Original Article

Exploring the Impact of 12-week Direct Acting Antiviral Therapy on Laboratory Parameters in HCV Patients: A Comparative Study

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ABSTRACT

Objective: The present study was designed to understand the hematological and chemical aspects of the patients undergoing 12-week DAA treatment therapy

Study Design: A prospective study

Place and Duration of Study: This study was conducted at the Department of Urology & Dialysis, District Headquarter Hospital Jhelum, from December 2022 to November 2023.

Methods: For clinical chemistry evaluation, serum creatinine, total bilirubin, aspartate transaminase (AST) and alanine transaminase (ALT) was tested on Cobas c701 (Roche®). For hematological evaluation, complete blood count (CBC) was done using an automated hematology analyzer (Sysmex KX-21, Japan).

Results: In this study, 380 HCV patients, including 253 male (66.5%) and 127 females (33.4%), are evaluated for the impact of Direct-Acting Antiviral (DAA) treatment. The hemoglobin (HGB) levels of males were found to start at 14.51±1.21g/dL and those of females at 12.22±1.38g/dL, according to the hematological analysis. There were 234.21±53.26x10^6/µL of platelets in the males and 218.53±42.17x10^6/µL in the females. With a decrease from 41.72±3.47% to 36.41±1.95% for males and from 39.18±2.62% to 35.74±1.67% for females, hematocrit (HCT) levels were seen in HCV patients. The concentration and mean corpuscular hemoglobin (MCH) varied significantly across the HCV patients. Reduced levels of ALT (from 50.2±8.4 IU/L to 22.35.1 IU/L) and AST (from 42.5±6.3 IU/L to 19.6±4.9 IU/L) were indicative of beneficial effects on liver function, according to hepatic parameters. HCV patients (male & females) showed improvement in renal indicators, including urea and creatinine levels.

Conclusion: The study provides a comprehensive understanding of the demographic, laboratory parameters and physiological intricacies associated with DAA therapy. The study also identified gender-based variations underscore the inevitability for initialed approaches in DAA treatment.

Key Words: HCV-Patients, Males & Females, DAA treatment, Hematological parameters, and Biochemical parameters

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INTRODUCTION

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Hepatitis C virus (HCV) is a major cause of liver-related mortality and morbidity, including cirrhosis and hepatocellular carcinoma, globally. The goal of treating this infection is to achieve a sustained virological response (SVR), which means that there is no detectable viral ribonucleic acid (RNA) six months after completing the treatment (Pawlotsky et al., 2020)[1]. Typically, an SVR is linked to the normalization of liver enzymes and the improvement or regression of liver necroinflammation and fibrosis, as well as an enhancement in liver function (Carrat et al., 2019; Mandorfer et al., 2020; Mauro et al., 2018)[2-4]. Patients with cirrhosis who clear HCV experience a notable reduction in the risk of HCC and liver-related mortality (Van Der Meer et al., 2012)[5]. However, it is important to note that the risk is not completely eliminated. This is particularly true for patients who have cofactors of liver morbidity, such as the metabolic syndrome, harmful alcohol consumption, and/or concurrent

hepatitis B virus (HBV) infection (Ioannou et al., 2018; Li et al., 2018; Nahon et al., 2017)[6-8].

There appears to be a correlation between achieving rapid virological response (RVR) and complete early virological response (cEVR) and the chances of achieving sustained virological response (SVR) in the treatment of HCV infection (Van Der Meer et al., 2012)[5]. In order to achieve a sustained virological response (SVR), it is crucial for patients to meet specific milestones throughout their treatment. These milestones involve the lack of detectable HCV RNA after 12 weeks of treatment (cEVR) or a notable reduction in HCV RNA levels at the 12th week of treatment (pEVR). Patients who fail to meet these milestones have a reduced likelihood of achieving SVR, even with an additional 36 weeks of treatment (Cacoub, Commarmond, Sadoun, & Desbois, 2017; Li et al., 2018; Thi Thu et al., 2023)[9,7,10].

