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Letter

The impact of a successful treatment of HCV on glyco-metabolic control in diabetic patients

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Dear Editor,

We read with interest the review by Adinolfi *et al* highlighting the need to evaluate all persons with Hepatitis C Virus (HCV) infection for diabetes, in view of extrahepatic benefits of viral eradication, the reduced risk of diabetic complications and improved glyco-metabolic control in HCV-infected patients [1]. Previous studies have shown that HCV impairs glucose metabolism directly via viral proteins and indirectly by altering pro-inflammatory cytokine levels [2–4]; thus, in turn, HCV clearance may positively impact on glucose metabolism, as evidenced by decreased mean haemoglobin A1c (HbA1c) and fasting plasma glucose (FPG) levels [5,6] in diabetic patients exposed to new Direct Acting Antiviral (DAA) agents that produce a Sustained Virological Response (SVR) in nearly all cases. However, there are limited data on the effect of viral eradication with DAAs on established type 2 diabetes (T2DM) and whether the benefits are persistent [7,8].

In view of the clinical importance of the above issue, we assessed if a correlation between HCV eradication following DAA-based therapy and improvement in glyco-metabolic control occurred in our study population and if it was maintained after the end of treatment (EOT). We retrospectively compared HbA1c and FPG levels at baseline and post-SVR (at 12 weeks) in 93 patients with T2DM exposed to DAAs for HCV eradication (Figure 1 show the selection process of patients with HCV and diabetes enrolled in the study). To evaluate the glycometabolic response, we used a composite end-point given by the reduction of plasma glucose levels of at least 20 mg/dl (1.1 mmol/L) and a reduction of HbA1c of 0.5% compared to baseline values as a significant improvement in the glyco-metabolic response, as previously reported in some studies that addressed the issue [9,10].

As reported in Table 1, we found a significant post-SVR level reduction both of plasma glucose (P=0.0378) and HbA1c values (P=0.0039), as previously reported by four similar retrospective studies [5,9–11]. In contrast with our findings, no change in HbA1c was found 12-weeks post SVR by Stine *et al* among 26 HCV diabetic patients treated with SOF/LED (P=0.268) [12] and also Carvalho *et al* failed to identify maintained post-SVR benefits in terms of plasma glucose level reduction in patients without diabetes exposed to DAAs [8]. Furthermore, two previous studies found no significant difference in changes in HbA1c and glucose levels from baseline to the last follow-up in subjects who achieved SVR in a mixed cohort of

diabetic and non-diabetic patients [7,13]. These conflicting results may be in part attributable to the fact that our median HbA1c levels at baseline were higher (59.19±16.31 mmol/mol; 7.6%) than the ones reported in the studies mentioned before, suggesting that an improvement in glyco-metabolic response is more likely to occur in patients with established diabetes and with high baseline levels of HbA1c. In line with this hypothesis, as correctly reported by Adinolfi *et al* in their interesting review [1], Hum et al found drops in HbA1c associated with SVR restricted to diabetic patients with a high baseline HbA1c (mean HbA1c >7.2%), whereas among diabetic patients with pre-treatment HbA1c ≤7.2% there was no significant difference based on SVR [5].

A recent meta-analysis quantifying variations of glyco-metabolic indicators attributed to DAA therapy in diabetic patients detected a significant improvement in glyco-metabolic control after HCV eradication, in terms of HbA1c (-0.45% ; P<0.001) and mean plasma glucose (-22.03 mg/dL; P=0.03) levels reduction, following DAA treatment in patients with established diabetes [14]. However, these promising findings came from a limited number of studies performed in a wide variety of clinical settings and need to be confirmed.

In conclusion, an increasing number of evidence seems to suggest that the eradication of HCV with DAA therapy may play a role in improving glycemic control in patients with established T2DM, highlighting the need to explore the issue through more wide-ranging studies, with a more complete baseline assessment and a prolonged follow-up, with a view to a possible tapering of anti-diabetic drugs in order to avoid hypoglycaemic events.

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Conflict of interest

The authors declare that there is no conflict of interest regarding the publication of this article

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Table 1. Baseline demographics and effect of treatment of HCV with DAAs on glyco-metabolic parameters

Baseline demographics for HCV patients with diabetes with pre-and post-treatment laboratory values			
Age (years), mean±SD	64**±**11	-	-
Male, gender, n (%)	72 (73%)	-	-
Genotype, n (%)			
1	47 (55,9%)		
2	18 (21,4%)	-	-
3	13 (15,4%)	-	-
4	8 (9,5%)	-	-
not performed	9 (10,7%)	-	-
Changes in laboratory values			
	Before [mean ± SD]	**After [mean ± SD]**	***P* value***
Mean plasma glucose levels, mg/dL	166.9**±**50.63	149.9**±**49.53	**0.0378**
Hemoglobin A1c, mmol/mol	59.19±16.31	49.81±16.25	**0.0039**
Total cholesterol,	164.2±35.13	182.4±38.54	**0.0010**
Triglycerides, mg/dL	186.3±83.27	173.9±101.6	0.5268

SD: standard deviation; HCV: Hepatitis C Virus ; DDA: Direct Acting Antiviral.
* Statistical significance assessed by paired Student's t-test. P values < 0.05 were considered statistically significant.

Figure 1. Selection process of patients with HCV and diabetes enrolled in the study