RESEARCH ARTICLE

Usefulness of Sofosbuvir and Daclatasvir combination in the treatment of HCV infection in childhood cancer patients: Experience from a tertiary care hospital

Uzma Imam[1], Arit Parkash[2], Nandlal Daryani[3], Fahad Mumtaz[4]

Abstract

Objective: To determine the usefulness of Sofosbuvir-Daclatasvir combination in the treatment of hepatitis c virus infection in paediatric cancer.

Method: The retrospective study was conducted at the Oncology Department of the National Institute of Child Health, Karachi, and comprised medical charts of patients who received sofosbuvir and daclatasvir from January 2018 to January 2022. Efficacy was documented by clearance of hepatitis C virus ribonucleic acid as rapid viral response, early viral response and sustained viral response at weeks 4, 12 and 24, respectively. Drug efficacy was determined by monitoring and recording adverse effects. Chemotherapy protocol for the treatment of patients concomitantly receiving direct acting antivirals was modified while looking at drug-drug interactions. The total duration of direct acting antiviral therapy was 12 weeks. Data was analysed using SPSS 24.

Results: Of the 804 patients with different malignancies, 132(16.4%) were found positive for hepatitis C virus. Of them, 28(21.21%) patients were started on direct acting antivirals; 17(60.71%) boys and 11(39.28%) girls. The overall mean age was 9.93±6.12 years. The diagnosis was pre-B acute lymphoblastic leukaemia in 18(64.28%) cases, 16(57.14%) were on maintenance chemotherapy, and 18(64.28%) had genotype 1. Pre- and post-treatment mean alanine transaminase levels were 328.00±324.00IU and 36.00±29.00IU, respectively (p=0.003). Pre- and post-treatment mean serum bilirubin levels were 3.13±3.95mg/dl and 0.61±0.21mg/dl (p=0.022). Rapid viral response was achieved in 26(92.85%) children, while early viral response and sustained viral response were achieved in all 28(100%) patients. Minor side effects were noted in 4(14.28%) patients and chemotherapy was continued in all 28(100%) cases as per the designed protocol.

Conclusion: The sofosbuvir-daclatasvir combination was found to be effective in hepatitis C virus treatment in paediatric cancer patients.

Keywords: Childhood cancer, HCV infection, Direct acting antiviral agents. (JPMA 73: 2183; 2023)

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Introduction

Chronic hepatitis C virus (HCV) infection in paediatric patients is mostly asymptomatic, but in cases of co-morbidities like malignancies, it becomes challenging because of rapid course of progression to liver fibrosis. There is a significant need of transfusion of blood products in cancer patients either due to disease consequences or due to myelosuppression secondary to chemotherapeutic agents.[1,2] There can be complications associated with such transfusion, especially the transmission of viruses, including hepatitis B, hepatitis C and human immunodeficiency virus (HIV), if appropriate screening protocols are not followed. While in high-income countries (HICs), there is decreased incidence of infection transmission with the utilisation of proper screening procedures, the situation is alarming in low- and middle-income countries (LMICs). The prevalence rates for HCV infection in cancer patients ranges from 1.50% to 32%.[3,4] As severe adverse effects are expected with the recommended interferon-ribavirin treatment, this combination is not to be given simultaneously with chemotherapy. Direct acting antivirals (DAAs) were introduced in 2013 and after the emergence of new generations of drugs, the eradication rate of HCV infection has been reported between 90% and 95% with very few side effects.[5,6] DAAs in combination have now been recommended in children aged <3 years for chronic HCV infection for a duration of 3 months, and also have been reported safe in paediatric population in various international and local studies.[7-11] A study about the concomitant use of DAAs in adult patients on cancer chemotherapy reported 95% eradication of HCV infection and no significantly increased side-effects except some drug-drug interactions.[12] The concomitant use of these drugs with chemotherapy in children, however, has not been studied. Keeping in view the severity of HCV infection in cancer patients, the current study was planned to determine the efficacy of sofosbuvir-daclatasvir

[1,3,4]Department of Paediatric Oncology, National Institute of Child Health, Karachi, Pakistan; [2]Department of Paediatric Gastroenterology, National Institute of Child Health, Karachi, Pakistan.

