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Original Article

Care Seeking Patterns of STIs-Associated Symptoms in Iran: Findings of a Population-Based Survey

Maryam Nasirian¹, Mohammad Karamouzian^{1,2}, Kianoush Kamali³, Amir Reza Nabipour⁴, Ahmad Maghsoodi⁵, Roja Nikaeen⁵, Ali Reza Razzaghi⁶, Ali Mirzazadeh^{7,1}, Mohammad Reza Baneshi⁵, Ali Akbar Haghdoost^{5*}

Abstract

Background: Understanding the prevalence of symptoms associated with sexually transmitted infections (STIs) and how care is sought for those symptoms are important components of STIs control and prevention. People's preference between public and private service providers is another important part of developing a well-functioning STIs surveillance system.

Methods: This cross-sectional survey was carried out in spring 2011, using a nonrandom quota sample of 1190 participants (52% female) in 4 densely-populated cities of Tehran, Kerman, Shiraz, and Babol. Two predictive logistic regression models were constructed to assess the association between the socio-demographic determinants (independent variables) and the dependent variables of history of STIs-associated symptom and seeking care. **Results:** Around 57% (677 out of 1190; men: 29.70% and women: 81.80%) had experienced at least one STIs-associated symptom during the previous year. History of experiencing STIs-associated symptoms among men, was negatively significantly associated with older age (adjusted odds ratio [AOR]=0.34, CI 95%: 0.17-0.67). Women who were married, in older ages, and had higher educations were more likely to report a recent (past year) STIs symptom, however all were statistically insignificant in both bivariate and multivariable models. Among those who have had STIs-associated symptoms in the last year, 31.15% did nothing to improve their symptoms, 8.03% attempted self-treatment by over-the-counter (OTC) medications or traditional remedies, and 60.93% sought care in health facilities. In both bivariate and multivariable analyses, care seeking among men was insignificantly associated with any of the collected demographic variables. Care seeking among women was positively significantly associated with being married (AOR=2.48, 95% CI: 1.60-3.84).

Conclusion: The reported prevalence of STIs-associated symptoms among our participants is concerning. A considerable number of participants had delayed seeking care and treatment or self-medicated. People should be informed about their sexual health and the consequences of delaying or avoiding seeking care for STIs. Participants preferred seeking care at private sectors which calls for engaging both public and private health sectors for reporting and following up STIs cases.

Key words: Sexually Transmitted Infections (STIs), Care-Seeking, Symptoms, Epidemiology, Iran Copyright: © 2016 by Kerman University of Medical Sciences

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*Correspondence to: Ali Akbar Haghdoost Email: ahaghdoost@kmu.ac.ir

Key Messages

Implications for policy makers

- Unfolding these patterns of care seeking for sexually transmitted infections-associated (STIs-associated) symptoms among the general population can help policy-makers improve the quality of STIs care and treatment and provide a better provision over STIs services.
- Policy-makers should prioritize establishment of a sentinel-based STIs case reporting system.
- STIs prevalence assessment surveys among the general population would be a valuable asset in monitoring the trend of STIs across the country.
- Policy-makers should monitor the pharmacies effectively and force them to stop selling non-prescribed antibiotics for STIs treatment.
- The considerable prevalence of STIs-associated symptoms could be partly addressed by highlighting sexual health education in the educational system.

Implications for public

We conducted a population-based survey on the general population and understood that around 57% of our participants had a history of previous sexually transmitted infections-associated (STIs-associated) symptom in the past year. People should realize that STIs can increase the risk of sexual transmission of HIV infection and if untreated, can lead to development of infertility, ectopic pregnancy, severe psychological problems, cervical cancer, premature delivery, stillbirth, low birth weight and neonatal infections. Although most STIs can be cured by timely access to treatment regimens, over one-third of participants with STIs-associated symptoms sought no treatment. People should not delay seeking treatment for STIs and should avoid practicing self-medication for them.