Interferon based treatment regimens developed initially for HCV infection, have been associated with low cure rates and numerous adverse effects (Mandorfer et al., 2020)[3]. With the introduction of direct-acting antivirals (DAAs), significant advancements have been made in the treatment of HCV infection. Cure rates have soared to nearly 100%, and the duration of therapy has been significantly reduced, resulting in fewer side effects (Sarrazin et al., 2016)[11]. In recent years, there has been a notable shift in hepatitis C treatment guidelines due to the emergence of DAAs. Targeting key stages of the HCV life cycle, DAAs have been found to result in a higher treatment response and fewer side effects compared to traditional therapy involving interferon and ribavirin (RBV) (Bhattacharjee, Singh, Das, Chaudhuri, & Mukhopadhyay, 2021; Gutierrez, Lawitz, & Poordad, 2015)[12-13].

So, the present study was designed to understand the hematological and chemical aspects of the patients undergoing 12-week DAA treatment therapy. This could potentially help clinicians in fashioning the therapeutic regimen as per individual groups in correspondence to their response to DAA treatment. For this purpose, we recruited patients presenting with clinically diagnosed PCR confirmed HCV patients and analyzed their blood parameters for different age and gender groups.

METHODS

It was a prospective study which was conducted from December 2022 to November 2023 at department of Urology & Dialysis, District Headquarter Hospital Jhelum. A total of 380 PCR confirmed chronic HCV infected patients met the inclusion criteria were included.

Patient assessment and data collection: Data for the research study were obtained by electronic medical records and through physical examinations conducted by clinicians. Patients were examined to evaluate their adherence to medication and assess their test results. At the beginning of the study, all patients underwent an evaluation that included taking their medical history and obtaining a comprehensive clinical profile. Sustained virological response (SVR) was assessed at the conclusion of therapy using quantitative evaluation of HCV RNA using PCR along with hematological and biochemical profile (Wai et al., 2003)[14].

Clinical chemistry and hematological assessment: For clinical chemistry evaluation, serum creatinine, total bilirubin, aspartate transaminase (AST) and alanine transaminase (ALT) was tested on Cobas c701 (Roche®). For hematological evaluation, complete blood count (CBC) was done using an automated hematology analyzer (Sysmex KX-21, Japan). These tests were performed before (baseline) and after the completion of the study. Appropriate sample collection and timely processing of samples were ensured throughout this process (Ibrahim, Elsaied, & Research, 2023)[15].

Ethical considerations: The study protocols underwent a thorough assessment and received approval from the Institutional Review Board (IRB) of District Headquarter Hospital, Jhelum, under registration no. 0311 prior to the initiation of the research, the study methods, expected outcomes and benefits were explained to each participant. Since it was not an intervention-based study, so there was no harm to the patients. Informed consent forms were signed by all the study participants (Hussein, Nafady, Hassan, & Diseases, 2022)[16].

Inclusion criteria: Only those patients who willingly agreed to participate from both genders were diagnosed with chronic HCV infection, belonged to age group over 25-55 years and were not diagnosed with any other illness, included in this study. Only HCV PCR-confirmed patients were recruited for the study (Hussein et al., 2022)[16].

Exclusion criteria: The study exclusion criteria were set so that these aspects cannot affect the outcome of this study. These included the age group over 60 and below 18, patients who had known pathological/hematological abnormalities or diseases, comorbidities, patients who were diagnosed with hepatocellular carcinoma, pregnant women and those who refused to participate in the study (Hussein et al., 2022)[16].

Data Interpretation: All the data from medical reports and clinical charts were gathered in Microsoft Excel (2016). The analysis was conducted using SPSS version 20. The continuous data was presented as the mean ± standard deviation, while the nominal data was presented as frequencies and percentages. Baseline continuous data were compared to the data collected after the course of therapy using probability. The level of confidence was maintained at 95%, so a P value was

deemed significant if it was less than 0.05 (Mauro et al., 2018)[4].

RESULTS

Demographics of patients with Hepatitis-C

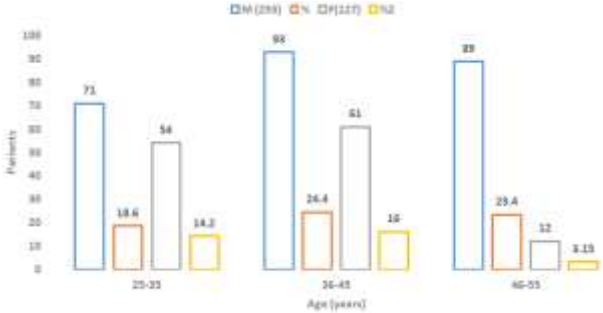

Figure No. 1: Demographic distribution of age groups among patients with Hepatitis-C

