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RESEARCH ARTICLE

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Comparison and evaluation of Abbott chemiluminescent microparticle immunoassay and ChIVD light-initiated chemiluminescent assay in the detection of *Treponema pallidum* antibody

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Abstract

Background: Laboratory tests play an important role in the diagnosis of syphilis. This study aimed to compare and assess the performance of the Abbott chemiluminescent microparticle immunoassay (CMIA) and the ChIVD light-initiated chemiluminescent assay (LICA) in the detection of *Treponema pallidum* (*TP*) antibody.

Methods: A total of 10 498 serum samples were detected with two assays, and the *Treponema pallidum* particle agglutination assay (TPPA) and recombinant immunoblot assay (RIBA) methods were used for confirmation. The sensitivity, specificity, positive predictive value, and negative predictive value of the Abbott CMIA and ChIVD LICA were calculated. The coincidence rate between two assays was also evaluated. The causes of false positive and false negative of two assays were studied.

Results: For the Abbott CMIA and ChIVD LICA, the sensitivity was 94.44% and 98.15%, the specificity was 99.89% and 99.81%, the positive predictive value was 93.29% and 88.83%, and the negative predictive value was 99.91% and 99.97%, respectively. The coincidence rate between Abbott CMIA and ChIVD LICA was 99.26%, and κ value was .790. The disease of infertility, hypertensive disease, liver disease, and cancer were the common causes of false positive in both assays, while infertility was also the main reason lead to false negative.

Conclusion: Our results demonstrated that the Abbott CMIA and ChIVD LICA generally had high sensitivity and specificity and therefore may be suitable for the detection of *TP* antibody and screening for syphilis.

KEYWORDS

Abbott chemiluminescent microparticle immunoassay, ChIVD light-initiated chemiluminescent assay, recombinant immunoblot assay, syphilis, *Treponema pallidum*, *Treponema pallidum* particle agglutination

Xiaohui Chen and Ruifeng Yang are contributed equally to this work.

1 | INTRODUCTION

Syphilis is a sexually transmitted disease caused by *Treponema pallidum* (*TP*) which can be spread by sexual contact, blood transfusion, and vertical transmission. Syphilis remains a significant health problem in the world. In recent years, the incidence of syphilis in China is rising. The number of syphilis increased from 135 210 in 2005 to 441 818 in 2014 and the incidence increased faster than 27 other Class B notifiable disease, ranking the third in proportion in China.[1]

Syphilis can cause neurosyphilis, cardiovascular, multisystem damage, and finally even death. So, timely diagnosis and treatment of syphilis patients is important.[2] At present, the diagnosis of syphilis is based on the clinical manifestations and laboratory serology tests. The serological tests provide a presumptive diagnosis for syphilis.[3] It can be divided into nontreponemal and treponemal tests. The nontreponemal tests mainly include rapid plasma reagin (RPR), Venereal Disease Research Laboratory (VDRL) test, and Tolulized Red Unheated Serum test (TRUST). However, these tests lack the sensitivity and specificity in different stages of syphilis and in many other clinical situations, such as pregnancy and autoimmune disease.[4,5] If the result was positive, then a confirmed treponemal test such as treponema pallidum particle agglutination (TPPA) was performed. In recent years, more and more laboratories have applied treponemal immunoassays, such as enzyme immunoassay (EIA), chemiluminescence immunoassay (CIA), and TPPA. The sensitivity and specificity of these assays are high.[6,7] But there is no accepted gold standard method in syphilis detection.[3]

The chemiluminescent microparticle immunoassay (CMIA) and the light-initiated chemiluminescent assay (LICA) are two methods for syphilis detection. The CMIA has been applied in many laboratories, while the LICA is a new method derived from the luminescent oxygen channeling immunoassay (LOCI) and it has been used for detection sIgE against egg white allergens, 5-α-dihydrotestosterone (5-α-DHT), allergen-specific IgG4 (sIgG4) and estradiol (E2) and exhibited satisfactory performance with rapid, high sensitivity, excellent reproducibility and broad analytical range.[8-11] But the performance of LICA in the detection of *TP* antibody remains unknown.

