International Journal of Infectious Diseases 108 (2021) 610–616

Contents lists available at ScienceDirect

International Journal of Infectious Diseases

journal homepage: www.elsevier.com/locate/ijid

Prevalence of cervical HPV infection, sexually transmitted infections and associated antimicrobial resistance in women attending cervical cancer screening in Mali

Aude Jary[a,*], Ibrahima Teguete[b], Younoussa Sidibé[c], Amadou Kodio[d], Oumar Dolo[e], Sonia Burrel[a], David Boutolleau[a], Laurianne Beauvais-Remigereau[f], Sophie Sayon[a], Mamadou Kampo[g], Fatoumata Tata Traoré[e], Mariam Sylla[h], Chad Achenbach[i], Robert Murphy[i], Béatrice Berçot[j], Cécile Bébéar[k], Vincent Calvez[a], Anne-Geneviève Marcelin[a], Almoustapha I. Maiga[d,e]

[a] Sorbonne Université, INSERM, Institut Pierre Louis d'Epidémiologie et de Santé Publique, AP-HP, Hôpital Pitié Salpêtrière, Service de Virologie, Paris, France
[b] CHU Gabriel Toure, Département de Gynéco-obstétrique, Bamako, Mali
[c] CERKES, Kenedougou Solidarité, Sikasso, Mali
[d] CHU Gabriel Toure, Département de Biologie Médicale, Bamako, Mali
[e] Université des Sciences Techniques et des Technologies de Bamako, USTTB, Centre de Recherche et de Formation sur le VIH et la Tuberculose SEREFO, Bamako, Mali
[f] Fondation GSK France, Marly Le Roi, France
[g] Hopital Régional de Tombouctou, Tombouctou, Mali
[h] CHU Gabriel Toure, Département de Pédiatrie, Bamako, Mali
[i] Northwestern University, Institute for Global Health, Chicago, IL, USA
[j] University of Paris, IAME and St Louis Hospital, Department of Bacteriology, Associated Laboratory of the National Reference Centre for Bacterial STIs, Paris, France
[k] CHU de Bordeaux and University of Bordeaux, Department of Bacteriology, National Reference Centre for Bacterial STIs, Bordeaux, France

ARTICLE INFO

Article history:
Received 16 November 2020
Revised 23 May 2021
Accepted 12 June 2021

Keywords:
HIV
HPV
Cervical lesions
STIs
Antimicrobial resistance
Mali

ABSTRACT

Objectives: To assess the prevalence of sexually transmitted infections (STIs), antimicrobial resistance and cervical lesions among women from Sikasso, Mali.

Methods: Women infected with human immunodeficiency virus (HIV) (n=44) and HIV-negative women (n=96) attending cervical cancer screening were included. Screening for human papillomavirus (HPV), *Chlamydia trachomatis* (CT), *Mycoplasma genitalium* (MG), *Neisseria gonorrhoeae* (NG) and *Trichomonas vaginalis* (TV) was performed using polymerase chain reaction assays, and herpes simplex virus (HSV-1/2) serological status was assessed using enzyme-linked immunosorbent assays. Antibiotic resistance tests were performed for MG- and NG-positive cases.

Results: A high prevalence of high-risk HPV (hrHPV) infection (63%) was found. This was associated with cervical lesions in 7.5% of cases. An unusual distribution was found, with HPV31, HPV56 and HPV52 being the most prevalent. The hrHPV distribution differed by HIV status, with HIV-positive cases having HPV35/31/51-52-56 and HIV-negative cases having HPV31/56/52. The seroprevalence of HSV-2 was 49%, and the prevalence of other STIs was as follows: CT, 4%; MG, 9%; NG, 1%; and TV, 7%. Five of nine MG-positive specimens and the NG strains obtained were resistant to fluoroquinolone.

Conclusions: These results showed high prevalence of hrHPV and fluoroquinolone resistance in several NG and MG strains. Further studies are required to confirm these data in Mali, and to improve prevention, screening and management of cervical cancer and other STIs in women.

