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Influence of Hepatitis C (HCV) Co-Infection and HCV Treatment on Risk of Chronic Kidney Disease in HIV Positive Persons

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INTRODUCTION

- HCV infection has been associated with increased risk of chronic kidney disease (CKD).[1,2]
- Case reports have shown that achievement of a sustained virological response (SVR) resulted in improvement in kidney function in persons with HCV-related glomerulonephritis.[3]
- Cohort studies, where most of the participants have no known underlying renal pathology, have been unable to document an improvement in kidney function in those with SVR compared with those treated without SVR.[4,5]

AIMS

- To investigate the impact of HCV treatment outcome on the risk of incident CKD in HIV/HCV co-infected individuals in the EuroSIDA study.

METHODS

- HIV-positive persons with known HCV status and >3 serum creatinine measurements after 1/1/2004, were included in five groups based on time-updated HCV-RNA, using last observation carried forward (LOCF) and use of HCV treatment:

Group	Anti-HCV	HCV RNA	HCV treatment	HCV Group
1	Negative	Negative	N/A	Anti-HCV negative
2	Positive	Negative	Untreated	Spontaneous HCV-RNA clearers
3	Positive	Positive	Untreated	Chronic HCV infection
4	Positive	Negative	Treated	Successfully treated
5	Positive	Positive	Treated	HCV-RNA positive despite HCV treatment

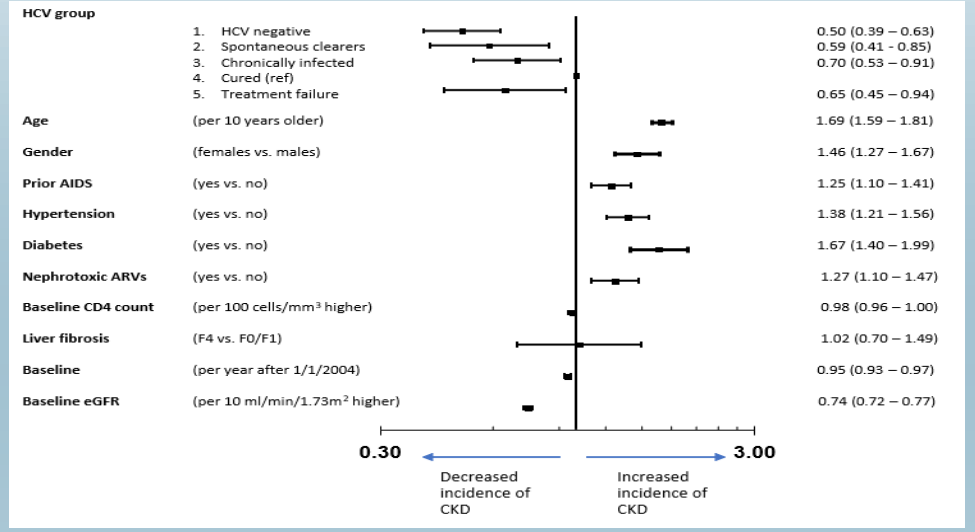
- Successful treatment (group 4) was defined as HCV-RNA negative after starting HCV treatment using LOCF while HCV-RNA positive despite treatment (group 5) was defined as HCV-RNA positive at any point after starting HCV treatment using LOCF.
- CKD was defined as either confirmed (≥3 months apart) estimated glomerular filtration rate (eGFR) of ≤60 mL/min/1.73m^2 for persons with an eGFR >60 ml/min/1.73m^2 at baseline or confirmed 25% decline in GFR for persons with an eGFR ≤60 ml/min/1.73m^2 at baseline. The eGFR was calculated using the CKD-EPI equation.
- Poisson regression was used to compare the incidence rates of CKD between HCV groups
- Persons were followed until their last visit (median June 2018), date of death, or CKD, whichever occurred first.

