Systematic Review / Meta-analysis

ANNALS OF MEDICINE & SURGERY

OPEN

Efficacy and safety of azithromycin in treating sinusitis patients: a systematic review and meta-analysis of randomized controlled trails

Wafa Elnaseeh, MBBS[a], Mohamed Yousif Elamin[b,*], Rahaf Bandar Alsliham, MBBS[c], Lujain Bandar Alotaibi, MBBS[d], Hissa Abdulaziz Alaiban, MBBS[d], Mawadah Fouzy Kattan, MBBS[e], Sadeem Khalid Alquraini, MBBS[f], Ahmed Khalid Alkhateeb, MBBS[a], Shaima ShamsEldeen KhalfAllah Ahmed, MBBS[b], Ziyad Jamal Alamer, MBBS[a], Ahmed Mohammed Alawdah, MBBS[a], Mohammed Hamad Alhushayyish, MBBS[g], Muhanna Jubayr Mohammed Altalhi, MBBS[h], Nojuod Fares Abdullah Alhadidi, MBBS[i], Albatul Omar Alghamdi, MBBS[j]

Background: Sinusitis is an inflammation of the paranasal sinuses and is commonly treated with antibiotics. The widely used antibiotics for this condition are macrolides, especially azithromycin. However, its effectiveness and side effects are still questionable compared to the other antibiotics. Therefore, this systematic review and meta-analysis assessed the efficacy and safety profile of azithromycin in sinusitis.

Methods: We adhered to PRISMA guidelines. A comprehensive literature review was performed to find out about randomized controlled trials concerning azithromycin compared with other antibiotics in sinusitis treatment. The main outcomes were the cure rate, pathogen eradication rate, and relapse rate. The secondary outcome was the adverse events rate.

Results: Fourteen trials were considered for review, with a sample size of 4201 patients. The pooled analysis for included studies indicated a high cure rate (70.86%) and pathogen eradication rate (74.55%), as well as a low relapse rate (4.82%) and adverse events rate (14.33%) for azithromycin in treating sinusitis patients. The quality of the included studies was considered to be moderate. In a meta-analysis, azithromycin demonstrated superiority in the cure rate to other antibiotics in the study but no difference in pathogen eradication rate, relapse rate, or adverse events rate.

Conclusion: Our results showed promising efficacy and safety of azithromycin in the management of sinusitis patients. However, moderate heterogeneity among studies and a 14.33% rate of adverse effects, primarily gastrointestinal, indicate the importance of individualized treatment decisions. Further research is needed to address variability and optimize its clinical application.

Keywords: antibiotic therapy, azithromycin, efficacy, macrolides, meta-analysis, safety, sinusitis, systematic review

Introduction

Sinusitis is a common disease that usually occurs as a complication of viral upper respiratory tract infections or allergic inflammation.

HIGHLIGHTS

- A systematic review and meta-analysis of randomized controlled trials.
- Azithromycin demonstrated efficacy in treating sinusitis, achieving a 70.86% clinical cure rate.
- The pathogen eradication rate for azithromycin was notably high, reaching 74.55%.
- Azithromycin exhibited a low relapse rate 4.83%, suggesting improved long-term outcomes.
- While gastrointestinal disturbances and other adverse events were observed in a small percentage of patients, azithromycin was generally well-tolerated, with a low adverse event rate of 14.33%.
- Fourteen trials were included in this study.

Both conditions are associated with swelling of the mucosa that reduces the patency of sinus ostia, impairment of ciliary action, and mucus overproduction. These abnormalities frequently cause retention of secretions within the sinus, favoring a secondary bacterial infection and the conversion of mucus to mucopus. Mucopus further impairs ciliary function and increases swelling around the ostia, creating a vicious cycle[1]. Non-severe, uncomplicated acute

[a]College of Medicine, King Faisal University, [b]Faculty of Medicine, University of Khartoum, [c]College of Medicine, Princess Nourah Bint Abdulrahman University, [d]Aldiriyah Hospital, [e]College of Medicine and Surgery King Abdulaziz University Hospital, [f]College of Medicine and Surgery, Imam Mohammad Ibn Saud Islamic University, [g]Saudi Board Residency Program, [h]College of Medicine, University of Taif, [i]College of Medicine, Vision College and [j]Jeddah University

Sponsorships or competing interests that may be relevant to content are disclosed at the end of this article.

*Corresponding author. Address: Faculty of Medicine, University of Khartoum, Omdurman, Khartoum, Sudan. E-mail: mohamedyousif621@gmail.com (M. Yousif Elamin).

Annals of Medicine & Surgery (2025) 87:2324–2335

Received 21 September 2024; Accepted 3 March 2025

Published online 20 March 2025

http://dx.doi.org/10.1097/MS9.0000000000003182

sinusitis often occurs with, or subsequent to, the common cold or other upper respiratory tract infections and is one of the most frequently seen infections in outpatient clinics. Accurate diagnosis on clinical grounds alone is not always easy, especially in an outpatient setting[2]. Clinical presentations are mucopurulent nasal discharge, nasal congestion, fever, and facial pain or tenderness lasting 7 to 28 days. Culturing is the most distinguishing means of diagnosis; however, it is invasive, requires up to 72 hours for identification, and does not always grow causative pathogens. Diagnosis is therefore often presumptive, being based on clinical presentation and diagnostic interpretation, and may include culturing. Diagnostic techniques include sinus radiography, sinus transillumination, fiber-optic endoscopy, and computerized tomography, although all but sinus radiographs may be highly costly[3]. Unfortunately, the documented data and statistics of sinusitis, including all of its types (acute or chronic), are only from developed countries; for example, the most common reason for clinical visits in the United States is sinusitis (also known as rhinosinusitis). It is also one of the top reasons that antibiotics are prescribed. Over one year, there were up to 73 million restricted-activity days related to sinusitis and total direct medical costs of almost 2.4 billion United States dollars (USD), not including surgery or radiographic imaging[4]. On the other hand, the prevalence of chronic sinusitis in Saudi Arabia is estimated to be 25% among the total Saudi population of 36 million individuals, and the estimated prevalence of chronic rhinosinusitis is 9 million individuals[5].

Most sinus infections are viral, and only a small proportion develops a secondary bacterial infection. Rhinoviruses, influenza viruses, and parainfluenza viruses are the most common causes of sinusitis. The frequently isolated bacteria from pediatric and adult patients with community-acquired acute purulent sinusitis are Streptococcus pneumoniae, Haemophilus influenzae, Moraxella catarrhalis, and Streptococcus pyogenes. Staphylococcus aureus and anaerobic bacteria (Prevotella and Porphyromonas, Fusobacterium, and Peptostreptococcus spp.) are the main isolates in chronic sinusitis. Pseudomonas aeruginosa and other aerobic and facultative gram-negative rods are commonly isolated from patients with nosocomial sinusitis, the immunocompromised host, those with HIV infection, and in cystic fibrosis. Fungi and Pseudomonas aeruginosa are the most common isolates in neutropenic patients[6]. The treatment of sinusitis involves several options: nasal spray, decongestants, and antibiotics. Unfortunately, the distinguishing of sinusitis cause (viral or bacterial) is difficult; that's why antibiotics are commonly prescribed to patients by doctors or pharmacies. Commonly used antibiotics include amoxicillin, penicillin, azithromycin, and co-amoxiclav.

