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# A RETROSPECTIVE OBSERVATIONAL STUDY OF CLINICAL PROFILE, MANAGEMENT AND OUTCOME OF HEPATITIS C AND VIRAL HEPATITIS B PATIENTS ENROLLED UNDER NATIONAL VIRAL HEPATITIS CONTROL PROGRAMME AT TERTIARY CARE CENTER

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## ABSTRACT
Direct-acting antiviral (DAA) drugs have been effective in the treatment of hepatitis C infection. We aim to evaluate the treatment response of Sofosbuvir based DAA in Hepatitis C patients as limited data exists in the real-world community setting.
Similarly, Data of safety and tolerability of Hepatitis B treatment with Tenofovir is also discussed.
A retrospective analysis was carried out including patients enrolled under government's scheme of National viral Hepatitis control programme for Hepatitis C infection and Hepatitis B treatment between 1/1/2021 to 1/1/2024 where patients were treated according to guidelines offered by national scheme in order to achieve SVR (Sustained Viral Response), preventing disease progression to Cirrhosis and Hepatocellular carcinoma.

## INTRODUCTION
Hepatitis A, B, C, D, E viruses are hepatotropic virus infecting hepatocytes where Hepatitis B And Hepatitis C are blood borne infections usually spread through contact of infected person's blood, blood products and they are responsible for cirrhosis and hepatocellular carcinoma. Hepatitis A and Hepatitis E are majorly self-resolving infections which are spread through fecal oral routes.
A meta-analysis undertaken by SGPGI, Lucknow showed that there can be estimated 5.2 to 13 million anti-HCV positive persons in India. Chronic HCV infection is associated with 12-20% of cirrhosis and 12-32% of hepatocellular carcinoma (HCC) [Anonymous, No Date]. Developed nations such as the USA are having between 3.2 and 5 million people with chronic hepatitis C (CHC) infection which if untreated can develop into cirrhosis, hepatocellular carcinoma, and death [Ly *et al.,* 2016; Rumgay *et al.,* 2022].
Hepatocellular carcinoma (HCC) comprises approximately 75%–80% of all liver cancer types in most countries [Rumgay *et al.,* 2022]. HCC is the sixth most common cancer worldwide, comprising approximately 5% of the total cancer incidence, and causes approximately six deaths per 100000 people annually [Rumgay *et al.,* 2022b].
At present, India contributes to approximately 18% of the incidence and 4% of the mortality. By 2040, the global burden of new cases and deaths from liver cancer may increase by up to 55% (an estimated 1.3 million cases and 1.4 million deaths) [Rumgay *et al.,* 2022b; Nelson, 2022]. However, India still has a low 5-year survival rate for HCC (< 15%) despite the advancement of curative and palliative treatment options over the last two decades [Paul *et al.,* 2009; Koshy *et al.,* 2023].
Newer drugs that directly inhibit the virus replication cycle have led to the advent of oral HCV treatment regimens known as direct-acting antiviral (DAAs) [Afdhal *et al.,* 2014].
Due to the relative novelty of DAA regimens, there is a paucity of literature establishing safety, tolerability, and efficacy of DAA in the real-world community care setting. As a result, we aim to analyze DAA's safety, tolerability and efficacy at Tertiary care centre.

WHO estimates that 254 million people were living with chronic hepatitis B infection in 2022, with 1.2 million new infections each year. In 2022, hepatitis B resulted in an estimated 1.1 million deaths, mostly from cirrhosis and hepatocellular carcinoma (primary liver cancer). In Hepatitis B infection life time treatment with tenofovir 300 once a day is given.

## MATERIALS AND METHODS

31 consecutive patients were registered for Hepatitis C infection treatment out of which 31 patients were eligible for treatment between January 2021 and December 2022 were included in this retrospective cohort study and received at least twelve weeks of treatment with one of the recommended combination regimens in standard doses for HCV infection guided by National Viral Hepatitis Control programme. Similarly, 100 patient were treated for Hepatitis B infection.