Introduction

Sexually transmitted infections (STIs) are significant and increasing public health concerns worldwide.1 The World Health Organization (WHO) has estimated that annually an approximate 340 million new cases of curable STIs such as syphilis, gonorrhoea, and chlamydia, occur worldwide.¹ Despite being serious infections on their own, STIs can increase the risk of sexual transmission of HIV. The presence of untreated STIs can raise the risk of both acquisition and transmission of HIV up to four times.^{2,3} Moreover, the secondary health outcomes of untreated STIs could lead to infertility, ectopic pregnancy, long-term disability, severe psychological problems, cervical cancer, premature delivery, stillbirth, low birth weight and neonatal infections.⁴ Although most STIs can be cured by timely access to treatment, they are frequently asymptomatic or go undetected. Women are disproportionately affected; for example, gonorrhoea and syphilis are asymptomatic in less than 10% of men against 50%-80% of women.5

Given the negative health consequences associated with STIs, there is a strong public health impetus to test and treat the infected individuals. While early detection and early response are key components of the surveillance systems in turning the tide of STIs, detection is impossible unless those who are infected seek care. Therefore, understanding how these symptoms are diagnosed and care is sought is vital for providing efficient care and treatment. Moreover, people's preference between public and private service providers are of outmost importance for health policy-makers in controlling STIs. Studies in Tanzania and India suggest that despite varying care seeking patterns across different sociodemographics, there is a general preference for the private sector due to its higher accessibility and quality of care.6,7 A similar situation has been reported in Lebanon, where of all outpatient visits for reproductive health matters, 78% take place in the private sector compared to 9% in the public facilities.8,9

Unfortunately, care seeking patterns of STIs-associated symptoms in the general population as well as their preferred choice of private or public settings for STIs treatment, is far less understood in Iran. Data on the prevalence of STIs in Iran is very sparse with very limited generalizability to the general population. For example, a study in Northeast of Iran has reported Chlamydia trachomatis in 10.6% of men. Another study in the Western parts of the country has reported Trichomonas vaginalis to be present in 2.1% of women who referred to health clinics.^{10,11} Hence, the current study was designed to explore the prevalence of STIs-associated symptoms in the general population and the dynamics of how, when, and where an individual decides to seek care for STIs-associated symptoms in Iran. Unfolding the patterns of care seeking for STIs-associated symptoms among the general population can help policy-makers improve the quality of STIs care and treatment and provide a better provision over existing STIs services.

Material and Methods

Context

Universal STIs case reporting was established in 1998 in Iran. It was then revised in 2007 when the list of reportable STIs was modified to urethral discharge, genital ulcer, *Chlamydia trachomatis, Neisseria gonorrhoeae*, and syphilis.¹² Iran benefits from a passive STIs reporting system consisting of routine STIs case reporting by healthcare providers at the primary healthcare level and monitoring STIs prevalence among female sex workers and pregnant population. Care and treatment for STIs is provided at health centers, hospitals, private clinics (ie, general practitioners, urologists, gynaecologists, dermatologists, midwives, and infectious disease specialists), as well as drop-in centers for vulnerable populations (eg, females sex workers, people who inject drugs and their partners).¹² In rural areas, however, midwives are the primary STIs care provider due to infrastructural deficits and limitations.¹²

Study Design and Research Instrument

This cross-sectional survey on the general population, was carried out between March and May 2011. To collect data, an interviewer-administered checklist (21 questions) was designed including questions about socio-demographics (4 questions), history of STIs signs and symptoms (7 questions), and care seeking practices (10 questions). To design the checklist, similar international and regional studies were reviewed and key points in designing the checklist were extracted. These points were then assessed and modified thoroughly in a number of sessions with HIV/STIs experts, medical doctors, and behavior consultants. To evaluate the validity of the checklist, it was pilot tested in each city and revised accordingly.