Correspondence: Uzma Imam. e-mail: druzmaimam@yahoo.com

ORCID ID. 0000-0001-6883-1407

combination in the treatment of HCV infection in paediatric cancer patients.

Patients and methods

The retrospective study was conducted at the Oncology Department of the National Institute of Child Health, Karachi, and comprised medical charts of patients who received sofosbuvir (SOF) and daclatasvir (DAC) from January 2018 to January 2022. After approval from the institutional ethics review board, data was retrieved from medical records. Clinical and laboratory data of children with different malignancies who received sofosbuvir-daclatasvir combination was recorded in a proforma. The potential drug-drug interactions of DAAs and chemotherapeutic agents were checked online (www.hep-druginteractions.org).[13] SOF was safe with chemotherapeutic agents, while DAC had theoretical interaction with a few agents, including methotrexate with increase chances of haematological toxicities. Dexamethasone, on the other hand, enhances enzyme CYP3A4 metabolism, decreasing the DAC concentration. Serum concentration of dactinomycin was reported to be increased when combined with DAC. While looking at these interactions, chemotherapy protocols of patients concomitantly receiving DAAs were modified (Annexure) in line with studies where rapid viral response (RVR) was one of the most important tools to predict DAA treatment outcomes.[11,14,15]

Annexure:

Dose modification of chemotherapeutic agents in use concomitantly with DAA therapy (sofosbuvir & daclatasvir)

Patient category: ALL (Pre B ALL, T ALL), B-LL (Lymphoblastic Lymphoma)

Phase of chemotherapy: Maintenance phase

Age: 4 years and above

First 2 weeks: no chemotherapy, Monitor CBC, LFTS, Cr, PT, INR

WK 2-4: Monitor CBC, ANC, Cr, LFTs

PO 6- MP at 25%-50% of total dose

WK 4: PCR Results, Monitor CBC, ANC, LFTs, Cr, PT, INR

PCR Negative patients: Vincristine + Oral *Prednisolone (5 days), PO 6-Mercaptopurine, Methotrexate@ 50% dose [*Dexamethasone replaced]

PCR Positive patients:

– With normal labs (CBC, ANC, LFTs, and Cr): Vincristine + Oral *Prednisolone (5 days), Continue PO 6- Mercaptopurine @ 50% dose. No Methotrexate [*Dexamethasone replaced]

– With abnormal labs: Hold chemotherapy for 1 week & repeat labs

WK 5 - 12:

PCR Negative patients: Monitor CBC, ANC, LFTs, Creatinine. Adjust chemotherapy drugs with ANC& LFTs [replace dexamethasone with prednisolone]. Repeat PCR after 12 weeks OF DAA

PCR Positive patients:

- With normal labs: 50% dose of VCR+ Prednisolone, PO 6MP/MTX. Monitor CBC, ANC, LFTs. Repeat PCR AFTER 12 WEEKS OF DAA
- With Abnormal labs: No chemo, Monitor CBC, ANC, LFTs, Cr, PT, INR, albumin. .Repeat PCR AFTER 12 WEEKS OF DAA

After WK 12:

PCR Negative Patients will receive chemotherapy as per standard of care treatment protocol

PCR Positive patients:

- With normal labs: 50% dose of VCR + Prednisolone, 6MP. No MTX. Discuss DAA replacement option with hepatologist
- With Abnormal labs: No chemo, discuss DAA replacement option with hepatologist

Patient category: Pilocytic Astrocytoma (ICT)

