Journal of Advances in Medicine and Medical Research

Volume 36, Issue 6, Page 266-281, 2024; Article no.JAMMR.117621
ISSN: 2456-8899, NLM ID: 101711724
(Past name: British Journal of Medicine and Medical Research, Past ISSN: 2231-0614, NLM ID: 101570965)

Direct-Acting Antivirals' Safety Profile in Patients with Advanced Liver Cirrhosis with Hepatitis C: A Systematic Review and Meta-Analysis

Shahroz M. Khan [a], Farhana Nazmin [b], Rubela Ray [c], Rauann Hachem [d++], Briannah Wade [e++], Manal A. Bhinder [f], Muhammad B. Chaudhry [f], Marya Syed [g], Ayesha Khan [h], Eman Fatima [i] and Imdad Ullah [j*]

[a] KHSC College of Osteopathic Medicine, Wichita, USA.
[b] Bronx Care Health System, Bronx, USA.
[c] Bankura Sammilani Medical College, Bankura, India.
[d] Saint James School of Medicine, Illinois, USA.
[e] American University of Antigua, New York, USA.
[f] CMH Lahore Medical College and Institute of Dentistry, Lahore, Pakistan.
[g] Fatima Jinnah Medical University, Lahore, Pakistan.
[h] Karachi Medical and Dental College, Karachi, Pakistan.
[i] Akhtar Saeed Medical and Dental College, Lahore, Pakistan.
[j] Khyber Medical College, Peshawar, Pakistan.

Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

Article Information

DOI: https://doi.org/10.9734/jammr/2024/v36i65469

Open Peer Review History:
This journal follows the Advanced Open Peer Review policy. Identity of the Reviewers, Editor(s) and additional Reviewers, peer review comments, different versions of the manuscript, comments of the editors, etc are available here: https://www.sdiarticle5.com/review-history/117621

Systematic Review Article

Received: 02/04/2024
Accepted: 05/06/2024
Published: 07/06/2024

[++] Medical Student;
**Corresponding author;*

Cite as: *Khan, Shahroz M., Farhana Nazmin, Rubela Ray, Rauann Hachem, Briannah Wade, Manal A. Bhinder, Muhammad B. Chaudhry, Marya Syed, Ayesha Khan, Eman Fatima, and Imdad Ullah. 2024. "Direct-Acting Antivirals' Safety Profile in Patients With Advanced Liver Cirrhosis With Hepatitis C: A Systematic Review and Meta-Analysis". Journal of Advances in Medicine and Medical Research 36 (6):266-81. https://doi.org/10.9734/jammr/2024/v36i65469.*

ABSTRACT

Chronic hepatitis C with cirrhosis is treated with direct-acting antibiotics (DAAs). The aim of this study was to investigate the effect of direct-acting antibodies in the treatment of hepatitis C in cirrhosis. It also examines the proportion of drug-related problems, side effects, and mortality. The Cochrane Library and PubMed were thoroughly searched for the required literature. Fifteen articles were extracted for inclusion in this systematic review and meta-analysis. A total of 16 studies were thoroughly screened. The included studies provided a comprehensive picture of the effects of DAA therapy, spanning multiple study designs and sites Our analysis showed that good responses were observed with DAA regimens and that treatment discontinuation was low due to adverse events a stirring that. Few adverse events were reported, but all were mostly uncontrolled to prevent treatment discontinuation or death. In addition, meta-analytic studies on specific outcomes such as encephalopathy, ascites, hepatocellular carcinoma (HCC), adverse events, and death provided quantitative analysis about the safety of DAAs. Research also shows that DAAs have fewer side effects, deaths, and complications than other treatments.

Keywords: Hepatitis C; direct-acting antivirals (DAAs); liver cirrhosis; systematic review; meta-analysis; safety profile; adverse events; treatment efficacy; chronic liver disease; viral eradication.

1. INTRODUCTION

Hepatitis is the leading cause of cirrhosis and other chronic liver diseases (CLD). About 71 million people worldwide are infected with hepatitis C [1]. The prevalence in Eastern European countries is 2-3% [2-4]. Patients with advanced liver disease or fibrosis should be treated promptly [5]. Patients with decompensated cirrhosis (CTP classes B or C) do not have access to the same range of options [5,6]. The number of patients receiving treatment for chronic HCV infection has significantly increased after direct-acting antiviral (DAA) therapy [7]. Most patients who are seen in clinical settings in the near future will have recovered from HCV, and almost all of them achieve a sustained virologic response (SVR) [8]. After HCV cure, managing liver disease after it has progressed mainly focuses on reducing the residual risk of complications [9]. Because they can effectively remove the virus from the body, direct-acting antivirals (DAAs) are the recommended treatment for hepatitis C virus (HCV) infection, according to several studies. Even in cases of advanced cirrhosis, this treatment option is very effective, usually achieving viral clearance in a relatively short period of 12 to 24 weeks. Compared to earlier treatment plans, patients receiving DAA therapy frequently report significantly better clinical outcomes, fewer side effects, and shorter treatment times. Regardless of the severity of hepatic fibrosis, the advent of novel antiviral drugs with genotypic and pan-genotypic effects has improved treatment outcomes even more, with viral eradication occurring in more than 95% of cases [10-13].

In a management plan it shows that HCV should be eradicated by 2030 [14]. Patients with fibrosis or cirrhosis are given utmost importance while devising the treatment plan [15,16].

