



**TO STUDY THE PREVALENCE OF HEPATITIS C VIRUS INFECTION AND  
EFFECTIVENESS OF SOFOSBUVIR/ VALPATASVIR REGIMEN IN PATIENTS WITH END  
STAGE RENAL DISEASE ON MAINTENANCE HEMODIALYSIS - A MULTICENTRIC  
STUDY ACROSS KASHMIR VALLEY**

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### ABSTRACT

**Background:** Hepatitis C virus (HCV) infection is a significant global health concern, particularly among patients undergoing maintenance dialysis. The immunosuppressed state and frequent vascular access in dialysis patients make them highly susceptible to blood-borne infections like HCV. Chronic HCV infection in this population is associated with increased morbidity and mortality, hepatic complications, and adverse cardiovascular outcomes.

**Objective:** This study aims to determine the prevalence of HCV infection in patients receiving dialysis and to evaluate the effectiveness and safety of the pan-genotypic antiviral regimen— Sofosbuvir/ Valpatasvir — in treating HCV in this population. **Methods:** A cross-sectional observational study was conducted among patients undergoing hemodialysis in selected dialysis centers. HCV infection was diagnosed using anti- HCV antibody testing and confirmed by HCV RNA PCR. Patients with confirmed HCV infection received a once-daily fixed-dose combination of Sofosbuvir 400 mg and Valpatasvir 100 mg for 12 weeks. Effectiveness was assessed based on the sustained virologic response at 12 weeks post-treatment (SVR12), while safety was evaluated by monitoring clinical and laboratory parameters during therapy. **Results:** Out of the total dialysis population screened, the prevalence of HCV infection was found to be X%. Among the patients treated with Sofosbuvir /Valpatasvir, Y% achieved SVR12, indicating a high rate of viral clearance. The regimen was well- tolerated, with no significant adverse events necessitating discontinuation. Minimal alterations in hemoglobin levels and liver enzymes were observed, with no serious drug-related toxicity reported. **Conclusion:** The prevalence of HCV remains a critical concern in the dialysis population. However, the Sofosbuvir/Valpatasvir regimen demonstrates excellent efficacy and safety, making it a viable and effective treatment option for managing HCV in patients on dialysis. Early screening and timely antiviral treatment can significantly reduce disease burden and improve the quality of life and survival outcomes in this vulnerable group.

### KEYWORDS:

#### Hepatitis C virus

Hepatitis C virus which before its identification was labeled, “non A non B hepatitis” was identified in 1988 and termed as hepatitis C virus.<sup>[8]</sup> HCV is an important / health problem because it is a major cause of chronic hepatitis, cirrhosis and HCC and major indication for

liver transplant worldwide. The most tracking feature of this virus is its ability to induce persistent Infection in at least 85% of the infected persons despite vigorous humoral and cellular host immune response.

The hepatitis C virus (HCV) is a small (55–65nm in

size), enveloped, positive-sense single- stranded RNA virus of the family Flaviviridae.<sup>[9]</sup>

Based on genetic differences between HCV isolates, the hepatitis C virus species is classified into six genotypes (1–6) with several subtypes within each genotype.<sup>[10,11]</sup>

Infection begins as acute and usually asymptomatic during early stages.<sup>[12]</sup> Over many years, the chronic infection of the liver, can lead to complications like a fatty liver, cirrhosis, and liver cancer.<sup>[13]</sup> Worldwide hepatitis C is the cause of 27% of cirrhosis cases, and 25% of hepatocellular carcinomas.<sup>[14]</sup>

The clinical picture is not significantly different whether a patient has renal failure or not. Sometimes transaminase peaks are a little lower in the dialysis groups.<sup>[15]</sup> But histological damage and prognosis do not differ.<sup>[16]</sup> The uremic immune defect does not have much influence on the course of disease.

Transmission of the hepatitis C virus is related to.

1. Transfusion<sup>[17]</sup>
2. Intravenous Drug use<sup>[18]</sup>
3. Sexual transmission and perinatal<sup>[19,20]</sup>
4. In haemodialyzed patients, environmental surface contamination<sup>[21]</sup>

The world Health organization (WHO) estimates that the global prevalence of HCV infection averages 3%, which corresponds to about 170 million infected person's worldwide.<sup>[22]</sup>

Rates are high (>3.5% population infected) in Central and East Asia, North Africa and the Middle East, they are intermediate (1.5–3.5%) in South and Southeast Asia, sub-Saharan Africa, Andean, Central and Southern Latin America, Caribbean, Oceania, Australasia and Central, Eastern and Western Europe; and they are low (<1.5%) in Asia-Pacific, Tropical Latin America and North America.<sup>[23]</sup>

In Egypt, the country managed to bring down the infection rates of Hepatitis C from 22% in 2011 to just 2% in 2021.<sup>[24]</sup>

In general, between 1990 and 2005, the prevalence of, and the number of people carrying, anti- HCV antibodies increased from 2.3% (95% UI, 2.1-2.5%) to 2.8% (95% UI, 2.6-3.1%) and from >122 million to > 185 million respectively.<sup>[25]</sup>

Globally, genotype 1 is estimated to account for more HCV prevalence of Gen-1 cases than any other genotype. HCV genotype 3 is the next most common genotype and is estimated to account for 54.3 million cases globally. Genotype 2,4,6 are responsible for majority of the remaining cases of HCV worldwide, corresponding to an estimated 16.5 million, 15 million and 9.8 million cases respectively.<sup>[26]</sup>

For a long time the true prevalence in patients with renal insufficiency has been in doubt because of the use of first generation assays which underestimate the prevalence in general. But in hemodialysis patients the production of specific antibodies is impaired due to uremic defect. Therefore the errors were even greater in these patients.

The prevalence of HCV among HD patients varies worldwide, ranging from as low as 1 to up to 70%, and the dialysis-related risk of HCV infection is estimated at 2% per year.<sup>[27]</sup> Overall, the HCV prevalence in patients in HD is below 5% in most countries of Northern Europe, around 10% in most countries of Southern Europe and the United States, and between 10 and 50% and up to 70% in many parts of the developing world, including many Asian, Latin American and North-African countries.<sup>[28]</sup>

In India, a very wide range of prevalence rates for HCV (4.3-45.2%) in the HD population have been reported.<sup>[29,30,31,32,33,34]</sup> These prevalence rate are higher than the average HCV prevalence in general population in India.<sup>[35]</sup> The prevalence is influenced by.

- a. The country of survey
- b. The frequency of blood transfusion
- c. The length of time the patient underwent haemodialysis.<sup>[36]</sup>

In patients on hemodialysis there is an increased mortality in Anti HCV positive patients (33%) mostly due to liver failure and hepatocellular carcinoma.<sup>[37]</sup>

#### High risk group for hepatitis C infection are

- 1) Patient requiring blood and blood products, thalassemic and hemophilic and CRF patients.
- 2) Immunocompromised e.g., HIV, alcoholic, CKD, patients on hemodialysis and renal transplant recipient.
- 3) Infant born to carrier mother.
- 4) Prostitutes and homosexual.
- 5) Medical personals and drug abuse.

