Prevalence of syphilis among antenatal clinic attendees in Karachi: Imperative to begin universal screening in Pakistan

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Abstract

Objectives—Sexually transmitted infections are thought by some to be rare in socially conservative Muslim countries. Little is known about prevalence of syphilis in Pakistani women from the general population. We determined syphilis prevalence in a multi-center cross-sectional study of low risk pregnant women in Karachi, Pakistan.

Methods—We administered a structured questionnaire and obtained a blood sample for syphilis serology (rapid plasma reagin test with *Treponema pallidum* hemagglutination assay confirmation) from all women giving informed consent over six weeks in 2007.

Results—The prevalence of confirmed syphilis was less than one percent (0.9%; 95%CI: 0.4, 1.8) in a sample size of 800 women recruited from three urban sites (≈1% refusal rate). Women who lived in an area where male drug use is prevalent (Ibrahim Hyderi Hospital) had 1% (1.5%) higher prevalence rates than women from the other two sites 0.5%.

Conclusions—We documented higher-than-expected syphilis seroprevalence rates in a low risk population of antenatal clinic attendees in Pakistan. Bridge populations for syphilis may include drug users, who are usually married, and Hijras or their clients. Hijras are transgender and/or transvestite men who may provide sex for money to men. In accordance with our results, the national policy for syphilis control in Pakistan should be modified to include universal syphilis screening in antenatal clinics with subsequent partner notification.

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INTRODUCTION

As in most resource-limited countries, widespread screening is not conducted in Pakistan for many important infectious and metabolic diseases during pregnancy and in newborns, including syphilis, HIV, gonorrhea, chlamydia, and inborn errors of metabolism[1]. In addition, Pakistan has one of the highest fertility rates of any country in the world, estimated by UNICEF to be 3.6 per women [2]. Syphilis in pregnant women is associated with low birth weight, prematurity, and intrauterine death[3]. The World Health Organization (WHO) estimated that 1 million pregnancies are affected by syphilis worldwide in 2004 [4]. Nearly half (n=460 000) will result in abortion or perinatal death, 270 000 will be born with low birth weight and/or prematurity, and 270 000 will be born with congenital syphilis [4]. Because of the serious complications of syphilis in pregnancy, WHO has recommended universal antenatal screening; WHO further recommended screening for syphilis at the first antenatal visit, as early as possible in pregnancy, repeating in the third trimester if resources permit, to detect infection acquired during pregnancy [5, 6]. The effectiveness of such antenatal syphilis screening and its treatment for the prevention of adverse pregnancy outcomes has been well documented [7]. However among Pakistani opinion leaders or most government officials, moat sexually transmitted infections (STIs), including syphilis, are not considered to be problems of public health significance. There is social stigma associated with STIS, along with a paucity of published data, and a generalized lack of STIs awareness among the lay public and medical practitioners alike. Many believe that STIs cannot be very important in a sexually conservative Muslim nation.

This study was therefore conducted to assess the prevalence of (1) syphilis among antenatal clinic (ANC) attendees in Karachi, Pakistan, and (2) associated risk factors.

METHODS

Study design and study site

This was a cross-sectional prevalence study of women attending ANC in Karachi, the principal port, the largest city, and the economic hub of Pakistan (2007 estimate population >12 million). To improve the generalizability of our findings, we included three antenatal clinics of Karachi: (1) the Civil Hospital, (2) the Kharadar General Hospital Karachi, and (3) the Ibrahim Hyderi Hospital. The Civil Hospital is a tertiary care teaching hospital affiliated with Dow University of Health Sciences and located in the center of Karachi. It provides health care services not only to the people of Karachi, but also to a large number of patients from the interior of Sindh and other provinces. All three hospitals mostly provide services to patients from poor and/or middle socio-economic class. The Ibrahim Hyderi Hospital is located near the harbour and mainly serves the fishermen community. The majority of inhabitants are poor and drug use is common, the drug users are all men and most are married.

Recruitment

A trained research officer conducted a daily session with all the pregnant women in the ANC who were 18 to 45 years old and willing to participate. After signing an informed consent form, the women were enrolled for the questionnaire and syphilis test. The study protocol and questionnaire were approved by all relevant Pakistani and United States Ethical Review Boards.

Data Collection

Data were collected through a face-to-face interviewer-administered structured questionnaire. The study questionnaire was originally developed in English, and was then

translated into Urdu. Reverse translation of the questionnaire ensured the correctness and compatibility of the first translation. The questionnaire included information about socio-demographic characteristics and sexual behaviors of study subjects and their husbands. Obstetrical histories of study subjects were obtained, including history of spontaneous or therapeutic abortions, stillbirths and low birth weight babies. Prior to data collection, the questionnaire was pre-tested among five women and appropriate changes were made according to the feedback received. Data collectors were trained in research techniques, the purpose of the study, and ethical considerations. As blood is routinely drawn during the antenatal checkup for hemoglobin, a free syphilis test was offered to all participants. Five mL of blood were drawn by a trained phlebotomist and transferred to a designated laboratory.

