Evaluation of Chagas RDTs Shows High Accuracy in Endemic Region

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NEW YORK – A head-to-head evaluation of two commercial rapid diagnostic tests to screen for the pathogens that cause Chagas disease has shown high accuracy in an endemic region. Researchers comparing tests from Chembio Diagnostic Systems and InBios International noted that the two tests worked well under very rugged field-testing conditions and might someday be useful as diagnostic tools, in addition to their use for rapid infection screening.

Chagas disease results from a bite from insect vectors infected with *Trypansoma cruzi*, a single-celled protozoa parasite. The vector species is triatomine bugs, also called "kissing bugs" because they suck blood from people's faces while they are sleeping. Infected kissing bugs excrete the protozoan parasites in feces while biting, and the itch of the bite can cause a person to rub the parasites into the wound or into an eye, potentially leading to a chronic infection.

According to the World Health Organization, as many as 7 million people are infected with *T. cruzi*, primarily in Latin America. Like related *Trypanosoma* protist parasites which cause African sleeping sickness and Leishmaniasis, *T. cruzi* infection can be carried for decades with serious health consequences.

In the short term, in can cause a tell-tale swelling of the eye where the parasite entered, known as Romaña's sign. If treated early, the infection is easily cured. Chronic infection is not so easily treated, however. It also leads to a buildup of the parasite in tissues, with cardiac complications in 30 percent of infections, digestive problems such as enlargement of the esophagus or colon in another 10 percent of cases, and an increased likelihood of sudden death due to heart failure.

The WHO has noted that a tremendous reservoir of infected animals, which in turn sustain kissing bug infection, means that eradication of *T. cruzi* is nearly impossible, so controlling transmission and providing early healthcare access is critical.

To these ends, a study published last month in *PLoS Neglected Tropical Diseases* compared the Chembio Chagas Stat-Pak and InBios Chagas Detect Plus tests, with a test called a WL-Check RDT kit from Wiener Laboratories used in cases of discordance.

In samples from 700 untreated volunteers at two Bolivian hospitals the combined tests showed 98 percent sensitivity and 96 percent specificity when compared to ELISA testing.

According to Julio Alonso-Padilla, a researcher at the Barcelona Institute for Global Health in Spain and corresponding author on the study, the research was motivated by the fact that currently available diagnostics are not adapted for the conditions found in many highly endemic regions, where poor access to diagnosis is hindering treatment.

In current practices, diagnosing chronic Chagas requires a patient to have two different conventional ELISA tests with positive results, Alonso-Padilla said in an email, and a third test is needed if the two tests have different results.

The ELISA tests also are usually run in batches, which in practice delays the return of results to patients by several weeks, he said.

On the other hand, RDTs "allow an almost immediate turnaround of results." And, they also use a tiny volume of blood, so there is no need for a blood draw, or a lab, or any additional expertise or equipment, Alonso-Padilla said.

The group chose to evaluate the Chembio and InBios tests specifically because it had used them before in a study performed as part of a program called the Platform for Integral Care of Chagas Disease in Sucre, Bolivia, and "They had a very good performance," Alonso-Padilla said.

In terms of percentage of disease prevalence, Bolivia is the country most affected by Chagas disease in the world, and within Bolivia, the Chaco region where the study was performed registers some of the highest prevalence rates, he explained.

Alonso-Padillo said that ISGlobal has been working in six locations in Bolivia since 2008 in collaboration with local partners, and over 180,000 people have been screened for *T. cruzi* infection. "Almost 58,000 were reported as positives, and more than 18,500 have now been treated," he said.

In the *PLoS NTD* study, 44 percent of people screened for *T. cruzi* were seropositive. Alonso-Padilla said this rate is higher than expected, which may have been due to high active vector transmission in the Chaco region and the fact that people suspecting they might be infected may have been drawn to the testing.

The sensitivity and specificity of the two RDTs was quite high, and the two tests were 93 percent concordant. The group found that the Chembio test performed slightly better in this particular population, with a 98 percent agreement with ELISAs, and that it was also easier to use in the field, Alonso-Padilla said.

"The main conclusion of the present work is that we saw a very good performance of the RDTs using them outdoors, in the form of highly-demanding field screening campaigns," he emphasized.

Improvements in immunoassay design have led to some surprising results recently in terms of test accuracy. Alonso-Padilla said that the Chagas tests are mostly based on recombinant antigens, even on antigens that combine epitopes from many different parasite antigens. "The use of these highly sensitive and specific antigens might be one of the reasons they have improved their performance," he said.

In an email, Wendy Bagnato, senior marketing and sales manager at InBios, concurred. "We believe careful selection of target antigens and assay conditions combined with high prevalence setting might be the reason for high accuracy" seen in this study, she said.

Regarding RDTs performance in this particular study, although more studies in regions with other epidemiological characteristics are required, there is agreement in the research community that higher levels of prevalence favor test accuracy, Alonso-Padilla added. In addition, it is possible that the antigens the RDTs are based on happen to nicely mirror those from circulating parasite strains in Bolivia.

"It is known that *T. cruzi* has a very wide antigenic profile and there are diagnostics that work very well in some regions but fail in others due to the different parasite genotypes predominant in each area," Alonso-Padilla said.

Company executives for Chembio could not be reached for comment, but according to Alonso-Padilla, the company's test is used for primary screening in Bolivia, so it is already readily available in the country. And, the test is supplied with a sample collector and dispenser device. "This was a major advantage over other RDTs that require micropipettes for their use," he said.

Bagnato noted that while InBios' US Food and Drug Administration-cleared kit does not include sample collection devices, customers can certainly request that they be included for a small additional cost.

Furthermore, Bagnato noted that Chagas is a very important product in the InBios infectious disease portfolio that was developed through National Institutes of Health funding. "We are currently marketing our FDA-cleared test in the US and expanding this business worldwide and [we] are also developing an ELISA," she said.

The firm's prospective and retrospective studies for FDA clearance were performed at a low-risk endemic site in Chile and high-risk endemic site in Bolivia, where the test demonstrated overall greater than 95 percent sensitivity and specificity, Bagnato said. The test has also recently been evaluated for testing of blood donor specimens, also showing high sensitivity.

Generalizing RDTs for use in confirmatory diagnosis of the infection, not just as primary screening tools for Chagas disease, should now be further explored, Alonso-Padilla said. The specificity of the tests also needs to be evaluated in areas where co-infection of Chagas and Leishmaniasis is a possibility. That said, "there are ample areas of Latin America where both infections are endemic and the implementation of RDTs could benefit both."

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