. Kariadi General Hospital, Semarang, Indonesia.

METHODS

Study Design and Population

This retrospective descriptive study was conducted at Dr. Kariadi General Hospital, a tertiary referral hospital in Semarang, Indonesia. This hospital serves as a referral center for hepatitis management in Central Java and the surrounding area. The study included all patients (aged ≥ 18 years) who tested positive for anti-HCV antibodies between January 1, 2019, and

November 30, 2024. Individuals with incomplete or missing essential baseline data were excluded from the analysis. No interventions were implemented, and patient management followed national guidelines as applied in routine clinical practice.

Data Collection

Patient data were extracted from the hospital's electronic medical record and laboratory information system. Variables collected included demographic characteristics (age and sex), screening data (anti-HCV antibody results), confirmatory testing (HCV RNA test results), treatment-related data (dates of initiation and termination of DAA treatment and DAA regimen used), and outcome data, including completion status and sustained virologic response (SVR12) at 12 weeks post-treatment. Patient comorbidities were also recorded.

Statistical Analysis

Descriptive statistics were used to analyze the data. Categorical variables were expressed as frequencies and percentages. The HCV cascade of care was categorized into five sequential stages: (1) Detection of anti-HCV antibodies; (2) Undergoing confirmatory HCV RNA testing; (3) HCV RNA positivity; (4) Initiation of antiviral therapy; and (5) Achieving SVR12 (sustained virologic response 12 weeks after completion of therapy).

Data were analyzed and presented as numbers and proportions for each stage. The proportion (%) of patients at each stage was calculated relative to the population of the previous stage to assess progression through the cascade of care. A descriptive comparison of baseline characteristics between patients who achieved SVR12 and those who did not was also performed. Inferential statistics were not performed due to the descriptive nature of the study and the small sample size in subgroup analyses. Patients with incomplete outcome data, particularly SVR12, were not excluded entirely but were included in the analysis where applicable. Outcome evaluation was performed based on available data, and missing data were reported descriptively without imputation. Data analysis was performed using SPSS Statistic version 26.

Ethical Considerations

This study was approved by the Health Research Ethics Committee of Dr. Kariadi Hospital, with protocol number 16627/EC/KEPK-RSDK/2025. Patient identities were kept confidential by anonymizing the data prior to analysis. Informed consent was not required due to the retrospective nature of this study and the use of deidentified data.

RESULTS

Patient Characteristics

Of the 346 patients with positive anti-HCV results, 29 patients were excluded due to incomplete baseline data. A total of 317 patients with positive anti-HCV antibody tests were enrolled in this study. The majority were male (n = 175, 55%), with a median age of 56 years. At diagnosis, 158 patients (49.8%) had liver cirrhosis, 16 patients (5%) had hepatitis B virus (HBV) coinfection, 6 patients (1.9%) had human immunodeficiency virus (HIV) coinfection, and 18 patients (5.7%) had hepatocellular carcinoma (HCC). Comorbidities included diabetes mellitus in 68 patients (21.5%) and regular hemodialysis in 65 patients (20.5%). **Table 1** summarizes the baseline clinical characteristics of the study population.

Table 1. Patients Characteristics

Characteristics	n	%
Age (median)	56 years	
Male	175	55.2
Female	142	44.8
Cirrhosis	158	49.8
HBV co-infection	16	5.0
HIV co-infection	6	1.9
Hepatocellular carcinoma	18	5.7
Regular hemodialysis	65	20.5
Diabetes Mellitus	68	21.5

HCV CASCADE OF CARE

Among 317 patients with confirmed anti-HCV positive results, 280 (88%) underwent confirmatory HCV RNA testing. Thus, 37 patients (12%) were lost to follow-up or did not undergo confirmatory testing due to unstable conditions and limited availability of HCV RNA testing. Of those tested, 213 (76%) were confirmed to have active viremia.

Of the 213 patients with detectable HCV RNA, 185 (87%) initiated direct-acting antiviral (DAA) treatment, while 28 (13%) did not initiate therapy. Of those who initiated treatment, 144 (78%) completed the full course. At the time of data collection, 6 patients (3%) were still on treatment, and 35 (19%) had discontinued treatment or were lost to follow-up before completing therapy.

Of the 144 patients who completed treatment, 108 (75%) achieved a sustained virologic response (SVR12) at 12 weeks post-treatment. Six patients (4%) did not achieve SVR12, while 30 patients (21%) had no SVR12 data due to incomplete follow-up or unavailable laboratory confirmation. Among patients with available SVR12 evaluation, the treatment efficacy rate was 94.7% (108/114).

