Dynamics of vaginal immune correlates and microbiota in women from Sub-Saharan Africa

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Background

Alterations in vaginal microbiota (VMB) have been shown to increase HIV acquisition and transmission in women. We carried out a longitudinal characterization of the VMB, soluble cervicovaginal immune mediators and their determinants in women from Sub-Saharan Africa.

Methods

Cervicovaginal lavages from two cohorts of sexually active women from Kenya, South Africa and Rwanda were analysed for IL-1α, IL-1β, IL-6, IL-12(p70), MIP-1β, IP-10, IL-8, GM-CSF, G-CSF, Elafin, SLPI, IL-1RA and total protein. qPCR was used to quantify total *Lactobacillus*, *L. crispatus, L. iners, L. jensenii*, *L. gasseri, L. vaginalis, A. vaginae, G. vaginalis, P. bivia* and *E. coli* in vaginal swab samples. Cohort A had 40 women with a healthy VMB (Nugent score < 4) at all five bi–weekly visits. Cohort B consisted of 40 women with incident bacterial vaginosis (BV) (Nugent score > 7) in the course of their visits.

Results

Cohort A: Individual *Lactobacillus* species were consistently present or absent within each woman over five study visits (Fig. 1). Sexual activity was associated with reduced counts of total *Lactobacillus*, *L. iners* and *Prevotella bivia* (Table 1) but increased concentrations of IL-6, IL-12(p70) and IP-10. pH was positively associated with IL-1RA and IL1RA/IL1(α+β) ratio but negatively associated with total protein and SLPI. The amount of total *Lactobacillus* was significantly lower and total soluble immune mediators, MIP-1β and IL-8 higher in 14 women on progesterone-only contraception compared to those with a cycle (20 not on any contraceptives and 6 on combined pill) (Table 1). Cohort B: Total *Lactobacillus*, *L. crispatus*, IP-10, GM-CSF, Elafin, SLPI and total protein were all reduced during the first visit with BV. Conversely, *G. vaginalis, A. vaginae, E. coli* and IL-1β were increased with incident BV (Table 2 & 3).

Table 1 Cohort A: Longitudinal analysis of microbiome qPCR results over 8 weeks

	Progesterone only		Day 21 of Cycle		PSA		Recent Vaginal Washing	
	Est.	P-Val.	Est.	P-Val.	Est.	P-Val.	Est.	P-Val.
PC Score 1	-0.06	0.793	0.14	0.048	-0.12	0.174	-0.20	0.093
PC Score 2	-0.03	0.928	0.02	0.796	0.05	0.570	-0.01	0.965
Total Lactobacillus	**-0.55**	**0.023**	0.20	0.124	**-0.39**	**0.010**	-0.27	0.146
L. crispatus	-1.33	0.091	0.49	0.245	-0.30	0.529	-0.05	0.939
L. iners	0.08	0.811	-0.25	0.356	**-0.75**	**0.008**	-0.32	0.272
L. jensenii	-0.30	0.785	0.85	0.066	0.36	0.476	0.12	0.842
L. vaginalis	0.75	0.192	-0.19	0.545	0.01	0.980	0.50	0.239
E. coli	0.14	0.637	**-0.75**	**0.020**	0.10	0.757	-0.26	0.373
P. bivia	0.27	0.199	-0.16	0.346	**-0.38**	**0.045**	0.03	0.880

Fig. 1 Cohort A (women with healthy VMB)
Presence/Absence and amount of microbiota species over 8 weeks