Patients with HCV Viral load and eligible for treatment without any complications were treated with Sofosbuvir (400 mg) + Daclatasvir (60 mg) for 84 days, that is 12 weeks. Patient selected for Hepatitis B infection treatment as per NVHCP guidelines were treated with Tenofovir (300mg) OD.

Treatment Safety And Tolerability of treatment were assessed by reviewing documented adverse events, treatment completion rates.

Laboratory studies were conducted both pretreatment and posttreatment. Laboratory values were then compared to look for any abnormalities associated with SVR antiviral therapy.

## RESULTS AND DISCUSSION

1) Hepatitis C

Out of 31 eligible patients 31 patient completed treatment

Out of 31 treated patient SVR was attained at 12th week in 28 Patients.

3 Patients achieved SVR after continuing treatment for more 12 weeks

**Demographic and clinical characteristics of patients at baseline**

| | | |
|---|---|---|
| **Age** | 31 year (Mean) | |
| **Sex** | Male: 22 | Female: 9 |
| **BMI (Kg/m2)** | 24.2 kg/m2 | |
| **HCV RNA (IU/ml)** | >80000 20 | |
| **MELD score** | <10: 31 | > 10: 0 |
| **Diabetes** | 2 patients | |
| **Hypertension** | 5 patients | |
| **Anemia** | 6 patients | |
| **Cirrhosis on USG** | 0 patient | |

Baseline investigations week 1 before treatment in patient whom SVR achieved and not achieved.

| | **SVR achieved (28 patients)** |
|---|---|
| Hemoglobin (mg/dl) | 12+- 2 |
| Platelet per cubicmm | 262000 +- 50000 |
| Serum Albumin (g/dl) | |
| AST (Aspartate aminotransferase) (IU/ml) | 54 |
| (Alanine aminotransferase) (IU/ml) | 48 |
| Bilirubin (mg/dl) | 1.1 |
| FIB 4 Score | 0.96 |
| APRI score | 0.687 |

Investigation after 12 weeks of treatment in patients whom SVR achieved and not achieved

| | **SVR achieved (28 patients)** |
|---|---|
| Hemoglobin (mg/dl) | 11 |
| Platelet per cubicmm | 262000 +- 50000 |
| Serum Albumin (g/dl) | 4 |
| AST (Aspartate aminotransferase) (IU/ml) | 34 |
| ALT (Alanine aminotransferase) (IU/ml) | 40 |
| Bilirubin (mg/dl) | 1.2 |
| FIB 4 score | 0.66 |
| APRI score | 0.433 |

Using the lower cut off value of 1.45, a FIB-4 score <1.45 had a negative predictive value of 90% for advanced fibrosis.
In contrast, a FIB-4 >3.25 would have a 97% specificity and positive predictive value of 65% for advanced fibrosis [Sterling *et al.*, 2006] Therefore there is no need of going for Liver biopsy for a low FIB-4 score.

In our study patients FIB 4 mean scores were 0.96 at starting of treatment and it reduced to 0.66 that suggests the effect of antiviral agents against development of cirrhosis in hepatitis C patients.
In a meta-analysis of 40 studies it was concluded that an APRI Score greater than 1.0 has sensitivity of 76% and specificity 72% for predicting cirrhosis [Lin *et al.*, 2011].
APRI Score was also reduced from 0.687 to 0.433 suggesting effect of antiviral drug against development of cirrhosis in hepatitis C patients.

