






The Antibiotic Susceptibility of *Brucella spp.* Isolated from Human Samples: A Systematic Review and Meta-Analysis

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ABSTRACT

Background and Aim: Effective brucellosis treatment necessitates antibiotics that can penetrate macrophages. This study systematic review and meta-analysis aimed at assessing the antibiotic susceptibility profile of *Brucella spp.* isolated from humans, addressing this critical gap in understanding *Brucella* infections and their treatment.

Materials and Methods: Two authors conducted a systematic search across PubMed, Web of Science, and Scopus, with no time restrictions, encompassing English studies. Data extraction employed a standardized sheet, with two independent authors, and disagreements were resolved by a third. The data sheet included study characteristics and susceptibility/resistance information for various antibiotics. Statistical analysis involved random effects models, Mantel-Haenszel methods, I^2 tests, z-tests, and funnel plots using R and RStudio.

Results: Based on the pooled susceptibility ratios, among the 630 samples of *Brucella spp.*, 98% (95% CI: 85% - 100%) were susceptible to trimethoprim. Among the 1255 samples of *Brucella spp.*, 82% (95% CI: 54% - 95%) were susceptible to rifampicin. Among the 1344 samples of *Brucella spp.*, 100% (95% CI: 78% - 100%) were susceptible to doxycycline. Among the 942 samples of *Brucella spp.*, 100% (95% CI: 85% - 100%) were susceptible to tetracycline. Among the 893 samples of *Brucella spp.*, 100% (95% CI: 82% - 100%) were susceptible to ciprofloxacin. Among the 906 samples of *Brucella spp.*, 97% (95% CI: 96% - 98%) were susceptible to gentamicin.

Conclusion: Based on our results, trimethoprim, doxycycline, tetracycline, ciprofloxacin, and gentamicin were effective, but rifampicin had lower susceptibility. This informs antibiotic selection for *Brucella* infections, underscoring its importance in managing the disease.

Keywords: *Brucella*, Brucellosis, Antibiotic Susceptibility, Resistance, MIC

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1. Introduction

Brucellosis, a zoonotic disease impacting both animals and humans, poses significant economic and public health challenges globally. *Brucella melitensis* and *Brucella abortus* are the primary culprits behind epidemic brucellosis (1, 2). Additionally, human

brucellosis can stem from various *Brucella* species, including *B. canis* and *B. suis*, often transmitted through infected animal organs or the consumption of unpasteurized dairy products. This disease notably contributes to economic losses due to reduced milk

production and livestock abortion. Despite therapeutic efforts, brucellosis treatment has not yielded absolute success, with instances of disease relapses documented. Moreover, widespread and inappropriate antibiotic use has raised concerns about antibiotic resistance in *Brucella* isolates (3-6).

It is now firmly established that *Brucella* is an intracellular bacterium capable of evading macrophage defenses. Furthermore, it induces significant mitochondrial fragmentation within 48 hours of entering various cell types. Consequently, effective antibiotics for brucellosis treatment must possess the ability to penetrate macrophages and eliminate the bacteria. However, in many clinical laboratories, routine antibiotic susceptibility testing is not feasible due to the absence of biosafety level 3 facilities (7-9). Consequently, there is limited available data regarding the antibiotic susceptibility of *Brucella* species, making it imperative to investigate. Thus, this study aimed to assess the antibiotic susceptibility profile of *Brucella* spp. isolated from humans in a systematic review and meta-analysis.

2. Materials and Methods

This systematic review and meta-analysis study was conducted based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guideline 2020 (1).

Search Strategy

Two authors performed a systematic search of literature in the following electronic databases: PubMed, Web of Science, and Scopus. No time limitation was defined and all English studies from the beginning until September 2023 were included. The relevant medical subject heading (MeSH) terms and related keywords were used in combination to build the search strategy; ("brucella" OR "brucellosis" OR "brucel*") AND ("antibiotic" OR "susceptibility" OR "resistance" OR "sensitivity" OR "sensitive" OR "resistant").

Eligibility Criteria

Our eligibility criteria were defined based on the PICO framework: (P) Population: patients with brucellosis. (I) antibiogram test. (C) susceptibility or resistance. (O) Not applicable. Those studies that did not include human samples, did not report outcomes, or performed any

antibiogram tests were excluded. Studies that were not in English, were also excluded.

Data Extraction and Outcome Measures

A standardized Excel sheet was prepared for data extraction. Two independent authors performed the data extraction. Disagreement between these two authors was discussed and resolved by a third author. The data extraction sheet included the following study characteristics: first author's name, year of publication, country, total number of samples, susceptible and resistant samples for trimethoprim, rifampicin, doxycycline, tetracycline, ciprofloxacin, gentamicin, and streptomycin.

Data Synthesis and Statistical Analysis

The pooled susceptibility/resistance ratios were calculated using the random effects model and Mantel-Haenszel method along with the 95% confidence intervals. For assessing the heterogeneity of the included studies, the I^2 (I square) test was used. The Mantel-Haenszel method and random effects model were used for pooling the effect sizes. For testing the overall significance of the random model, a z-test was performed. Potential publication bias was graphically assessed by creating funnel plots for each of the aforementioned groups. R (R Foundation for Statistical Computing, Vienna, Austria) and RStudio (RStudio, Inc., Boston, MA) were used for the statistical analysis and creation of forest and funnel plots.

