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Research Article

Comparative Evaluation of Brucella Immunocapture Agglutination and Coombs Gel Tests in the Serological Diagnosis of Human Brucellosis

İnsan brusellozunun serolojik tanısında brucella immunocapture aglütinasyon ve coombs jel testlerinin karşılaştırmalı değerlendirilmesi

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Aim: This study aimed to compare the diagnostic performance and agreement between the Brucella Immunocapture Agglutination Test (Brucella Capt, BICA) and the Brucella Coombs Gel Test (BCGT) in the serological diagnosis of human brucellosis.

Material and Method: Serum samples from 51 Rose Bengal Test (RBT)–positive and 50 RBT–negative patients with a preliminary diagnosis of brucellosis were analyzed using the BICA and BCGT assays. The agreement between the two methods was evaluated using Cohen's kappa (κ) coefficient, and positive and negative percent agreements (PPA, NPA) were calculated.

Results: A very high level of concordance was observed between the two tests, with an overall agreement of 96.0 % (κ = 0.92). The PPA and NPA were 95.9 % and 100 %, respectively. A substantial correlation was also found between antibody titers of the two assays (weighted κ = 0.64).

Conclusion: Brucella Capt (BICA) and Brucella Coombs Gel Test (BCGT) demonstrated substantial agreement and comparable diagnostic performance in the serological diagnosis of brucellosis. The complementary use of these assays may be particularly beneficial in clinically challenging situations, such as cases with low antibody titers or atypical serological profiles. Integration of these methods with clinical evaluation and, when available, molecular or culture-based approaches may further enhance diagnostic confidence.

Keywords: Brucellosis, Brucella Capt, Brucella Coombs Gel Test, Serological Diagnosis, Cohen's Kappa

Amaç: Bu çalışmada insan brusellozunun serolojik tanısında kullanılan Brucella İmmünokap¬tür Aglütinasyon Testi (Brucella Capt, BICA) ile Brucella Coombs Jel Testi'nin (BCGT) tanısal performanslarının ve aralarındaki uyumun karşılaştırılması amaçlanmıştır.

Gereç ve Yöntem: Bruselloz ön tanısı alan 51 Rose Bengal Testi (RBT) pozitif ve 50 RBT negatif hastaya ait serum örnekleri BICA ve BCGT testleriyle analiz edilmiştir. Testler arasındaki uyum Cohen's kappa (κ) katsayısı ile değerlendirilmiş; pozitif ve negatif yüzde uyum (PPA, NPA) oranları hesaplanmıştır.

Bulgular: İki test arasında çok yüksek düzeyde uyum saptanmıştır (genel uyum %96.0, κ = 0.92). Pozitif ve negatif uyum oranları sırasıyla %95.9 ve %100 olarak bulunmuştur. Antikor titreleri arasında da anlamlı bir ilişki belirlenmiştir (ağırlıklı κ = 0.64).

Sonuç: Brucella Capt (BICA) ve Brucella Coombs Jel Testi (BCGT), brusellozun serolojik tanısında yüksek düzeyde uyum ve karşılaştırılabilir tanısal performans göstermiştir. Bu testlerin birlikte kullanımı, özellikle düşük antikor titreleri veya atipik serolojik profillerin bulunduğu klinik olarak zorlayıcı durumlarda tanısal değerlendirmeye katkı sağlayabilir. Klinik bulgularla birlikte ve olanaklar dâhilinde moleküler veya kültür temelli yaklaşımlarla desteklenmesi, tanısal güvenilirliği daha da artırabilir.

Anahtar Kelimeler: Bruselloz, Brucella Capt, Brucella Coombs Jel Testi, Serolojik Tanı, Cohen's Kappa

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INTRODUCTION

Brucellosis is a zoonotic disease caused by bacteria of the Brucella genus. It is transmitted to humans from infected animals such as cattle, sheep, goats, pigs, and dogs, primarily through the consumption of unpasteurized milk and dairy products, direct contact with infected animal tissues, urine, or birth materials, and by inhalation of infectious aerosols (1). Veterinarians, farmers, butchers, and laboratory personnel are at increased risk due to occupational exposure (2).

Brucellosis is a multisystem disease with a wide spectrum of clinical manifestations, ranging from subclinical infections to non-specific symptoms such as fever, sweating, lymphadenopathy, anorexia, fatigue, arthritis, hepatosplenomegaly, and neurological involvement (1). Diagnosis is generally based on clinical, epidemiological, and serological findings; however, isolation of the organism from blood or other clinical specimens remains the definitive diagnostic method (3). Although culture is considered the gold standard, Brucella species are fastidious, slow-growing organisms that require special media and prolonged incubation, and the infection often presents with low levels of bacteremia (3). Consequently, culture isolation rates are low and turnaround times are long. In addition, the risk of laboratory-acquired infection and biohazard concerns further limit its routine use (3).

