Genital chlamydia trachomatis infection: an underestimated sexually transmitted disease in China

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Abstract

Background

Genital chlamydia trachomatis infection is one of the most prevalent sexually transmitted disease globally. The diagnosis and reporting of genital chlamydia trachomatis infection mainly rely on effective laboratory testing available. The prevalence of genital chlamydia trachomatis infection in China may be largely underestimated, based on the reported data.

Methods

A survey was conducted among hospitals provided clinical services for STD in Shandong Province in 2018. Basic information on the hospitals, type of laboratory tests provided and cases reported of GCTI were collected and analysed in SPSS 22.

Results

Among 456 hospitals surveyed, antigen testing, PCR testing, and either antigen or PCR testing were available among 200 (43.9%), 88 (19.3%) and 268 (58.8%) hospitals, respectively. PCR testing was more available among tertiary and secondary hospitals than primary hospitals ($X^2 = 28.560$, $P=0.000$). Significant differences were observed in the availability of antigen testing, PCR testing, and either antigen or PCR testing among different type of hospitals ($X^2 = 15.708$, $P=0.003$; $X^2 = 22.494$, $P=0.000$; $X^2 = 21.729$, $P=0.000$). In 2018, a total of 1532 cases of GCTI were reported in 99 hospitals. More cases were reported by tertiary and secondary hospitals than primary hospitals ($X^2 = 24.082$, $P=0.000$). The proportion of different kind of hospitals that reported case of GCTI cases was consistent with that of hospitals provided laboratory testing for GCTI.

Conclusion

The availability of laboratory testing for GCTI in Shandong province was poor, which may lead to underestimation of prevalence of GCTI. More effort needs to improve the availability of GCTI laboratory testing in order to effectively control of GCTI in Shandong province.

Background

Genital chlamydia trachomatis infection (GCTI) is a chronic inflammatory disease mainly caused by d-k type of chlamydia trachomatis (CT) through the infection of 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 will increase the risk of ectopic pregnancy and tubal factor infertility.[1-3] Additionally, GCTI increases the risk of acquiring HIV infection, ovarian cancer and cervical cancer.[4-8]

Early diagnosis of GCTI has an important clinical significance for early cure of symptomatic patients and elimination of asymptomatic infections. Screening and treatment of GCTI in early can decrease the incidence of PID.[9] Early diagnosis and treatment of GCTI has economic benefits in women less than 30 years old or with pregnancies.[10, 11] The Centers for Disease Control and Prevention in the USA recommends that pregnant women who are younger than 25 years or women who are older than 25 years and at increased risk for GCTI should be routinely screened for CT,[12] whereas the Public Health Agency in Canada recommends screening among all pregnant women.[13]

There are 130 million new cases were infected by CT worldwide aged 15–49 years in 2012.[14] GCTI is the most common sexually transmitted disease (STD) in Europe and the United States.[15, 16] In 2016, about 230,000 and 1.6 million cases were reported in the UK and the United States, with an incidence of nearly 351 per 100,000 population and 497 per 100,000 population, respectively.[17, 18] It was estimated that the incidence of GCTI could reach to 15%-20% in some regions.[19, 20] In populations actively screened, the positive rate was as high as 30.2%.[21] In contrast, reports on the prevalence of GCTI in China are limited.

Our recent study found that the prevalence of GCTI among general population in Shandong was 2.3% in females and 2.7% in males.[22] It was estimated that the prevalence of GCTI could be as high as 14.3% in some areas of China.[23] However, the reported prevalence of GCTI was 37 per 100,000 population in China in 2015,[24] which was much lower than that in Europe and the United States, where annual screening and treatment programmes for GCTI in young women were recommended.[12, 25] We suppose that the prevalence of GCTI in China may be largely underestimated, based on the reported data.

The reported prevalence of GCTI is closely related to screening programmes implemented. The diagnosis and reporting of GCTI mainly rely on effective laboratory testing available, because
50%-70% of GCTIs are asymptomatic.[26] It is necessary to understand the availability of CT laboratory testing and to evaluate its role in estimation of the prevalence of GCTI in China. Hospitals are in a unique position to deal with high risk population of STD, and are responsible for screening, diagnosing and reporting of GCTI. Therefore, we conducted a survey on availability of CT laboratory testing among hospitals provided STD clinical service in Shandong province in 2018.