Figure 1 illustrates the distribution of patients across each stage of the HCV cascade of care, demonstrating a stepwise decrease in patient numbers from diagnosis to SVR12 evaluation. A descriptive comparison of baseline characteristics between patients who achieved SVR12 and those who did not is presented in **Table 2**. Overall, the characteristics appeared broadly similar between groups. However, interpretation is limited by the small number of patients in the non-SVR12 group.

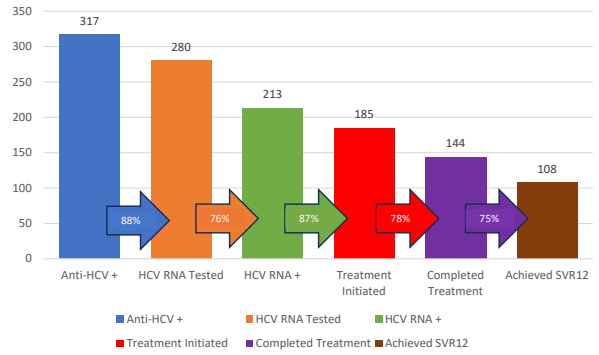

Figure 1. HCV Cascade of Care at Dr. Kariadi General Hospital

The figure illustrates the number of patients at each stage of care, including diagnosis, treatment initiation, treatment completion, and sustained virologic response at 12 weeks (SVR12) evaluation, demonstrating a stepwise decrease in patient numbers across the cascade

Table 2. Comparison of Baseline Characteristics Based on SVR 12 Outcome

Variables	SVR12 (n=108)	Non-SVR12 (n=6)
Age (years), median	56	55.5
Sex, n (%)		
Male	62 (57.4%)	5 (83.3%)
Female	46 (42.6%)	1 (16.7%)
Presence of comorbidities, n (%)	94 (87%)	6 (100%)
DAA regimen, n (%)		
Sofosbuvir-based	93 (86.1%)	2 (33.3%)
Other regimens	15 (13.9%)	4 (66.7%)

Data are presented as mean or frequency (percentage). No inferential statistical analysis was performed due to the small sample size in the non-SVR12 group

DAA Regimens

The majority of treated patients (77.8%) received the sofosbuvir–daclatasvir regimen, followed by grazoprevir–elbasvir (16.7%) and sofosbuvir–velpatasvir (3.5%). SVR12 outcomes according to treatment regimen are presented in **Table 3**. In a subgroup analysis, among patients undergoing hemodialysis, SVR12 was achieved in 22 of 33 patients (66.7%). Among patients with diabetes mellitus and liver cirrhosis, SVR12 was achieved in 26 of 29 patients (89.6%) and 65 of 80 patients (81.3%), respectively. These findings should be interpreted with caution due to the limited sample size in each subgroup.

DISCUSSION

This study highlights persistent gaps across multiple stages of the hepatitis C care cascade in a tertiary referral setting in Indonesia. Although a high proportion of patients with positive anti-HCV results proceeded to confirmatory HCV RNA testing and treatment initiation, attrition remained evident at each step. These findings are consistent with challenges reported globally in HCV care delivery.

At the early stages of the cascade, despite the availability of government-supported DAA therapy and HCV RNA testing, 12% of patients did not undergo confirmatory testing, and 13% of confirmed cases did not initiate treatment. While this study did not directly assess underlying causes, these gaps may reflect challenges commonly described in similar settings, such as limited access to diagnostic services, variations in clinical stability, and suboptimal patient awareness. Previous studies in low- and middle-income countries have also highlighted delayed care-seeking behavior, limited awareness of the asymptomatic nature of HCV infection, and knowledge gaps among healthcare providers as potential contributing factors.[7,10]

In terms of treatment outcomes, the proportion of patients achieving SVR12 among treatment completers (75%) was higher than some real-world reports from low- to middle-income countries but lower than the >90% efficacy reported in clinical trials and well-

Table 3. SVR12 Outcomes by Treatment Regimen

Treatment Regimen	Total (n)	SVR12 Achieved, n (%)	Non-SVR12, n (%)	Missing SVR12, n (%)
Sofosbuvir–daclatasvir	112	86 (76.8%)	1 (0.9%)	25 (22.3%)
Grazoprevir–elbasvir	24	15(62.5%)	4 (16.7%)	5 (20.8%)
Sofosbuvir–velpatasvir	5	4 (80.0%)	1 (20.0%)	0
Other regimens	3	3 (100%)	0	0
Total	144	108 (75.0%)	6 (4.2%)	30 (20.8%)

Data are presented as frequency (percentage). Percentages in the total row are calculated based on the total number of patients who completed treatment (n=144). No statistical comparison was performed due to the limited sample size in some treatment groups

resourced settings.[8,11,12] Importantly, when restricted to patients with available SVR12 evaluation, the treatment efficacy reached 94.7%, which is comparable to previously published data.[12] This discrepancy underscores the impact of incomplete follow-up on observed treatment outcomes in real-world settings.