Rationale: The rationale behind the systematic review and meta-analysis of the safety profile of direct-acting antivirals (DAAs) in patients with advanced liver cirrhosis who have hepatitis C is the necessity to study the effect of these drugs.

Objectives: This study aimed to critically examine the safety profile of direct-acting antibiotics (DAAs) in individuals with hepatitis C and advanced liver disease Objectives include to investigate the frequency and severity of DAA treatment adverse events in this particular group of patients.

2. METHODOLOGY

Study Design: Study Design of this study is given in the table [Table 1].

Eligibility Criteria: Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) guidelines were followed in order to determine the eligibility requirements for studies. The following are the inclusion criteria: 1. Participants: Individuals with hepatitis C-related advanced liver cirrhosis (Child–Turcotte–Pugh [CTP] class B or C). 2. Intervention: Hepatitis C infection treatment with direct-acting antivirals

(DAAs). 3. Outcome: Research detailing the incidence and seriousness of adverse events, the rate at which treatment is stopped because of side effects, and any differences in safety outcomes depending on the DAA regimen, and the existence of comorbidities. 4. Study Design: Clinical Trials 5.

Language: English-language studies.

The exclusion criteria involve 1. Research with inadequate information. 2. Research that only reports efficacy results without disclosing safety information. 3. Reviews, editorials, letters, conference abstracts, case reports, and studies involving animals. 4. Research that has been published in languages besides English. 5. Overlapping datasets from the same research population or duplicate publications [Table 2].

Search Strategy: Different databases were searched as a part of the search approach used for this systematic review. PRISMA guidelines were adhered to during the article search process. There were various full-text articles, abstracts, and journal titles. The search strategy made use of the Boolean operators AND/OR. To further refine the article search, more filters were suggested [Table 3].

Selection Process: We looked for pertinent literature in peer-reviewed journals and publications. Based on the inclusion and exclusion criteria, we attempted to "include" or "exclude" relevant studies. (1) There was a problem with the population; (2) High bias reported in studies; (3) The research measured inaccurate results; or (4) The study's design was subpar for the purposes of our analysis. Occasionally, there was a compounding effect from several exclusionary factors.

Statistical Analysis: R studio was used to generate the forest plots. A P 0.1 threshold was used to determine whether heterogeneity—that is, actual variation in effect sizes—was present. The degree of variation between studies was measured using heterogeneity.

Heterogeneity and reporting bias: The Cochran Q statistic can be used to assess the likelihood that variations in study outcomes are caused by real differences in the population being studied rather than by chance.

Quality Assessment: We searched for digital and online resources to assess the possibility of bias in the studies selected for the meta-analysis. Five risk domains included in the primary studies were assessed [17-19].

Table 1. PICO Framework

Population (P)	People with advanced liver cirrhosis due to hepatitis C (Child–Turcotte–Pugh [CTP] class B or C).
Intervention (I)	direct-acting antivirals (DAAs).
Comparison (C)	alternative treatments for hepatitis C infection or placebo/no treatment.
Outcomes (O)	Primary safety, efficacy, complications, adverse effects, and mortality.

Table 2. Inclusion and Exclusion Criteria

Inclusion Criteria	Exclusion Criteria
Patients with advanced chronic Hepatitis C and cirrhosis	Research with inadequate information.
Hepatitis C infection treatment with direct-acting antivirals (DAAs).	Research that only report efficacy results without disclosing safety information.
Research detailing the incidence and seriousness of adverse events, the rate at which treatment is stopped because of side effects, and any differences in safety outcomes depending on the DAA regimen, and the existence of comorbidities.	Reviews, editorials, letters, conference abstracts, case reports, and studies involving animals.
All types of Clinical Trials.	Overlapping datasets from the same research population or duplicate publications.
English-language studies.	Research that has been published in languages besides English.

Table 3. Search Strategy for the SRMA

Database	Search String	Number of Hits
PubMed	("Hepatitis C" OR "HCV" OR "Chronic Hepatitis C") AND ("Antiviral Agents" OR "Direct-Acting Antivirals" OR "DAAs") AND ("Liver Cirrhosis" OR "Cirrhosis") AND ("Safety" OR "Adverse Effects" OR "Side Effects" OR "Toxicity") AND ("Advanced Liver Cirrhosis" OR "End-stage Liver Disease") AND ("Treatment Safety" OR "Drug Safety" OR "Adverse Drug Reactions")	1344
Cochrane Library	("Hepatitis C" OR "HCV" OR "Chronic Hepatitis C") AND ("Direct-Acting Antivirals" OR "DAAs") AND ("Liver Cirrhosis" OR "Cirrhosis" OR "End-stage Liver Disease") AND ("Safety" OR "Adverse Events" OR "Adverse Effects" OR "Side Effects" OR "Toxicity" OR "Complications")	112

3. RESULTS

Data Items: Studies were made part of this review through the following process illustrated in Fig. 1 It involves identifying, screening, and determining eligibility [20].