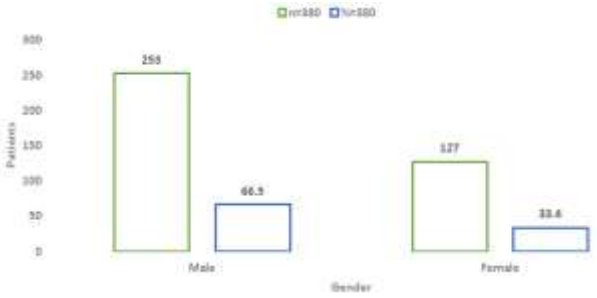

Figure 2: Demographic distribution of Gender among patients with Hepatitis-C

Hematological Profiling before Direct-Acting Antiviral therapy in HCV-Patients

Table No. 1: Comparison of Baseline Hematological Parameters between Males and Females before Direct-Acting Antiviral Therapy in HCV patients

Lab parameters	SI (Unit)	Baseline (Makhlouf et al.[17])	Baseline (Female)	P-value
HGB	g/dL	14.51±1.21	12.22±1.38	>0.05
Platelets	$x10^3/\mu L$	234.21±53.26	218.53±42.17	>0.06
WBCs	$x10^6/\mu L$	4.93±0.45	4.19±0.36	0.5
HCT	%	41.72±3.47	39.18±2.62	<0.05*
MCV	fl	88.13±5.22	83.43±4.67	<0.06
MCH	pg	26.73 ±3.21	25.33 ±1.95	<0.001**
MCHC	g/dL	32.17±0.93	31.29±0.91	<0.05*

Femtoliter (Towfighi et al.)[18], Pictogram (pg), Gram per deciliter (g/dL), Hemoglobin (HGB), White Blood Cells (WBCs), Hematocrit (HCT), Mean Corpuscular Volume (MCV), Mean Corpuscular Hemoglobin (MCH), Mean Corpuscular Hemoglobin Concentration (MCHC), Hepatitis-C (HCV) and **Significant at <0.05.

Hematological Profiling After 12-week of Direct Acting Antiviral (DAA) Therapy

Table No. 2: Hematological Parameter Changes during 12-week of Direct-Acting Antiviral Therapy in Males in HCV patients

Lab parameters	**SI (Unit)**	**Baseline (M)**	**DAA 4-weeks**	**DAA 8-weeks**	**DAA 12-weeks**
HGB	g/dL	14.51±1.21	12.22±1.38	11.8±1.15	11.2±1.03
Platelets	$x10^3/\mu L$	234.21±53.26	218.53±42.17	205.64±38.52	198.29±34.79
WBCs	$x10^6/\mu L$	4.93±0.45	4.19±0.36	3.98±0.31	3.72±0.27
HCT	%	41.72±3.47	39.18±2.62	37.93±2.18	36.41±1.95
MCV	fl	88.13±5.22	83.43±4.67	80.72±4.15	78.49±3.71
MCH	pg	26.73±3.21	25.33±1.95	24.57±1.72	23.84±1.48
MCHC	g/dL	32.17±0.93	31.29±0.91	30.85±0.82	30.42±0.75

Femtoliter (Towfighi et al.)[18], Pictogram (pg), Gram per deciliter (g/dL), Hemoglobin (HGB), White Blood Cells (WBCs), Hematocrit (HCT), Mean Corpuscular Volume (MCV), Mean Corpuscular Hemoglobin (MCH), Mean Corpuscular Hemoglobin Concentration (MCHC), Hepatitis-C (HCV) and Direct Acting Antiviral (DAA).

Table No. 3: Hematological Parameter Changes during 12-week of Direct-Acting Antiviral Therapy in Females in HCV patients

Lab parameters	SI (Unit)	Baseline (F)	DAA 4-weeks	DAA 8-weeks	DAA 12-weeks
HGB	g/dL	12.22±1.38	11.8±1.15	11.5±1.08	11.2±1.03
Platelets	$x10^3/\mu L$	218.53±42.17	205.64±38.52	198.29±34.79	192.15±31.62
WBCs	$x10^6/\mu L$	4.19±0.36	3.98±0.31	3.82±0.27	3.68±0.24

HCT	%	39.18±2.62	37.93±2.18	36.82±1.91	35.74±1.67
MCV	fl	83.43±4.67	80.72±4.15	78.95±3.81	77.21±3.48
MCH	pg	25.33±1.95	24.57±1.72	23.94±1.48	23.32±1.25
MCHC	g/dL	31.29±0.91	30.85±0.82	30.47±0.74	30.12±0.68

Femtoliter (Towfighi et al.)[18], Pictogram (pg), Gram per deciliter (g/dL), Hemoglobin (HGB), White Blood Cells (WBCs), Hematocrit (HCT), Mean Corpuscular Volume (MCV), Mean Corpuscular Hemoglobin (MCH), Mean Corpuscular Hemoglobin Concentration (MCHC), Hepatitis-C (HCV) and Direct Acting Antiviral (DAA).

