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*Original Research Article*

# Clinical Spectrum of Sexually Transmitted Infections and Treponemal Serological Profile Among Patients Living with HIV at a Tertiary Dermatovenereology Clinic in Surakarta, Indonesia: A Retrospective Cross-Sectional Study (2020–2026)

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**ABSTRACT**

**Background:** Sexually transmitted infections (STIs) and human immunodeficiency virus (HIV) infection interact biologically, but data from Indonesian tertiary dermatovenereology clinics are scarce.

**Objective:** To describe the clinical STI spectrum, coinfection multiplicity, and Venereal Disease Research Laboratory (VDRL) and Treponema pallidum hemagglutination assay (TPHA) results of HIV-positive patients at Dr. Moewardi Regional General Hospital, Surakarta, Indonesia (2020–2026).

**Methods:** This retrospective cross-sectional study analyzed medical records of 74 HIV-positive patients with STIs (ethics approval: 865/V/HREC/2026). Sociodemographics, STI diagnoses, multiplicity, and VDRL/TPHA results were summarized descriptively with Wilson 95% confidence intervals; agreement used Cohen's kappa (κ), and TPHA reactivity was explored by logistic regression.

**Results:** Of 74 patients, 68 (91.89%) were male and 36 (48.65%) were aged 21–30 years (mean 29.70 years). Isolated condyloma acuminata predominated (n = 43, 58.11%), followed by isolated syphilis (n = 17, 22.97%), condyloma acuminata plus syphilis (n = 6, 8.11%), other polymicrobial STIs (n = 6, 8.11%), and molluscum contagiosum (n = 2, 2.70%). Single STIs occurred in 62 patients (83.78%) and multiple STIs in 12 (16.22%). VDRL was positive in 32 patients (43.24%; modal titer 1:16; maximum 1:512) and not done in 19 (25.68%). TPHA was reactive in 34 patients (45.95% overall; 61.82% of 55 tested; κ = 0.924); 11 of 51 patients with non-syphilitic STIs (21.57%) were TPHA-reactive without a syphilis diagnosis. Multiple STIs were associated with TPHA reactivity (aOR = 4.890, p = 0.0344).

**Conclusion:** Condyloma acuminata and young adult male predominance characterized HIV-associated STIs here, and TPHA reactivity without a syphilis diagnosis supports considering paired VDRL/TPHA screening.

*All authors have reviewed and approved the final version of the manuscript.*

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## 1. Introduction

Sexually transmitted infections (STIs) and human immunodeficiency virus (HIV) infection are overlapping epidemics. They share transmission networks. They also influence each other biologically.[1–3] Global surveillance estimates put the number of curable STIs acquired each day above one million. Most arise from *Treponema pallidum*, *Neisseria gonorrhoeae*, *Chlamydia trachomatis*, and *Trichomonas vaginalis*. Viral infections with human papillomavirus (HPV) and herpes simplex virus type 2 (HSV-2) add hundreds of millions of prevalent cases.[1,3,4] In the Asia-Pacific region, including Indonesia, the combined burden of HIV and STIs has shifted toward young adults of reproductive age. Key populations are especially affected, namely men who have sex with men (MSM), transgender people, and those in commercial sex networks.[5–8] Biologically, ulcerative and non-ulcerative STIs damage the stratified squamous and columnar anogenital epithelium. They draw activated CD4+ CCR5+ CXCR4+ T lymphocytes and dendritic cells into the mucosal lamina propria and raise

local levels of tumor necrosis factor-alpha (TNF-α), interleukin-1 beta (IL-1β), and interleukin-6 (IL-6). The result is easier acquisition of HIV-1. Viral shedding in the genital tract also increases.[2,5,9] In the other direction, HIV-1 depletes systemic and mucosal T-helper 1 (Th1) and T-helper 17 (Th17) subsets and exhausts epidermal Langerhans cells and natural killer (NK) cells, which weakens local cell-mediated surveillance.[5,6,8] People living with HIV (PLHIV) are therefore more susceptible to opportunistic and classical venereal pathogens. They often present with florid, multifocal, refractory, or atypical mucocutaneous lesions, faster neoplastic progression, and polymicrobial coinfection.[6–8]

Among the viral STIs seen in HIV-positive people, anogenital HPV infection, which appears clinically as condyloma acuminata (external anogenital warts), is one of the commonest and hardest to treat in dermatovenereology.[7,8,10] Low-risk mucosotropic genotypes HPV-6 and HPV-11 cause about 90% of macroscopic condyloma acuminata in immunocompetent hosts. In HIV-associated immunodeficiency, infection tends to persist with several genotypes at once. Several oncogenic high-risk types (HPV-16, HPV-18, HPV-31, HPV-33, and HPV-52) co-colonize the epithelium, and viral replication proceeds unchecked in basal keratinocytes.[8,10,11] At the molecular level, the HIV-1 transactivator of transcription (Tat) protein and extracellular envelope glycoproteins enter neighboring mucosal keratinocytes and increase transcription of the HPV early oncoproteins E6 and E7. These degrade the tumor suppressors p53 and retinoblastoma protein (pRb), block keratinocyte apoptosis, and push local tissue macrophages toward an immunosuppressive M2-like phenotype.[5,8,12,13] Clinically, the outcome is larger, coalescent, exophytic perianal and genital warts. These recur often after ablation. The long-term risk is higher still, because they also carry a much higher long-term risk of progressing to high-grade squamous intraepithelial lesions (HSIL), anal intraepithelial neoplasia (AIN), penile intraepithelial neoplasia (PeIN), and invasive anogenital squamous cell carcinoma.[7,8,11,14] Impaired mucocutaneous immunity in PLHIV also favors other viral, fungal, and bacterial venereal dermatoses: umbilicated molluscum contagiosum papules, recurrent genital herpes from HSV-2 reactivation, symptomatic vulvovaginal candidiasis, and purulent gonococcal urethritis.[1,4,6]

Syphilis, a chronic systemic spirochetal infection caused by *Treponema pallidum* subspecies pallidum, has resurged worldwide over the past two decades and falls disproportionately on HIV-positive populations and MSM networks.[9–12] In people with HIV, coinfection creates diagnostic and therapeutic difficulties for dermatovenereologists.[9,10] Syphilis in these hosts is known for overlapping primary and secondary stages, multiple or deeply indurated chancres, and ulcerative lues maligna. It may progress early to symptomatic neurosyphilis, ocular syphilis, and otosyphilis. Plasma HIV-1 RNA can rise transiently while peripheral CD4+ T-cell counts fall sharply.[9–12] Laboratory diagnosis adds another difficulty. It depends on reading two kinds of test together. Non-treponemal lipoidal flocculation assays, chiefly the quantitative Venereal Disease Research Laboratory (VDRL) or Rapid Plasma Reagin (RPR) tests, measure immunoglobulin M (IgM) and immunoglobulin G (IgG) against a cardiolipin–lecithin–cholesterol antigen. Specific treponemal assays such as the *Treponema pallidum* hemagglutination assay (TPHA) detect antibodies to treponemal cell components.[9,10,15] In HIV infection, polyclonal B-cell dysregulation and hypergammaglobulinemia can distort serology. Antibody excess may give a false-negative undiluted non-treponemal result (the prozone phenomenon), seroconversion may be delayed, biological false-positive reactions occur, and low-titer reactivity can persist after adequate benzathine penicillin G treatment (the serofast state).[15–19]

Even though HIV, HPV-related condyloma acuminata, and resurgent syphilis are well known to intersect, real-world clinical and serological datasets from tertiary dermatovenereology centers in Indonesia remain scarce.[7,8,20–24] Two gaps stand out. Most Indonesian reports describe either community HIV cohorts without detailed dermatovenereological phenotyping, or isolated STI syndromes without looking at coinfection multiplicity, the distribution of quantitative VDRL endpoint dilutions, and confirmatory TPHA status.[7,8,21,24] The second gap is practical. In routine practice at resource-limited referral hospitals, syphilis serology is sometimes ordered only for patients with classic genital ulcers or palmoplantar rashes, and that habit may leave a large reservoir of asymptomatic latent or occult treponemal coinfection undiagnosed among patients who come mainly with viral anogenital warts.[17,25,26] This retrospective cross-sectional study therefore set out to describe several features among HIV-positive patients attending the Dermatology and Venereology Outpatient Clinic of Dr. Moewardi Regional General Hospital, Surakarta, Indonesia, over the period from 2020 to 2026. These were the sociodemographic profile, the spectrum of dermatovenereological STI diagnoses, and the split between single and multiple coinfections. We also examined the quantitative VDRL titer distribution, TPHA seroreactivity, the concordance of the two assays, and the multivariable predictors of treponemal coinfection.

Managing HIV-associated STIs in Southeast Asian tertiary centers also depends on how diagnostic algorithms behave under real-world immunovirological conditions.[15–18,25,26] Algorithms matter here. In classical teaching, non-treponemal flocculation tests (VDRL and RPR) and treponemal hemagglutination or immunoassay platforms (TPHA, TPPA, and chemiluminescence immunoassays) are used in sequence. The traditional algorithm screens with quantitative VDRL/RPR and confirms with TPHA; the reverse algorithm screens with an automated treponemal immunoassay or TPHA and then titrates VDRL/RPR to gauge disease activity and treatment response.[9–11,18] In PLHIV, relying on symptoms alone to trigger testing, that is, ordering syphilis serology only when genital chancres, condyloma lata, or secondary palmoplantar eruptions are visible, misses a sizeable

group of patients. These are patients with macroscopic viral dermatoses such as condyloma acuminata or molluscum contagiosum who at the same time carry asymptomatic early latent, late latent, or serofast treponemal infection.[17,25,26] Polymicrobial venereal coinfection (more than one STI alongside HIV, that is >1) is also a marker of high-exposure sexual networks and heavy mucosal barrier damage. Its relation to treponemal seroreactivity and VDRL dilution patterns has rarely been modeled by multivariable regression in Indonesian tertiary hospital cohorts.[7,8,21,24] By combining complete clinical phenotyping, coinfection multiplicity, quantitative VDRL endpoint dilutions (spanning 1:1 to 1:512), paired VDRL–TPHA concordance testing, and multivariable logistic regression across a cohort spanning 2020–2026 at Dr. Moewardi Regional General Hospital, this study offers local descriptive data that can inform discussion of STI screening in HIV care.

## 2. Methods

### 2.1. Study design, setting and ethical oversight

This was a retrospective, observational, cross-sectional study with descriptive and analytical components, using secondary clinical and laboratory data from the institutional medical records registry of the Dermatology and Venereology Outpatient Clinic at Dr. Moewardi Regional General Hospital, Surakarta, Central Java, Indonesia. The hospital is a large provincial tertiary referral and academic teaching hospital affiliated with the Faculty of Medicine, Universitas Sebelas Maret, and it serves a wide catchment area across Central Java and eastern Yogyakarta. Records were reviewed from January 2020 through May 2026, a window of about six and a half years (January 2020 to May 2026) that spans the years of pandemic service disruption and the later expansion of integrated HIV–STI outpatient care. The Health Research Ethics Committee (*Komite Etik Penelitian Kesehatan*) of Dr. Moewardi Regional General Hospital reviewed and approved the protocol under ethical clearance number 865/V/HREC/2026, issued on 13 May 2026. All procedures followed the ethical principles of the Declaration of Helsinki (2013 Fortaleza revision) and the International Council for Harmonisation Good Clinical Practice (ICH-GCP) standards. Reporting followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines.[27] Consent was waived. Because only de-identified routine records were analyzed and no patient was approached, the ethics committee waived individual written informed consent. Names, residential addresses, and hospital registration numbers were removed before statistical coding.

### 2.2. Study population, sampling and eligibility criteria

All electronic and physical medical records of patients seen at the Dermatology and Venereology Outpatient Clinic of Dr. Moewardi Regional General Hospital between 2020 and 2026 were screened by total enumerative (consecutive) sampling. Patients entered the analytical cohort if they met three criteria: (1) confirmed HIV infection by the national three-test serial serological algorithm of the Ministry of Health of the Republic of Indonesia, or documented enrollment in the hospital antiretroviral therapy (ART) registry; (2) a definitive clinical and/or laboratory diagnosis of at least one sexually transmitted infection (STI), made by board-certified dermatovenereologists at the clinic during 2020–2026; and (3) core sociodemographic and clinical diagnostic documentation available in the chart. Records were excluded when HIV status was unconfirmed or indeterminate. Non-venereal dermatoses (for example non-infectious inflammatory balanitis, psoriasis, fixed drug eruption, or irritant contact dermatitis) were also excluded, as were entries that duplicated a follow-up visit for the same patient episode. For such episodes only the index comprehensive STI evaluation was kept. Verification of the records left a clear result. N = 74 unique HIV-positive patients with STIs met all criteria and formed the final cohort.