Sample Size Calculation

Four cities of Iran including Tehran, Kerman, Shiraz, Babol (located in the Center, Southeast, Southwest, and North of the country, respectively) were selected to provide a geographically dispersed sample. In a nonrandom sampling scheme, 1190 quota samples were interviewed. Since there was no previous data about the prevalence of STIs in Iran, the sample size was calculated based on the single proportion formula, assuming a prevalence of 50% with 5% marginal error, a 95% Confidence Interval (CI), and a nonresponse rate of 20%. The calculated sample size was adjusted based on expert opinions of Ministry of Health and Medical Education (MoHME). Consequently, 393 samples in Tehran, 383 in Shiraz, 198 in Kerman, and 216 in Babol were recruited.

Sampling Strategy

Asking sensitive questions about stigmatized topics such as STIs in the traditional and religious context of Iran can be very challenging. However, our prior research in Iran indicates a preference for street-based surveys over household-level, and telephone-based surveys, when it comes to asking sensitive questions.¹³ Therefore, we recruited equal number of men and women, aged 18 to 55 years, on street corners, outside markets, and in busy public places during different times of the day (morning, noon, and evening). Participants were excluded if they were pregnant, nonresidents of the city of interest, sexually inactive, or had been interviewed on earlier days. Pregnant women were excluded due to the possible influence of pregnancy on their self-reported STIs-associated symptoms.

Potential participants were approached by experienced university-trained interviewers and briefed on the objectives of the survey. Participants could choose to be interviewed by a male or female interviewer. The interviewers showed their university employee card and an introduction letter from the faculty of medicine along with documents to ensure full anonymity of the interview and information provided. Interviewers were trained to carry out the interview in a relatively quiet and private space. Interviews were conducted after obtaining verbal informed consent and lasted between 25-30 minutes. In men, data was collected on urethral discharge, genital pain, inflammation, and genital ulcer and in women on abnormal vaginal discharge, genital ulcer, genital pain, itching, and lower abdominal pain. In order to avoid misunderstanding of symptoms and signs, interviewers were trained to provide the participants with sufficient information about STIs symptoms. While no incentive was provided, all participants were orally briefed about STIs prevention and treatment. They were also provided with an illustrated educational pamphlet after the interview.

Data Analysis

Data were entered via double data entry into Stata version 11 (Stata Corp.) software, cleaned and checked for errors before coding. Since participants were recruited from different cities, the cities were considered as sampling units and their clustering effects were adjusted using Stata survey package. Chi-square test was used to compare the proportions between subgroups of socio-demographic variables and one-way analysis of variance (ANOVA) was used to compare the mean age of groups. In all tests, P values less than 5% were considered statistically significant. Two predictive logistic regression models were constructed to investigate the socio-demographic determinants (independent variables) associated with dependent variables of history of STIsassociated symptom (yes/no) and seeking care (yes/no). Odds ratios (ORs) and 95% CIs for variables of interest were calculated.

Results

Participants' Demographics

A total number of 1500 participants were approached and 1190 (52% female) consented and participated in the survey. Overall, the response rate was 81% (equal among men and women). Mean age of all participants was 30.40 (CI 95%: 29.78-31.41) ranging from 18-55 years. Around 43% had some college or university education and only 1.80% were illiterate. All participants were urban residents and more than half were married (55.29%) at the time of the survey. Women were significantly older (31.21 vs. 29.56, P=.008) and less married (44.44% vs. 65.42%, P<.0001) than men. Educational level was not significantly different across genders (P=.097) while men appeared to have a slightly higher level of education compared to women (Table 1).

Younger men (18-25 years old) reported the highest prevalence of genital pain (26.64%), urethral discharge (9.27%), and inflammation (7.34%) among men. On the other hand, older women (35-55 years old) reported the highest prevalence of genital pain (32.14%), inflammation (29.76%), itching (61.10%), lower abdominal pain (55.36%), and ulcer (17.86%) among women (Table 2).

