HIV Drug Therapy
GLASGOW 2022 | HYBRID 30 YEARS

Could we consider U=U as a potential driver of new syphilis infection in HIV population during the Covid-19 pandemic?

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❖ BACKGROUND

Partner 1&2 studies support risk-zero of HIV transmission through condomless sex in serodiscordant couples with the HIV positive partner virally suppressed (HIV RNA <200 copies/ml) by taking ART. This message has been considered as a revolutionary perspective for people living with HIV infection (PLWH).

Paradoxically, a wide and acritical interpretation of this message could reduce the perception of the risk of transmission of other STIs .

❖ METHODS

This is a retrospective observational study. We analyzed the trend of syphilis infection in general population (PLWoH) and among People Living with HIV (PLWH) in the period between January 1st, 2014, and June 30th, 2022.

We collected data about demographic characteristics (age, sex, sex orientation), year of diagnosis, stages of syphilis, re-infections, prescribed therapy, and HIV-RNA viremia at the time of diagnosis.

All data has been collected in a worksheet before analysis.

Categorical variables are expressed as count (percentages), while continuous variables as as mean ±SD when normally distributed or median (IQR) when non-normally distributed.

T-test for paried data and ANOVA test were applied to find any statistically significant difference between normally distributed variables. Wilcoxon test was applied to find any significant difference over time among non-normally distributed variables.

Statistically significant level was set at a p value < 0.05, confidence interval (CI) was set at 95%.

Statistical analysis was performed with SPSS 28.0 for MacOS.

❖ RESULTS

261 patients were enrolled for a total of 320 cases of syphilis infection (261 first diagnosis, 59 (18.4%) re-infections).

| Median (IQR) age	37 (29,9-47,7)
Female sex	40 (12,5%)
Sex orientation	
- Heterosexual	78 (24,4%)
- MSM	173 (54,0%)
- Unknown	69 (21,6%)
Stage of Syphilis	
- Primary	25 (7,8%)
- Secondary	69 (21,6%)
- Lantent	226 (70,6%)
Re-infection	59 (18,4%)
Prescribed therapy	
- BBP 2.4 MU x3	265 (82,8%)
- BBP 2.4MU x1	37 (11,6%)
- Tetracyclines	5 (1,6%)
- Other	13 (4,0%)

Table 1. Demographics and disease characteristics of general population

147 (45.9%) were HIV-positive, 113 (35.3%) were on antiretroviral treatment, 34 (10.6%) received both the diagnosis of HIV and syphilis.

- HIV -
- HIV+ (on ART)
- HIV+ (naïve)

10,6%
35,3% 54,1%
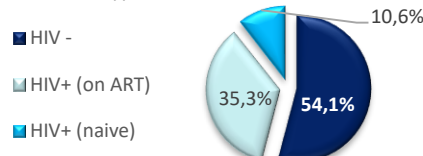
Figure 1. Proportion of PLWoH, PLWH on ART and PLWH naïve among the population

Median age was 37.4 years (IQR 29.9-47.7), with a significant difference between PLWoH [33 (IQR 27.9-43.6)] and PLWH [41 (IQR 34.3-51.7)] (**p<0.001**).

SEX PLWH
F   M   M2F
0,7%   1,4%
98,0%

SEX PLWoH
F   M   M2F
0,6%   22,0%
77,5%
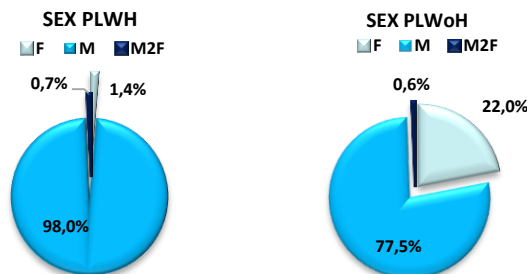
Figure 2. Distribution of populations (PLWH and PLWoH) by sex

Re-infections occurred in 59 patients (18.4%), 10 (16.9%) PLWoH and 49 (83.1%) in PLWH (**p<0.001**).