* Corresponding author. Sorbonne Université, INSERM, Institut Pierre Louis d'Epidémiologie et de Santé Publique, AP-HP, Hôpital Pitié Salpêtrière, Service de Virologie, 47–83 boulevard de l'hôpital, 75013 Paris, France. Tel.: +33142177406.
E-mail address: aude.jary@aphp.fr (A. Jary).

https://doi.org/10.1016/j.ijid.2021.06.024

Background

Cervical cancer is the fourth most common female cancer in the world, and the second most common female cancer in developing countries, with approximately 530,000 new cases diagnosed each year, approximately 90% of which occur in low-and-middle-income countries (LMICs) (de Martel et al., 2017; Cohen et al., 2019). In West Africa, approximately 32,000 new cases of cervical cancer are diagnosed each year, and the prevalence of human papillomavirus (HPV) in the general population is approximately 20% (ICO/IARC Information Centre on HPV and Cancer, 2019). However in several countries, there are dissimilarities in the prevalence and types of HPV involved in infections, and precancerous and cervical cancers (Piras et al., 2011; Ferre et al 2018; Bah Camara et al., 2018; Krings et al., 2019). Current World Health Organization (WHO) recommendations endorse national HPV vaccination programmes targeting girls aged 9–14 years. If implemented widely, HPV vaccination is likely to prevent millions of deaths from cervical cancer, particularly in LMICs. The choice between bivalent, quadrivalent and nonavalent HPV vaccines is an important decision for decision-makers, who must balance the expected impact of the programme against cost considerations in the context of local epidemiological trends and competing health priorities.

Other sexually transmitted infections (STIs) remain a public health concern because they affect the health and lives of people worldwide. The worldwide seroprevalence of herpes simplex virus 2 (HSV-2) in 2012 was estimated to be 11.3%, with the highest prevalence in Africa (31.5%), and higher prevalence in females compared with males (14.8% vs 8.0%, respectively) (Looker et al., 2015). In 2016, WHO estimated that prevalence rates of *Chlamydia trachomatis* (CT), *Neisseria gonorrhoeae* (NG) and *Trichomonas vaginalis* (TV) in women living in Africa were 5.0%, 1.9% and 11.7%, respectively (Rowley et al., 2019). These prevalence rates were similar, both globally and by world region, to rates in 2012, showing that STIs are persistently endemic worldwide (Rowley et al., 2019). However, there is considerable geographic variation in both the burden of disease and prevalence of resistance, and this could influence guidelines for treatment.

Recent data are not yet available on the burden of HPV and other STIs in women from Mali. As such, this study was undertaken among women screened for cervical cancer in Sikasso, Mali to assess the prevalence of HPV infection, subtype distribution and associated cervical lesions, the seroprevalence of HSV-1/2 and other STIs, and antimicrobial resistance.

Methods

Study population

A cross-sectional study was conducted at Kénédougou Solidarité Clinic, Sikasso, Mali, which is a non-government organization that specializes in human immunodeficiency virus (HIV) counselling, offers HIV screening and manages HIV-positive patients. The clinic is fully integrated in the local healthcare system, and collaborates with the district referral health centre and the regional hospital in Sikasso. Educational talks are organized regularly for patients who consult in this centre, and cervical cancer is one of the topics covered in addition to HIV infection and STIs.

This study included women who presented at the clinic between May and June 2018. An educational talk on cervical cancer was offered, and women were invited for screening if they were eligible (age >18 years, not pregnant, not immediate post-partum, not had a hysterectomy, not menstruating at the time of consultation) and gave consent. The inclusion criteria did not consider the presence of symptoms of other STIs. All the HIV-positive women included were followed and treated in the clinic. As the study centre is involved in the management of HIV and STIs, the recruited women may have included key populations such as female sex workers and intravenous drug users; however, these groups were not differentiated in this study.

For each woman, cervical cancer screening was performed by visual inspection with acid (VIA) and Lugol's iodine (VILI), as recommended in LMICs by WHO, and liquid-based cytology and sera were collected for biological analysis. Sociodemographic data including age, marital status, marital age, number of pregnancies, contraception used, polygamous or not, education level and geographical setting were also collected during medical consultation.

Cervical cancer screening and HPV testing

Each woman with a positive VIA/VILI result underwent a punch biopsy. The specimen was conveyed to Bamako where histological analysis was performed at the Department of Pathology, Point G Teaching Hospital, Mali. Before HPV testing, 1 mL of liquid-based cytology was centrifuged, the supernatant was discarded, and the cell pellet was stored at -20°C in Mali, then sent for analysis at the Virology Department, Pitié-Salpêtrière Hospital, France.

The cell pellet was resuspended in 400 µL of phosphate buffered serum 1X, and DNA extraction was performed using the NucliSENS EasyMAG total nucleic acid extractor (BioMérieux, Marcy l'Etoile, France) according to the manufacturer's instructions. HPV testing was performed with the AnyplexII HPV28 (Seegene, Seoul, South Korea) which enabled the detection of 28 HPV types. According to the International Agency for Research on Cancer classification, 12 HPV types were defined as high-risk HPV (hrHPV, Category 1: 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58 and 59); eight HPV types were defined as intermediate risk (Categories 2A and 2B: 26, 53, 66, 68, 69, 70, 73 and 82); and eight HPV types were defined as low-risk HPV (lrHPV) or non-classified HPV (6, 11, 40, 42, 43, 44 54 and 61).

