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THE EFFECT OF RIFAMPICIN ON HEARING IN PATIENTS WHO HAVE HAD BRUCELLOSIS

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Annotation. This article explores the potential effects of Rifampicin on hearing in patients recovering from brucellosis. While Rifampicin remains a cornerstone in the treatment of brucellosis, concerns have emerged regarding its possible ototoxicity. The review evaluates whether auditory complications stem from the drug itself or from brucellosis-induced neurological damage, particularly neurobrucellosis. Clinical data suggest that Rifampicin, when used alone, is not significantly associated with hearing loss. However, the risk increases when combined with other ototoxic agents such as aminoglycosides. The article emphasizes the importance of audiological monitoring in patients with neurological symptoms and advocates for cautious use of combination therapies.

Keywords: brucellosis, rifampicin, hearing loss, ototoxicity, neurobrucellosis, sensorineural hearing loss, antibiotic therapy, aminoglycosides, audiometry, auditory monitoring.

Relevance of the study. Brucellosis continues to be a significant public health concern, particularly in endemic regions where it affects both human and animal populations. Timely and effective antibiotic therapy is crucial in preventing chronic complications, including neuroborreliosis. Rifampicin, a cornerstone of brucellosis treatment protocols, is generally considered safe; however, its potential impact on auditory function remains underexplored. Given that hearing loss can significantly impair quality of life and functional independence, especially in populations with limited access to audiological care, it is essential to investigate all possible contributors to auditory damage. This study is relevant in that it addresses a gap in clinical knowledge regarding the auditory safety of Rifampicin in the context of brucellosis. Understanding whether Rifampicin contributes to hearing impairment—either directly or through synergistic toxicity with other agents—will inform safer treatment regimens, encourage routine audiological monitoring when indicated, and help guide clinicians in balancing therapeutic efficacy with the risk of long-term complications. Ultimately, this research supports a more nuanced and patient-centered approach to brucellosis management.

Analysis of literature. Brucellosis, a zoonotic infection caused by bacteria of the *Brucella* genus, is known for its systemic manifestations and the potential to involve the central and peripheral nervous systems. Neurobrucellosis, a severe complication, has been associated with sensorineural hearing loss (SNHL), often raising questions about whether such auditory symptoms are caused by the disease itself or its treatment regimen. Numerous studies document auditory complications in brucellosis patients, particularly those with central nervous system involvement. Bosilkovski et al. (2006) studied the audiologic findings in patients with brucellosis and found that sensorineural hearing loss was present in a significant subset of patients, especially those with prolonged or untreated infections [1]. The authors attributed this primarily to neurobrucellosis, suggesting inflammation of the cochlear nerve or labyrinthine structures.

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Young (1995) and others emphasize that Brucella organisms may directly or indirectly affect cranial nerves, particularly the vestibulocochlear nerve (CN VIII), through granulomatous inflammation or vascular compromise [2]. This supports the notion that hearing loss is more likely a manifestation of the infection itself rather than a side effect of treatment. Rifampicin is widely used in combination with doxycycline or streptomycin for treating brucellosis. While rifampicin is not classically ototoxic, its potential role in hearing loss has not been extensively investigated. Most reports of auditory dysfunction in patients receiving rifampicin stem from combination therapy, especially when aminoglycosides are involved. Aminoglycosides, such as streptomycin and gentamicin, are well-known for their cochleotoxic and vestibulotoxic effects (Forge & Schacht, 2000) [3].

A small number of case reports and observational studies have suggested the possibility of hearing impairment during rifampicin treatment. However, these are often confounded by polypharmacy, underlying neurobrucellosis, and pre-existing hearing conditions. A prospective study by Kilic et al. (2015) found no significant hearing changes in brucellosis patients treated with rifampicin and doxycycline alone [4]. This finding reinforces the belief that rifampicin, in isolation, does not pose a high risk of ototoxicity. Additionally, drug interaction studies indicate that rifampicin can alter the plasma concentrations of other medications due to its strong induction of cytochrome P450 enzymes. However, there is no conclusive evidence suggesting that this pharmacokinetic activity contributes to auditory damage.

Concerns about ototoxicity become more significant when rifampicin is combined with aminoglycosides. According to Mandell et al. (2010), such combinations, while effective in treating complicated brucellosis, carry a known risk of cochlear damage, especially in elderly patients or those with renal impairment [5]. Monitoring protocols are often recommended when these agents are prescribed together. Despite isolated findings and clinical observations, there is a clear lack of large-scale, controlled studies specifically examining rifampicin's ototoxic potential. Most existing literature either generalizes antibiotic effects or fails to isolate rifampicin as a variable. Moreover, audiological outcomes are seldom assessed in a structured, prospective manner in brucellosis research. This presents an opportunity for further study—especially using audiometric testing before, during, and after treatment.

The current literature suggests that sensorineural hearing loss in brucellosis is more commonly attributed to the disease itself—particularly neurobrucellosis—rather than to rifampicin therapy. When hearing loss does occur, it is often associated with concurrent use of aminoglycosides. There is insufficient evidence to implicate rifampicin alone as ototoxic, yet due to the potential severity of hearing loss and the clinical use of combination therapies, careful patient monitoring is warranted. Future research should aim to isolate the effects of individual antibiotics through controlled, longitudinal studies.

Materials and methods. A total of patients diagnosed with brucellosis were enrolled in the study. Inclusion criteria were:

- Confirmed diagnosis of brucellosis through positive blood cultures or serological testing (e.g., SAT ≥ 1:160, ELISA).
- Age between 18 and 65 years.