Hepatitis is known to be a major cause in hemodialysis patients and staff, since the introduction of maintenance hemodialysis which was first time performed in 1960.<sup>[38,39]</sup> Hepatitis is a risk to CKD and renal transplant patients. From the early 1970s the disease entity Non-A, Non-B hepatitis (NANBH) has been associated with transfusion therapy.<sup>[40]</sup> Transmission of NANBH in a dialysis unit might however occur unrelated to blood transfusion.<sup>[41]</sup>

The epidemiology of NANBH has been characterized but the diagnosis has earlier been based on exclusion of other diseases.<sup>[42]</sup> The discovery of essential parts of Hepatitis C virus (HCV) genome has enabled the introduction of a serologic test for antibodies to hepatitis C virus (anti-HCV). This test has shown HCV to be the major etiologic agent of NANBH.<sup>[8]</sup>

CRF patients on haemodialysis constitute a high risk group for both HBV and HCV as these patients are immunosuppressed and receive multiple blood transfusions for anemia. Moreover, in the course of standard haemodialysis treatment with shared equipments each patient is parenterally exposed by IV procedures at least one thousand time every year.

These observations together with a negative history of blood transfusion in several cases of HBs Ag and HCV positive patients suggest that HBV and HCV may be transmitted within the haemodialysis environment.<sup>[43,44]</sup>

The efficacy rate of a DNA derived vaccine in HD population is similar to the plasma derived vaccines and lower than in healthy subjects.<sup>[45]</sup>

Currently no vaccine is available for hepatitis

C. For the management of HCV in hemodialysis patients, previously it was challenging to treat patients due to associated toxicities of interferon therapy.<sup>[47]</sup> In addition to the safety concerns, the effectiveness of interferon regime was also not promising with low sustained virological response (SVR) rates (33-37%) and discontinuation rates (17-30%) that further limited its applicability.<sup>[48]</sup> The toxicity of IFN was also aggravated by the concomitant use of RBV that is minimally eliminated by hemodialysis; thus combination of regime associated with substantial hematologic toxicity and risk for anemia.<sup>[47,48,49]</sup> Over the last years, direct acting antiviral agents have been approved for use in patients with HCV infection and CKD. However, approved HCV treatments for patients with ESRD are associated with drug –drug interactions, baseline resistance testing, risk of hepatotoxicity and contraindications for those with decompensating liver disease.<sup>[50,51,52]</sup>

Additionally, some of these regimens are not pangenotypic.

Treatment regimens containing the NS5B inhibitor, Sofosbuvir, are the most widely prescribed treatments for HCV infection worldwide. The predominant circulating etabolite of Sofosbuvir, GS-331007, is renally cleared and accumulates in patients with severe renal impairment or ESRD which has resulted in the exclusion of this population in prior clinical trials, and consequently, a lack of dosing recommendations for patients with ESRD. However a real-world case series in patients with ESRD undergoing dialysis demonstrate substantial use of Sofosbuvir based regimens in this population with no safety concerns identified.<sup>[53,54,55,56,57,58,59]</sup> Also in countries like India use of DAA'S like Grazoprevir-elbasvir, Glecaprevir- Pibrentasvir as recommended by KDIGO for treatment of hepatitis C in ESRD patients can be difficult due to high cost and non-availability of these regimens. There are some studies in India who have studied the safety and efficacy of Sofosbuvir based regimens in ESRD patients and have shown that they are

safe and effective in treating these patients.<sup>[80,82]</sup>

The fixed dose combination of Sofosbuvir and Velpatsavir, an NS5A inhibitor, provides a treatment option for HCV infected patients regardless of HCV genotype, Patient demographics and other disease characteristics.<sup>[60,61]</sup>

The present study has been undertaken to determine the prevalence of HCV infection and to evaluate the safety and efficacy of Sofosbuvir/Velpatsavir in patients with ESRD who are undergoing dialysis to expand our knowledge regarding the use of Sofosbuvir – based regimens in these patients with severe renal impairment and ESRD.

## MATERIALS AND METHODS

This prospective study was conducted from December 2023 to june 2025 in the department of Nephrology at AGA SYED YOUSUF MEMOREAL DISTRICT HOSPITAL, Budgam, Kashmir. A total of 1330 patients on maintenance haemodialysis were enrolled from 11 haemodialysis centers and followed in a longitudinal manner. All the patients were screened for anti-HCV antibodies by enzyme linked immunosorbent assay (ELISA) and for HCV-RNA by real time reverse transcription polymerase chain reaction (RT-PCR). 188 patients came positive for anti-HCV antibodies during the study period. Among positive ones, 82 patients were excluded from study because of lost to followup ,no consent ,death and not received drug treatment for HCV. Data on 106 HCV patients were finally evaluated.

### Inclusion criteria

1. Patients who were on maintenance haemodialysis for greater than 3 months.
2. Patients who were anti HCV negative before entry into dialysis.

Informed consent was taken from all the patients before proceeding with the study. The following individual data were collected from patients:

- Patient ID,BMI, Age/Gender
- Underlying cause of CKD
- Vascular access
- Duration and Frequency of HD
- Number of centers attended
- Blood group
- History of blood transfusion
- History of previous surgery and dental check-up
- Time between initiation of haemodialysis and HCV detection.
- ELISA and card method results
- HCV RNA load (Quantitative), Genotype
- Treatment of HCV, Duration of treatment
- Effectiveness & SVR of treatment
- Adverse events, Prior HCV Treatment
- Complete haemogram
- Liver function test

- Kidney function test
- Serum phosphorus ,Serum Calcium, Serum Uric acid
- USG findings of liver ,Fibroscan of liver

- positive, anti HCV positive were excluded from study.
- 2. Acute renal failure patients who underwent dialysis.
- 3. No consent

**Exclusion criteria**

1. The patients already suffering from liver disease or having deranged liver function tests, HBs Ag
- Lost to follow-up.

**OBSERVATIONS AND RESULTS**

**Table 1: Age and Sex distribution of HCV positive patients on maintenance dialysis.**

		GENDER		Total
		MALE	FEMALE	
Age	<= 20	1 0.9%	0 0.0%	1 .9%
	21-35	15 14.2%	9 8.5%	24 22.6%
	36-50	23 21.7%	11 10.4%	34 32.1%
	51-65	16 15.1%	16 15.1%	32 30.2%
	66-80	8 7.5%	5 4.7%	13 12.3%
	81+	2 1.9%	0 .0%	2 1.9%
	Total	65 61.3%	41 38.7%	106 100.0%

Chi-square value: 4.209,  
P value: 0.520

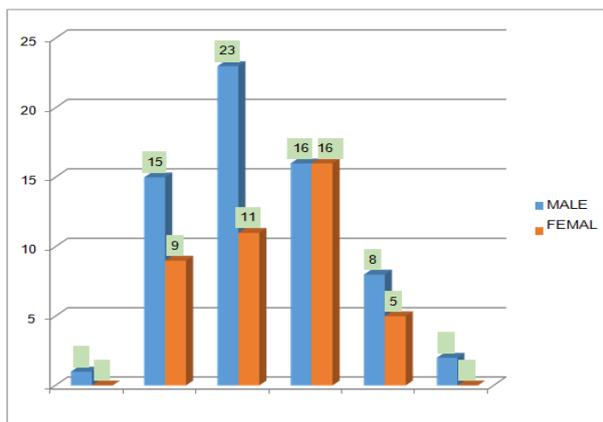
**Mean age**

Male patients: 48.81 years

**Minimum age:** 19 years

**Female patients:** 48.90 years

**Maximum age:** 88years



**Fig. 1.**

1					2
0					0
0 <=20	21-35	36-50	51-65	66-80	81+

Table 1 and Fig.1- shows that majority of the patients were male (61.3%) and female (38.7%).The majority of patients were in age group of 36 to 50 years, There were

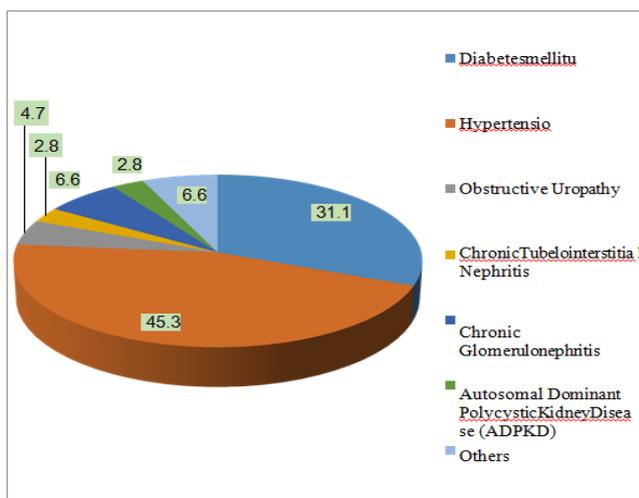
same proportion of patients in the age group of 51 to 65 years. Age group ranges from 19 years to 88 years.

