Disparity in availability of laboratory testing for syphilis among different hospitals in Shandong province, eastern China

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Research article

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Abstract

Background Availability of laboratory testing is the prerequisite for early diagnosis of syphilis. This study aimed to understand the availability of laboratory testing for syphilis among different hospitals in Shandong province.

Methods Basic information on hospitals provided clinical health service for sexually transmitted infections in Shandong province and type of laboratory tests for syphilis provided was collected and analyzed using Chi-square test.

Results A total of 410 and 456 hospitals provided sexually transmitted infection (STI) clinical services were surveyed in 2012 and 2018, respectively. Significant differences in the availability of nontreponemal tests were observed among hospitals with different levels (X^2 =6.624, p=0.010) and types (X^2 =17.752, p=0.001) in 2012 but not in 2018. A significant difference in the availability of treponemal tests was observed at different levels in 2012 (X^2 =9.937, p=0.002) but not in 2018. Significant differences in the availability of nontreponemal tests, titre of nontreponemal tests, and treponemal tests were observed among hospitals with different affiliations in 2018 (p=0.000; X^2 =15.274, p=0.000; p=0.021) but not in 2012. The availability of both nontreponemal test and treponemal test for syphilis among hospitals in 2018 was higher than that in 2012 (90.13% vs. 57.56%, X^2 =121.219, p=0.000).

Conclusions Further efforts are needed to reduce the disparity in availability of laboratory testing for syphilis among different hospitals in China.

Background

Syphilis continues to be an important global public health issue.[1] An estimated 17.721 million cases of syphilis occurred in people aged 15–49 years globally in 2012, including 5.6 million new cases.[2] Approximately one-third of undiagnosed and untreated patients with syphilis or received inadequate treatment progress to late stages of the disease, which can lead to irreversible damage to cardiovascular, bone and joint, and central nervous systems and even death finally.[3, 4] Syphilis, especially primary and secondary syphilis can enhance HIV acquisition and transmission.[5–7] If left untreated during pregnancy, then syphilis can cause early foetal loss, premature birth, stillbirth, low birth weight, and congenital infection.[8] More than 900,000 pregnant women globally were infected with syphilis in 2012, generating approximately 350,000 adverse outcomes.[9] The harms resulting from maternal and congenital syphilis among children may exceed those caused by HIV in some developing countries.

The clinical manifestations of syphilis often mimic those of various skin diseases, or the disease may exist in a latent state. Identifying atypical symptoms and asymptomatic infection, especially among pregnant women, by laboratory testing is a very important component of syphilis control and prevention.[10] Most adverse outcomes can be controlled with early detection and timely treatment. Early diagnosis and treatment is a cost-effective strategy for syphilis control.[11, 12] A survey reported that the screening

rate of prenatal HIV test was 95%, and that of syphilis test was only 47%.[13] The availability of laboratory testing is a prerequisite for early diagnosis of syphilis.

Many test methods with high sensitivity and specificity are available technically for syphilis. Etiological detection methods, such as dark-field microscopy (DF), polymerase chain reaction (PCR) and serologic detection, including nontreponemal and treponemal tests are commonly used.[14] Either a nontreponemal or treponemal test can be used for screening.[15] According to the case definition, the diagnosis of syphilis requires that at least one of the following tests is positive: DF, PCR, both positive of nontreponemal test and treponemal test.[16, 17] However, the availability of laboratory testing for syphilis remains poor in some nations or regions. Some medical institutions still use either a nontreponemal or a treponemal test alone for the diagnosis of syphilis,[18] leading to the poor accuracy of the diagnosis.

