Journal of Tropical Diseases
ISSN: 2329-891X

Gupte and Kaur, J Trop Dis 2015, 4:1
DOI: 10.472/2329-891X.1000e109

Editorial Open Access

# Diagnostic Approach to Brucellosis

**Satish Gupte* and Tanveer Kaur**

*Department of Microbiology, Gian Sagar Medical College and Hospital, Rajpura, India*

## Editorial

Brucellosis is a worldwide zoonosis with a high degree of morbidity in humans. According to WHO data about 500,000 cases of this disease are registered in the world every year [1,2]. The presence of brucellosis in India was first established early in the previous century and since then has been reported from almost all states [3]. It is mainly transmitted from cattle, sheep, goats, pigs and camels through direct contact with blood, placenta, fetuses or uterine secretions, or through consumption of contaminated raw animal products (especially unpasteurized milk and soft cheese). Furthermore, brucellosis is the most common bacterial laboratory-acquired infection worldwide [4]. The disease primarily presents as fever of unknown origin with multiple clinical signs and symptoms. Patients regularly suffer serious focal complications such as spondylitis, neurobrucellosis or *Brucella* endocarditis [5]. The clinical picture is not specific and laboratory testing should support the diagnosis. Presumptive diagnosis of brucellosis can be made by the use of several serological tests to *Brucella* antibodies, but the "gold standard" remains isolation and identification of the bacterium. Despite the vigorous attempt for more than one century to come up with a definitive diagnostic technique for brucellosis, diagnosis still relies on the combination of several tests to avoid false negative results [6]. Certain newer molecular techniques have also been introduced for the diagnosis of brucellosis.

Among serological tests, Serum Agglutination Test (SAT) suffers from high false-negative rates in complicated and chronic cases. The Rose Bengal Plate Agglutination test (RBT) is a rapid test which was designed originally for screening use in veterinary medicine, but is now often used for the diagnosis of human brucellosis [7]. Its high sensitivity, ease and speed of use, as well as its low cost, have made it very popular in hospital emergency departments for the diagnosis of febrile syndromes [8]. Lateral flow assay is simple and easy to perform. The sensitivity of this test calculated is 95% and specificity is 97%. Complement fixation test is a widely used confirmatory test for brucellosis. Coombs' test may be more suitable for confirmation of brucellosis in relapsing patients or patients with persisting disease. The combination of positive rose Bengal test and Coombs' test ≥ 1/320 was the best diagnostic criterion with 80% specificity and 100% sensitivity. The enzyme linked immunosorbent assay (ELISA) is a sensitive and rapid method for diagnosis of brucellosis. Detection of specific immunoglobulin by a single, simple and rapid test is a major advantage with ELISA [9]. Brucellacapt is a single stage proprietory test kit and is a new form of the agglutination test to test for brucellosis antibodies with 95.1% sensitivity and 99% specificity. Brucellacapt is more sensitive and usually shows higher titers than the Coombs test.

Culture from the blood of a patient provides definite proof of brucellosis [10]. There is a range of commercially available culture media for growing *Brucella*. The Castaneda two-phase system is the most convenient. Now semi-automated blood culture techniques like such as the BACTEC™ the time to detection has been significantly reduced. Brucellae can be detected in the blood of infected patients after four days of culture or less [11]. Molecular techniques such as Polymerase chain reaction (PCR) assays can be used to amplify and detect *Brucella* DNA in pure cultures and in clinical specimens. The QIAamp™ DNA Mini Kit and the UltraClean™ DNA BloodSpin Kit are among the many commercial kits that have been successfully used to extract *Brucella* DNA from whole-blood, serum and tissue samples [12]. For the diagnosis of human brucellosis, a PCR assay with one pair of primers is developed, which amplifies the target genomic sequence of *Brucella* species. Studies showed that standard PCR appeared to be a more sensitive technique than microbiological methods, not only for the diagnosis of a first episode of infection, but also for the early detection of relapses. Real-time PCR is a valuable technique in quantification of nucleic acids in individual blood samples. It is highly reproducible, rapid, sensitive and specific [13].

G.Vrioni *et al.* [14] employed a simple Polymerase Chain Reaction-Enzyme Immunoassay (PCR-EIA) for the rapid laboratory diagnosis of human brucellosis directly from peripheral blood. Following the amplification of a 223-bp sequence of a gene that codes for the synthesis of an immunogenic membrane protein specific for the *Brucella* genus, the amplified product was detected in a microtiter plate by hybridization with specificity of 100% and sensitivity of 81.5% for whole blood specimens and 79% for serum specimens. Results suggest that PCR-EIA assay is a sensitive and specific method that could assist the rapid and accurate diagnosis of acute human brucellosis [15]. The Loop- Mediated Isothermal Amplification Assay (LAMP) assay is for the quantitative detection of *Brucella spp.* is highly sensitive and specific. A simple and inexpensive apparatus such as a water bath or heat block that provides a constant temperature of 63°C is sufficient for the assay, and, unlike PCR, the reactivity is directly observed with the naked eye neglecting the need for electrophoretic analysis. Moreover, the LAMP assay can be performed on site, as special equipment such as a thermal cycler is not required. Recently, a more rapid and inexpensive method based on the Lab on a chip technology has been proposed i.e. Multiple Locus VNTR Analysis (MLVA) Typing For *Brucella* Based On Microfluidics Technology**.** This miniaturized platform for electrophoresis applications is able to size and quantify PCR fragments, and was previously used for studying the genetic variability of *Brucella spp*. The strain and biovar typing of *Brucella* field samples isolated in outbreaks, detected by this method is useful for tracing back source of infection and may be crucial for discriminating naturally occurring outbreaks versus bioterrorist events, being *Brucella* a potential biological warfare agent [16].