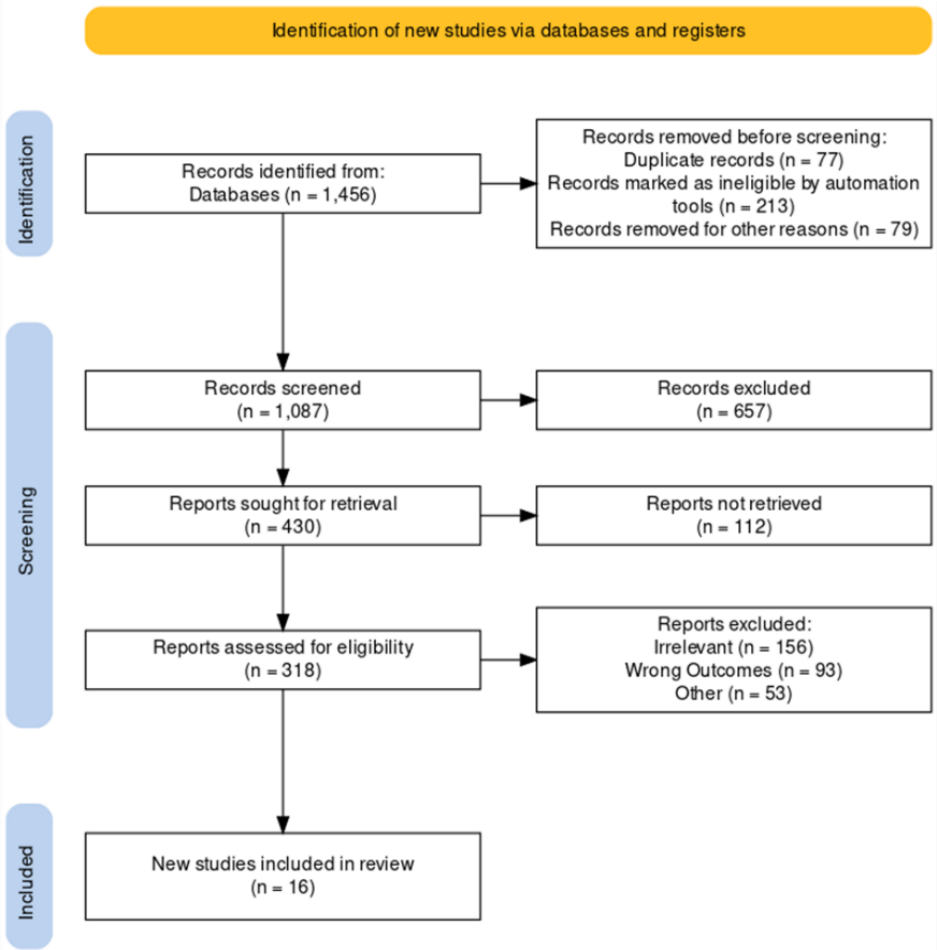

Fig. 1. PRISMA Flow Chart of the included studies

Data Characteristics: The detailed summary of all the included studies is given in Table 4.

Table 4. Summary Table of the included studies [21-36]

Sr No.	Study	Location	Study Design	Sample Size	Population	Intervention	Comparison	Drugs Used	Outcome Measures	Main Findings
1	Solomon et al 2022 [21]	Brazil, South Africa, Thailand, Uganda, and the USA	open-label, single-arm trial	400	Patients who have compensated cirrhosis, are at least 18 years old, exhibit active HCV infection (HCV RNA >1000 IU/mL), and are not receiving treatment for the virus	Pangenotypic direct-acting antivirals that do not require interferon or ribavirin	Placebo	sofosbuvir–velpatasvir	primary efficacy and safety	379 out of the 399 individuals who started therapy had an overall SVR (95·0%, 95% CI 92·4–96·7). Between week 28 and the start of treatment, 14 (4%) of the 397 participants reported serious adverse events; none of these were connected to the medication, resulted in treatment discontinuation, or resulted in death. Of the 399 participants, 15 (4%) had unscheduled visits; none of them had anything to do with therapy.
2	Abd Alla et al 2018 [22]	Egypt	Clinical Trial	75	Seventy-five post-HCV cirrhotic patients who were not on treatment were categorized	direct-acting antivirals	3 groups based on Child-Turcotte-Pugh (CTP) scoring system	sofosbuvir (SOF) (400 mg) plus ledipasvir (LDV) (90 mg)	primary efficacy and safety	Only 18.75% had HCV after treatment and only a smaler number of patients reported encephalopathy.

					using the Child-Turcotte-Pugh (CTP) scoring system.					
3	Quaranta et al 2021 [23]	Italy	Cohort Study	1350	Individuals diagnosed with HCV liver cirrhosis prior to treatment	direct acting antivirals	HIV/HCV monoinfected and coinfected	DAA	Efficacy, safety, and complications	After the virus was eradicated, a new decompensating event happened in 7 of 15 coinfected patients (46.6%) and in 61 of 133 (45.8%) monoinfected patients who had previously experienced decompensation. 53 of 1109 (4.8%) monoinfected patients and 4 of 93 (4.3%) coinfected patients had a first decompensating event on record (p = 0.83).
4	Dhiman et al 2019 [24]	India	Clinical Trial	48088	Individuals with Chronic Hepatitis C (CHC)	direct acting antivirals	different drug groups	daclatasvir, ledipasvir, ribavirin, sofosbuvir	primary efficacy and safety	According to protocol, 91.6% of patients achieved sustained virological response (SVR12) at 12 weeks post-treatment completion. In an intention-to-treat