HSV-1/2 and other STI testing

Sera were tested for the HSV-1/2 IgG antibody with the LIAISON HSV-1 IgG/HSV-2 IgG (DiaSorin, Stillwater, MN, USA) and HSV-1/2 DNA-genital with the Artus HSV-1/2 RG polymerase chain reaction (PCR) kit (Qiagen, Hilden, Germany) on the same acid nucleic extracts used for HPV detection. Screening for other STIs was performed with the Allplex STI Essential Assay (Seegene), which is able to detect seven STIs: CT, NG, *Mycoplasma genitalium* (MG), TV, *Mycoplasma hominis* (MH), *Ureaplasma parvum* (UP) and *Ureaplasma urealyticum* (UU). Only CT, NG, MG and TV were considered as pathogenic STIs in further analysis. MH, UU and UP were considered to reflect vaginal microbiota.

Bacterial resistance testing

The identification of macrolide resistance for MG strains was performed by FRET real-time PCR and 23S rRNA Sanger sequencing (Touati et al., 2014); when amplification failed, samples were tested with the ResistancePlus MG (SpeeDx) kit (Le Roy et al., 2017). The identification of fluoroquinolone resistance was performed by amplification and Sanger sequencing of the *parC* gene (Le Roy et al., 2016).

The identification of cephalosporin resistance for NG strains was performed using amplification and Sanger sequencing of the *penA* gene (de Curraize et al., 2016). The identification of fluoroquinolone resistance was performed by amplification and Sanger sequencing of the *gyrA* gene (Poncin et al., 2019).

Statistical analysis

Continuous variables are reported as median and interquartile range (IQR), and discrete variables are reported as number and percentage. Group comparison was performed using Chi-squared test or Fisher's test for categorical variables, and Mann–Whitney *U*-test for continuous variables.

Univariable and multi-variable (including age; polygamy; contraception; number of pregnancies; education level; and HIV, HSV-2, CT, MG, NG and TV infections) logistic regression analyses were performed with R v3.6.1 to identify risk factors associated with hrHPV infection. Factors with $P<0.20$ on univariate logistic regression analyses were included in the multiple logistic regression model.

Results

Patient characteristics

In total, 144 patients were included in this study. The median age was 37 (IQR 29–44) years (Table S1, see online supplementary material). The majority lived in urban areas (98%, $n=141$), were married (78%, $n=113$) and had a median age at marriage of 19 (IQR 17–22) years, and 34% ($n=40$) were polygamous. Seventy-eight percent ($n=112$) of women had a primary school education or less. Forty-four (31%) patients were infected with HIV. Compared with HIV-negative patients, the HIV-positive patients tended to be older (P=0.086), used less contraception ($P=0.06$) and were less educated ($P=0.032$) (Table 1).

HPV prevalence and associated lesions

The prevalence rates of any HPV types, hrHPVs, intermediate HPVs and lrHPVs were 74% ($n=104$), 63% ($n=90$), 55% ($n=55$) and 25% ($n=36$), respectively, and women harboured a median of 2 (IQR 0–4), 1 (IQR 0–2), 0 (IQR 0–1) and 0 (IQR 0–0.25) different HPV types, respectively. Among the hrHPVs, HPV31 was the most prevalent (28%), followed by HPV56 (25%) and HPV52 (18%). The prevalence rates of HPV16 and HPV18 were 9.7% and 7.6%, respectively. Among the lrHPVs, HPV42 was the most common (11%), followed by HPV6 (7%) and HPV54 (6%) (Figure 1). Among hrHPV-positive women, 26% ($n=23$) harboured at least one hrHPV included in the bi- or quadrivalent vaccines. This percentage increased to 79% ($n=71$) considering at least one hrHPV included in the nonavalent-vaccine. However, 72% ($n=65$) also harboured at least one hrHPV that was not included in any of the HPV vaccines.

The prevalence of hrHPV types was higher in HIV-positive women compared with HIV-negative women (77% vs 55%, $P=0.014$) (Table 1), as was the prevalence of multiple hrHPV infections (55% vs 33%, $P=0.03$). In HPV-positive women, the prevalence of hrHPV types differed according to HIV status. Specifically, among HIV-positive women, HPV35 (36%) was the most prevalent HPV type, followed by HPV31 (31%) and HPV51/52/56 (each at 28%). Among HIV-negative women, HPV31 (41%) was the most prevalent HPV type, followed by HPV56 (36%) and HPV52 (22%) (Figure 2A).

