Poster # 950

Is Syndromic Diagnosis of Reproductive Tract Infections Antiquated in the HIV Era?

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BACKGROUND

- Syndromic diagnosis (SD) of reproductive tract infections (RTIs), based on patient signs and symptoms, is a widely implemented strategy in sub-Saharan Africa.
- Where laboratory services are limited, SD is expected to address the majority of RTIs, especially those with the most adverse outcomes.
- We assessed prevalence of RTIs by SD and laboratory testing, and examined sensitivity and specificity of SD against laboratory testing for RTIs among newly-diagnosed HIV-infected patients in Tanzania.

METHODS

- A cross-sectional study among sexually-active HIV-positive adults ≥ 18 years
- Consecutively recruited adults newly enrolling at the regional hospital HIV clinic in Bukoba Tanzania, 2012-2014.
- Participants interviewed on current RTI symptoms (sores, discharge, dysuria, lower abdominal pain), followed by full general body examination and a genital exam, including speculum insertion for women.
- Study nurse made the SD of genital ulcer disease (GUD) urethral discharge syndrome (UDS), vaginal discharge syndrome (VDS) or lower abdominal pain/pelvic inflammatory disease (LAP/PID) according to national RTI guidelines. This was verified by a medical doctor.
- Regardless of symptoms, laboratory testing was done as shown in **Table 1.**
- Analyzed the sensitivity and specificity (with 95% confidence intervals) of syndromic RTI diagnosis of major syndromes against laboratory testing for transmittable RTIs (CT, NG, TP and HSV-2), and all RTIs.
- Determined the positive and negative predictive values, PPV and NPV (with 95% confidence intervals).

Table 1: Laboratory testing

Pathogen	Men	Women	Lab Assay
Chlamydia Trachomatis (CT), Nesseiria Gonorrhoeae (NG)	Urine	Vaginal swab	PCR
Troponema Pallidum (TP)	Blood	Blood	RPR → TPPA
Herpes Simplex Virus (HSV)-2 (if ulcer present)	Blood	Blood	Kalon ELISA
Trichomonas Vaginalis (TV)	-	Vaginal swab	In pouch, culture
Bacterial Vaginosis (BV), Vulvovaginal Candidiasis (VVC)	-	Vaginal swab	Gram stain

RESULTS

- Enrolled 615 participants: 301 men, median age 36 years (Inter quartile range, IQR 30-41) and 314 women, median age, 33 years (IQR 27-38). Half the men (56%) and 43% of women were married, median number of sexual partners in the previous 6 months was 1 for both.
- Median CD4 cell count, cells/μL (IQR) was 249 (82-398) among men and 294 (132-486), among women.
- One third of men were circumcised (34%) at a median age of 10 years (IQR 3-19).
- **Figure 1** summarizes syndromic and laboratory RTI diagnosis among men and women. The most common RTI syndromes and laboratory pathogens are shown in **Figure 2**.
- **MEN:** 59 (20%) reported genital symptoms, and 52 (17%) had signs on examination. Of the 242 men who did not report symptoms, 24 (10%) had RTI signs on examination.
  - RTI prevalence by SD was 83(28%): 21 (7%) with GUD and 46 (15%) with UDS, and 16 (19%) with other syndromes e.g. buboes, warts and abscesses. Few men 14 (5%) had more than one syndrome.
  - RTI prevalence by laboratory testing was 107 (36%), 46 (15%) men had more than 1 RTI on laboratory testing
  - SD had sensitivity of 47% (36-58%) and a specificity of 69% (62-75%), with a PPV of 37% (27-46%) and NPV of 77% (71-83%).
- **WOMEN:** 95 (30%) reported RTI symptoms, and 168 (54%) had signs on examination. Half the women (89/168, 53%) who did not report any symptoms were found to have RTI signs on examination.
  - RTI prevalence by SD was 184 (59%): 158 (50%) with VDS, 56 (18%) with LAP and 17 (5%) with GUD. One in five women (64, 20%) had more than one syndrome.
  - RTI prevalence by laboratory testing was 247 (79%), 138 (44%) women had more than one RTI detected on laboratory testing.
  - SD had a sensitivity of 59% (51-66%) and a specificity of 51% (42-60%), with a PPV of 63% (55-70%) and a NPV of 47 (39-55%). Inclusion of BV and VVC in overall estimate increased sensitivity to 82% but decreased specificity to 27%.
- **Tables 2 and 3** show the sensitivity and specificity by syndrome.
- SD had higher sensitivity in the youngest age group (18-24 years) for both men 67% and women 76%. SD sensitivity was lowest among men who reported to be taking antibiotics (30%). SD specificity was higher among circumcised men (78%). No significant differences were observed in SD sensitivity or specificity by CD4 count.