										(ITT) analysis, 67.6% of patients had successful SVR12.
5	Heo et al 2023 [25]	Korea	Clinical Trial	53	At screening, participants' BMI was ≥18 kg/m2, they were ≥19 years old, and they had a chronic hepatitis C infection with detectable HCV RNA (≥ 15 IU/mL).	direct acting antivirals	different drug groups	sofosbuvir–velpatasvir and sofosbuvir–velpatasvir–voxilaprevir	primary efficacy and safety	All things considered, sofosbuvir-velpatasvir and sofosbuvir-velpatasvir-voxilaprevir exhibited good safety and tolerability.
6	Meyer et al 2022 [26]	Switzerland	Clinical Trial	301	Individuals with HCV who are between the ages of 18 and 69 who have compensated cirrhosis or without cirrhosis	direct acting antivirals	different drug groups and timings	ravidasvir plus sofosbuvir	primary efficacy and safety	There were no fatalities or treatment stops as a result of significant side effects from the study medications. SVR12 rates were unaffected by prior interferon therapy or HIV co-infection.
7	Poordad et al 2018 [27]	USA	Clinical Trial	22	Patients without cirrhosis or with compensated cirrhosis	direct acting antivirals		Ombitasvir/paritaprevir/ritonavir and dasabuvir with or without sofosbuvir	primary efficacy and safety	95.5% (21/22) of the patients in part 1 of the study and 85.7% (6/7) of the patients in part 2 of the study achieved SVR12. The majority of adverse events (AEs)

										had moderate to mild severity.
8	Sølund et al 2018 [28]	Denmark	a clinical randomized study	90	patients with chronic hepatitis C	direct-acting antivirals	different drug groups	either paritaprevir/ombitasvir/ritonavir/dasabuvir/ribaviriin (RBV) or ledipasvir/sofosbuvir (SOF)/RBV	primary efficacy and safety	Twelve weeks following treatment, the investigator found that seven (11%) patients still had adverse events that may have been connected to their DAA regimen.
9	Lawitz et al 2016 [29]	USA	Clinical Trial	40	HCV patients	direct acting antivirals	groups based on Child-Turcotte-Pugh (CTP) scoring system	Simeprevir, daclatasvir and sofosbuvir	primary efficacy and safety	In 26 out of 40 patients (65%), grade 1/2 adverse events (AEs) happened.
10	Younossi et al 2016 [30]	USA	Clinical Trial	267	HCV patients	direct acting antivirals	groups based on Child-Turcotte-Pugh (CTP) scoring system	sofosbuvir and velpatasvir with or without ribavirin	primary efficacy and safety	All PROs showed mean improvements of +5·3 to +16·0 points by the end of the treatment, with the exception of the work productivity metrics by WPAI:HCV.
11	Wei et al 2019 [31]	Asia-Pacific region and Russia	RCT	489	participants with HCV genotype 1, 4, or 6 infection	direct acting antivirals	placebo	elbasvir/grazoprevir	primary efficacy and safety	The immediate treatment group experienced higher rates of adverse events and drug-related adverse events (51.0% vs. 50.4% and 21.4% vs. 21.1%) than the

										deferred treatment group's placebo phase.
12	Degasperi et al 2018 [32]	Italy	Clinical Trial	452	HCV cirrhotic patients	direct acting antivirals		not specified	primary efficacy and safety	Even after accounting for an extra set of 348 noncirrhotic patients, the incidence of HCC remained unaffected by TLL1 genotypes (P = 0.58; 2% in AA vs. 1% in AT/TT patients).
13	Waked et al 2018 [33]	Egypt	Clinical Trial	60	hepatitis C	direct acting antivirals		ombitasvir, paritaprevir, and ritonavir plus ribavirin	primary efficacy and safety	12-week arm showed significant improvements. Analogous outcomes were documented in the 24-week segment.
14	Chayama et al 2018 [34]	Japan	Clinical Trial	129	hepatitis C virus infection	direct acting antivirals	compensated cirrhosis and without cirrhosis	glecaprevir/ pibrentasvir	primary efficacy and safety	SVR12 was attained by all 38 (100%) patients with compensated cirrhosis; no TESAEs were noted in this group, and one patient stopped therapy as a result of an AE.
15	Lawitz et al 2015 [35]	USA	Clinical Trial	82	Patients With Chronic Hepatitis C Virus, With and Without	direct acting antivirals	Hepatitis C	Ombitasvir, Paritaprevir, and Ritonavir	Adverse effects, mortality	SVR12 rates for cirrhosis patients who had never received treatment before and those

					Cirrhosis					who had were 97.9% and 96.2%, respectively. There were no discernible clinically significant variations in SVR12 rates between patients with and without cirrhosis.
16	Asselah et al 2018 [36]	France, USA	Clinical Trial	111	Chronic hepatitis C	direct acting antivirals	Placebo	sofosbuvir-velpatasvir	primary efficacy and safety, adverse effects, mortality	Patients receiving a placebo experienced a similar safety profile during their course of treatment. Headache, exhaustion, and nausea were the most frequent adverse events. An adverse event (AE) of gallbladder carcinoma occurred in one patient (1%), but it was not thought to be related to the treatment. Out of five documented severe adverse events, none were linked to the experimental medication.