In this study, the performance of the Abbott CMIA and ChIVD LICA in the detection of *TP* antibody were evaluated and compared. Furthermore, the main causes of the false-positive and false-negative results of Abbott CMIA and ChIVD LICA were analyzed.

2 | MATERIALS AND METHODS

2.1 | Patients and serum samples

A total of 10 498 patients for routine *TP* antibody testing in Peking University Third Hospital from June 2018 to September 2018 were enrolled in this study. The study was approved by the Ethics Committee of Peking University Third Hospital.

2.2 | Serum samples testing

All the fresh serum samples were tested in Architect i2000SR (Abbott) and LICA 500 (ChIVD). Residual samples were preserved in −80°C condition for further use. The results were expressed with sample-to-cutoff ratio (S/CO), the S/CO <1.0 indicating a negative result and S/CO ≥1.0 indicating a positive result. The inconsistent results between the two assays were confirmed by TPPA (Fujirebio) and RIBA (Mikrogen Diagnostic). The results were expressed as negative, indeterminate, and positive. All tests were performed following the manufacturer's instructions.

2.2.1 | Architect i2000SR Syphilis *TP* test

The Abbott CMIA based on paramagnetic microparticle chemiluminescent technology. The reaction principle is as follows: Microparticle is coated with three recombinant antigens (Ag) (TpN15, TpN17, TpN47) to band IgG and IgM antibodies specific for *TP*. After incubating the microparticles with serum (30 μL), the acridinium-labeled anti-human IgG/IgM antibody conjugates were added, and chemiluminescent reaction was measured.

2.2.2 | LICA 500 Syphilis *TP* test

The principle of ChIVD LICA is based on two types of nanoparticles with the diameter of 200 nm. One is a chemiluminescent nanoparticle which was coated with *TP*-Ag (TpN15, TpN17, TpN47) and the other contains a streptavidin-coated photosensitizer which binds to bioavidin labeled *TP*-Ag, and after incubating them with serum (25 μL), these *TP*-Ag can band IgG and IgM antibodies specific for *TP* and form Ag-Ab-Ag complex. Under the excitation of the 680 nm laser, ionic oxygen transfers between two particles, producing chemiluminescent emission. By single photon counter and mathematical fitting, the photon number is converted to the target molecule concentration.

2.2.3 | *Treponema pallidum* particle agglutination assay

The TPPA test is based on the agglutination of colored gelatin particles that coated with *TP* (Nichols Strain) antigen. After incubating the particle with 25 μL serum samples, it can produce particle agglutination.

2.2.4 | Recombinant immunoblot assay

The recomLine Treponema IgG and IgM is an immunoassay for the qualitative determination of IgG and IgM antibodies to *TP*. Nitrocellulose membrane strips containing Tp47, TmpA, Tp257,

Tp453, Tp17, and Tp15 antigens were incubated with 20 μL serum samples, then incubated with anti-human IgG and/or IgM which are coupled to horseradish peroxidase. After addition of the substrate solution, a dark band will appear on the strip at the corresponding point if an antigen-antibody reaction. The band intensity was assessed by comparison with the intensity of the cutoff control band. The test was considered as positive when at least two of six bands were recognized as reactive.

2.3 | Statistical analysis

Statistical analysis was performed using statistical software SPSS 17.0 (SPSS Inc). The sensitivity, specificity, negative predictive value, positive predictive value, and the coincidence rate were calculated. Kappa (κ) test was conducted to evaluate the consistency between the two assays. The κ value of .41-.60 indicates moderate agreement, .61-.80 indicates substantial agreement, and .81-1.00 indicates almost perfect agreement.

3 | RESULTS

3.1 | Serum samples test and final diagnosis

A total of 10 498 serum samples were tested with two assays, 4473 of which were male and 6025 were female, and the ages ranged from 18 to 100 years old. Overall, the results of 10 420 samples were consistent between the Abbott CMIA and ChIVD LICA, while 78 samples were inconsistent. The inconsistent results were confirmed by TPPA and RIBA, which showed 29 were negative, 1 was positive and 48 were inconsistent. We used the RIBA as the reference method if the TPPA and RIBA assays results inconsistent. The result which the RIBA showed indeterminate was excluded. The testing algorithms for *TP* antibody detection and diagnose is shown by the flow diagram in Figure 1.

