INTRODUCTION

Genital Chlamydia trachomatis infection (GCTI) is a chronic inflammatory disease mainly caused by the D–K type of Chlamydia trachomatis (CT) which infects the human genitourinary tract. It can lead to urethritis and epididymitis in men, pelvic inflammatory disease (PID) or infertility in women, and spontaneous preterm birth or stillbirth in pregnant women. Delayed treatment increases the risk of ectopic pregnancy and tubal factor infertility (1–3). Moreover, GCTI increases the risk of HIV infection, and may also be related to ovarian cancer and cervical cancer (4–8).

Early diagnosis of GCTI is crucial in ensuring that symptomatic patients are promptly treated and asymptomatic infections are eliminated. GCTI screening and treatment can decrease the incidence of PID (9).

Early diagnosis and treatment of GCTI have economic and health benefits for women less than 30 years old or those who are pregnant (10,11). The Centers for Disease Control and Prevention in the USA has advised that all sexually active women younger than 25 years old should be routinely screened for CT (12), whereas the Public Health Agency in Canada has recommended screening of all pregnant women for this disease (13). In 2012, 130 million people aged 15-49 years were infected by CT worldwide (14). GCTI is the most common sexually transmitted disease (STD) in Europe and the USA (15,16). In 2016, approximately 230,000 and 1.6 million cases were reported in the UK and the USA, respectively (17,18). These equate to an incidence of nearly 351 per 100,000 population in the UK and 497 per 100,000 population in the USA (17,18). The incidence of GCTI was estimated to have reached 15%–20% in some regions (19,20). In populations that had been actively screened, the positive rate has been reported to be as high as 30.2% (21). However, reports on the prevalence of GCTI in Shandong province, China are limited.

A study estimated that the prevalence of GCTI in several areas of China could be as high as 14.3% (22). However, the reported incidence of GCTI in the country in 2015 was 37 per 100,000 population (23), which was substantially lower than that in Europe and the USA,
where annual screening and treatment programs for GCTI in young women have been recommended (12,24). Based on the data reported in the literature (25), we hypothesized that the prevalence of GCTI in Shandong province or even in the whole of China may have been severely underestimated.

GCTI diagnosis and reporting mainly rely on the availability of laboratory testing, because 50-70% of cases are asymptomatic (26). Therefore, the availability of CT laboratory testing must be determined and its role in the estimation of GCTI prevalence in Shandong province should be evaluated. Hospitals are in a unique position to manage populations at high risk of contracting STDs, and they are responsible for screening, diagnosing, and reporting GCTI cases. Accordingly, we surveyed the availability of CT laboratory testing in hospitals in Shandong province that provided clinical service for patients with STDs in 2018.

MATERIALS AND METHODS

Study objects: The study was conducted in Shandong province in December 2018. Shandong province is subdivided into 17 prefecture-level cities and 137 county-level units. As of 2017, the total number of hospitals registered in the province was 2,450; of which, 166 are tertiary hospitals and 2,284 are primary and secondary hospitals, 1,856 are general western medicine hospitals, 48 are specialized dermatological hospitals, 161 are maternal and child healthcare hospitals; 300 are Chinese medicine hospitals, and 85 are other specialized hospitals. Of these, 863 are public hospitals and 1,587 are private hospitals (27). The classification of these hospitals was strictly conducted by the administration of the Department of Health according to a guideline based on scale, staff, beds, and scope of service provided by these medical institutions.

Survey hospitals: All hospitals that provided clinical services for patients with STDs in Shandong province were included in the survey (n = 496). A hospital was included in the survey if it reported at least one STD case (syphilis, gonorrhea, GCTI, condyloma acuminatum, or genital herpes) in 2017.