Twenty patients were positive for VIA/VILI screening. Of these, one had normal histology, six had cervical intra-epithelial neoplasia grade 1 (CIN1), and five had CIN2 or higher. Among the remaining women, five had cervicitis/endocervicitis, and the histology of the biopsies did not contribute to the definitive diagnosis for three women. No significant difference according to sociodemographic data was found between women with and without cervical lesions (Table S2, see online supplementary material). Seven of the 11 patients with cervical lesions tested positive for hrHPV, and only one was infected with HIV. HPV16 was involved in one case, and multiple hrHPV infections occurred in four of the seven cases (HPV31/56/73/82, HPV31/33, HPV16/35/58/82 and HPV35/51/52/58/66/68). HPV31, HPV35 and HPV66 mono-infection were involved in the other three cases (Figure 2B). Overall, the prevalence of cervical lesions was 7.5%, with prevalence rates of 2.3% (1/44) and 10.4% (10/96) in HIV-positive and HIV-negative women.

Prevalence of other STIs and antimicrobial resistance

The seroprevalence rates of HSV-1 and HSV-2 antibodies were 99% and 49%, respectively. Among the HSV-seropositive women, seven (11%) were positive for HSV2-DNA but none were positive for HSV1-DNA in the genital tract. The prevalence rates of NG, CT, MG and TV were 1% ($n=2$), 4% ($n=6$), 9% ($n=13$) and 7% ($n=10$), respectively. Among the analysed parameters, the prevalence of HSV-2 was higher in HIV-positive women than in HIV-negative women (84% vs 32%, $P<0.0001$), and was higher in women with hrHPV infection compared with those with non-hrHPV infection (56% vs 37%, $P=0.035$) (Table 1). No differences in the prevalence rates of HSV-1 or other STIs tested were found based on HIV infection or hrHPV infection.

Considering antimicrobial resistance, none of the MG-positive specimens had macrolide-resistance-associated mutations, but five of nine sequenced specimens were resistant to fluoroquinolone (mutation Ser83(80)Ile on *parC* gene). Furthermore, the two NG strains were also resistant to fluoroquinolone (mutation Ser91Phe on *gyrA* gene), whereas only one strain had decreased susceptibility to cephalosporin (*penA* 19.01 variant) (Table S3, see online supplementary material).

The presence of UU, UP or MH in the cervical tractus was not significantly associated with hrHPV infection (Table 1) or cervical lesions (Table S2, see online supplementary material).

Risk factors associated with hrHPV cervical infection

Univariate and multi-variate logistic regression analyses were performed to assess independent associations between sociodemographic data, and STI and hrHPV infections. On univariate analysis, HIV and HSV-2 infections were significantly associated with cervical hrHPV infection [odds ratio (OR) 2.76, 95% confidence interval (CI) 1.42–5.61, $P=0.014$; OR 2.14 (95% CI 1.18–3.92), $P=0.037$, respectively]. On multi-variate analysis, HIV and MG infections tended to be significantly and independently associated with hrHPV infection [OR=2.17 (95% CI 1.01–4.78), $P=0.098$; OR 6.55 (95% CI 1.47–66.6), $P=0.081$, respectively] (Table 2).

Discussion

To the authors' knowledge, this is the first study performed in Sikasso, Mali to evaluate the prevalence rates of HPV and other

Table 1
Characteristics of 144 women screened for cervical cancer in Sikasso, Mali, according to human immunodeficiency virus status and high-risk human papillomavirus infection.