Laboratory analysis

Blood samples were tested by rapid plasma reagin (RPR) card test. RPR-reactive specimens were confirmed with a *Treponema pallidum* hemagglutination assay (TPHA) test. Specimen positive on both RPR and TPHA were considered as syphilis seroreactive (syphilis positive). All syphilis positive study participants were provided counseling and free treatment with injectable benzathine penicillin 2.4 million units intramuscularly once every week for three consecutive weeks as per Sindh Provincial guidelines.

Data management and analysis

All questionnaires were checked for completeness and double data entry was performed by trained data entry operators in Statistical Package for Social Sciences (SPSS) version 13.0™ (SPSS, Inc., College Station, TX, USA). Before final analysis, data were validated and cleaned for possible data entry errors. The prevalence of syphilis infection was computed with 95% confidence intervals (95% CI) for the entire group and for risk-defined subgroups. Syphilis prevalence was compared between the high-risk and the low-risk women using a prevalence odds ratio (POR) with 95%CI. When PORs could not be computed because of zero cells, a Chi-square test or a Fisher's exact test was used to assess the extent to which differences might be due to chance alone. Exact logistic regression procedures were used to adjust for multiple risk factors. A potential risk factor was included in the multivariable model if there was moderate association in either direction (positive or inverse) between the risk factor and the prevalence of syphilis (that is, POR ≥ 2 or ≤ 0.5). Data analysis was conducted using the SAS version 9.1™ (SAS, Inc., Cary, NC, USA).

RESULTS

Among 800 pregnant women, the prevalence of TPHA-confirmed syphilis was 875 per 100,000 women (0.9%; 95%CI: 0.4, 1.8). The prevalence of syphilis among women attending Ibrahim Hyderi was 1.5% (1%) higher than among women from the other two sites. Women married to men with a lower educational background had a higher syphilis prevalence (p =0.04). Women >25 years of age, of Sindhi ethnicity, of a lower educational background, married to self-employed men, employed as housewives, and with an income <5,000 rupees/month had a higher syphilis prevalence rates, but these differences may have been due to chance (Table 1). Multiparous women, women with more than one child still alive, women with a history of stillbirth, abortion or low birth weight, women married for >5 years, women with genitourinary symptoms, and women who never used contraceptives had a higher syphilis prevalence rate, but again these differences might have been due to chance (Table 2).

None of the seven infected women were aware of any symptoms in their husbands or partners. Women's extramarital relations and drug use predicted significantly higher syphilis

prevalence, while a husband's extramarital relations and drug use predicted higher syphilis prevalence but differences may have been due to chance (Table 3). Of the seven infected women, four were from the Ibrahim Hyderi Hospital (4/264, 1.5%) and three were from either the Civil Hospital, or the Kharadar General Hospital (3/536, 0.5%)

Multivariate analysis

Ten risk factors were included in multivariable analysis based on the strength of association criteria cited in methods above: maternal age, husband's occupation, income, gravidity, number of live children, previous history of low birth weight infant, years of marriage, extramarital relations, husband's extramarital relations, and husband's habitual drug use. None of these associations were statistically significant with our comparisons of seven infected and 793 uninfected women.

DISCUSSION

The 0.9% seroprevalence rate for syphilis among ANC attendees in three major hospitals of Karachi, Pakistan was relatively high when compared to rates in Europe and North America. While it is true that several studies have found few or no cases of syphilis among the general population [8, 9], women in Pakistan who have sex with high-risk men such as drug users or sex partner of hijras can be at considerable risk. Baqi et al reported a 37% prevalence of syphilis among Hijras (male transvestites and/or transgenders) in Karachi[10]. A 2004 survey of high-risk subgroups in Lahore and Karachi by the National AIDS Control Program reported a syphilis prevalence of 60% among Hijras and 36% among other male sex workers (MSM) [11]. Altaf et al reported a13.1% prevalence among registered male injection drug users (IDUs) at a needle exchange and harm reduction program in Karachi [12]. Thus, Hijras, their male sexual clients, and male IDUs are likely STI bridge populations to women; Hijras practice sex work with married men while IDUs are likely to be married unless they are very young. Given the survey data among Hijras, MSM, and IDUs, the potential for increasing syphilis rates in Pakistani women is therefore substantial with the current syphilis situation reminiscent of the HIV epidemic where the problem is worst in one specific subgroup (IDUs), but has the potential to jump to others very quickly.