China is one of the countries with the high prevalence of syphilis worldwide. In 2017, 475,860 new cases of syphilis were reported in China.[19] Approximately 67.6% of maternal syphilis were latent syphilis, and 71.8% of maternal syphilis were reported in eastern areas, such as Shandong province.[20] A survey in Guangdong province showed that 81% of newly reported syphilis cases were diagnosed in hospitals, but only 22% were diagnosed early.[21] Another survey found that the coverage rate of syphilis screening in sexually transmitted infection(STI) clinics was only 40% in 2014.[22]

Availability of laboratory testing plays a key role in syphilis prevention and control programs. Several indicators related to syphilis testing contribute to the ultimate goal of the National Program for Prevention and Control of Syphilis in China (2010–2020). This goal includes the availability of laboratory tests for syphilis among 90% institutions that provide STI clinical service, and the testing of 90% pregnant women in city and 70% in rural areas for syphilis by the end of 2020. Disparity in availability of laboratory testing for syphilis may exist among different hospitals and effect achieving the goal of the program. To understand the availability of laboratory testing for syphilis and evaluate the effectiveness of the program, we conducted two surveys among hospitals that reported syphilis cases in Shandong province, China.

Methods

Study site

The study was conducted in Shandong province, eastern of China, which is subdivided into 17 prefecture-level cities and 137 county-level units. There were a total of 1,377 and 2,450 registered hospitals in the province in 2010 and 2017, respectively. [23]

Study objects

All hospitals providing clinical services for STIs in Shandong province were included in the study. The inclusion was based on the list of hospitals that reported syphilis cases in the past few years. Some army

and enterprise hospitals were included and classified according to their scale, affiliation and services provided.

Data collection

A unified questionnaire designed by the National Center for STD Control, China CDC was used in each survey for data collection. Contents related to this study were covered, including basic information of the hospitals (level, type, and affiliation) and the types of laboratory tests for syphilis provided. In the survey, rapid plasma regain test (RPR), toluidine red unheated serum test (TRUST) and venereal disease research laboratory (VDRL) test belong to nontreponemal tests. *Treponema pallidum* particle agglutination assay (TPPA), *T. pallidum* hemagglutination assay (TPHA), *T pallidum* enzyme-linked immunosorbent assays (TP-ELISA), *T. pallidum* chemiluminescence immunoassay (TP-CLIA) and *T pallidum* rapid test (TP-RT) belong to treponemal tests.

The first survey was conducted in 2012 as a part of the baseline assessment for the National Program for Prevention and Control of Syphilis in China (2010-2020). To assess the effectiveness of the program, we conducted a second survey in 2018. Health staff from the Centre for Disease Control and Prevention at county- level visited each hospital in their respective jurisdictions and filled in the questionnaires.

Data analysis

Data collected were entered into Microsoft Excel for Windows (2012) and analysed in SPSS (version 22). The percentages of providing each laboratory test for syphilis among hospitals according to levels, types, and affiliation were analysed and compared. Descriptive analysis and Chi-square were used for statistical analysis. P values<0.05 were considered statistically significant.

Results

General information

A total of 410 and 456 valid questionnaires were collected in 2012 and 2018 among hospitals that reported syphilis cases in the past year in Shandong province, respectively. The percentages of surveyed hospitals in each category by level, type and affiliation in Shandong province are listed in Table 1.

Seventeen (4.15%) hospitals in 2012 and 14 (3.07%) in 2018 reported being able to provide DF, but none actually provided this test. No hospitals in 2012 and 3 (0.66%) in 2018 reported using PCR for *T. pallidum* test. TRUST or RPR was used among 300 (73.17%) hospitals in 2012 and among 415 (91.01) in 2018. Furthermore, 140 (34.15%) hospitals in 2012 and 352 (77.19%) in 2018 provided the titre of RPR or TRUST assay. No hospitals reported using VDRL and USR in 2012 and 2018. TPPA was used among 188 (45.85%) hospitals in 2012 and among 266 (58.33%) in 2018. TP-RT was used among 122 (29.76%) hospitals in 2012 and among 214 (46.93%) in 2018. TP-CLIA was used among 20 (4.89%) hospitals in 2012 and among 187 (41.01%in 2018. TP- ELISA was used among 109 (26.59%) hospitals in 2012 and among 113 (24.78%) in 2018. No hospitals provided either TPHA or FTA-Abs in 2012 and 2018.