Chemical pathology of patients before Direct Acting Antiviral therapy HCV-Patients

Table No. 4: Comparison of Baseline Biochemical Parameters between Males and Females before Direct-Acting Antiviral Therapy

Lab Parameters	Baseline (M)	Baseline (F)
ALT	50.2±8.4	43.0±7.2
AST	42.5±6.3	39.2±5.8
Bilirubin	2.8 ± 0.8	1.9±0.6
ALP	80.6 ± 13.2	76.5±12.0
Urea	28.4 ± 6.1	21.0±5.5
Creatinine	0.9 ± 0.2	0.6±0.1

Alanine Aminotransferase (ALT), Aspartate Aminotransferase (AST), Alkaline Phosphatase (Berkman, Sheridan, Donahue, Halpern, & Crotty)[19], Hepatitis-C (HCV).

Table No. 5: Biochemical Parameter Changes in Males during 12 weeks Direct-Acting Antiviral Therapy in HCV patients

Lab Parameters	Baseline (M)	DAA 4 Weeks	DAA 6 Weeks	DAA 12 Weeks	P-value
ALT	50.2±8.4	30.1 ± 8.7	25.5 ± 6.3	22.3 ± 5.1	0.03
AST	42.5±6.3	25.7 ± 6.2	21.8 ± 5.8	19.6 ± 4.9	0.05
Bilirubin	2.8 ± 0.8	1.2 ± 0.3	1.1 ± 0.2	1.0 ± 0.2	0.07
ALP	80.6 ± 13.2	75.3 ± 10.9	72.2 ± 9.7	70.5 ± 8.6	0.05
Urea	28.4 ± 6.1	22.1 ± 3.6	20.3 ± 2.9	18.7 ± 2.5	0.04
Creatinine	0.9 ± 0.2	0.8 ± 0.1	0.8 ± 0.1	0.7 ± 0.1	0.001**

Alanine Aminotransferase (ALT), Aspartate Aminotransferase (AST), Alkaline Phosphatase (Berkman et al.)[19], Hepatitis-C (HCV) and **Significant at <0.05.

Table No. 5(a): Biochemical Parameter Changes in Females during 12 weeks Direct-Acting Antiviral Therapy in HCV patients

Lab Parameters	Baseline (F)	DAA 4 Weeks	DAA 6 Weeks	DAA 12 Weeks	P-value
ALT	43.0±7.2	38.5±7.3	31.0±5.8	21.2±4.9	0.05
AST	39.2±5.8	38.3±6.0	26.5±5.5	19.2±4.5	0.03
Bilirubin	1.9±0.6	1.4±0.2	1.2±0.2	0.9±0.2	0.001**
ALP	76.5±12.0	68.2±9.5	65.0±8.2	66.3±7.0	0.07
Urea	21.0±5.5	20.2±3.2	18.5±2.5	17.0±2.0	0.06
Creatinine	0.6±0.1	0.7±0.1	0.7±0.1	0.6±0.1	0.02

Alanine Aminotransferase (ALT), Aspartate Aminotransferase (AST), Alkaline Phosphatase (Berkman et al.)[19], Hepatitis-C (HCV) and **Significant at <0.05.

DISCUSSION

This comprehensive study explores the multifaceted impact of Direct-Acting Antiviral (DAA) therapy on 380 HCV patients, offering insights into demographic, hematological, and physiological parameters. In the demographic analysis, the gender distribution revealed 253 males (66.5%) and 127 females (33.4%). Further delineation by age groups disclosed intriguing patterns, emphasizing the need for nuanced considerations in DAA therapy across various demographics.

