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HIV/Malaria and HIV/syphilis Co-infections among HIV-Infected Persons attending a Tertiary Hospital in Umuahia, Abia State, Nigeria

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Abstract: The trio of HIV, Malaria, and Syphilis represents three major infectious diseases with significant global health burdens especially in sub-Saharan Africa. This study analyzed co-infection rates of syphilis and malaria in a cohort of 200 HIV/AIDS patients. The overall syphilis co-infection rate was 7.0% (14/200), and the malaria co-infection rate was 4.5% (9/200). HIV/Syphilis co-infection was highest rate in 41-50 age group (10.0%, 7/70), lowest in ≤30 (0%) with no significant association (χ^2=1.04, p=0.52). Males had higher co-infection (9.8%, 6/61) vs. females (5.8%, 8/139), but not significant (p=0.22). Higher rates of HIV/syphilis co-infection were found in middle-aged groups (41-50 years: 10.0%) and singles (10.1%). No significant association (χ^2=2.61, p=0.16) was found between viral load and HIV/syphilis co-infection. It was found from this study that 18.5% and 9.1% of the HIV/Syphilis co-infected persons had viral loads of 40-1000copies/ml and >1000copies/ml respectively. Males had higher (6.6%, 4/61) malaria/HIV co-infection than the female respondents (3.6%, 5/139) (p=0.39). Occupational status showed that the co-infection was most common amongst those who were employed and students each with a 5.6% prevalence. Singles had higher co-infection rate (7.6%) than the married category (5.5%). However, no statistically significant association was found between co-infection status and marital status (p=0.08). The prevalence of *Plasmodium falciparum* infection among HIV patients in relation to age groups revealed that the highest prevalence of 7.1% was observed among patients within the age group of <30years. Co-infection with HIV/malaria also showed no significant difference with regards to the HIV viral load (χ^2=4.61, p=0.33) as 36.4% of malaria co-infected HIV subjects had higher levels of HIV viral load (>1000copies/ml). Owing to the fact that increased viral load enhances transmission of the disease, this study suggests that individuals living with HIV/AIDS should prioritize monitoring their viral load as it was found that co-infection with either syphilis or malaria resulted in increase in viral load.

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Keyword: Malaria; Syphilis; Infection

1. Introduction

The triad of HIV, Malaria, and Syphilis represents three major infectious diseases with profound global health burdens especially in sub-Saharan Africa. Infection with HIV has been documented to impair immunity (Eickhoff & Decker, 2016), thus increasing susceptibility to other diseases, including malaria and syphilis (WHO, 2024) while malaria infection transiently elevates HIV viral load by activating immune cells, potentially accelerating HIV progression. In 2022, there were an estimated 249 million cases of malaria worldwide, resulting in 0·61 million related deaths (WHO, 2023). Sub-Saharan Africa accounted for approximately 94% of all malaria cases and 95% of all malaria-related deaths (WHO, 2023). Nigeria contributes about 23% of the

global malaria cases and around 250,000 Nigerians especially children die from malaria every year (WHO, 2024). It is also estimated that 97% of Nigerian population is at risk of malarial infection.

Globally, there were an estimated 39 million people living with HIV in 2022, approximately 1·3 million new diagnoses, and 0·63 million HIV-related deaths.7 Similar to malaria, the global HIV epidemic has the greatest impact in sub-Saharan Africa, with an estimated 67% of people living with HIV worldwide residing in this region (UNAIDS, 2022). Syphilis on the other hand is a chronic bacterial infection caused by *Treponema pallidum subspecies pallidum*. The organism is an obligate human pathogen, which can spread by sexual transmission, mother-to-child transmission, and blood transfusion. Without treatment, the disease can progress over years through a series of clinical stages, leading to irreversible neurological, ocular, and internal organ damage, and even death. Studies have demonstrated a relationship between HIV and a number of STIs, including syphilis (Fan et al., 2021; Gong et al., 2020; Bagheri-Amiri et al., 2016). The prevalence of co-infection with HIV and syphilis varies from 8% to 25% (Sarigul et al., 2019). The prevalence of syphilis co-infections was reported to be 13% in sub-Saharan Africa (SSA) (Getaneh and Lusida, 2023). The increase in rates of syphilis is concurrent with an increase in the rate of human immunodeficiency virus (HIV) infection (Feng et al., 2015; Luppi et al., 2018; Riley et al., 2020). Infection with *T. pallidum* and HIV has worse clinical outcomes as there is an increased viral load, decreased CD4 count, and therefore a higher risk of contracting other diseases (Eickhoff & Decker, 2016).

