Vaginal Immune Dysregulation in Transgender/Non-Binary Individuals on Masculinizing Hormone Therapy

1175

Matilde Jacobson[1], Janja Kovacic[1], Eleanor Capozzi[1], Megan Gooding[1], Huberth Garcia[1], Fernando Cabezas Mejia[1], Christopher Cannon[2], Lynsay Ehui[2], Janelle Schrag[2], Mimi Ghosh[1]

[1]George Washington University, Washington, DC, USA; [2]Whitman-Walker Institute, Washington, DC,USA

BACKGROUND

Many transgender men and nonbinary (TMNB) people receiving gender-affirming care take supplemental testosterone as part of their masculinizing hormone therapy (MHT) regimen. This is a diverse population encompassing a variety of sexual orientations and behaviors. They are disproportionately affected by sexually transmitted infections, particularly HIV[1,2]. Testosterone is known to have immunosuppressive activity and may modulate HIV/STI susceptibility[3,4]. However, little is known about the immunological characteristics of the vaginal mucosa of people assigned female at birth (AFAB) on MHT.

OBJECTIVE

To characterize the vaginal immune microenvironment of AFAB, TMNB individuals on MHT and provide baseline immunological data to guide future research.

METHODS

We conducted a cross sectional study with 72 AFAB, sexually active, pre-menopausal, and HIV-negative participants recruited from the Washington DC metro area.

Group 1: No MHT
36 participants not taking any supplemental testosterone

Group 2: MHT
36 participants taking testosterone as gender-affirming hormone therapy for ≥6 months

Following GWU IRB approval, participants provided informed consent, completed a demographic and behavioral survey, had blood drawn, and self-collected vaginal swabs. Enzyme-linked immunosorbent assays (ELISAs) were used to assess the concentrations of inflammatory and antimicrobial immune biomarkers (R&D Systems) in vaginal swab supernatants, as well as hormone concentrations (DRG International) in blood plasma. For statistical analyses, Mann-Whitney U tests were used to compare vaginal biomarker concentrations between study groups, and simple linear regression to assess the correlations between biomarker concentrations in vaginal samples and testosterone levels in plasma (GraphPad Prism 10.0.2). Demographic and behavioral characteristics were compared between groups using Mann-Whitney U, Chi-squared, and Fisher's exact tests, as appropriate (R Studio 2023.09.0).

Individuals assigned female at birth who are taking testosterone show evidence of an inflammatory vaginal immune profile

RESULTS

Table 1. Demographics

	Group 1 (No MHT) n=36	Group 2 (MHT) n= 36	P-value
Age			
Mean [Min, Max]	28.6 [21, 42]	27.8 [18, 44]	0.5879[a]
	n (%)	**n (%)**	
Race			
White	15 (41.7)	24 (66.7)	0.1234[c]
Black or African American	7 (19.4)	5 (13.9)	
Asian	3 (8.3)	3 (8.3)	
Other or mixed	11 (30.6)	4 (11.1)	
Ethnicity			
Hispanic	11 (30.5)	5 (13.9)	0.0890[b]
Gender Identity (All participants AFAB)			
Cisgender woman	29 (80.6)	--	**<0.0001[c]**
Transgender man or trans masculine	--	33 (91.7)	
Nonbinary or other	7 (19.4)	3 (8.3)	
Annual Income			
Less than $25,000	8 (22.2)	10 (27.8)	0.1071[c]
$25,000 to $49,999	14 (38.9)	15 (41.7)	
$50,000 to $74,999	12 (33.3)	4 (11.1)	
$75,000 to $99,999	2 (5.6)	5 (13.9)	
$100,000 or more	--	2 (5.6)	
Education			
High school or GED	6 (16.7)	--	**0.0342[c]**
Some college	2 (5.6)	8 (22.2)	
Associate level degree or trade certification	2 (5.6)	2 (5.6)	
Bachelor's degree	19 (52.8)	20 (55.6)	
Master's/Doctoral/Professional degree	7 (19.4)	6 (16.7)	