We found aligned results as (Ibrahim & Elsaied, 2023)[15] reported in their study, HCV patients (males) exhibited higher baseline hemoglobin (HGB) levels (14.51±1.21 g/dL) compared to females (12.22±1.38 g/dL). Platelet counts for HCV patients (males) were 234.21±53.26x10^6/µL, and for females, they were 218.53±42.17x10^6/µL, with similar trends over the 12-week DAA therapy period. White blood cell counts demonstrated a decline from 4.93±0.45x10^3/µL at baseline to 3.72±0.27x10^3/µL at 12 weeks in HCV patients (males). HCV patients (females) exhibited a

decline from 4.19±0.36x10^3/µL to 3.68±0.24x10^3/µL over the same period.

Regarding hematocrit (HCT), HCV patients (males) showed a decline from 41.72±3.47% at baseline to 36.41±1.95% at 12 weeks, while females exhibited a decline from 39.18±2.62% to 35.74±1.67%. Mean Corpuscular Volume (MCV) demonstrated a decreasing trend in both genders, with HCV (males) declining from 88.13±5.22 fl to 78.49±3.71 fl, and females from 83.43±4.67 fl to 77.21±3.48 fl as described by (Lishnevska & Chemych, 2020b)[20].

The study of (Makhlouf et al., 2021)[17] delved into mean corpuscular hemoglobin (MCH) and mean corpuscular hemoglobin concentration (MCHC), showing significant gender-based differences. HCV patients (males) exhibited MCH levels of 26.73±3.21 pg and MCHC levels of 32.17±0.93 g/dL, while females had lower values at 25.33±1.95 pg and 31.29±0.91 g/dL, respectively.

Moving to hepatic parameters, HCV patients (males) displayed higher baseline ALT levels (50.2±8.4 IU/L) than females (39.2±5.8 IU/L), showcasing gender variations in liver health. DAA therapy demonstrated a consistent positive effect on liver function, with ALT levels decreasing to 22.35±1.1 IU/L in HCV patients (males) and 21.2±4.9 IU/L in females at 12 weeks as aligned with (Desai, Ansari, Makwana, Jadeja, & Gusani, 2020)[21]. AST levels followed a similar trend, dropping from 42.5±6.3 IU/L in HCV patients (males) and 39.2±5.8 IU/L in females at baseline to 19.6±4.9 IU/L and 19.2±4.5 IU/L, respectively, at 12 weeks (Lishnevska & Chemych, 2020a)[22]. Bilirubin levels showed a decreasing trend in both genders, with HCV (males) decreasing from 2.8±0.8 mg/dL to 1.0±0.2 mg/dL and females from 1.9±0.6 mg/dL to 0.9±0.2 mg/dL at 12 weeks. Alkaline Phosphatase (Berkman et al.)[19] levels exhibited a decline in HCV patients (males) from 80.6±13.2 IU/L to 70.5±8.6 IU/L and in females from 76.5±12.0 IU/L to 66.3±7.0 IU/L at 12 weeks, indicating a positive effect of DAA therapy on liver health (El Kassas et al., 2022)[23].

Renal parameters demonstrated noteworthy changes. Urea levels in HCV patients (males) decreased from 28.4±6.1 mg/dL at baseline to 18.7±2.5 mg/dL at 12 weeks (Saif-Al-Islam et al., 2020)[24]. Creatinine levels in HCV patients (males) decreased from 0.9±0.2 mg/dL to 0.6±0.1 mg/dL at 12 weeks. In HCV patients (females), urea levels decreased from 21.0±5.5 mg/dL to 17.0±2.0 mg/dL, and creatinine levels fluctuated from 0.6±0.1 mg/dL to 0.6±0.1 mg/dL at 12 weeks, signifying positive changes in renal function due to DAA therapy (Shiha et al., 2020)[25].

CONCLUSION

In conclusion, this study provides a comprehensive understanding of the demographic and physiological intricacies associated with DAA therapy. We identified HCV patient's variations underscore the necessity for personalized approaches in DAA treatment. These findings contribute valuable insights to the evolving landscape of DAA therapy, emphasizing the importance of considering gender-specific factors for optimized patient care. Further research is warranted to validate and extend these observations, fostering a deeper understanding of the nuanced effects of DAA therapy across diverse patient populations.

Author's Contribution:

Concept & Design of Study:	Saeed Anwar
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Data Analysis:	Sajid Ali Ahmad, Muhammad Tariq, Saeeda Itrath Batool
Revisiting Critically:	Saeed Anwar, Hira Arif
Final Approval of version:	Saeed Anwar

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Ethical Approval: No. 0311/SMI dated 13.09.2022

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