	Total *n*=144 *n*		HIV+*n*=44		HIV-*n*=96		*P*-value	hrHPV+*n*=90 *n*		hrHPV-*n*=54 *n*		*P*-value
Age, *n*, median (IQR)		37 (29–44)		40 (33.75–44)		35 (27–45)	0.086		37 (31–44.75)		38 (28–44)	0.77
Geographical setting, *n* (%)	144		44		96			90		54		
Urban		141 (98)		42 (95)		95 (99)	0.23		87 (97)		54 (100)	0.29
Rural		3 (2)		2 (5)		1 (1)			3 (3)		0 (0)	
Marital status, *n* (%)	144		44		96			90		54		
Single		4 (3)		0 (0)		4 (4)	<0.0001		2 (2)		2 (4)	0.01
Married		112 (78)		23 (52)		86 (90)			63 (70)		49 (90)	
Widower		24 (16)		17 (39)		6 (6)			22 (25)		2 (4)	
Divorced		4 (3)		4 (9)		0 (0)			3 (3)		1 (2)	
Marital age (years), *n*, median (IQR)		19 (17–22)		20 (17–25)		18 (16.75–22)	0.18		19 (16.75–22)		20 (17–22)	0.49
Polygamy, *n* (%)	116		27		86			67		49		
Yes		40 (34)		10 (37)		29 (34)	0.75		20 (30)		20 (41)	0.22
No		76 (66)		17 (63)		57 (66)			47 (70)		29 (59)	
Contraception, *n* (%)	144		44		96			90		54		
Yes		34 (24)		6 (14)		27 (28)	0.06		22 (24)		12 (22)	0.76
No		110 (76)		38 (86)		69 (72)			68 (76)		42 (78)	
Duration of contraception (years), *n*, median (IQR)		3 (1.25–5)		2 (1–3.75)		3 (2–5)	0.51		3 (1.25–5)		2.5 (1.75–4.5)	0.99
Pregnancy, *n*, median (IQR)		4 (2–6)		4 (2–6)		4 (2–6)	0.94		4 (2–6)		4 (2–6.75)	0.57
Education level, *n* (%)	144		44		96			90		54		
None		75 (52)		27 (61)		47 (49)	0.032		49 (54)		26 (48)	0.42
Primary		37 (26)		13 (30)		23 (24)			22 (25)		15 (28)	
Secondary		29 (20)		4 (9)		24 (25)			18 (20)		11 (20)	
Higher		3 (2)		0 (0)		2 (2)			1 (1)		2 (4)	
STI, *n* (%)												
HIV +	140	44 (31)	-	-	-	-	-	87	34 (39)	53	10 (19)	0.012
hrHPV +	144	90 (63)	44	34 (77)	96	53 (55)	0.012	-	-	-	-	-
HSV-1 + (Ab)	135	133 (99)	44	43 (98)	91	90 (99)	0.55	84	83 (99)	51	50 (98)	>0.99
HSV-2 + (Ab)	135	66 (49)	44	37 (84)	91	29 (32)	<0.0001	84	47 (56)	51	19 (37)	0.035
CT +	144	6 (4)	44	3 (7)	96	3 (3)	0.38	90	4 (4)	54	2 (4)	>0.99
MG +	144	13 (9)	44	5 (11)	96	8 (8)	0.55	90	11 (12)	54	2 (4)	0.13
NG +	144	2 (1)	44	1 (2)	96	1 (1)	0.53	90	1 (1)	54	1 (2)	>0.99
TV +	144	10 (7)	44	4 (9)	96	6 (6)	0.72	90	7 (8)	54	3 (5)	0.74
UU +	144	45 (31)	44	17 (39)	96	28 (29)	0.33	90	36 (40)	54	9 (17)	0.005
UP +	144	84 (58)	44	20 (46)	96	64 (68)	0.025	90	57 (63)	54	37 (69)	0.59
MH +	144	52 (36)	44	20 (46)	96	32 (34)	0.18	90	33 (37)	54	19 (35)	>0.99

Ab, antibody; CT, *Chlamydia trachomatis*; MG, *Mycoplasma genitallium*; MH, *Mycoplasma hominis*; NG, *Neisseria gonorrhoeae*; TV, *Trichomonas vaginalis*; UP, *Ureaplasma parvum*; UU, *Ureaplasma urealyticcum*; HIV, human immunodeficiency virus ; hrHPV, high-risk human papillomavirus; *n*, number; STI, sexually transmitted infection; +, positive ; -, negative ; IQR, interquartile range.
Statistical comparisons were performed using Chi-squared test or Fisher's test for categorical variables, and Mann–Whitney *U*-test for continuous variables.

