



Effect of Direct Acting Antiviral Drugs on HbA1c in Type 2 Diabetic Patients Infected with Chronic Hepatitis C Infection

Amna Ehsan¹, Wajeeha Gull², Arwa Shahid³, Zubia Jamil¹

¹Department of Medicine, Fauji Foundation Hospital, Rawalpindi, Pakistan

²Department of Medicine, CMH Gujranwala, Gujranwala, Pakistan

³Department of Medicine, CMH Multan, Multan, Pakistan

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Correspondence to: Amna Ehsan, Department of Medicine, Fauji Foundation Hospital, Rawalpindi, Pakistan. Email: amna.ehs11@gmail.com

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ABSTRACT

Background: There is emerging evidence that direct acting antiviral therapy in HCV patients affect insulin resistance. This study is being conducted to study the impact of direct acting antiviral drugs on glycaemic control in terms of pre- and post-treatment mean HbA1C among hepatitis C virus positive diabetic patients, treated at tertiary care hospital of northern Pakistan. **Material and Methods:** This Quasi-Experimental Model study was conducted between 6 Feb 2025 to 31st May 2025 at the Hepatology Department, Fauji Foundation Hospital, Islamabad. A total of 60 male and female diabetic patients with confirmed HCV positive and planned for DAA therapy and having age between 18-75 years were enrolled using the non-probability consecutive sampling after getting a written informed consent. Baseline HbA1c was determined and patients were followed up monthly. After four weeks of the treatment, the HbA1c and values were repeated. Data was analyzed using SPSS software version 25. Study confounders like were controlled by the stratification. Post stratification, paired *t*-test was used to see the statically significant difference (*p*-value ≤ 0.05). **Results:** The mean age was 51.42 ± 13.35 years, with a predominance of female participants (70%). Paired sample analysis showed that the mean pre-treatment HbA1c was $8.90 \pm 2.19\%$, which significantly decreased to $7.42 \pm 1.41\%$ following completion of DAA therapy. The mean reduction in HbA1c was 1.48% (95% CI: 1.20–1.76). This improvement was statistically significant (paired *t*-test: $t = 10.60$, $df = 59$, $p < 0.001$). A strong positive correlation was observed between pre- and post-treatment HbA1c values ($r = 0.91$, $p < 0.001$). **Conclusion:** The current research proves that a direct-acting antiviral (DAA) treatment of hepatitis C virus (HCV) infection is linked to a meaningful increase in glycaemic control in patients with type 2 diabetes mellitus (T2DM), indicating that the glycated haemoglobin (HbA1c) level declined consistently within all the investigated groups. HCV treatment does not only reduce hepatic complications but also enhances the management of diabetes, which may reduce long-term vascular complications and healthcare expenses, as well.

INTRODUCTION

Hepatitis C virus constitutes a major healthcare burden among low resource countries such as Pakistan, where it is estimated to affect 4.8% of the general population; however, it affects around 58 million peoples globally [1]. Lack of preventive measures during sexual relationships and unsafe healthcare practices are among the major causes of transmission [2,3].

Past studies reflected that chronic HCV infection may leads to severe insulin resistance and indicated a potential reciprocal link between diabetes and HCV infection [4].

Since direct-acting antiviral (DAA) medications have equally high cure rates among diabetic patients, there is increasing interest in the study of impact of this

medication on glyceimic control by studying the HbA1c levels [5]. According to recent research, individuals with type 2 diabetes may have improvements in their HbA1c and insulin sensitivity after successfully eradicating their HCV with DAAs [6]. The extent and durability of this impact, however, are still up for question; whilst some studies demonstrate considerable decreases in HbA1C [7]. In a recent study, Hagag RY et al, investigated the impact of DAAs therapy on glyceimic status among HCV patients and they found that pretreatment mean HbA1C was 8.34 ± 1.59 while post treatment mean HbA1C was 7.51 ± 0.86 in the same population with no change in standard treatment. This was a statistically significant difference (*p*-value 0.001) [8].