Data collection and analysis: The basic information on the hospitals (level, type, and affiliation) and types of laboratory testing for CT (antigen or PCR testing) were collected using a questionnaire. National healthcare staff from the Centers for Disease Control and Prevention were trained for data collection. They visited each hospital in their respective jurisdictions and completed the questionnaires. The questionnaires were collected by the staff from the Shandong Provincial Institute of Dermatology and Venereology, and 5% of the surveyed hospitals were randomly contacted by phone. Questionnaires with consistent and complete information were regarded as valid after the phone verification. Records of GCTI cases in Shandong province in 2018 were downloaded from the China Information System for Disease Control and Prevention. Data were entered in Microsoft Excel for Windows (2012) and analyzed using SPSS (version 22). Distribution of laboratory tests provided for CT and GCTI cases as reported by the hospitals according to level, type, and affiliation were analyzed and compared via descriptive analysis and Chi-square test. P-values < 0.05 were considered statistically significant. Data quality reviews were completed through desk review which focused on checking and analyzing the statistics aggregated and reported by each district and field investigation. This strategy was used because it is more comprehensive and informative.

RESULTS

Availability of CT laboratory testing in hospitals in Shandong province in 2018: A total of 496 questionnaires were collected, 456 of which were deemed valid after a quality check of the information. These questionnaires were obtained from 116 (25.4%) tertiary hospitals, 340 (74.6%) primary and secondary hospitals, 229 (50.2%) general Western medicine hospitals, 37 (8.1%) specialized dermatological hospitals, 95 (20.8%) maternal and child healthcare hospitals, 78 (17.1%) Chinese medicine hospitals, and 17 (3.7%) other specialized hospitals. Among these hospitals, 419 (91.9%) were publicly managed and 37 (8.1%) were privately owned.

Antigen and PCR testing were available in 200 (43.9%) and 88 (19.3%) hospitals, respectively. No significant difference in the availability of antigen testing was observed among hospitals at different levels. PCR testing was more available in tertiary hospitals than in primary and secondary hospitals (χ² = 28.560, P = 0.000). By contrast, significant differences in the availability of antigen testing (χ² = 15.708, P = 0.003) and PCR testing (χ² = 22.494, P = 0.000) were observed among different types of hospitals. The availability of antigen testing in specialized dermatological hospitals was significantly higher than that in general Western medicine hospitals (χ² = 11.997, P = 0.001), maternal and child health hospitals (χ² = 8.830, P = 0.003), Chinese medicine hospitals (χ² = 14.824, P = 0.000), and other specialized hospitals (χ² = 5.050, P = 0.025). The availability of PCR testing in general Western medicine hospitals was also significantly higher than that in specialized dermatological hospitals (χ² = 8.186, P = 0.004) and maternal and child healthcare hospitals (χ² = 10.638, P = 0.001). No significant difference in the availability of antigen testing and PCR testing was observed among hospitals with different affiliations (Table 1).

Either antigen or PCR testing was available in 268 (58.8%) hospitals. Both tests were more available in tertiary hospitals than the primary and secondary hospitals (χ² = 22.728, P = 0.000). Significant differences in the availability of either antigen or PCR testing were observed among the different types of hospitals (χ² = 21.729, P = 0.000). These tests were more available in general Western medicine hospitals than in maternal and child healthcare hospitals (χ² = 5.139, P = 0.023), Chinese medicine hospitals (χ² = 9.880, P = 0.002), and other specialized hospitals (χ² = 6.018, P = 0.014). They were also more available in specialized dermatological hospitals than in maternal and child healthcare hospitals (χ² = 7.912, P = 0.005), Chinese medicine hospitals (χ² = 11.416, P = 0.001), and other specialized hospitals (χ² = 9.418, P = 0.001).
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Table 1. Availability of CT laboratory testing in hospitals of Shandong province in 2018