Azithromycin is approved for sinusitis as monotherapy for sinusitis in Europe and other continents. The recommended dose is 500 mg once daily for 3 days for sinusitis but not the definitive one, as there are other options available[7]. Azithromycin belongs to macrolides and achieves its antimicrobial effect by binding to the 50S ribosomal subunit of susceptible microorganisms and interfering with bacterial protein synthesis. However, azithromycin is different from all other macrolides in its structure and chemical components, which leads to an expanded antimicrobial spectrum and a novel pharmacokinetic profile. The in vitro antimicrobial spectrum of azithromycin includes the gram-positive organisms susceptible to erythromycin and gram-negative bacteria, including the previously mentioned pathogens associated with sinusitis[7]. Compared to other macrolides, azithromycin has fewer interactions with medications metabolized by the cytochrome P450 system, making it safer for patients on multiple drugs[8-12].

This systematic review evaluates the effectiveness of azithromycin in treating sinusitis, a prevalent condition that significantly impacts both healthcare systems and patients. The review employs a rigorous methodology, including systematic search strategies and strict inclusion criteria, to critically analyze the current evidence on the use of azithromycin for sinusitis management. The goal is to not only summarize existing studies but also assess their quality, providing insights to guide clinical practice, policy development, and future research in this area.

Methods

Study design

This is a systematic review and meta-analysis of randomized controlled trials (RCTs). The study was conducted according to PRISMA guidelines for systematic reviews[13].

Eligibility criteria

RCTs were included, either published in peer-reviewed journals or posting results on clinicaltrials.gov; studying patients with sinusitis of any age and gender who used antibiotics and comparing azithromycin to placebo, azithromycin with different doses, or other antibiotics.

The primary outcomes were the cure rate of sinusitis and the relapse rate of sinusitis. The secondary outcomes were the pathogens eradication rate and the incidence of adverse effects.

Studies were included if they met the following criteria:

Population: Adults or children who were diagnosed with sinusitis based on validated criteria.

Intervention: Azithromycin, Zithromax, or Azasite as the primary treatment arm.

Comparator: Placebo, standard antibiotic therapy, or other relevant control group.

Outcomes: Clinical cure of sinusitis (defined by specific criteria established in the studies) and adverse events associated with Azithromycin treatment.

Study design: RCTs.

Exclusion criteria

We excluded other types of studies, like case reports, cohorts, and review articles. Clinical trials with no control group were also excluded.

Search strategy

We conducted a comprehensive search of electronic databases, including PubMed, MEDLINE, Embase, and the Cochrane Central Register of Controlled Trials (CENTRAL) from March to April 2024. The search strategy was composed of keywords like "Azithromycin," "Zithromax," "Azasite," "sinusitis," and "efficacy." There was no restriction on publication date or language, but all non-English studies' full texts and patient data were not available to include. Also, we manually searched the references and similar articles in the included articles. The process of screening was reported using the PRISMA flow chart (Fig. 1) [14].

Data extraction and management

Two independent reviewers screened titles and abstracts for eligibility. The full-text articles were screened for eligibility

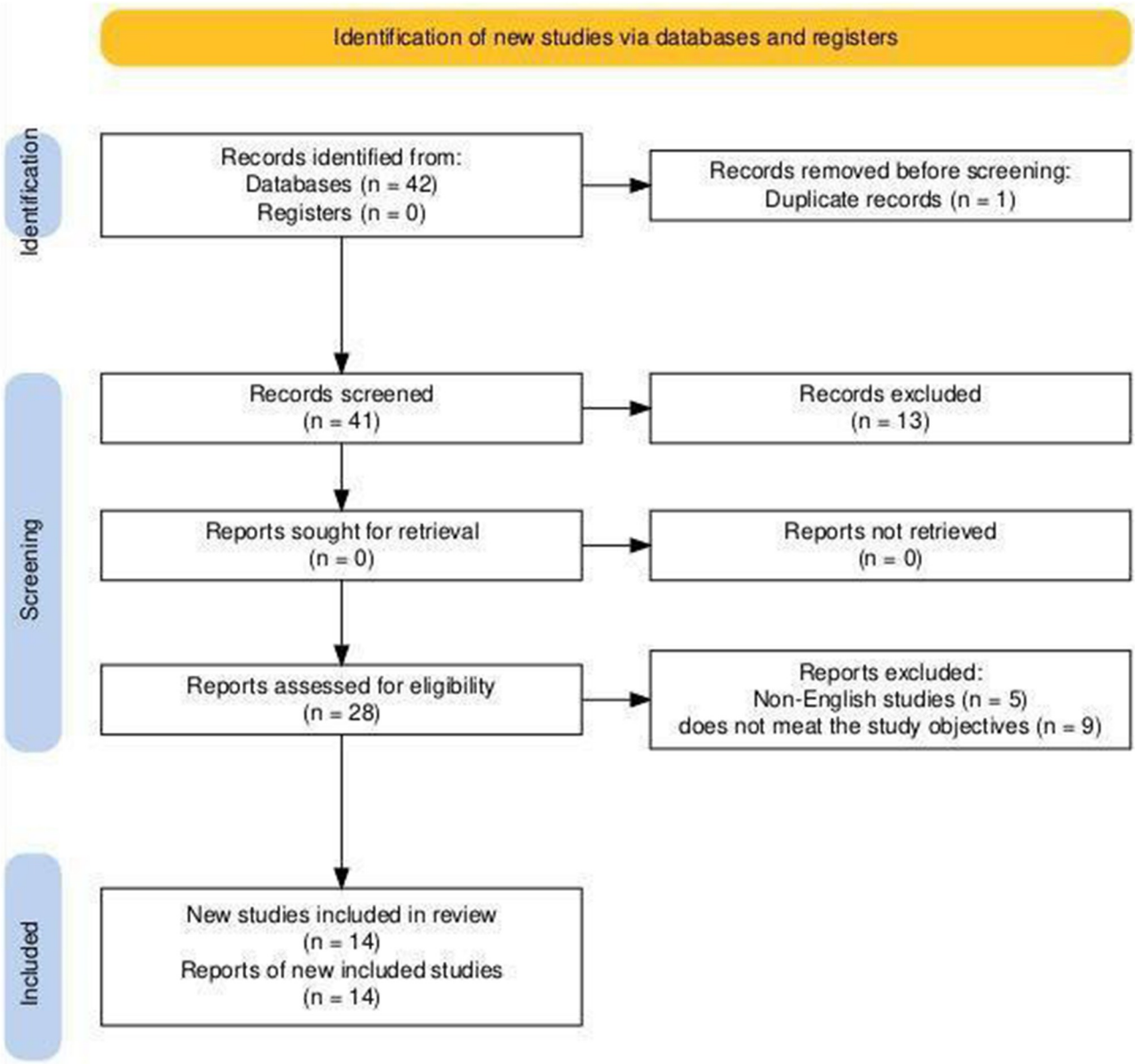

Figure 1. Preferred reporting items for the systematic review and meta-analysis (PRISMA) flowchart of the systematic review process.

based on their methodology and relevant outcomes. The discrepancy during the screening was solved by a third author. Data was extracted using Google Spreadsheets by three independent authors and revised by a fourth one for any conflict. These data include study characteristics, participant details, intervention specifics, and outcomes.