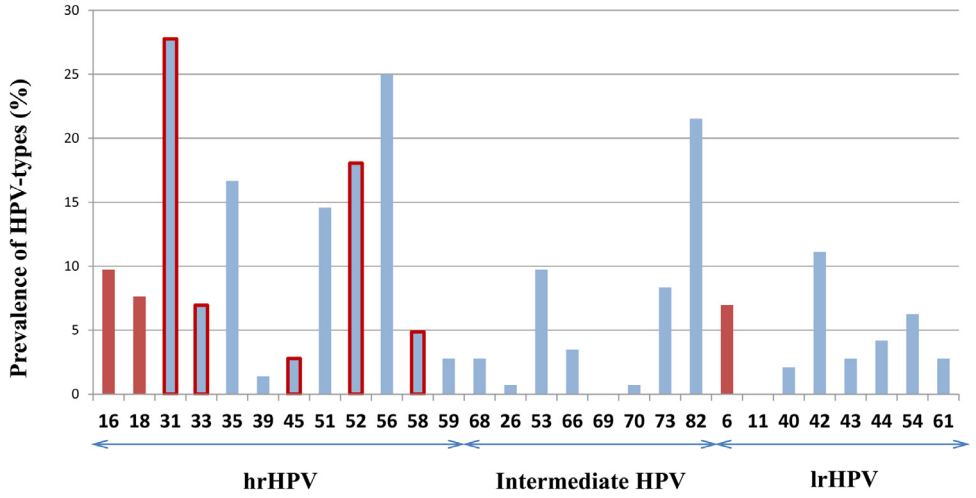

Figure 1. Prevalence of human papillomavirus (HPV) types among the 144 women screened for cervical cancer in Sikasso, Mali. All types of HPV identifiable by the Anyplex II HPV-28 detection test (Seegene, Seoul, South Korea) are represented on the x-axis and the proportions (as percentages) of each HPV type identified in the population are represented on the y-axis. Red columns, HPV types included in the HPV quadrivalent vaccine; blue columns with red outline, additional HPV types included in the HPV nonavalent vaccine. hrHPV, high-risk human papillomavirus; lrHPV, low-risk human papillomavirus.

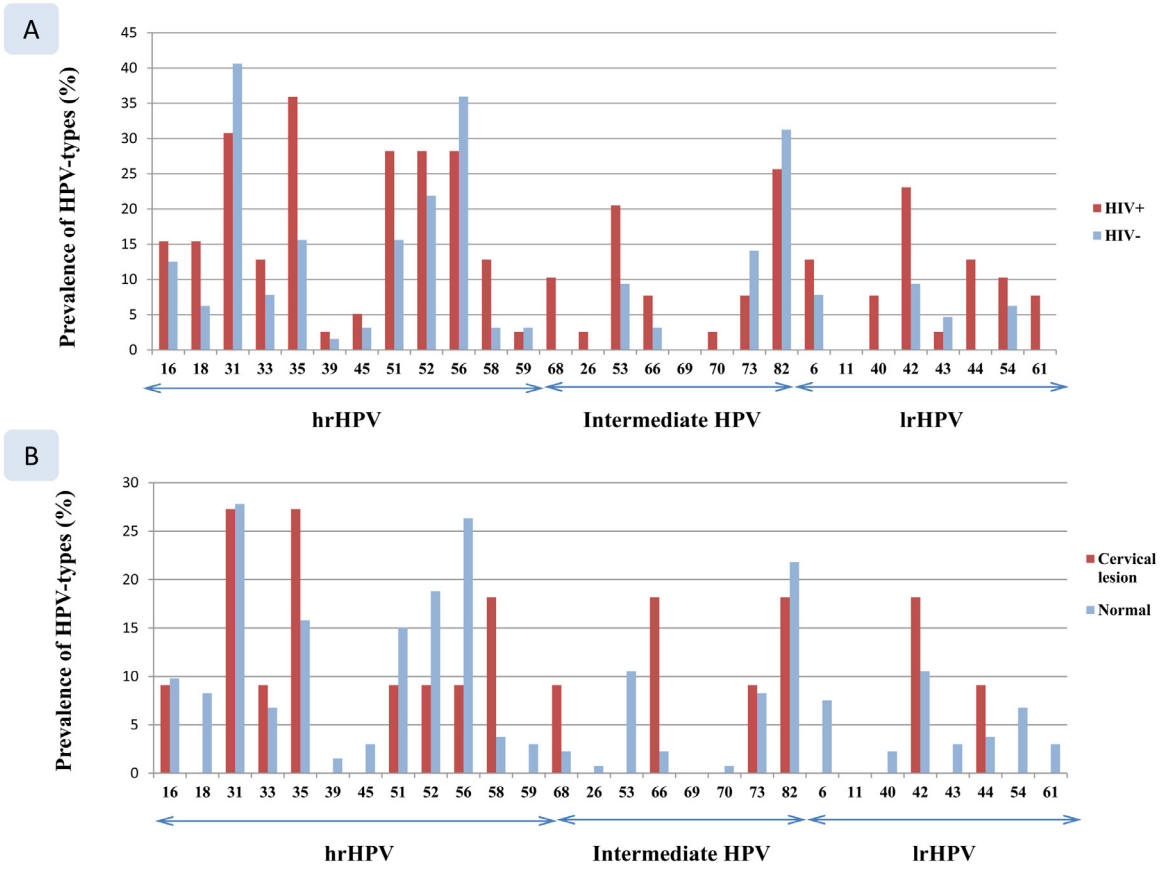

Figure 2. Prevalence of human papillomavirus (HPV) types according to human immunodeficiency virus (HIV) status (A) or associated cervical lesions (B). All types of HPV identifiable by the Anyplex II HPV-28 detection test (Seegene, Seoul, South Korea) are represented on the x-axis and the proportions (as percentages; 2A: among HPV-positive women, 2B: among all women tested) of each HPV type identified are represented on the y-axis. Red columns, prevalence of each HPV type among HIV-positive women (2A) or women with cervical lesions (2B); blue columns, prevalence of each HPV type among HIV-negative women (2A) or women without cervical lesions (2B). hrHPV, high-risk human papillomavirus; lrHPV, low-risk human papillomavirus.