Meta-Analysis:

(i) Hepatic Encephalopathy (Fig. 2):

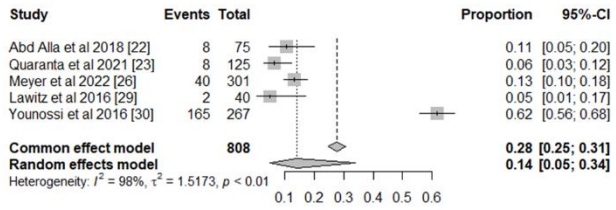

Fig. 2. Forest Plot for Hepatic Encephalopathy [22] [23] [26] [29] [30]

(ii) Ascites (Fig. 3):

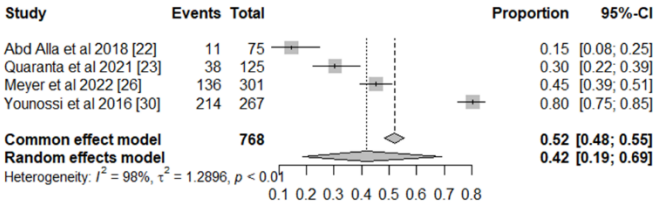

Fig. 3. Forest Plot for Ascites [22] [23] [26] [30]

(iii) Hepatocellular Carcinoma (HCC) (Fig. 4):

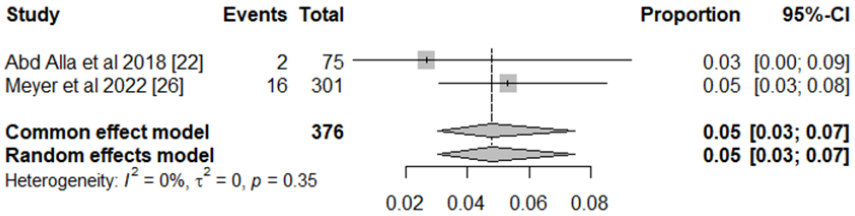

Fig. 4. Forest Plot for Hepatocellular Carcinoma [22] [26]

(iv) Adverse Events (Fig. 5):

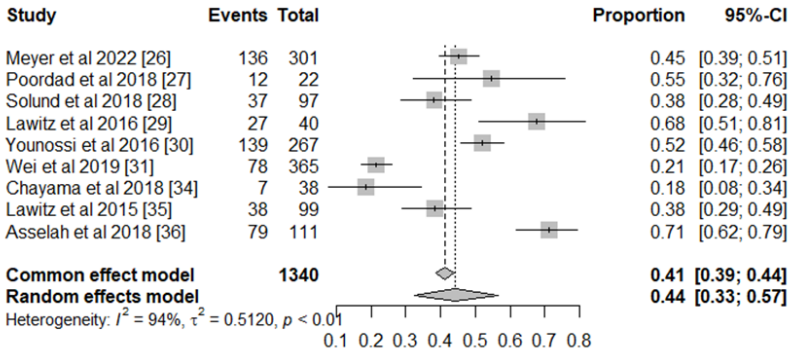

Fig. 5. Forest Plot for Adverse Events [26] [27] [28] [29] [30] [31] [34] [35] [36]

(v) Deaths (Fig. 6):

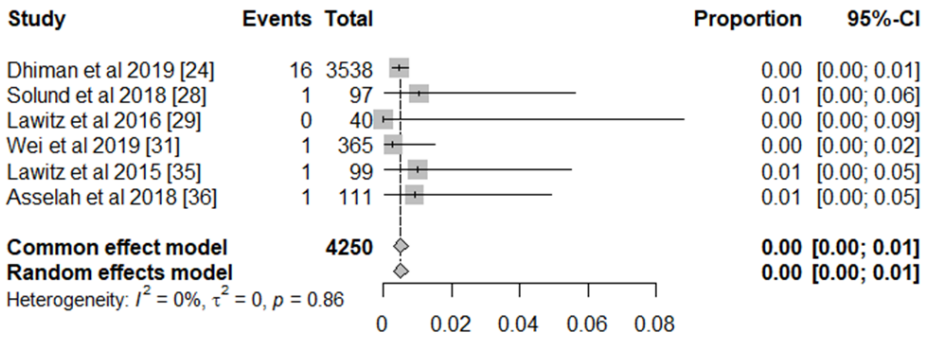

Fig. 6. Forest Plot for Hepatocellular Carcinoma [24] [28] [29] [31] [35] [36]

Risk of Bias Assessment: The researchers evaluated and displayed the bias risk in the 18 chosen studies using a "traffic lights" plot, which they created using the Cochrane Risk-of-Bias tool (Fig. 7).