| Categories               | Number of hospitals in 2017 (n) | Surveyed in 2018 (n, %) | Antigen testing (n, %) | PCR testing (n, %) |
|--------------------------|---------------------------------|-------------------------|------------------------|--------------------|
| Total                    | 2,450                           | 456 (18.6)              | 200 (43.9)             | 88 (19.3)          |
| Level                    |                                 |                         |                        |                    |
| Tertiary hospitals       | 166                             | 116 (69.9)              | 58 (50.0)              | 42 (36.2)          |
| Primary and secondary hospitals | 2,284                       | 340 (14.9)              | 142 (41.8)             | 46 (13.5)          |
| Type                     |                                 |                         |                        |                    |
| General western medicine hospitals | 1,856                  | 229 (12.3)              | 97 (42.4)              | 62 (27.1)          |
| Specialized dermatological hospitals | 48                            | 37 (77.1)               | 27 (73.0)              | 2 (5.4)            |
| Maternal and child health care hospitals | 161                       | 95 (59.0)               | 42 (44.2)              | 10 (10.5)          |
| Chinese medicine hospitals | 300                            | 78 (26.0)               | 27 (34.6)              | 13 (16.7)          |
| Other specialized hospitals | 85                            | 17 (20.0)               | 7 (41.2)               | 1 (5.9)            |
| Affiliation              |                                 |                         |                        |                    |
| Public hospitals         | 863                             | 419 (48.6)              | 184 (43.9)             | 79 (18.9)          |
| Private hospitals        | 1,587                           | 37 (2.3)                | 16 (43.2)              | 9 (24.3)           |

\( \chi^2, P \)

Table 2. Comparison on the availability of antigen or PCR testing and case reporting among hospitals in 2018

| Categories               | Hospitals with antigen testing or PCR testing 2018 (n, %) | Hospitals with case reporting (n, %) |
|--------------------------|----------------------------------------------------------|-----------------------------------|
| Total                    | 268 (58.8)                                               | 99 (21.7)                         |
| Level                    |                                                          |                                   |
| Tertiary hospitals       | 90 (77.6)                                                | 44 (37.9)                         |
| Primary and secondary hospitals | 178 (52.4)                   | 55 (30.9)                         |
| \( \chi^2, P \)          | 22.728, 0.000                                            | 24.082, 0.000                     |
| Type                     |                                                          |                                   |
| General western medicine hospitals | 149 (65.1)            | 60 (26.2)                         |
| Specialized dermatological hospitals | 29 (78.4)          | 15 (40.5)                         |
| Maternal and child health care hospitals | 49 (51.6)          | 13 (13.7)                         |
| Chinese medicine hospitals | 35 (44.9)                                                | 10 (12.8)                         |
| Other specialized hospitals | 6 (35.3)                                                 | 1 (5.9)                           |
| \( \chi^2, P \)          | 21.729, 0.000                                            | 20.604, 0.000                     |
| Affiliation              |                                                          |                                   |
| Public hospitals         | 244 (58.2)                                               | 94 (22.4)                         |
| Private hospitals        | 24 (64.9)                                                | 5 (13.5)                          |
| \( \chi^2, P \)          | 0.617, 0.432                                             | 1.592, 0.207                      |

\( \chi^2, P = 0.002 \). No significant difference in the availability of either antigen or PCR testing was observed between public and private hospitals (Table 2).

**Distribution of GCTI cases reported from different hospitals in Shandong province in 2018:**

Distribution of reported GCTI cases from different hospitals was consistent with the hospitals that provided laboratory testing for GCTI. In 2018, 1,532 GCTI cases were reported to the Shandong Provincial Institute of Dermatology and Venereology by 99 hospitals, including 44 (37.9%) tertiary hospitals and 55 (30.9%) primary and secondary hospitals, 60 (26.2%) general Western medicine hospitals, 15 (40.5%) specialized dermatological hospitals, 13 (13.7%) maternal and child healthcare hospitals, 10 (12.8%) Chinese medicine hospitals, and 1 (5.9%) other specialized hospital. Among them, 94 (22.4%) were public hospitals and 5 (13.5%) were private hospitals.

Tertiary hospitals reported more cases than that in primary and secondary hospitals (\( \chi^2 = 24.082, P = 0.000 \)). Significant differences in the distribution of cases reported by different types of hospitals were observed (\( \chi^2 = 20.604, P = 0.000 \)). General western medicine hospitals reported more cases than that in Chinese medicine hospitals (\( \chi^2 = 5.918, P = 0.015 \) and other specialized hospitals (\( P = 0.079 \)). Specialized dermatological hospitals reported more cases than that in maternal and child healthcare hospitals (\( \chi^2 = 11.492, P = 0.001 \), Chinese medicine hospitals (\( \chi^2 = 11.334, P = 0.001 \), and other specialized hospitals (\( \chi^2 = 6.710, P = 0.010 \)) (Table 2).