Factors Associated With the Presence of Sexually Transmitted Infections-Associated Symptoms

Participants were asked about their health seeking behaviours regarding STIs-associated symptoms. Based on our self-reported data, 56.89% (29.70% men and 81.80% women) had ever experienced STIs-associated symptoms during the past year. In the bivariate analysis, history of ever experiencing STIs-associated symptoms during the past year among men was negatively significantly associated with being married (OR=0.63, CI 95%: 0.43-0.90) and older age (OR=0.34, CI 95%: 0.20-0.58) and positively insignificantly associated with higher education (OR=1.17, CI 95%: 0.83-1.88). In the multivariable analysis however, only older age remained statistically significant and the odds of having ever experienced STIs-associated symptoms in the previous year

Table 1. Demographic Characteristics of the Participants of an STIs Survey in Iran

Demographic Characteristics		Male n = 569	Female n = 621	P Value
Age groups				
18-25		259 (45.52)	237 (38.16)	
26-35		181 (31.81)	216 (34.78)	.000ª
35-55		129 (22.67)	168 (27.05)	
Age: Mean (95% CI)		29.56 (28.67-30.44)	31.21 (30.35-32.06)	.008 ^b
Education				
Illiterate		7 (1.23)	15 (2.42)	
Under Diploma		96 (16.87)	131 (21.10)	0073
Diploma		197 (34.62)	188 (30.27)	.097°
Graduated		269 (47.28)	287 (46.22)	
Marital status				
Single		184 (32.31)	343 (55.20)	
Married		372 (65.42)	276 (44.44)	< 00013
Divorced		9 (1.62)	2 (0.35)	<.0001-
Widowed		4 (0.65)	0 (0.00)	

Abbreviation: STIs, sexually transmitted infections.

Data are n (%) unless specified; ^aP values were obtained from chi-square test; ^bP values were obtained from one-way ANOVA test.

Table 2. History of Specific and Nonspecific Lifetime STIs-Associated Symptoms

	Lifetime STIs-Associated Symptoms, n (%) ^a							
	No.	Vaginal Discharge	Urethral Discharge	Ulcer	Lower Abdominal Pain	Itching	Inflammation	Genital Burning and Pain
Men (age groups)								
18-25	259	-	24 (9.27)	11 (4.25)	-	-	19 (7.34)	69 (26.64)
26-34	181	-	15 (8.29)	14 (7.73)	-	-	12 (6.63)	42 (23.20)
35-55	129	-	8 (6.20)	3 (2.33)	-	-	3 (2.33)	16 (12.40)
Women (age groups)								
18-25	237	79 (33.33)	-	21 (8.86)	127 (53.59)	122 (51.48)	37 (15.61)	72 (30.38)
26-34	216	98 (45.37)	-	33 (15.28)	112 (51.58)	127 (58.80)	49 (22.69)	56 (25.93)
35-55	168	69 (41.07)	-	30 (17.86)	93 (55.36)	103 (61.10)	50 (29.76)	54 (32.14)

Abbreviation: STIs, sexually transmitted infections.

^aAs some participants reported more than one symptom, sum of all percentages does not add up to 100%. Data are % unless specified.

Table 3. Effect of Demographic Characteristic on the Occurrence of STIs-Associated Symptoms and Care Seeking