**Table 2: Etiological profile of HCV positive patients on maintenance haemodialysis.**

Etiology	Frequency	Percent
Diabetes mellitus	33	31.1
Hypertension	48	45.3
Obstructive Uropathy	5	4.7
Chronic Tubelointerstitial Nephritis	3	2.8
Chronic Glomerulonephritis	7	6.6
Autosomal Dominant Polycystic Kidney Disease (ADPKD)	3	2.8
Others	7	6.6
<b>Total</b>	<b>106</b>	<b>100.0</b>

Table 2 - shows that Hypertension, Diabetes mellitus and Chronic glomerulonephritis were the main etiological

causes in our HCV positive patients on maintenance haemodialysis.



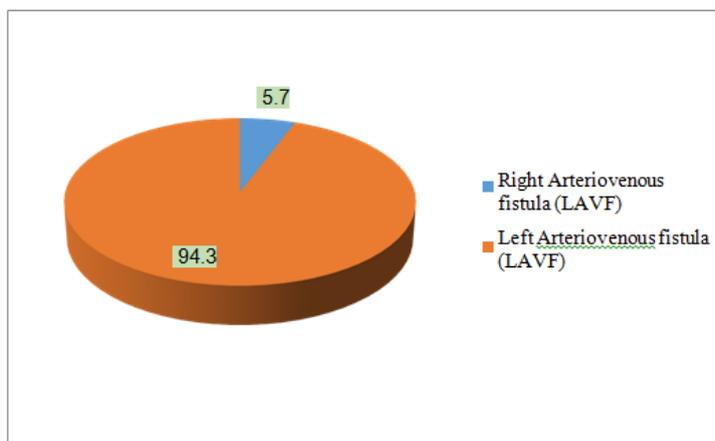
**Fig. 2.**

Fig 2- shows that Hypertension (45.3%), Diabetes mellitus (31.1%) and chronic glomerulonephritis (6.6%),

were the main etiological causes in our HCV positive patients on maintenance haemodialysis.

**Table 3: Vascular Access of patients on maintenance haemodialysis**

Vascular Access	Frequency	Percent
Right Arteriovenous fistula (RAVF)	6	5.7
Left Arteriovenous fistula (LAVF)	100	94.3
<b>Total</b>	<b>106</b>	<b>100</b>



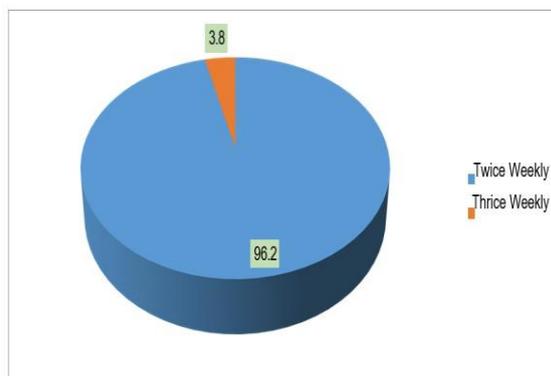
**Fig. 3.**

All the HCV+ patients had arterio venous fistula as venous vascular access.94.3% patients had LAVF while

only 5.7% of patients had RAVF as shown in table 3 and fig. 3.

**Table 4: Haemodialysis Frequency of maintenance haemodialysis patients.**

Haemodialysis Frequency	Frequency	Percentage
Twice Weekly	102	96.2
Thrice Weekly	4	3.8
<b>Total</b>	<b>106</b>	<b>100.0</b>

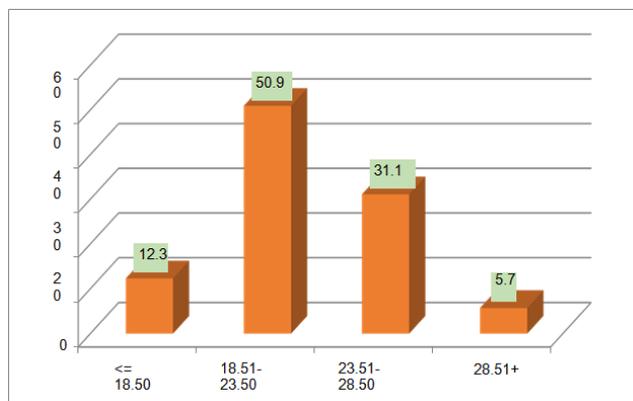


**Fig. 4.**

As shown in the table 4 and fig. 4-majority of patients (96.2%) were on twice weekly dialysis schedule and only 3.8% were on thrice weekly schedule.

**Table 5: Body Mass Index (BMI) of HCV patients on maintenance haemodialysis.**

BMI(kg/m <sup>2</sup> )	Frequency	Percent
<=18.50	13	12.3
18.51-23.50	54	50.9
23.51-28.50	33	31.1
28.51+	6	5.7
<b>Total</b>	<b>106</b>	<b>100.0</b>



**Fig. 5.**

As shown in the table 5 and fig 5-most of the patients (50.9%), had their BMI (kg/m<sup>2</sup>) in the range of 18.5-23.5.

**Table 6: Blood group of HCV + patients on maintenance haemodialysis**

Blood group	Frequency	Percent
A+	19	17.9
A-	0	0.0
B+	22	20.8
B-	03	2.8
AB+	10	9.4
O+	37	34.9
O-	03	2.8
Unknown	12	11.3
<b>Total</b>	<b>106</b>	<b>100.0</b>

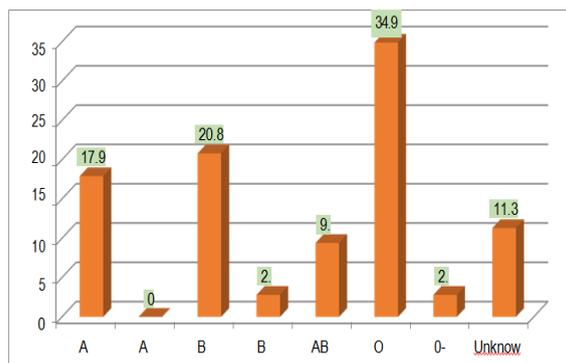


Fig 6:

Table 6 and fig.6-shows us that the most common blood group in our study population was O+ (34.9%), followed by B+ (20.8%), A+ (17.9%), AB+ (9.4%) and O- (2.8%).

Table 7: History of previous surgery and Dental checkup of HCV+ patients on maintenance haemodialysis.

Previous surgery Or Dental checkup	Frequency	Percent
No	69	65.1
Yes	37	34.9
Total	106	100.0

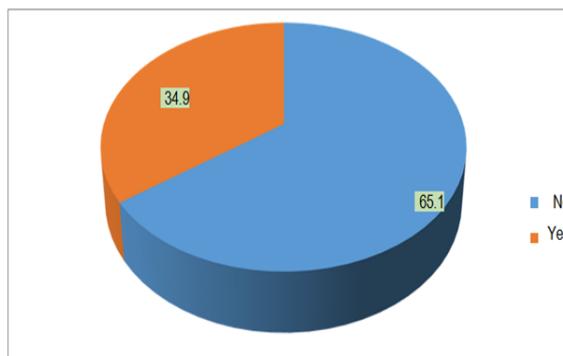


Fig. 7.