In addition it should be noted that in neighboring India, the prevalence of syphilis ranges between 2.0-4.8 % among women of reproductive age [13-16]. In Bangladesh a largely Muslim nation that shares many customs with Pakistan, a cross sectional clinic based study conducted in two urban primary health care level clinics among 1103 women found 1.5% prevalence of syphilis [17]. Another study conducted in Dhaka Bangladesh among 284 pregnant women found an estimated prevalence of 3% [18]. A preponderance of our syphilis cases were among the attendees of the Ibrahim Hyderi Hospital; unlike the catchment area serving the other two sites (the Civil Hospital and the Kharadar General Hospital), Ibrahim Hyderi Hospital serves a peri-urban settlement around the fish harbor of Karachi. Persons working in the fishing industry include men on fishing boats and trawlers that remain at-sea for weeks or even months. Many Pakistani fishermen run afoul of actual or perceived fishing or national boundaries and may be imprisoned in neighboring countries for a time, thus increasing their chances for potential sexual contact with high-risk infected partners.

The strengths of our study include a sample size of 800 women and the use of three diverse sites representing all of the major ethnic and socio-economic levels, as well as both urban and peri-urban areas. The Ibrahim Hyderi Hospital population is the poorest, has a high illiteracy rate, especially among wives of fisherman. Drug use, including IDU, is more common in this district. In contrast, the Civil Hospital and the Kharadar General Hospital are located in the center of Karachi, and serve a lower and middle class population. The Civil Hospital is the teaching hospital of Dow University of Health Sciences and gets

patients from throughout Karachi and from elsewhere in Sindh or Balochistan Provinces. Kharadar General Hospital is a charitable institution established by the business community (Memon Community) and is situated in the old town, catering mainly to the needs of the Memon ethnic population and other communities in the area. The limitations included the absence of data from very rural areas and an insufficient sample size to determine risk factors given the 0.9% syphilis prevalence rate.

Gestational syphilis is of particular concern in under-equipped health systems and wherever access to health care is a major limiting factor for program effectiveness. Adverse pregnancy outcomes include direct placental, fetal, or neonatal infection, or preterm birth associated with some long term neurological damage. Infant mortality rates in Pakistan were estimated at 66.95/1000 live births in 2008 [19]. Congenital syphilis poses a significant challenge especially because infants may be stillborn, asymptomatic at birth but nonetheless infected, or present with a highly variable clinical picture, thereby precluding easy clinical diagnosis. The high risk of congenital syphilis in untreated or inadequately treated mothers (14%) is one reason why 40% of these pregnancies end in fetal loss or perinatal death [20]. All these adverse outcomes continue to make syphilis a global problem of major medical and public health consequences [21-23]. Moreover, syphilis predisposes to HIV infection and can, in turn, increase the transmissibility of HIV [24, 25].

A seroprevalence of nearly 1% among low-risk Pakistani women suggests the need to recommend that universal syphilis screening in pregnancy be instituted in Pakistan with subsequent partner notification, to reduce the prevalence of a potentially dangerous disease, reduce gestational and congenital syphilis, and reduce the potential risk of HIV transmission.

Acknowledgments

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Summary

A study conducted in Karachi, among antenatal clinic attendees displayed higher-than-expected syphilis rates for such a low-risk population. Syphilis bridge populations in Pakistan may include married IDUs and Hijras (transgender and/or transvestite) and/or their clients.

Table 1

Prevalence (%), crude prevalence odds ratio (PORs) and corresponding 95% confidence interval (CI) of syphilis by socio-demographic risk factors in a population of pregnant woman attending antenatal care in Karachi, Pakistan

Socio-demographic risk factors	N*/T#	Prevalence % (95% CI)	POR (95% CI) or p-value¶
Total	7/800	0.9 (0.4 – 1.8)	
Age (years)			
25	2/403	0.5 (0.1 – 1.8)	1.0
>25	5/396	1.3 (0.4 – 2.9)	2.6 (0.5 – 13.3)
Ethnicity			
Punjabi/Pashto/Balochi	3/415	0.7 (0.1 – 2.1)	1.0
Sindhi/Urdu	4/385	1.0 (0.3 – 2.6)	1.4 (0.3 – 6.5)
Education			
Matriculate/College	1/175	0.6 (0.0 – 3.1)	1.0
No School/Primary	6/625	1.0 (0.4 – 2.1)	1.7 (0.2 – 14.1)
Occupation			
Employed	0/53	0.0 (0.0 – 6.7)	
Housewife	7/740	0.9 (0.4 – 1.9)	0.50
Husband's education			
Matriculate/College	0/299	0.0 (0.0 – 1.2)	
No School/Primary	7/501	1.4 (0.6 – 2.9)	0.04¶¶
Husband's occupation			
Government/Private	2/374	0.5 (0.1 – 1.9)	1.0
Self-employed/Other	5/426	1.2 (0.4 – 2.7)	2.2 (0.4 – 11.5)
Husband's job involves travel			
No	7/643	1.1 (0.4 – 2.2)	
Yes	0/157	1.0 (0.0 – 2.3)	0.19
Monthly income (Pak Rupees)			
5,000+	1/356	0.3 (0.0 – 1.6)	1.0
5,000	6/443	1.4 (0.5 – 2.9)	4.9 (0.6 – 40.7)

