Are self-reported STI symptoms an accurate measure of disease? A comparison of STI symptom reporting versus etiological diagnosis among three different high-risk populations – men who have sex with men, female sex workers, and persons living with HIV/AIDS – in El Salvador, 2008

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Abstract

Background: Treatment of sexually transmitted infections (STIs) can help prevent the spread of HIV. However, resource-limited countries have limited laboratory capability and rely on syndromic management to diagnose STIs. El Salvador, which has the highest rates of HIV and STIs in Central America, uses syndromic management. Currently, data to validate syndromic management as a STI control strategy in El Salvador are limited.

Methods: From March–September 2008, men who have sex with men (MSM), female sex workers (FSW) and people living with HIV/AIDS (PLWHA) were recruited for a STI surveillance study. Participants provided information on demographic characteristics, sexual behaviors, STI history, and service utilization. Biological specimens were collected and tested for genital inflammatory infections (gonorrhea, chlamydia, Mycoplasma genitalium, Trichomonas vaginalis) and ulcerative infections (syphilis and HSV-2). Z-scores were calculated to compare the sensitivity, specificity, and positive predictive value (PPV) of self-reported STI symptoms to laboratory-confirmed STIs among different populations.

Results: Prevalence of ulcerative infections was 48.8% among MSM, 82.2% among FSW, and 84.6% among PLWHA. Prevalence of inflammatory infections was higher in women (FSW 75.2%; female PLWHA 52.7%) than men (MSM 11.9%; male PLWHA 9.0%). Most participants (82.0% to 96.7%) reported no ulcerative symptoms. Sensitivity and PPV of inflammatory symptoms were poor among female PLWHA (52% and 52%, respectively), male PLWHA (28% and 15%, respectively) and MSM (17% and 14%, respectively). Sensitivity of inflammatory symptoms among FSW was 75%. Specificity (88% - 96%) and PPV (63% - 92%) of ulcerative symptoms were high among all populations. Significant differences were seen when comparing sensitivity, specificity, and PPV between FSW and female PLWHA (p<0.01), FSW and MSM (p<0.01), and male and female PLWHA (p<0.01).

Conclusions: The high proportion of asymptomatic individuals with laboratory-confirmed STIs suggests missed STI treatment opportunities. Reliance on self-reporting is not an effective STI control strategy for these high-risk study populations. Prevention programs should focus on STI symptoms recognition and consider routine screening for high-risk populations.

Background

El Salvador

- El Salvador is one of 7 countries in Central America, bordered by the Pacific Ocean, Guatemala, and Honduras.
- It is the smallest and most densely populated country in the Americas with a population size of approximately 7 million.
- Capital City: San Salvador (1.4 million)
- Languages: Spanish, Nahua

STI burden

- 340 million new cases of STIs globally among adults aged 15-49 years
- > 75% of the STI burden in the developing world
- In addition to causing significant morbidity, mortality and economic costs, STIs also increase the risk of HIV transmission

STI syndromic management

- Developed by WHO as a response to limited laboratory capacity in developing countries
- Syndromic management approach groups easily-recognized signs and consistent groups of symptoms into syndromes, which are then assigned treatment regimens that will deal with the majority of, or the most serious, organisms responsible for producing the respective syndrome
- Currently there is no universal consensus on the efficacy of these guidelines

STIs in El Salvador

- According to a study among high-risk populations conducted in five Central American countries, men who have sex with men (MSM) in El Salvador had the highest rates of HIV, syphilis, gonorrhea, chlamydia, and Herpes simplex virus -2 (HSV-2) infections compared with other countries (Soto, 2007)
- Female sex workers (FSWs) in El Salvador were also amongst the groups with the highest rates of HIV, HSV-2, bacterial vaginosis (BV) and syphilis compared to other countries.
- Compared to other countries, MSM in El Salvador reported highest frequency of bisexual behavior and FSWs reported lowest frequency of condom use with clients

El Salvador and STI syndromic management

- STI syndromic management is practiced in El Salvador; however, there are limited data regarding the rates of STIs in El Salvador
- Currently, there are no data evaluating efficacy of STI syndromic management in El Salvador especially in high-risk populations such as MSM, FSWs and persons living with HIV/AIDS (PLWHA)
- Given the high prevalence of STIs in FSWs and MSM, there is urgent need to accurately identify and promptly treat STIs in El Salvador
- Gaining knowledge about efficacy of STI syndromic management is critical for informing future STI prevention programs and can be a key component for HIV prevention programs