### 2.3. Variable definitions and serological assays

Four domains of clinical and laboratory variables were abstracted with a standardized data collection instrument. These were biological sex (male or female). Age at presentation was recorded in years, grouped into six 10-year intervals of 11–20, 21–30, 31–40, 41–50, 51–60, and 61–70 years, and dichotomized at ≤30 versus >30 years. The remaining variables were primary and secondary dermatovenereological STI diagnoses with STI coinfection multiplicity, and syphilis serology results.[7–11] Diagnoses rested on a full anogenital and mucocutaneous examination. Targeted microbiological and serological work-up followed the national Indonesian Society of Dermatology and Venereology (PERDOSKI) and Centers for Disease Control and Prevention (CDC) guidelines.[1,10] Condyloma acuminata was diagnosed clinically from flesh-colored to hyperpigmented, papillomatous, verrucous, or cauliflower-like papules and plaques on the external genitalia, perineum, perianal skin, or anal canal, with 5% acetic acid (acetowhite) testing where indicated.[7,8,28] Syphilis was diagnosed by correlating mucocutaneous lesions (a primary painless indurated chancre, secondary maculopapular or palmoplantar syphilids, condyloma lata, or mucous patches) or latent clinical staging with reactive non-treponemal and treponemal serology.[9–11] Reactive serology was therefore part of the case definition of syphilis. Other STIs were recorded both individually and by coinfection multiplicity. Genital herpes was identified by vesiculoulcerative clusters with multinucleated giant cells on Tzanck cytology. Vulvovaginal candidiasis showed pruritic erythematous vulvovaginitis with pseudohyphae or blastospores on 10% potassium hydroxide wet mount and Gram stain. Gonococcal urethritis presented with purulent urethral discharge and intracellular Gram-negative diplococci within polymorphonuclear leukocytes. Molluscum contagiosum showed umbilicated pearly papules with Henderson–Paterson intracytoplasmic molluscum bodies.[1,6,29–31] Patients were classed by the number of

concurrent venereal diagnoses alongside HIV infection. A single STI coinfection (1 Infection) meant isolated condyloma acuminata, isolated syphilis, or isolated molluscum contagiosum. Multiple STI coinfections (>1 Coinfection) meant condyloma acuminata plus syphilis, or polymicrobial combinations of genital herpes, vulvovaginal candidiasis, and gonococcal urethritis. Syphilis serology was run at the Central Clinical Pathology Laboratory of Dr. Moewardi Regional General Hospital with two assays. The first was the quantitative non-treponemal Venereal Disease Research Laboratory (VDRL) slide flocculation test. Results were reported as Negative (non-reactive), Positive undiluted (1:1), or an endpoint dilution (1:2, 1:4, 1:8, 1:16, 1:32, 1:128, 1:320, or 1:512), and were further grouped as low-titer reactive (≤1:4) or high-titer reactive (≥1:8). The second was the specific treponemal *Treponema pallidum* hemagglutination assay (TPHA), reported as Reactive or Non-reactive.[9,10,17] Patients without VDRL and TPHA testing at the outpatient visit were coded as Not tested (n = 19, 25.68%). This keeps denominators transparent for both the whole cohort (N = 74) and the serologically tested subcohort (n = 55).

### 2.4. Statistical analysis

All analyses used Python (version 3.11; NumPy and SciPy libraries). Categorical variables are given as exact counts (n) and percentages rounded to two decimal places (summing to 100.00%), with two-sided 95% Wilson score confidence intervals (CIs), which keep adequate coverage in small strata. Age and log-transformed reciprocal VDRL dilutions were checked for normality with the Shapiro–Wilk test (W statistic and exact p-value). They are shown parametrically as mean ± standard deviation (SD) with 95% CIs (and the geometric mean titer [GMT] for VDRL) and non-parametrically as median with interquartile range [IQR: 25th–75th percentile] and minimum–maximum range. The departure of the sex distribution from 1:1 parity was tested with a one-sample binomial chi-square ($\chi^2$) goodness-of-fit test and quantified by Cohen's h. The expected sex ratio of HIV–STI clinic attenders is not 1:1, so this test is reported for completeness and the proportion with its confidence interval is the primary estimate. Agreement between paired VDRL and TPHA results in the serologically tested subcohort (n = 55) was assessed by overall percentage agreement and Cohen's unweighted kappa (κ with 95% CI). Sensitivity, specificity, Pearson's $\chi^2$ test, Fisher's exact test, and Cramér's V were also computed. Bivariate associations were examined in 2 × 2 tables. Predictors were age ≤30 vs. >30 years, male vs. female sex, multiple >1 vs. single 1 STI coinfection, and overt clinical syphilis vs. non-syphilitic STI presentation. Outcomes were isolated condyloma acuminata, confirmed TPHA reactivity, and high-titer VDRL ≥1:8. Pearson's $\chi^2$ p-values are reported with Fisher's exact p-values; Fisher's exact test was regarded as governing when the smallest expected cell count was below 5. We report crude odds ratios (ORs) with 95% Woolf/Haldane–Anscombe CIs, Pearson's $\chi^2$, two-tailed Fisher's exact p-values, and Cramér's V. Finally, a multivariable binary logistic regression model was fitted by maximum likelihood (Newton–Raphson iteratively reweighted least squares) in the total cohort (N = 74) to explore associations with confirmed TPHA reactivity. It yielded regression coefficients (β), standard errors (SE), Wald z-statistics, adjusted odds ratios (aORs) with 95% CIs, the omnibus likelihood ratio $\chi^2$ test, and McFadden's pseudo-$R^2$. Statistical significance was set a priori at a two-tailed p-value < 0.05.

### 2.5. Sensitivity analysis of the untested subcohort and VDRL dilution standardization

A sensitivity analysis was needed. In 19 of the 74 patients (25.68%), no VDRL or TPHA was performed at the index outpatient visit, so the effect of incomplete serological coverage had to be gauged. First, all main serological proportions and 95% Wilson score CIs were reported against two denominators: the conservative total cohort (N = 74), which treats untested patients as unconfirmed, and the complete-case serologically tested group (n = 55). Second, we estimated the treponemal burden possibly missed among the 19 untested patients, all of whom had non-syphilitic primary STIs. For this we applied the TPHA reactivity rate seen in the 32 tested non-syphilitic STI patients (11/32 = 34.38%). The rate was used to project the number of undiagnosed infections in the untested group and an adjusted cohort-wide seroprevalence range. In line with clinical pathology quality-control practice, quantitative VDRL endpoint dilutions were also analyzed in two ways. One used the exact recorded laboratory categories. These were the standard two-fold serial dilutions (1:1, 1:2, 1:4, 1:8, 1:16, 1:32, 1:128, and 1:512) plus the ten-fold/two-fold hybrid endpoint of 1:320. That endpoint arises from a 1:10 initial serum pre-dilution followed by five two-fold dilutions (1:20, 1:40, 1:80, 1:160, and 1:320). The other used a base-2 logarithmic transformation ($\log_2$ reciprocal titer) to compute the exact geometric mean titer (GMT) and the non-parametric median [IQR] dilution.

## 3. Results

### 3.1. Baseline sociodemographic characteristics and age distribution

Over the observation period from January 2020 to May 2026, 74 consecutive HIV-positive patients with sexually transmitted infections at the Dermatology and Venereology Outpatient Clinic of Dr. Moewardi Regional General Hospital met all inclusion criteria and formed the analytical cohort (N = 74). Male patients clearly predominated: 68 (91.89%; 95% Wilson CI: 83.42–96.23%) versus 6 female patients (8.11%; 95% CI: 3.77–16.58%), a male-to-female ratio of 11.33:1 (one-sample binomial goodness-of-fit $\chi^2 = 51.946$, df = 1, $p < 0.001$; Cohen's h = 0.993, a large effect). By 10-year age bracket, the cohort was concentrated in young reproductive-age adults. The largest group was 21–30 years with 36 patients (48.65%; 95% CI: 37.61–59.82%), followed by 31–40 years with 22 patients (29.73%; 95% CI: 20.53–40.93%) and the adolescent and late-teen 11–20 years group with 10 patients (13.51%; 95% CI: 7.51–23.12%). Middle-aged and older adults were few: 3 patients aged 41–50 years (4.05%;

95% CI: 1.39–11.25%), 2 aged 51–60 years (2.70%; 95% CI: 0.74–9.33%), and 1 aged 61–70 years (1.35%; 95% CI: 0.24–7.27%).

Combined into reproductive age brackets, 58 of the 74 patients (78.38%; 95% CI: 67.73–86.23%) were aged 21–40 years. Patients aged ≤30 years (11–30 years combined) numbered 46 (62.16%; 95% CI: 50.78–72.35%), against 28 (37.84%; 95% CI: 27.65–49.22%) aged >30 years (31–70 years combined). Continuous age had a mean ± SD of 29.70 ± 9.01 years (95% CI: 27.62–31.79 years; grouped class-midpoint mean ± SD = 29.28 ± 9.61 years) and a median of 28.00 years [IQR: 24.00–34.00 years; overall range: 17–64 years]. The Shapiro–Wilk test showed significant positive (rightward) skewness toward the younger strata ($W = 0.901$, $p = 2.63 \times 10^{-5}$, $p < 0.001$), which is why both parametric and non-parametric age summaries are given. Table 1 lists the baseline sociodemographic distribution and normality parameters, and Figure 1 displays them.

### 3.2. STI diagnosis spectrum and coinfection multiplicity

By primary dermatovenereological diagnosis, HPV-associated condyloma acuminata (anogenital warts) was the most frequent STI syndrome among HIV-positive patients at Dr. Moewardi Regional General Hospital. Isolated condyloma acuminata was diagnosed in 43 patients (58.11%; 95% CI: 46.74–68.68%), almost three-fifths of the cohort. Isolated clinical syphilis came second, in 17 patients (22.97%; 95% CI: 14.87–33.75%). Concurrent condyloma acuminata and syphilis was documented in 6 patients (8.11%; 95% CI: 3.77–16.58%), and another 6 patients (8.11%; 95% CI: 3.77–16.58%) had other polymicrobial STI coinfections combining genital herpes, vulvovaginal candidiasis, and gonococcal urethritis. Isolated molluscum contagiosum was diagnosed in 2 patients (2.70%; 95% CI: 0.74–9.33%).

Grouped by the number of concurrent STI coinfections alongside HIV, most patients had a single STI (1 Infection: n = 62, 83.78%; 95% CI: 73.76–90.47%), made up of 43 patients with isolated condyloma acuminata (58.11%), 17 with isolated syphilis (22.97%), and 2 with isolated molluscum contagiosum (2.70%) (43 + 17 + 2 = 62; 83.78%). Multiple STI coinfections (>1 Coinfection) occurred in 12 patients (16.22%; 95% CI: 9.53–26.24%): 6 with concurrent condyloma acuminata plus syphilis (8.11%) and 6 with other polymicrobial combinations of genital herpes, vulvovaginal candidiasis, and gonococcal urethritis (8.11%) (6 + 6 = 12; 16.22%). Counting pathogens across both isolated and dual diagnoses, condyloma acuminata involved 49 of the 74 patients (66.22%; 95% CI: 54.88–75.96%), and overt clinical syphilis at presentation involved 23 of 74 (31.08%; 95% CI: 21.69–42.34%). Table 2 gives the full breakdown of STI diagnoses and coinfection multiplicity, and Figure 2 illustrates it.