Risk of bias assessment

The methodological quality of the included studies was critically appraised using the Cochrane Collaboration's tool for assessing the risk of bias in randomized trials (RoB 2.0)[15]. This tool evaluates bias arising from factors such as randomization, allocation concealment, blinding, incomplete outcome data (attrition bias), selective outcome reporting, and other sources of bias (Figs. 2 and 3).

Data synthesis

Data were analyzed using a meta-analysis approach when a sufficient number of studies with similar interventions and outcomes were available. We used a random-effects model to account for potential heterogeneity (variation) across studies. Pooled effect sizes were calculated for key outcomes (e.g., cure rate, improvement rate). Statistical heterogeneity was assessed using the I^2 statistic.

Ethical considerations

This systematic review and meta-analysis adhered to ethical principles for conducting research involving human participants. We ensured that the included studies obtained ethical approval from relevant institutional review boards.

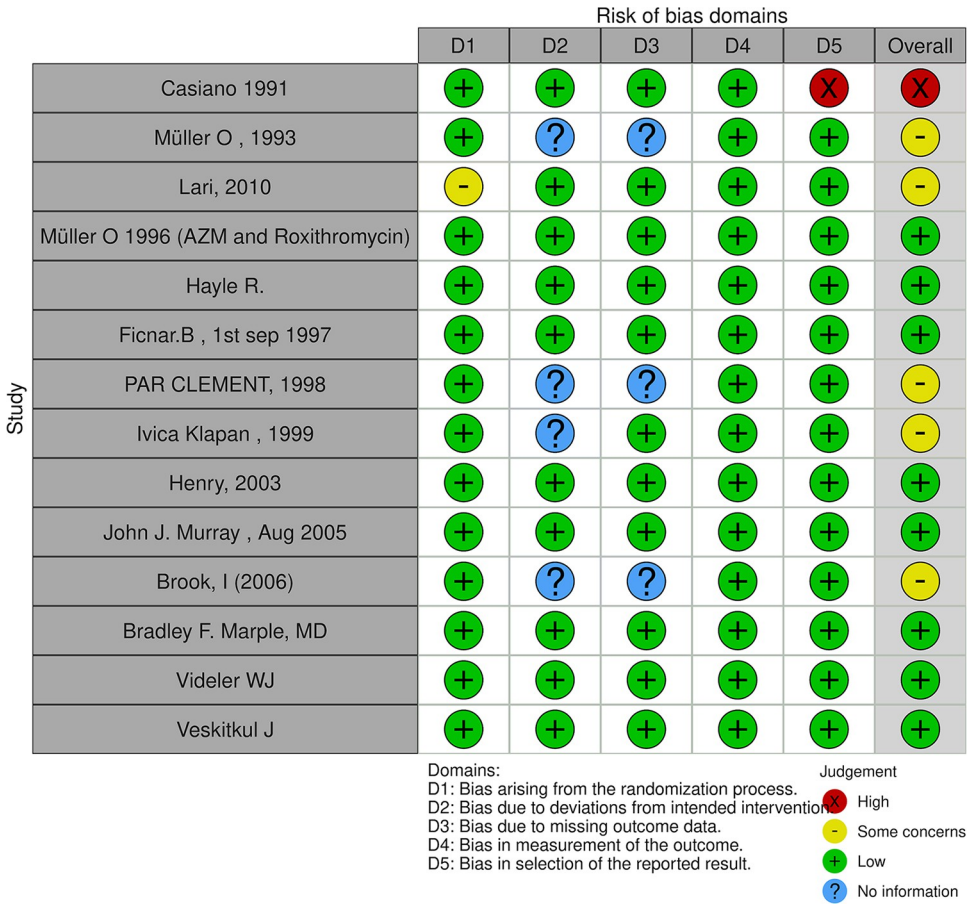

Figure 2. Risk of bias graph of included studies.

Results

The PRISMA flow diagram depicting the selection of studies for the meta-analysis of azithromycin in patients with sinusitis is shown in Fig. 1. The total number of records considered from all databases (PubMed, Embase, ICTRP, CT.gov, CINAHL) was 1271 RCTs. Of these 1271 RCTs, we rejected 1264 RCTs, as definitely not meeting the inclusion criteria simply based on title or abstract (1190 RCTs) or because they were duplicates (74 RCTs). The main reasons for irrelevance were studies with interventions other than AZM and incomplete studies.

We retrieved a total of 138 new records after duplicates were removed from searches in MEDLINE (60 records), EMBASE (137 records), CENTRAL (20 records), and OpenGrey (three records).

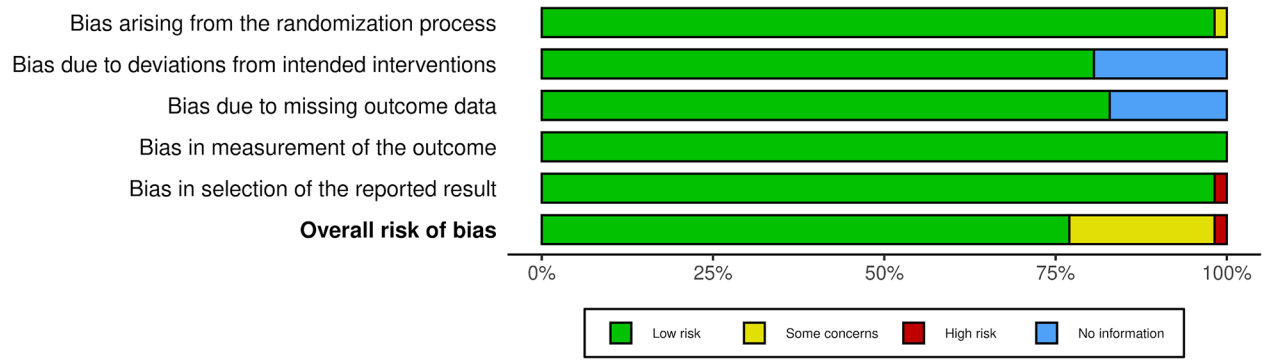

Figure 3. Risk of bias summary of included studies.

We identified 28 reports to be evaluated in detail. We excluded non-English reports because their full texts were not available (5 records) and reports that did not meet the specific study objectives (9 records), leaving 14 individual studies to be eligible for inclusion in the review.

Patient characteristics and baseline data

Four of the 14 included studies compared azithromycin treatment to amoxicillin-clavulanate (co-amoxiclav)[1,2,7,16]. Three studies compared azithromycin to other macrolides (one study for clarithromycin[17], one study for roxithromycin[18], and one for telithromycin[19]); two studies compared azithromycin to levofloxacin[20,21]; two studies compared azithromycin to placebo[22,23]; one study compared azithromycin to amoxicillin[24]; one study compared azithromycin to phenoxymethylpenicillin[25]; and the last study compared 3-day azithromycin therapy to 5-day azithromycin therapy[26]. With a total of 4125 sinusitis patients, of whom 2421 were female. There were 2257 patients in all azithromycin groups and 1858 in all control groups. The overall age of patients treated with azithromycin for sinusitis is approximately 37.08 years (95% CI 24.25–49.91) (Table 1).