3. Results

Our initial search retrieved 931 articles from PubMed, Scopus, and Web of Science, from which 185 duplicates were removed. After screening the title and abstract of 746 records, 66 full texts were retrieved, among which 15 studies (Figure 1) were included based on our eligibility criteria (4, 5, 10-22). More detail regarding the study characteristics of the included studies is summarised in Table 1.

Based on the pooled susceptibility ratios, among the 630 samples of *Brucella* spp., 98% (95% CI: 85% - 100%) were susceptible to trimethoprim. Further information regarding the susceptibility of *Brucella* spp. against trimethoprim is available in Figure 2. The pooled resistance ratio of *Brucella* spp. against trimethoprim is available in Appendix 1.

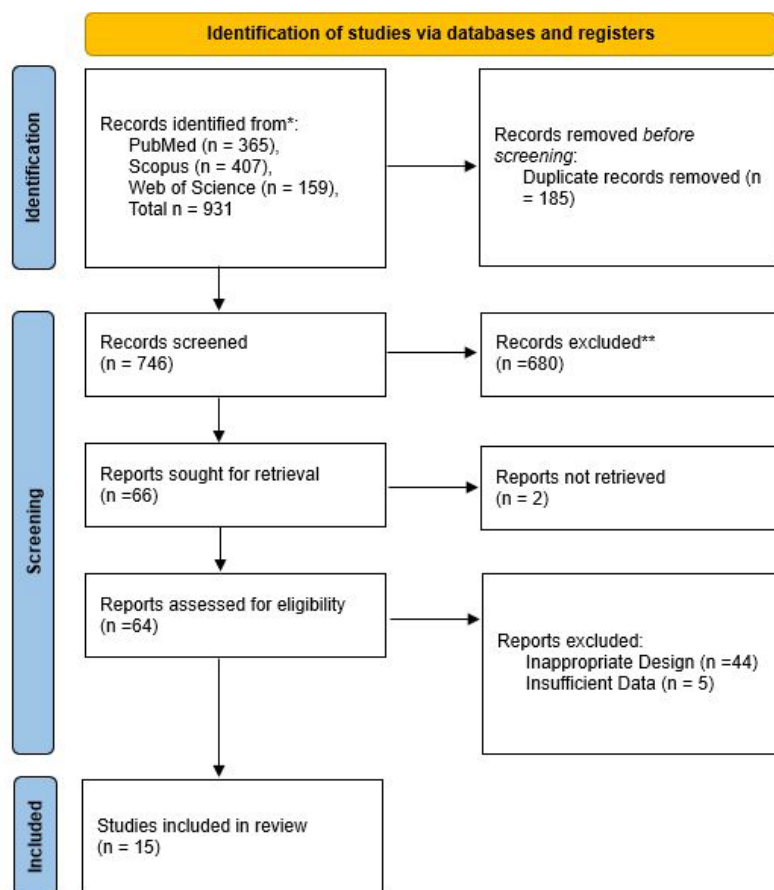


Figure 1. PRISMA flowchart of the included studies

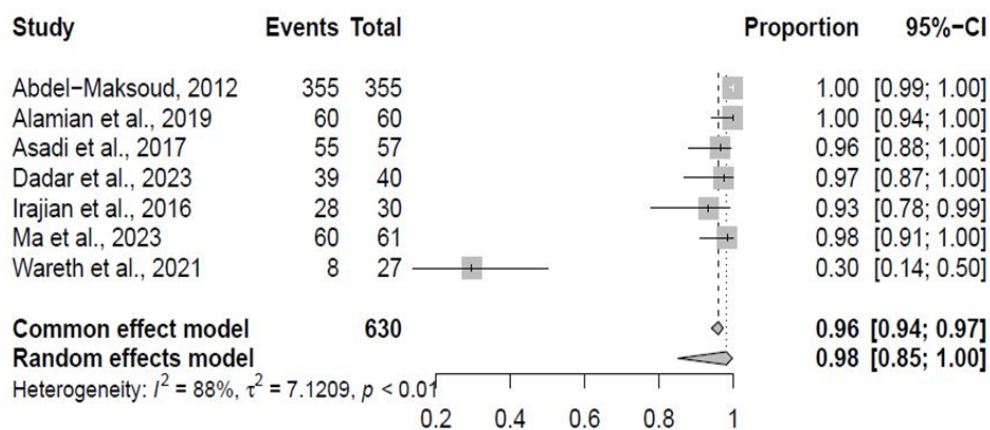


Figure 2. The pooled susceptibility ratio of *Brucella spp.* against trimethoprim

Based on the pooled susceptibility ratios, among the 1255 samples of *Brucella spp.*, 82% (95% CI: 54% - 95%) were susceptible to rifampicin. Further information regarding the susceptibility of *Brucella spp.* against rifampicin is available in [Figure 3](#). The pooled resistance ratio of *Brucella spp.* against rifampicin is available in Appendix 2.

Based on the pooled susceptibility ratios, among the 1344 samples of *Brucella spp.*, 100% (95% CI: 78% - 100%) were susceptible to doxycycline. Further information regarding the susceptibility of *Brucella spp.* against doxycycline is available in [Figure 4](#). The pooled resistance ratio of *Brucella spp.* against doxycycline is available in Appendix 3.