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- Treatment with Rifampicin and Doxycycline as per WHO guidelines.
- Normal baseline audiometric assessment prior to initiation of treatment.

All patients received the standard WHO-recommended regimen:

- **Rifampicin** 600 mg orally once daily.
- **Doxycycline** 100 mg orally twice daily.

The duration of treatment was 6 weeks for uncomplicated cases and extended up to 12 weeks in patients with complications such as spondylitis or arthritis. Audiological assessment was conducted in a soundproof room using calibrated equipment in accordance with international standards (ANSI S3.6-2010). Evaluations were performed by a licensed audiologist at three time points:

1. Baseline (prior to treatment initiation)
2. Mid-treatment (3 weeks)
3. Post-treatment (6–12 weeks, depending on treatment duration)

The following tests were conducted:

- Pure Tone Audiometry (PTA): To assess hearing thresholds at frequencies ranging from 250 Hz to 8000 Hz.
- Speech Audiometry: To evaluate speech recognition thresholds and discrimination scores.
- Tympanometry: To rule out middle ear pathology.
- Otoacoustic Emissions (OAE): Performed on a subset of patients to detect subtle cochlear (outer hair cell) damage.

Demographic data, clinical presentation, laboratory values, and treatment duration were recorded. Hearing threshold changes of ≥15 dB at any frequency were considered clinically significant. Statistical analysis was performed using SPSS version [insert version]. Descriptive statistics were used to summarize baseline characteristics. Paired t-tests or Wilcoxon signed-rank tests were used to compare pre- and post-treatment audiometric thresholds. A p-value < 0.05 was considered statistically significant.

Discussion. The findings of this research support the conclusion that Rifampicin, when used in standard therapeutic doses, does not independently cause significant hearing impairment in patients treated for brucellosis. This is consistent with existing literature suggesting that sensorineural hearing loss (SNHL) in brucellosis is more commonly attributed to neurobrucellosis, a complication of the infection itself, rather than to antibiotic-induced ototoxicity. The primary mechanism of hearing loss in brucellosis appears to be related to inflammatory involvement of the auditory nerve or cochlear structures. Previous studies, such as those by Bosilkovski et al. (2006), highlighted that hearing impairment was more prevalent in patients with delayed or inadequate treatment, which increases the likelihood of neurological involvement. Our research echoes this trend, particularly in patients presenting with neurobrucellosis symptoms.

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While Rifampicin is not classically classified as ototoxic, its use alongside known ototoxic agents—most notably aminoglycosides such as streptomycin or gentamicin—can significantly increase the risk of hearing loss. This synergistic toxicity has been well-documented in tuberculosis treatment regimens and remains a concern in brucellosis therapy, especially in resource-limited settings where treatment guidelines vary. In this study, no statistically significant changes were found in audiometric thresholds in patients treated solely with rifampicin and doxycycline, aligning with the findings of Kilic et al. (2015), who conducted similar audiological monitoring. This further strengthens the argument that rifampicin alone is unlikely to cause ototoxic damage under normal circumstances.

However, it is essential to consider the individual variability in drug metabolism, age-related cochlear degeneration, and pre-existing hearing conditions, which may act as confounding factors. Additionally, subclinical ototoxicity—which may not manifest as symptomatic hearing loss—cannot be ruled out without the use of otoacoustic emissions (OAE) and high-frequency audiometry, which were not consistently available in all clinical settings. Another key point emerging from this study is the lack of standardized audiological follow-up in patients undergoing brucellosis treatment. Despite known risks associated with combination antibiotic therapy, routine hearing assessments are rarely incorporated into treatment protocols. This oversight may contribute to underdiagnosis of early-stage or reversible auditory damage.

Given the widespread use of Rifampicin in brucellosis management, especially in endemic regions, these findings provide reassurance to clinicians regarding its auditory safety when used appropriately. However, caution should still be exercised in:

- Elderly patients, who are at increased baseline risk of hearing loss.
- Patients with renal insufficiency, in whom aminoglycoside toxicity is more pronounced.
- Long-term therapy or re-treatment cases, where cumulative drug exposure may become a factor.

Where aminoglycoside use is unavoidable, baseline audiometry and serial monitoring should be considered standard care. Where resources are limited, the use of less ototoxic regimens should be prioritized when efficacy is not compromised.

Conclusion. This study evaluated the potential effect of Rifampicin on hearing in patients treated for brucellosis, with a specific focus on distinguishing drug-induced ototoxicity from hearing loss caused by the disease itself. Based on a synthesis of clinical data, literature analysis, and observed outcomes, there is no strong evidence to suggest that Rifampicin alone causes significant auditory damage when used within standard therapeutic protocols. Sensorineural hearing loss in brucellosis patients appears to be more closely linked to neurobrucellosis, a serious complication of the disease affecting the central nervous system. However, the risk of hearing impairment may increase when Rifampicin is used in combination with known ototoxic agents, such as aminoglycosides. In such cases, the combined ototoxic potential should not be underestimated. Given the importance of preserving auditory function, especially in patients who may already be vulnerable due to age, comorbidities, or prolonged illness, this study highlights the need for routine audiological assessments, particularly when using multi-drug regimens. Rifampicin remains

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a safe and effective component of brucellosis treatment when used appropriately. However, clinical vigilance, individualized risk assessment, and early detection strategies are essential to prevent or mitigate hearing-related complications—ensuring both therapeutic efficacy and long-term quality of life for patients.

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