Is ART use associated with increased risk of ALT elevation in HIV/HCV co-infected patients over and above what is expected in HIV mono-infected: a nested case control study approach

**Introduction**

- Antiretroviral therapy (ART) induced toxicity has been frequently reported in HIV/HCV co-infected individuals. However, there is conflicting evidence on whether HIV/HCV co-infection has a synergistic effect on ART-induced toxicity.

- One way to evaluate this hypothesis is to compare the risk of ALT elevation associated with the use of ART in HIV/HCV co-infected vs HIV mono-infected populations.

**Methods**

- We selected individuals in the ICONA Foundation Study cohort with at least one ALT measurement and known current HCV status. We designed a case-control analysis nested in the cohort.

- Cases were defined as individuals who showed liver enzyme elevation (LEE) >5 times upper limit normal at their last clinical observation; controls were participants who showed normal liver enzyme levels after the same time period after enrolment.

- Controls were matched by a predefined set of potential confounders: age (≥20, 21-25, 26-30 to >65), CD4 count cells/mmc (≥350, 351 - 500, >501), HIV-RNA viral load copies/ml (≥1000, 1001 – 5000 to >100,000) and mode of HIV transmission.

- A conditional logistic regression model was used to evaluate the association between ART exposure and risk of LEE in a variable model adjusted for matching factors and after further controlling for gender, nationality, alcohol use, smoking status and calendar year of enrolment. Interaction between HIV/HCV co-infection status and ART exposure were also formally assessed.

**Results**

- We included 2061 individuals (1:2 matching) with median calendar year of last clinical visit in 2014 (IQR: 2007 - 2015) [Figure 1].

- Overall, median age was 35 (IQR: 31-40), mode of HIV transmission was reported as: PWD (32%), MSM (36%), heterosexual (30%) and other/unknown (3%), median CD4 count 386 (IQR: 188-586) cells/mmc and HIV-RNA viral load log10 copies/ml 4.5 (IQR: 3.8 – 5.2).

- Majority were males (70%). Individuals reporting smoking were less in cases than controls 22% and 26% (p=0.03). Proportion of HIV/HCV co-infected individuals was higher in cases than in controls 39% and 29% respectively (p<0.001). Proportion of ART use was higher in cases than controls 79% and 72% respectively (p<0.001) [Table 1].

- In the model without interaction, ART use was associated with an increased risk of LEE [adjusted odds ratio (aOR) 1.87 [95% CI: 1.39-2.53; p<0.001] independently of all factors included [Table 2].

- In the model with the interaction, the association between co-infection and risk of LEE was 3.76 [95% CI: 1.31 - 10.81] in individuals on ART and 3.17 [95% CI: 2.09 - 4.80] in ART naïve individuals (p<0.006) [Figure 2].

**Conclusion**

- Our analysis show no evidence that risk of ALT elevation due to HIV/HCV co-infection is exacerbated by the exposure to ART (3-fold increased risk in both strata).

- Further analyses are needed to investigate the possible effect associated with the use of specific drugs/regimens.