Table 1

Characteristics of included studies

Study	Country	Follow-up	N	Intervention	Control	Outcome	Cure rate	Side effects
Casiano, 1991[23]	USA	11 days	78	Azithromycin (5 doses, 5 days)	Amoxicillin (30 doses, 10 days)	Azithromycin was as effective, with better tolerability and compliance.	73.91%	• Headache • Nausea
Müller, 1996[16]	Germany	25–30 days	380	Azithromycin (3 days)	Clarithromycin (10 days)	Azithromycin was equally effective and well-tolerated.	66.21%	Gastrointestinal tract disturbances: • Abdominal pain • Diarrhea • Gastroenteritis • Nausea • Vomiting Other: • Dizziness • Somnolence • Pruritus • Glossitis • Tongue discoloration • Hypokalemia • Increase blood urea nitrogen • Hematological disturbances
Müller, 1996[17]	Germany	25–30 days	441	Azithromycin (3 days)	Roxithromycin (10 days)	Azithromycin was equally effective and well-tolerated.	73.52%	Gastrointestinal tract disturbances: • Diarrhea • Gastritis • Gastroenteritis • Nausea • Vomiting Central nervous system events Hematological changes Elevated serum hepatic enzyme activities Increased blood urea concentrations
Hayle, 1996[25]	Norway	23–27 days	438	Azithromycin (10 days)	Phenoxymethylpenicillin (10 days)	No significant difference in efficacy between the treatments.	79.09%	Gastrointestinal tract disturbances
Ficnar.B, 1997 Sep[26]	Croatia	10 days	371	Azithromycin (3 days)	Azithromycin (5 days)	No significant difference in efficacy between the treatments but 3 days course is faster and better tolerated.	60.93%	Gastrointestinal tract disturbances Hematological changes
Clement, 1998[1]	Belgium	4 weeks	254	Azithromycin (3 days)	Co-amoxiclav (10 days)	Azithromycin was as effective, with fewer compliance issues.	75%	Gastrointestinal tract disturbances: • Abdominal pain

(*Continued*)

Table 1

(Continued)

Study	Country	Follow-up	N	Intervention	Control	Outcome	Cure rate	Side effects
								• Diarrhea • Nausea Central nervous system • Headaches • Vertigo
Culig, 1999[2]	USA	4 weeks	100	Azithromycin (3 days)	Amoxicillin (10 days)	No significant difference in bacteriological response.	93.61%	Gastrointestinal tract disturbances: • Nausea • Vomiting
Henry, 2003[7]	USA	4 weeks	941	Azithromycin (3 or 6 days)	Amoxicillin-Clavulanate (10 days)	Azithromycin was as effective, with better safety and compliance.	72.80%	Gastrointestinal tract disturbances: • Nausea • Diarrhea • Flatulence
Murray, 2005[20]	USA	17–24 days	538	Azithromycin (single dose)	Levofloxacin (10 days)	Azithromycin was as effective as Levofloxacin.	98.37%	Gastrointestinal tract disturbances: • Nausea • Diarrhea • Vomiting • Abdominal pain
Brook, 2006[19]	USA	12 days	105	Azithromycin (3 days)	Telithromycin (5 days)	No significant differences in pathogen eradication.	45.65%	Not mentioned
Marple, 2007[21]	USA, Europe, India, Latin America	11 months	534	Azithromycin (single dose)	Levofloxacin (10 days)	Azithromycin led to earlier symptom resolution.	32.59%	Gastrointestinal tract disturbances: • Nausea • Diarrhea • Abdominal pain
Lari, 2010[16]	Iran	4 weeks	76	Azithromycin (5 days)	Co-amoxiclav (10 days)	Azithromycin was more efficient, with fewer side effects and better compliance.	80%	Not mentioned
Videler, 2011[22]	Netherlands	3 months	60	Azithromycin (12 weeks)	Placebo	No significant advantage of Azithromycin over placebo for chronic rhinosinusitis.	9.09%	Gastrointestinal tract disturbances: • Diarrhea Central nervous system • Headaches
Veskitkul J, 2017[23]	USA	12 months	40	Azithromycin (3 days)	Placebo	There's significant advantage of Azithromycin over placebo for chronic rhinosinusitis	85%	Well tolerated without any adverse events.

Efficacy of azithromycin in sinusitis treatment using pooled analysis

Azithromycin cure rate

Assessment of cure included data from 13 studies (Fig. 4). The pooled cure rate of azithromycin for treating sinusitis is approximately 70.86% (95% CI 59.04%–80.40%, *P* 0.00087). The I^2 value of 52.81% suggests moderate heterogeneity among the included studies, indicating some variability in the cure rates reported across different studies.

Azithromycin pathogen eradication rate

Assessment of pathogen eradication included data from eight studies (Fig. 5). The overall event rate (pathogen eradication rate) of azithromycin for treating sinusitis is approximately 74.55%. The confidence interval ranges from 57.89% to 86.20% (95% CI, *P* 0.0054). The I^2 value of 59.72% suggests moderate to substantial heterogeneity among the included studies, indicating significant variability in the pathogen eradication rates reported across different studies.

Azithromycin relapse rate

Assessment of relapse included data from seven studies (Fig. 6). The overall relapse rate of sinusitis is approximately 4.83% (95% CI 2.9%–7.96%, $P < 0.001$). The I^2 value of 0 suggests minimum heterogeneity among the included studies.

Azithromycin adverse effects and safety

Assessment of adverse effects included data from 11 studies (Fig. 7). The pooled adverse effects rate among sinusitis patients treated with azithromycin is approximately 14.33% (95% CI 7.64%–25.27%, $P < 0.001$). The I^2 value of 32.86% suggests moderate heterogeneity among the included studies.

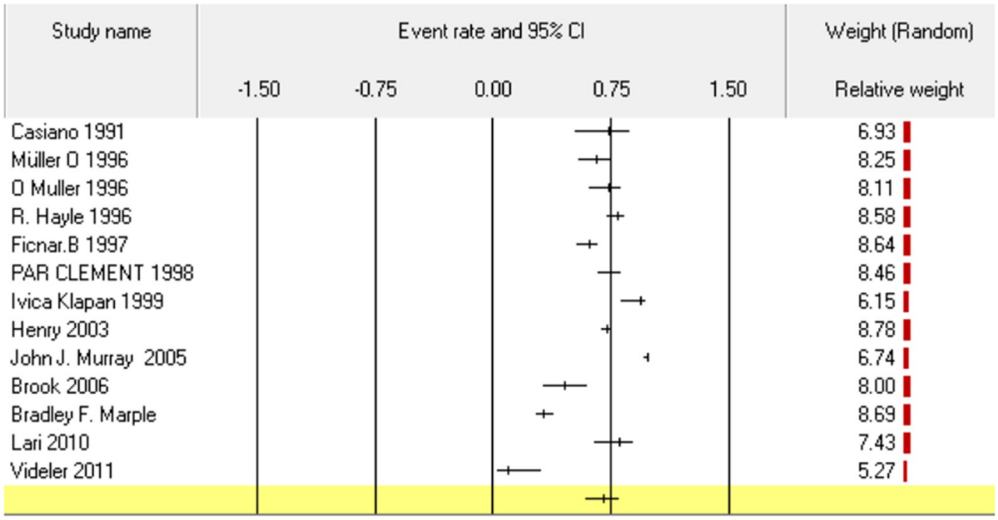

Figure 4. Forest plot for the cure rate among sinusitis patients treated with azithromycin.