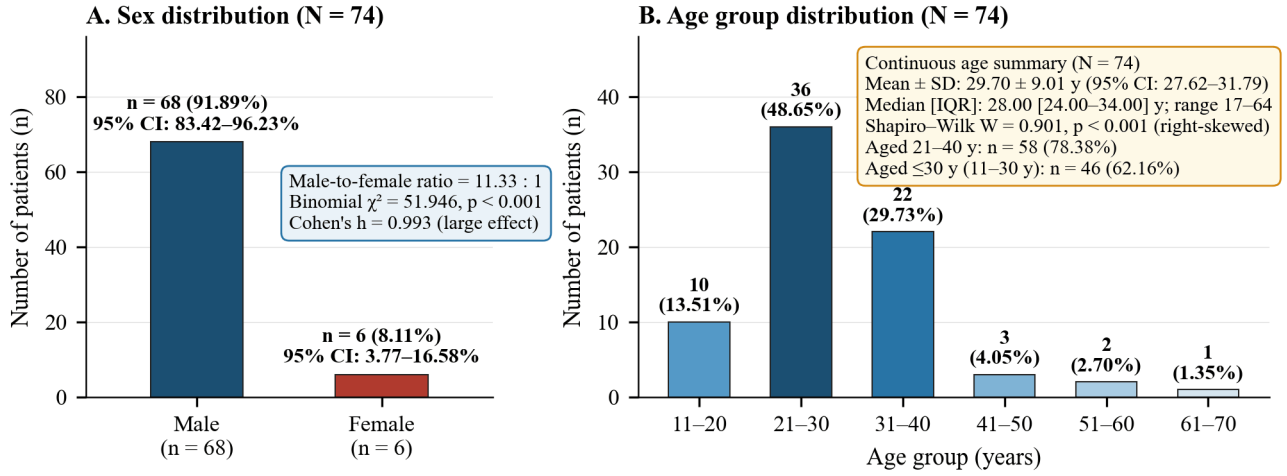


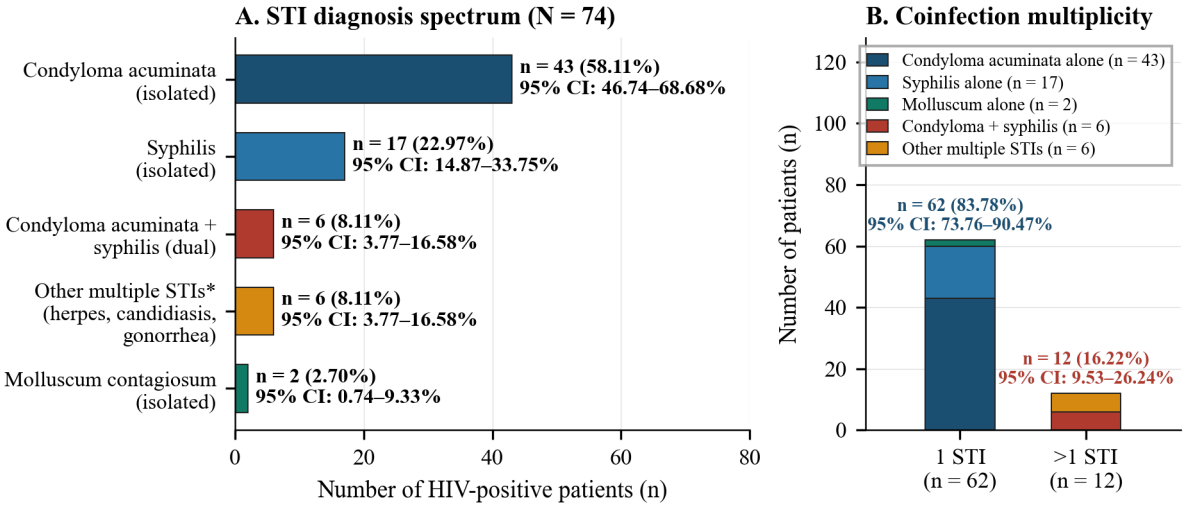

**Figure 1.** Sociodemographic profile of HIV-positive patients with STIs (N = 74): (A) sex distribution (male-to-female ratio 11.33:1; Cohen's h = 0.993); (B) age distribution by 10-year stratum, with the continuous age summary (mean 29.70 ± 9.01 years; median 28.00 years).

**Table 1.** Baseline sociodemographic characteristics and continuous age profile of HIV-positive patients with sexually transmitted infections (N = 74, 2020–2026).

| Sociodemographic Characteristic | Frequency (n) | Percentage (%) | 95% Wilson CI (%) | Parametric / Non-Parametric Summary & Normality Test |
|---|---|---|---|---|
| Sex Distribution (N = 74) | | | | Male-to-Female Ratio = 11.33 : 1; $\chi^2$ = 51.946, p < 0.001; Cohen's h = 0.993 |
| Male | 68 | 91.89% | 83.42–96.23% | Predominant biological sex stratum |
| Female | 6 | 8.11% | 3.77–16.58% | Minority biological sex stratum |
| Age Group Distribution, 10-Year Strata (N = 74) | | | | Mean ± SD = 29.70 ± 9.01 years (95% CI: 27.62–31.79); Grouped Midpoint Mean = 29.28 ± 9.61 years |
| 11–20 years (Adolescent / Late Teen) | 10 | 13.51% | 7.51–23.12% | Stratum midpoint = 15.5 years |

| Sociodemographic Characteristic | Frequency (n) | Percentage (%) | 95% Wilson CI (%) | Parametric / Non-Parametric Summary & Normality Test |
|---|---|---|---|---|
| 21–30 years (Young Adult Peak) | 36 | 48.65% | 37.61–59.82% | Modal age group; Median cohort age = 28.00 years [IQR: 24.00–34.00; Range: 17–64] |
| 31–40 years (Early Middle Adult) | 22 | 29.73% | 20.53–40.93% | Second largest age stratum; 21–40 years combined: n = 58 (78.38%; 95% CI: 67.73–86.23%) |
| 41–50 years (Middle Adult) | 3 | 4.05% | 1.39–11.25% | Stratum midpoint = 45.5 years |
| 51–60 years (Older Adult) | 2 | 2.70% | 0.74–9.33% | Stratum midpoint = 55.5 years |
| 61–70 years (Elderly) | 1 | 1.35% | 0.24–7.27% | Stratum midpoint = 65.5 years |
| Dichotomized Age Brackets (N = 74) | | | | Shapiro–Wilk Normality Test: W = 0.901, p < 0.001 (Right-skewed toward young adults) |
| Aged ≤30 years (11–30 years) | 46 | 62.16% | 50.78–72.35% | Primary young reproductive-age subcohort |
| Aged >30 years (31–70 years) | 28 | 37.84% | 27.65–49.22% | Older adult comparison subcohort |
| Total Study Cohort | 74 | 100.00% | — | 100% complete ascertainment |

***Notes:*** *Abbreviations: CI, confidence interval; HIV, human immunodeficiency virus; IQR, interquartile range; SD, standard deviation; STI, sexually transmitted infection. Percentages may not sum to 100.00% because of rounding (the six age strata sum to 99.99%). The youngest patient was 17 years; the lowest stratum (11–20 years) follows the stratification defined in Methods.*




**Genital herpes, vulvovaginal candidiasis and gonococcal urethritis in polymicrobial combinations.*

**Figure 2.** STI diagnosis spectrum and coinfection multiplicity (N = 74): (A) primary STI diagnoses with 95% Wilson confidence intervals; (B) single STI (1 infection, n = 62 = 43 + 17 + 2) versus multiple STIs (>1 infection, n = 12 = 6 + 6).

### *3.3. Quantitative VDRL endpoint dilution spectrum and TPHA serological profile*

Paired VDRL and TPHA assays were performed in 55 of the 74 patients (74.32%; 95% CI: 63.35–82.90%), whereas 19 patients (25.68%; 95% CI: 17.10–36.65%) had no serological testing at their outpatient visit. For non-treponemal VDRL across the total cohort, 23 patients were negative (non-reactive) (31.08% of the total cohort; 41.82% of the 55 tested; 95% CI: 21.69–42.34%) and 32 were positive (reactive) at various dilutions (43.24% of the total; 58.18% of the 55 tested; 95% CI: 32.57–54.59%). The 32 VDRL-positive patients spread across nine dilution categories: positive undiluted (1:1) in 1 patient (1.35% of total cohort; 1.82% of tested), 1:2 in 6 (8.11% of total; 10.91% of tested), 1:4 in 6 (8.11%; 10.91%), 1:8 in 4 (5.41%; 7.27%), 1:16 in 8 (10.81%; 14.55%), 1:32 in 4 (5.41%; 7.27%), 1:128 in 1 (1.35%; 1.82%), 1:320 in 1 (1.35%; 1.82%), and 1:512 in 1 (1.35%; 1.82%). The most frequent (modal) positive titer was 1:16 (n = 8; 10.81% of the total cohort and 25.00% [8/32] of all VDRL-positive cases), and the highest endpoint dilution was 1:512 (n = 1, 1.35%).

By clinical titer threshold, low-titer VDRL reactivity (≤1:4, covering undiluted 1:1, 1:2, and 1:4) was seen in 13 patients (17.57% of the total cohort; 23.64% of tested; 40.63% of VDRL-positive cases), and high-titer reactivity (≥1:8, covering 1:8 through 1:512) in 19 patients (25.68% of total; 34.55% of tested; 59.38% of VDRL-positive cases). Among the 32 reactive patients, reciprocal VDRL titers gave a geometric mean titer (GMT) of 1:10.0 (mean $\log_2$ reciprocal titer = 3.32 ± 2.13) and a median of 1:8.0 [IQR: 1:4.0–1:16.0; range: 1:1–1:512; Shapiro–Wilk W = 0.391, p < 0.001]. For the specific treponemal TPHA assay across 74 patients, 34 were reactive (45.95% of the total cohort, 95% CI: 35.07–57.22%; 61.82% [34/55] of the tested subcohort, 95% CI: 48.61–73.48%), 21 were non-reactive (28.38% of total, 95% CI: 19.37–39.52%; 38.18% [21/55] of tested, 95% CI: 26.52–51.39%), and 19 were not tested (25.68%; 95% CI: 17.10–36.65%). Table 3 summarizes the full VDRL and TPHA distributions, and Figure 3 shows them.

**Table 2.** Dermatovenereological STI diagnosis spectrum and coinfection multiplicity among HIV-positive patients (N = 74).

| Clinical STI Diagnostic Category | Patients (n) | Percentage of Cohort (%) | 95% Wilson CI (%) | Coinfection Multiplicity Assignment & Etiological Classification |
|---|---|---|---|---|
| Primary Mutually Exclusive STI Diagnosis (N = 74) | | | | Categorized by clinical and laboratory dermatovenereological evaluation |
| Condyloma acuminata (Isolated genital warts) | 43 | 58.11% | 46.74–68.68% | Single STI coinfection (1 Infection); Human papillomavirus (HPV) types 6/11 & high-risk co-genotypes |
| Syphilis (Isolated clinical syphilis) | 17 | 22.97% | 14.87–33.75% | Single STI coinfection (1 Infection); *Treponema pallidum* subsp. pallidum |
| Condyloma acuminata + Syphilis (Dual coinfection) | 6 | 8.11% | 3.77–16.58% | Multiple STI coinfections (>1 Coinfection); Concurrent viral (HPV) and spirochetal (*T. pallidum*) disease |
| Other multiple STI coinfections (Genital herpes, vulvovaginal candidiasis, gonococcal urethritis) | 6 | 8.11% | 3.77–16.58% | Multiple STI coinfections (>1 Coinfection); Polymicrobial HSV-2, *Candida* spp., and *Neisseria gonorrhoeae* combinations |
| Molluscum contagiosum (Isolated poxviral lesions) | 2 | 2.70% | 0.74–9.33% | Single STI coinfection (1 Infection); Molluscum contagiosum virus (MCV) |
| Number of STI Coinfections in HIV (N = 74) | | | | Exact mathematical decomposition across single vs. polymicrobial STI strata |
| 1 Infection (Single STI coinfection in HIV) | 62 | 83.78% | 73.76–90.47% | Sum of Condyloma acuminata alone (43) + Syphilis alone (17) + Molluscum contagiosum alone (2) = 62 |
| >1 Coinfection (Multiple STI coinfections in HIV) | 12 | 16.22% | 9.53–26.24% | Sum of Condyloma acuminata + Syphilis (6) + Other multiple STI coinfections (6) = 12 |
| Cumulative Pathogen Involvement Across Cohort | | | | Accounts for both isolated and dual-diagnosed cases |
| Any Condyloma acuminata (Isolated 43 + Dual 6) | 49 | 66.22% | 54.88–75.96% | Two-thirds of HIV-positive STI patients exhibited HPV-driven anogenital warts |
| Any Overt Clinical Syphilis (Isolated 17 + Dual 6) | 23 | 31.08% | 21.69–42.34% | Excludes 11 TPHA-reactive patients without a syphilis diagnosis, identified through TPHA/VDRL screening |