Methods
Study objects
The study was conducted in Shandong province, eastern China, which is subdivided into 17 prefecture-level cities and 137 county-level units. A total of 2450 hospitals had been registered in the province by 2017, including 761 tertiary and secondary hospitals and 1689 primary hospitals; 1856 general western medicine hospitals, 48 specialized dermatological hospitals, 161 maternal and child health hospitals, 300 Chinese medicine hospitals and 85 other specialized hospitals; 863 public hospitals, and 1,587 private hospitals.[27] All hospitals provided clinical services for STDs in Shandong province were eligible for inclusion criteria of the survey.

Data collection and analysis
The survey was conducted in 2018. The basic information on the hospitals (level, type and affiliation) provided clinical services for STDs and types of laboratory testing for CT available were collected. A questionnaire was used for data collection. Health staff from the Centers for Diseases Control and Prevention at county-level visited each hospital in their respective jurisdictions and filled in the questionnaires. The records of cases of GCTI reported in Shandong in 2018 were downloaded from the China Information System for Disease Control and Prevention (CISDCP). Data collected were entered into Microsoft Excel for Windows (2012) and analysed in SPSS (version 22). The percentages of each laboratory testing for CT provided and GCTI cases reported among hospitals by level, type and affiliation were analysed and compared. Descriptive analysis and Chi-square were used for statistical analysis. P values < 0.05 was considered statistically significant.

Result
Availability of CT laboratory testing in hospitals of Shandong province in 2018
Among 2450 hospitals registered in the province by 2017, clinical service for STD were available in 496 (20.24%) hospitals. A total of 456 valid questionnaires were collected from 116(25.4%) tertiary
and secondary hospitals, and 340 (74.6%) primary hospitals; 229 (50.2%) general western medicine hospitals, 37 (8.1%) specialized dermatological hospitals, 95 (20.8%) maternal and child health hospitals, 78 (17.1%) Chinese medicine hospitals, and 17 (3.7%) other specialized hospitals; 419 (91.9%) public hospitals and 37 (8.1%) private hospitals.

Antigen and PCR testing were available among 200 (43.9%) and 88 (19.3%) hospitals, respectively. No significant differences were observed in the availability of antigen testing among hospitals at different levels. PCR testing was more available in tertiary and secondary hospitals than primary hospitals ($X^2 = 28.560, P = 0.000$). Significant differences were observed in the availability of antigen testing and PCR testing among different type of hospitals ($X^2 = 15.708, P = 0.003; X^2 = 22.494, P = 0.000$). Antigen testing was more available among specialized dermatological hospitals than general western medicine hospitals ($X^2 = 11.997, P = 0.001$), maternal and child health hospitals ($X^2 = 8.830, P = 0.003$), Chinese medicine hospitals ($X^2 = 14.824, P = 0.000$), and other specialized hospitals ($X^2 = 5.050, P = 0.025$). PCR testing was more available among general western medicine hospitals than specialized dermatological hospitals ($X^2 = 8.186, P = 0.004$), and maternal and child health hospitals ($X^2 = 10.638, P = 0.001$). No significant differences were observed in the availability of antigen testing and PCR testing among hospitals with different affiliations. (Table 1)