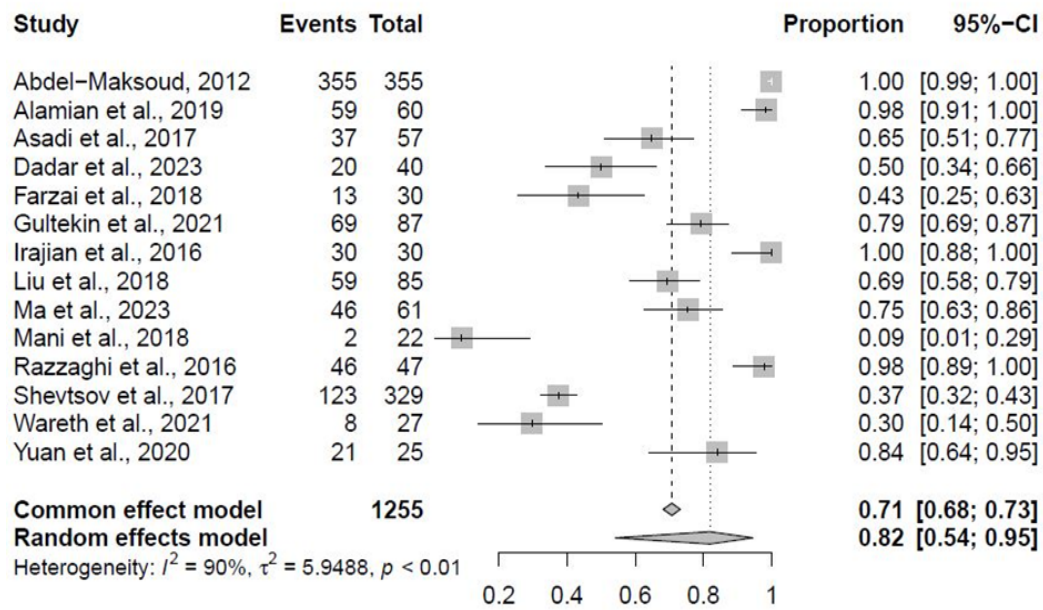


Figure 3. The pooled susceptibility ratio of *Brucella spp.* against rifampicin

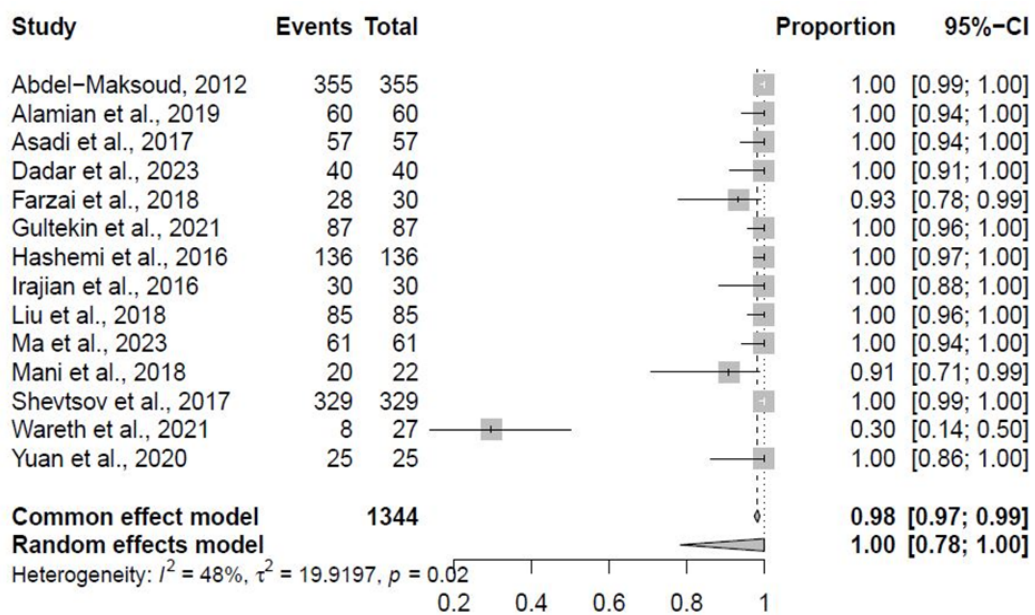


Figure 4. The pooled susceptibility ratio of *Brucella spp.* against doxycycline

Based on the pooled susceptibility ratios, among the 942 samples of *Brucella spp.*, 100% (95% CI: 85% - 100%) were susceptible to tetracycline. Further information regarding the susceptibility of *Brucella spp.* against tetracycline is available in Figure 5. The pooled resistance ratio of *Brucella spp.* against tetracycline is available in Appendix 4.

Based on the pooled susceptibility ratios, among the 893 samples of *Brucella spp.*, 100% (95% CI: 82% - 100%) were susceptible to ciprofloxacin. Further information regarding the susceptibility of *Brucella spp.* against ciprofloxacin is available in Figure 6. The pooled resistance ratio of *Brucella spp.* against ciprofloxacin is available in Appendix 5.