For these reasons, serological methods have become indispensable in the diagnosis of brucellosis (1,3). Several serological tests are available, including agglutination tests, complement fixation, and immunocapture assays. Among them, the standard tube agglutination test (STA) is the most widely used for detecting Brucella-specific IgM and IgG antibodies (4). However, the presence of blocking antibodies may occasionally result in false-negative STA results (4,5). The Coombs anti-human globulin test overcomes this limitation by detecting incomplete or blocking antibodies and is particularly useful in chronic or atypical cases (5). Nevertheless, the Coombs test is labor-intensive and time-consuming, limiting its practicality in routine laboratories (5,6).

Recently, newer agglutination-based serological methods such as the Brucella Immunocapture Agglutination Test (Brucella Capt) and the Brucella Coombs Gel Test (BCGT) have been developed to improve diagnostic performance (7,8). Both tests can detect total antibodies, including blocking antibodies, while offering faster and easier procedures (5–8). The Brucella Capt assay yields results within 24–48 hours, whereas the BCGT can provide results on the same day, often within 2 hours (5,6,8).

In the present study, we aimed to prospectively compare Brucella Capt and the Brucella Coombs Gel Test (BCGT), two contemporary serological methods increasingly used in routine laboratories, in patients with suspected brucellosis. Rather than evaluating diagnostic accuracy against a reference standard, the primary objective was to assess the level of agreement and concordance between these two assays under real-life laboratory conditions. The original contribution of this study lies in providing a direct agreement-based comparison of these methods, thereby offering practical value for clinicians and microbiology laboratories when selecting reliable, rapid, and complementary serological tools, particularly in endemic settings.,

MATERIALS AND METHODS

Serum samples from 51 Rose Bengal Test (RBT)–positive and 50 RBT–negative patients with a preliminary diagnosis of brucellosis, sent to the Microbiology Unit of Aksaray University Training and Research Hospital, were included in the study. This study was approved by the Aksaray University Ethics Committee (Decision No: 2025/286, December 11, 2025).

2.1. Rose Bengal Test

The Rose Bengal Test (RBT; Redcell Diagnostics, Spain) is a rapid slide agglutination assay used for the qualitative detection of Brucella-specific antibodies. After all reagents were brought to room temperature, 50 µL of patient serum and 50 µL of saline were placed on a glass slide, and one drop of BRUCEL-RB antigen suspension was added to the circle on the slide. The mixture was gently rotated for 4 minutes at room temperature. During evaluation, the presence of visible agglutination, observed macroscopically, indicates the presence of Brucella antibodies (IgM and/or IgG) at or above 25 IU/mL in the patient serum.

2.2. Coombs Agglutination Test

The Brucella Coombs Gel Test (BCGT; Redcell Diagnostics, Spain) is based on the Coombs agglutination principle and uses a gel matrix system for antibody detection. After the patient serum and test reagents that tested positive with the Rose Bengal test were brought to room temperature, 50 µL of each serum sample, diluted serially from 1:40 to 1:1280, was pipetted into the wells of the BCGT plate. The plates were then centrifuged for 20 minutes according to the manufacturer's instructions. During evaluation, if Brucella-specific antibodies are absent in the serum, the Brucella

antigens migrate through the gel and settle at the bottom of the tube, indicating a negative result. In contrast, if antibodies are present, the antigen–antibody complexes are retained within the gel as a distinct pink line, representing a positive reaction. According to the Coombs agglutination method, titers of 1:160 and above were considered positive.

2.3. Brucella Immunocapture Agglutination Test

The Brucella Immunocapture Agglutination Test (Brucella Capt; Vircell, S.L., Spain) consists of U-bottomed microplate wells coated with anti-human immunoglobulins. Patient sera were diluted according to the manufacturer's instructions, and Brucella antigen was added to each well. The plates were incubated for 18–24 hours at room temperature to allow agglutination to occur. In the absence of Brucella-specific antibodies, the antigen particles form a compact blue dot that settles at the bottom of the well, indicating a negative result. In contrast, a homogeneous blue layer adhering to the inner surface of the well indicates a positive reaction.

2.4. Statistical Analysis

The agreement between the Brucella Capt and Brucella Coombs Gel Tests (BCGT) was evaluated using Cohen's kappa (κ) coefficient. The strength of agreement was interpreted according to the following criteria: values of κ<0.00 were considered poor, κ=0.00–0.20 slight, κ=0.21–0.40 fair, κ=0.41–0.60 moderate, κ=0.61–0.80 good, and κ=0.81–1.00 very good agreement.

RESULTS

A total of 101 serum samples were analyzed, including 51 RBT-positive and 50 RBT-negative specimens. Brucella Capt and Brucella Coombs Gel Test (BCGT) results were concordant in 97 of 101 samples (96.0%).