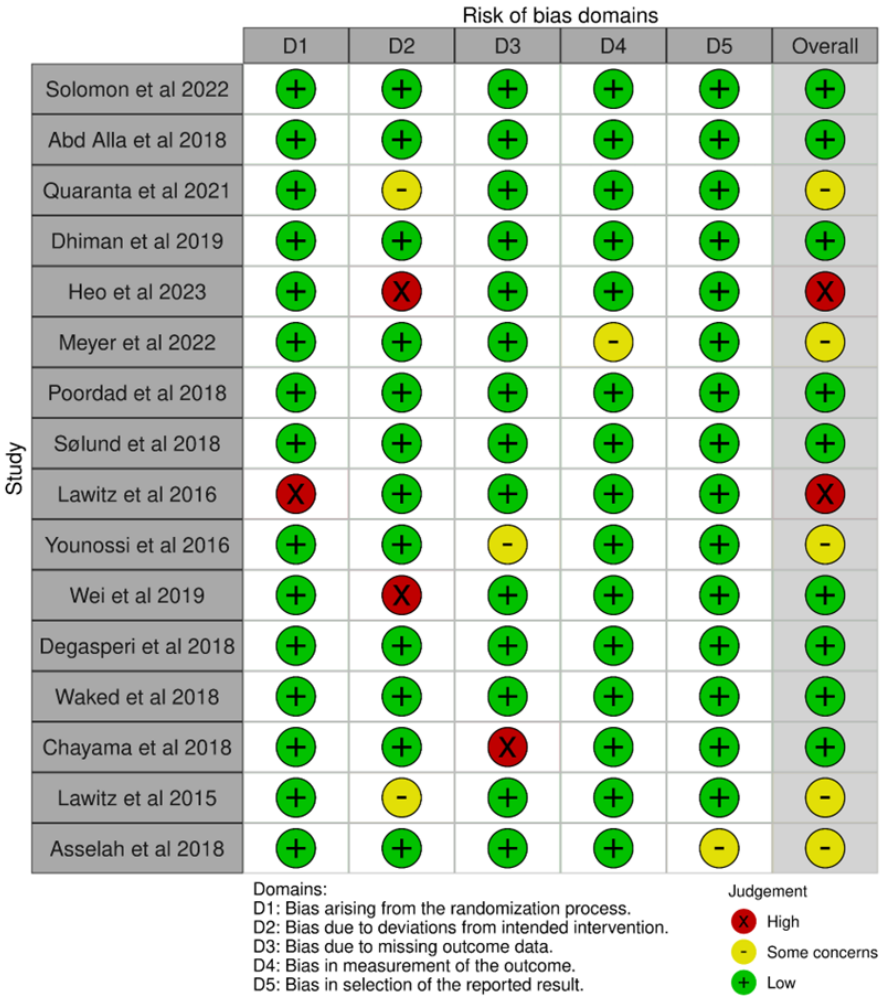

Fig. 7. Traffic Light Plot of the Included Studies

4. DISCUSSION

The included sixteen studies showed that DAAs have a safety profile and efficacy in Hepatitis C. When combined with creative case-finding techniques, this tactic may be essential to the global HCV eradication effort [21]. Most cirrhosis patients showed improvement in liver function after HCV eradication; however, in patients who were coinfected or monoinfected, viral eradication did not always result in liver disease recovery [23]. In this diverse adult patient population with chronic HCV infection, ravidasvir plus sofosbuvir proved to be an effective and well-tolerated treatment in the first phase. When combined with sofosbuvir, ravidasvir may offer a further low-cost, easy-to-use, and effective public health tool that could be widely used to end HCV as a cause of illness and death [26]. The findings offer patients who have historically had few treatment options a promising outcome [27]. AEs that may have been caused by the DAA regimen did not differ in patients with CHC; however, a considerable proportion of patients continued to experience AEs that may have been caused by the DAA regimen even after treatment. This finding may be significant for clinicians when it comes to patient information regarding adverse events (AEs) that may be connected to DAA treatment [28]. After receiving simeprevir, daclatasvir, and sofosbuvir for 12 weeks, all patients with portal hypertension or decompensated liver disease achieved SVR12 [29]. For those without prior medical experience, a 12-week course of elbasvir/grazoprevir is an efficient and well-tolerated treatment option for genotype 1 infection in individuals from Russia and the Asia-Pacific region [31]. Regardless of treatment duration, combination therapy with ombitasvir/paritaprevir/ritonavir and RBV improved injury and liver function [33].

Burden et al. Genotype 3 has provided important information regarding the relative efficacy of direct-acting antiviral agents (DAAs). The most effective treatment of choice for patients with HCV genotype 3 infection was chemotherapy with velpatasvir and sofosbuvir. These findings highlight the need for individualized therapies to maximize outcomes for patients infected with HCV genotype 3, particularly with regimens including ribavirin, sofosbuvir, and velpatasvir [37]. The findings of Villani et al. suggested that patients with DAAs may have some changes in their lipid profile that persist after completion of treatment. This finding underscores the importance of ongoing lipid monitoring in patients taking these medications, as well as the potential for consideration of interventions to address abnormal lipids and reduce associated risks [38].

Systematic reviews and meta-analyses have some limitations. First, there are not many studies looking at the effects of direct-acting antiviral drugs in hepatitis C patients with ulcerative colitis. Proportion analysis A meta-analysis was necessary because there was no comparison of placebo-controlled trials. The heterogeneity of the meta-analysis reflects bias in the included studies. Finally, these systematic reviews and meta-analyses are limited by the high risk of bias in some studies.

5. CONCLUSION

Hepatitis C is a viral infection that primarily affects the liver and can lead to both acute and chronic disease. It is caused by the Hepatitis C virus (HCV), which is transmitted primarily through direct contact with infected body fluids, typically through intravenous drug use, improperly sterilized medical equipment, and blood transfusions. Unlike Hepatitis A and B, there is no vaccine for Hepatitis C, making prevention focused largely on reducing the risk of exposure to the virus. This Systematic review and meta-analysis concluded that Patients with Hepatitis C with cirrhosis who were treated using DAA were found to be safe and effective; the complications, mortality, and adverse effects of DAA were less reported in patients who use DAA clearly show that DAAs can be prescribed to treat H C with cirrhosis without developing adverse complications towards the body.

CONSENT AND ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Blach S, Zeuzem S, Manns MP, et al.: Global prevalence and genotype distribution of hepatitis C virus infection in 2015: a modelling study. the Lancet Gastroenterology & Hepatology. 2017;2:161–76. DOI:10.1016/s2468-1253(16)30181-9
2. Razavi H, Scott SR, Zeuzem S, et al. Hepatitis C virus prevalence and level of

intervention required to achieve the WHO targets for elimination in the European Union by 2030: a modelling study. the Lancet Gastroenterology & Hepatology. 2017;2:325–36.
DOI:10.1016/s2468-1253(17)30045-6.