Figure 1: Syndromic and laboratory RTI diagnosis among men and women in the survey

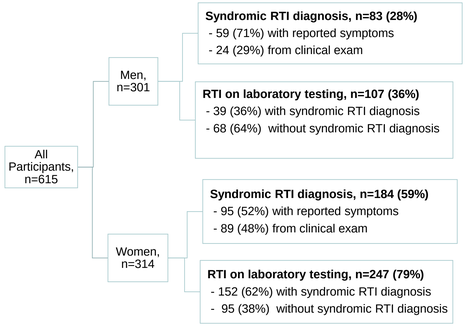

Figure 2: Prevalence of RTIs by syndromic diagnosis and laboratory testing among men and women

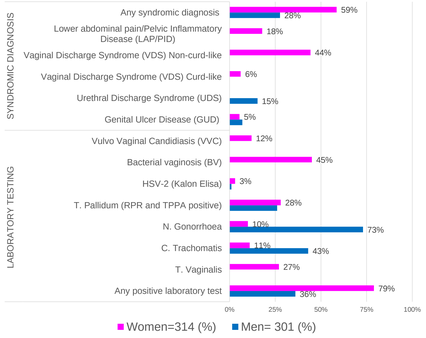

Table 3: Sensitivity and specificity of SD versus laboratory testing among men and women for urethral discharge syndrome (UDS), vaginal discharge syndrome (VDS) and lower abdominal pain/pelvic inflammatory disease (LAP/PID)