TABLE 1: BASELINE CHARACTERISTICS

		Group 1 Anti-HCV negative	Group 2 Spontaneously resolved HCV infection	Group 3 Chronic untreated HCV infection	Group 4 Successfully treated HCV infection	Group 5 HCV-RNA positive despite HCV treatment
All (%)		9273 (62.9)	696 (4.7)	3021 (20.5)	922 (6.2)	842 (5.7)
Age, median (IQR) years		43 (36 – 51)	44 (38 – 51)	41 (35 – 47)	48 (41 – 53)	46 (40 – 52)
Male (%)		7023 (75.7)	454 (65.2)	2125 (70.3)	694 (75.3)	621 (73.8)
HIV risk group (%)	IDU	245 (2.6)	391 (56.2)	1974 (65.3)	485 (52.6)	493 (58.6)
	MSM	4856 (52.4)	103 (14.8)	393 (13.0)	241 (26.1)	169 (20.1)
Fibrosis stage (%)	F4	44 (0.5)	26 (3.7)	197 (6.5)	96 (10.4)	121 (14.4)
	Unknown	5151 (55.5)	166 (23.9)	771 (25.5)	73 (7.9)	102 (12.1)
CD4 (median cells/µl)		461 (320 – 653)	484 (344 – 714)	440 (282 – 643)	558 (376 – 782)	543 (370 – 741)
DAD high CKD risk score* (%)		2842 (30.6)	303 (43.5)	1128 (37.3)	545 (59.1)	425 (50.5)

*https://chip.dk/Tools-Standards/Clinical-risk-scores, Baseline=latest of first prospective eGFR, 1/1/2004, EuroSIDA enrolment, known HCV group

FIGURE 1: MULTIVARIATE INCIDENCE RATE RATIOS OF CHRONIC KIDNEY DISEASE



* Adjusted for gender, HIV exposure group, region, baseline eGFR, HIV VL, prior AIDS, cardiovascular disease, non-AIDS defining malignancies, end-stage liver disease, smoking status, hypertension, BMI, diabetes, use of nephrotoxic ARVs (tenofovir, atazanavir, indinavir, lopinavir), use of nephrotoxic other drugs, CD4, nadir CD4, age, liver fibrosis and date of baseline (all fixed at baseline)

RESULTS

- We included a total of 14,754 HIV positive persons of which 5,481 (37.1%) were anti-HCV positive.
- The characteristics according to HCV group are shown in table 1.
- During 115,335 person-years of follow-up (PYFU); median 7.0 (IQR 3.7–12.4) per person, 1130 (7.7%) developed CKD
- The crude incidence rate per 1000 PYFU (95% confidence interval) of CKD was 9.9 (9.2 – 10.5), 8.7 (6.0 – 11.3), 8.6 (7.1 – 10.1), 12.9 (10.4 – 15.3), 7.7 (5.2 – 10.1) in group 1-5, respectively.
- In multivariable analysis (figure 1), the incidence rate of CKD was significantly higher among those with successfully treated HCV infection compared with all other HCV groups.
- Analysis in those without F3/F4 fibrosis showed similar results.
- Excluding persons who have received direct acting antivirals attenuated the differences in CKD incidence between the groups. After adjustment, compared to group 4, group 3 had a 21% decreased incidence of CKD (aIRR 0.79; 95% CI 0.57-1.09) and a 30% reduced incidence in group 5 (aIRR 0.70; 95% CI 0.45-1.08.

LIMITATIONS

- We were not able to characterize the type of CKD, as data on kidney biopsies and proteinuria are not available.
- Successful HCV treatment was not defined as in HCV guidelines

CONCLUSIONS

- This large study of more than 5000 HIV/HCV co-infected persons found that successful HCV treatment was associated with a higher incidence of CKD compared with other HCV groups.
- Confounding by indication, where those with highest risk of CKD were prioritized for HCV treatment, especially in the DAA era could have influenced these results.

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

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