Phase of chemotherapy: Continuation phase

Age: 4 years and above

First 2 weeks: No Chemotherapy, Monitor CBC, LFTS, Cr, PT, INR

WK 2-4: Monitor CBC, ANC, Cr, LFTs

Vinblastine @50% dose

WK 4: PCR Results, Monitor CBC, ANC, LFTs, Cr, PT, INR

PCR Negative patients: Vinblastine @ 100% dose

PCR Positive patients:

- With normal labs (CBC, ANC, LFTs, and Cr): Vinblastine @75% dose
- With abnormal labs: Hold chemotherapy for 1 week & repeat labs

WK 5 - 12:

PCR Negative patients: Monitor CBC, ANC, LFTs, Cr. Vinblastine @ 100% dose, Repeat PCR AFTER 12 WEEKS OF DAA

PCR Positive patients:

- With normal labs: Vinblastine @75% dose. Repeat PCR AFTER 12 WEEKS OF DAA
- With Abnormal labs: No chemo, Monitor CBC, ANC, LFTs, Cr, PT,INR, albumin Repeat PCR AFTER 12 WEEKS OF DAA

After WK 12:

PCR Negative Patients will receive chemotherapy as per standard of care treatment protocol

PCR Positive patients:

-With normal labs: Vinblastine @ 75% doses, discuss DAA replacement option with hepatologist

-With Abnormal labs: No chemo, discuss DAA replacement option with hepatologist

Patient category: Wilm's Tumor (WT)

Phase of chemotherapy: Continuation phase

Age: 4 years and above

First 2 weeks: NO CHEMOTHERAPY, Monitor CBC, LFTS, Cr, PT, INR

WK 2-4: Monitor CBC, ANC, Cr, LFTs

Vincristine @50% dose

WK 4: PCR Results, Monitor CBC, ANC, LFTs, Cr, PT, INR

PCR Negative patients: Vincristine @ 100% dose, Doxorubicin @ 50% dose, No Dactinomycin

PCR Positive patients:

- With normal labs (CBC, ANC, LFTs, and Cr): Vincristine @75% dose, Doxorubicin @25% dose, No Dactinomycin
- With abnormal labs: Hold chemotherapy for 1 week & repeat labs

WK 5 - 12:

PCR Negative patients: with normal CBC, ANC, LFTs, Cr. Chemotherapy as per standard of care treatment protocol. Repeat PCR AFTER 12 WEEKS OF DAA

PCR Positive patients:

- **With normal labs:** Vincristine @75% dose, Doxorubicin @25% dose, No Dactinomycin. Repeat PCR AFTER 12 WEEKS OF DAA
- **With Abnormal labs:** No chemo, Monitor CBC, ANC, LFTs, Cr, PT,INR, albumin. Repeat PCR AFTER 12 WEEKS OF DAA

After WK 12:

PCR Negative Patients will receive chemotherapy as per standard of care treatment protocol

PCR Positive patients:

- **With normal labs:** Vincristine @ 75% doses, Doxorubicin @50% dose. Discuss DAA replacement option with hepatologist
- **With Abnormal labs:** No chemo, discuss DAA replacement option with hepatologist

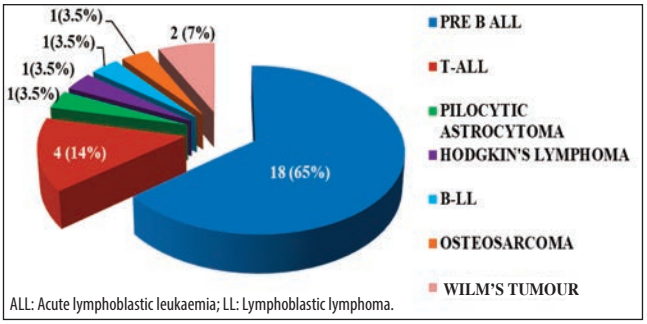
Data analysed related to paediatric cancer patients of either gender aged 3-18 years who were in remission and having baseline HCV polymerase chain reaction (PCR) data available. Data of patients with relapse of primary disease, patients who were not in remission and whose records were incomplete was excluded. Also excluded was data of patients who had concomitant hepatitis B virus (HBV) infection.