***Notes:*** *Abbreviations: CI, confidence interval; HIV, human immunodeficiency virus; HPV, human papillomavirus; HSV-2, herpes simplex virus type 2; MCV, molluscum contagiosum virus; STI, sexually transmitted infection.*

**Table 3.** Quantitative VDRL endpoint dilution spectrum and TPHA serological profile (N = 74 total cohort; n = 55 serologically tested subcohort).

| Syphilis Serological Parameter & Titer Stratum | Frequency (n) | % of Total Cohort (N = 74) | % of Tested Subcohort (n = 55) | 95% Wilson CI in Total Cohort (%) | Quantitative & Clinical Serological Interpretation |
|---|---|---|---|---|---|
| VDRL Non-Treponemal Assay (N = 74) | | | | | Quantitative lipoidal flocculation titer profile |
| Negative (Non-reactive) | 23 | 31.08% | 41.82% | 21.69–42.34% | Absence of detectable anti-cardiolipin/lecithin/cholesterol reaginic antibodies |
| Positive (Undiluted / 1:1) | 1 | 1.35% | 1.82% | 0.24–7.27% | Low-titer reactive (≤1:4); early seroconversion, treated serofast, or late latent state |
| Positive 1:2 | 6 | 8.11% | 10.91% | 3.77–16.58% | Low-titer reactive (≤1:4); accounts for 18.75% (6/32) of VDRL-positive cases |
| Positive 1:4 | 6 | 8.11% | 10.91% | 3.77–16.58% | Low-titer reactive (≤1:4); cumulative low-titer ≤1:4: n = 13 (17.57% total; 40.63% of VDRL+) |
| Positive 1:8 | 4 | 5.41% | 7.27% | 2.12–13.09% | High-titer reactive (≥1:8); indicative of active treponemal replication |
| Positive 1:16 (Modal Positive Titer) | 8 | 10.81% | 14.55% | 5.58–19.90% | Most frequent positive dilution (25.00% [8/32] of VDRL-positive cases) |
| Positive 1:32 | 4 | 5.41% | 7.27% | 2.12–13.09% | High-titer active syphilis; elevated risk of central nervous system invasion in HIV |
| Positive 1:128 | 1 | 1.35% | 1.82% | 0.24–7.27% | Markedly elevated non-treponemal antibody activity |
| Positive 1:320 | 1 | 1.35% | 1.82% | 0.24–7.27% | High-titer non-standard laboratory serial dilution endpoint |
| Positive 1:512 (Maximum Endpoint Titer) | 1 | 1.35% | 1.82% | 0.24–7.27% | Highest recorded dilution; cumulative high-titer ≥1:8: n = 19 (25.68% total; 59.38% of VDRL+) |

| Syphilis Serological Parameter & Titer Stratum | Frequency (n) | % of Total Cohort (N = 74) | % of Tested Subcohort (n = 55) | 95% Wilson CI in Total Cohort (%) | Quantitative & Clinical Serological Interpretation |
|---|---|---|---|---|---|
| Total VDRL Positive (Any Reactive Titer) | 32 | 43.24% | 58.18% | 32.57–54.59% | GMT = 1:10.0 ($log_2$ mean 3.32 ± 2.13); median = 1:8.0 [IQR: 1:4.0–1:16.0] |
| Not tested (VDRL not performed) | 19 | 25.68% | — | 17.10–36.65% | Clinical diagnostic gap in patients presenting with non-ulcerative viral STIs |
| TPHA Specific Treponemal Assay (N = 74) | | | | | Qualitative hemagglutination assay for specific anti-*T. pallidum* antibodies |
| Reactive | 34 | 45.95% | 61.82% | 35.07–57.22% | Confirmed current or lifetime exposure/infection with *Treponema pallidum* |
| Non-reactive | 21 | 28.38% | 38.18% | 19.37–39.52% | Seronegative for specific treponemal antibodies among tested patients |
| Not tested (TPHA not performed) | 19 | 25.68% | — | 17.10–36.65% | Identical 19-patient untested subcohort as VDRL |

***Notes:*** *Abbreviations: CI, confidence interval; GMT, geometric mean titer; IQR, interquartile range; TPHA, Treponema pallidum hemagglutination assay; VDRL, Venereal Disease Research Laboratory. Shapiro–Wilk test on reciprocal VDRL titers (n = 32): W = 0.391, p < 0.001. The median, geometric mean titer, standard deviation of $log_2$ titer and Shapiro–Wilk W were recomputed from the printed titer distribution.*

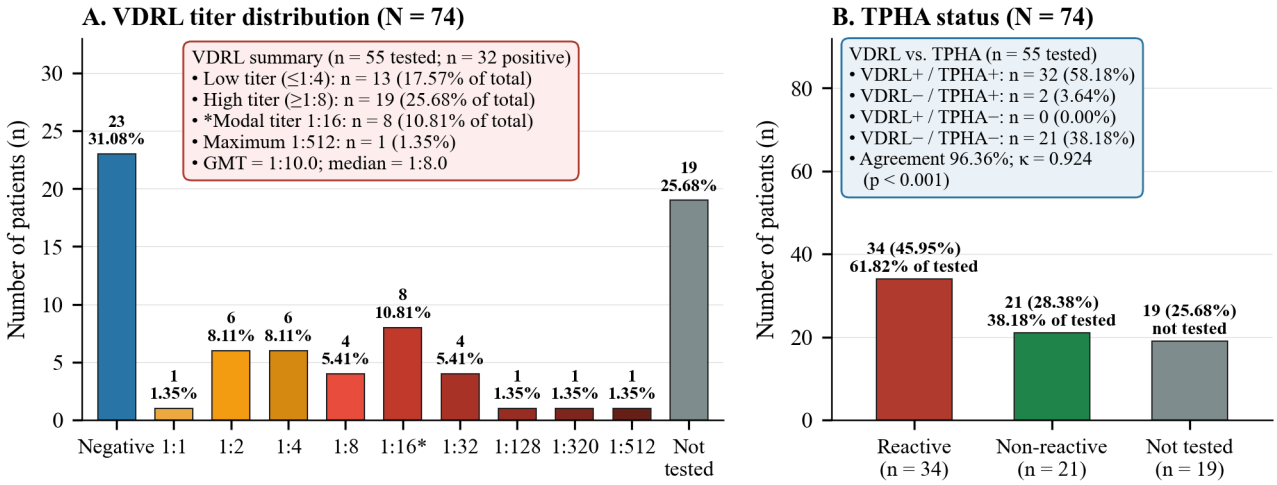



**Figure 3.** Syphilis serology (N = 74; n = 55 tested; n = 19 not tested): (A) quantitative VDRL endpoint dilution distribution (modal titer 1:16, marked with an asterisk; geometric mean titer 1:10.0; median 1:8.0); (B) TPHA status and VDRL–TPHA concordance (agreement 96.36%; Cohen's κ = 0.924; p < 0.001).

### *3.4. VDRL–TPHA concordance and TPHA-reactive patients without a syphilis diagnosis*

Cross-tabulating paired VDRL and TPHA results in the serologically tested subcohort (n = 55) showed near-perfect concordance between the non-treponemal and treponemal assays. Of the 55 tested patients, 32 (58.18%) were both VDRL-positive and TPHA-reactive and 21 (38.18%) were both VDRL-negative and TPHA-non-reactive. 2 patients (3.64%) were discordant, VDRL-negative but TPHA-reactive, which may reflect prior treated syphilis with non-treponemal seroreversion, persistent late latent treponemal reactivity, or an undiluted prozone phenomenon. 0 patients (0.00%) showed a biological false-positive VDRL (VDRL-positive / TPHA-non-reactive). Overall agreement between VDRL and TPHA was therefore 96.36% (53/55), with a Cohen's unweighted κ of 0.924 (95% CI: 0.821–1.000; Pearson's $\chi^2 = 47.263$, $p = 6.21 \times 10^{-12}$, Fisher's exact $p = 3.01 \times 10^{-13}$, Cramér's V = 0.927). With TPHA reactivity as the treponemal reference standard, qualitative VDRL had a sensitivity of 94.12% (32/34; 95% CI: 80.91–98.37%) and a specificity of 100.00% (21/21; 95% CI: 84.54–100.00%).

Comparing clinical STI diagnoses with TPHA results across the total cohort (N = 74) revealed a sizeable number of TPHA-reactive patients without a syphilis diagnosis (possible subclinical, latent, or previously treated syphilis) among patients whose primary STI was not syphilis. All 23 patients with overt clinical syphilis (17 isolated syphilis plus 6 condyloma acuminata plus syphilis; 31.08% of the total cohort) were TPHA-reactive and VDRL-positive (23/23, 100.00%). Among the other 51 patients, whose primary STIs were non-syphilitic (43 isolated condyloma acuminata, 2 molluscum contagiosum, and 6 other polymicrobial STIs; 68.92% of the total cohort), routine serology found 11 additional TPHA-reactive cases (21.57% of all 51 non-syphilitic STI patients, and 34.38% [11/32] of the 32 serologically tested non-syphilitic STI patients). Comparing clinical syphilis with

all other patients, with the untested counted as non-reactive, gave $\chi^2$ = 39.262 (p < 0.001; Cramér's V = 0.728); because clinical syphilis required reactive serology, this contrast is descriptive. Of these 11 TPHA-reactive patients without a syphilis diagnosis, 9 were also VDRL-positive (7 with low-titer VDRL ≤1:4 and 2 with high-titer VDRL ≥1:8) and 2 were VDRL-negative. Among the 32 VDRL-positive patients, high-titer VDRL (≥1:8) was present in 17 of 23 (73.91%) with overt clinical syphilis but in only 2 of 9 (22.22%) with seropositive non-syphilitic presentations, a 9.917-fold higher odds of high-titer VDRL ≥1:8 in overt clinical syphilis (crude OR = 9.917, 95% CI: 1.596–61.599, $\chi^2$ = 7.166, p = 0.0074, Fisher's exact p = 0.0147, Cramér's V = 0.473). Table 4 and Figure 4 present these concordance findings and the TPHA-reactive patients without a syphilis diagnosis.

### 3.5. Bivariate and multivariable determinants of condyloma acuminata and TPHA seroreactivity

Bivariate analyses examined the sociodemographic and clinical determinants of isolated condyloma acuminata and of confirmed TPHA reactivity (Table 5 and Figure 5). For isolated condyloma acuminata (n = 43 vs. n = 31 other primary STI diagnoses), patients aged ≤30 years had a significantly higher prevalence than those aged >30 years (Pearson p = 0.038, smallest expected count 11.7; Fisher exact p = 0.0525) (31/46 [67.39%] vs. 12/28 [42.86%]; crude OR = 2.756, 95% CI: 1.045–7.267, $\chi^2$ = 4.304, p = 0.0380, Cramér's V = 0.241). Men also had a higher proportion of isolated condyloma acuminata than women (41/68 [60.29%] vs. 2/6 [33.33%]; crude OR = 3.037, 95% CI: 0.520–17.751, $\chi^2$ = 1.646, p = 0.1995), but with so few women this difference was not statistically significant.