Table 7 and fig.7-reveals that only 37 (34.9%) patients had undergone surgery and dental checkup.

Table 8: Marital status of HCV + patients on Maintenance haemodialysis.

Marital Status	Frequency	Percent
Married	94	88.7
Unmarried	12	11.3
Total	106	100.0

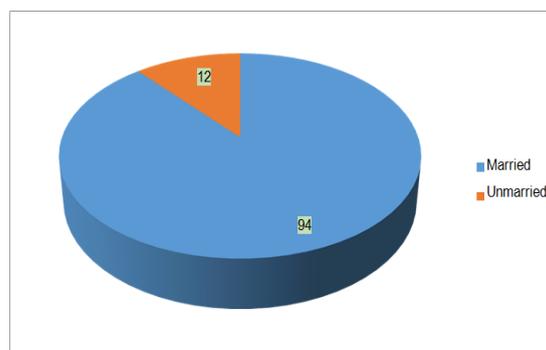
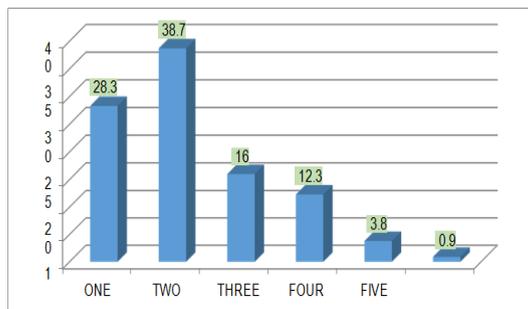


Fig. 8.

Table 8 and fig.8-shows that 94 patients were married and only 12 patients were unmarried.

**Table 9: Number of haemodialysis centers attended by HCV + patients.**

HD centers	Frequency	Percent
1	30	28.3
2	41	38.7
3	17	16.0
4	13	12.3
5	4	3.8
7	1	0.9
Total	106	100.0



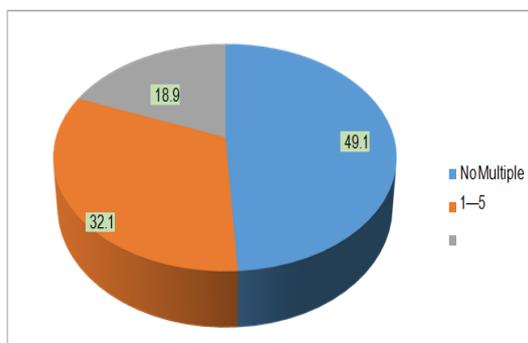
**Fig. 9.**

Table 9 and fig.9-shows that majority of the patients had attended more than one centre. Among all the patients

only 28.3% patients had been dialysed in single HD center.

**Table 10: Blood transfusion history of HCV + patients.**

Blood transfusions received by patient	Frequency	Percent
No	52	49.1
Multiple	34	32.1
1—5	20	18.9
Total	106	100.0



**Fig. 10.**

Table 10 and fig. 10 - summarizes the blood transfusion history of HCV + patients. Fifty two Patients (49.1%) had no previous history of blood transfusion. 34 patients

received multiple blood transfusions. Twenty patients had received 1to5 units of blood transfusions.

**Table 11: Time between initiation of haemodialysis and HCV detection.**

Years	Frequency	Percentage
0-1	30	28.3
1-2	37	34.9
2—3	19	17.9
3—4	11	10.4
4—5	4	3.8
5—6	3	2.8
6—7	2	1.9
Total	106	100.0

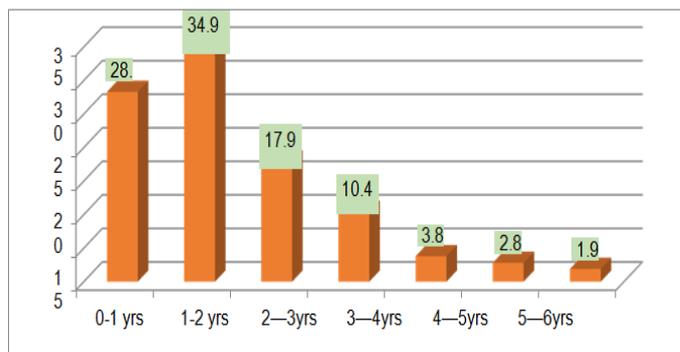


Fig. 11.

Table 11 and fig.11 summarize that most of the patients came positive for HCV during the first two years of haemodialysis. In the first and 2<sup>nd</sup> year of MHD 30 (28.3%) and 37 (34.9%) patients came positive for HCV.

Table 12: Genotypes of HCV + patients on maintenance haemodialysis.

Genotype	Frequency	Percent
1A	74	69.8
1	1	0.9
3	2	1.9
Not Done	29	27.4
Total	106	100.0

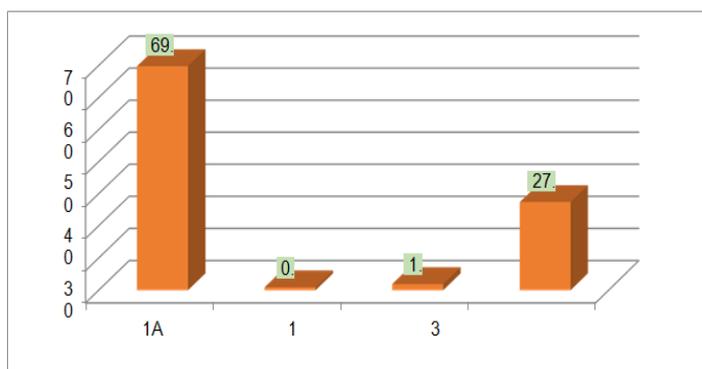


Fig. 12.

Genotype 1A was the most common genotype in our study population followed by genotype 2 and genotype 1 as depicted in the table 12 and fig 12. Genotyping was not available in 29 patients.

Table 13: Fibrosis stages of liver of HCV + Patients on Maintenance haemodialysis.

Fibrosis stages/ LSM (Kpa)	Frequency	Percentage
F0/F1count	7	6.6
F2count	7	6.6
F3count	26	24.5
F4count	7	6.6
Not Done	59	55.7
Minimum	4.80	
Maximum	66.40	
Mean ±SD	12.58±2.310	

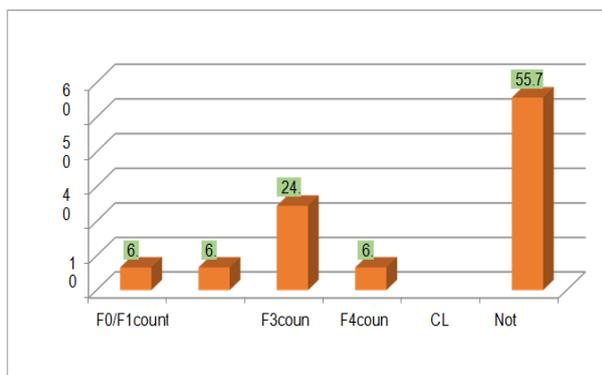


Fig. 13.

Table 13 and fig. - 13 shows various fibrosis stages of liver of HCV+ patients on MHD before starting antiviral treatment. F3 count was seen in maximum number of

patients. F4 count or cirrhosis was seen in 7 patients. 59 patients had not their fibroscan available.

Table 14: HCV RNA Load (IU/ml) of HCV + patients on MHD.