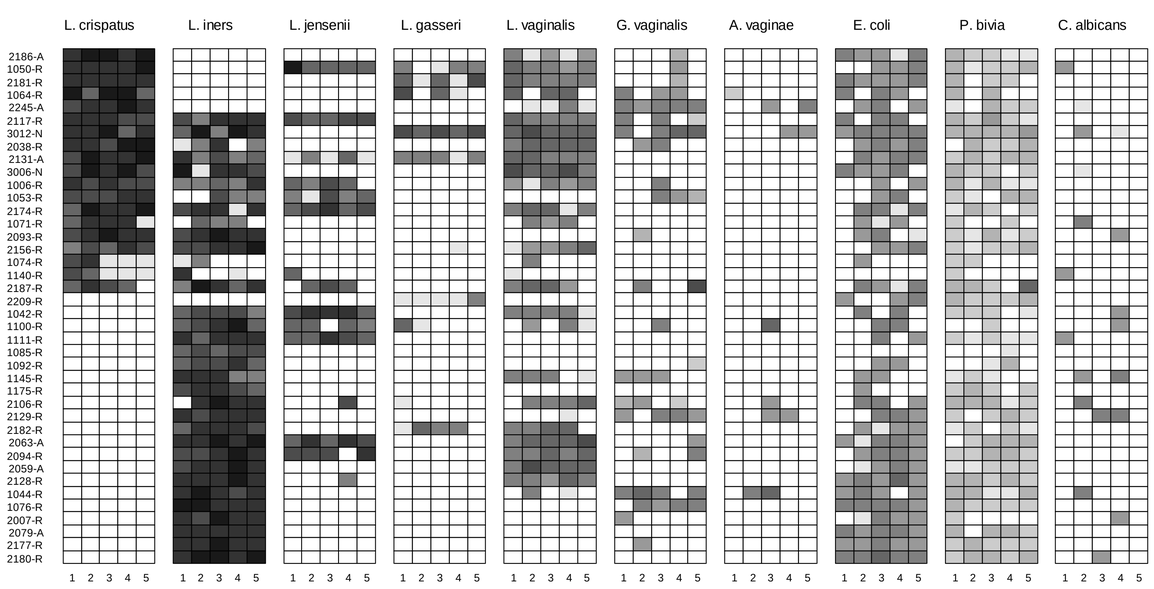

Fig. 2 Cohort B (women with incident BV)
Presence/Absence and amount of microbiota species over 8 weeks

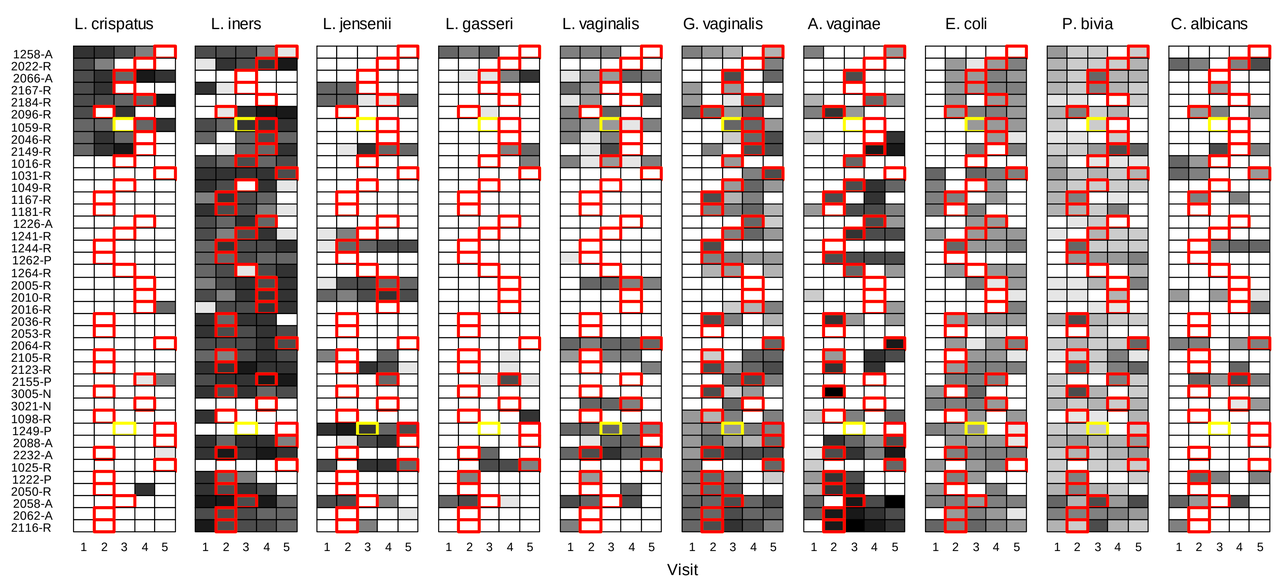

Table 2 Cohort B Microbiota qPCR difference between baseline visit and visit before BV/BV visit