The prevalence of malaria and HIV co-infection has been estimated to be 19% overall in sub-Saharan Africa, with values of 26% in non-pregnant adults, 12% in pregnant women, and 9% in children (Niang et al., 2016). Furthermore, Kwenti (2018) reported varying prevalence of malaria and HIV co-infection across different populations and regions in sub-Saharan Africa, ranging from 0·7% to 72%, with values of 0·7% to 47·5% in non-pregnant adults, 0·94% to 37% in pregnant women, and 1·2% to 27·8% in children. Some complications, such as anaemia, which are common to both HIV and malaria, are also likely to be worse with the co-infection (Tay et al., 2015).

Among people living with HIV, both *in vitro* and *in vivo* studies have revealed that malaria co-infection causes a transient increase in HIV viral load for several weeks post-antimalarial treatment, threatening ART effectiveness and heightening the risk of HIV transmission (Yegorov et al., 2019; Kwenti, 2018). HIV therapy reduces the effectiveness of antimalarial medications and may exacerbate side effects (Ssentongo et al., 2020). Thus, the likelihood of HIV patients also having malaria is very high (Gumel et al., 2021). Hence, malaria and HIV co-infection might have an effect on HIV disease progression and transmission, potentially contributing to the high prevalence of HIV in sub-Saharan Africa. Immunity to malaria is both humoral and cell-mediated (Munyenyembe et al., 2020) and HIV has been described to have direct effect on both the cell-mediated and antibody-mediated immunity. HIV infection depletes CD4+ T cells, causes deterioration of antigen-specific humoral responses and leads to alteration of innate immunity through impairment of cytolytic activity and cytokine production by natural killer (NK) cells (Finney et al., 2013; Subramaniam et al., 2015). By this mechanism, HIV reduces the host's immunity to infecting agents of malaria, thus allows propagation of the risk of malaria infection. This expands both diseases in areas where their burden is high and their interaction will have profound public health effect (Jegede et al., 2017).

The progressive use of ART has remarkably reduced the episodes of HIV-related morbidity and mortality and increased life expectancy worldwide. However, comorbidities with malaria and syphilis infection could pose significant clinical challenges in managing HIV patients (Kwenti, 2018). This is because co-infections increase disease severity, make diagnosis and treatment difficult, and increase mortality. This study was thus aimed at evaluating the proportion of HIV infected individuals co-infected with syphilis and malaria in Umuahia, Abia State Nigeria.

2. Materials and Methods

The study was a cross-sectional study involving 200 HIV/AIDS patients from the Federal Medical Centre (FMC), Umuahia, Abia State, Nigeria.

2.1. Inclusion criteria: Confirmed HIV-1 positive patients who willingly gave their consent.

2.2. Exclusion criteria: Patients who declined consent. Ethical approval for the study was obtained from the Federal Medical Centre, Umuahia (FMC) ethical review board/committee. Ethical approval was also obtained from the University of Port Harcourt (UPH) ethics review board/committee. A written informed consent was received from each study participant.

2.3. Sample collection: Five milliliters of whole blood was drawn from each subject into an EDTA tube and centrifuged at 3000 rpm for 5 min. A structured questionnaire was administered to consenting participants in order to collect demographic data (age, sex), marital status, religious belief, occupational status, educational background.

2.4. Serological Analysis: Serum samples were tested for detection of syphilis antibodies using ELISA kit (DIA. PRO Diagnostic Bioprobes, Italy). The tests were conducted following the manufacturer's instructions. The test results were computed using a cut-off value based on the mean OD450nm value of the negative control (NC), using the formula NC + 0.050 = Cut-Off (Co). Calculated as the ratio of the sample OD450nm (S) and the Cut-Off value (Co), test results are interpreted as follows: 0.9 = negative, 0.9 - 1.1 = equivocal, and > 1.1 = positive.

2.5. Viral Load Assay: Plasma viral load of HIV present in the body was estimated using Abbott Real-Time PCR Assay as described by (Sollis et al., 2014).

2.6. Statistical Analysis: The data obtained was collated and presented in tables and figures and analysed using chi-square for the categorical variables. This was done using SPSS with statistical significance set at $p<0.05$.