Minimum	Maximum	Mean
85.8IU/ml	1400000000IU/ml	15880748.54IU/ml

Table 14 shows-HCV RNA level of positive patients before starting treatment. The minimum and maximum

ranges are show in the table.

Table 15: Anti-viral drug treatment received by HCV + patients.

Drug treatment	Frequency	Percent
Sofosbuvir400mg/Velpatsavir 100mg	94	88.7
Sofosbuvir400mg/Daclatsavir Dihydrochloride60mg	12	11.3
Total	106	100.0

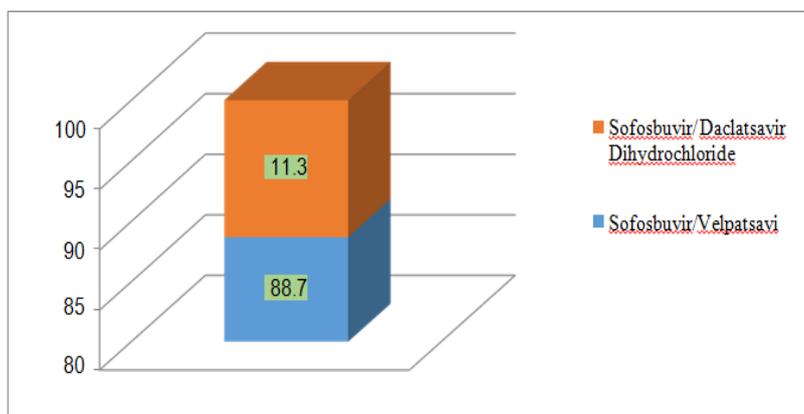


Fig. 15.

As shown in the table 15 and fig. 15 - the most common anti-viral treatment received by our patients was Sofosbuvir 400mg/Velpatsavir 100mg (88.7%) and

Sofosbuvir 400mg/Daclatasvir Dihydrochloride 60 mg (11.3%).

Table 16: Duration of anti-viral Treatment received by HCV + patients.

Treatment Duration	Frequency	Percent
3 Months	78	73.5
6 Months	28	26.5
Total	106	100.0

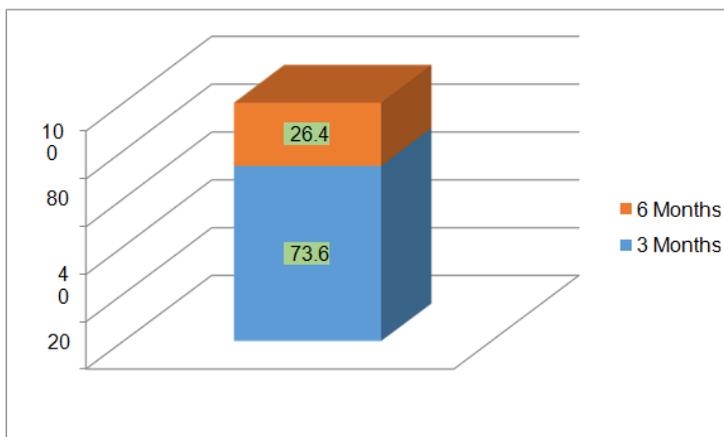


Fig. 16.

Table 16 and fig16-shows that majority of patients (73.5%) received treatment for 3 months while only (26.5%) of patients received treatment for 6 months.

Table 17: Sustained virological response (SVR) of treatment.

SVR 12/24 Weeks	Frequency	Percent
SVR achieved at 12 weeks	78	73.5
SVR achieved at 24 Weeks	28	26.5
Total	106	100.0

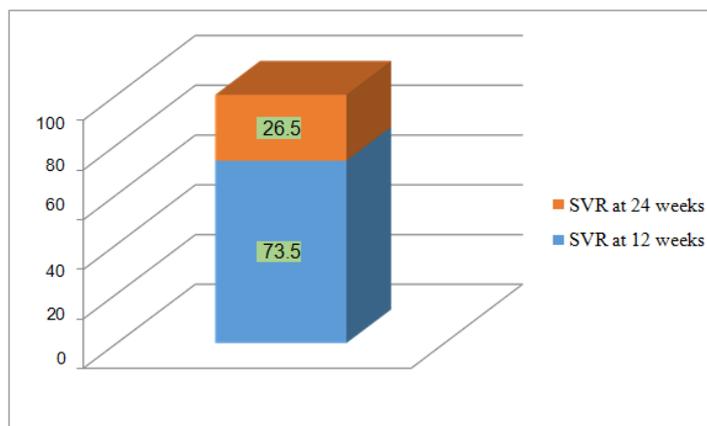


Fig 17:

Table 17 and fig.17 - shows SVR at 12 and 24 weeks after stopping treatment was seen in 100% of patients. SVR at 12 weeks was seen in 73.5% and SVR at 24 weeks was seen in 26.5% of patients.

Table 18: Adverse events experienced by patients.

Adverse events	Frequency	Percent
No	77	72.6
Asthenia ,Fatigue	12	11.3
Epigastric Pain, Anorexia	4	3.8
Anemia ,Thrombocytopenia	2	1.9
Polydipsia	6	5.2
Nausea ,Vomiting	2	1.9
Others	3	2.8
Total	106	100.0

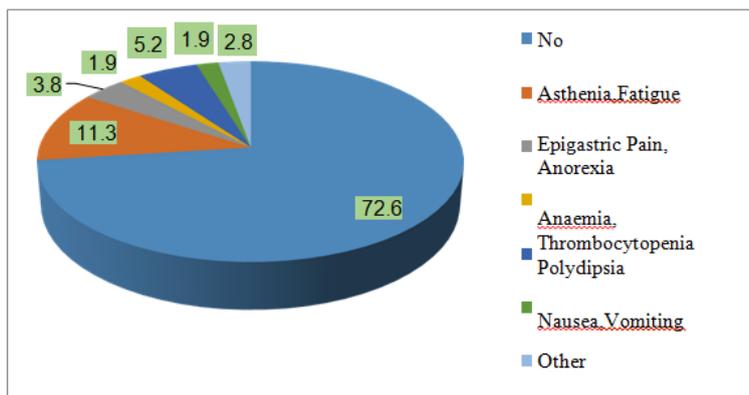


Fig 18:

Table 18 & fig 18- shows adverse events experienced by patients who received anti-viral treatment for HCV. Most of our patients (72.6%) did not experience any adverse

event. Asthenia and fatigue were the common adverse events experienced by other patients.

Table 19: Prior HCV treatment received by positive patients.

Prior HCV treatment	Frequency	Percent
No	96	90.6
Yes	10	9.4
Total	106	100.0

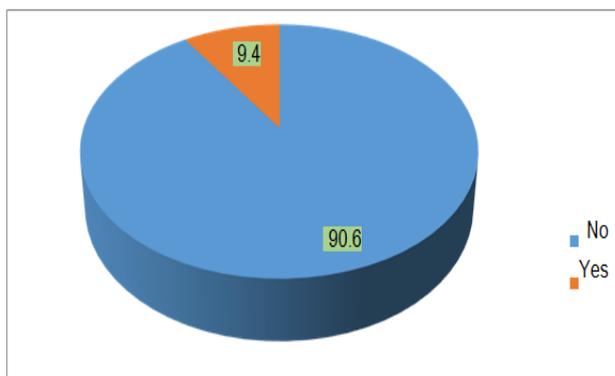


Fig. 19.

Table 19 and fig.19 –reveals that only 10 patients had previous experience with anti- viral treatment for HCV.

Ninety six patients had not received any treatment.

Table 20: Correlation of Sustained virological response (SVR) with Age.