Statistical Tests: α=0.05. *Significant results in* ***bold***
[a]Mann-Whitney U Test, [b]Chi-square Test of Independence, [c]Fisher's Exact Test
Abbreviations:
MHT: Masculinizing hormone therapy
AFAB: Assigned female at birth

Table 2. Sexual Behaviors

	Group 1 (No MHT) n (%)	Group 2 (MHT) n (%)	P value
Sexual Activity			
Sexually active in last month, one partner	32 (88.9)	24 (66.7)	0.0557[b]
Sexually active in last month, multiple partners	3 (8.3)	10 (27.8)	
None	1 (2.8)	2 (5.6)	
Sexual Practices			
Receptive vaginal intercourse	32 (88.9)	30 (83.3)	0.4955[a]
Receptive anal intercourse	4 (11.1)	9 (25.0)	0.1255[a]
Gender of Sexual Partners			
Cisgender men	22 (61.1)	14 (38.9)	0.1082[b]
Cisgender women	4 (11.1)	4 (11.1)	
Transgender men or trans masculine people	--	3 (8.3)	
Transgender women or trans feminine people	--	3 (8.3)	
Non-binary or gender fluid	5 (13.9)	7 (19.4)	
Multiple genders	3 (8.3)	5 (13.9)	
Contraceptives			
None	24 (66.7)	24 (66.7)	0.8974[b]
Hormonal Pill	--	--	
Copper IUD	3 (8.3)	2 (5.6)	
Hormonal IUD	8 (22.2)	6 (16.7)	
Hormonal Implant	1 (2.8)	2 (5.6)	
Hysterectomy	--	1 (2.8)	
Condoms only	--	1 (2.8)	
Condom use during receptive vaginal sex			
Never or less than half the time	20 (62.5)	22 (73.3)	0.8369[b]
About half the time	2 (6.3)	2 (6.7)	
Most of the time	6 (18.8)	4 (13.3)	
Every time	4 (12.5)	2 (6.7)	
HIV Pre-Exposure Prophylaxis			
Currently Taking	--	9 (25.0)	**0.0022[b]**

Statistical Tests: α=0.05. *Significant results in* ***bold***
[a]Chi-square Test of Independence, [b]Fisher's Exact Test
Abbreviations:
MHT: Masculinizing Hormone Therapy

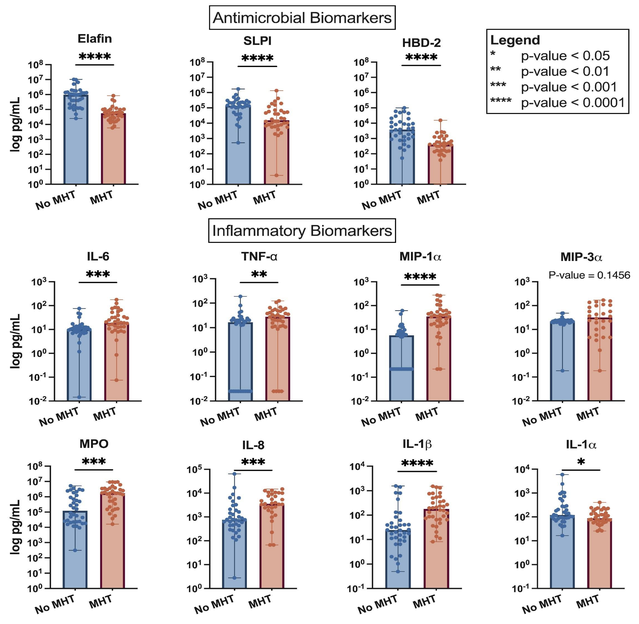


Figure 1. Decreased antimicrobial and elevated inflammatory biomarker concentrations in vaginal samples from MHT group.