Availability of serologic test for syphilis among hospitals at different levels in 2012 and 2018

A significant difference in the availability of RPR or TRUST was observed among hospitals at different levels in 2012 (X^2=6.624, p=0.010) but not in 2018 (X^2=2.773, p=0.096). Significant differences in the availability of titre of RPR or TRUST were observed at different levels in 2012 (X^2=12.909, p=0.000) and 2018 (X^2=5.872, p=0.015). A significant difference in the availability of TPPA or ELISA or RT or CLIA was observed at different levels in 2012 (X^2=9.937, p=0.002) but not in 2018 (p=0.425, Fisher's exact test) (Table 2 and 3

Availability of serologic test for syphilis among different types of hospitals in 2012 and 2018

A significant difference in the availability of RPR or TRUST was observed among different types of hospitals in 2012 (X^2=17.752, p=0.001) but not in 2018. This availability was significantly higher among specialized dermatological hospitals than in general western medicine hospitals (X^2=10.855, p=0.001), maternal and child health hospitals (X^2=11.527, p=0.001), Chinese medicine hospitals (X^2=12.568, p=0.000) and other specialized hospitals (p=0.012, Fisher's exact test) in 2012. Significant differences in the availability of titre of RPR or TRUST were observed among different types of hospitals in 2012 (X^2=24.607, p=0.000) and 2018 (X^2=11.132, p=0.025). The availability of this test was significantly higher among specialized dermatological hospitals than in general western medicine hospitals (X^2=13.811, p=0.000) in 2012. However, the availability was significantly lower among Chinese medicine hospitals than general western medicine hospitals (X^2=6.969, p=0.008), specialized dermatological hospitals (X^2=7.864, p=0.005) and maternal and child health hospitals (X^2=4.013, p=0.045) in 2018. No significant differences in the availability of treponemal tests were observed among hospitals with different type in 2012 and 2018(X^2=2.809, p=0.590; X^2=7.069, p=0.132) (Table 1 and 2

Availability of serologic tests for syphilis among hospitals with different affiliations in 2012 and 2018

A significant difference in the availability of RPR or TRUST was observed in 2018 (p=0.000, Fisher's exact test) among hospitals with different affiliations, but not in 2012(X^2=0.083, p=0.773). A significant difference in the availability of titre of RPR or TRUST was observed in 2018 (X^2=15.274, p=0.000) but not in 2012 (X^2=0.311, p=0.577). A significant difference in the availability of treponemal tests was observed in 2018(p=0.021, Fisher's exact test) but not in 2012(X^2=1.602, p=0.206) (Table 2 and 3

Changes in the capacity of laboratory diagnosis for syphilis among hospitals by level, type, and affiliation from 2012 to 2018

The availability of both nontreponemal test and treponemal test for syphilis among hospitals was higher in 2018 than in 2012 (90.13% vs. 57.56%, X^2=121.219, p=0.000). The availability was significantly improved from 2012 to 2018 among tertiary hospitals (72.57% vs. 93.97%, X^2=18.939, p=0.000), secondary and primary hospitals (51.85% vs. 88.82%, X^2=106.529, p=0.000), general western medicine hospitals (59.26% vs. 96.51%, X^2=91.147, p=0.000), maternal and child health hospitals (50.00% vs.

88.42%, X^2=31.314, p=0.000), Chinese medicine hospitals (47.37% vs. 84.62%, X^2=21.318, p=0.000) and public hospitals (56.99% vs. 92.34%, X^2=134.425, p=0.000) (Table 4)

Changes in the availability of titre of RPR or TRUST for syphilis among hospitals by level, type, and affiliation from 2012 to 2018

The availability of titre of RPR or TRUST for syphilis among hospitals in 2018 was higher than that in 2012 (77.19% vs. 34.15%, X^2=163.045, p=0.000). The availability was significantly improved from 2012 to 2018 among tertiary hospitals (47.79% vs. 85.34%, X^2=36.413, p=0.000), secondary and primary hospitals (28.96% vs. 74.41%, X^2=131.563, p=0.000), general western medicine hospitals (35.19% vs. 79.04%, X^2=87.615, p=0.000), maternal and child health hospitals (25.61% vs. 77.89%, X^2=48.387, p=0.000), Chinese medicine hospitals (24.56% vs. 64.10%, X^2=20.652, p=0.000 and public hospitals (33.77% vs. 79.67%, X^2=171.675, p=0.000) (Table 4

Discussion

In this study, we found that aetiological diagnostic tests for syphilis, such as DF and PCR, were seldom used in Chinese hospitals, although they have advantages in diagnosis of early syphilis as immediate and definitive methods.[24] The high requirement for specific expertise in DF and the need of expensive equipment and reagents in PCR tests may prevent hospitals from adopting these methods. Although the sensitivity and specificity of treponemal and nontreponemal tests vary with the types of tests and the stages of syphilis infection, the mainstay of diagnosis for syphilis still depends on serologic testing in China.