Safety of DAA combination was determined by recording adverse effects, like symptoms, signs and laboratory derangements, while efficacy was documented by clearance of HCV ribonucleic acid (RNA) in terms of rapid viral response (RVR) at 4 weeks after initiation of treatment, early viral response (EVR) or end of treatment response (ETR) at 12 weeks after initiation of treatment, and sustained viral response (SVR) at 12 weeks after completion of treatment. History, examination and baseline investigations, including complete blood count (CBC), liver functions tests (LFTs), serum creatinine, quantitative HCV PCR and HCV genotypes, were recorded. The subjects represented a special immunocompromised paediatric population being treated for their underlying malignancy for whom there was no standard of care related to DAA therapy. As such, they were evaluated with quantitative HCV PCR and genotype assessment. Besides, the facility of conducing these tests was available at the study site, and these were done free of cost to the patients. Dose of once daily 200mg and 400mg SOF was prescribed to patients aged ≤5–11 years and >11 years, respectively. Once daily dose of DAC 30mg and 60mg was given to patients aged ≤5–11 years and >11 years, respectively. Laboratory investigations were recorded at week 1 and 2, followed by 2 weekly assessments till completion of 12 weeks of DAA therapy. After initiation of DAAs, quantitative HCV PCR analysis was performed at weeks 4, 12 and 24. As was the case in previous paediatric studies,[11,16,17] patients in the current study were given 12-week DAA therapy while keeping an eye on their serial RVR, EVR and ETR levels. These children with cancer had no concomitant chronic liver disease, therefore fibrosis-4 index (Fib-4) or aspartate aminotransferase-to-platelet ratio index (APRI) or fibroscan were not utilised.

Data was analysed using SPSS 24. Descriptive statistics were calculated for qualitative and quantitative variables. Qualitative variables were presented as frequencies and percentages. Quantitative variables were presented as mean and standard deviation. Data normality was tested and Shapiro-Wilk test was used for pre-treatment (baseline) and post-treatment biochemical parameters, including alanine transaminase (ALT), which was earlier known as serum glutamic-pyruvic transaminase (SGPT), AST, which was earlier known as serum glutamic-oxaloacetic transaminase (SGOT), and serum creatinine. For normally distributed data, paired T test was used, while non-parametric Wilcoxon sign rank test was used if the variables did not meet the assumption of normality. $P<0.05$ was taken as significant.

Results

Of the 804 patients with different malignancies, 132(16.4%) were found positive for HCV. Of them, 28(21.21%) patients were started on DAAs; 17(60.71%) boys and 11(39.28%) girls. The overall mean age was 9.93±6.12 years. The diagnosis was pre-B acute lymphoblastic leukaemia (ALL) in 18(64.28%) cases (Figure), 16(57.14%) were on maintenance chemotherapy, and 18(64.28%) had genotype 1. The mean weight was 26.85±10.73kg and 26(93%) subjects weighed <45kg. Mean viral load was 1950819.00±2440842.00IU (Table 1). Presenting complaints were jaundice in 9(32%) cases, abdominal pain 8(28.5%), loss of appetite 7(25%) and nausea and vomiting 5(17.8%).



ALL: Acute lymphoblastic leukaemia; LL: Lymphoblastic lymphoma.

Figure: Diagnosis of the patients (n=28).

Table-1: Patient characteristics (n=28).

