No CSF Study in Neuro Asymptomatic Syphilis in People With HIV: Clinical and Serologic Outcomes

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BACKGROUND

Syphilis is common in people living with HIV (PLHIV), and central nervous system involvement is more frequent, although mostly asymptomatic, in which case it seems to be mostly a benign condition, leading to a growing trend to not perform a lumbar punction (LP) in this cases. During the COVID-19 pandemic restrictions, LPs were not performed in neuro asymptomatic patients with low CD4+ cell count and high VDRL titers, as previously done at this HIV care center, and participants received benzathine penicillin, as in no neurologic involvement, generating an opportunity to evaluate outcomes after this noninvasive practice

Neuro-asymptomatic syphilis in PLHIV with low CD4 counts and *high VDRL titers with no CSF study* treated with benzathine penicillin had proper VDRL decline, and **none developed clinical neurological signs/symptom** on follow up

METHODS

- Retrospective, longitudinal observational study
- Study population: PLHIV diagnosed with syphilis at the Infectious Diseases Center of San Borja Arriarán Clinical Hospital between 03/2020 and 08/2022
- Eligibility criteria: VDRL ≥ 1:32, no neurological symptoms, no cerebrospinal fluid (CSF) analysis at diagnosis and minimum of 12 months of follow-up
- Data were analyzed using Stata 15.1 to calculate central tendency measures, associations were explored using linear regression, logistic regression, and the Kruskal-Wallis test.
- Treponemal tests were not used for syphilis diagnosis confirmation

Gender	98.5% male
Median age	34 years (IQR 29–45)
Undetectable viral load	73% (n=131)
Median CD4 count*	533 cells/mm^3 (IQR 400–734)
CD4 <200 cells/mm^3*	8.4% (n=17)
Median initial VDRL titer	1:32 (IQR 1:32–1:64)
Syphilis stages	Early latent (51.7%) Late latent (27.5%) Secondary (17%) Primary (4%)
Treatment	Benzathine penicillin (99%), doxycycline (1%)
Median follow-up	20 months (IQR 13.2–25.3)

Table 1. Baseline Characteristics of the Study Population

RESULTS

- Of 868 adult PLHIV, 220 met inclusion criteria; 17 were excluded (7 with CSF analysis, 10 lost to follow-up).
- A ≥2-dilution VDRL titer decline was observed in 83.3% at 2, 95% at 6, 83.6% at 12, and 94.3% at 24 months, respectively.
- VDRL became non-reactive in 21.1% (median: 12.9 months, IQR 9–18).
- No association between initial VDRL titers and CD4 count (p=0.46) or viral load (p=0.65) were found.
- No association was found between CD4 count or viral load and VDRL decline.
- **No neurological symptoms were observed during follow-up. Six lumbar punctures were performed due to persistently high VDRL titers; all had non-reactive VDRL in CSF and <5 cells.**

VDRL (N/%)	Initial (203/100%)	2 – 3 months (68/33.5%)	6 – 9 months (110/54.2%)	12 months (98/48.3%)	18 – 24 months (116/57.1%)
Median	1/32	1/8	1/4	1/4	1/2
	IQR (1/32 - 1/64)	IQR (1/4 – 1/16)	IQR (1/1 – 1/8)	IQR (1/1 – 1/8)	IQR (1/1 – 1/8)
Decrease ≥ 2 dil/initial	-	82.4%	90.9%	83.7%	91.4%
Decrease ≥ 2 dil/previous control	-	82.4%	65.5%	22.2%	23.6%

Table 2. Serological follow-up from initial VDRL, 2–3 months, 6–9 months, 12 months, and 18–24 months

CONCLUSIONS

- In PLHIV with syphilis, CD4 count and viral load were not associated with initial VDRL titers or their decline. While most patients showed an adequate VDRL response, only 21% achieved seroreversion at a median follow-up of 20 months.
- This study provides **real-world clinical data** showing that PLHIV with neuro-asymptomatic syphilis and high VDRL titers previously indicative of a CSF study—but managed without one—had an adequate serological response, with no cases of clinical neurosyphilis during follow-up.
- **Not performing routine lumbar punctures in this real-world clinical context did not lead to different clinical or serological outcomes compared to previous practices, as observed in studies from developed countries. These findings are significant and may be applicable to other resource-limited countries, where syphilis remains highly prevalent and access to neurological evaluation and neuroimaging is often limited**.

Despite study limitations, these findings support a more selective approach to CSF studies in neurologically asymptomatic syphilis among PLHIV.

- While the follow-up period was sufficient to rule out early neurosyphilis, long-term studies are needed to assess late forms and further refine management strategies

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