3.2 | Evaluation of Abbott CMIA and ChIVD LICA based on the diagnosis

The sensitivity, specificity, positive predictive value, and negative predictive value of the Abbott CMIA were 94.44%, 99.89%, 93.29%, and 99.91%, respectively. The ChIVD LICA was 98.15%, 99.81%, 88.83%, and 99.97%, respectively (Table 1).

3.3 | Consistency of Abbott CMIA and ChIVD LICA

10 270/10 498 results were negative, and 150/10 498 were positive by both assays (Table 2). The negative coincidence rate between Abbott CMIA and ChIVD LICA was 99.71%, and the positive coincidence rate was 75.76%. The coincidence rate was 99.26%, and κ value was .790, indicating a substantial agreement between two assays.

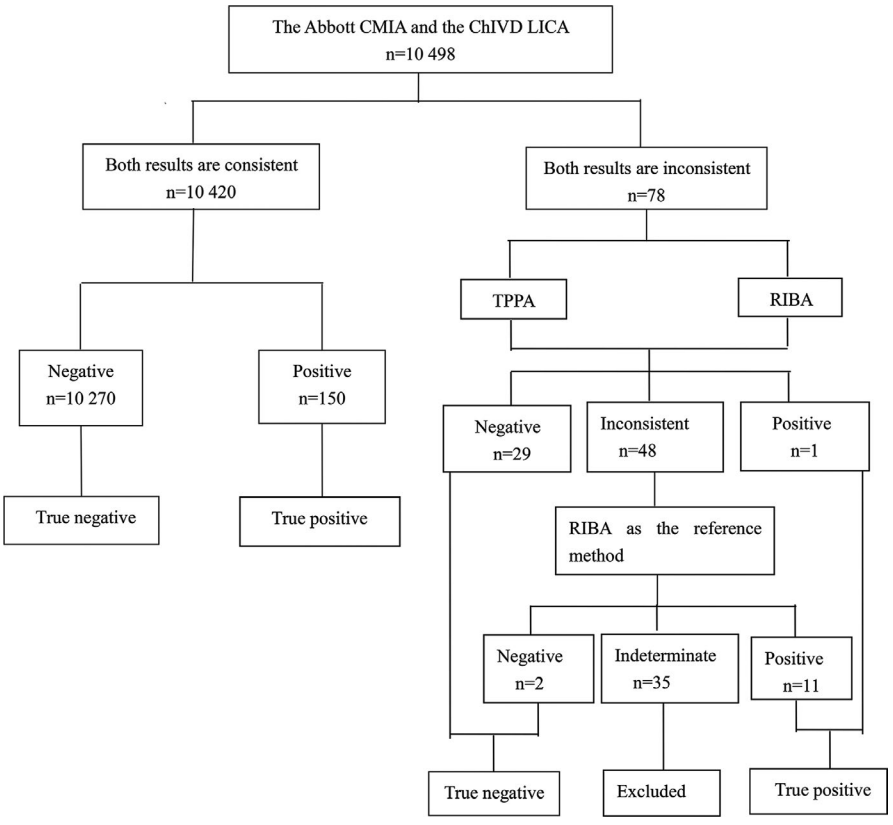

FIGURE 1 Testing algorithms of Treponema pallidum antibody detection. Abbreviations: CMIA, chemiluminescent microparticle immunoassay; LICA, light-initiated chemiluminescent assay; RIBA, recombinant immunoblot assay; TPPA, treponema pallidum particle agglutination

TABLE 1 Evaluation of Abbott CMIA and ChIVD LICA with the diagnose

	Diagnose (n)					
	Positive	Negative	Sensitivity	Specificity	PPV	NPV
Abbott CMIA						
Positive	153	11	94.44%	99.89%	93.29%	99.91%
Negative	9	10 290				
ChIVD LICA						
Positive	159	20	98.15%	99.81%	88.83%	99.97%
Negative	3	10 281				

Abbreviations: CMIA, chemiluminescent microparticle immunoassay; LICA, light-initiated chemiluminescent assay; NPV, negative predictive value; PPV, positive predictive value.