Feature	Findings [n (%)]
Mean Age (years)	9.93±6.12
Age groups (years)	
≤ 5	05 (18.0)
5.1-10	18 (64.0)
> 10	05 (18.0)
Mean Weight (kg)	26.85±10.73
Gender	
Male:	17(60.7)
Female:	11(39.3)
Diagnosis	
Pre-B ALL	18 (64.5)
T-ALL	04 (14.0)
Others	06 (21.5)
Phase of chemotherapy	
Maintenance phase	16 (57.0)
End of chemotherapy	10 (36.0)
Continuation phase	02 (7.0)
Genotype	
1	18 (64.5)
3	08 (28.5)
4	01 (3.6)
Combined 1 and 3	01 (3.6)
Mean viral load	1950819.00 IU±2440842.00 IU

SD: Standard deviation, ALL: Acute lymphoblastic leukaemia.

Table-2: Laboratory Investigations pre- and post-treatment.

Parameters with units	Pre-treatment Mean±SD	Post-treatment Mean±SD	*p*-value
Haemoglobin (gm/dl)	12.35±1.80	12.31±1.81	0.851
WBC (/µl)	5420.00±2840.00	4243.00±2214.00	0.183
ANC (/µl)	3847.00±2018.00	2561.00±1135.00	0.032
Platelets (/µl)	212133.00±77029.00	233200.00±94334.00	0.444
Serum bilirubin (mg/dl)	3.13±3.95	0.61±0.21	0.022
ALT(SGPT) (IU)	328.00±324.00	36.00±29.00	0.003
Serum creatinine (mg/dl)	0.41±0.08	0.43±0.11	0.575

SD: Standard deviation, WBC: White blood cell, ANC: Absolute neutrophil count, ALT: Alanine transaminase, SGPT: Serum glutamic-pyruvic transaminase.

Hepatomegaly was present in 10(37%) patients. There were 3(10.7%) patients who did not complain of any specific symptoms and only had deranged laboratory parameters.

Mean haemoglobin (Hb) level, mean platelets and white blood cell (WBC) counts, absolute neutrophil count (ANC) value and serum creatinine level were in normal range prior to initiation of SOF-DAC combination and there were no significant changes post-treatment (p>0.05). Post-treatment values for both the mean ALT and mean serum bilirubin levels showed significant decline (Table 2).

Of the 24(85.71%) children who had ALT value >50mg/dl prior to DAA therapy, 20(83.33%) achieved a significant (p<0.05) reduction and the levels came down to the desirable level of <50mg/dl, resulting in uninterrupted chemotherapy scheduling.

Table-3: Efficacious impact of DAAs on bilirubin and ALT levels.

Pre- treatment total bilirubin	n (%)	Post- treatment total bilirubin	n (%)
<1 mg/dl	16 (57.0)	<1 mg/dl	23 (82.1)
1-2 mg/dl	3 (10.8)	1-2 mg/dl	4 (14.3)
>2 mg/ dl	9 (32.2)	>2 mg/ dl	1 (3.6)
Pre- treatment ALT (SGPT)	**n (%)**	**Post- treatment ALT (SGPT)**	**n (%)**
<50	4 (14.3)	< 50	24 (85.7)
50-100	5 (18.0)	50-100	2 (7.0)
101-200	4 (14.3)	101-200	1 (3.6)
201-300	4 (14.3)	201-300	1 (3.6)
301-400	3 (10.8)	301-400	0
401-500	2 (7.0)	401-500	0
>500	6 (21.5)	> 500	0

DAA: Direct acting antivirals, ALT: Alanine transaminase, SGPT: Serum glutamic-pyruvic transaminase.

RVR was achieved in 26(92.85%) children, and only 2(7.14%) patients had RNA load <12.00IU, while EVR and SVR were achieved in all 28(100%) patients. Minor side effects were noted in 4(14.28%) patients; 2(50%) had generalised body ache, 1(25%) developed headache in the first two weeks of treatment, and 1(25%) experienced pruritus while on SOF-DAC therapy. All 4(100%) patients were treated symptomatically, and chemotherapy was continued in all 28(100%) cases as per the designed protocol. Treatment was well tolerated, and no drug-drug interaction was reported.