		MEN		WOMEN					
		UDS		VDS (curd-like)		VDS (non-curd-like)		LAP/PID	
		Yes, n=46	No, n=255	Yes, n=19	No, n=295	Yes, n=139	No, n=175	Yes, n=56	No, n=258
Laboratory testing results		**n (%)**	**n (%)**	**n (%)**	**n (%)**	**n (%)**	**n (%)**	**n (%)**	**n (%)**
N. Gonorrhoea	Yes	13 (28)	9 (4)	0 (0)	30 (10)	16 (12)	14 (8)	9 (16)	21 (8)
	No	33 (72)	246 (96)	19 (100)	265 (90)	123 (88)	161 (92)	47 (84)	237 (92)
	Sensitivity (95% CI)	**28 (16-44)**		–		**12 (7-18)**		**16 (8-28)**	
	Specificity (95% CI)	97 (93-98)		90 (86-93.0)		92 (87-96)		92 (88-95)	
	PPV (95% CI)	59 (36-79)		–		53 (34-72)		30 (15-49)	
	NPV (95% CI)	88 (84-92)		93 (90-96)		57 (51-63)		84 (79-88)	
C. Trachomatis	Yes	3 (7)	10 (4)	1 (5)	33 (11)	18 (13)	16 (9)	8 (14)	26 (10)
	No	43 (93)	245 (96)	18 (95)	262 (89)	121 (87)	159 (91)	48 (86)	232 (90)
	Sensitivity (95% CI)	**7 (1-18)**		5 (0-26)		**13 (8-20)**		**14 (6.-26)**	
	Specificity (95% CI)	96 (93-98)		89 (85-92)		91 (86-95)		90 (86-93)	
	PPV (95% CI)	23 (5-54)		3 (0-15)		53 (35-70)		24 (11-41)	
	NPV (95% CI)	85 (80-89)		94 (90-96)		57 (51-63)		82 (78-87)	
T. Vaginalis	Yes			5 (26)	80 (27)	35 (25)	50 (29)	12 (21)	73 (28)
	No			14 (74)	215 (73)	104 (75)	125 (71)	44 (79)	185 (72)
	Sensitivity (95% CI)			26 (9-51)		**25 (18-3)**		**21 (12-34)**	
	Specificity (95% CI)			73 (67-78)		71 (64-78)		72 (66-77)	
	PPV (95% CI)			6 (2-13)		41 (31-52)		14 (8-23)	
	NPV (95% CI)			94 (90-97)		55 (48-61)		81 (75-86)	
C. Albicans*	Yes			8 (42)	30 (10)	13 (9)	25 (14)	9 (16)	29 (11)
	No			11 (58)	263 (89)	125 (90)	149 (85)	47 (84)	227 (88)
	Sensitivity (95% CI)			**42 (20-67)**		9 (5-16)		16 (8-28)	
	Specificity (95% CI)			89 (85-93)		85 (79-90)		88 (83-92)	
	PPV (95% CI)			21 (10-37)		34 (20-51)		24 (11-40)	
	NPV (95% CI)			96 (93-98)		54 (48-60)		83 (78-87)	
Bacterial Vaginosis*	Yes			5 (26)	135 (46)	75 (54)	65 (37)	21 (36)	119 (46)
	No			9 (47)	139 (47)	54 (39)	94 (53)	27 (48)	121 (47)
	Sensitivity (95% CI)			26 (9-51)		**54 (45-62)**		38 (25-51)	
	Specificity (95% CI)			47 (41-53)		54 (46-61)		47 (41-53)	
	PPV (95% CI)			4 (1-8)		54 (45-62)		15 (10-22)	
	NPV (95% CI)			94 (89-97)		64 (55-71)		82 (75-88)	

** 2 women had indeterminate laboratory results for candida albicans; 26 women had indeterminate laboratory results for bacterial vaginosis*

Table 2: Sensitivity and specificity of SD versus laboratory testing for genital ulcer disease (GUD) among men and women

		MEN		WOMEN	
		Yes, n=21	No, n=280	Yes, n=17	No, n=297
Laboratory testing results		**n (%)**	**n (%)**	**n (%)**	**n (%)**
T. pallidum serology	Positive	5 (24)	74 (26)	9 (53)	80 (27)
	Negative	16 (76)	206 (74)	8 (47)	217 (73)
	Sensitivity (95% CI)	**24 (8-47)**		**53 (23-77)**	
	Specificity (95% CI)	74 (68-79)		73 (68-78)	
	PPV (95% CI)	6 (2-14)		10 (5-18)	
	NPV (95% CI)	93 (89-96)		96 (93-99)	
HSV2 serology	Positive	3 (14)	0 (0)	7 (41)	1 (0)
	Negative	18 (86)	280 (100)	10 (59)	296 (100)
	Sensitivity (95% CI)	**14 (3-36)**		**41 (18-67)**	
	Specificity (95% CI)	100 (99-100)		100 (98-100)	
	PPV (95% CI)	100 (29-100)		88 (47-100)	
	NPV (95% CI)	94.0 (91-96)		97 (94-98)	

CONCLUSIONS

- RTI prevalence was high, particularly among women.
- Only a small proportion of participants reported current RTI symptoms, even with questions directly assessing for symptoms. The majority of SD was made through a thorough physical examination.
- Use of SD among adults newly diagnosed with HIV underestimated RTI prevalence, particularly among men. However, SD had relatively high specificity.
- Routine RTI screening through physical exam, even when no symptoms are reported should be implemented in this population.
- Laboratory testing should be explored for more sensitive RTI diagnosis among all adults recently diagnosed with HIV.
- Investment to develop point of care tests for RTIs is needed.

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