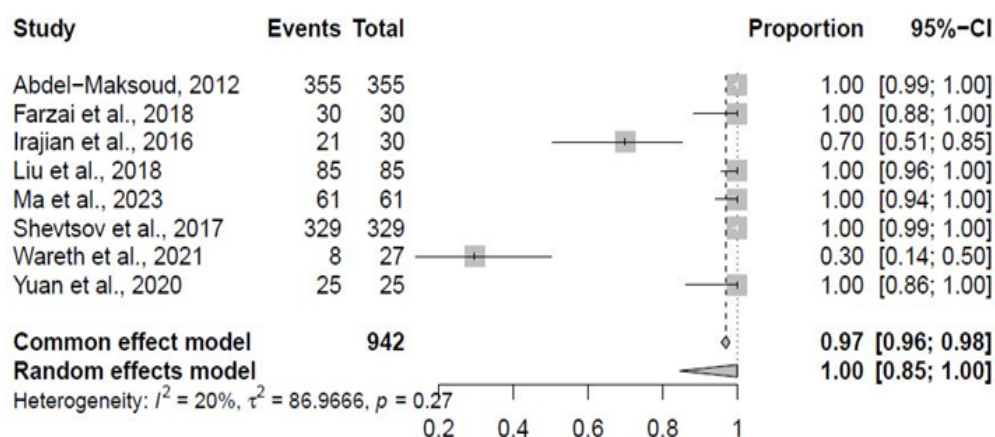


Figure 5. The pooled susceptibility ratio of *Brucella spp.* against tetracycline

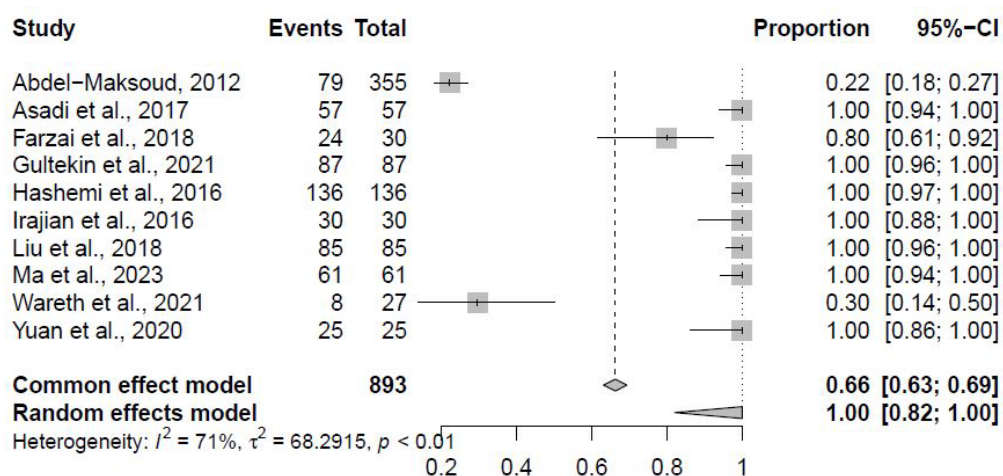


Figure 6. The pooled susceptibility ratio of *Brucella spp.* against ciprofloxacin

Based on the pooled susceptibility ratios, among the 906 samples of *Brucella spp.*, 97% (95% CI: 96% - 98%) were susceptible to gentamicin. Further information regarding the susceptibility of *Brucella spp.* against

gentamicin is available in [Figure 7](#). The pooled resistance ratio of *Brucella spp.* against gentamicin is available in Appendix 6.

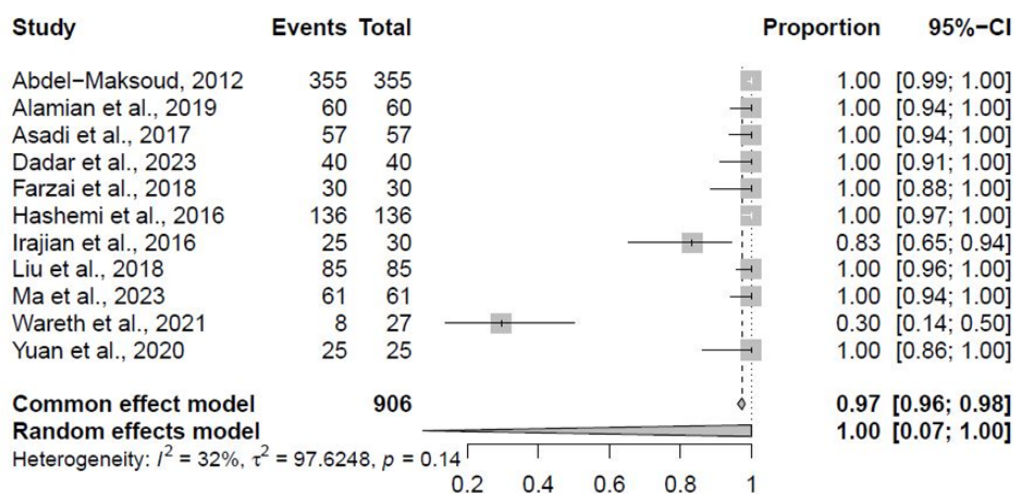


Figure 7. The pooled susceptibility ratio of *Brucella spp.* against gentamicin

4. Discussion

In our systematic review and meta-analysis study, we evaluated the susceptibility of *Brucella* spp. to various antibiotics. The results demonstrated varying levels of susceptibility among these samples, indicating that certain antibiotics, such as trimethoprim, doxycycline, tetracycline, ciprofloxacin, and gentamicin, were effective against *Brucella* spp. infections. However, susceptibility to rifampicin was lower in comparison. These findings provide insights into potential treatment options for *Brucella* infections, supporting the importance of antibiotic selection in managing this disease.