Discussion

To the best of our knowledge, the current study is the first to evaluate the usefulness of DAA in paediatric oncology population. Standard of care anti-HCV therapy is not defined in patients with cancer. In addition, there are no guidelines for the timing of DAA administration with respect to the individual anti-cancer treatment schedule in patients with HCV and cancer.

HCV infection affects millions of people worldwide and the main mode of its transmission is the use of contaminated medical material. The fact that the highest prevalence of HCV antibodies is in LMICs, including Egypt (4.6%), Pakistan (4.7%) and Taiwan (4.4%), is definitely alarming.[18-20] For the oncology population, in some regions of Europe and Asia, HCV antibodies have been reported in up to 2.8% of patients with solid tumours and 30% of those with haematological malignancies.[21,22]

The management of HCV-infected patients was compromised in the past, likely due to difficulties in treating them concomitantly with chemotherapy and older HCV therapy, such as interferon. With the arrival of DAAs, their treatment standards have changed as the virological clearance rate is documented even in cancer patients

having HCV infection. Torres HA et al.[23] showed that the SVR rates, regarded as indicating HCV cure, are now similar in HCV-infected patients with and without cancer.

The current study provided some insight into the usefulness of DAA therapy in immunocompromised paediatric cancer patients with concomitant HCV infection. There are recent similar studies done in adult cancer patients with liver disease.[24] In the paediatric population, encouraging results regarding the use of DAAs including the SOF-DAC combination are available, indicating their positive efficacy and favourable safety profiles.[15,25]

Nothing, however, has been published for this special subset of patients with childhood cancer that is likely to receive multiple injectable medications and repeated blood transfusions during the illness and treatment. In the current study, there were 5 children aged <5 years. This is because the most common underlying malignancy was ALL.

As reported earlier,[26] hepatitis flare occurs in 26% to 45% of HCV-infected cancer patients in the absence of liver infiltration by tumour or use of hepatotoxic drugs other than chemotherapeutics, and can lead to liver dysfunction that necessitates discontinuation or dose reduction of potentially life-saving chemotherapy. In our study, ALT levels were abnormal in 24(86%) patients; of them, 6(25%) had levels >500mg/dl and if they were not started on DAAs, chances of chemotherapy completion were bleak. In these circumstances, with the use of DAA therapy, the parameters normalised signifying the fact that these alterations were secondary to HCV infection. When the liver functions improved, it was possible to continue with the chemotherapy. Hence, chances of their disease remission also enhanced. In addition to this huge benefit, the use also helped in the prevention of progressive liver damage in terms of the development of chronic liver disease (CLD) and liver cirrhosis.

The guidelines issued by the American Association for the Study of Liver Diseases (AASLD) and the Infectious Diseases Society of America (IDSA)[27] mentioned that a ≥10-fold increase in ALT values from baseline, especially with signs or symptoms of liver inflammation or increasing conjugated bilirubin, alkaline phosphatase, or international normalised ratio (INR) at any time during treatment should prompt discontinuation of DAA therapy. In the current series, none was observed. Once the LFT normalises, patients do not have to wait for another 24 weeks to resume chemotherapy.

In order to maintain the balance of treating HCV infection while also taking care of their primary disease and without subjecting them to unnecessary exposure to adverse events (AEs) during the initial 4 weeks of therapy, patients were closely monitored. RVR is one of the most powerful tools for predicting treatment response[14] and RVR in the current study was achieved in 93% of the children.

AEs were earlier reported with simultaneous use of anti-neoplastic agents[28-30] and were largely attributed to chemotherapy. This issue together with the possibility of drug interactions poses a challenge while managing children with cancer. It is therefore crucial to monitor patients and recognise any serious AE timely. It is also important to note that when AEs occur, they usually appear within the first 2-4 weeks of concomitant therapy.[24] In the current patients, only a few AEs were observed while no toxic effect was observed that required discontinuation of either agent.