3. Results

This study analyzed co-infection rates of syphilis and malaria in a cohort of 200 HIV/AIDS patients. The overall syphilis co-infection rate was 7.0% (14/200), and the malaria co-infection rate was 4.5% (9/200). HIV/Syphilis co-infection was highest rate in 41-50 age group (10.0%, 7/70), lowest in ≤30 (0%) with no significant association ($\chi^2=1.04$, $p=0.52$). Males had higher co-infection (9.8%, 6/61) vs. females (5.8%, 8/139), but not significant ($p=0.22$). Participants who were singles had highest rate (10.1%, 11/109) relative to the married category (3.8%, 3/79) ($p=0.18$). Secondary education had highest rate (13.2%, 9/68); no cases in primary/tertiary groups ($p=0.64$). None of the demographic factors showed statistically significant associations with syphilis co-infection ($p>0.05$). No significant association ($\chi^2=2.61$, $p=0.16$) was found between viral load and HIV/syphilis co-infection. It was seen that 18.5% (5/27) of the co-infected persons had viral load in the range of 40–1000 copies/mL while 6.9 % (8/115) and 9.1% (1/11) had viral loads of <40 copies/mL and >1000 copies/mL respectively. For syphilis, the highest co-infection rate was in the 40-1000 copies/ml group (18.5%), but the association with viral load was not significant ($p=0.16$).

Malaria/HIV co-infection seemed to be common in the younger population in this study (≤30 group) as they recorded the highest proportion (7.1%) while the least was seen for the 31–40 age group (1.9%, 1/53). Males higher (6.6%, 4/61) malaria/HIV co-infection than the female respondents (3.6%, 5/139) ($p=0.39$). Occupational Status showed that the co-infection was most common amongst those who were employed and students each with a 5.6% prevalence. Singles had higher co-infection rate (7.6%) than the married category (5.5%). No significant demographic associations (all $p>0.05$) was observed amongst the variables. The findings from this study revealed that 36.4% (4/11) of the co-infected persons had viral load in the range of >1000 copies/mL while 7.4 % (2/27) and 2.6% (3/115) had viral loads of 40-1000copies/mL and <40 copies/mL respectively. Co-infection with HIV/malaria showed no significant difference with regards to the HIV viral load ($\chi^2=4.61$, $p=0.33$). However, the 36.4% observed for >1000 copies/mL shows a strong trend.

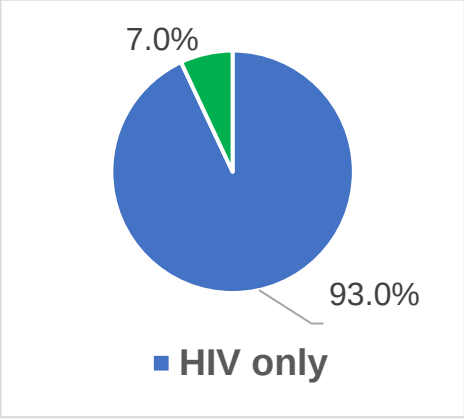

Fig 1: HIV-1 co-infection rate with Syphilis

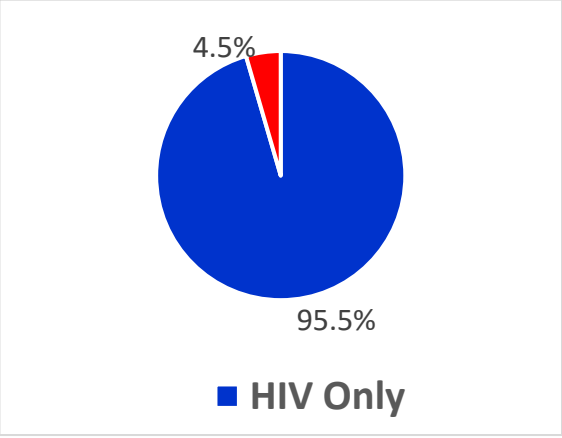

Fig 2: HIV-1 co-infection rate with Malaria

Table 1: HIV/Syphilis Co-infection Rate in HIV/AIDS patients in relation to their demographic characteristic

VARIABLES	Number tested	Percentage (%)	Syhpilis +ve	% Syhpilis +ve	χ-value	P-value
Age						
≤30	28	14.0	0	0.0	1.04	0.52
31-40	53	26.5	4	7.5		
41-50	70	35.0	7	10.0		
≥51	49	24.5	3	6.1		
Sex						
Males	61	30.5	6	9.8	0.49	0.22
Females	139	69.5	8	5.8		
Marital Status						
Married	79	39.5	3	3.8	2.42	0.18
Single	109	54.5	11	10.1		
Others	12	6.0	0	0.0		
Educational Status						
None	56	28.0	5	8.9		
Primary	35	17.5	0	0.0	0.94	0.64
Secondary	68	34.0	9	13.2		
Tertiary	41	20.5	0	0.0		
Occupations						
Student	72	36.0	4	5.6	1.24	0.33
Unemployed	25	12.5	10	40.0		
Self Employed	33	16.5	0	0.0		
Employed	70	35.0	0	0.0		
Religion						
Christianity	141	70.5	12	8.5		
Islam	38	19.0	0	0.0	1.42	0.92
Others	21	10.5	2	9.5		
Total	**200**		**14**	**7.0**		