Brucellosis primarily affects individuals who come into contact with farm animals, particularly cattle, sheep, and goats. Additionally, cases have been reported in those who consume raw milk, driven by traditional beliefs in its health benefits. Diagnosis typically relies on serological tests for antibodies or isolating the *Brucella* bacterium (10, 23, 24). However, the gold standard involves isolating the causative agent, which requires high-level biosafety laboratories due to the organism's high infectivity. Consequently, limited efforts are made to isolate and identify *Brucella* spp. from clinical samples, leading to potential misidentifications (11, 25-27).

Similarly, Lopez-Merino et al. found that cotrimoxazole and rifampin exhibited limited inhibitory activity against *Brucella* strains. In an endemic region for human brucellosis in Turkey, *B. melitensis* isolates demonstrated the highest resistance rate to cotrimoxazole (46.3%), while resistance to rifampin was observed in only 9.7%. In many developing countries, inappropriate antibiotic use is the primary driver of antibiotic resistance, resulting in the annual consumption of a multitude of antibiotics (28-31). Furthermore, Iran has reported significantly higher usage of systemic antibacterial agents like broad-spectrum penicillin, third-generation cephalosporins, and quinolones compared to other countries. It is known to exert an in vitro inhibitory effect against *Brucella* spp. due to its efficient intracellular diffusion. In our study, 98.5% (59/60) of the tested *Brucella* isolates with MIC \leq 1 μ g/mL were classified as sensitive to rifampin based on the CLSI breakpoints for slow-growing bacteria. However, one *Brucella* strain exhibited resistance to rifampin with a MIC of 1.5 μ g/mL. Notably, a high rate of rifampin resistance has been previously documented in Egyptian field strains (64%), as well as in Brazil (36.73%), Turkey (9.7%), and Malaysia (70%) (13, 32-35).

It's important to take into account that a significant portion of individuals with brucellosis cannot endure extended rifampin therapy due to its adverse

gastrointestinal effects. Consequently, the concurrent use of streptomycin and doxycycline has been identified as the preferred treatment regimen, followed by the combination of rifampin and doxycycline, as there have been no reported treatment failures or relapses with these regimens. Nevertheless, several studies have cautioned against the indiscriminate use of rifampin due to the increased occurrence of intermediate sensitivity to these drugs (15, 36-39).

The World Health Organization has provided treatment recommendations for adults with acute brucellosis, endorsing a six-week regimen that combines doxycycline with either rifampicin or streptomycin. These guidelines remain applicable today. Nonetheless, there have been reports indicating that cases of brucellosis accompanied by osteoarticular and visceral complications are less prone to relapse when treated with a triple therapy approach involving streptomycin, rifampicin, and doxycycline (17, 40-44). Furthermore, an extensive review and meta-analysis of 30 randomized controlled trials have suggested that the preferred treatment should include combinations like doxycycline with gentamicin or triple regimens (e.g., doxycycline, rifampicin, and gentamicin). Despite combination therapy, there have been reports of relapse rates as high as 10%. Importantly, these relapses were primarily attributed to inadequate treatment due to issues such as incorrect dosing or poor patient compliance, rather than antimicrobial resistance. As a result, antimicrobial susceptibility testing is currently not considered indispensable in the management of brucellosis cases. Also, doxycycline has become the preferred tetracycline derivative for *Brucella* infection treatment due to its favorable pharmacokinetics (45-49).

5. Conclusion

In our systematic review and meta-analysis, we assessed the susceptibility of *Brucella* spp. to different antibiotics. Our findings revealed varying degrees of susceptibility among these samples. Notably, trimethoprim, doxycycline, tetracycline, ciprofloxacin, and gentamicin exhibited effectiveness against *Brucella* spp. infections. In contrast, rifampicin showed lower susceptibility. These results offer valuable insights into potential antibiotic choices for treating *Brucella* infections, emphasizing the significance of antibiotic selection in the management of this disease.

Acknowledgment

Not applicable.

Conflict of Interest

The authors declare that they don't have any conflict of interest.