It is significant that the primary disease of all the current subjects remained in remission after completion of DAA therapy. Therefore, HCV infection and its treatment should not be considered contraindications to cancer treatment. HCV-targeted DAA can be used concomitantly with selective anti-neoplastic agents. However, a dedicated, multidisciplinary approach with close monitoring is mandatory.

The current study has limitations, including the sample size which was too small to allow meaningful generalisation of the findings. Also, the patients were in the less intensive phase of chemotherapy when DAAs were used. Further prospective trials of DAAs and chemotherapeutic agents in HCV-infected paediatric oncology population are required.

Conclusion

The SOF-DAC combination was found to be effective in HCV treatment, and it may be used in patients with selected chemotherapy drugs with due monitoring and modification of treatment protocols.

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References

1. Torres HA, Mahale P, Blechacz B, Miller E, Kaseb A, Herlong HF, et al. Effect of hepatitis C virus infection in patients with cancer: addressing a neglected population. J Natl Compr Canc Netw 2015; 13: 41-50.
2. Fong IW. Blood Transfusion-Associated Infections in the Twenty-First

Century: New Challenges. Current Trends and Concerns in Infectious Diseases 2020: 191–215.

3. Liang TJ, Ghany MG. Current and future therapies for hepatitis C virus infection. N Engl J Med 2013; 368: 1907-17.
4. Torres HA, McDonald GB. How I treat hepatitis C virus infection in patients with hematologic malignancies. Blood 2016; 128: 1449-57.
5. Gudeloglu E, Albayrak D. Blood product requirement in childhood Acute Lymphoblastic Leukaemia in relation to chemotherapy regimens. Iran J Pediatr 2020; 30: 1-10.e100823.
6. Vermehren J, Park JS, Jacobson IM, Zeuzem S. Challenges and perspectives of direct antivirals for the treatment of hepatitis C virus infection. J Hepatol 2018; 69: 1178-87.
7. Karnsakul W, Schwarz KB. Management of hepatitis C infection in children in the era of Direct-acting Antiviral Agents. J Viral Hepat 2019; 26: 1034-9.
8. Schwarz KB, Rosenthal P, Murray KF, Honegger JR, Hardikar W, Hague R, et al. Ledipasvir-Sofosbuvir for 12 weeks in children 3 to <6 years old with chronic hepatitis C. Hepatology 2020; 71: 422-30.
9. Malik F, Bailey H, Chan P, Collins IJ, Mozalevskis A, Thorne C, et al. Where are the children in national hepatitis C policies? A global review of national strategic plans and guidelines. JHEP Rep 2021; 3: 100227.
10. Indolfi G, Serranti D, Resti M. Direct-acting antivirals for children and adolescents with chronic hepatitis C. Lancet Child Adolesc Health 2018; 2: 298-304.
11. Hashmi MA, Cheema HA. Effectiveness and safety of Sofosbuvir in treatment-näive children with hepatitis C infection. J Coll Physicians Surg Pak 2017; 27: 423-6.
12. Economides MP, Mahale P, Kyvernitakis A, Turturro F, Kantarjian H, Naing A, et al. Concomitant use of direct-acting antivirals and chemotherapy in hepatitis C virus-infected patients with cancer. Aliment Pharmacol Ther 2016; 44: 1235- 41.
13. The Hepatology Drug Interactions website [Internet]. University of Liverpool: HEP Drug Interactions Board: 2010. Prescribing resources. Interactions with HCC Treatment. [Online] 2010 July 13 [Cited 2022 Nov 15]. Available from: URL: https://www.hep-druginteractions.org/
14. Navaneethan U, Kemmer N, Neff GW. Predicting the probable outcome of treatment in HCV patients. Therap Adv Gastroenterol 2009; 2: 287-302.