	Years	SVR		Total	P Value
		12 weeks	24 weeks		
AGE	<=20	1	0	1	0.793 (NS)
		1.3%	.0%	0.9%	
	21–35	20	4	24	
		25.3%	14.8%	22.6%	
	36–50	24	10	34	
		30.4%	37.0%	32.1%	
	51–65	23	9	32	
		29.1%	33.3%	30.2%	
66–80	10	3	13		
	12.7%	11.1%	12.3%		
81+	1	1	2		
	1.3%	3.7%	1.9%		
Total	79	27	106		
	100.0%	100.0%	100.0%		

Table 20 - shows that there is no significant association between Sustained virological response and age (P=0.793).

**Table 21: Correlation of Sustained Virological response with Gender.**

		SVR		Total	P value
		12 weeks	24 weeks		
Gender	Male	48	17	65	0.839 (NS)
		60.8%	63.0%	61.3%	
	Female	31	10	41	
		39.2%	37.0%	38.7%	
Total		79	27	106	
		100.0%	100.0%	100.0%	

Table 21 - reveals that SVR was independent of gender. There is a non-significant (P= 0.839) association between SVR and gender.

**Table 22: Correlation of Sustained Virological Response with Genotype.**

		SVR		Total	P Value
		12 weeks	24 weeks		
Genotype	1A	56	18	74	0.778 (NS)
		70.9%	66.7%	69.8%	
	1	1	0	1	
		1.3%	.0%	.9%	
	3	1	1	2	
		1.3%	3.7%	1.9%	
	Not Done	21	8	29	
		26.6%	29.6%	27.4%	
Total		79	27	106	
		100.0%	100.0%	100.0%	

As shown in table 22 - Sustained virological response was independent of genotype as shown in our study. P value (0.778) is non-significant.

**Table 23: Correlation of Sustained virological response with Treatment received (SOF/VEL & SOF/DAC).**

		SVR		Total	P value 0.906
		SVR at 12 weeks	SVR at weeks		
Treatment of HCV	SOFOSBUVIR/ VELPATASVIR	69	25	94	
		88.5%	89.3%	88.7 %	
	SOFOSBUVIR/ DACLATSAVIR DIHYDROCHLORIDE	9	3	12	
		11.5%	10.7%	11.3%	
Total		78	28	106	
		100.0%	100.0%	100.0%	

**Table 24: Correlation of Sustained virological response with Duration of treatment.**

		Duration of treatment		Total	P value 0.889
		3 Months	6 Months		
Treatment of HCV	Sofosbuvir/ Velpatsavir	69	25	94	
		88.5%	89.3%	88.7%	
	Sofosbuvir/ Daclatsavir Dihydrochloride	9	3	12	
		11.5%	10.7%	11.3%	
Total		78	28	106	
		100.0%	100.0%	100.0%	

Table 23 and 24 - summarizes correlation of SVR with treatment received (SOF/VEL & SOF/DAC) and duration of treatment (3 and 6 months). SVR was independent of treatment type and duration.

**Table 25: Values of Various Lab parameters of HCV+ patients on maintenance haemodialysis.**

Parameter	Minimum	Maximum	Mean	Std. Deviation
White blood cell count (WBC $\times 10^3 \mu\text{l}$ )	2.00	17.70	5.6169	1.964
Hemoglobin(g/dl)	4.80	13.20	8.8835	1.534
Platelet count( $\times 10^3 \mu\text{l}$ )	30.00	318.00	164.33	57.32
Urea(mg/dl)	39.00	298.00	149.03	45.91
Creatinine (mg/dl)	4.88	21.00	9.8936	2.96
Calcium(mg/dl)	4.40	10.80	8.5291	0.975
Uric Acid(mg/dl)	2.54	16.30	5.9146	1.91
Bilirubin (mg/dl)	0.11	13.50	0.8727	1.49
SGPT(ALTU/L)	8.00	688.00	104.23	111.11
SGOT(ASTU/L)	3.00	1200.00	85.4874	135.27
ALP(IU/ml)	39.00	680.00	223.77	102.60

Table 25-indicate values of the various lab parameters in hepatitis C positive patients.

## DISCUSSION

Chronic kidney disease (CKD) is a worldwide public health problem, due to the continuous increase in the number of patients. Irrespective of the etiology of CKD, the progressive loss of kidney functions has a strong impact on the health status of the patient. Renal replacement therapy (RRT) by dialysis (hemodialysis or peritoneal dialysis) or kidney transplant, is the necessary treatment for advanced stage CKD.<sup>[91,92]</sup> The infection risk in hemodialysis patients is considerable, explained by impaired immunity and by the need for frequent hospitalizations and surgical interventions. Moreover, hemodialysis itself involves frequent and/or prolonged exposure to blood by means of vascular access and the extracorporeal circuit, and by the proximity of other patients during dialysis, contact with the medical staff, and change of the dialysis machine. The infection with hepatitis C virus (HCV), a particular type of blood-borne viral infection, is relatively common in hemodialysis patients.<sup>[93]</sup> Infection with HCV is a real public health problem worldwide. In 2018, WHO estimated that 3% of the world population was infected with this virus and that 71 million people are chronic carriers' of Hepatitis C. The risk of hepatitis is still a serious problem despite the availability of serological tests for hepatitis and vaccination for hepatitis B virus infection, universal precaution standards and infection control measures.

The present study was conducted in the department of Nephrology at Aga Syed Yousuf Memoreal District hospital Budgam, Kashmir during the years 2023 & 2024 to find out the prevalence of Hepatitis C virus infection in our haemodialysis centers and to evaluate the effectiveness of Sofosbuvir/Velpatasvir and Sofosbuvir/Daclatasvir regime in ESRD patients on maintenance haemodialysis. All the patients were screened for anti-HCV antibodies by third generation ELISA test. HCV-RNA by RT-PCR was used in patients in whom anti-viral treatment was started. The prevalence of Hepatitis C virus was determined in 1330 patients who were on maintenance haemodialysis.

The hypertension was the commonest etiological cause

of CRF (45.3%) in hepatitis C positive patients followed by diabetes (31.3%) and chronic glomerulonephritis (CGN) (6.6%). This was consistent with other studies.<sup>[85,94]</sup> The mean age of hepatitis C positive patients was 48 ranges from 19 to 88 years. The majority of patients were in age group of 36 to 50 years.

The majority of the patients were male (61.3% male & 38.7% females) as with other studies.<sup>[66,100]</sup> The prevalence of hepatitis C virus infection in our study was 14.1% i.e., 188 out of 1330 patients on maintenance haemodialysis.

The prevalence of HBV and HCV in various HD units varies from country to country across the globe and the prevalence in the Indian HD centers continues to be high.

Hinrichsen et al ; (2002) [65] done a multi centric study in 2796 patients from 43 dialysis centers, the overall prevalence of hepatitis C virus (HCV antibody and HCV RNA positivity) was 7% (195 patients). Antibody positivity occurred in 171 patients (6.1%). Viraemia was detected in 111 patients (4%). 24 of 111 HCV RNA positive (21.6%) were negative for HCV antibodies. Thus (0.8%) of the entire study population was HCV positive but could not be diagnosed by routine HCV antibody testing. Major risk factors identified by a standard questionnaire in 1717 of 2796 patients were number of blood transfusions had received and duration of dialysis and concluded that HCV is common in German haemodialysis patients but screening for HCV antibody does not exclude infection with HCV.