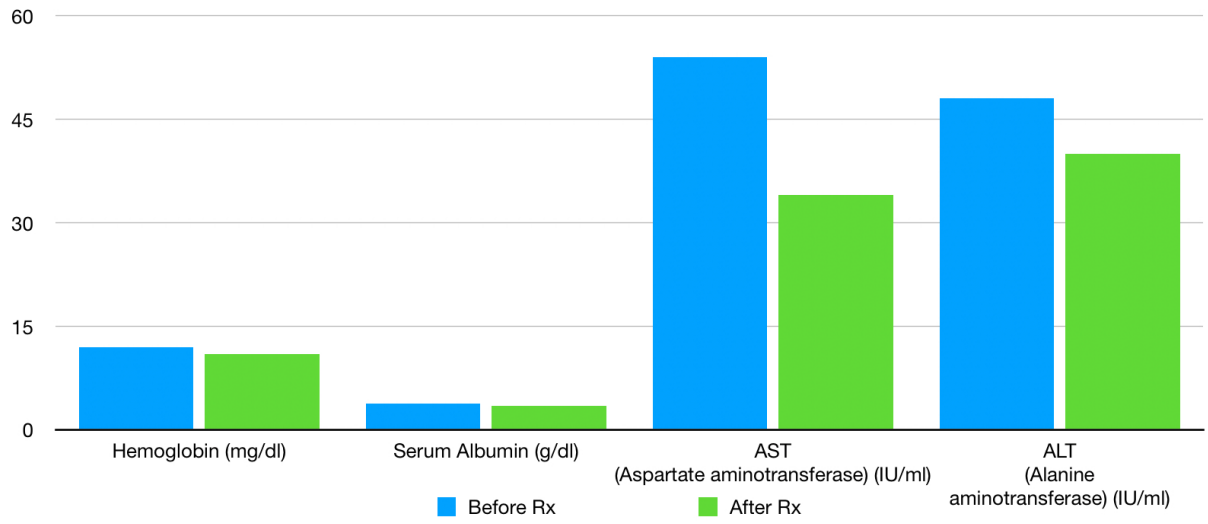
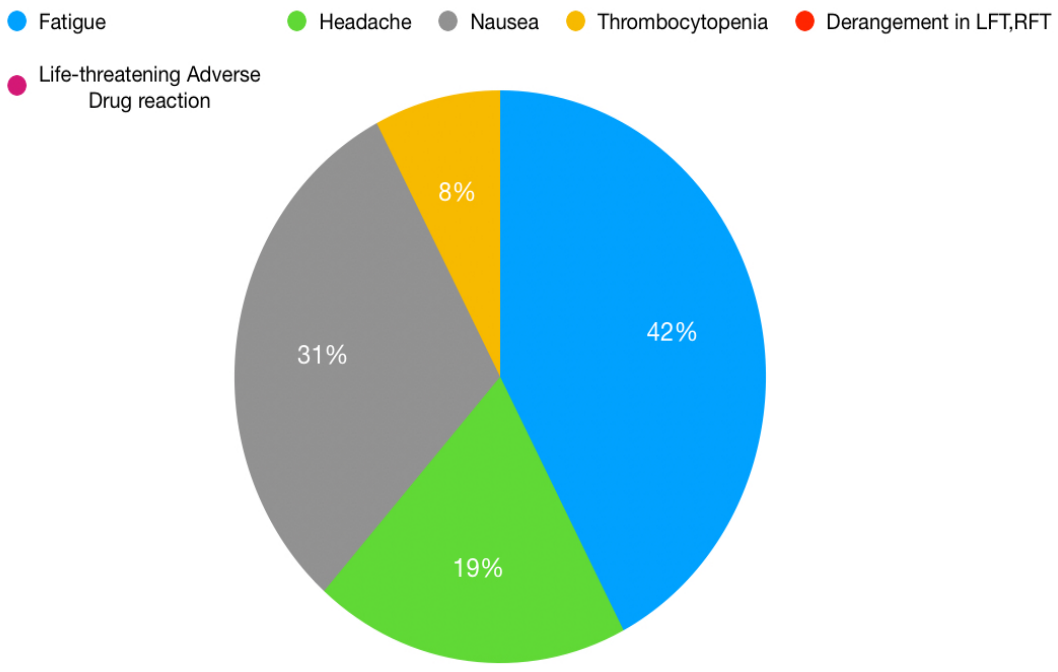