Even while research from throughout the world is expanding, there isn't much information from South Asia, especially Pakistan, where T2DM and HCV are both widespread. Furthermore, differences in healthcare accessibility, socioeconomic position, and genetic makeup may affect how the DAA treatment responds to the body and how that affects HbA1c levels [9]. Thus, in order to provide important insights into the potential metabolic benefits of HCV eradication in our local population, where both diseases impose significant public health and economic burdens, this study intends to evaluate the effect of DAA therapy on HbA1c in T2DM patients with chronic HCV infection. While DAAs have shown great promise in achieving sustained virological responses, the potential for these therapies to also improve glycaemic control remains underexplored in our local population. So, it is crucial to understand whether successful HCV treatment via DAAs can positively impact HbA1c levels and, by extension, diabetes management. This study will contribute to filling this knowledge gap, providing valuable information that could guide clinical practice in a region with limited access to specialized diabetes care.

MATERIAL AND METHODS

This Quasi-Experimental Model study was conducted between 6 Feb 2025 to 31st May 2025 at the Hepatology Department, Fauji Foundation Hospital, Islamabad. A total of 60 male and female diabetic patients with confirmed HCV positive and planned for DAA therapy and having age between 18-75 years were enrolled using the non-probability consecutive sampling after getting a written informed consent. Sample size was calculated using the WHO sample size calculator used for hypothesis testing for a population mean by taking significance level as 5%, power of the test as 95%, population standard deviation as 1.225⁸, test value of the population means as 7.51⁸, anticipated population mean as 8.34⁸, the sample size would be calculated as 60 patients. Patients with Liver Cirrhosis/failure, renal failure, pregnant female, patients with thyroid or auto immune disorder, patients with malignancy (any kind) and having ischemic cardiovascular disease were excluded from the study. After taking study permission from ethical review board and taking a written consent from patient a detailed physical examination and clinical work-up, pre-treatment HbA1C was done. After that patient were advised the DAAs by the consultant gastroenterologist/hepatologist and instructed to continue the standard medication as per routine. Patient were followed up monthly. After four weeks of the treatment, the HbA1C and values were repeated. Demographic details and HbA1C findings recorded on the pre-designed data collection form. Data was analyzed using SPSS software version 25. Quantitative variables such as age, BMI, duration of diabetes, duration of HCV, baseline HbA1C and post-treatment HbA1C would be computed as mean and standard deviation. While, qualitative variables such as gender and type of oral diabetic treatment will be presented as frequency and

percentages. Pre- and post-treatment mean HbA1C will be compared in the study population and paired *t*-test would be applied to see the statically significant difference (*p*-value ≤ 0.05). Study confounders like age, gender, BMI, duration of T2DM, type of oral diabetic and duration of HCV will be controlled by the stratification. Post stratification, paired *t*-test was used to see the statically significant difference (*p*-value ≤ 0.05).

RESULTS

A total of 60 patients were included in the analysis. The mean age was 51.42 ± 13.35 years, with a predominance of female participants (70%). The mean BMI was 28.66 ± 4.11 kg/m², with the majority of patients being overweight or obese (80%). Most participants had a diabetes duration of ≥ 5 years (80%) and HCV duration of ≥ 3 years (73.3%). Paired sample analysis showed that the mean pre-treatment HbA1c was $8.90 \pm 2.19\%$, which significantly decreased to $7.42 \pm 1.41\%$ following completion of DAA therapy. The mean reduction in HbA1c was 1.48% (95% CI: 1.20–1.76). This improvement was statistically significant (paired *t*-test: $t = 10.60$, $df = 59$, $p < 0.001$). A strong positive correlation was observed between pre- and post-treatment HbA1c values ($r = 0.91$, $p < 0.001$). Both age groups (<50 years and ≥ 50 years) showed comparable reductions in HbA1c. Similarly, significant improvements were observed in both males and females, across normal, overweight, and obese BMI categories, and irrespective of shorter or longer duration of diabetes and HCV infection. Patients receiving monotherapy as well as combination oral antidiabetic therapy also demonstrated significant post-treatment reductions in HbA1c.