Yakaryilmaz F et al; (2006)<sup>[67]</sup> reported that Hepatitis B and Hepatitis C virus infections are important causes of morbidity and mortality in maintenance haemodialysis patients. Although their exact prevalence is not known, HBV and HCV viral infections and occult viral infections are frequent in these patients. Among the patients screened, 25 (13.3%) had HBV infection alone and 38 (20.2%) had HCV infection alone, While 7 (3.7%) had dual infection of both viruses. Serological markers for

occult hepatitis B and occult hepatitis C were positive in five (2.7%) and nine (4.8%) of the patients, respectively. Concluded that both occult and non-occult forms of HCV infection are more prevalent than HBV infection in haemodialysis patients.

Sun J *et al.*; (2009)<sup>[69]</sup> reviewed that pooled prevalence of HCV infection among HD patients in China was 41.1%. No significant difference was found in HCV infection rates between male and female HD patients. HD patients with blood transfusion were 5.65 times more likely to be infected with HCV than HD patients without blood transfusion. A longer duration of HD was associated with increased HCV prevalence. Co-infection with hepatitis B virus did not increase the probability of HCV infection among HD patients.

Aman K *et al.*; (2015)<sup>[72]</sup> done a cross sectional study among patients on maintenance hemodialysis (HD) in three centers in Aden, Yemen. The data from 219 patients and their records over the period between 2000-2013, was extracted and analyzed. Eighty-eight of 219 (40.2%) patients were anti-HCV positive. In this study sample, the prevalence of HCV was significant. Patients attending more than one center and those who underwent HD for longer durations were found to be more likely to contract HCV.

Gomez-Gutierrez C *et al.*; (2015)<sup>[73]</sup> found that the prevalence of hepatitis C infection in hemodialysis patients ranged from 4.2 to 83.9% in Latin America, which was greater than that detected in developed countries. The most common genotype was genotype 1, and subtype 1b was most prevalent, followed by genotype 1a, and concluded patients with pre-existing liver disease, high ALT levels, blood transfusions, transplant surgeries, intravenous drug use are at higher risk of acquiring HCV. PCR is crucial for diagnosing of HCV infection in HD patients.

Masoodi I *et al.*; (2019)<sup>[84]</sup> conducted prospective study from January 2009 to April 2018 at Sheri Kashmir Institute of Medical Sciences, Srinagar, Kashmir. A cohort of 459 end-stage renal disease patients on hemodialysis was enrolled from four dialysis centers and followed in a longitudinal manner. Their seroconversion rates, risk factors were studied. Positive patients were treated and followed up. This study demonstrated HBV seroconversion rate of 7.4 % (n = 34) and HCV seroconversion rate of 10% (n = 46) in a cohort of 459 patients on hemodialysis attending four dialysis centers of Kashmir. Seroconversion was associated with longer duration of dialysis (80.30 ± 30.92 vs 61 ± 9.41 months, P < 0.000).

As per literature review, anti-HCV positive HD patients had received significantly more units of blood products than anti-HCV negative patients.<sup>[90]</sup> The risk of acquiring post-transfusion HCV infection has significantly declined primarily because of availability of better

screening test for HCV and erythropoietin [96]. In our study out of 106 patients only 54 had received blood transfusions.

Duration of dialysis has been reported to be significantly longer among anti-HCV positive patients compared to anti-HCV negative patients. Our results were in contrast to others, we found that most of our patients (63.2%) came positive for HCV in the first two years of their maintenance haemodialysis because of various reasons, most of the patients who were included in our study had a less time on maintenance haemodialysis, frequency of change in HD units during first few months of MHD, most patients were anemic during initial phase of MHD so they have received more blood transfusions and nosocomial transmission could be there as on for this increased prevalence.

Furthermore, it has been shown by various studies that the prevalence of HCV infection among HD patients was significantly associated with history of receiving HD at more than one HD center.<sup>[72,100]</sup> In the present study out of 106 patients, 76 patients had attended more than one Centre.

HCV RNA level was available in all patients who received treatment for HCV. The minimum range was 85.8 IU/ml and the maximum range was 14×10<sup>8</sup> IU/ml. Genotyping was available for 77/106 (72.6%) patients. The most common genotype in our study population was 1a, followed by genotype 3 and genotype 1. Seventy four patients or 69.8% were carriers of genotype 1a, 2 patients or 1.9% were carriers of genotype 3 and 1 patient or 0.9% was a carrier of genotype 1. This was consistent with other studies.<sup>[74,85,86]</sup>

All the HCV + patients had arteriovenous fistula as venous vascular access, 96.2% of patients were on dialysis two times a week while 3.8% were receiving dialysis three times a week. Among 106 HCV positive patients, 34.9% of patients had a history of previous surgery and dental check. 88.7% of patients were married. 50.9% of patients had a BMI (kg/m<sup>2</sup>) in the range of 18-23.

Blood grouping was available in 94/106 (88.6%) patients. The most prevalent blood groups were blood group O (37.7%), blood group B (23.6%), blood group A (17.9%) and blood group AB (9.4%) in accordance with other studies.<sup>[97]</sup>

Hepatic fibrosis was assessed by Fibroscan before the start of drug therapy. Assessment of liver stiffness measurement (LSM) using Fibroscan was available in only 47 patients. No liver scarring or mild scarring (Fo-F1) was seen in 7 patients (6.6%), moderate liver scarring (F2) was seen in 7 patients (6.6%), severe liver scarring was seen in 26 patients (24.5%), and advanced liver scarring (cirrhosis) was seen in 7 patients (6.6%). All HCV positive (106) patients received antiviral

treatment for moderate to severe viral hepatitis. 94 patients (88.7%) received Sofosbuvir/Velpatsavir while 12 patients (11.3%) received Sofosbuvir/Daclatsavir Dihydrochloride. 78 patients (73.6%) received treatment for 3 months while 28 patients (26.4%) received treatment for 6 months. 10/106 (9.4%) patients had been previously treated for HCV. 9 patients had an experience with Sofosbuvir/Velpatsavir while 1 patient was treated with interferon therapy previously.

Sustained virologic response (SVR) defined as a negative viral load at 12/24 weeks after therapy, was achieved by all patients. Plasma levels of HCV RNA declined rapidly with treatment, with all patients (100.0%) having HCV RNA < lower limit of quantitation (LLOQ) after 4 weeks of treatment. No patients experienced on-treatment virologic failure. Regarding the safety of antiviral treatment/therapy, most of the patients (72.6%) in our study did not experience any adverse event. Remaining 27% of patients experienced mild to moderate adverse events. The most common adverse events were asthenia or fatigue (11.3%), polydipsia (5.2%), epigastric pain/Dyspepsia (3.8%), anorexia (3.8%), nausea and vomiting (2%) anemia and thrombocytopenia (1.9%), others (2.8%). No patient had treatment discontinuation due to side effects.

Treatment with Sofosbuvir/Velpatsavir was generally safe and well tolerated, with a safety profile consistent with that expected for patients with ESRD undergoing dialysis. There were no treatment related discontinuations or serious adverse events. Overall, the safety and efficacy results from this study are consistent with those observed in the ASTRAL-1, ASTRAL-2, ASTRAL-3, ASTRAL-5, POLARIS-2, and POLARIS-3 clinical trials of Sofosbuvir/Velpatsavir, which demonstrated that treatment with Sofosbuvir/Velpatsavir for 12 weeks was well tolerated and resulted in high SVR rates across HCV genotypes in patients with or without compensated cirrhosis.<sup>[74,75]</sup>

Feld JJ *et al.* (2015)<sup>[74]</sup> conducted a multicenter phase 3, double-blind, placebo-controlled study involving untreated and previously treated patients with chronic HCV genotype 1, 2, 4, 5, or 6 infection, including those with compensated cirrhosis. Patients with HCV genotype 1, 2, 4, or 6 were randomly assigned in a 5:1 ratio to receive the nucleotide polymerase inhibitor Sofosbuvir and the NS5A inhibitor Velpatsavir in a once-daily, fixed-dose combination tablet or matching placebo for 12 weeks. Of the 624 patients who received treatment with Sofosbuvir-Velpatsavir, 34% had HCV genotype 1a, 19% genotype 1b, 17% genotype 2, 19% genotype 4, 6% genotype 5, and 7% genotype 6. The rate of sustained virologic response among patients receiving Sofosbuvir-Velpatsavir was 99%. Two patients receiving Sofosbuvir-Velpatsavir, both with HCV genotype 1, had a virologic relapse. None of the 116 patients receiving placebo had a sustained virologic response. Serious adverse events were reported in 15 patients (2%) in the

Sofosbuvir-Velpatsavir group and none in the placebo group.

