Influence of HCV coinfection and HCV treatment on risk of diabetes mellitus in HIV infected persons

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1 INTRODUCTION

- HCV infection has been associated with an increased risk of diabetes mellitus (DM)[1].
- However, a large cohort study among HIV infected people found that DM was associated with cirrhosis, but not HCV infection per se[2].
- Other studies have found that a sustained virologic response (SVR) improved insulin resistance[3] and was associated with a lower incidence of DM compared with people who did not achieve an SVR[4,5].

2 AIM

- To investigate the association between HCV coinfection status and DM, and the impact of HCV treatment outcome in HIV-infected individuals.

3 METHOD

- All HIV positive individuals in the EuroSIDA cohort with known HCV status after January 2001 were included in one of five groups based on time-updated HCV-RNA and use of HCV treatment:

  1) Anti-HCV negative
  2) Spontaneously resolved HCV infection
  3) Chronic untreated HCV infection
  4) Successfully treated HCV infection
  5) HCV-RNA positive despite previous HCV treatment

- DM was defined as either HbA1C >48 mmol/mol or 6.5%, a single blood glucose >11.1 mmol/l, use of antidiabetic drugs or diagnosis of DM mentioned in medical chart.
- Individuals with DM at baseline were excluded.
- Poisson regression was used to investigate the association between HCV groups and DM.

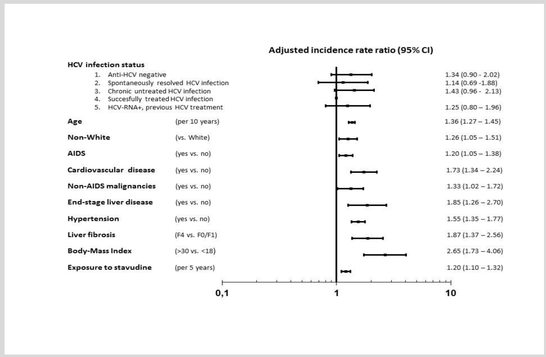
4 RESULTS

- We included a total of 16,034 HIV positive persons of which 6109 (38.1%) were anti-HCV positive of whom 460 (2.9%) had cirrhosis at baseline.
- At baseline, overall the majority were male (74%), White (85%), and on ART (85%) with a median (IQR) age of 41 (35-49) years and CD4 cell count of 446 (290-639) cells/µl. The characteristics according to HCV groups are shown in table 1.
- During 123610 person-years of follow-up (PYFU); median 6 years (IQR 3–12) per person, 1019 (6.4%) developed DM.
- The crude incidence rate per 1000 PYFU (95% confidence interval) of DM was 8.7 (8.1–9.3), 6.3 (4.2–8.5), 7.4 (6.1–8.7), 6.7 (4.4–8.9), 7.4 (5.4–9.5) in group 1-5, respectively.
- In multivariable analysis (figure 1), there was a 43% increased incidence of DM in those with chronic untreated HCV (group 3) compared to those successfully treated (group 4), although this was marginally significant (p=0.08).
- The incidence of DM was significantly higher among persons with F4 (cirrhosis) vs. F0/1 fibrosis (incidence rate ratio, IRR, 1.87, 95% CI 1.37-2.56, p=0.0001) and in those with end-stage liver disease (ESLD) vs. no ESLD (IRR 1.85, 95% CI 1.26-2.70, p=0.0015). There was no difference in incidence of DM when comparing F2 or F3 with F0/F1 (p>0.6).
- In addition, development of AIDS or serious non-AIDS events (cardiovascular events, malignancies) and hypertension, as well as older age and non-white ethnicity and higher body-mass index were associated with increased incidence of DM.
- People who were HBsAg positive had similar incidence of DM as those HBsAg negative (IRR, 0.95, 95% CI 0.76-1.16, p=0.64).
- Among a priori selected antiretroviral drugs (didanosine, stavudine and zidovudine) increased incidence of DM was only seen for cumulative exposure to stavudine. CD4 cell count or HIV-RNA levels did not increase the incidence of DM.
- Limitation: most follow up was prior to the introduction of direct-acting antivirals against HCV.

Table 1
Characteristics at baseline according to HCV group

		Group 1	Group 2	Group 3	Group 4	Group 5
		Anti-HCV negative	Spontaneously resolved HCV infection	Chronic untreated HCV infection	Successfully treated HCV infection	HCV-RNA positive despite HCV treatment
All (%)		9925 (61.9)	864 (5.4)	3471 (21.6)	864 (5.4)	910 (5.7)
Age (median years)		41 (34-48)	42 (36-49)	40 (34-46)	48 (40-53)	46 (39-52)
Male (%)		7529 (75.9)	571 (66.1)	2429 (70.0)	638 (73.8)	665 (73.1)
HIV transmission risk (%)	IDU	275 (2.8)	516 (59.7)	2336 (67.3)	464 (53.7)	518 (56.9)
	MSM	5225 (52.6)	114 (13.2)	394 (11.4)	219 (25.3)	199 (21.9)
Fibrosis stage (%)	F4	30 (0.3)	34 (3.9)	195 (5.6)	92 (10.6)	109 (12.0)
	Unknown	6525 (65.7)	272 (31.5)	1209 (34.8)	76 (8.8)	116 (12.7)
CD4 (median cells/µl)		436 (284-617)	463 (290-670)	421 (270-629)	546 (362-765)	544 (368-760)
HIV-RNA (% <500 cp/ml)		6508 (65.6)	656 (75.9)	2418 (69.7)	787 (91.1)	775 (85.2)
BMI (%)	<18	204 (2.1)	27 (3.1)	133 (3.8)	27 (3.1)	22 (2.4)
	18-25	4968 (50.1)	459 (53.1)	1909 (55.0)	436 (50.5)	454 (49.9)
	25-30	1763 (17.8)	152 (17.6)	534 (15.4)	153.(17.7)	166 (18.2)
	30	338 (3.4)	38 (4.4)	104 (3.0)	45 (5.2)	36 (4.0)
	Unknown	2652 (26.2)	188 (21.8)	791 (22.8)	203 (23.5)	232 (25.5)
Ever exposed to stavudine (%)		4201 (42.3)	333 (38.5)	1321 (38.1)	222 (25.7)	264 (29.0)

Figure 1
Factors associated with incidence of diabetes mellitus



Model adjusted for factors shown and gender, HIV transmission risk group, region, nadir CD4, baseline blood glucose/HbA1c level, baseline date (as fixed values at baseline), and HBsAg, HIV viral load, CD4, smoking, chronic kidney disease, exposure to didanosine and zidovudine (as time updated values). Factors not included in the figure were not statistically significantly associated with incidence of DM.
DM was defined as either blood glucose >11.1 mmol/L, HbA1C >6.5% or >48 mmol/mol, starting antidiabetic medicine or physician reported date of DM onset.

5 CONCLUSIONS

- In a large cohort of HIV infected persons, cirrhosis and ESLD were associated with increased risk of DM.
- There was some evidence that those with successfully treated HCV infection had a lower incidence of DM than those with chronic untreated HCV, but our results did not reach statistical significance. More follow up is required to confirm our findings.
- Increased risk of DM was also associated with both HIV related and well-known general risk factors for DM.

6 ACKNOWLEDGEMENTS

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https://chip.dk/Studies/EuroSIDA/Study-group

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Poster can be downloaded at www.chip.dk