References

1. Yang XW, Wang YZ, Li JQ, Chen JJ, Liu JY, Tian GZ, et al. Genetic characteristics of an amikacin-resistant *Brucella abortus* strain first isolated from Marmota himalayana. *Microb Pathog.* 2022;164:105402. [DOI:10.1016/j.micpath.2022.105402] [PMID]
2. Tscherne A, Mantel E, Boskani T, Budniak S, Fasanella A, Feruglio SL, et al. Adaptation of *Brucella melitensis* Antimicrobial Susceptibility Testing to the ISO 20776 Standard and Validation of the Method. *Microorganisms.* 2022;10(7):1470. [PMID] [DOI:10.3390/microorganisms10071470] [PMCID]
3. Sheng X, Lu W, Li A, Lu J, Song C, Xu J, et al. ANT(9)-Ic, a Novel Chromosomally Encoded Aminoglycoside Nucleotidyltransferase from *Brucella intermedia*. *Microbiol Spectr.* 2023;11(3):e00620-23. [DOI:10.1128/spectrum.00620-23] [PMID] [PMCID]
4. Ma HR, Xu HJ, Wang X, Bu ZY, Yao T, Zheng ZR, et al. Molecular characterization and antimicrobial susceptibility of human *Brucella* in Northeast China. *Front Microbiol.* 2023;14:1137932. [PMID] [PMCID] [DOI:10.3389/fmicb.2023.1137932]
5. Dadar M, Alamian S, Brangsch H, Elbadawy M, Elkharsawi AR, Neubauer H, Wareth G. Determination of Virulence-Associated Genes and Antimicrobial Resistance Profiles in *Brucella* Isolates Recovered from Humans and Animals in Iran Using NGS Technology. *Pathogens.* 2023;12(1):82. [PMID] [DOI:10.3390/pathogens12010082] [PMCID]
6. Celik E, Kayman T, Buyuk F, Saglam AG, Abay S, Akar M, et al. The canonical *Brucella* species-host dependency is changing, however, the antibiotic susceptibility profiles remain unchanged. *Microbial Pathogenesis.* 2023;182:106261. [DOI:10.1016/j.micpath.2023.106261] [PMID]
7. Manafe RP, Bhembe-Magadaza NL, Green E. Antibigram Screening and Detection of Virulence-Associated Genes in *Brucella* Species Acquired from Cattle in South Africa's Eastern Cape Province. *Int J Environ Res Public Health.* 2022;19(5):2813. [DOI:10.3390/ijerph19052813] [PMID] [PMCID]
8. Elbehiry A, Aldubaib M, Al Rugaie O, Marzouk E, Abaalkhail M, Moussa I, et al. Proteomics-based screening and antibiotic resistance assessment of clinical and sub-clinical *Brucella* species: An evolution of brucellosis infection control. *PLoS One.* 2022;17(1):e0262551. [PMID] [PMCID] [DOI:10.1371/journal.pone.0262551]
9. Arapović J, Kompes G, Dedić K, Teskeredžić S, Ostojić M, Travar M, et al. Antimicrobial resistance profiles of human *Brucella melitensis* isolates in three different microdilution broths: the first multicentre study in Bosnia and Herzegovina. *J Glob Antimicrob Resist.* 2022;29:99-104. [DOI:10.1016/j.jgar.2022.02.005] [PMID]
10. Wareth G, El-Diasty M, Abdel-Hamid NH, Holzer K, Hamdy MER, Moustafa S, et al. Molecular characterization and antimicrobial susceptibility testing of clinical and non-clinical *Brucella melitensis* and *Brucella abortus* isolates from Egypt. *One Health.* 2021;13:100255. [PMID] [PMCID] [DOI:10.1016/j.onehlt.2021.100255]
11. Gültekin E, Uyanık MH, Albayrak A, Kılıç S. Investigation of antibiotic susceptibilities of *Brucella* Strains isolated from various clinical samples in eastern Turkey. *Eur J Med Res.* 2021;26(1):57. [DOI:10.1186/s40001-021-00527-5] [PMID] [PMCID]
12. Yuan HT, Wang CL, Liu LN, Wang D, Li D, Li ZJ, Liu ZG. Epidemiologically characteristics of human brucellosis and antimicrobial susceptibility pattern of *Brucella melitensis* in Hinggan League of the Inner Mongolia Autonomous Region, China. *Infect Dis Poverty.* 2020;9(1):79. [PMID] [PMCID] [DOI:10.1186/s40249-020-00697-0]
13. Alamian S, Dadar M, Etemadi A, Afshar D, Alamian MM. Antimicrobial susceptibility of *Brucella* spp. isolated from Iranian patients during 2016 to 2018. *Iran J Microbiol.* 2019;11(5):363-7. [DOI:10.18502/ijm.v11i5.1953] [PMID] [PMCID]
14. Mani SSR, Gunasekaran K, Iyyadurai R, Prakash JAJ, Veeraraghavan B, Mishra AK, et al. Clinical spectrum, susceptibility profile, treatment and outcome of culture-confirmed brucellosis from South India. *Indian J Med Microbiol.* 2018;36(2):289-92. [DOI:10.4103/ijmm.IJMM_18_236] [PMID]
15. Liu ZG, Di DD, Wang M, Liu RH, Zhao HY, Piao DR, et al. In vitro antimicrobial susceptibility testing of human *Brucella melitensis* isolates from Ulanqab of Inner Mongolia, China. *BMC Infect Dis.* 2018;18(1):43. [DOI:10.1186/s12879-018-2947-6] [PMID] [PMCID]
16. Farazi A, Hoseini SD, Ghaznavirad E, Sadekhoo S. Antibiotic Susceptibility of *Brucella Melitensis* in Markazi Province of Iran. *Int J Infect Dis.* 2018;73:124. [DOI:10.1016/j.ijid.2018.04.3697]