Table 1
Descriptive Statistics of Quantitative Variables (n = 60)

Variable	N	Minimum	Maximum	Mean	SD \pm
Age (years)	60	31.00	73.00	51.42	13.35
Body Mass Index (kg/m ²)	60	19.00	37.60	28.66	4.11
Duration of Diabetes (months)	60	13.00	179.00	112.92	48.47
Duration of HCV (months)	60	12.00	120.00	64.22	33.06

Table 2
Distribution of Qualitative Variables (n = 60)

Variable	Category	Frequency	Percentage (%)
Gender	Female	42	70.0
	Male	18	30.0
Age Groups (years)	30–49	26	43.3
	50–75	34	56.7
BMI Groups	Normal	12	20.0
	Overweight	25	41.7
Duration of Diabetes	Obese	23	38.3
	< 5 years	12	20.0
Duration of HCV	≥ 5 years	48	80.0
	< 3 years	16	26.7
Type of Oral Antidiabetic Drugs	≥ 3 years	44	73.3
	Combination Therapy	38	63.3
	Mono Therapy	22	36.7

Table 3*Effect of Direct-Acting Antiviral Therapy on HbA1c: Overall and Stratified Analysis*

Subgroup	N	Pre-treatment HbA1c (Mean ± SD)	Post-treatment HbA1c (Mean ± SD)	Mean Difference	95% CI	p-value
Overall population	60	8.90 ± 2.19	7.42 ± 1.41	1.48	1.20 – 1.76	<0.001
Age < 50 years	26	8.93 ± 2.29	7.52 ± 1.29	1.40	0.89 – 1.92	<0.001
Age ≥ 50 years	34	8.89 ± 2.15	7.35 ± 1.50	1.54	1.21 – 1.86	<0.001
Male	18	9.47 ± 2.13	7.72 ± 1.54	1.75	1.28 – 2.21	<0.001
Female	42	8.66 ± 2.20	7.30 ± 1.34	1.37	1.01 – 1.72	<0.001
Normal BMI	12	9.28 ± 2.19	7.46 ± 1.52	1.82	1.23 – 2.42	<0.001
Overweight	25	8.46 ± 2.39	7.20 ± 1.39	1.26	0.72 – 1.79	<0.001
Obese	23	9.19 ± 1.95	7.65 ± 1.39	1.54	1.17 – 1.92	<0.001
Diabetes < 5 years	12	9.36 ± 2.48	7.91 ± 1.60	1.45	0.80 – 2.10	<0.001
Diabetes ≥ 5 years	48	8.79 ± 2.12	7.30 ± 1.34	1.49	1.17 – 1.81	<0.001
HCV < 3 years	16	9.09 ± 2.23	7.51 ± 1.49	1.58	1.08 – 2.09	<0.001
HCV ≥ 3 years	44	8.84 ± 2.20	7.39 ± 1.39	1.44	1.10 – 1.79	<0.001
Monotherapy	22	9.30 ± 1.91	7.77 ± 1.30	1.53	1.18 – 1.88	<0.001
Combination therapy	38	8.68 ± 2.33	7.22 ± 1.44	1.45	1.05 – 1.85	<0.001

DISCUSSION

The findings showed a significant reduction in the HbA1c after completion of the antiviral treatment. This improvement was observed in the overall study of the population and in all of the stratified subgroups based on their age, gender, body mass index (BMI), duration of diabetes, duration of HCV infection, and type of the antidiabetic therapy. These results support the hypothesis that eradication of the HCV through DAA therapy contributes positively in the glucose metabolism and for the diabetic control as well as in line with the previous findings of a Chinese study conducted by Weidner P and colleagues [10]. The majority of the participants were overweight or either obese, which is a known contributor to the insulin resistance and of the poor glycaemic control. Long duration of diabetes and the chronic HCV infection among most of the patients indicates prolonged metabolic stress and a viral enduringness, both of which may worsen the insulin sensitivity.

