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N. **Title:**

OC 50 **Impact of HCV treatment with Direct-Acting Antivirals on glucose levels in diabetic HIV/HCV co-infected patients in the ICONA and HepaICONA cohorts**

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Abstract:

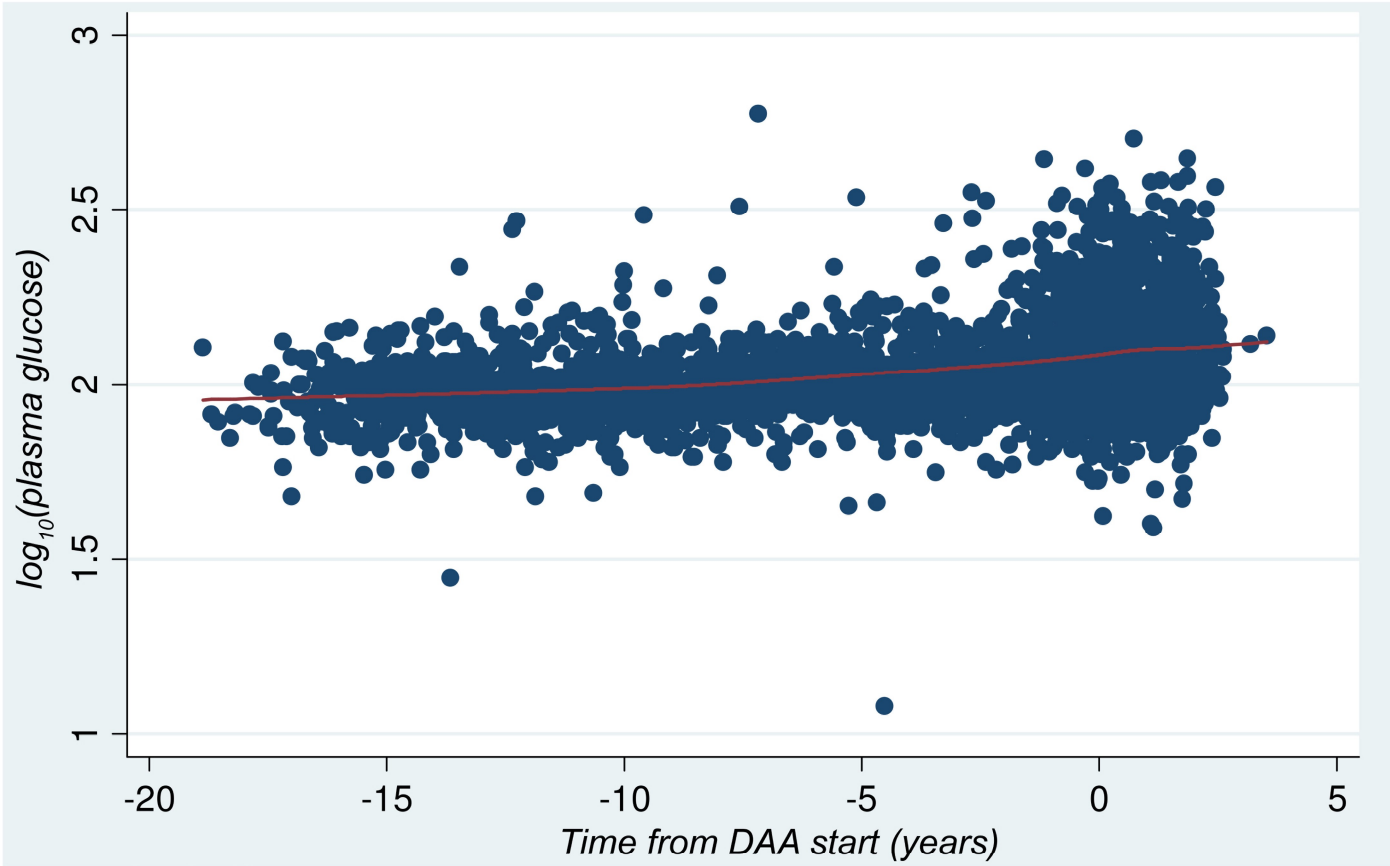
Background: Chronic HCV infection has been associated with a number of extrahepatic manifestations and comorbidities, including diabetes mellitus (DM). Some large observational studies found that treatment response in HIV/HCV co-infected patients was associated with a significant decrease in the risk of DM. Data on the impact of HCV treatment in HIV/HCV co-infected patients with known DM are lacking. We conducted a longitudinal analysis to explore if the HCV treatment with Direct-Acting Antivirals (DAA) had an impact on glucose levels in diabetic individuals.

Material and methods: Any patient in the ICONA and HepaICONA cohorts, who have started DAA treatment and had a diagnosis of DM at or before DAA initiation, with fasting glucose levels before and after DAA completion, have been included in the analysis. Successful DAA treatment was defined by HCV RNA not detected 12 weeks (SVR12) after the end of treatment (EOT). DM was defined by the presence of at least one of the following conditions: i. diagnosis of DM as reported by the treating clinician, ii. use of antidiabetic drugs, iii. single blood glucose level >125 mg/dL at a verified fasting status. Stepwise mixed linear models with random intercept/slope were fitted to identify if HCV eradication could have an effect on the slope of glucose levels comparing periods before and after DAA therapy start. Multivariable model was adjusted for main potential confounding factors (demographic, clinical, treatment-related).

Results: A total of 185 patients were included in the analysis. Females 14%, median age (IQR) 54 (51, 56) years, CD4+ count 580 (323, 816) cells/mm3, HIV-RNA 0.95 (0, 1.6) Log10 cp/mL. HCV genotypes were: 1 in 60% and 3 in 26%. Subjects were prescribed sofosbuvir- and ombitasvir/paritaprevir-based regimens in 73% and 15%, respectively. Patients with available data 12 weeks after EOT were 162 and SVR12 was achieved in 149 cases (92%). We observed an increase in glucose levels before DAA starting [mean +0.008 (CI 95% +0.008, +0.009) Log10 mg/dL/year] and a significant reduction of this increase after DAA treatment [-0.015 (-0.023, -0.007) Log10 mg/dL/year]. The finding was similar after adjusting for potential confounding factors in intercept (see figure 1).

Conclusions: Based on these preliminary data, DAA treatment seemed to have a beneficial effect on glucose levels, in HIV/HCV co-infected patients with DM. This finding underscores the need to accelerate DAA treatment in individuals affected by this comorbid condition. Longer follow up is required to confirm this observation and to better investigate the real impact of HCV eradication on glucose metabolism in HIV/HCV co-infected population.

Figure 1.



Univariable	***Beta***	***95% CI***		***p-value***
Slope before DAA starting	0.008	0.006	0.009	<0.001
Slope change after DAA starting	-0.015	-0.023	-0.007	<0.001
Multivariable*	***Beta***	***95% CI***		***p-value***
Slope before DAA starting	0.007	0.004	0.010	<0.001
Slope change after DAA starting	-0.013	-0.023	-0.003	0.010

*adjusted for age, gender, mode of HIV transmission, race, nadir and current $CD4^+$ count, Log_{10} HIV RNA, AIDS diagnosis, ART regimen change before starting DAA (yes or no), Log_{10} HCV RNA, HCV genotype 3, SVR12 (yes or no), DAA regimen (paritaprevir/ritonavir yes or no), F4 fibrosis stage.