Study objective of El Salvador BSS

- To determine if self-reported STI symptoms were an accurate measure for STI diagnosis by comparing them to laboratory diagnoses for three high-risk populations: FSWs, MSM, and PLWHA
- To determine if there were differences in gender in accuracy of self-reported STI symptoms in comparison to laboratory diagnoses
- To provide information to assist partners with STI and HIV prevention program planning

Methods

- From March to September 2008, the El Salvador Ministry of Health conducted integrated behavioral and biologic surveys among MSM, FSW, and PLWHA
- Sexually active individuals ≥ 18 years were recruited from 4 cities: San Salvador, Santa Ana, San Miguel, and Sonsonate
- PLWHA were identified and sampled consecutively through clinical programs providing AIDS prophylaxis or HIV treatment, or through HIV well-being programs or support groups from 8 hospitals in San Salvador that treat 80% of the country's HIV-infected individuals
- MSM and FSWs were recruited using respondent driven sampling (RDS) in San Salvador, San Miguel, and Sonsonate
- Eligible participants consented to a behavioral survey, clinical examination, and sample collection for STD testing
- Behavioral survey was administered through audio computer-assisted self-interview (ACASI)
- Survey variables included: socio-demographic characteristics, attitudes regarding sexual behavior, history of sexual behavior, use of condoms with different partner types, knowledge of STIs, STI symptoms and health seeking behaviors, knowledge and attitudes on HIV and AIDS, use of alcohol and drugs

Methods for STI detection

Specimen	Test	Laboratory
Serum	RPR and TPPA for syphilis	Central Laboratory El Salvador
Serum	HSV-2 serology	Central Laboratory El Salvador
Serum	Rapid HIV tests	On site with confirmation by Central Laboratory El Salvador
Urine (males)	*C. trachomatis, N. gonorrhea, M. genitalium, T. vaginalis* PCR	Regional Laboratory Panama
Vaginal swab (females)	*C. trachomatis, N. gonorrhea, M. genitalium, T. vaginalis* PCR	Regional Laboratory Panama
Vaginal swab (females)	Bacterial vaginosis gram stain	Regional Laboratory Panama

- Participants with STI symptoms on clinical examination were treated syndromically following national STI treatment guidelines
- Blood, urine (males only), anal swab (males only), and vaginal swab (females only) specimens were collected and tested for STIs (see Table)
- STI testing was conducted at the central laboratory in El Salvador and the regional laboratory in Panama. Quality control testing was conducted at CDC Atlanta
- Participants were provided an anonymous voucher with their study identification number and were asked to return to the survey site after 2 weeks to receive final STI results and free treatment if needed

Methods for statistical analysis

- For female participants: sensitivity, specificity, and positive predictive values (PPVs) of self-reported vaginal discharge symptoms (discharge, pain/odor, lower back pain, itching) and laboratory-confirmed diagnoses of 1) Neisseria gonorrhoeae (GC) or Chlamydia trachomatis (CT); 2) BV, Trichomonas vaginalis (TV), or Mycoplasma genitalium (MG); and 3) GC, CT, BV, TV, or MG were calculated
- For male participants: sensitivity, specificity, and PPVs of self-reported penile discharge symptoms (discharge, pain/odor, lower back pain, itching) and laboratory-confirmed diagnoses of 1) GC or CT; 2) TV or MG; and 3) GC, CT, TV, or MG were calculated
- All participants: sensitivity, specificity, and PPV were calculated for self-reported genital ulcer symptoms and laboratory-confirmed diagnoses of syphilis or HSV-2 infections
- Statistical software used: SAS version 9.2

Results

- 807 MSM, 810 FSW, 411 male PLWHA, and 397 female PLWHA were recruited for the study.
- After excluding individuals without laboratory results and those who did not answer STI symptom questions, the final analyses included
  - For genital inflammatory infection analysis (GC, CT, BV [women only], TV and MG results): 503 MSM, 518 FSW, 356 male PLWHA and 245 female PLWHA
  - For ulcerative infection analysis (HSV-2 and syphilis results): 703 MSM, 768 FSW, 366 male PLWHA and 366 female PLWHA