Azithromycin outcomes summary

In Fig. 8, you can find a summary for all azithromycin outcomes rate in treating sinusitis patients.

Efficacy of azithromycin in sinusitis treatment compared with specific control groups using meta-analysis

The meta-analysis included 12 studies with (n) patients with rhinosinusitis treated with azithromycin (intervention) versus other antibiotics or placebo (control) (Table 1). The mean age of patients in the intervention groups is 39.76 (CI 38.15–41.36) with 50.4% males (CI 44.1–56.7), while the mean age of patients in the control group is 39.47 (CI 37.64–41.30) with 47.8% males (CI 41–54.7).

Cure rate

The overall effect size is 1.49 (CI 1.25–1.97, *P* 0.005) in favor of azithromycin, suggesting that azithromycin is generally more effective than other antibiotics, with 49% higher odds of a successful outcome across the studies included in this meta-analysis (Fig. 9). The I^2 value was 21.78, indicating moderate heterogeneity, while subgroup analysis for azithromycin versus penicillins (odds ratio 1.26, CI 0.95–1.65, *P* 0.097) and azithromycin versus clarithromycin family (odds ratio 1.174, CI 0.62–2.21, *P* 0.619) showed no statistical preference for azithromycin over the specific group.

Pathogen eradication

The overall effect size is 1.23 (CI 0.78–1.92, *P* 0.364) in favor of azithromycin, suggesting no significant preference for azithromycin over other antibiotics in pathogen eradication (Fig. 10). I^2 value was 0, indicating consistent results (Q = 3.78, Q (df) = 5, I^2 = 0.00).

Relapse

The overall effect size is 0.934 (CI 0.71–1.22, *P* 0.626) in favor of azithromycin, suggesting no significant difference between

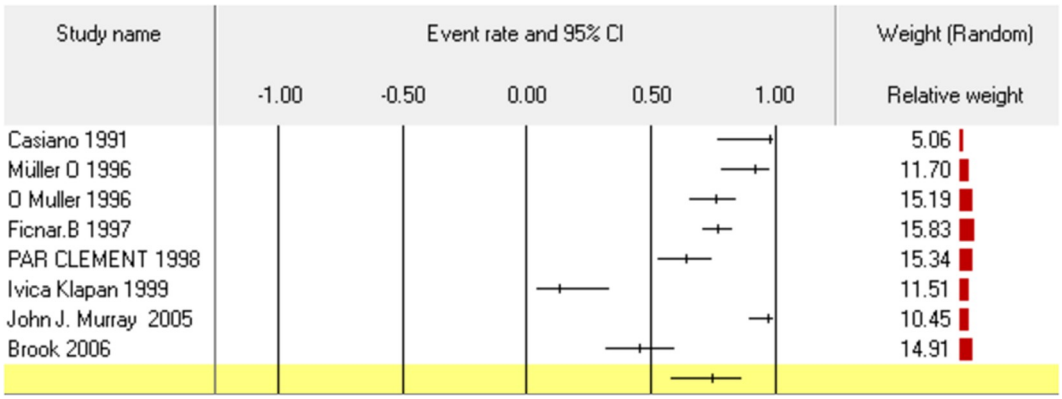

Figure 5. Forest plot for the pathogen eradication rate among sinusitis patients treated with azithromycin.

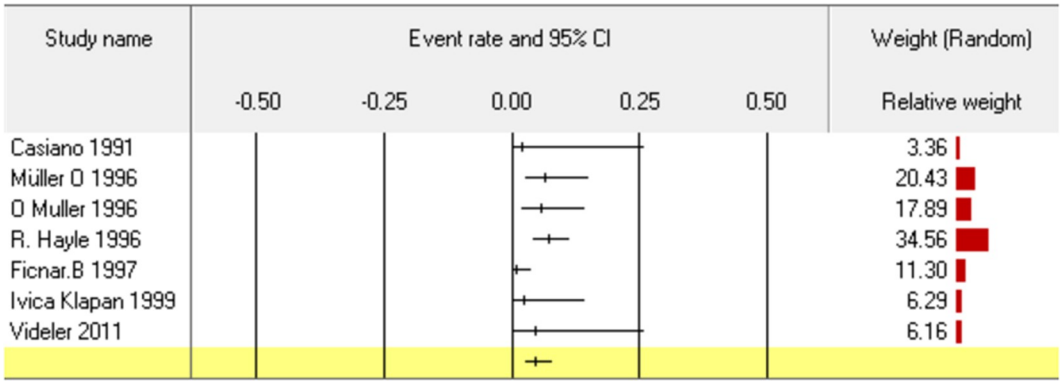

Figure 6. Forest plot for the relapse rate among sinusitis patients treated with azithromycin.

azithromycin and other antibiotics in pathogen relapse rates (Fig. 11). The I^2 value was 0, indicating consistent results (Q = 3.8, Q (df) = 4, I^2 = 0.00).

Adverse effects

The overall effect size is 0.846 (CI 0.566–1.26, *P* 0.413) in favor of azithromycin, suggesting no significant difference between azithromycin and other antibiotics in adverse effect rates (Fig. 12). The I^2 value was 0, indicating consistent results (Q = 5.85, Q (df) = 8, I^2 = 0.00).

Discussion

The findings of the current review provided valuable insights into the role of azithromycin in the management of sinusitis, though it also highlighted the need for further research addressing existing gaps and heterogeneity among the studies. The meta-analysis included data from 14 studies, which revealed a pooled cure rate of approximately 70.86% for azithromycin in the treatment of sinusitis. This suggested that a substantial proportion of patients experience complete resolution of symptoms when treated with azithromycin. This result was noted to be consistent with the known antimicrobial properties of azithromycin, which targets the 50S ribosomal subunit of susceptible bacteria, causing inhibition of protein synthesis leading to bacterial death. In addition, the pooled event rate for pathogen eradication was 74.55%, which indicated the effectiveness of azithromycin in clearing the causative pathogens of sinusitis. Pathogen eradication is essential as it is often associated with clinical improvement and reduced rates of relapse. The low rate of relapse noted at 4.38% further supports the efficacy of azithromycin in providing sustained relief from sinusitis, thereby reducing the likelihood of recurrent infections. These findings collectively suggest that azithromycin is a viable treatment option for sinusitis, particularly in cases where pathogen eradication and sustained relief from symptoms are the primary goals. One of the significant challenges encountered in the meta-analysis was moderate to substantial heterogeneity observed across the studies, particularly when outcomes were related to cure, improvement, and pathogen eradication rates. The I^2 values for these outcomes ranged from 44.29% to 59.72%, indicating considerable variability in the results. This heterogeneity can be attributed to factors such as differences in study populations, variations in diagnostic criteria, and discrepancies in treatment protocols. For instance, studies from varying geographical locations such as the United States and Europe, the