Foster GR, *et al.* (2015)<sup>[75]</sup> conducted multicenter two randomized, phase 3, open-label studies involving patients who had received previous treatment for HCV genotype 2 or 3 and those who had not received such treatment, including patients with compensated cirrhosis. In one trial, patients with HCV genotype 2 were randomly assigned in a 1:1 ratio to receive Sofosbuvir-Velpatsavir, in a once-daily, fixed-dose combination tablet (134 patients), or Sofosbuvir plus weight-based ribavirin (132 patients) for 12 weeks. In a second trial, patients with HCV genotype 3 were randomly assigned in a 1:1 ratio to receive Sofosbuvir-Velpatsavir for 12 weeks (277 patients) or Sofosbuvir-ribavirin for 12 weeks (275 patients). The primary end point for the two trials was a sustained virologic response at 12 weeks after the end of therapy. Among patients with HCV genotype 2, the rate of sustained virologic response in the Sofosbuvir-Velpatsavir group was 99% which was superior to the rate of 94% in the Sofosbuvir-ribavirin group ( $P=0.02$ ). Among patients with HCV genotype 3, the rate of sustained virologic response in the Sofosbuvir-Velpatsavir group was 95% which was superior to the rate of 80% in the Sofosbuvir-ribavirin group ( $P<0.001$ ). The most common adverse events in the two studies were fatigue, headache, nausea, and insomnia. They concluded that patients with HCV genotype 2 or 3 with or without previous treatment, including those with compensated cirrhosis, 12 weeks of treatment with Sofosbuvir-Velpatsavir resulted in rates of sustained virologic response that were superior to those with standard treatment with Sofosbuvir-ribavirin.

The response rates are also consistent with the study of Khan RA *et al.* (2018).<sup>[81]</sup> They conducted observational, prospective, single-center study from December 2017 till September 2018 at the Nawaz Sharif Kidney Hospital, Swat, Pakistan. Total 27 HCV- HD subjects on SOF/DAC regime for 12 weeks, were enrolled in the study. As per the results of 27 subjects', ( $n=$  female 12, 44.5% and  $n=$  male 15, 55.5%), 21 subjects were naive and 6 belonged to treatment experienced group with a mean age of  $35.5 \pm 9.6$  years. On SOF/DAC treatment for 12 weeks, the sustained virological response rate was 100% (27 of 27) at 12 weeks. 95% confidence interval, (95 to 100). No patients had a virologic failure during treatment. They reported that regime of full dose SOF and DAC therapy is well tolerated, safe and with a high rate of Sustained Viral Response (SVR) in both naive and treatment experienced group of HD Pakistani patients with HCV.

The safety profile and response rates are also consistent with results from a phase IIb study, which demonstrated that treatment of ledipasvir (an NS5A inhibitor) combined with Sofosbuvir once daily for 12 weeks in HCV-infected patients with ESRD was well tolerated and resulted in an SVR12 rate of 100%.<sup>[98]</sup>

We studied the correlation of sustained virological response (SVR) with gender, age, and genotype.

In our study there was no significant association between genotype and SVR. The response rate was same with all genotypes. This is consistent with other studies<sup>[80,88]</sup> where they found that there was no difference in response rates in relation to genotype.

We did not find a significant difference of sustained virological response with age and gender in accordance with other studies.<sup>[99]</sup>

We also studied the biochemical profile of hepatitis C positive patients. The mean range of urea and creatinine was  $149 \pm 45.9$  and  $9.8 \pm 2.96$ . Calcium was in the range of 4.4 to 10.8. There was no marked elevation of uric acid in hepatitis C positive patients, mean uric acid level was  $5.9 \pm 1.9$ . Most of our patients were anemic, mean Hb level was  $8.8 \pm 1.5$ g/dl.

Bilirubin was slightly increased in some patients, mean bilirubin level was  $0.87 \pm 1.49$ . The ALT and AST levels were markedly high in these patients, mean level of ALT was  $104 \pm 111$  and AST  $85 \pm 135$ . Similarly ALP was also in the higher range, mean value  $223 \pm 102$ .

#### SUMMARY AND CONCLUSION

A total of 1330 patients on maintenance haemodialysis were enrolled from 11 haemodialysis centers to study the prevalence of Hepatitis C virus infection and effectiveness of Sofosbuvir/Velpatsavir and Sofosbuvir/Daclatasvir Dihydrochloride regimen in patients with end stage renal disease (ESRD) on maintenance hemodialysis. The data obtained was analyzed to find out the prevalence of hepatitis C virus infection in patients on maintenance haemodialysis and to evaluate the safety and efficacy of antiviral therapy received by our patients so as to ensure the better management of already infected ones. The following conclusions were drawn from study:

- The prevalence of hepatitis C virus infection in hemodialysis units in our setup was 14.1%.
- The hypertension was the leading cause of CRF (45.3%) in hepatitis C positive patients followed by diabetes (31.3%) and chronic glomerulonephritis (CGN) (6.6%).
- Male predominance over females was seen in study group patients.
- Most of the patients (88.7%) were married.
- All the HCV + patients had arteriovenous fistula as venous vascular access.
- The most common genotype in our study population was 1a, followed by genotype 3 and genotype 1.
- The most prevalent blood group among Hep.C positive patients was blood group O (37.7%), blood group B (23.6%), blood group A (17.9%) and blood group AB (9.4%).
- There was marked elevation of AST and ALT levels

in hepatitis C positive patients.

- Severe liver scarring was seen in most of our patients (24.5%) while advanced liver scarring (cirrhosis) was seen in 7 patients (6.6%) patients.
- Most of the hepatitis C positive patients were anemic.

Lack of an effective vaccine and the increased risk of serious complications, have made prevention and early detection of HCV extremely important. One of the main concerns in HCV transmission is its potential for nosocomial spread. Stringent universal precautions in the dialysis units and availability of isolated area and separate dialysis machines for infected patients will lead to reduced cross-contamination and nosocomial infection among patients.

CDC recommends that special precautions should be observed in dialysis units. These include wearing and changing of gloves and water-proof gowns between patients, systematic decontamination of the equipment circuit and surfaces after each patient treatment and no sharing of instruments (e.g., tourniquets) or medications (e.g., multidose vials of heparin) among patients.

The high percentage of HCV prevalence in this study could be partly attributed to the shortage of nursing staff, in an environment of a high prevalence of HCV positivity in our region. Further, invariably our HD units remain crowded units due to limited resources. Last but not least there are inadequate infection control policies and procedures in this part of the globe.

- All our patients received Sofosbuvir/Velpatsavir or Sofosbuvir/Daclatasvir Dihydrochloride treatment for moderate to severe viral hepatitis for 12 and 24 weeks.
- Sustained virological response at 12 and 24 weeks after stopping treatment was seen in 100% of the patients.
- No patients experienced on-treatment virologic failure.
- No patient had treatment discontinuation due to side effects.
- Sustained virological response was independent of age, gender, genotype and drug received.

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