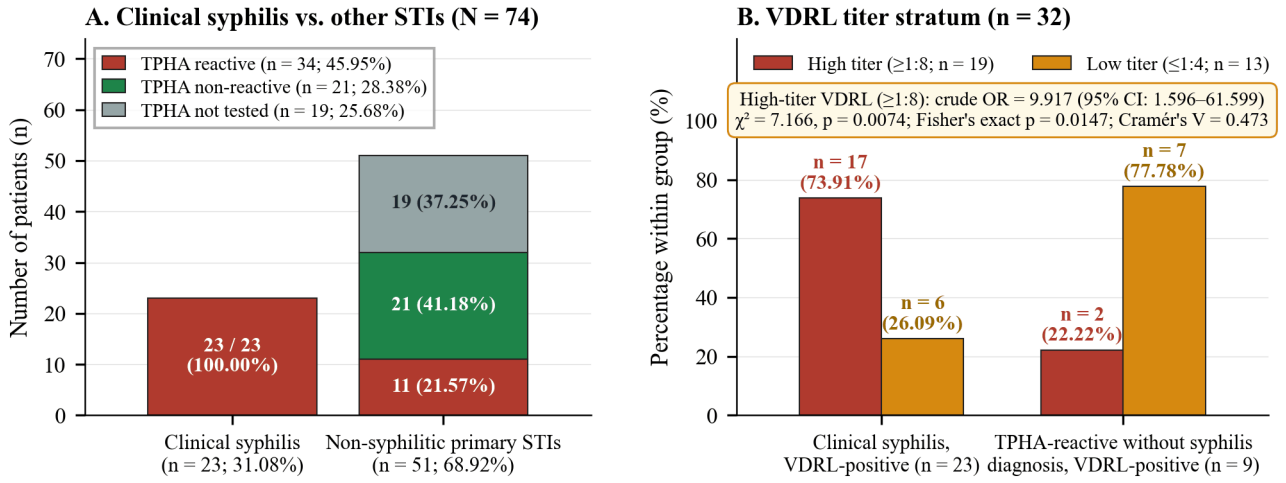



**Figure 4.** Clinical diagnosis and serology: (A) TPHA status in patients with clinical syphilis (n = 23) and in patients with non-syphilitic primary STIs (n = 51), including the 11 TPHA-reactive patients without a syphilis diagnosis (34.38% [11/32] of those tested); (B) VDRL titer stratum among the 32 VDRL-positive patients (crude OR = 9.917; p = 0.0074).

**Table 4.** Two-by-two concordance matrix between VDRL and TPHA, and TPHA status by clinical diagnosis (n = 55 tested; N = 74 total cohort).

| Serological Cross-Classification / Clinical Stratum | TPHA Reactive, n (%) | TPHA Non-Reactive, n (%) | TPHA Not Tested, n (%) | Row Total, n (%) | Agreement / Effect Size & Statistical Significance |
|---|---|---|---|---|---|
| A. Paired VDRL vs. TPHA Concordance in Tested Subcohort (n = 55) | | | | | Overall Agreement = 96.36% (53/55); Cohen's κ = 0.924 (95% CI: 0.821–1.000) |
| VDRL Positive (Any Titer 1:1 to 1:512) | 32 (58.18%) | 0 (0.00%) | 0 (0.00%) | 32 (58.18%) | VDRL Specificity vs. TPHA = 100.00% (21/21; 0% biological false-positive VDRL) |
| VDRL Negative (Non-reactive) | 2 (3.64%) | 21 (38.18%) | 0 (0.00%) | 23 (41.82%) | VDRL Sensitivity vs. TPHA = 94.12% (32/34); 2 discordant VDRL−/TPHA+ cases |
| Total Serologically Tested Subcohort | 34 (61.82%) | 21 (38.18%) | 0 (0.00%) | 55 (100.00%) | $\chi^2$ = 47.263, p = 6.21 × $10^{-12}$ (Fisher's exact p = 3.01 × $10^{-13}$); Cramér's V = 0.927 |
| B. Clinical Syphilis Diagnosis vs. TPHA Status Across Total Cohort (N = 74) | | | | | Quantifies occult treponemal burden in non-syphilitic STI presentations |
| Overt Clinical Syphilis (Syphilis alone n=17 + Condyloma+Syphilis n=6) | 23 (100.00%) | 0 (0.00%) | 0 (0.00%) | 23 (31.08%) | 100.00% (23/23) serologically confirmed by both reactive TPHA and positive VDRL |

| Serological Cross-Classification / Clinical Stratum | TPHA Reactive, n (%) | TPHA Non-Reactive, n (%) | TPHA Not Tested, n (%) | Row Total, n (%) | Agreement / Effect Size & Statistical Significance |
|---|---|---|---|---|---|
| Non-Syphilitic Primary STIs (Condyloma n=43, Molluscum n=2, Others n=6) | 11 (21.57%) | 21 (41.18%) | 19 (37.25%) | 51 (68.92%) | 11 TPHA-reactive patients without a syphilis diagnosis (21.57% of 51; 34.38% [11/32] of tested non-syphilitic STIs) |
| Total Study Cohort (N = 74) | 34 (45.95%) | 21 (28.38%) | 19 (25.68%) | 74 (100.00%) | OR = 165.522 (95% CI: 9.322–2939.025), $\chi^2$ = 39.262, p < 0.001, Cramér's V = 0.728 |

***Notes:*** *Abbreviations: CI, confidence interval; OR, odds ratio; STI, sexually transmitted infection; TPHA, Treponema pallidum hemagglutination assay; VDRL, Venereal Disease Research Laboratory. The odds ratio in the last row compares clinical syphilis, which required reactive serology, with all other patients and counts the 19 untested patients as non-reactive; it is descriptive.*

For confirmed TPHA reactivity in the total cohort (N = 74: 34 reactive vs. 40 non-reactive/untested), patients with multiple STI coinfections (>1 STI, n = 12) had a significantly higher prevalence of reactivity than those with a single STI (smallest expected count 5.5, so Pearson's test applies) (1 STI, n = 62) (9/12 [75.00%] vs. 25/62 [40.32%]; crude OR = 4.440, 95% CI: 1.093–18.036, $\chi^2$ = 4.868, p = 0.0274, Cramér's V = 0.256). Patients aged ≤30 years showed a higher prevalence of TPHA reactivity than those aged >30 years that did not reach significance, both in the total cohort (25/46 [54.35%] vs. 9/28 [32.14%]; crude OR = 2.513, 95% CI: 0.941–6.714, $\chi^2$ = 3.455, p = 0.0630, Cramér's V = 0.216) and in the serologically tested subcohort (25/35 [71.43%] vs. 9/20 [45.00%]; crude OR = 3.056, 95% CI: 0.971–9.614, $\chi^2$ = 3.766, p = 0.0523, Cramér's V = 0.262). Within the tested subcohort (n = 55), male sex was also associated with TPHA reactivity compared with female sex (Pearson p = 0.0435; Fisher exact p = 0.0643) (33/50 [66.00%] vs. 1/5 [20.00%]; crude OR = 7.765, 95% CI: 0.804–75.017, $\chi^2$ = 4.075, p = 0.0435, Cramér's V = 0.272).

To adjust for possible confounding by age, sex, and STI multiplicity, a multivariable binary logistic regression model of confirmed TPHA reactivity was fitted in the total cohort (N = 74; Table 6 and Figure 5). Restricted to the 55 tested patients, the crude odds ratio for multiple STIs was 3.420 (95% CI: 0.661–17.705; Pearson p = 0.1269; Fisher's exact p = 0.1742; Table 5), so the association was not significant when untested patients were excluded. The omnibus model was statistically significant (likelihood ratio $\chi^2$ = 10.889, df = 3, p = 0.0123; log-likelihood = −45.605 vs. null log-likelihood = −51.049; McFadden's pseudo-$R^2$ = 0.107). After adjustment, multiple STI coinfections (>1 STI vs. 1 STI) was associated with TPHA seroreactivity, with 4.890-fold higher adjusted odds of confirmed treponemal infection (β = 1.587, SE = 0.751, Wald z = 2.115, aOR = 4.890, 95% CI: 1.123–21.290, p = 0.0344). Age ≤30 years had a positive adjusted association that approached significance (β = 0.928, SE = 0.531, Wald z = 1.748, aOR = 2.529, 95% CI: 0.893–7.159, p = 0.0805), and male sex had an adjusted odds ratio of 5.558 (β = 1.715, SE = 1.229, Wald z = 1.395, 95% CI: 0.499–61.862, p = 0.1630).

**Table 5.** Bivariate analysis of determinants of isolated condyloma acuminata, TPHA seroreactivity, and high-titer VDRL (≥1:8).

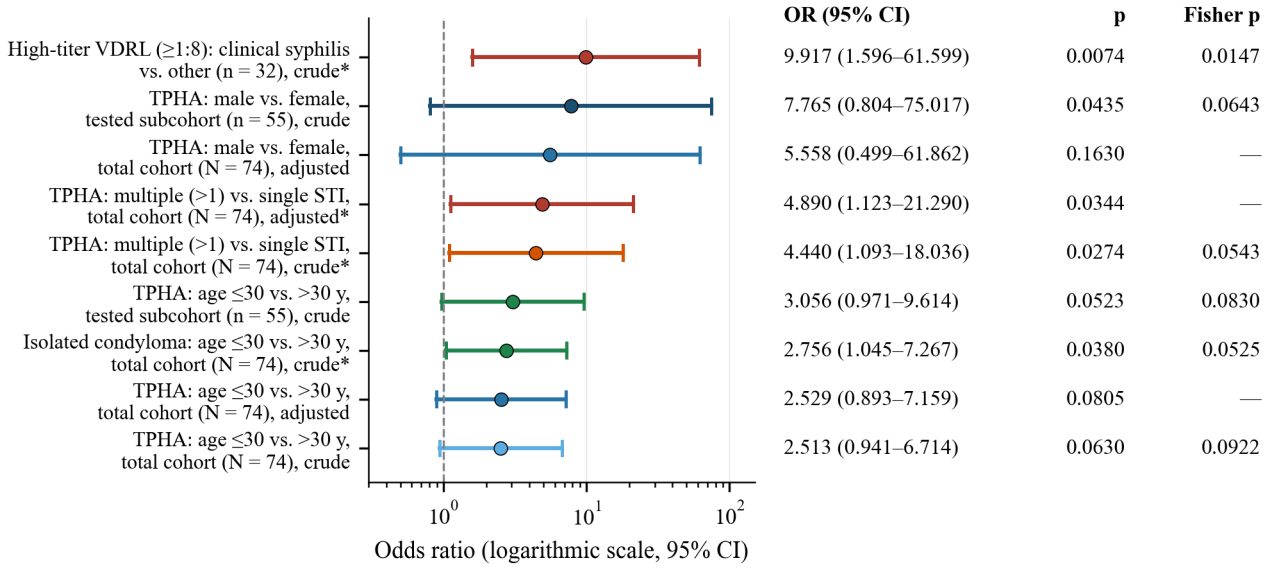
| Analytical Comparison & Predictor Stratum | Outcome Present, n / N (%) | Outcome Absent, n / N (%) | Crude Odds Ratio (95% CI) | Chi-Square ($\chi^2$) & Cramér's V | p-value (Pearson $\chi^2$ / Fisher's Exact) |
|---|---|---|---|---|---|
| **1. Isolated Condyloma Acuminata Presentation (N = 74; n = 43 vs. n = 31)** | | | | | |
| Age ≤30 years (n = 46) vs. >30 years (n = 28) | 31/46 (67.39%) vs. 12/28 (42.86%) | 15/46 (32.61%) vs. 16/28 (57.14%) | 2.756 (1.045–7.267) | $\chi^2$ = 4.304; V = 0.241 | p = 0.0380* (Fisher p = 0.0525) |
| Male sex (n = 68) vs. Female sex (n = 6) | 41/68 (60.29%) vs. 2/6 (33.33%) | 27/68 (39.71%) vs. 4/6 (66.67%) | 3.037 (0.520–17.751) | $\chi^2$ = 1.646; V = 0.149 | p = 0.1995 (Fisher p = 0.2297) |
| **2. Confirmed TPHA Reactivity Across Total Cohort (N = 74; n = 34 vs. n = 40)** | | | | | |
| Multiple STIs (>1 STI, n = 12) vs. Single STI (1 STI, n = 62) | 9/12 (75.00%) vs. 25/62 (40.32%) | 3/12 (25.00%) vs. 37/62 (59.68%) | 4.440 (1.093–18.036) | $\chi^2$ = 4.868; V = 0.256 | p = 0.0274* (Fisher p = 0.0543) |
| Age ≤30 years (n = 46) vs. >30 years (n = 28) | 25/46 (54.35%) vs. 9/28 (32.14%) | 21/46 (45.65%) vs. 19/28 (67.86%) | 2.513 (0.941–6.714) | $\chi^2$ = 3.455; V = 0.216 | p = 0.0630 (Fisher p = 0.0922) |
| Male sex (n = 68) vs. Female sex (n = 6) | 33/68 (48.53%) vs. 1/6 (16.67%) | 35/68 (51.47%) vs. 5/6 (83.33%) | 4.714 (0.523–42.509) | $\chi^2$ = 2.254; V = 0.175 | p = 0.1333 (Fisher p = 0.2088) |
| **3. Confirmed TPHA Reactivity in Serologically Tested Subcohort (n = 55; n = 34 vs. n = 21)** | | | | | |
| Male sex (n = 50) vs. Female sex (n = 5) | 33/50 (66.00%) vs. 1/5 (20.00%) | 17/50 (34.00%) vs. 4/5 (80.00%) | 7.765 (0.804–75.017) | $\chi^2$ = 4.075; V = 0.272 | p = 0.0435 (Fisher p = 0.0643) |
| Age ≤30 years (n = 35) vs. >30 years (n = 20) | 25/35 (71.43%) vs. 9/20 (45.00%) | 10/35 (28.57%) vs. 11/20 (55.00%) | 3.056 (0.971–9.614) | $\chi^2$ = 3.766; V = 0.262 | p = 0.0523 (Fisher p = 0.0830) |
| Multiple STIs (>1 STI, n = 11) vs. Single STI (1 STI, n = 44) | 9/11 (81.82%) vs. 25/44 (56.82%) | 2/11 (18.18%) vs. 19/44 (43.18%) | 3.420 (0.661–17.705) | $\chi^2$ = 2.330; V = 0.206 | p = 0.1269 (Fisher p = 0.1742) |
| **4. High-Titer VDRL (≥1:8 vs. ≤1:4) Among VDRL-Positive Patients (n = 32; n = 19 vs. n = 13)** | | | | | |
| Overt Clinical Syphilis (n = 23) vs. Occult Seropositive STI (n = 9) | 17/23 (73.91%) vs. 2/9 (22.22%) | 6/23 (26.09%) vs. 7/9 (77.78%) | 9.917 (1.596–61.599) | $\chi^2$ = 7.166; V = 0.473 | p = 0.0074* (Fisher p = 0.0147*) |