3. Isakov V, Цыркунов BM, Nikityuk DB: Is elimination of hepatitis C virus realistic by 2030: Eastern Europe. Liver International. 2021;41:50–5.
DOI:10.1111/liv.14836.
4. Petruzziello A, Marigliano S, Loquercio G, Cacciapuoti C: Hepatitis C virus (HCV) genotypes distribution: an epidemiological up-date in Europe. Infectious Agents and Cancer. 2016;11.
DOI:10.1186/s13027-016-0099-0.
5. Liver EA for SO: Corrigendum to 'EASL recommendations on treatment of hepatitis C: Final update of the series' [J Hepatol 73 (2020) 1170–1218]. Journal of Hepatology. 2023;78:452.
DOI:10.1016/j.jhep.2022.10.006
6. Recommendations for testing, managing, and treating hepatitis C | HCV Guidance.
Available:http://www.hcvguidelines.org/.
7. Programmes GHH and Sti: Global progress report on HIV, viral hepatitis and sexually transmitted infections, 2021.
Available:https://www.who.int/publications/i/item/9789240027077.
8. Spearman CW, Dusheiko G, Hellard M, Sonderup M: Hepatitis C. Lancet. 2019;394:1451–66.
DOI:10.1016/s0140-6736(19)32320-7.
9. Ioannou GN, Green PK, Berry K. HCV eradication induced by direct-acting antiviral agents reduces the risk of hepatocellular carcinoma. Journal of Hepatology. 2018;68:25–32.
DOI:10.1016/j.jhep.2017.08.030.
10. Mangia A, Milligan S, Khalili M, et al. Global real-world evidence of sofosbuvir/velpatasvir as simple, effective HCV treatment: Analysis of 5552 patients from 12 cohorts. Liver International. 2020;40:1841–52.
DOI:10.1111/liv.14537.
11. Lawitz E, Flisiak R, Abunimeh M, et al. Efficacy and safety of glecaprevir/pibrentasvir in renally impaired patients with chronic HCV infection. Liver International. 2019;40:1032–41.
DOI:10.1111/liv.14320.
12. Scotto R, Buonomo AR, Moriello NS, et al. Real-World Efficacy and Safety of Pangenotypic Direct-Acting antivirals against Hepatitis C virus infection. Reviews on Recent Clinical Trials. 2019;14:173–82.
DOI:10.2174/1574887114666190306154650.
13. Goel A, Chen Q, Chhatwal J, Aggarwal R: Cost-effectiveness of generic pan-genotypic sofosbuvir/velpatasvir versus genotype-dependent direct-acting antivirals for hepatitis C treatment. Journal of Gastroenterology and Hepatology. 2018;33:2029–36.
DOI:10.1111/jgh.14301.
14. Razavi H, Scott SR, Zeuzem S, et al. Hepatitis C virus prevalence and level of intervention required to achieve the WHO targets for elimination in the European Union by 2030: a modelling study. the Lancet Gastroenterology & Hepatology. 2017;2:325–36.
DOI:10.1016/s2468-1253(17)30045-6.
15. Foster GR, Irving WL, Cheung M, et al. Impact of direct acting antiviral therapy in patients with chronic hepatitis C and decompensated cirrhosis. Journal of Hepatology. 2016;64:1224–31.
DOI:10.1016/j.jhep.2016.01.029.
16. Pawlotsky J, Aghemo A, Dusheiko G, Forns X, Puoti M, Sarrazin C: EASL Recommendations on Treatment of Hepatitis C 2018. Journal of Hepatology. 2018;69:461–511.
DOI:10.1016/j.jhep.2018.03.026.
17. Higgins JPT. et al. (2011) The Cochrane Collaboration's tool for assessing risk of bias in randomised trials, BMJ. 2011;343(oct18 2):5928.
Available:https://doi.org/10.1136/bmj.d5928.
18. Schulz, et al . The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. BMJ. 2011;343(oct18 2):d5928.
Available:https://doi.org/10.1136/bmj.d5928.
19. Review Manager (RevMan) [Computer program]. Version 5.4. The Cochrane Collaboration, 2020.
Available:https://training.cochrane.org/system/files/uploads/protected_file/RevMan5.4_user_guide.pdf.
20. Haddaway N, Page MJ, Pritchard CC, McGuinness LA: PRISMA2020: An R package and Shiny app for producing PRISMA 2020-compliant flow diagrams, with interactivity for optimised digital

transparency and Open Synthesis. Campbell Systematic Reviews. 2022;18. DOI:10.1002/cl2.1230.