Table 1

| | Before Rx | After Rx | | |
|---|---|---|---|---|
| **Hemoglobin (mg/dl)** | 12 | 11 | | |
| **Serum Albumin (g/dl)** | 4 | 4 | | |
| **AST (Aspartate aminotransferase) (IU/ml)** | 54 | 34 | | |
| **ALT (Alanine aminotransferase) (IU/ml)** | 48 | 40 | | |

**Drug side effect profile**

| Side effects | Number of patients |
|---|---|
| Fatigue | 11 |
| Headache | 5 |
| Nausea | 8 |
| Thrombocytopenia | 2 |
| Derangement in LFT,RFT | 0 |
| Life-threatening Adverse Drug reaction | 0 |



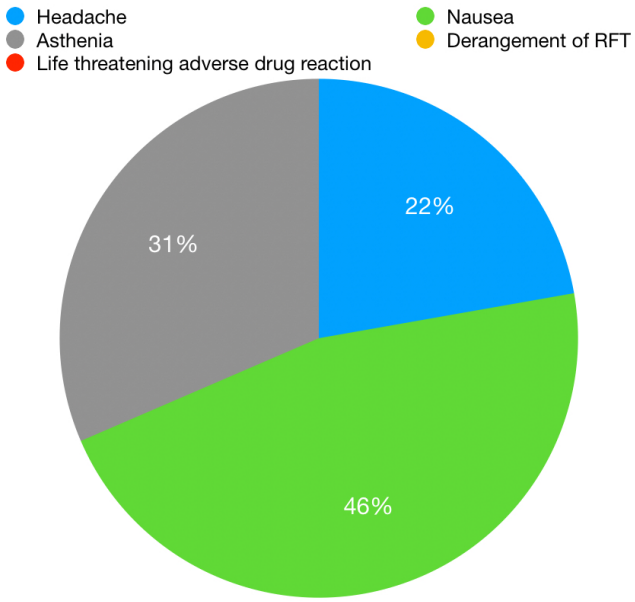
**2) Hepatitis B**

Out of 130 patients who are found to be HbSAg positive during screening undergone for HBV DNA loads where 109 patients were having positive results for DNA 100 patients were started on treatment. Drug safety and side effect were observed

| | | |
|---|---|---|
| **Age** | **42 year (Mean)** | |
| **Sex** | **Male: 70** | **Female: 30** |
| **BMI (Kg/m2)** | **23 kg/m2** | |
| **MELD score** | **<10: 98** | **> 10: 2** |
| **Diabetes** | **8 patients** | |
| **Hypertension** | **12 patients** | |
| **Anemia** | **10 patients** | |
| **Cirrhosis on USG** | **2 patient** | |
| **Average APRI score** | **0.66** | |

In our study average APRI was 0.66 where most of the patients were having less than 1 score therefore patients were unlikely to end up with complications of cirrhosis.

| Drug side effect | Number of patient |
|---|---|
| **Headache** | **12** |
| **Nausea** | **25** |
| **Asthenia** | **17** |
| **Derangement of RFT** | **0** |
| **Life threatening adverse drug reaction** | **0** |
| | |




**CONCLUSION**

The Government of India has implemented the Scheme of National Viral Hepatitis Programme through which costly treatment of HBV and HCV infection are available to all patients at our center. It was implemented in 2018.

Early detection of infection through screening helps to diagnose the condition and early treatment for both infections prevents further risk to develop cirrhosis and Hepatocellular carcinoma.

12-week course of Sofosbuvir and Daclatasvir have shown remarkable results where more than 95% of patient have shown negative viral load after 12 weeks of completion of treatment

Drugs used in both Hepatitis B and C virus infection treatment have shown minor drugs side effects but such possibility of life-threatening adverse reaction in our sample.

Regimens should be promoted and early detection and treatment should be the goal for both infections, especially achieving the goal of elimination of Hepatitis C virus from India as per Nation viral hepatitis control programme.
More awareness and strong implementation of DAA Drugs is key to achieve the desired goal. All viral hepatitis elimination is the target by the government of India 2030 by Sanitization improvement, public awareness and DAA drugs.

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