Table 2
Risk factors associated with high-risk human papillomavirus (hrHPV) cervical infection in women screened for cervical cancer at Kénédougou Solidarité community health centre, Sikasso, Mali.

Risk factors	Univariate analysis			Multi-variate analysis		
	OR	95% CI	*P*-value	OR	95% CI	*P*-value
hrHPV infection						
Age	1.00	0.98–1.03	0.80	–	–	–
Polygamy	0.62	0.32–1.18	0.22	–	–	–
Contraception	1.13	0.58–2.25	0.76	–	–	–
Number of pregnancies	0.95	0.86–1.06	0.43	–	–	–
Education level (none and primary vs secondary and higher)	0.84	0.43–1.67	0.68	–	–	–
HIV	2.76	1.42–5.61	0.014[a]	2.17	1.01–4.78	0.098
HSV-2	2.14	1.18–3.92	0.037[a]	1.56	0.79–3.1	0.28
NG	0.60	0.04–8.1	0.72	–	–	–
CT	1.21	0.30–6.16	0.83	–	–	–
MG	3.62	1.13–16.7	0.10	6.55	1.47–66.6	0.081
TV	1.43	0.74–5.19	0.61	–	–	–

CI, confidence interval; HIV, human immunodeficiency virus; HSV-2, herpes simplex virus 2; NG, *Neisseria gonorrhoeae*; CT, *Chlamydia trachomatis*; MG, *Mycoplasma genitalium*; TV, *Trichomonas vaginalis*; OR, odds ratio; –, parameter not included in multi-variate analysis.
[a] <0.05.

STIs in a population of women screened for cervical cancer. A high rate of hrHPV infection associated with cervical lesions was found in 7.5% of cases. The prevalence rates of other STIs were similar to data reported previously (Rowley et al., 2019).

This study found high prevalence of any type of HPV as well as hrHPV (74% and 63%, respectively). Previous studies in Mali reported prevalence rates ranging from 11.9% (95% CI 8.1–17.1%) to 23.1% (95% CI 17.9–29.2) in apparently healthy women with no history of precancerous cervical lesions or cancer (Sankaranarayanan et al., 2004; Tracy et al., 2011; Schluterman et al., 2013). The main differences between the present study and these previous studies are based on the HPV test (AnyplexII HPV28 vs Digene Hybrid), and on the geographical setting in Mali (Sikasso vs Bamako and Naréna, 100 km south-west of Bamako), and may explain the higher prevalence in the present study population. Indeed, the prevalence of HPV has been reported to be higher in rural areas than in urban areas, and it has been hypothesized that this may be due to riskier sexual behaviours and

cultural factors facilitating the transmission of HPV to almost all women soon after the start of sexual activity (Schluterman et al., 2013). Limited access to the healthcare system for women living in rural areas could also be associated with a high rate of untreated STIs. On the other hand, Sikasso is a town close to the border, which could imply more passages, exchanges, truck drivers or sex workers. Some potential female sex workers were included in this study, and these women are at higher risk of being exposed to HPV or other STIs. Finally, 24% of the women in this study were HIV-positive (HIV status was not available in the other two studies), and this also contributed to higher hrHPV infection.

Although HPV16 is the most common HPV type in women with normal cytology (2.7%) and remains the first hrHPV type identified in low-grade squamous intra-epithelial lesions (14.8%), high-grade squamous intra-epithelial lesions (23.9%) and cervical cancer (35.5%) (ICO/IARC Information Centre on HPV and Cancer, 2019) in West Africa, HPV16 was only the sixth most common HPV type in the present study. This study also found an unusual distribution of hrHPV types (HPV31/56/52 were the most prevalent) compared with the hrHPV types usually involved in precancerous and cancerous cervical lesions. This unusual distribution was also observed between hrHPV types harboured by HIV-positive or HIV-negative women. However, these results are consistent with several studies carried out in Africa, which reported infections or precancerous cervical lesions with a wide variety of hrHPVs, different from conventional HPV16 or HPV18 (Piras et al., 2011; Mbaye et al., 2014; Traore et al., 2016; Ferre et al 2018).