*Notes:* *Significant at $p < 0.05$ by the governing test: Pearson's $\chi^2$ when the smallest expected count is at least 5 (age and condyloma acuminata, 11.7; multiple STIs, 5.5), Fisher's exact test otherwise (sex comparisons, 2.5, 2.8 and 1.9; multiple STIs in the tested subcohort, 4.2; high-titer VDRL, 3.7). The sex comparison in the tested subcohort (Pearson p = 0.0435) is therefore not significant (Fisher p = 0.0643). Abbreviations: CI, confidence interval; OR, odds ratio; STI, sexually transmitted infection; TPHA, Treponema pallidum hemagglutination assay; VDRL, Venereal Disease Research Laboratory.

**Table 6.** Multivariable logistic regression of predictors of confirmed TPHA reactivity among HIV-positive patients with STIs (N = 74).

| Explanatory Variable (Predictor) | Regression Coefficient (β) | Standard Error (SE) | Wald z-Statistic | Adjusted Odds Ratio (aOR) | 95% Confidence Interval for aOR | p-value |
|---|---|---|---|---|---|---|
| Multiple STI Coinfections (>1 STI vs. 1 STI [Reference]) | 1.587 | 0.751 | 2.115 | 4.890 | 1.123–21.290 | 0.0344* |
| Young Adult Age Group (≤30 years vs. >30 years [Reference]) | 0.928 | 0.531 | 1.748 | 2.529 | 0.893–7.159 | 0.0805 |
| Biological Sex (Male vs. Female [Reference]) | 1.715 | 1.229 | 1.395 | 5.558 | 0.499–61.862 | 0.1630 |
| Model Intercept (Constant $\beta_0$) | −2.603 | 1.284 | −2.028 | 0.074 | 0.006–0.916 | 0.0425* |

*Notes:* *Statistically significant at $\alpha = 0.05$ (Wald test). Model diagnostics (N = 74): log-likelihood = −45.605; null log-likelihood = −51.049; likelihood ratio omnibus test $\chi^2 = 10.889$ (df = 3, p = 0.0123); McFadden pseudo-$R^2 = 0.107$. Exploratory model: the outcome counts the 19 untested patients as non-reactive and includes syphilis cases, which are TPHA-reactive by definition; 34 events for three predictors.




*Significant at $p < 0.05$ by the governing test (Pearson if the smallest expected count is ≥5, otherwise Fisher). p = Pearson $\chi^2$ (crude) or Wald test (adjusted). Multivariable model (N = 74): likelihood ratio $\chi^2 = 10.889$, df = 3, p = 0.0123; McFadden pseudo-$R^2 = 0.107$.

**Figure 5.** Forest plot of crude and adjusted odds ratios with 95% confidence intervals (logarithmic scale) for determinants of TPHA seroreactivity (N = 74 total, n = 55 tested), isolated condyloma acuminata, and high-titer VDRL (≥1:8; n = 32). The multivariable model (N = 74) had a likelihood ratio $\chi^2 = 10.889$ (df = 3, p = 0.0123) and McFadden pseudo-$R^2 = 0.107$. Asterisks mark $p < 0.05$ by the governing test (Pearson's $\chi^2$ when the smallest expected count is at least 5, otherwise Fisher's exact test).

## 4. Discussion

### *4.1. Sociodemographic vulnerability: young adult male predominance in HIV–STI networks*

This retrospective cross-sectional study gives a broad clinical and serological picture of sexually transmitted infections in 74 HIV-positive patients at a major tertiary referral dermatovenereology clinic in Central Java, Indonesia. The first main finding is the high share of men (n = 68, 91.89% vs. female n = 6, 8.11%; male-to-female ratio 11.33:1, p < 0.001). A sharp concentration in the 21–30 years (n = 36, 48.65%) and 31–40 years (n = 22, 29.73%) groups came with it. Reproductive-age patients (21–40 years) made up 78.38%, and the median age was 28.00 years [IQR: 24.00–34.00 years]. Adolescents and young adults aged ≤30 years formed nearly two-thirds of the cohort (n = 46, 62.16%). They had higher odds of isolated condyloma acuminata than adults aged >30 years (67.39% vs. 42.86%, OR = 2.756, Pearson p = 0.038; Fisher exact p = 0.0525). The pattern is familiar. It matches current surveillance across Indonesia and the wider Asia-Pacific region. New HIV infections and the bacterial and viral STI burden have shifted toward young adult men there, especially in urban and peri-urban MSM networks and digital partner-seeking settings.[7,8,20–24] Miwa et al. in a multi-country Asian cohort,[22] and Agung et al.[20] and Sudirman et al.[23] in Indonesian regional analyses, describe the vulnerabilities facing young men aged 18–30 years. These include early sexual debut, condomless receptive and insertive anal intercourse, dense concurrent sexual networks, and healthcare stigma that delays STI

screening. These factors amplify HIV and STI co-transmission. Our cohort fits that picture.

Table 7 sets our Surakarta cohort beside international HIV–STI populations, with both similarities and regional differences. In metropolitan HIV cohorts of Western Europe, North America, and East Asia, such as the Spanish cohort of Villoslada et al.[5] and the South Korean cohort of Lee et al.,[25] male predominance among PLHIV presenting with STIs usually lies between 88% and 100% and is driven mainly by cisgender MSM transmission networks. The picture differs elsewhere. Africa shows a different pattern. Sub-Saharan African HIV clinics, such as the Cameroonian cohort of Obase et al.,[6] typically show a female majority (about 81% female in that cohort), reflecting a generalized heterosexual epidemic. The 91.89% male share (male-to-female ratio 11.33:1, Cohen's h = 0.993) and the young adult peak (48.65% aged 21–30 years; 78.38% aged 21–40 years; mean age 29.70 ± 9.01 years) at Dr. Moewardi Regional General Hospital suggest that HIV-associated STIs in Central Java may resemble the key-population pattern of East Asia and Western Europe rather than a generalized heterosexual one.[20–24] Patients aged ≤30 years were 62.16% (n = 46) of our cohort and had 2.756-fold higher odds of isolated condyloma acuminata (67.39% vs. 42.86%, p = 0.0380). This points to a window for targeted prevention among adolescents and young adults entering HIV care in Indonesia. Catch-up HPV vaccination, barrier protection counseling, and youth-friendly, stigma-free dermatovenereological screening are the obvious components.[22,32]

### *4.2. Immunopathogenesis of condyloma acuminata and polymicrobial venereal coinfections in HIV*

Condyloma acuminata dominated our findings. It accounted for 58.11% (n = 43) of primary isolated STI diagnoses and affected 66.22% (n = 49) of the cohort once the 6 patients (8.11%) with condyloma acuminata plus syphilis are added. This agrees with recent tertiary hospital data from Surakarta (Mawardi et al.[7] and Yuliarto et al.[8]). It also agrees with a cohort of men with HIV from South Korea (Lee et al.[25]) and with anogenital wart series from Turkey (Biten et al.[26]) and India (Pal et al.[28]). These studies identify HPV-driven anogenital warts as a frequent mucocutaneous presentation (Table 7). The biological basis lies in HIV-1 disruption of cutaneous and mucosal cell-mediated immunity.[5,8,33,34] In immunocompetent people, primary anogenital infection with low-risk HPV-6 or HPV-11 is usually cleared within 6 to 18 months. Clearance relies on antigen presentation by epidermal Langerhans cells and cytotoxic activity of CD4+ Th1-polarized and CD8+ T lymphocytes that secrete interferon-gamma (IFN-γ) and interleukin-2 (IL-2).[33–35] In HIV-positive patients, systemic and mucosal CD4+ T-cell depletion, loss of CCR6+ Th17 mucosal barrier lymphocytes, and direct viral down-modulation of major histocompatibility complex (MHC) class I and II molecules weaken local HPV clearance.[5,8,34] Xie et al.[34] recently showed that in condyloma acuminata tissue, upregulated long non-coding RNA MIR31HG stimulates keratinocyte secretion of interleukin-4 (IL-4) and drives M2-like macrophage polarization, which creates an immunosuppressive niche that sustains wart growth. Immune escape is the common theme.

Yuliarto et al.[8] and Liu et al.[36] likewise showed that condyloma acuminata lesions in immunocompromised HIV-positive people often carry high-risk oncogenic genotypes (such as HPV-16, HPV-18, and HPV-52) alongside low-risk HPV-6 and HPV-11. Interaction between the HIV-1 Tat protein and the HPV E6/E7 oncoproteins speeds the ubiquitin-mediated proteasomal degradation of p53 and hypophosphorylated pRb, leading to genomic instability and intraepithelial dysplasia.[5,8,13,37–39] Antiretroviral therapy (ART) restores peripheral CD4+ T-cell counts. Control is incomplete. Even so, mucosal HPV persistence and recurrence of anogenital warts often stay high unless lesions are treated aggressively and followed for high-grade squamous intraepithelial lesions (HSIL), as systematic meta-analyses by Kelly et al.[39] and longitudinal cohorts by Faber et al.[38] and Palefsky et al.[37] indicate. Local reports add to this. Recent Indonesian clinical reports by Arrum et al.,[40] Zulfan et al.,[41] Shelly et al.,[42] and Nurhidayati and Saraswati[43] describe how often anogenital warts resist treatment in HIV-positive patients and why multimodal therapy is needed. It combines ablative methods (trichloroacetic acid, cryotherapy, electrocautery) with immunomodulators or quadrivalent/nonavalent HPV vaccination.[32,40–45] The 2 patients (2.70%) with isolated molluscum contagiosum and the 6 patients (8.11%) with polymicrobial coinfections of genital herpes (HSV-2), vulvovaginal candidiasis, and gonococcal urethritis fit a wider pattern. Opportunistic and classical venereal pathogens take advantage of impaired mucocutaneous Th1/Th17 immunity in PLHIV.[6,29–31]