	Visit before BV				BV visit			
	Baseline	Visit	Change		Baseline	Visit	Change	
	Mean	Mean	Mean	p-value	Mean	Mean	Mean	p-value
Microbiota qPCR								
PC Score1	0.54	0.67	0.14	0.403	0.33	-0.75	**-1.08**	**<.001**
PC Score2	0.04	-0.20	-0.24	0.104	-0.25	-0.24	0.01	0.459
Total Lactobacillus	6.96	7.60	0.64	0.166	7.10	6.09	**-1.00**	**0.021**
L. crispatus	2.45	1.91	-0.54	0.547	1.66	0.52	**-1.15**	**0.010**
L. iners	5.15	5.84	0.69	0.210	6.01	5.54	-0.47	0.358
L. vaginalis	2.11	2.76	0.66	0.626	1.83	1.14	-0.69	0.116
G. vaginalis	1.51	2.11	0.60	0.391	1.89	5.37	**3.47**	**<.001**
A. vaginae	1.04	0.20	-0.84	0.141	1.34	4.97	**3.63**	**<.001**
E. coli	1.53	3.04	1.51	0.054	1.57	2.83	**1.26**	**0.024**
P. bivia	2.51	1.76	**-0.75**	**0.034**	2.38	3.70	**1.33**	**<.001**

Table 3 Cohort B Immune markers difference between baseline visit and visit before BV/BV visit

	Visit before BV				BV visit			
	Baseline	Visit	Change		Baseline	Visit	Change	
	Mean	Mean	Mean	p-value	Mean	Mean	Mean	p-value
Soluble Markers								
PC Score 1	0.10	-0.31	-0.41	0.098	-0.03	-0.00	0.03	0.989
PC Score 2	-0.11	-0.13	-0.02	1.000	-0.16	-0.01	0.15	0.412
PC Score 3	-0.34	-0.25	0.10	0.956	-0.30	0.92	**1.22**	**<.001**
IL-1α	1.33	1.23	-0.10	0.698	1.30	1.55	0.26	0.093
IL-1β	0.91	0.69	-0.22	0.262	0.89	1.20	**0.31**	**0.030**
IL-6	1.02	0.77	**-0.24**	**0.049**	0.86	0.87	0.00	0.853
IL-12	0.15	-0.00	-0.15	0.058	0.12	0.22	0.11	0.103
IL-1RA	4.79	4.71	-0.08	0.157	4.73	5.00	0.27	0.096
IP-10	2.77	2.63	-0.14	0.274	2.73	2.11	**-0.62**	**<.001**
IL-8	2.25	2.07	-0.18	0.104	2.23	2.26	0.03	0.895
GM-CSF	0.48	0.34	**-0.15**	**0.005**	0.38	0.27	**-0.11**	**0.011**
G-CSF	2.06	1.96	-0.11	0.846	1.92	1.87	-0.05	0.396
Elafin	5.10	5.07	-0.02	0.657	5.17	4.89	**-0.28**	**<.001**
SLPI	4.95	4.80	-0.15	0.125	4.88	4.46	**-0.42**	**<.001**
Total protein	8.26	8.29	0.02	0.782	8.26	8.05	**-0.21**	**0.001**
IL-1α+β/IL-1RA	3.29	3.28	-0.00	0.598	3.25	3.19	-0.06	0.579

Conclusion

Sexual activity, progesterone, clinical symptoms of pathology and BV alter vaginal mucosal immunity in Sub-Saharan African women potentially increasing their susceptibility to HIV infection.

Disclosure of interest statement

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