We observed some peaks of diagnosis during 2018 (46), 2020 (42) and 2022 (51 only during the first semester). The distribution of diagnosis of syphilis by years is reported in the table below.

| Year	PLWoH (%)	PLWH (%)	PLWH on ART (%)	Tot
2014	21 (95,5%)	1 (4,5%)	0 (0,0%)	22
2015	16 (80,0%)	4 (20,0%)	1 (5,0%)	20
2016	16 (50,0%)	16 (50,0%)	12 (37,5%)	32
2017	22 (59,5%)	15 (40,5%)	8 (21,6%)	37
2018	**24 (52,2%)**	**22 (47,8%)**	**18 (39,1%)**	**46**
2019	17 (54,8%)	14 (45,2%)	12 (38,7%)	31
2020	**24 (57,1%)**	**18 (42,9%)**	**11 (26,2%)**	**42**
2021	24 (61,5%)	15 (38,5%)	13 (33,3%)	39
2022*	**9 (17,6%)**	**42 (82,4%)**	**38 (74,5%)**	**51**

*Table 2. Distribution of diagnosis of syphilis by years among People Living without HIV (PLWoH), People Living with HIV (PLWH) and PLWH on ART (*period between 1st Jan 2022 and 30th Jun 2022)*

Median (IQR) age	38 (30,9-48)
Sex	
- Male	112 (99,1%)
- M2F	1 (0,9%)
Sex orientation	
- Heterosexual	9 (8,0%)
- MSM	99 (87,6%)
- Unknown	5 (4,4%)
Stage of Syphilis	
- Primary	16 (14,2%)
- Secondary	23 (20,4%)
- Lantent	74 (65,4%)
Re-infection	46 (40,7%)

Table 3. Demographics and disease characteristics of PLWH on anti retroviral treatment-experienced (ARV)

Finally, only 71 (62.8%) HIV-positive subjects on antiretroviral treatment at the time of syphilis diagnosis were virally suppressed (VL <200 cps/mL).

Syphilis diagnosis 2014-2022 in PLWH ARNAS Garibaldi, Catania
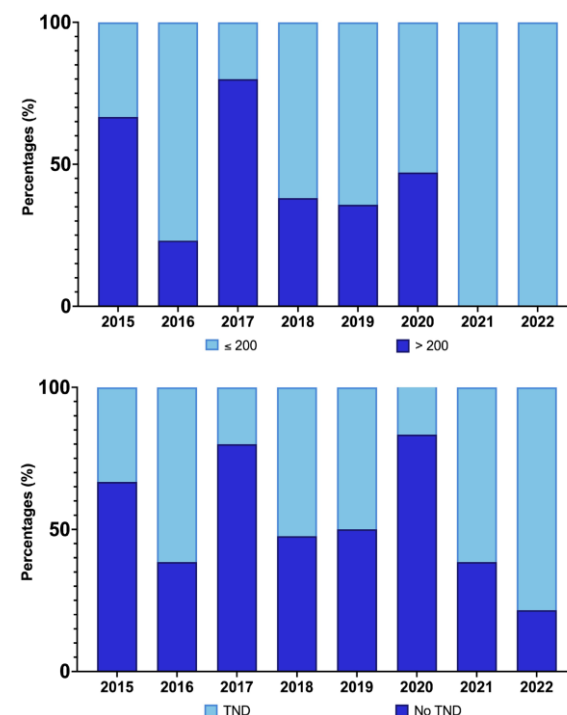
Figure 3. 1) HIV RNA ≤ 200 copies/mL or ≥ 200 copies/mL by years
Figure 3. 2) HIV RNA ≤ 20 copies/mL (Target Not Detected TND) or ≥ 20 copies/mL (No-TND) by years

❖ CONCLUSIONS

A remarkable increase in syphilis diagnosis has been observed during the last years, especially during the last 6 months, among general population and in PLWH assuming ART and followed in our clinics. One possible explanation could be the increase in condom-less sexual contacts, including oral ones, as reaction after the forced reduction due to COVID-19 restrictions. At the same time a compensatory increase in screening activities in our population after the pandemic could contribute to these results.

A slight increase in HIV-RNA viremia at the moment of syphilis diagnosis has been described and observed in some of our cases. Syphilis could be associated with transient HIV-RNA viremia increase in PLWH receiving ART. More data are necessary to evaluate the relationship between an undiagnosed STI, HIV-RNA replication (with value >200 copies/ml) and the risk of HIV transmission.

Considering the last five years, about 72,2% to 100% of PLWH on ART with syphilis infection had a viral load <200 copies/mL at the time of the diagnosis. The increased awareness of the meaning of U = U might have reduced the perception of the residual risk of transmitting and acquiring sexually transmitted infections.

As STIs, and in particular syphilis infections, can be considered as markers of unsafe-sex, should we have to wait for a significant increase of new HIV infection in the near future?