A closer look at the cellular architecture of the anogenital mucosa may help explain why condyloma acuminata dominated the clinical spectrum in our cohort, although none of these mechanisms was measured here (58.11% isolated; 66.22% overall). It may also explain why 16.22% (n = 12) of patients had multiple (>1) concurrent STI coinfections. The normal barrier is layered. Normally, the stratified squamous epithelium of the ectocervix, vagina, penis, perineum, and anal canal is protected by a layered immune barrier. Its parts are tight-junction claudins and occludins, antimicrobial peptides (human beta-defensins and cathelicidins), intraepithelial Langerhans cells, and tissue-resident memory CD4+ Th1, CD4+ Th17, and CD8+ cytotoxic T lymphocytes.[5,8,33,34] In acute and chronic HIV-1 infection, mucosal CCR5+ CD4+ T lymphocytes are depleted quickly and out of proportion, in particular the interleukin-17-producing Th17 cells and interleukin-22-producing Th22 cells that keep tight junctions intact. This happens in the lamina propria, often long before peripheral blood CD4+ counts fall sharply.[5,8,39] At the same time, the HIV-1 proteins gp120, Tat, and Nef impair the maturation, migration, and MHC class II antigen presentation of epidermal Langerhans cells. They also induce local expression of regulatory T-cell (Treg) cytokines such as transforming growth

factor-beta (TGF-β) and interleukin-10 (IL-10).[8,34] When basal keratinocytes meet HPV-6, HPV-11, or co-infecting high-risk genotypes (HPV-16, HPV-18, HPV-52) through micro-abrasions during sexual contact, extracellular HIV-1 Tat enters the keratinocytes through heparin-binding domains and directly transactivates the HPV long control region (LCR). This raises transcription of the early viral proteins E1, E2, E6, and E7.[5,8,13,35] The HPV E6 oncoprotein recruits the cellular ubiquitin ligase E6AP to degrade p53 and activate human telomerase reverse transcriptase (hTERT). E7 binds and degrades hypophosphorylated retinoblastoma protein (pRb), freeing E2F transcription factors that drive suprabasal keratinocytes into unscheduled S-phase DNA synthesis and exuberant verrucous proliferation.[8,34,37]

The same immunodeficient mucosal environment may account for the molluscum contagiosum (n = 2, 2.70%) and the polymicrobial coinfections of genital herpes, vulvovaginal candidiasis, and gonococcal urethritis (n = 6, 8.11%) in our cohort. Other infections follow the same logic. Molluscum contagiosum virus (MCV) is a double-stranded DNA poxvirus that encodes immune-evasion molecules: the MC148 chemokine antagonist, the MC159 FLICE-inhibitory protein (vFLIP) that blocks Fas/TNF-induced apoptosis, and the MC054 interleukin-18 binding protein. These go unchecked when CD4+ Th1 interferon-gamma signaling is weak, which leads to persistent or atypical giant anogenital molluscum lesions in PLHIV.[29,30,46] Loss of mucosal Th17 cells likewise reduces neutrophil recruitment and the histatin and beta-defensin defenses of the mucosa against *Candida albicans* and non-albicans *Candida* species, which predisposes HIV-positive women to recurrent, azole-refractory vulvovaginal candidiasis.[31] HSV-2 reactivation in the sacral dorsal root ganglia, in turn, produces frequent perigenital herpetic ulcers that attract activated CD4+ target cells and ease mucosal invasion by *Neisseria gonorrhoeae* and *Treponema pallidum*.[1,2,6]

### 4.3. Treponemal serological burden, VDRL titers, and the testing gap

Treponemal coinfection is equally important. Isolated syphilis was the second most common primary clinical diagnosis (n = 17, 22.97%), and another 6 patients (8.11%) had condyloma acuminata and syphilis together, so overt clinical syphilis was diagnosed in 23 patients (31.08%). TPHA, however, was reactive in 34 patients (45.95% of the total cohort of 74, and 61.82% [34/55] of the serologically tested subcohort). VDRL was positive in 32 (43.24% of the total cohort; 58.18% [32/55] of tested). The gap between overt clinical syphilis (n = 23, 31.08%) and confirmed TPHA seroreactivity (n = 34, 45.95%) means that 11 patients were TPHA-reactive without a syphilis diagnosis, which may reflect asymptomatic latent or previously treated syphilis. This is a sizeable share. They represent 21.57% of the 51 patients with non-syphilitic primary STIs and 34.38% (11/32) of those who were tested, and they would have been missed entirely without routine serology.[17,26,47] The multivariable model also indicated that multiple (>1) STI coinfections was associated with nearly five-fold odds of TPHA seroreactivity (aOR = 4.890, 95% CI: 1.123–21.290, p = 0.0344). This points to shared high-risk sexual exposure and mucosal barrier disruption driving concurrent HPV and treponemal transmission.[5,26,47]

The VDRL endpoint dilutions add insight into treponemal disease activity in PLHIV. Among the 32 VDRL-positive patients, endpoint titers ran from undiluted (1:1) to 1:512 (GMT = 1:10.0; median = 1:8.0 [IQR: 1:4.0–1:16.0]), and 1:16 was the modal positive dilution (n = 8, 10.81% of the total cohort; 25.00% of VDRL-positive cases). At the established ≥1:8 threshold, 19 patients (25.68% of the total cohort; 59.38% of VDRL-positive cases) had high-titer reactivity (1:8 in 4, 1:16 in 8, 1:32 in 4, 1:128 in 1, 1:320 in 1, and 1:512 in 1). This was strongly linked to overt clinical syphilis rather than seropositive non-syphilitic STI presentation (73.91% vs. 22.22%, OR = 9.917, p = 0.0074).[9–11,48] In 13 patients (17.57% of the total cohort; 40.63% of VDRL-positive cases) reactivity was low-titer (≤1:4: undiluted 1:1 in 1, 1:2 in 6, and 1:4 in 6). VDRL was negative in 2 TPHA-reactive patients (2.70% of total; 3.64% of tested). In HIV-positive people, low-titer VDRL (≤1:4) and VDRL-negative/TPHA-reactive profiles call for careful sorting among three possibilities: (1) late latent syphilis with waning non-treponemal antibody; (2) the serofast state or successful non-treponemal seroreversion after earlier benzathine penicillin G therapy; or (3) for VDRL-negative/TPHA-reactive results, a false-negative undiluted VDRL from the prozone phenomenon, in which excess anti-lipoidal antibody blocks lattice formation unless the serum is serially diluted.[15–19,49–51] Serum VDRL/RPR titers ≥1:16 or ≥1:32 in HIV-positive patients carry a higher risk of asymptomatic and symptomatic neurosyphilis, ocular syphilis, and treatment failure. Our observation that 15 patients (20.27% of the total cohort; 46.88% [15/32] of VDRL-positive cases) had titers ≥1:16 therefore supports quantitative endpoint titration and neurological vigilance in this population.[10–12,51,52]

We also found a quality-of-care gap. Of the 74 HIV-positive STI patients, 19 (25.68%) had no VDRL or TPHA performed during their clinic visit. This happened almost always because they presented with macroscopic, non-ulcerative condyloma acuminata without overt syphilitic lesions. Since 34.38% (11/32) of tested patients with non-syphilitic primary STIs were TPHA-reactive, applying that TPHA reactivity rate to the 19 untested patients suggests that roughly 6 to 7 further treponemal infections may have gone undetected among them. We therefore propose an integrated dermatovenereological clinical pathway (Figure 6) that proposes universal paired quantitative VDRL (with routine serial dilution) and confirmatory TPHA screening for 100% of HIV-positive patients presenting with any STI, whether or not mucocutaneous ulcers are present.

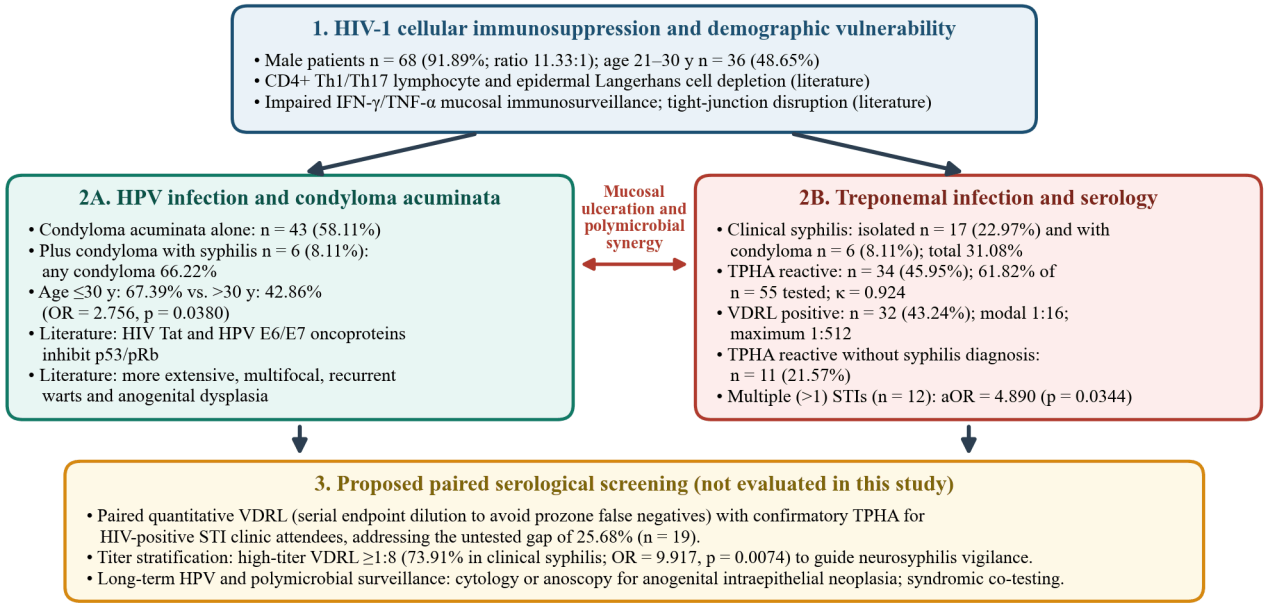



**Figure 6.** Immunopathogenic background and proposed paired serological screening pathway for HIV-positive patients with STIs: (1) HIV-1-related mucosal immunosuppression and demographic vulnerability (literature background); (2A) HPV infection and condyloma acuminata; (2B) treponemal infection and serology; (3) proposed paired VDRL and TPHA screening to address the untested gap (the pathway was not evaluated in this study).

This study has limitations. First, the retrospective single-center design relied on secondary medical records, so quantitative peripheral CD4+ T-lymphocyte counts, plasma HIV-1 RNA viral loads, duration of antiretroviral therapy, and detailed sexual behavior data (such as receptive versus insertive anal exposure and number of partners) could not be extracted systematically. Future prospective studies should include them. Second, molecular HPV genotyping by polymerase chain reaction (PCR) and high-resolution anoscopy or histopathology were not routinely done for all condyloma acuminata cases. Third, 25.68% (n = 19) of the cohort had no VDRL and TPHA testing. We handled this by reporting exact proportions and 95% Wilson CIs for both the total cohort (N = 74) and the serologically tested subcohort (n = 55). Fourth, syphilis serology was ordered at the clinicians' discretion, so tested and untested patients may differ. Fifth, treatment history for syphilis was not analyzed, so TPHA reactivity cannot be separated from previously treated infection. Finally, only 6 women and 12 patients with multiple STIs were included, which limits the precision of subgroup estimates.

From a pathophysiological and laboratory perspective, the high rate of TPHA reactivity (45.95% in the total cohort; 61.82% in the tested subcohort) and of quantitative VDRL positivity (43.24% in the total cohort; 58.18% in the tested subcohort; Cohen's κ = 0.924) reflects the immunobiology of *Treponema pallidum* subspecies pallidum in HIV-coinfected hosts.[9–12,17] The organism is unusual. Unlike Gram-negative bacteria with lipopolysaccharide-rich outer membranes, *T. pallidum* has an outer membrane with very few integral outer membrane proteins. This leaves the spirochete nearly invisible to innate pattern-recognition receptors (a 'stealth pathogen') and exposes abundant sub-surface lipoproteins (such as TpN47, TpN17, and TpN15) only when it is phagocytosed or lysed.[9,12] Rapid gene conversion across the seven variable regions (V1–V7) of the surface-exposed *Treponema pallidum* repeat protein K (TprK) generates antigenic diversity that lets the spirochete evade humoral opsonophagocytosis. The mechanism is made worse when HIV-1 impairs macrophage activation and T-cell-dependent B-cell affinity maturation.[9,12,47] In our cohort, VDRL titration showed that 19 of the 32 VDRL-positive patients (59.38%; 25.68% of the total cohort) had high-titer reactivity ≥1:8. They included 8 patients at the modal titer of 1:16 (10.81%), 4 at 1:32 (5.41%), 1 at 1:128 (1.35%), 1 at the hybrid laboratory dilution of 1:320 (1.35%), and 1 at 1:512 (1.35%). High-titer VDRL ≥1:8 had nearly ten-fold higher odds in overt clinical syphilis than in seropositive non-syphilitic STI presentations (73.91% vs. 22.22%, OR = 9.917, p = 0.0074). Titers carry biological meaning. Biologically, high non-treponemal titers (≥1:8, and especially ≥1:16 to 1:512) reflect active spirochetal proliferation and extensive tissue destruction. This releases mitochondrial cardiolipin, lecithin, and cholesterol into the circulation together with treponemal lipoproteins and drives strong IgM and IgG anti-lipoidal antibody synthesis.[9,18,49] International neurosyphilis cohorts and guidelines also establish that HIV-positive patients with serum VDRL/RPR titers ≥1:16 or ≥1:32 have a clearly greater probability of treponemal passage across the blood–cerebrospinal fluid (CSF) barrier, raised CSF CXCL13 B-cell chemoattractant, and symptomatic or asymptomatic neurosyphilis, ocular syphilis, or otosyphilis.[10–12,51,52] The clinical implication follows. That 15 patients in our cohort (20.27% of all 74 patients; 46.88% of the 32 VDRL-positive patients) had VDRL titers ≥1:16 supports routine neurological, fundoscopic, and audiological assessment in HIV-positive STI clinic attendees.