Table 1: Age, self-reported prevalence of signs or symptoms related to STI, and etiological prevalence of STIs among men who have sex with men, female sex workers, and persons living with HIV/AIDS in San Miguel, San Salvador, and Sonsonate, El Salvador, 2008

			PLWHA		
	MSM	FSW	Male	Female	Total
Age	n = 807	n = 810	n = 411	n = 397	n = 808
18 - 25	531 (65.8)	279 (34.4)	44 (10.7)	61 (15.4)	105 (13.0)
26 - 35	197 (24.4)	335 (41.4)	158 (38.4)	165 (42.6)	323 (40.0)
36 - 45	58 (7.2)	152 (18.8)	132 (32.1)	121 (30.5)	253 (31.3)
> 45	21 (2.6)	44 (5.4)	77 (18.7)	50 (12.6)	127 (15.7)
	n = 503	n = 518	n = 356	n = 245	n = 601
Self-reported genital inflammatory symptoms in the last 12 months					
Vaginal/penile discharge	15 (3.0)	327 (63.1)	12 (3.4)	103 (42.0)	115 (19.1)
Pain with urination	33 (6.6)	152 (29.3)	33 (9.3)	53 (21.6)	86 (14.3)
Itching around genital area	35 (7.0)	157 (30.3)	35 (9.8)	43 (17.6)	78 (13.8)
Pain in lower abdomen - women only		87 (16.8)		43 (17.6)	43 (17.6)
Any of the above vaginal or penile inflammatory symptoms	70 (13.9)	389 (75.1)	61 (17.1)	129 (52.7)	190 (31.6)
No genital inflammatory symptoms	433 (86.1)	129 (24.9)	295 (82.9)	116 (47.4)	411 (68.4)
Laboratory confirmed inflammatory infection†	60 (11.9)	411 (79.3)	32 (9.0)	129 (52.7)	161 (26.8)
	n = 703	n = 768	n = 366	n = 366	n = 732
Self-reported genital ulcer symptoms in the last 12 months					
Genital or anal ulcer	37 (5.3)	17 (2.2)	48 (13.1)	51 (13.9)	99 (13.5)
Genital warts	23 (3.3)	11 (1.4)	27 (7.4)	24 (6.6)	51 (7.0)
Any ulcerative symptoms	59 (8.4)	25 (3.3)	63 (17.2)	66 (18.0)	129 (17.6)
No ulcerative symptoms	644 (91.6)	743 (96.7)	303 (82.8)	300 (82.0)	603 (82.4)
Laboratory confirmed ulcerative infection*	343 (48.8)	631 (82.2)	296 (80.9)	323 (88.3)	619 (84.6)

†*Neisseria gonorrhea, Chlamydia trachomatis, Mycoplasma genitalium, Trichomonas vaginalis,* and Bacterial vaginosis (for women only)

*Herpes simplex virus-2 (HSV-2) and syphilis

- Laboratory results:
  - Among PLWHA and FSW participants the majority were between 26 – 45 years of age (40% and 41.4%, respectively). Among MSM the majority were between 18 – 25 years of age (65.8%)
  - There was a higher rate of laboratory confirmed genital inflammatory infection within women (FSW 79.3% and female PLWHA 52.7%) compared to men (MSM 11.9% and male PLWHA 9.0%)
  - Prevalence of genital ulcer infections was high among all populations
- Self-reported symptoms
  - Few MSM or male PLWHA reported any STI symptoms
  - FSWs and female PLWHA reported a high rate of genital inflammatory symptoms (75.1% and 52.7%, respectively)

Table 2: Performance of various self-reported symptoms and laboratory test results among FSWs and female PLWHA in Sonsonate and San Salvador, El Salvador, 2008