**DISCUSSION**

In this study, we found that the availability of CT laboratory testing was poor in different hospitals in the Shandong province of China. In 2018, only 20.24% (496/2,450) of the province’s hospitals reported STD cases. Among these hospitals, over 50% did not provide antigen testing for CT and over 80% did not have access...
to PCR testing. Furthermore, over 40% did not have access to either antigen or PCR testing. These results indicated that GCTI cases in these hospitals may not have been correctly diagnosed. As such, there may be numerous GCTI cases that have not been reported. The real status of GCTI in Shandong province may have been severely underestimated according to the surveillance data of case reporting.

We hypothesized that GCTI case reporting was largely related to the availability of laboratory testing for CT in the hospitals. To confirm our hypothesis, we compared the distribution of different hospitals that reported GCTI cases and those that provided laboratory testing for CT. As expected, the results were consistent. Therefore, the reported incidence of GCTI was determined by the availability of laboratory testing, and the actual disease burden of GCTI in Shandong province is inadequately described.

Although the sensitivity of antigen testing is as low as 65%–75% (28), it was more readily available than that of PCR testing in Shandong province. Given that antigen testing is convenient and easy to perform, the reagents used are inexpensive and commercially available, and its results can be rapidly reported, this type of testing is an attractive option in primary and secondary hospitals. These advantages somehow compensate for its low sensitivity. In contrast, the sensitivity and specificity of PCR testing are as high as 97% and 100%, respectively (29,30) and is strongly recommended for CT diagnosis (31–33). However, we found that this test was seldom used in Chinese hospitals. During routine supervision, we noted that the preference of doctors and patients for various testing methods may affect the availability and accessibility of CT screening, even if both of these tests were available in the hospitals. Although doctors are recommended to use CT screening tests based on nucleic acid amplification techniques, many doctors and patients still prefer the antigen-based test because it is rapid and cheap.

From the perspective of supervisors of programs for STD control, we posit that one of the primary reasons for the low availability of GCTI testing is the lack of training for medical staff. This is an unfortunate situation and has led to inadequate knowledge of the disease and low awareness of GCTI screening. A survey showed that only 21.2% of general practitioners could provide correct follow-up guidance for patients with GCTI (34). Another reason is that PCR testing requires expensive equipment and specialized facilities, and its operation is complicated. Cost-benefit analysis may affect the decision-making process of hospital administrators. PCR testing was more available in general Western medicine hospitals than in specialized dermatological hospitals and maternal and child healthcare hospitals because PCR is widely used in the former to test for various infectious diseases (35–37). Lastly, GCTI is not included in the 39 statutory infectious diseases in the country (38). CT screening and reporting are routinely requested in designated STD monitoring sites rather than in all the medical institutions in China. Unlike syphilis and gonorrhea, CT screening is not prioritized in some medical institutions.

Various efforts are needed to improve the situation of GCTI control in Shandong province as well as the whole of China. First, the Chinese government must initiate CT screening plans among sexually active and high-risk groups, especially women under 30 years of age, female sex workers, and bisexual or homosexual men. In England, the implementation of the National Chlamydia Screening Programmers from 2003 to 2008 initially resulted in an astonishing increase in chlamydia diagnoses and reporting, and the number of infections has decreased since the program’s culmination (17,39). Second, an effective referral process and laboratory outsourcing services must be introduced into the primary and secondary hospitals where CT testing is unavailable. Finally, ad hoc surveys, rather than passive case reporting, are recommended for GCTI surveillance to avoid underestimating the severity of GCTI in China.

This study has several limitations. First, the survey was conducted in a single province in China and the hospitals were not randomly selected. Therefore, the results and conclusion should be interpreted with utmost care. Second, aside from the availability of CT testing, various factors may have affected the reporting and estimation of the CT prevalence. Further studies investigating other issues concerning GCTI control in Shandong province or even the whole of China are warranted.

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Conflict of interest None to declare.

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