|                     | Number of hospitals in 2017 | Surveyed in 2018 (n,% ) | Antigen testing (n,% ) | PCR testing (n,% ) |
|---------------------|-----------------------------|--------------------------|-------------------------|-------------------|
| Total               | 2450                        | 456 (18.6)               | 200 (43.9)              | 88 (19.3)         |
| Level               |                             |                          |                         |                   |
| Tertiary and Secondary hospitals | 761                      | 116 (15.2)               | 58 (50.0)               | 42 (36.2)         |
| Primary hospitals   | 1689                        | 340 (20.1)               | 142 (41.8)              | 46 (13.5)         |
| X^2, P              |                             |                          | 2.382, 0.123            | 28.560, 0.000     |
| Type                |                             |                          |                         |                   |
| General western medicine hospitals | 1856                  | 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 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)           |
| X^2, P              |                             |                          | 15.708, 0.000           | 22.494, 0.000     |
| Affiliation         |                             |                          |                         |                   |
| Public hospitals    | 863                         | 419 (48.6)               | 184 (43.9)              | 79 (18.9)         |
| Private hospitals   | 1587                        | 37 (2.3)                 | 16 (43.2)               | 9 (24.3)          |
| X^2, P              |                             |                          | 0.006, 0.937            | 0.653, 0.419      |
Either antigen or PCR testing was available among 268 (58.8%) hospitals. It was more available in tertiary and secondary hospitals than primary hospitals ($X^2 = 22.728, P = 0.000$). A significant difference was observed in the availability of either antigen or PCR testing among different type of hospitals ($X^2 = 21.729, P = 0.000$). It was more available among general western medicine hospitals than maternal and child health hospitals ($X^2 = 5.139, P = 0.023$), Chinese medicine hospitals ($X^2 = 9.880, P = 0.002$), and other specialized hospitals ($X^2 = 6.018, P = 0.014$). It was more available among specialized dermatological hospitals than maternal and child health hospitals ($X^2 = 7.912, P = 0.005$), Chinese medicine hospitals ($X^2 = 11.416, P = 0.001$), and other specialized hospitals ($X^2 = 9.418, P = 0.002$). No significant differences were observed in the availability of either antigen or PCR testing in hospitals with different affiliations. (Table 2)

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

| Categories                  | Hospitals with antigen or PCR testing 2018(n, %) | Hospitals with case reporting (n, %) |
|-----------------------------|-------------------------------------------------|------------------------------------|
| **Total**                   | 268(58.8)                                       | 99(21.7)                           |
| **Level**                   |                                                 |                                    |
| Tertiary and Secondary hospitals | 90(77.6)                                       | 44(37.9)                           |
| Primary hospitals           | 178(52.4)                                       | 55(30.9)                           |
| $X^2$, 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 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)                             |
| $X^2$, P                    | 21.729, 0.000                                   | 20.604, 0.000(Likelihood)          |
| **Affiliation**             |                                                 |                                    |
| Public hospitals            | 244(58.2)                                       | 94(22.4)                           |
| Private hospitals           | 24(64.9)                                        | 5(13.5)                            |
| $X^2$, P                    | 0.617, 0.432                                    | 1.592, 0.207                       |

Distribution of GCTI cases reported among different hospitals in Shandong province in 2018

The proportion of different kind of hospitals that reported case of GCTI cases was consistent with that of hospitals provided laboratory testing for GCTI. In 2018, a total of 1532 GCTI cases were reported in 99 hospitals, including 44(37.9%) tertiary and secondary hospitals and 55(30.9%) primary hospitals; 60 (26.2%) general western medicine hospitals, 15(40.5%) specialized dermatological hospitals, 13(13.7%) maternal and child health hospitals, 10(12.8%) Chinese medicine hospitals and 1(5.9%)
other specialized hospitals; 94(22.4%) public hospitals and 5(13.5%) private hospitals.

More cases were reported by tertiary and secondary hospitals than primary hospitals ($X^2 = 24.082, P = 0.000$). A significant difference was observed in distribution of case reporting among different type of hospitals ($X^2 = 20.604, P = 0.000$). More cases were reported among general western medicine hospitals than Chinese medicine hospitals ($X^2 = 5.918, P = 0.015$) and other specialized hospitals ($P = 0.079$, fisher). More cases were reported among specialized dermatological hospitals than maternal and child health hospitals ($X^2 = 11.492, P = 0.001$), Chinese medicine hospitals ($X^2 = 11.334, P = 0.001$) and other specialized hospitals ($X^2 = 6.710, P = 0.010$). (Table 2)

Discussion:
In this study, we found that the availability of CT laboratory testing was still poor in different hospitals in China. In 2018, only one fifth (496/2450) of hospitals in Shandong reported STD cases, which meant that a few hospitals could provide related laboratory testing and STD clinical services. Among those provided STD clinical services, more than half could not provide antigen testing for CT, more than four fifths could not provide PCR testing, and more than two fifths could provide neither antigen nor PCR testing, indicating that GCTI cases in those hospitals were not correctly diagnosed and reported, which meant that a large number of GCTI cases were not screened and reported, and the real situation of GCTI epidemic in China may be largely underestimated according to surveillance data of case reporting.