15. Parkash A, Merchant A, Habib S, Hussain W, Hayat M, Memon N. Effectiveness and Safety of Direct Acting Antiviral Agents In Thalassaemic Patients With Chronic Hepatitis C. J Ayub Med Coll Abbotabad 2022; 34: 447-51.
16. Padhi S, Maharshi S, Gupta GK, Garg K, Nijhawan S. Efficacy and Safety of Direct Acting Antiviral Therapy for Chronic Hepatitis C in Thalassemic Children. J Pediatr Hematol Oncol 2018; 40: 511-4.
17. European Association for the Study of the Liver. Electronic address: easloffice@easloffice.eu; Clinical Practice Guidelines Panel: Chair:; EASL Governing Board representative:; Panel members:. EASL recommendations on treatment of hepatitis C: Final update of the series☆. J Hepatol 2015; 63: 199-236.
18. Hanafiah KM, Groeger J, Flaxman AD, Wiersma ST. Global epidemiology of hepatitis C virus infection: new estimates of age-specific antibody to HCV seroprevalence. Hepatology 2013; 57: 1333-42.
19. Sievert W, Altraif I, Razavi HA, Abdo A, Ahmed EA, Alomair A, et al. A systematic review of hepatitis C virus epidemiology in Asia, Australia and Egypt. Liver Int 2011; 31 Suppl 2: 61-80.
20. Waked I, Esmat G, Elsharkawy A, El-Serafy M, Abdel-Razek W, Ghalab R, etal. Screening and Treatment Program to Eliminate Hepatitis C in Egypt. N Engl J Med 2020; 382: 1166-74.
21. Silvestri F, Pipan C, Barillari G, Zaja F, Fanin R, Infanti L, et al. Prevalence of hepatitis C virus infection in patients with lymphoproliferative disorders. Blood 1996; 87: 4296–301.
22. Oguz A, Aykas F, Unal D, Karahan S, Uslu E, Basak M, et al. Hepatitis B and C seroprevalence in solid tumors - necessity for screening during chemotherapy. Asian Pac J Cancer Prev 2014; 15: 1411-4.
23. Torres HA, Economides MP, Angelidakis G, Hosry J, Kyvernitakis A, Mahale P, et al. Sofosbuvir-based therapy in hepatitis C virus-infected cancer patients: A prospective observational study. Am J Gastroenterol 2019; 114: 250-7.
24. Torres HA, Shigle TL, Hammoudi N, Link JT, Samaniego F, Kaseb A, et al. The oncologic burden of hepatitis C virus infection: A clinical perspective. CA Cancer J Clin 2017; 67: 411-31.
25. Arcaini L, Besson C, Frigeni M, Fontaine H, Goldaniga M, Casato M, et al. Interferon-free antiviral treatment in B-cell lymphoproliferative disorders associated with hepatitis C virus infection. Blood 2016; 128: 2527-32.
26. Mahale P, Kontoyiannis DP, Chemaly RF, Jiang Y, Hwang JP, Davila M, et al. Acute exacerbation and reactivation of chronic hepatitis C virus infection in cancer patients. J Hepatol 2012; 57: 1177-85.
27. Ghany MG, Morgan TR. Hepatitis C guidance 2019 update: American Association for the Study of Liver Diseases–Infectious Diseases Society of America recommendations for testing, managing, and treating hepatitis C virus infection. Hepatology 2019; 71: 686-721.
28. Medeiros T, Salviato CM, do Rosário NF, Saraiva GDN, Esberard EBC, Almeida JR, et al. Adverse effects of direct acting antiviral-based regimens in chronic hepatitis C patients: a Brazilian experience. Int J Clin Pharm 2017; 39: 1304-11.
29. Maan R, van Tilborg M, Deterding K, Ramji A, van der Meer AJ, Wong F et al. Safety and effectiveness of Direct-Acting Antiviral Agents for treatment of patients with chronic hepatitis C virus infection and cirrhosis. Clin Gastroenterol Hepatol 2016; 14: 1821-30.e6.
30. Spera AM. Safety of direct acting antiviral treatment for hepatitis C in oncologic setting: A clinical experience and a literature review. World J Hepatol 2022 27; 14: 525-34.