RPR, TRUST, TPPA, ELISA, RT and CLIA rather than VDRL, USR, FTA-Abs and TPHA were commonly used in China, in contract to other countries, such as the USA, Canada and the UK.[24–26] VDRL, USR, FTA-Abs and TPHA were unavailable in China mainly because of reagent shortage. Both VDRL and FTA-abs test are laborious and time consuming, although they are valuable in detecting neurosyphilis. Surveys suggested that FTA-ABS and VDRL tests can be replaced by CSF-TPPA and TRUST test in the diagnosis of neurosyphilis in case of lacking CSF-ABS and VDRL.[18, 27–29] However, RPR is not recommended for the diagnosis of neurosyphilis because its sensitivity is lower than that of VDRL.[30]

Some improvements in the availability of laboratory testing for syphilis were observed in Shandong in general. First, the proportion of providing syphilis laboratory testing and STI clinical services among maternal and child health hospitals increased with increasing of total number, indicating that the coverage for maternal and congenital syphilis screening had been extended. This contrasted with the increased proportion among specialized dermatological hospitals due to the decreased number of hospitals. Second, among hospitals providing STI clinical service, the availability of serologic tests was significantly improved at different level of hospitals in the past 6 years. The improvement was greater among secondary and primary hospitals than in tertiary hospitals. The availabilities of both treponemal and nontreponemal tests were significantly improved among some hospitals providing STI clinical

services, especially among secondary and primary hospitals, general western medicine hospitals, maternal and child health hospitals, Chinese medicine hospitals and public hospitals, indicating the increased diagnosis capacity and accuracy rate of case reports among these hospitals.

However, great disparities in availability of syphilis laboratory tests exist among different hospitals, especially between public and private sectors. In the 2012 survey, one third of hospitals in Shandong reported syphilis cases, indicating that those hospitals could provide syphilis laboratory testing and STI clinical services. The proportion decreased to less than one fifth in the 2018 survey, mainly because the total number of hospitals largely increased but the number of hospitals that provided syphilis laboratory tests did not increase proportionately, especially in the private sector. In the past six years, the number of private hospitals disproportionately increased, but few could provide syphilis laboratory testing. Private hospitals are encouraged to provide additional medical services and cooperate with public sectors in recent years.[31] Although until 2018, less than half of public hospitals provided STI clinical service, the proportion was higher than that among private hospitals. Public hospitals still play a leading role in STI health care, and private sectors still need to meet the increasing demand for STI health service in China. In addition, one tenth of the hospitals providing STI clinical services in Shandong could not offer both nontreponemal test and treponemal test until 2018 in Shandong, indicating that syphilis cases in those hospitals were not correctly diagnosed.

Further efforts are needed to improve the availability of laboratory tests for syphilis in China. First, the application of point-of-care (POC) tests needs to be promoted. One of the main reasons for the poor availability of some syphilis tests are the requirement of trained professional technicians, essential equipment, and complicated and time-consuming procedures. POC has equivalent sensitivity and specificity as TRUST and TPPA,[32, 33] and can provide results in 15–20 min without the need for a laboratory and equipment.[34] A diagnosis can be made at the first visit, so patients do not have to return for their results, and treatment can be immediately provided. Second, professional training and quality control management need to be strengthened. The quality control of syphilis diagnostic testing is a critical component of effective STI control programs. Internal and external quality assurance and quality control procedures are important to help ensure accurate testing and reduce the risk of misdiagnosis.[14] Staff training is one of the main determinants of quality control for laboratory.[35] As a provincial central laboratory, professional training and quality control management should be carried out regularly. Third, an effective referral system needs to be established. Referral service involves the outreach of medical personnel recommended to a suitable medical institution for service and help according to the needs of the target population. Any screened syphilis antibody-positive cases should be referred to proper medical institutions that can provide standardised clinical services if the screening institutions cannot provide. One of the advantages of a referral system is increasing accessibility by integrating and making good use of various resources in resource constrained countries or areas. However, the disadvantages include increasing burden of patients in costs, transportation and time. The referral rate for patients with suspected STIs can reach generally 95–100%, but the referral success rate is only 30–45%.[36] Fourth, laboratory outsourcing service is allowed or encouraged by health administrative authorities in China, which may be a beneficial for increasing the availability of syphilis laboratory testing. However, additional