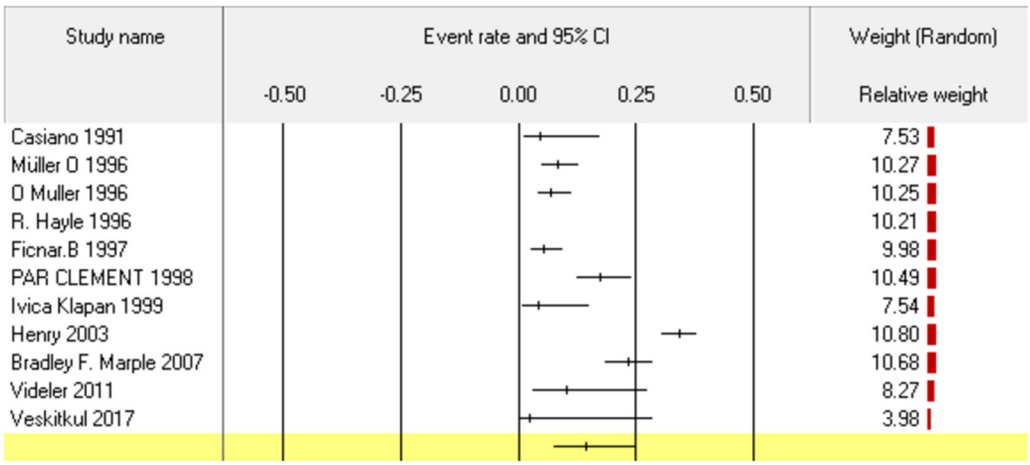

Figure 7. Forest plot for the adverse effects rate among sinusitis patients treated with azithromycin.

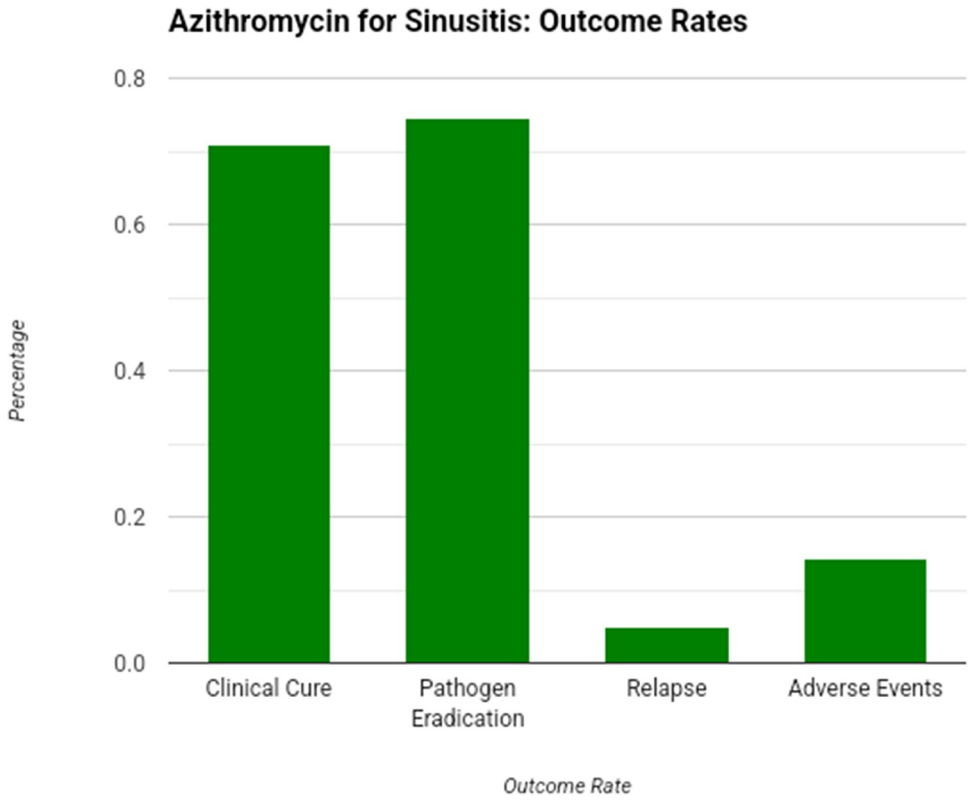

Figure 8. Outcomes rate summary of azithromycin for sinusitis treatment.

Middle East, and Asia may reflect variations in the prevalence of specific pathogens, patient demographics, and healthcare practices that could influence observed outcomes. Moreover, the study designs and methodologies employed across the analyzed studies were not uniform, with varied diagnostic criteria as well. This lack of standardization could contribute to observing heterogeneity as the accuracy of sinusitis diagnosis directly impacts the assessment of treatment efficacy. The results also revealed that the efficacy of azithromycin against the control group across multiple studies indicated that there is no statistically significant difference in efficacy between azithromycin and the control. A similar trend was noted in relation to the benefit of azithromycin over control treatments for sinusitis as indicated by the confidence intervals of individual studies. The safety profile of azithromycin was also evaluated in the meta-analysis, with the pooled analysis indicating an adverse effects rate of approximately 14.33%. The most commonly reported adverse effects were gastrointestinal disturbances, including nausea, vomiting, diarrhea, and abdominal pain. These side effects were noted to be consistent with the known safety profile of azithromycin, which is generally well tolerated; however, it can cause gastrointestinal issues in some patients. The I^2 value for adverse effects was 32.86%, suggesting moderate heterogeneity among the studies included in the meta-analysis. This variability in adverse effects rate could be owing to variances in study populations with certain groups, such as older adults or those with underlying gastrointestinal conditions, being more susceptible to adverse effects. While the adverse effects rate of azithromycin is comparable to that of other antibiotics commonly used to treat sinusitis, it is important to carefully weigh the benefits and risks of azithromycin on an individual basis. In the case of patients with a history of antibiotic-associated diarrhea or those at high risk of gastrointestinal side effects, alternative treatments with a more favorable safety profile may be preferable. In addition to this, the potential for antibiotic resistance is an important consideration in the use of azithromycin. Overuse or inappropriate use of antibiotics can contribute to the development of resistant bacterial strains, which can limit future treatment options. Overall, the findings of this meta-analysis have important implications for clinical practice, particularly in the management of sinusitis. The demonstrated efficacy of azithromycin in achieving clinical cure, improving symptoms of sinusitis, and eradicating pathogens supports its use as a treatment option for sinusitis. However, the moderate heterogeneity observed among the studies reviewed in the meta-analysis highlighted the need for caution in interpreting the results and underscored the importance of individualized treatment decisions. The meta-analysis also highlights the importance of considering factors such as patient characteristics, likelihood of bacterial and viral sinusitis, and potential adverse effects when deciding the prescription of azithromycin.