Two groups need careful interpretation here. One comprises the 13 patients (17.57% of the total cohort; 40.63% of VDRL-positive cases) with low-titer VDRL reactivity (≤1:4: undiluted 1:1 in 1, 1:2 in 6, and 1:4 in 6). The other comprises the 2 patients (2.70% of the total cohort; 3.64% of tested) with discordant VDRL-negative / TPHA-reactive serology. Of the 9 VDRL-positive patients whose treponemal infection was found while being evaluated for non-syphilitic primary STIs (such as condyloma acuminata), 7 (77.78%) had low-titer VDRL ≤1:4. This fits asymptomatic latent syphilis or a persistent serofast state after earlier antimicrobial exposure.[47–50] The 2 discordant cases are harder. For the 2 discordant VDRL-negative / TPHA-reactive cases, clinicians should weigh three non-exclusive explanations. One is successful non-treponemal seroreversion after historical treatment while lifetime treponemal IgG (TPHA) stays reactive. Another is late latent syphilis in which anti-lipoidal VDRL antibody has fallen below the qualitative detection threshold. The third is an undiluted false-negative VDRL from the prozone phenomenon.[15–18,51] Awake et al.,[15] Aboo et al.,[16] and Sanayama et al.[51] stress that the prozone phenomenon occurs disproportionately in HIV-coinfected patients because of polyclonal B-cell activation and extreme hypergammaglobulinemia. The excess anti-lipoidal antibody saturates the micellar cardiolipin antigen binding sites and prevents visible lattice flocculation in undiluted serum; the test turns strongly positive (often at 1:16 to 1:512) only after serial dilution.

The cost of selective testing is visible in the sensitivity analysis of the 19 untested patients (25.68%). All 23 patients with clinical signs of syphilis had VDRL/TPHA testing (100% coverage). Of the 51 patients with non-syphilitic primary STIs (mostly external condyloma acuminata), only 32 (62.75%) were tested and 19 (37.25%) were not. Because 11 of those 32 tested non-syphilitic STI patients (34.38%) were TPHA-reactive (and 9/32 [28.13%] VDRL-positive), the observed 34.38% TPHA reactivity rate can be applied to the 19 untested patients. This projects approximately 6.53 (6 to 7) further HIV-positive patients with TPHA reactivity in the 74-patient cohort, if untested patients resemble tested patients, an assumption that makes the projection illustrative because testing was ordered at the clinicians' discretion. Adding these 6 to 7 projected cases to the 34 confirmed TPHA-reactive patients puts the true treponemal seroprevalence across the cohort between 54.05% (40/74) and 55.41% (41/74), below the 61.82% (34/55) found in the tested subcohort. This calculation illustrates the possible size of the testing gap (Figure 6). In tertiary dermatovenereology practice, every HIV-positive patient with condyloma acuminata, molluscum contagiosum, genital herpes, vulvovaginal candidiasis, or gonococcal urethritis should be considered for bundled paired quantitative VDRL (with routine serial dilution) and confirmatory TPHA screening at the index visit.

**Table 7.** Selected studies of STI coinfection spectra, condyloma acuminata prevalence, and syphilis seroreactivity among people living with HIV, compared with the present study.

| Study / Author (Year) & Reference | Country & Clinical Setting | Sample Size & Study Design | Demographic Profile (Male % & Age Peak) | Condyloma Acuminata / HPV Burden & Syphilis / TPHA Seroprevalence | Key Mechanistic or Clinical Screening Insight |
|---|---|---|---|---|---|
| Present Study (Lisnawati et al., 2026) | Surakarta, Indonesia (Dr. Moewardi Tertiary Referral Hospital) | N = 74 HIV-positive STI patients (Retrospective, 2020–2026) | 91.89% Male (68/74); 48.65% aged 21–30 y (Mean 29.70 ± 9.01 y) | Condyloma acuminata alone: 58.11% (43/74; overall 66.22%); Syphilis alone: 22.97%; TPHA Reactive: 45.95% (61.82% of tested); VDRL+: 43.24% | Multiple STIs (16.22%) were associated with TPHA reactivity (aOR = 4.890, p = 0.0344); 21.57% of non-syphilitic STI patients were TPHA-reactive without a syphilis diagnosis. |
| Mawardi et al. (2026)[7] | Surakarta, Indonesia (Dr. Moewardi Regional General Hospital) | Cross-sectional medical-record study, 2020–2024; 132 condyloma acuminata outpatients | Not reported in the abstract | Recovery highest with trichloroacetic acid (71.2%); recurrence highest after excision (42.4%); HIV status associated with recurrence | Condyloma type, sexual orientation, and HIV status were associated with recurrence time; treatment modality was not significantly associated with recovery. |
| Yuliarto et al. (2023)[8] | Surakarta, Indonesia (tertiary dermatology and venereology clinic) | Cross-sectional study; 41 biopsied condyloma acuminata patients; immunohistochemistry for high-risk HPV | Mean age 31.2 ± 16.9 years (high-risk HPV group); 5 HIV-positive patients | High-risk HPV in all 5 HIV-positive patients and in none of the HIV-negative patients (p = 0.005) | HIV infection was significantly associated with a high-risk HPV strain in condyloma acuminata. |
| Lee et al. (2025)[25] | South Korea (single-center HIV cohort) | Retrospective study of 1,192 men living with HIV, 2002–2023 | Men only | Anogenital warts in 76 men (6.4%), mostly anal (n = 67); high-grade squamous intraepithelial lesion in 25% of biopsied anal warts; high-risk HPV in 42.9% of tested specimens | Routine screening and early detection of precancerous lesions are important in men living with HIV. |
| Biten et al. (2026)[26] | Turkey (two centers) | Retrospective cross-sectional study; 779 patients with anogenital warts, 2020–2025 | 75% male; mean age 35.8 ± 12.3 years | Concomitant STI seropositivity 2.4% (anti-HIV 0.2%; treponemal antibodies 1.6%; HBsAg 1.4%; anti-HCV 0.9%) | Findings support guideline-recommended serological screening in all patients with anogenital warts; seroprevalence was low but non-negligible. |
| Inci et al. (2026)[17] | Turkey (Istanbul training and research hospital) | Retrospective study of TPHA results in 1,436 patients, 2019–2021 | Male sex more frequent in the TPHA-positive group | TPHA positivity 22.3% of all patients; 24.6% (n = 353) of the patients were HIV-infected | Individuals diagnosed with one sexually transmitted infection should be screened for the other (syphilis and HIV). |

| Study / Author (Year) & Reference | Country & Clinical Setting | Sample Size & Study Design | Demographic Profile (Male % & Age Peak) | Condyloma Acuminata / HPV Burden & Syphilis / TPHA Seroprevalence | Key Mechanistic or Clinical Screening Insight |
|---|---|---|---|---|---|
| Casado et al. (2026)[47] | Not stated in the abstract | Prospective cohort; 362 syphilis episodes in 183 people with HIV, 2016–2024 | Not reported in the abstract | Secondary-stage presentation less frequent in repeated episodes (21%, 11%, 13%); serofast status rose from 33% to 62% and 64% | Serological response at 12 months was similar across episodes (75%–83%); findings are compatible with partial immune memory. |
| Villoslada et al. (2026)[5] | Mallorca, Spain (Son Llàtzer University Hospital) | Prospective study of 377 people living with HIV (370 men who have sex with men, 7 transgender women), 2017–2023 | Predominantly men who have sex with men; mean age 44 years | Anal *Chlamydia trachomatis* 5.9%, *Neisseria gonorrhoeae* 2.8%, Mycoplasma genitalium 10.3%; oncogenic HPV 62.6% | Bacterial STIs were associated with greater oncogenic HPV genotype diversity but not significantly with high-grade anal intraepithelial neoplasia; no causal inference. |

***Notes:*** *Abbreviations: aOR, adjusted odds ratio; HBV, hepatitis B virus; HCV, hepatitis C virus; HIV, human immunodeficiency virus; HPV, human papillomavirus; MSM, men who have sex with men; PLHIV, people living with HIV; STI, sexually transmitted infection; TPHA, Treponema pallidum hemagglutination assay; VDRL, Venereal Disease Research Laboratory.*

## 5. Conclusion

This retrospective cross-sectional study at the Dermatology and Venereology Outpatient Clinic of Dr. Moewardi Regional General Hospital, Surakarta (2020–2026, N = 74), shows that HIV-positive patients diagnosed with sexually transmitted infections are mostly young adult men (91.89% male, male-to-female ratio 11.33:1; 48.65% aged 21–30 years and 78.38% aged 21–40 years; mean age 29.70 ± 9.01 years). Isolated condyloma acuminata was the commonest clinical STI diagnosis (58.11%, or 66.22% overall when coinfections with syphilis are included). Isolated syphilis followed (22.97%), then condyloma acuminata plus syphilis (8.11%), other polymicrobial STI combinations of genital herpes, vulvovaginal candidiasis, and gonococcal urethritis (8.11%), and isolated molluscum contagiosum (2.70%). A single STI coinfection was the rule. It occurred in 83.78% (n = 62) and multiple (>1) STI coinfections in 16.22% (n = 12). Quantitative VDRL was positive in 43.24% (n = 32; modal titer 1:16 in 10.81% and maximum dilution 1:512 in 1.35%). TPHA was reactive in 45.95% of the total cohort (61.82% of the 55 tested patients; diagnostic agreement 96.36%, Cohen's $\kappa = 0.924$, $p < 0.001$). Hidden infection was common. TPHA reactivity without a syphilis diagnosis was found in 21.57% (11/51) of patients with non-syphilitic primary STIs. Multiple STI coinfection was associated with TPHA reactivity (aOR = 4.890, p = 0.0344). Closing the 25.68% (n = 19) serological testing gap through routine paired VDRL and TPHA screening, together with long-term anogenital HPV surveillance, may help to improve dermatovenereological care for people living with HIV in Indonesia.

## Declarations

**Use of Generative Artificial Intelligence.** The authors did not use any generative artificial-intelligence tools in writing, analyzing, or preparing this manuscript. All content was produced and verified by the authors, who take full responsibility for its integrity and accuracy.

**Author Contributions.** E.L.: conceptualization, methodology, investigation, data curation, formal analysis, visualization, writing – original draft. L.P.A.: investigation (literature search), data curation, writing – original draft. H.F.Y.: investigation (literature search), data curation, formal analysis, writing – review & editing. A.M.: supervision, methodology, validation, writing – review & editing. All authors read and approved the final manuscript.

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**Conflict of Interest.** The authors declare no conflict of interest.

**Ethical Approval.** This study was approved by the Health Research Ethics Committee of Dr. Moewardi Regional General Hospital, Surakarta, Indonesia, under ethical approval number 865/V/HREC/2026, and was conducted in accordance with the principles of the Declaration of Helsinki.

**Patient Consent.** Individual informed consent was waived by the ethics committee because the study used de-identified routine medical records. Consent for publication is not applicable.

**Data Availability.** The data underlying this study are not publicly available because they were obtained from institutional patient medical records containing confidential clinical information. De-identified analytical summaries are available from the corresponding author upon reasonable request and subject to institutional ethical restrictions.

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