			Ever had STIs-associated symptom		Sought Care		
	Demographics	No	OR (95% CI)		OR (95% CI)		
		NO.	Crude	Adjusted*	Crude	Adjusted	
Women	Marital statues						
	Single	343	Ref.	Ref.	Ref.	Ref.	
	Married	276	1.33 (0.87-2.04)	1.24 (0.72-2.15)	2.55 (1.79- 3.63)	2.48 (1.60- 3.84)	
	Age groups (year)				· ·		
	18-25	237	Ref.	Ref.	Ref.	Ref.	
	26-35	216	1.23 (0.76-1.99)	1.08 (0.64-1.81)	1.40 (0.96-2.02)	0.99 (0.66-1.50)	
	36-60	168	1.36 (0.81-2.28)	1.22 (0.66-2.25)	1.77 (1.19-2.65)	1.15 (0.72-1.84)	
	Education						
	Under Diploma	142	Ref.	Ref.	Ref.	Ref.	
	Over diploma	475	1.17 (0.73-1.89)	1.41 (0.83-2.38)	0.87 (0.62-1.27)	1.21 (0.79-1.82)	
	Marital statues						
Men	Single	184	Ref.	Ref.	Ref.	Ref.	
	Married	372	0 .63 (0.43-0.90)	1.05 (0.63-1.77)	0.99 (0.53- 1.83)	0.77 (0.34-1.78)	
	Age groups (year)						
	18-25	259	Ref.	Ref.	Ref.	Ref.	
	26-35	181	0.75 (0.50-1.12)	0.72 (0.44-1.18)	1.38 (0.69-2.77)	1.59 (0.70-3.60)	
	36-55	129	0.34 (0.20-0.58)	0.34 (0.17-0.67)	1.24 (0.57-2.72)	1.57 (0.55-4.48)	
	Education		1				
	Under Diploma	102	Ref.	Ref.	Ref.	Ref.	
	Over diploma	466	1.17 (0.83-1.88)	0.96 (0.58-1.60)	0.72 (0.38-1.36)	0.68 (0.35-1.36)	

Abbreviations: OR, odds ratio; STIs, sexually transmitted infections.

among 36-55 year-old men was 0.34 times that of 18-25 year-old men (adjusted odds ratio [AOR] = 0.34, CI 95%: 0.17-0.67). Married (OR = 1.33, CI 95%: 0.87-2.04; AOR = 1.24, CI 95%: 0.72-2.15), older (OR = 1.36, CI 95%: 0.81-2.28; AOR = 1.22, CI 95%: 0.66-2.25), and more educated (OR = 1.17, CI 95%: 0.73-1.89; A OR = 1.41, CI 95%: 0.83-2.38) women were more likely to report a recent (past year) STIs symptom, however all were statistically insignificant in both bivariate and multivariable models (Table 3).

Care Seeking Patterns for Sexually Transmitted Infections

Among those with STIs-associated symptoms in the last year, 31.15% did nothing to improve their symptoms (62.50% of men and 21.57% of women, P<.001), 7.92% attempted self-treatment by over-the-counter (OTC) medications or traditional remedies (4.41% of men and 8.99% of women,

P = .045), and 60.93% sought care (33.09% of men and 69.44% of women, P < .001) in health facilities. In both bivariate and multivariable analyses, care seeking among men was insignificantly associated with any of the collected demographic variables. However, men aged 25-36 were more likely to seek for STIs care (OR=1.38, CI 95%: 0.69-2.77; AOR=1.59, CI 95%: 0.70-3.60) and more educated individuals sought less care for STIs (OR=0.72, CI 95%: 0.38-1.36; AOR = 0.68, CI 95%: 0.35-1.36). Conversely, in the bivariate analysis, care seeking among women was positively significantly associated with being married (OR=2.55, CI 95%: 1.79- 3.63) and older age (OR = 1.77, CI 95%: 1.19-2.65). In the multivariable analysis, the odd of care seeking among married women was decreased but remained statistically significantly elevated compared to single women (AOR = 2.48, 95% CI: 1.60-3.84) (Table 3).

Delay between the appearance of symptoms and seeking medical care-defined as postponing care seeking for more than a week-was not significantly associated with age, gender, marital status, and educational level. On average, about half of the participants (46.98%) across different age groups sought treatment less than a week after their symptoms were found; however, the length of delay was wider for men (Figure 1). Overall, two-thirds of participants who had symptoms reported seeking treatment through the private sector. Majority of the participants referred to specialists to seek care or treatment. While most women reported referring to gynecologists and midwives (81.23% and 8.74%, respectively), men mainly referred to urologists and general practitioners (42.22% and 26.67%, respectively). Infectious disease specialists were visited only by 2 men and no women. Traditional healers were referred to by 3 women and no men. Only about 44% of women and men visited by specialists, general physicians or midwifes, were referred to laboratory to diagnose the etiology of symptoms (Table 4).