	Female Sex Workers					Female PLWHA				
	# identified infected by lab tests	# reporting STI symptoms with positive lab	Sensitivity	Specificity	PPV	# identified infected by lab tests	# reporting STI symptoms with positive lab	Sensitivity	Specificity	PPV
Reported any genital inflammatory symptoms for:			n = 518					n = 245		
Gonorrhea and/or chlamydia	70	52	0.74	0.25	0.13	4	1	0.25	0.47	0.08
Bacterial vaginosis and/ or Trichomonas and/or Mycoplasma genitalium	404	300	0.74	0.22	0.77	128	67	0.52	0.47	0.52
Any genital inflammatory infection*	411	307	0.75	0.23	0.79	129	67	0.52	0.47	0.52
Reported any genital ulcerative symptoms for:			n = 768					n = 366		
Syphilis and/or herpes	631	20	0.03	0.96	0.80	323	61	0.19	0.88	0.92

**Neisseria gonorrhea, Chlamydia trachomatis, Mycoplasma genitalium, Trichomonas vaginalis,* and Bacterial vaginosis

- Among FSWs:
  - Sensitivity for any self-reported vaginal inflammatory symptom compared with laboratory diagnoses was high (at least 74%)
  - Specificity and PPV of genital ulcerative symptoms compared with laboratory diagnoses were high (96% and 80%, respectively)
- Among female PLWHA
  - Sensitivity, specificity and PPV for any self-reported vaginal inflammatory symptoms compared with laboratory diagnosed STI were poor
  - Specificity of genital ulcer symptoms for laboratory diagnosed syphilis or HSV-2 was high (88%)
- Comparing FSWs and female PLWHA
  - Inflammatory infections: FSWs had a higher sensitivity and PPV
  - Ulcerative infections: female PLWHA had a higher sensitivity than FSWs

Table 3: Performance of various self-reported symptoms and laboratory test results among MSM and male PLWHA in San Miguel and San Salvador, El Salvador, 2008

	Men who have sex with men					Male PLWHA				
	# identified infected by lab tests	# reporting STI symptoms with positive lab	Sensitivity	Specificity	PPV	# identified infected by lab tests	# reporting STI symptoms with positive lab	Sensitivity	Specificity	PPV
Reported any genital inflammatory symptoms for:			n = 503					n = 356		
Gonorrhea and/or chlamydia	46	8	0.17	0.86	0.11	0	0	n/a	n/a	n/a
Bacterial vaginosis and/ or *Trichomonas* and/or *Mycoplasma genitalium*	17	2	0.12	0.86	0.03	32	9	0.28	0.84	0.15
Any genital inflammatory infection*	60	10	0.17	0.86	0.14	32	9	0.28	0.84	0.15
Reported any genital ulcerative symptoms for:			n = 703					n = 366		
Syphilis and/or herpes	343	37	0.11	0.94	0.63	296	56	0.19	0.90	0.89

**Neisseria gonorrhea, Chlamydia trachomatis, Mycoplasma genitalium,* and *Trichomonas vaginalis*

- Among MSM:
  - Sensitivity was low at < 18% for any self-reported penile inflammatory symptoms compared with laboratory diagnosed STI
  - High specificity (94%) of genital ulcerative symptoms compared with laboratory confirmed syphilis or HSV-2 infections
- Among male PLWHA, specificity for TV or MG and syphilis or HSV-2 was high (84% and 90%, respectively)
- When comparing ulcerative symptoms, male PLWHA had higher sensitivity and PPV than MSM
- Comparing genders:
  - Female PLWHA had higher sensitivity and PPV than male PLWHA for inflammatory symptoms
  - FSWs had higher PPV and lower sensitivity then MSMs for ulcerative symptoms

Discussion

- Study provided key data regarding STIs among high-risk sexual groups in El Salvador
- High rates of STIs were found in these populations, which is especially concerning for HIV prevention strategies
- High proportion of female PLWHA and male participants reported no STI symptoms
- Syndromic STI management based solely on self-reported symptoms would miss many infections which could lead to serious sequelae, especially in women

Limitations

- Results not generalizable to all FSWs, MSM and PLWHA in El Salvador as participants were only recruited from select areas
- STI and symptoms data were missing for some participants
- Study not specifically designed to address the question of STI syndromic management effectiveness
- Participants were recruited with different methods, which limited direct comparisons

Conclusions

- STI education and treatment efforts should be strengthened and concentrate on encouraging STI symptom recognition and routine physical exams for high-risk populations
- When feasible, clinical correlation should accompany symptom reporting
- STI evaluation should be part of routine screening for high-risk individuals
- Expanding laboratory capacity should be considered

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