Table 2: Seroprevalence of HIV/Syphilis in relation to immunological and virological markers

Viral load (copies/ml)	Number tested	Syphilis +ve	%Syphilis +ve	χ-test	p-value
TND	47 (23.5)	0	0.0		
<40	115 (57.5)	8	6.9		
40-1000	27 (13.5)	5	18.5	2.61	0.16
>1000	11 (5.5)	1	9.1		
Total	200	14	7.0		

TND: Target not detected

Table 4: Seroprevalence of HIV/Malaria in relation to immunological and virological markers

Viral load (copies/ml)	Number tested	Malaria +ve	%Malaria +ve	χ-test	p-value
TND	47 (23.5)	0	0.0		
<40	115 (57.5)	3	2.6		
40-1000	27 (13.5)	2	7.4	4.61	0.33
>1000	11 (5.5)	4	36.4		
Total	200	9	4.5		

Table 3: HIV/Malaria Co-infection Rate in HIV/AIDS patients in relation to their demographic characteristics

VARIABLES	Number tested	Percentage (%)	Malaria +ve	% Malaria +ve	χ-value	P-value
Age						
≤30	28	14.0	2	7.1	1.60	0.66
31-40	53	26.5	1	1.9		
41-50	70	35.0	4	5.7		
≥51	49	24.5	2	4.1		
Sex						
Males	61	30.5	4	6.6	0.74	0.39
Females	139	69.5	5	3.6		
Marital Status						
Married	79	39.5	3	3.8	2.88	0.08
Single	109	54.5	6	5.5		
Others	12	6.0	0	0.0		
Educational Status						
None	56	28.0	4	7.1		
Primary	35	17.5	1	2.9	2.77	0.64
Secondary	68	34.0	4	5.9		
Tertiary	41	20.5	0	0.0		
Occupations						
Student	72	36.0	4	5.6	1.84	0.61
Unemployed	25	12.5	1	4.0		
Self Employed	33	16.5	0	0.0		
Employed	70	35.0	5	5.6		
Religion						
Christianity	141	70.5	5	3.5		
Islam	38	19.0	2	5.3	1.24	0.72
Others	21	10.5	2	9.5		
Total	200		9	4.5		

4. Discussion

There has been variations in the prevalence of syphilis infection following its re-emergence as a public health problem especially in bisexuals and MSM (Sarigul et al., 2019). Different studies have equally reported varying rates of HIV/syphilis co-infection with 6.21% in Singapore (Ang et al., 2020), 8-25% in Turkey Sarigul et al., 2019; Yenilmez & Cetinkaya, 2019) 25% in Mexico (Mata-Marin et al., 2015), 46.5% in Taiwan (Chang et al., 2014), 16.42% in Morocco (Bourouache et al., 2019), 18.4% in Brazil (Santos), 16.1% in Thailand (Phanuphak et al., 2018), and 10% in Ghana (Asade-Beideko et al., 2018). The observed syphilis co-infection rate of 7.0% in this present study aligns with global reports. A meta-analysis of 351 studies found a global pooled prevalence of 9.5% (95% CI: 8.9–10.1) among people living with HIV (PLWH) (Kojima et al., 2020). The 7.0 % reported for HIV co-infection with syphilis in the present study is higher than the 0.3% reported in Eritrea by Siraj et al. (2018) and 2.2% prevalence among the general population in Ethiopia (Getaneh et al., 2023). Other studies done in different parts of Africa have also shown lower prevalence values of 2.9% and 2.3% (Kassa et al., 2019; Genetu et al., 2022). Co-infection with HIV was found in 8.21% of patients with syphilis in the study of Gong et al. (2020) a finding which is comparable with the 7.0% prevalence level in the current study.