Limitations and strengths

This meta-analysis has several limitations. The inclusion of studies with varying methodologies and patient populations may have influenced the pooled estimates. Additionally, the reliance on published studies might introduce publication bias. As a limitation too, the studies do not provide enough information

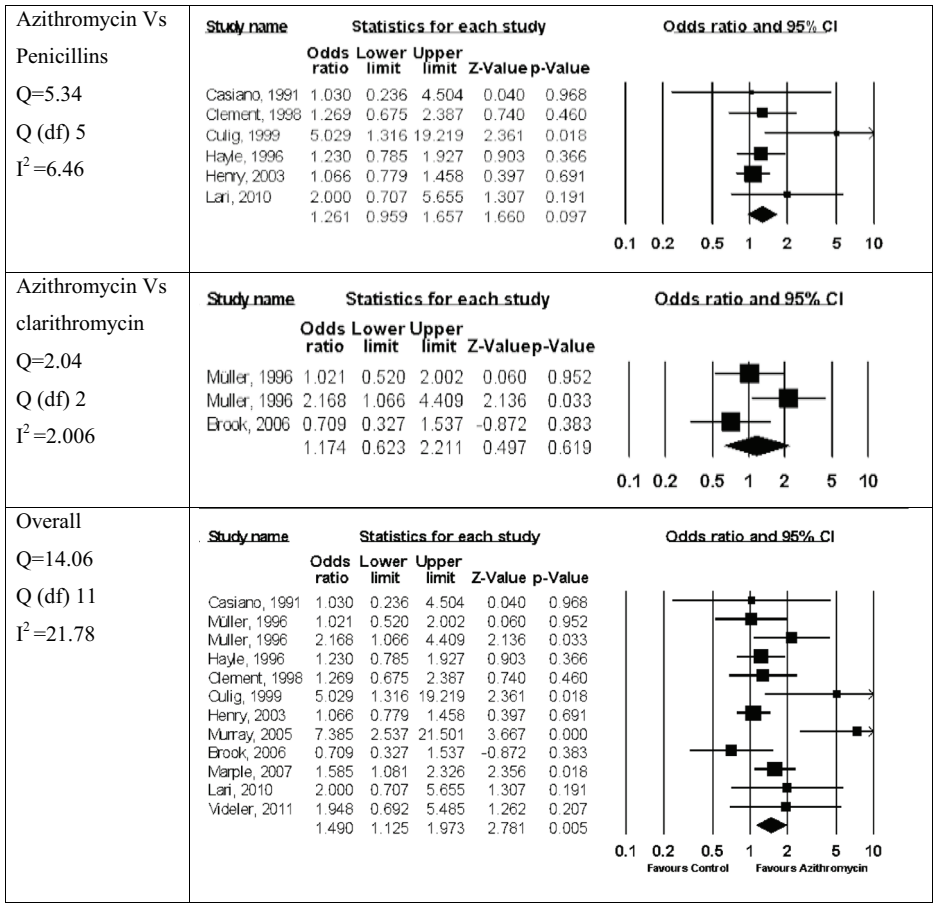

Figure 9. Meta-analysis for cure rate of azithromycin versus other controls.

to make finalized conclusions about the efficacy of Azithromycin in sinusitis treatment. On the other hand, the comprehensive search strategy and inclusion of relevant outcomes strengthen the study.

Conclusion

The findings of this meta-analysis suggest that azithromycin is an effective treatment option for sinusitis. While heterogeneity among studies limits definitive conclusions, the overall positive impact on cure and pathogen eradication is evident. However, careful consideration of potential adverse effects is necessary. Future research should focus on reducing heterogeneity and confounding variables, identifying predictors of treatment response, and exploring alternative therapeutic strategies.

Ethical approval

Ethics approval was not required for this systematic review.

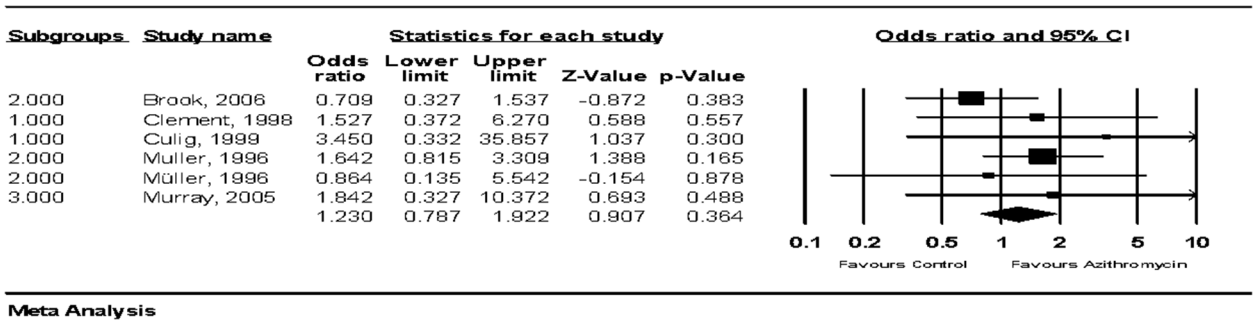

Figure 10. Meta-analysis for pathogen eradication of azithromycin versus controls.

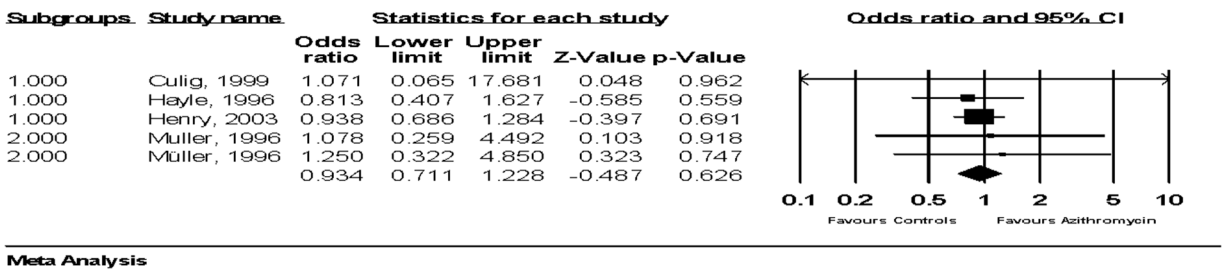

Figure 11. Meta-analysis for relapse of symptoms with azithromycin versus controls.

Consent

Informed consent was not required for this systematic review.

Sources of funding

No funding source.

Author's contribution

W.E. and M.Y.E. developed the research idea and study concept. All authors participated in literature review and searching for articles. A.K.K., A.M.A., M.J.M.A., N.F.A.A., and M.Y.E. participated in writing introduction and methods. M.Y.E., A.O.A., R.B.A., H.A.A., and L.B.A. participated in data extraction of included studies and revising it. M.Y.E., S.S.K.A., S.K.A., A.O.A., R.B.A., and N.F.A.A. participated in risk of bias assessment for the included studies. All authors participated in cleaning, analyzing, and interpreting data. M.Y.E., M.H.A., M.F.K., Z.J.A., and S.S.K.A. participated in writing discussion and abstract. All authors participated in revising and reviewing the manuscript.

Conflicts of interest disclosure

No conflict of interest to state.

Research registration unique identifying number (UIN)

PROSPERO 2024 CRD42024576523.

Guarantor

Wafa Elnaseeh and Mohamed Yousif Elamin.

Provenance and peer review

Not commissioned, internally peer-reviewed.