17. Torkaman Asadi F, Hashemi SH, Yousef Alikhani M, Moghimbeigi A, Naseri Z. Clinical and diagnostic aspects of brucellosis and antimicrobial susceptibility of brucella isolates in Hamedan, Iran. *Jpn J Infect Dis.* 2017;70(3):235-8. [DOI:10.7883/yoken.JJID.2016.133] [PMID]
18. Shevtsov A, Syzdykov M, Kuznetsov A, Shustov A, Shevtsova E, Berdimuratova K, et al. Antimicrobial susceptibility of *Brucella melitensis* in Kazakhstan. *Antimicrob Resist Infect Control.* 2017;6:130. [DOI:10.1186/s13756-017-0293-x] [PMID] [PMCID]
19. Reza Irajian G, Masjedian Jazi F, Mirnejad R, Piranfar V, Zahraei Salehi T, Amir Mozafari N, et al. Species-specific PCR for the diagnosis and determination of antibiotic susceptibilities of brucella strains Isolated from Tehran, Iran. *Iran J Pathol.* 2016;11(3):238-47.
20. Razzaghi R, Rastegar R, Momen-Heravi M, Erami M, Nazeri M. Antimicrobial susceptibility testing of *Brucella melitensis* isolated from patients with acute brucellosis in a centre of Iran. *Indian J Med Microbiol.* 2016;34(3):342-5. [PMID] [DOI:10.4103/0255-0857.188336]
21. Hashemi SH, Alikhani MY, Asadi FT, Naseri Z. Antibiotic susceptibility pattern of *Brucella melitensis* clinical isolates in Hamedan, West of Iran. *Int J Infect Dis.* 2016;45:91-2. [DOI:10.1016/j.ijid.2016.02.244]
22. Abdel-Maksoud M, House B, Wasfy M, Abdel-Rahman B, Pimentel G, Roushdy G, Dueger E. In vitro antibiotic susceptibility testing of *Brucella* isolates from Egypt between 1999 and 2007 and evidence of probable rifampin resistance. *Ann Clin Microbiol Antimicrob.* 2012;11:24. [PMID] [PMCID] [DOI:10.1186/1476-0711-11-24]
23. Al-Afifi AH, Alewy Almashhadany D, Al-Azazi ASH, Khalaf AM, Naji Ahmed Odhah M, Al-Gabri NA. Prevalence of *Brucella* spp. in milk from aborted and non-aborted animals in Dhamar governorate, Yemen. *Ital J Food Saf.* 2022;11(4):10370. [DOI:10.4081/ijfs.2022.10370] [PMID] [PMCID]
24. Lama M, Chanakya PP, Khamari B, Peketi ASK, Kumar P, Muddu GK, et al. Genomic analysis of a multidrug-resistant *Brucella anthropi* strain isolated from a 4-day-old neonatal sepsis patient. *J Glob Antimicrob Resist.* 2021;26:227-9. [DOI:10.1016/j.jgar.2021.06.013] [PMID]
25. Castillo-Zeledón A, Ruiz-Villalobos N, Altamirano-Silva P, Chacón-Díaz C, Barquero-Calvo E, Chaves-Olarte E, Guzmán-Verri C. A *Sinorhizobium meliloti* and *Agrobacterium tumefaciens* ExoR ortholog is not crucial for *Brucella abortus* virulence. *PLoS ONE.* 2021;16(8):e0254568. [PMID] [PMCID] [DOI:10.1371/journal.pone.0254568]
26. Yang XW, Piao DR, Mao LL, Pang B, Zhao HY, Tian GZ, et al. Whole-genome sequencing of rough *Brucella melitensis* in China provides insights into its genetic features. *Emerg Microbes Infect.* 2020;9(1):2147-56. [DOI:10.1080/22221751.2020.1824549] [PMID] [PMCID]
27. Sofi-Mahmudi A, Masinaei M, Shamsoddin E, Tovani-Palone MR, Heydari M-H, Shoaee S, et al. Global, regional, and national burden and quality of care index (QCI) of lip and oral cavity cancer: a systematic analysis of the Global Burden of Disease Study 1990-2017. *BMC Oral Health.* 2021;21(1):1-11. [DOI:10.1186/s12903-021-01918-0] [PMID] [PMCID]
28. Khan S, Akhtar MU, Khan S, Javed F, Khan AA. Nanoniosome-encapsulated levofloxacin as an antibacterial agent against *Brucella*. *J Basic Microbiol.* 2020;60(3):281-90. [DOI:10.1002/jobm.201900454] [PMID]
29. del Villar-Perez VM, Barreras-Serrano A, Tamayo-Sosa AR, Tinoco-Gracia L, Melgarejo T. Evaluation of the antimicrobial activity of the K9CATH peptides of 21 and 38 amino acids against *Brucella abortus* and *Brucella melitensis*. *Thai J Vet Med.* 2020;50(4):593-7. [DOI:10.56808/2985-1130.3067]
30. Aslam M, Shehroz M, Shah M, Khan MA, Afridi SG, Khan A. Potential druggable proteins and chimeric vaccine construct prioritization against *Brucella melitensis* from species core genome data. *Genomics.* 2020;112(2):1734-45. [DOI:10.1016/j.ygeno.2019.10.009] [PMID]
31. Shoaee S, Masinaei M, Moghaddam SS, Sofi-Mahmudi A, Hessari H, Shamsoddin E, et al. National and Subnational Trend of Dental Caries of Permanent Teeth in Iran, 1990-2017. *Int Dent J.* 2023;74(1):129-37. [DOI:10.1016/j.identj.2023.07.012] [PMID] [PMCID]
32. Liu ZG, Cao XA, Wang M, Piao DR, Zhao HY, Cui BY, et al. Whole-Genome Sequencing of a *Brucella melitensis* Strain (BMWS93) Isolated from a Bank Clerk and Exhibiting Complete Resistance to Rifampin. *Microbiol Resour Announc.* 2019;8(33):e01645. [DOI:10.1128/MRA.01645-18] [PMID] [PMCID]
33. Khan AU, Shell WS, Melzer F, Sayour AE, Ramadan ES, Elschner MC, et al. Identification, Genotyping and Antimicrobial Susceptibility Testing of *Brucella* spp. Isolated from Livestock in Egypt. *Microorganisms.* 2019;7(12):603. [PMID] [PMCID] [DOI:10.3390/microorganisms7120603]
34. Cama BAV, Ceccarelli M, Rullo EV, Ferraiolo F, Paolucci IA, Maranto D, et al. Outbreak of *Brucella melitensis* infection in Eastern Sicily: Risk factors,