Definitive diagnosis of brucellosis remains a difficult task. No single test is perfect, clinical history coupled with combination of two or more tests reduces diagnostic errors. Despite the vigorous attempt for more than one century to come up with a definitive diagnostic technique for brucellosis, diagnosis still relies on the combination of several tests to avoid false negative results. A lot of work needs to be done to approach the best diagnostic techniques in

***Corresponding author**: Satish Gupte, Department of Microbiology, Gian Sagar Medical College and Hospital, Rajpura, India; Tel: +9915025865; E-mail: dr.satishgupte@hotmail.com

**Received** October 19, 2015; **Accepted** October 20, 2015; **Published** October 27, 2015

**Citation**: Gupte S, Kaur T (2015) Diagnostic Approach to Brucellosis. J Trop Dis 4: e101. doi:10.472/2329-891X.1000e109

brucellosis diagnosis.

## References

1. Young EJ (1995) An overview of human brucellosis. Clin Infect Dis 21: 283-289.
2. Corbel MJ (1997) Brucellosis: an overview. Emerging Infectious Diseases journal 3: 313-321.
3. Renukaradhya GJ, Isloor S, Rajasekhar M (2002) Epidemiology, zoonotic aspects, vaccination and control/eradication of brucellosis in India. Vet Microbiol 90: 183-195.
4. Yagupsky P, Baron EJ (2005) Laboratory exposures to brucellae and implications for bioterrorism. Emerg Infect Dis 11: 1180-1185.
5. Colmenero JD, Reguera JM, Martos F, Sánchez-De-Mora D, Delgado M, et al. (1996) Complications associated with Brucella melitensis infection: a study of 530 cases. Medicine (Baltimore) 75: 195-211.
6. Poiester FP, Nielsen K, Samartino LE, Yu WL (2010) Diagnosis of Brucellosis. The Open Veterinary Science Journal 4: 46-60.
7. Morgan WJ, MacKinnon DJ, Lawson JR, Cullen GA (1969) The rose bengal plate agglutination test in the diagnosis of brucellosis. Vet Rec 85: 636-641.
8. Ruiz-Mesa JD, Sánchez-Gonzalez J, Reguera JM, Martín L, Lopez-Palmero S, et al. (2004) Rose Bengal test: diagnostic yield and use for the rapid diagnosis of human brucellosis in emergency departments in endemic areas. Clinical Microbiology and Infection 11: 221-225.
9. Osoba AO, Balkhy H, Memish Z, Khan MY, Al-Thagafi A, et al. (2001) Diagnostic value of Brucella ELISA IgG and IgM in bacteremic and non-bacteremic patients with brucellosis. J Chemother 13 Suppl 1: 54-59.
10. Al Dahouk S, Tomaso H, Nöckler K, Neubauer H, Frangoulidis D (2003) Laboratory-based diagnosis of brucellosis--a review of the literature. Part I: Techniques for direct detection and identification of Brucella spp. Clin Lab 49: 487-505.
11. De Santis R, Ciammaruconi A, Faggioni G, Fillo S, Gentile B, et al. (2011) High throughput MLVA-16 typing for Brucella based on the microfluidics technology. BMC Microbiol 11: 60.
12. Cetin ES, Kaya S, Demirci M, Aridogan BC (2007) Comparison of the BACTEC blood culture system versus conventional methods for culture of normally sterile body fluids. Adv Ther 24: 1271-1277.
13. Al Dahouk S, Sprague LD, Neubauer H (2013) New developments in the diagnostic procedures for zoonotic brucellosis in humans. Rev Sci Tech 32: 177-188.
14. Wang Y, Wang Z, Zhang Y, Bai L, Zhao Y, et al. (2014) Polymerase chain reaction-based assays for the diagnosis of human brucellosis. Ann Clin Microbiol Antimicrob 13: 31.
15. Vrioni G, Gartzonika C, Kostoula A, Boboyianni C, Papadopoulou C, et al. (2004) Application of a Polymerase Chain Reaction Enzyme Immunoassay in Peripheral Whole Blood and Serum Specimens for Diagnosis of Acute Human Brucellosis. Eur J Clin. Microbiol Infect Dis 23: 194-199.
16. De Santis R, Ciammaruconi A, Faggioni G, D'Amelio R, Marianelli C, et al. (2009) Lab on a chip genotyping for Brucella spp. based on 15-loci multi locus VNTR analysis. BMC Microbiol 9: 66.