*
The sum of subjects in some categories was less than 800 because some participants did not respond to some questions.

#N/T = number of women with syphilis/total number of women in the risk factor category.

¶chi-square p-value presented when POR could not be computed due to a cell containing zero.

¶¶p<0.05.

Table 2

Prevalence (%), crude prevalence odds ratio (PORs) and corresponding 95% confidence interval (CI) of syphilis by obstetric history in a population of pregnant woman attending antenatal care in Karachi, Pakistan

Obstetric history:	N*/T#	Prevalence % (95% CI)	POR (95% CI) Or p-value¶
Gravidity	1/201	0.5 (0.0 – 2.7)	1.0
1	6/597	1.0 (0.4 – 2.2)	2.0 (0.2 – 17.0)
>1			
No. of live children			
0	1/235	0.4 (0.0 – 2.3)	1.0
1	6/563	1.1 (0.4 – 2.3)	2.5 (0.3 – 21.1)
H/o of abortion or stillbirth			
No	5/648	0.8 (0.3 – 1.8)	1.0
Yes	2/152	1.3 (0.2 – 4.7)	1.7 (0.3 – 8.9)
H/o of low birth weight			
No	5/695	0.7 (0.2 – 1.7)	1.0
Yes	2/103	1.9 (0.2 – 6.8)	2.7 (0.5 – 14.0)
H/o congenital anomaly			
No	7/766	0.9 (0.4 – 1.9)	
Yes	0/27	0.0 (0.0 – 12.8)	0.62
H/o of contraceptive use before pregnancy			
Any use	1/159	0.6 (0.0 – 3.5)	1.0
None	6/641	0.9 (0.3 – 2.0)	1.5 (0.2 – 12.5)

¶¶ p<0.05.

*
The sum of subjects in some categories was less than 800 because some participants did not respond to some questions.

#
N/T = number of women with syphilis/total number of women in the risk factor category.

¶
chi-square p-value presented when POR could not be computed due to a cell containing zero.

Table 3

Prevalence (%), crude prevalence odds ratio (PORs) and corresponding 95% confidence interval (CI) of syphilis by other risk factors in a population of pregnant woman attending antenatal care in Karachi, Pakistan

Other risk factors	N*/T#	Prevalence % (95% CI)	POR (95% CI) or p-value¶
Years of marriage	2/405	0.5 (0.1 – 1.8)	1.0
<5	5/393	1.3 (0.4 – 2.9)	2.6 (0.5 – 13.5)
5+			
Genitourinary symptoms			
None	4/505	0.8 (0.2 – 2.0)	1.0
Present	3/295	1.0 (0.2 – 2.9)	1.3 (0.3 – 5.8)
Husband's genitourinary symptoms			
None	7/778	0.9 (0.4 – 1.8)	
Present	0/22	0.0 (0.0 – 15.4)	0.66
Extramarital relations			
No	6/788	0.8 (0.3 – 1.6)	1.0
Yes	1/12	8.3 (0.2 – 38.5)	11.8 (1.3 – 106.8)
Husband's extramarital relations			
No	5/585	0.9 (0.3 – 2.0)	1.0
Yes	2/117	1.7 (0.2 – 6.0)	2.0 (0.4 – 10.5)
Habitual drug use			
No	5/611	0.8 (0.3 – 1.9)	1.0
Yes	2/189	1.1 (0.1 – 3.8)	1.3 (0.2 – 6.7)
Husband's habitual drug use			
No	1/444	0.2 (0.0 – 1.2)	1.0
Yes	6/355	1.7 (0.6 – 3.6)	7.6 (0.9 – 63.6)
H/o blood transfusion			
No	7/697	1.0 (0.4 – 2.0)	
Yes	0/103	0.0 (0.0 – 3.5)	0.31

*The sum of subjects in some categories was less than 800 because some participants did not respond to some questions.

#N/T = number of women with syphilis/total number of women in the risk factor category.

¶chi-square p-value presented when POR could not be computed due to a cell containing zero.