Discussion

We conducted a population-based survey among the public and realized that more than half of our participants had ever had STIs symptoms in the year preceding the survey. The prevalence of STIs in our sample was different with that of Pakistan (46%) and Kenya (75%) which could be partly due to differences in reporting, the nonexclusive nature of



Figure 1. Care Seeking Delay for Sexually Transmitted Infections (STIs) Symptoms Among Participants of a Survey in Iran.

 Table 4.
 Venues
 Where
 Participants
 Sought
 Care
 for
 Their
 STIs-Associated
 Symptoms

Ever Had STIs-Associated Symptoms in the Past Year ^a					
Location	Women (n = 309)	Men (n = 45)			
Gynecologist	250 (81.23)	0 (0.00)			
Urologist	1 (0.32)	19 (42.22)			
Infectious disease specialist	0 (0.00)	2 (4.44)			
Internist	4 (1.29)	3 (6.67)			
General practitioner	13 (4.21)	12 (26.67)			
Midwife	27 (8.74)	0 (0.00)			
Health center	11 (3.56)	1 (2.22)			
Traditional healers	3 (0.97)	0 (0.00)			

Abbreviation: STIs, sexually transmitted infections.

^aData are n (%); As some participants reported more than one choice, sum of all percentages does not add up to 100%.

certain reported symptoms, and the self-reported nature of our survey.¹² While increasing age in our study appeared to a protective factor in men, it was not significantly associated with the presence of STIs-associated symptoms in women. This could be attributed to higher sexual risky behaviours of young men which is observed across different contexts.¹⁴ This could also be related to decreased stigma towards getting tested or treated for STIs among older men. Several studies suggest that youth face higher levels of internalized and external stigma regarding seeking STIs testing or care.14,15 History of STIs-associated symptoms was also associated with gender, and women reported a significantly higher frequency of STIs-associated symptoms compared to men. Several studies have associated higher rates of STIs in women compared to men with differences in biological, sociocultural, and physiological factors.5,16

The most frequent STIs-associated symptoms were reported to be itching in women and genital pain in men; both of which are nonspecific symptoms of STIs. These findings could be due to over-reporting of these symptoms due to misdiagnosis. On the other hand, while inflammation, itching, and pain in the genital organs are not necessarily indicative of STIs diagnosis, they are important as presence of symptoms leads to seeking treatment.¹⁷ For example, a study in India reported that 72% of symptomatic women who showed up in an STIs clinic, had a confirmed clinical diagnosis.7 In our study, less than half of STIs cases were referred to laboratory settings which was reportedly accompanied by reluctance from the patients. Nonetheless, providing interviewees with more precise explanations regarding the symptoms as well as collecting data on the exclusive symptoms of STIs should be taken into account in later studies.

We realized that over one-third of participants with a STIsassociated symptom sought no treatment. Not seeking treatment was significantly lower among women. As several studies have reported, women in general, tend to seek care more often than men.¹⁸ This is consistent with the results of a study in Kenya that reported around 20% of women and 35% of men had sought no treatment.¹⁹ While data on the reasons behind not seeking treatment was not collected in our study, several studies have reported economic pressure, stigma, accessibility of clinics, confidentiality, quality of services, and attitude of staff as some of the underlying reasons for avoiding seeking care.²⁰⁻²³

Our findings also revealed that around 10% of the participants with STIs-associated symptoms had practiced self-medications with OTC drugs or traditional medicines. Similar to other studies' findings, practicing self-medication was higher among women.²⁴ Self-medication for STIs is a common practice worldwide; for example, studies in England or the Unites States have reported that up to 60% of their STIs patients had practiced self-treatment before seeking professional care.^{24,25} In Iran, patients can purchase most of the routinely prescribed antibiotics as an OTC drug without any prescriptions from a healthcare provider. This has contributed to an increase in the incidence of antibiotic resistance in *Neisseria gonorrhoea*.^{12,26} Therefore, policy-makers should come up with strategies to limit such easy access to nonprescribed antibiotics in Iran.