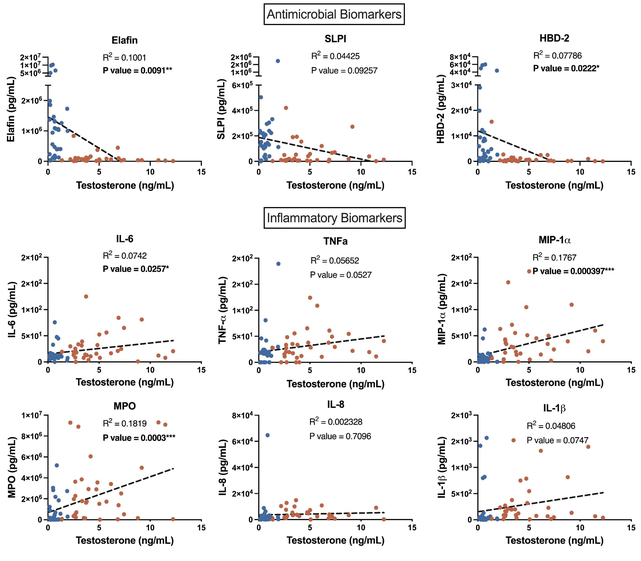


Figure 2. Significant correlations between plasma testosterone concentrations and vaginal biomarker concentrations.

CONCLUSIONS

Overall, we found evidence of vaginal immune dysregulation in TMNB individuals receiving MHT.

- 6 of 8 inflammatory biomarkers tested were significantly higher in the MHT group compared to the No MHT group
- All 3 antimicrobial biomarkers tested were significantly lower in the MHT group
- Testosterone concentrations in participant plasma positively correlated with inflammatory and negatively correlated with antimicrobial biomarker concentrations in vaginal samples
- 83% of TMNB participants reported engaging in vaginal sex in the last month, underscoring the relevance of vaginal immune status in this population

Our findings do not negate gender-affirming hormone therapy as a life-saving standard of care for transgender and non-binary individuals. We recommend integrating HIV prevention services, such as PrEP counseling, into broader gender-affirming care services.

ACKNOWLEDGEMENTS

We would like to thank the team at Whitman-Walker Institute for their invaluable role recruiting and conducting study visits, and our study participants for enabling this research.

FUNDING

"Genital Health of Trans-men on Testosterone", NIH R21AI157927-02 (MG)

CONTACT

Presenting Author: matildejacobson@gwu.edu
Principal Investigator: mghosh@gwu.edu

Abbreviations used:

TMNB: transgender men and nonbinary people
MHT: masculinizing hormone therapy
AFAB: assigned female at birth
GWU IRB: George Washington University Institutional Review Board
ELISA: enzyme-linked immunosorbent assay
PrEP: pre-exposure prophylaxis
SLPI: secretory leukocyte protease inhibitor
HBD-2: human beta-defensin-2
MPO: myeloperoxidase
TNF-α: tumor necrosis factor-alpha
MIP-1α and MIP-3α : macrophage inflammatory protein 1 and 3-alpha
IL-1α, IL-1β, IL-6 and IL-8: interleukin 1-alpha, 1-beta, 6, and 8

REFERENCES

1. Van Gerwen OT, Jani A, Long DM, Austin EL, Musgrove K, Muzny CA. Prevalence of Sexually Transmitted Infections and Human Immunodeficiency Virus in Transgender Persons: A Systematic Review. Transgend Health. 2020;5(2):90-103. doi:10.1089/trgh.2019.0053
2. Stutterheim SE, van Dijk M, Wang H, Jonas KJ. The worldwide burden of HIV in transgender individuals: An updated systematic review and meta-analysis. *PloS One*. 2021;16(12):e0260063. doi:10.1371/journal.pone.0260063
3. Trigunaite A, Dimo J, Jørgensen TN. Suppressive effects of androgens on the immune system. *Cell Immunol*. 2015;294(2):87-94. doi:10.1016/j.cellimm.2015.02.004
4. Ragupathy V, Devadas K, Tang S, et al. Effect of sex steroid hormones on replication and transmission of major HIV subtypes. *J Steroid Biochem Mol Biol*. 2013;138:63-71. doi:10.1016/j.jsbmb.2013.03.002