21. Solomon SS, Wagner-Cardoso S, Smeaton L, et al.: A minimal monitoring approach for the treatment of hepatitis C virus infection (ACTG A5360 [MINMON]): a phase 4, open-label, single-arm trial. the Lancet Gastroenterology & Hepatology. 2022;7:307–17. DOI:10.1016/s2468-1253(21)00397-6.
22. Alla MDAA, Awady MKE, Dawood RM, Elhawary M, Al-Azhari SS, Galal A-SGM: Hepatitis C virus serologic relapse after treatment with direct-acting antivirals is dependent on viral RNA levels in peripheral blood mononuclear cells and the grade of liver cirrhosis. Archives of Virology. 2018;163:2765–74. DOI:10.1007/s00705-018-3922-7.
23. Quaranta MG, Ferrigno L, Tata X, et al.: Liver function following hepatitis C virus eradication by direct acting antivirals in patients with liver cirrhosis: data from the PITER cohort. BMC Infectious Diseases. 2021;21. DOI:10.1186/s12879-021-06053-3.
24. Dhiman RK, Grover GS, Premkumar M, et al.: Decentralized care with generic direct-acting antivirals in the management of chronic hepatitis C in a public health care setting. Journal of Hepatology. 2019;71:1076–85. DOI:10.1016/j.jhep.2019.07.006.
25. Heo J, Kim YJ, Lee SW, et al.: Efficacy and safety of sofosbuvir–velpatasvir and sofosbuvir–velpatasvir–voxilaprevir for hepatitis C in Korea: a Phase 3b study. The Korean Journal of Internal Medicine/Korean Journal of Internal Medicine. 2023, 38:504–13. DOI:10.3904/kjim.2022.252
26. Andrieux-Meyer I, Tan S, Thanprasertsuk S, et al.: Efficacy and safety of ravidasvir plus sofosbuvir in patients with chronic hepatitis C infection without cirrhosis or with compensated cirrhosis (STORM-C-1): interim analysis of a two-stage, open-label, multicentre, single arm, phase 2/3 trial. the Lancet Gastroenterology & Hepatology. 2021;6:448–58. DOI:10.1016/s2468-1253(21)00031-5.
27. Poordad F, Bennett M, Sepe T, et al.: Ombitasvir/paritaprevir/ritonavir and dasabuvir with or without sofosbuvir for patients with hepatitis C virus genotype 1 infection who failed a prior course of direct-acting antiviral therapy. Journal of Medical Virology. 2019; 91:1307–12. DOI:10.1002/jmv.25448.
28. Sølund C, Andersen ES, Mössner BK, et al.: Outcome and adverse events in patients with chronic hepatitis C treated with direct-acting antivirals: a clinical randomized study. European Journal of Gastroenterology & Hepatology. 2018;30:1177–86. DOI:10.1097/meg.0000000000001192.
29. Lawitz E, Poordad F, Gutiérrez J, et al.: Simeprevir, daclatasvir, and sofosbuvir for hepatitis C virus-infected patients: Long-term follow-up results from the open-label, Phase II IMPACT study. Health Science Reports. 2020;3. DOI:10.1002/hsr2.145.
30. Younossi ZM, Stepanova M, Charlton M, Curry M, O'Leary JG, Brown RS, Hunt S: Patient-reported outcomes with sofosbuvir and velpatasvir with or without ribavirin for hepatitis C virus-related decompensated cirrhosis: an exploratory analysis from the randomised, open-label ASTRAL-4 phase 3 trial. the Lancet Gastroenterology & Hepatology. 2016;1:122–32. DOI:10.1016/s2468-1253(16)30009-7.
31. Wei L, Jia JD, Wang FS, et al.: Efficacy and safety of elbasvir/grazoprevir in participants with hepatitis C virus genotype 1, 4, or 6 infection from the Asia–Pacific region and Russia: Final results from the randomized C-CORAL study. Journal of Gastroenterology and Hepatology. 2018;34:12–21. DOI:10.1111/jgh.14509.
32. Degasperi E, Galmozzi E, Facchetti F, et al.: TLL1 variants do not predict hepatocellular carcinoma development in HCV cirrhotic patients treated with direct-acting antivirals. Journal of Viral Hepatitis. 2019;26:1233–6. DOI:10.1111/jvh.13155.
33. Waked I, Esmat G, Fouad R, et al. Change in the hepatic profile of hepatitis C virus genotype 4–infected patients with compensated cirrhosis receiving ombitasvir, paritaprevir, and ritonavir plus ribavirin: A subanalysis of the AGATE-II study. Journal of Medical Virology. 2018;90:1739–44. DOI:10.1002/jmv.25243.
34. Chayama K, Suzuki F, Karino Y, et al. Efficacy and safety of glecaprevir/

pibrentasvir in Japanese patients with chronic genotype 1 hepatitis C virus infection with and without cirrhosis. Journal of Gastroenterology. 2017;53:557–65.
DOI:10.1007/s00535-017-1391-5.

35. Lawitz E, Makara M, Akarca US, et al.: Efficacy and safety of ombitasvir, paritaprevir, and ritonavir in an Open-Label study of patients with genotype 1B chronic hepatitis C virus infection with and without cirrhosis. Gastroenterology. 2015;149:971-980.e1.
DOI:10.1053/j.gastro.2015.07.001.

36. Asselah T, Shafran SD, Bourgeois S, et al.: Deferred treatment with a fixed-dose combination of sofosbuvir-velpatasvir for chronic hepatitis C virus genotype 1, 2, 4 and 6 infection. Journal of Viral Hepatitis. 2019;26:1229–32. DOI:10.1111/jvh.13159.

37. Berden F a. C, Aaldering BRRZ, Groenewoud H, IntHout J, Kievit W, Drenth JPH: Identification of the Best Direct-Acting Antiviral Regimen for patients with Hepatitis C Virus genotype 3 infection: a systematic review and network meta-analysis. Clinical Gastroenterology and Hepatology. 2017;15:349–59.
DOI:10.1016/j.cgh.2016.10.034.

38. Villani R, Di Cosimo F, Romano AD, Sangineto M, Serviddio G: Serum lipid profile in HCV patients treated with direct-acting antivirals: a systematic review and meta-analysis. Scientific Reports. 2021;11.
DOI:10.1038/s41598-021-93251-3.

Peer-review history:
The peer review history for this paper can be accessed here:
https://www.sdiarticle5.com/review-history/117621