Data availability statement

It is available upon request.

References

[1] Clement P, de Gandt JB. A comparison of the efficacy, tolerability and safety of azithromycin and co-amoxiclav in the treatment of sinusitis in adults. J Int Med Res 1998;26:66–75.

[2] Klapan I, Culig J, Oreškovoć K, *et al*. Azithromycin versus amoxicillin/clavulanate in the treatment of acute sinusitis. Am J Otolaryngol 1999;20:7–11.

[3] Heidary M, Ebrahimi Samangani A, Kargari A, *et al*. Mechanism of action, resistance, synergism, and clinical implications of azithromycin. J Clin Lab Anal 2022;36:e24427.

[4] Battisti AS, Modi P, Pangia J. Sinusitis. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025.

[5] Alfallaj R, Obaid SB, Almousa H, *et al*. Demographic and clinical profile of patients with chronic rhinosinusitis in Saudi Arabia. Saudi Med J 2023;44:401–05.

[6] Brook I. Microbiology of sinusitis. Proc Am Thorac Soc 2011;8:90–100.

[7] Henry DC, Riffer E, Sokol WN, *et al*. Randomised double-blind study comparing 3- and 6-day regimens of azithromycin with a 10-day amoxicillin-clavulanate regimen for treatment of acute bacterial sinusitis. Antimicrob Agents Chemother 2003;47:2770–74.

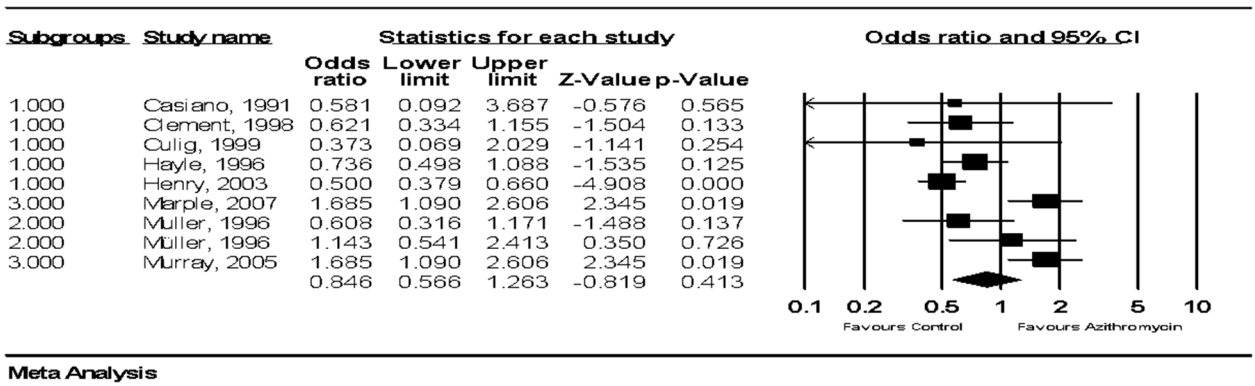

Figure 12. Meta-analysis for adverse effects with azithromycin versus controls.

[8] Wallwork B, Coman W, Mackay-Sim A, *et al*. A double-blind, randomized, placebo-controlled trial of macrolide in the treatment of chronic rhinosinusitis. Laryngoscope 2006;116:189–93.
[9] Kuruvilla M, de la Morena MT. Antibiotic prophylaxis in primary immune deficiency disorders. J Allergy Clin Immunol Pract 2013;1:573–82.
[10] Florescu DF, Murphy PJ, Kalil AC. Effects of prolonged use of azithromycin in patients with cystic fibrosis: a meta-analysis. Pulm Pharmacol Ther 2009;22:467–72.
[11] Altenburg J, de Graaff CS, Stienstra Y, *et al*. Effect of azithromycin maintenance treatment on infectious exacerbations among patients with non-cystic fibrosis bronchiectasis: the BAT randomized controlled trial. JAMA 2013;309:1251–59.
[12] Leach AJ, Morris PS. Antibiotics for the prevention of acute and chronic suppurative otitis media in children. Cochrane Database Syst Rev 2006;2006:CD004401.
[13] Page MJ, McKenzie JE, Bossuyt PM, *et al*. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. Int J Surg 2021;88:105906.
[14] Haddaway NR, Page MJ, Pritchard CC, *et al*. PRISMA2020: an R package and Shiny app for producing PRISMA 2020-compliant flow diagrams, with interactivity for optimised digital transparency and open synthesis. Campbell Syst Rev 2022;18:e1230.
[15] Risk of Bias 2 (RoB 2) tool Cochrane Methods [Internet]. [cited 2024 Jul 18]. Available from: https://methods.cochrane.org/risk-bias-2.
[16] Lari AR, Ghaffariyeh A, Etesam N, *et al*. A randomized controlled trial of 5-day regimen of azithromycin and a 10-day regimen of co-amoxiclav for treatment of acute sinusitis. Iran J Clin Infect Dis 2010;5:137–41.
[17] Muller O. Comparison of azithromycin versus clarithromycin in the treatment of patients with upper respiratory tract infections. J Antimicrob Chemother 1993;31:137–46.
[18] Muller O. An open comparative study of azithromycin and roxithromycin in the treatment of acute upper respiratory tract infections. J Antimicrob Chemother 1996;37:83–92.
[19] Brook I, Hausfeld JN. Effect of telithromycin and azithromycin on nasopharyngeal bacterial flora in patients with acute maxillary sinusitis. Arch Otolaryngol Head Neck Surg 2006;132:442.
[20] Murray JJ, Emparanza P, Lesinskas E, *et al*. Efficacy and safety of a novel, single-dose azithromycin microsphere formulation versus 10 days of levofloxacin for the treatment of acute bacterial sinusitis in adults. Otolaryngol Head Neck Surg 2005;133:194–200.
[21] Marple B, Roberts C, Decaprariis P, *et al*. Onset of symptom resolution in adults with acute bacterial rhinosinusitis treated with a single dose of azithromycin extended release compared with 10 days of levofloxacin: a retrospective analysis of a randomized, double-blind, double-dummy trial. Clin Ther 2007;29:2690–98.
[22] Videler WJ, Badia L, Harvey RJ, *et al*. Lack of efficacy of long-term, low-dose azithromycin in chronic rhinosinusitis: a randomized controlled trial. Allergy 2011;66:1457–68.
[23] Veskitkul J, Wongkaewpothong P, Thaweethamchareon T, *et al*. Recurrent acute rhinosinusitis prevention by azithromycin in children with nonallergic rhinitis. J Allergy Clin Immunol Pract 2017;5:1632–38.
[24] Casiano RR. Azithromycin and amoxicillin in the treatment of acute maxillary sinusitis. Am J Med 1991;91:S27–30.
[25] Haye R, Lingaas E, Høivik HO, *et al*. Efficacy and safety of azithromycin versus phenoxymethylpenicillin in the treatment of acute maxillary sinusitis. Eur J Clin Microbiol Infect Dis 1996;15:849–53.
[26] Ficnar B, Huzjak N, Oreskovic K, *et al*. Azithromycin: 3-day versus 5-day course in the treatment of respiratory tract infections in children. J Chemother 1997;9:38–43.