Seroprevalence of syphilis co-infection was high among the age group of 41-50 (10.0%). This finding is in alliance with a similar study carried by Aydin et al. (2022) who found that co-infection was high among age range of 26-45. Similarly, Riley et al. (2020) found that syphilis infection occurs most frequently between the ages of 25 and 44years old while the reports of Mata-Marin et al. (2015) and Asade-Beideko et al. (2018) also corroborated the findings of this study. This trend could be because younger age group has more sexual activity, and their tendency to engage with multiple partners is higher relative to the elderly population.

Among the participant it was observed that the male had syphilis co-infection rate of 9.8% which was in contrast with the 5.1% observed by Mike-Ogburia et al. (2023). The higher risk of syphilis co-infection among male is supported by similar studies by Aydin et al. (2022) which reported higher male predominated syphilis/HIV co-infection. However, the findings of Asare-Bediako et al. (2018) in Ghana where females had more predominance is in contrast with the result of this current study. It has been reported that males are engaged in having multiple sexual partners compared to the females thus increasing their chances of acquiring these infections (Bourouache et al., 2019). Equally, because Syphilis infection remains asymptomatic in females for a long time, they become risk factors which favour the spread of the disease.

The higher rates in middle-aged groups (41-50 years: 10.0%) and singles (10.1%) align with previous studies linking syphilis risk to sexual networks and behaviors. For instance, studies in sub-Saharan Africa report higher STI rates among unmarried PLWH due to multiple partnerships (Maughan-Brown et al., 2018). However, the lack of statistical significance in our data ($p>0.05$) may reflect regional variations.

It was found from this study that 18.5% and 9.1% of the HIV/Syphilis co-infected persons had viral loads of 40-1000copies/ml and >1000copies/ml respectively. Taken together, these findings suggests that co-infection with syphilis contributes to poor immune recovery and subsequently increases the likelihood of virologic failure. The study of Fan et al. (2021), found that individuals co-infected with HIV/syphilis before initiation of ART had a higher probability of virologic failure. Syphilis is known to have a negative impact on immune recovery during HIV infection and our results are consistent with previous studies which have reported virological failures following co-infections (Tsachouridou et al., 2016; Wang et al., 2018; Spagnuolo et al., 2019). The work of Getaneh et al. (2023), also reported increased rate of HIV virologic failure (46.2%), immunosuppression (39.1%) among syphilis positive patients. Similarly, the study of Kotsafti et al. (2016) reported decreased CD4 T lymphocyte count and increased HIV viral load in HIV/syphilis co-infected patients which is in agreement with results of this investigation further affirming the virologic failure associated with such co-infection.

In this study, the prevalence of malaria co-infection among individuals with HIV infection is 4.5%; this was significantly lower than the 18.9% reported from Anambra, Southeastern Nigeria (Onyenekwe et al., 2007) and 21% from Jos, North-central Nigeria (Uneke et al., 2005). Also, the overall prevalence of *Plasmodium falciparum* infection among HIV patients in the study of Muhammad et al. (2022) was 14.3%. However, the prevalence rate recorded in this study is in unison with those of Okonko et al. (2023) in a related study which recorded a 5% prevalence. The difference could be due to differing methodologies used in the respective studies. In this study, the prevalence of the co-infection did not differ significantly between males and females and is not associated with age. This agrees with findings from a study in Kano, North-West Nigeria (Jegede et al. (2017) but contrary to another one from Jos North-Central Nigeria (Uneke et al., 2005). The prevalence observed in this study is also in variance with the 14.2% reported by Amadi et al. (2018) in Uyo, Nigeria, 59.2% reported by Abioye et al. (2014) in Kaduna, Nigeria and 33.0% reported by Gennaro et al. (2018) in Mozambique. The prevalence of Plasmodium/HIV co-infection as reported in a study in Cameroon varied from one region to the other; ranging from 2.24% in Bamenda (Njunda et al., 2012) to 29.5% in Douala (Nkuo-Akenji et al., 2011) while Sandie et al. (2019) found an overall malaria parasites prevalence of 14.1%. The study of Mahittikorn et al. (2021), showed a pooled prevalence of 43.0% severe malaria in individuals with both malaria and HIV in a meta-analysis involving 23 studies. The odds of severe malaria were significantly higher in individuals with both malaria and HIV than in individuals with *P. falciparum* alone. The prevalence of *Plasmodium falciparum* infection (4.5%) in this study is however, in agreement with the 4.8% reported by Dada (2015) in Ondo State, Nigeria. The finding from this study is also comparable with the prevalence of 7.3% reported by Njunda et al. (2016) in Cameroun. The 4.5% co-infection rate aligns with findings of Cuadros et al. (2011) who reported a pooled prevalence of 4.3% across 15 sub-Saharan African countries. Similarly, a Kenyan study documented 4.6% co-infection rate which are comparable to those of this present study. The low prevalence may be attributed to the to the period of study (dry season) which coincided with low malaria parasite transmission or care seeking behaviour of the people living with HIV as reported by Muhammad et al. (2022).