3.4 | Analysis of the samples with false-positive results

The incidence of false positive of Abbott CMIA was associated with 9 different diseases in the 11 samples, 72.7% (8/11) of them were male, and 36.4% (4/11) were aged people (≥60 years old). However, the number of false positive in male and female of ChIVD LICA was equal and associated with 12 different diseases in the 20 samples, 25% (5/20) of them were aged people. The false-positive results of Abbott CMIA mainly occurred in patients with infertility and hypertensive disease (Table 3). Compared with Abbott CMIA, infertility, lumbar spinal stenosis, liver disease, and cancer were the key factors that cause the false-positive results of ChIVD LICA (Table 4).

3.5 | Analysis of the samples with false-negative results

There were 8 different diseases involved in the false-negative results of Abbott CMIA and 77.8% (7/9) was male and 55.6% (5/9) were aged people. However, the number of false-negative results of ChIVD LICA was 3 and they were all female and 33.3% (1/3) were aged people. The major disease that causes false-negative of Abbott CMIA was hypertensive disease and infertility (Table 5), while the infertility was also the factor for the false negative of ChIVD LICA (Table 6).

TABLE 2 The comparison of Abbott CMIA and ChIVD LICA

		Abbott CMIA		
		Positive (n)	Negative (n)	Total (n)
ChIVD LICA	Positive (n)	150	30	180
	Negative (n)	48	10 270	10 318
	Total (n)	198	10 300	10 498

Abbreviations: CMIA, chemiluminescent microparticle immunoassay; LICA, light-initiated chemiluminescent assay.

4 | DISCUSSION

In recent years, the number of syphilis has been increasing. As a notifiable disease, it can be cured as long as being diagnosed early. The prompt diagnosis and treatment in early syphilis can not only prevent transmission but also prevent the serious consequences.[6] So, a rapid and accurate assay for syphilis diagnosis is important. Despite the nontreponemal test is easy to perform and cheaper, but the results are susceptible to many factors, they are commonly used to determine serological activity and to monitor the therapeutic effects.[12] However, the treponemal tests have been found to show superior performance than nontreponemal test in the detection of *TP* antibody.[13]

The Abbott CMIA has been widely used to detect *TP* antibody in clinical laboratories as the advantage of automation, higher throughput, good sensitivity, and specificity. A multicenter report involved 13 independent laboratories in 10 different regions in China reported that the sensitivity of Abbott CMIA in detect *TP* antibody was 98.26% and specificity was 99.74%.[14] Another study containing 2420 samples showed that the sensitivity and specificity of Abbott CMIA were 98.80% and 99.58%.[15] In our study, the Abbott CMIA

TABLE 3 The characteristics of Abbott CMIA false positive

Characteristic	False positive (n)	Male (n)	Female (n)
Male infertility	2	0	2
Hypertensive disease	2	2	0
Female infertility	1	1	0
Spinal cord injury	1	1	0
Retinal detachment	1	1	0
Lung cancer	1	1	0
HBV	1	0	1
Cirrhosis	1	1	0
Chest pain	1	1	0
Total	11	8	3

Abbreviations: CMIA, chemiluminescent microparticle immunoassay; HBV, hepatitis B virus.

TABLE 4 The characteristics of ChIVD LICA false positive

Characteristic	False positive (n)	Male (n)	Female (n)
Male infertility	5	5	0
Female infertility	4	0	4
Lumbar spinal stenosis	2	0	2
HBV	1	1	0
HCV	1	0	1
Prostate cancer	1	1	0
Skin tumor	1	0	1
Non-Hodgkin lymphoma	1	1	0
Coronary heart disease	1	0	1
Hypertensive disease	1	1	0
pregnancy	1	0	1
Cervical spondylosis	1	1	0
Total	20	10	10

Abbreviations: HBV, hepatitis B virus; HCV, hepatitis C virus; LICA, light-initiated chemiluminescent assay.