- clinical characteristics and complication rate. *New Microbiol.* 2019;42(1):43-8.
35. Moscowchi A, Moradian-Lotfi S, Koohi H, Sarrafan Sadeghi T. Levels of smoking and outcome measures of root coverage procedures: a systematic review and meta-analysis. *Oral Maxillofac Surg.* 2023. [DOI:10.1007/s10006-023-01172-4] [PMID]
 36. Trott DJ, Abraham S, Adler B. Antimicrobial Resistance in *Leptospira*, *Brucella*, and Other Rarely Investigated Veterinary and Zoonotic Pathogens. *Microbiol Spectr.* 2018;6(4):A11. [PMID] [DOI:10.1128/microbiolspec.ARBA-0029-2017]
 37. Singh DK, Kumar B, Shrinet G, Singh RP, Das A, Mantur BG, et al. Draft genome sequence of field isolate *Brucella melitensis* strain 2007BM/1 from India. *J Glob Antimicrob Resist.* 2018;13:152-3. [DOI:10.1016/j.jgar.2018.04.008] [PMID]
 38. Monti SM, Meccariello A, Ceruso M, Szafranski K, Sławiński J, Supuran CT. Inhibition studies of *Brucella suis* β -carbonic anhydrases with a series of 4-substituted pyridine-3-sulphonamides. *J Enzyme Inhib Med Chem.* 2018;33(1):255-9. [PMID] [PMCID] [DOI:10.1080/14756366.2017.1413097]
 39. Shoaee S, Saeedi Moghaddam S, Masinaei M, Sofi-Mahmudi A, Hessari H, Heydari M-H, et al. Trends in dental caries of deciduous teeth in Iran: a systematic analysis of the national and sub-national data from 1990 to 2017. *BMC Oral Health.* 2022;22(1):634. [DOI:10.1186/s12903-022-02634-z] [PMID] [PMCID]
 40. Basyony AF, Aboulwafa MM, Hafez MM, Abou-Gazia KAS. Antimicrobial susceptibility profile, Adherence and invasion to mammalian cells of *Brucella melitensis* isolates. *Pak J Pharm Sci.* 2018;31(6): 2379-90.
 41. Zuo SW, Ni ZL, Yao YB, Yang RS, Wang SK, Zhou YH. [Study on antimicrobial susceptibility of *Brucella* in a city]. *Zhonghua Lao Dong Wei Sheng Zhi Ye Bing Za Zhi.* 2017;35(12):939-41.
 42. Qian J, Bu Z, Lang X, Yan G, Yang Y, Wang X, Wang X. A safe and molecular-tagged *Brucella canis* ghosts confer protection against virulent challenge in mice. *Vet Microbiol.* 2017;204:121-8. [DOI:10.1016/j.vetmic.2017.04.027] [PMID]
 43. Monti SM, Meccariello A, Ceruso M, Szafranski K, Slawinski J, Supuran CT. Inhibition studies of *Brucella suis* beta-carbonic anhydrases with a series of 4-substituted pyridine-3-sulphonamides. *J Enzyme Inhib Med Chem.* 2017;33(1):255. [PMCID] [DOI:10.1080/14756366.2017.1413097] [PMID]
 44. Mortazavi H, Sadeghian A, Hazrati P, Heydari M-H, Madihi S. Oral hemorrhagic blister and its possible related factors: Analyses of reported cases in the literature. *J Oral Maxillofac Surg Med Pathol.* 2023; 35(4):358-67. [DOI:10.1016/j.ajoms.2022.12.009]
 45. Khazaei Z, Najafi A, Piranfar V, Mirnejad R. Microarray-based long oligonucleotides probe designed for *Brucella* Spp. detection and identification of antibiotic susceptibility pattern. *Electron Physician.* 2016;8(4):2297-303. [DOI:10.19082/2296] [PMID] [PMCID]
 46. Wu T, Wang S, Wang Z, Peng X, Lu Y, Wu Q. A multicopper oxidase contributes to the copper tolerance of *Brucella melitensis* 16M. *FEMS Microbiol Lett.* 2015;362(12):fnv078. [DOI:10.1093/femsle/fnv078]
 47. Maansi M, Upadhyay AK. Antibiotic susceptibility of smooth *Brucella Abortus* S99 and rough *Brucella Melitensis* B115 strains. *Indian Vet J.* 2015;92(7):80-1.
 48. Deshmukh A, Hagen F, Sharabasi OA, Abraham M, Wilson G, Doiphode S, et al. In vitro antimicrobial susceptibility testing of human *Brucella melitensis* isolates from Qatar between 2014 - 2015. *BMC Microbiol.* 2015;15:121. [PMID] [PMCID] [DOI:10.1186/s12866-015-0458-9]
 49. Shoaee S, Rezaie F, Payab M, Bakhtiari F, Heydari M-H. Experiences from the management of COVID-19 pandemic in a nursing home in Iran (March-April, 2020). *J Diabetes Metab Disord.* 2022;21(1):1195-9. [DOI:10.1007/s40200-022-01005-3] [PMID] [PMCID]