In this study, males had relatively higher prevalence of *Plasmodium falciparum* infection (6.6%) than their female counterparts (3.6%) despite the females having more participants. Similar obsevations was also made by Muhammad et al. (2022) as well as

Hwida et al. (2019) while Abioye et al. (2014) in Kaduna, reported that HIV positive females were at higher risk of contracting malaria than their male counterparts. This result is in line with a study carried out by Baume et al. (2019) and contrary to what has been reported in other studies (Kimbi et al., 2013) where females had a higher prevalence of malaria parasite. The findings of this study with regards to males having higher prevalence rate is supported by earlier studies including those of Onankpa et al. (2017), Ejike et al. (2020), and John et al. (2020) with the exception of Oyeniran et al. (2022), which found that the prevalence of malaria was statistically significantly higher in female patients than in male patient. The higher prevalence of malaria/HIV co-infection is males (6.6% vs. 3.6%) is consonance with literature on gender-based exposure differences (e.g., occupational hazards, less bed net use).

The prevalence of *Plasmodium falciparum* infection among HIV patients in relation to age groups revealed that the highest prevalence of 7.1% was observed among patients within the age group of <30years. This finding is in conformity with those of Onankpa et al. (2017) and Ahmed et al. (2016) who reported high prevalence of *Plasmodium falciparum* infection in younger populations. This result could have been due to the fact that the age group ≤30years includes children who are a vulnerable group when it comes to malaria as their immune system is still developing. This finding is in line with results reported form other studies carried out in the Southwest region of Cameroon by Apinjoh et al. (2015); Ebai et al. (2016); and Sumbele et al. (2018). There was no statistically significant association between co-infection of *P. falciparum*/HIV with age and sex.

A higher rate of HIV/malaria co-infection was observed among the single participants compared to the married respondents. However, no statistically significant association was found between co-infection status and marital status ($p = 0.08$). This finding contradicts earlier studies by Okonko et al. (2023) which reported higher proportion of married individuals being co-infected. However, the findings of our study is supported by those of Ejike et al. (2020), and John et al. (2020), which reported higher prevalence among single/divorced populations. The reasons for increased predominance in singles cannot be ascertained but could be because single individuals may demonstrate lower adherence to malaria prevention (e.g., inconsistent bed net use) due to unstable housing thus, they have higher exposure to mosquitoes (Tusting et al., 2019). Equally, it may also be because singles are typically younger and could increase their exposure through Night-time social activities thus increasing mosquito bites.

This study found that 36.4% of malaria co-infected HIV subjects had higher levels of HIV viral load (>1000copies/ml) supporting earlier propositions that malaria infection causes an increase in transitory viral load (Muhammad et al., 2022). These findings agree with several similar studies and theories. Kwenti (2018) indicated that malaria infection is associated with an increase in the HIV viral load *in vivo* and *in vitro*. The 36.4% malaria rate in >1000 copies/mL group (high viral load) suggests HIV uncontrolled replication may increase malaria susceptibility. This thus suggests that an additional significant risk factor for malaria in HIV patients is a viral load greater than 1000 copies/mL, which is probably caused by weakened immunity from uncontrolled HIV or declining ART effectiveness, which opens the door to opportunistic infections. HIV reduces $CD4^+$ T-cell-mediated responses to *Plasmodium*, increasing susceptibility and severity (Van geertruyden et al., 2006). Our data show a stronger association between HIV viral load and malaria infection, underscoring the critical role of ART in malaria prevention.

5. Conclusion

The overall co-infection rates (7.0% for syphilis and 4.5% for malaria) suggest that these co-infections are present in the HIV population, though not extremely high. The lack of significant associations with demographics might indicate that these co-infections are not strongly driven by the demographic factors considered. The trend for higher syphilis co-infection in the 40-1000 copies/ml group and higher malaria co-infection in the >1000 copies/ml group might indicate a relationship with HIV viral load. For malaria, the high rate in the >1000 copies/ml group (36.4%) is striking and might suggest that uncontrolled HIV replication (high viral load) could be associated with increased susceptibility to malaria. However, the association was not statistically significant, so this needs further investigation with a larger sample.

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