We supposed that GCTI case reporting was largely related to laboratory testing for CT provided in hospitals. To confirm the hypothesis, we compared the proportion of different kind of hospitals reported GCTI cases with that of hospitals provided laboratory testing for CT, and found that they were completely consistent as expected. In other words, the reported incidence of GCTI is determined by the availability of laboratory testing and can not reflect the real disease burden of GCTI in China.

We found that antigen testing was more available than PCR in Shandong province, although its sensitivity is as low as 65%-75\%.[28] The advantages of convenient operation, cheap and available reagents and rapid reporting make it an attractive option in primary hospitals and counterbalance the
impact of its lower sensitivity. PCR testing, with sensitivity and specificity as high as 97% and 100% respectively,[29, 30] was strongly recommended for diagnosis of CT,[31-33] but was seldom used in Chinese hospitals.

From the point of view of programmes supervisors for STD control, we suppose that one of the main reasons for the low availability of GCTI testing is lack training of medical staffs, which leads to inadequate knowledge of the disease and low awareness of GCTI screening. A survey showed that only 21.2% of general practitioners were able to provide correct follow-up guidance for patients with GCTI.[34] Another reason is expensive equipments needed and complicated process for PCR testing. Cost-benefit analysis may affect decision making of hospitals. We found that PCR testing was more available among general western medicine hospitals than specialized dermatological hospitals and maternal and child health hospitals because PCR was widely used as an auxiliary diagnosis for various infectious diseases including CT.[35-37] Lastly, GCTI is not included in 39 statutory infectious diseases,[38] and CT screening and reporting are routinely requested in pointed STD monitoring sites rather than all medical institutions in China. CT screening is not given priority in some medical institutions.

Some efforts are needed to improve the situation of GCTI control in Shandong province as well as in China. First, the governments need to attach great importance to initiate CT screening plans among sexually active and high-risk groups, especially among women under 30 years old, female sex workers and man who have sex with man. National Chlamydia Screening Programmes (NCSP) was rolled out between 2003 and 2008 in England, which resulted in a large increase of chlamydia diagnoses and reporting from 2008 onwards at first and a reduction in numbers of infections then.[17, 39] Second, urine testing for CT by PCR or ligase chain reaction (LCR) needs to be promoted in tertiary and secondary hospitals. One of the main reasons for the poor availability of PCR tests for GCTI is inconvenient swab specimen collection. Urine testing has a high sensitivity and specificity as well as using swab specimens.[40] Third, effective referral service and laboratory outsourcing service are suggested to be introduced among primary hospitals where CT testing are unavailable. Fourth, ad hoc survey rather than passive case reporting is recommended for GCTI surveillance in order of
avoiding underestimation of the epidemic situation. 

There are some limitations in the study. First, the investigation was conducted in a province of China, and generalization of the results and referring of the conclusion should be careful. Second, many factors may affect reporting and estimation of CT prevalence beside availability of CT testing, and more issues concerning GCTI control are need to be addressed in China in further studies. 

Conclusion 

The availability of laboratory testing for GCTI in Shandong province was poor, which may lead to underestimation of prevalence of GCTI. More effort needs to improve the availability of GCTI laboratory testing in order to effectively control of GCTI in Shandong province.

Abbreviations 

GCTI: Genital chlamydia trachomatis infection; GCT: Genital chlamydia trachomatis; CT: chlamydia trachomatis; PID: pelvic inflammatory disease; STD: sexually transmitted disease; CISDCP: China Information System for Disease Control and Prevention; NCSP: National Chlamydia Screening Programmes; LCR: ligase chain reaction.

Declarations 

Ethical approval and consent to participate This study was approved by the institutional review board at the Shandong Provincial Institute of Dermatology and Venereology. We received permissions to access data from the China Information System for Disease Control and Prevention (CISDCP).

Consent for publication Not Applicable.

Availability of data and materials The datasets used and analysed during the current study are available from the corresponding author on reasonable request.

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. YG, QC, ZR and FL contributed to collecting the data, the interpretation of the results and critical revision of the
manuscript for important intellectual content and approved the final version of the manuscript. All authors have read and approved the final manuscript. DL is the study guarantors.

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