regulations are needed to monitor and manage these organisations providing laboratory outsourcing service. In summary, further efforts are needed to survey and discuss these issues.

This study has some limitations. First, the survey was conducted in Shandong province, representing eastern coastal economically developed areas in China. Thus the results cannot be generalised to all regions of China. Second, the study focused on the availability of laboratory tests for syphilis, issues related to the accessibility of syphilis testing and laboratory quality control, which are very important for screening and laboratory diagnosis of syphilis, were not considered.

Conclusion

The availability of laboratory testing for syphilis in Shandong province showed improvements in the past 6 years in general. However further efforts are needed to reduce the disparity in availability of laboratory testing for syphilis among different hospitals in China.

Abbreviations

DF: dark-field microscopy; PCR: polymerase chain reaction; RPR: rapid plasma regain test; TRUST: toludine red unheated serum test; VDRL: venereal disease research laboratory test; TPPA: treponema pallidum particle agglutination assay; TPHA: treponema pallidum hemagglutination assay; TP-ELISA: treponema pallidum enzyme-linked immunosorbent assays; TP-CLIA: treponema pallidum chemiluminescence immunoassay; TP-RT: treponema pallidum rapid tests; STI: sexually transmitted infection; POC: point-of-care tests; WHO-AFRO: the World Health Organization Regional Office for Africa.

Declarations

Ethics Approval and Consent to Participate

This study was approved by the institutional review board at the Shandong Provincial Institute of Dermatology and Venereology.

Consent for publication

Not applicable.

Availability of data and materials

The data used and analyzed are available upon reasonable request by emailing dianchangliu@163.com.

Competing Interests

The authors declare no conflicts of interest.

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Authors' contributions

DL who is corresponding author obtained funding and designed the study. XC is first author. DL and XC collected and analyzed the data, drafted the manuscript. TC, YG, FL and LC contributed to collecting the data. DC, XM and QC contributed to the interpretation of the results and critical revision of the manuscript for important intellectual content. All authors have read and approved the final manuscript. DL is the study guarantors.

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Tables

Table 1 Percentages of surveyed hospitals in Shandong in 2012 and 2018

Categories		Number of hospitals in 2010	Surveyed in 2012 (%)	Number of hospitals in 2017	Surveyed in 2018 (%)
Overall		1377	410(29.77)	2450	456(18.61)
Levels	Tertiary hospitals	117	113(96.58)	166	116(69.88)
	Secondary and primary hospitals	1200	297(24.75)	2284	340(14.89)
Types	General western medicine hospitals	950	216(22.74)	1856	229(12.34)
	Specialized dermatological hospitals	55	37(67.27)	48	37(77.08)
	Maternal and child health hospitals	148	82(55.41)	161	95(59.01)
	Chinese medicine hospitals	157	57(36.33)	300	78(26.00)
	Other specialized hospitals	67	18(26.87)	85	17(20.00)
Affiliation	Public hospitals	844	379(44.91)	863	418(48.44)
	Private hospitals	533	31(5.82)	1587	38(2.39)

Table 2 Availability of serologic test for syphilis among hospitals in Shandong province in 2012