The primary outcome of this study was a statistically significant decrease in the mean HbA1c from 8.90% before the treatment to 7.42% afterwards of the treatment. A reduction of the 1.48% is clinically significant because even a one percent decrease in the HbA1c is also associated with the reduced risk of the microvascular complications such as the neuropathy, nephropathy, and the retinopathy [10,11]. The Stine JG et al. [12] reported a significant decline in the HbA1c levels following the DAA therapy in the diabetic patients with the HCV infection. Similarly, Chen B et al. [13] also observed an improved insulin sensitivity after the uninterrupted virological response (SVR). There is also a case-control study by Adinolfi et al. [14] which demonstrated that the HCV eradication is very much associated with the improved glucose metabolism and the reduced relative incidence of the new-onset diabetes. The correspondence between this study and the previous research provide more strength in the reliability of the results.

Stratification analysis of our study suggests that the age does not limit the metabolic benefit of the antiviral therapy and similar associations were reflected by Pavone et al. [15], who found that the improvement in the glucose metabolism occurred across the different age groups after the viral eradication. This indicates that patients of all ages

may benefit from the DAA therapy in terms of the diabetes management. Similarly, we noticed improvement in both gender which is inline with the findings of Hum [16]. This difference can be related to the hormonal factors, body fat distribution, or adherence to the treatment [10,16]. The improvement observed in the obese patients suggests that the viral eradication can partly counteract the metabolic dysfunction even in the presence of the excess body weight [17]. Similar the outcomes were reported by the Hagag RY et al [8], who explained the improved glycaemic control after the antiviral therapy regardless of their BMI category. As we noticed that duration of diabetes as well as hepatitis C didn't significantly affect the treatment outcome, this factor illustrates that the metabolic benefits of DAA are not linked with the chronicity of either disease. Marzaban RN and colleagues also reported the similar findings [18]. Duration of the diabetes, duration of the HCV infection and type of therapy did not significantly affect treatment outcomes. Patients with both the short and long disease duration have experienced comparable improvements. This suggests that the metabolic benefits of the viral eradication are not only limited by the chronicity of the illness. These findings are supported by the Dawood et al. (2019), who determined the improved HbA1c levels in the patients with long-standing diabetes following the antiviral treatment.

The findings of our study are especially very important for Pakistan and other low- and middle-income countries where both for the HCV and T2DM are extremely prevalent and has one of the highest burdens of HCV and diabetes around the globe and on increase as well [19]. Demonstrating that the DAA therapy increases the glycaemic control provides additional justification for the early antiviral treatment in diabetic patients. Improved glucose control may also reduce the long-term complications and the healthcare costs among HCV infected subjects [20].

Contempt its strengths, this study has the several limitations. The quasi-experimental design without a control group limits the causal representation. Other factors such as dietary changes, increased health awareness, or the improved medication adhesiveness during the follow-up may have contributed to the observed improvement. The sample size was relatively

small and taken from a single center, which limits the generalizability. Additionally, the follow-up period was limited to the 12 weeks, and the long-term sustainability of the metabolic improvement could not be measured. The study also did not assess the insulin resistance indices such as fasting glucose, or the lipid profiles. Including these parameters would have provided a more comprehensive understanding of the metabolic changes following antiviral therapy. Future studies should use randomized controlled designs, larger samples, and the longer follow-up periods to confirm these findings and explore long-term outcomes.

CONCLUSION

This study concludes that the direct-acting antiviral therapy importantly improves the glycaemic control in the patients with type 2 diabetes mellitus and the chronic hepatitis C infection. A meaningful reduction in HbA1c was also seen after the completion of the antiviral treatment across all the demographic and clinical subgroups. The

improvement in the HbA1c regardless of the age, gender, BMI, duration of diabetes, duration of HCV infection, and the type of antidiabetic therapy establish that the effect of the DAA therapy on glycaemic control is more consistent and reliable. From a clinical perspective, these results emphasize the importance of the early detection and treatment of HCV in the diabetic patients. The antiviral therapy not only prevents the liver-related complications but also improves diabetes management and may reduce the risk of the long-term microvascular and macrovascular complications. The improved glycaemic control through the viral eradication could lower healthcare costs and improve patient quality of life. The DAA therapy should be considered as valuable component of the comprehensive care for patients with coexisting the HCV infection and type 2 diabetes. Future research should focus on the long-term outcomes, multicenter studies, and the evaluation of additional metabolic parameters to strengthen the evidence base for the integrated treatment approaches.

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