A modelling study showed that switching from the bivalent or quadrivalent HPV vaccine to the nonavalent HPV vaccine would reduce the incidence of CIN2/3 by 9–13% in the long term due to the coverage of additional high-risk HPV types (Van de Velde et al., 2012). The present results strongly suggest that the nonavalent HPV vaccine provides better hrHPV coverage than the quadrivalent vaccine in the study population (79% vs 26%, respectively).

According to extensive research around the world, the prevalence of hrHPV, as well as hrHPV multi-infection, was higher in HIV-positive women, and these findings were also supported by univariate and multi-variate regression analysis. Indeed, chronic immunosuppression induced by HIV infection provides an environment for persistent HPV infection, and thus increases the risk of malignant transformation (Liu et al., 2018). However, in the present study, associated cervical lesions were mainly found in HIV-negative women (only one HIV-positive women had CIN1) and regardless of any sociodemographic characteristics. Although the persistence of hrHPV infection was not evaluated, the results suggest that both nonavalent HPV vaccination and cervical cancer screening are necessary in women in Mali.

Considering the other STIs, this study found prevalence rates similar to those reported previously (Rowley et al., 2019), with higher seroprevalence of HSV-2 in HIV-positive patients as well as in patients with hrHPV infection. In fact, it has been shown that HSV-2 infection increases the risk of HIV-1 acquisition (Looker et al., 2017; Kouyoumjian et al., 2018), and is higher in patients with HPV infection (Finan et al., 2006). However, the role of HSV-2 in the development of cervical intra-epithelial cancer remains uncertain with conflicting results (Smith et al., 2002; Finan et al., 2006). Importantly, this is the first study to report antimicrobial resistance in STIs in Mali. Current international, European and American guidelines recommend treatment with combination therapy with extended-spectrum cephalosporin and azithromycin for uncomplicated gonococcal infections to maximize efficacy, and theoretically reduce the risk of emergence of resistance in gonococcal isolates. MG has intrinsic resistance to many antibiotics, and the prevalence of resistance to first- and second-line regimens (macrolides and fluoroquinolones) is increasing worldwide, with limited alternative therapeutic options. The present study found fluoroquinolone resistance in the two NG strains and in half of the MG strains. This could be related to the extended use of this class of antibiotics, especially ciprofloxacin, in Mali, where diagnosis of STIs is based on a syndromic approach and antibiotic use is based on WHO recommendations. This should be monitored carefully, as antibiotic resistance surveillance informs optimal empiric antibiotic regimens.

Although an association between vaginal microbiota and increased risk of HPV persistence and progression of HPV-related cervical disease has been reported (Parthenis et al., 2018), the present study did not find any evidence to support this.

This study has two main limitations: the small number of women enrolled and the lack of population characterization, specifically the presence of STI symptoms and sexual risk factors. The lack of longitudinal follow-up is another important missing element, as it was not possible to assess the progression of cervical lesions or the persistence of hrHPV infection. Further studies should be performed in a large cohort, including women from the general population and from different centres to confirm these data, and to improve knowledge about cervical cancer, HPV infection and other STIs in women in Mali.

In conclusion, this study reported high prevalence rates of viral and bacterial STIs in HIV-positive and HIV-negative women, and fluoroquinolone resistance in different strains involved in STIs. Further studies are required to confirm these data in Mali, and to improve prevention, screening and management of cervical cancer and other STIs in women.

Declaration of Competing Interest

None declared.

Acknowledgments

The authors wish to thank Marie Gardette for technical assistance. This work was presented, in part (HPV data), as an oral communication at Eurogin, 4–7 December 2019, Monte-Carlo, Monaco.

Funding

This work was funded by the Agence Nationale de Recherche sur le SIDA et les Hépatites Virales AC43 ‘Sexually Transmitted Infections’ Working Group and GSK France.

Ethical approval

This study was approved by the Comité d’Ethique Institutionnel de la Faculté de Médecine, de Pharmacie et d’Odontostomatologie, Université des Sciences Techniques et des Technologies de Bamako.

Author contributions

Conception and design of the study: CA, RM, VC, AGM, AIM.

Patient enrolment and acquisition of clinical data: IT, YS, AK, OD, MK, FTT, MS.

Execution of experiments: SS.

Data analysis: AJ, SB, DB, LBR, BB, CB.

Drafting a significant portion of the manuscript or figures: AJ, IT, SB, DB, CB.

All the authors read, corrected and approved the final manuscript.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.ijid.2021.06.024.

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