Table 1. Comparison of Brucella Capt and Brucella Coombs Gel Test (BCGT) Results

		BCGT		
		Positive	Negative	Total
Brucella Capt	Positive	47	0	47
	Negative	4	50	54
	Total	51	50	101

As shown in Table 1, 47 samples were positive and 50 were negative by both methods, while four samples were positive by BCGT but negative by Capt. No samples were positive by Capt and negative by BCGT.

When evaluated separately, the agreement rate between Brucella Capt and BCGT was 92.2% for positive samples and 100% for negative samples. The overall Cohen's κ coefficient was 0.92 (95% CI: 0.84–0.99), indicating almost perfect agreement.

In the analysis of antibody titers, a weighted Cohen's κ value of 0.64 was obtained, indicating a good level of agreement across serial dilution levels.

DISCUSSION

In the present study, the Brucella Immunocapture Agglutination Test (Brucella Capt) and the Brucella Coombs Gel Test (BCGT) were compared for their diagnostic concordance in human brucellosis. A very high level of agreement was observed between the two assays (overall agreement=96.0%, κ=0.92), indicating almost perfect consistency. The positive and negative agreement rates were 92.2% and 100%, respectively, while the weighted κ value based on antibody titers was 0.64, reflecting a substantial degree of correlation between serial dilutions. These findings are consistent with previous reports demonstrating good-to-very-good agreement between immunocapture-based and Coombs-gel serological methods (4–8).

The Brucella Capt test, based on the principle of immunocapture agglutination, efficiently detects total antibodies, including blocking antibodies, and yields results within 24–48 hours (3,6,8). In contrast, the BCGT—performed using gel-supported microtubes—offers same-day results (approximately 2 hours) and provides a more objective endpoint compared with the classical Coombs test (4,5). In the present study, both assays demonstrated comparable positivity rates among RBT-positive sera, and all RBT-negative samples were concordantly negative by both methods, supporting a high level of agreement in negative samples. These results are in line with earlier studies emphasizing the reliability and rapid applicability of BCGT in routine laboratory settings (4,5).

Recent investigations have highlighted the importance of combining different serological approaches to improve diagnostic accuracy across disease stages (2,5,8,9). Previous studies have reported that Brucella Capt performs particularly well during acute infection, while gel-based Coombs methods may demonstrate higher sensitivity in chronic or relapsing cases (5,8,11). Modern immunocapture assays have also been shown to reduce false-negative results associated with the prozone effect and may serve as confirmatory tests when standard agglutination or ELISA results are inconclusive (5,9,12). Furthermore, several recent publications have emphasized the integration of new serological technologies into endemic-area screening programs to enhance early detection and case confirmation (9,10,13).

Overall, the findings of the present study support that both Brucella Capt and BCGT are reliable and complementary tools in the serological diagnosis of brucellosis. BCGT provides faster and more objective results, while Brucella Capt may be advantageous in detecting low antibody titers or blocking antibodies. However, as with all serological methods, these assays should be interpreted in conjunction with clinical findings and, when available, supported by molecular or culture-based methods.

Despite the strengths of the present study, several limitations should be acknowledged. First, the absence of a definitive reference standard, such as culture or molecular testing, limits the assessment of true diagnostic accuracy. However, this was not the primary objective of the study. The main aim was to evaluate the agreement between two widely used serological methods in routine practice. Therefore, the lack of culture or molecular confirmation should be interpreted in the context of an agreement-based comparative design rather than as a methodological shortcoming. In addition, the single-center design and relatively modest sample size may limit the generalizability of the findings.

CONCLUSION

Brucella Capt (BICA) and Brucella Coombs Gel Test (BCGT) demonstrated substantial agreement and comparable diagnostic performance, indicating that both assays can be reliably used in the serological diagnosis of brucellosis. Their complementary use may be particularly beneficial in challenging clinical scenarios, such as cases with low antibody titers or atypical serological profiles. Integration of these methods with clinical evaluation and, when available, molecular or culture-based approaches may further enhance diagnostic confidence.

Declarations

Ethics Committee Approval: Ethics committee approval was obtained from the Health Sciences Scientific Research Ethics Committee (Date: December 11, 2025; Decision No: 2025/286; Protocol No: SAGETİK 2025-193). The study was conducted at Aksaray Training and Research Hospital, Medical Microbiology Laboratory. This study was carried out in accordance with the principles of the Declaration of Helsinki.

Authors' Contributions: F.G. conceived the manuscript and served as the corresponding author. S.T. performed the statistical analysis. A.A. conducted the serological tests. Y.D. designed the study and contributed to the creation and approval of the manuscript. All authors read and approved the final version of the manuscript.

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