TABLE 5 The characteristics of Abbott CMIA false negative

Characteristic	False negative (n)	Male (n)	Female (n)
Hypertensive disease	2	1	1
Male infertility	1	1	0
Female infertility	1	0	1
Ligament rupture	1	1	0
Hernia	1	1	0
Lumbar spinal stenosis	1	1	0
Cataract	1	1	0
Diabetes	1	1	0
Total	9	7	2

Abbreviation: CMIA, chemiluminescent microparticle immunoassay.

TABLE 6 The characteristics of ChIVD LICA false negative

Characteristic	False negative (n)	Male (n)	Female (n)
Female infertility	2	0	2
Gastric cancer	1	0	1
Total	3	0	3

Abbreviation: LICA, light-initiated chemiluminescent assay.

demonstrated the sensitivity and specificity amounted to 94.44% and 99.89% by using the RIBA as the final confirmatory test. A study conducted by Tao C et al[14] showed the positive predictive value as 88.25% and the negative predictive value as 99.97%; so compared with it, our positive predictive value was superior but the negative predictive value was lesser. The difference may be attributed to different populations.

Different from CMIA, LICA requires no washing steps. Despite the LICA system has been developed, the performance of LICA in detecting *TP* antibody has not been reported previously. The sensitivity, specificity, positive predictive value, and negative predictive value of ChIVD LICA in detection *TP* antibody were 98.15%, 99.81%, 88.83%, and 99.97% in our study, which were similar to the results of Abbott CMIA reported in previous study.[14] So in the present study, the sensitivity and negative predictive value of ChIVD LICA were greater than Abbott CMIA, while the specificity and positive predictive value of ChIVD LICA were lesser than Abbott CMIA.

In the present study, the negative coincidence rate between Abbott CMIA and ChIVD LICA can reach to 99.71%, but the positive coincidence rate was only 75.76% due to the higher false-positive rate of ChIVD LICA. In order to study and compare the causes of false-positive and false-negative results of the two assays, we also analyzed these results. In Abbott CMIA, the higher incidence of false positive mainly occurred in people with pregnancy, aged, tumor, dialysis, and autoimmune disease, it may be anti-lipid antibodies or syphilis cross-antigen in these patients,[16,17] while the influence of these factors on the results of LICA has not been reported. It is reported that the test result of LICA may be affected by a few substances at higher concentrations such as severe hemolysis but cannot affected by hemoglobin, bilirubin, lipid, ascorbic acid, and biotin at concentrations that might be expected in a routine clinical laboratory settings.[18] In our study, the aged people also accounted for a large proportion in the false-positive results in both two assays. The infertility and hypertensive disease were the main causes lead to false positive in Abbott CMIA, in addition, cancer and liver disease can also lead to false positive. In the ChIVD LICA, infertility also the main reason, lumbar spinal stenosis, cancer, and liver disease accounted for a large proportion. In the disease that causes the false-negative results of two assays, the infertility was also the major reason. The proportion of male is higher in Abbott CMIA while the number of female and male in the false-positive results of ChIVD LICA is equal, and all of them were inconsistent with previous studies which showed it tend to be more prevalent in women than men.[5,19] The false-negative results were mainly male in the Abbott CMIA but female in the ChIVD LICA. The difference of our results between previous reports maybe the number of false positive and false negative is smaller, and a study of large sample size is needed to validate our results.

This study has several limitations. Firstly, there were no syphilis stages of the true positive because of insufficient information, so the sensitivity and specificity of Abbott CMIA and ChIVD LICA in different stages cannot be analyzed. Secondly, the reasons of false positive and false negative of two assays were might not represent the true situation because the sample size was small. If the sample size is increased, the results will be more representative.

5 | CONCLUSION

In conclusion, our study demonstrated the Abbott CMIA and ChIVD LICA generally have the high levels of sensitivity and specificity and showed a substantial agreement, so they may be suitable for the detection of *TP* antibody and screening for syphilis.

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