Subgroup analyses suggested lower SVR12 rates among patients undergoing hemodialysis, as well as those with diabetes mellitus and cirrhosis; however, these findings should be interpreted cautiously due to small sample sizes and the descriptive nature of the analysis. Prior studies have demonstrated high SVR12 rates in these populations[13-15], suggesting that the lower rates observed in this study may be influenced by incomplete follow-up rather than reduced treatment efficacy.

Notably, a substantial proportion of patients (21%) who completed treatment did not have documented SVR12 results, indicating a substantial gap in post-treatment monitoring. Similar challenges have been reported in other settings, although at lower rates, including 8.4% in a Japanese cohort and 2.7% in a multicenter study in Poland.[16,17] This gap may reflect barriers such as loss to follow-up or limited access to confirmatory testing, although these factors were not directly evaluated in this study.

In addition, these gaps may be further influenced by programmatic challenges such as inconsistencies in DAA availability and the use of multi-drug regimens, which can affect treatment continuity. Patient adherence also plays an important role in treatment success. Previous real-world studies have shown that suboptimal adherence is associated with lower SVR12 rates, particularly in patients with early treatment discontinuation or prolonged interruptions.[18,19] Therefore, interruptions in therapy or follow-up may contribute to suboptimal outcomes in this setting.

Given these findings, improving the HCV care cascade requires strengthening coordination between healthcare providers and national programs, as well as enhancing systems for patient tracking and follow-up. Digital health tools and structured monitoring systems may help reduce loss to follow-up and improve continuity of care. In addition, patient education and adherence support are likely important components in optimizing treatment outcomes. Overall, these findings suggest that continued efforts to strengthen service delivery, supply chains, and patient follow-up systems are essential to achieving the WHO 2030 HCV elimination target.

This study provides real-world insights into HCV care delivery at a tertiary referral hospital in Indonesia. A key strength of this study is the comprehensive evaluation of the HCV care cascade using real-world clinical data over five years, including patients with diverse clinical characteristics. However, several limitations should be acknowledged. The retrospective single-center design may limit generalizability, and the absence of inferential statistical analysis precludes assessment of associations between variables. In addition, incomplete SVR12 data may introduce bias in estimating treatment outcomes. These findings emphasize the importance of strengthening programmatic implementation and follow-up systems to optimize the effectiveness of HCV elimination strategies in similar healthcare settings.

CONCLUSION

This study highlights persistent gaps across several stages of the hepatitis C virus (HCV) care cascade, particularly in confirmatory HCV RNA testing, treatment initiation, and post-treatment monitoring. Despite the availability of free HCV RNA testing and direct-acting antivirals (DAAs) through the national program, challenges such as drug stockouts, fragmented care pathways, and inconsistent combination regimen availability may contribute to the gaps observed and should be considered in efforts to strengthen HCV program implementation.

To advance progress toward HCV elimination, strengthening coordination between healthcare providers, government health agencies, and supporting stakeholders is essential. Furthermore, implementing an integrated digital system for patient tracking and follow-up, along with patient-centered strategies to improve adherence, may help optimize sustained virologic response and overall program outcomes in similar healthcare settings.

CONFLICT OF INTEREST

None

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AUTHORS CONTRIBUTIONS

Lily Chandrawati: Concept, design, acquisition of data, analysis, interpretation of data, drafting the manuscript, and final approval.

Cecilia Oktaria Permatadewi: Design, acquisition of data, analysis, interpretation of data, and final approval.

Hesti Triwahyu Hutami: Analysis, interpretation of data, drafting the manuscript, and final approval.

Didik Indiarso: Interpretation of data, revised the manuscript for important intellectual content, and final approval.

Hery Djagat Purnomo: Concept, design, interpretation of data, revised the manuscript for important intellectual content, and final approval.

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DATA AVAILABILITY

Not applicable

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