Categories		Total	RPR or Trust	Titre of RPR or TRUST	TPPA or ELISA or RT, or CLIA
Overall		410(100)	300(73.17)	140(34.15)	320(78.05)
Levels	Tertiary hospitals	113(27.56)	93(82.30)	54(47.79)	100(88.50)
	Secondary and primary hospitals	297(72.44)	207(69.70)	86(28.96)	220(74.07)
	X^2, P		6.624, 0.010	12.909, 0.000	9.937, 0.002
Types	General western medicine hospitals	216(52.68)	156(72.22)	76(35.19)	174(80.56)
	Specialized dermatological hospitals	37(9.02)	36(97.30)	25(67.57)	30(81.08)
	Maternal and child health hospitals	82(20.00)	57(69.51)	21(25.61)	62(75.61)
	Chinese medicine hospitals	57(13.90)	38(66.67)	14(24.56)	41(71.93)
	Other specialized hospitals	18(4.39)	13(72.22)	4(22.22)	13(72.22)
	X^2, P		17.752, 0.001	24.607, 0.000	2.809, 0.590
Affiliation	Public hospitals	379(92.44)	278(73.35)	128(33.77)	293(77.31)
	Private hospitals	31(7.56)	22(70.97)	12(38.71)	27(87.10)
	X^2, P		0.083, 0.773	0.311, 0.577	1.602, 0.206

Table 3 Availability of serologic test for syphilis among hospitals in Shandong province in 2018

Categories		Total	RPR or Trust	Titre of RPR or TRUST	TPPA or ELISA or RT or CLIA
Overall		456(100)	415(91.01)	352(77.19)	448(98.25)
Levels	Tertiary hospitals	116(25.44)	110□94.83□	99(85.34)	113(97.41)
	Secondary and primary hospitals	340(74.56)	305(89.71)	253(74.41)	335(98.53)
	X^2, P		2.773, 0.096	5.872, 0.015	0.425
Types	General western medicine hospitals	229(50.22)	213(93.01)	181(79.04)	225(98.25)
	Specialized dermatological hospitals	37(8.11)	35(94.59)	33(89.19)	37(100.00)
	Maternal and child health hospitals	95(20.83)	86(90.53)	74(77.89)	91(95.79)
	Chinese medicine hospitals	78(17.11)	66(84.62)	50(64.10)	78(100.00)
	Other specialized hospitals	17(3.73)	15(88.24)	14(82.35)	17(100.00)
	X^2, P		5.329, 0.255	11.132, 0.025	7.069, 0.132
Affiliation	Public hospitals	418(91.67)	390(93.30)	333(79.67)	414(99.04)
	Private hospitals	38(8.33)	25(65.79)	19(50.00)	34(89.47))
	X^2, P		0.000	15.274, 0.000	0.021

Table 4 Capacity of syphilis diagnosis among hospitals by level, type and affiliation from 2012 to 2018

	Both a non-treponemal test and a treponemal test			Titre of RPR or TRUST		
Categories	2012(n, %)	2018(n, %)	X^2, P	2012(n, %)	2018(n, %)	X^2, P
Overall	236(57.56)	411(90.13)	121.219, 0.000	140(34.15)	352(77.19)	163.045, 0.000
Tertiary hospitals	82(72.57)	109(93.97)	18.939, 0.000	54(47.79)	99(85.34)	36.413, 0.000
Secondary and primary hospitals	154(51.85)	302(88.82)	106.529, 0.000	86(28.96)	253(74.41)	131.563, 0.000
General western medicine hospitals	128(59.26)	221(96.51)	91.147, 0.000	76(35.19)	181(79.04)	87.615, 0.000
Specialized dermatological hospitals	30(81.08)	35(94.59)	0.152	25(67.57)	33(89.19)	5.103, 0.024
Maternal and child health hospitals	41(50)	84(88.42)	31.314, 0.000	21(25.61)	74(77.89)	48.387, 0.000
Chinese medicine hospitals	27(47.37)	66(84.62)	21.318, 0.000	14(24.56)	50(64.10)	20.652, 0.000
Other specialized hospitals	10(55.56)	15(88.24)	0.060	4(22.22)	14(82.35)	12.655, 0.000
Public hospitals	216(56.99)	386(92.34)	134.425, 0.000	128(33.77)	333(79.67)	171.675, 0.000
Private hospitals	20(64.52)	25(65.79)	0.012, 0.912	12(38.71)	19(50.00)	0.880, 0.348

Supplementary Files

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