Most participants in our study reported seeking STIs care

through the private sector. This finding highlights the important role of the private sector as the largest STIs service provider in the country. Overall, the general population in Iran prefers seeking care at private sectors over public ones.²⁷ Although our data did not capture the underlying reason of the tendency among the general population to seek STIs care at private setting, similar studies in developing countries have reported convenience, cleanness, sympathy of staff, not using expired drugs, providing adequate drug doses, accessibility, confidentiality, and shorter waiting hours, and higher quality of care as major drives for people to refer to the private sector^{21,22,27}; conditions that are very similar to what is observed in Iran. Therefore, to improve the STIs surveillance system and obtain more accurate data, we need to promote the private sector to take on a proactive role in reporting and following up the STIs cases. However, supervising several private sectors across the country would require numerous financial and human resources (HRs).

The findings of this study are limited primarily due to the street-based nonrandom sampling method taken and the self-reported nature of data. However, our prior experience in Iran suggests that asking sensitive questions on the street leads to more accurate responses compared to household-level or telephone surveys. This could be mainly related to the profound stigma toward STIs and people's confidentiality concerns in household-level and telephone-based surveys.¹³ Our sample was limited to urban population and we were unable to collect biological data as well as survey data on more sensitive questions regarding risky sexual behaviours among the participants. Hence, a random sample of participants including both urban and rural populations is necessary to provide a better estimate of the prevalence of STIs in Iran.

Conclusion

The reported prevalence of STIs-associated symptoms among our participants is concerning. Additionally, a considerable number of them had avoided seeking care or self-medicated. While sexual health education is very limited in Iran, people need to be informed about their sexual health and the consequences of self-medication or delaying seeking care for STIs.²⁸ Our findings also indicate a preference of seeking care at private sectors over public facilities. Therefore, MoHME should come up with a comprehensive and multisectoral plan using both public and private health sectors for reporting and following up STIs cases.

Ethical Issues

Kerman University of Medical Sciences, Kerman, Iran as well as the committee of ethics at the MoHME reviewed and approved the study. Before obtaining verbal informed consent, participants were informed about the anonymity of all collected data and the voluntary nature of their participation. Data was reported as aggregate data and did not identify subjects as individuals.

Competing interests

KK has participated in the implementation of Iran's HIV/STIs control program and is supported the Ministry of Health and Medical Education (MoHME). Other authors declare no conflict of interest.

Authors' contributions

Study design: MN, AH, MRB, KK, and AM; Data collection: MN, KK, ARN, AM, RN, and ARR; Data analysis: MN, MK, AH, KK, MRB, and AM; Manuscript

drafting: MK, MN, AM, and AH.

Authors' affiliations

¹Regional Knowledge Hub, and WHO Collaborating Centre for HIV Surveillance, Institute for Futures Studies in Health, Kerman University of Medical Sciences, Kerman, Iran. ²School of Population and Public Health, Faculty of Medicine, University of British Columbia, Vancouver, BC, Canada. ³Center for Disease Control (CDC), Ministry of Health and Medical Education, Tehran, Iran. ⁴Department of Biostatistics and Epidemiology, Faculty of Public Health, Kerman University of Medical Sciences, Kerman, Iran. ⁵Research Center for Modeling in Health, Institute for Futures Studies in Health, Kerman University of Medical Sciences, Kerman, Iran. ⁶Guilan Road Trauma Research Center, Guilan University of Medical Science, Guilan, Iran. ⁷Global Health Sciences Department, University of California, San Francisco, CA, USA.

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