

Unmasking Acne: Azithromycin Edges Out Doxycycline in Randomized Trial at a Tertiary Care Centre

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ABSTRACT

Objective: This study aimed to compare the efficacy of oral azithromycin with oral doxycycline in treating acne vulgaris at a tertiary care hospital in Islamabad.

Methodology: A randomized controlled trial was conducted. Patients aged 14-30 years (n=190) were enrolled and randomly assigned to either azithromycin or doxycycline treatment groups. Baseline and post-treatment (12 weeks) Global Acne Grading System (GAGS) scores were assessed. Percent reductions in GAGS score were categorized into four groups (<25%, 25-50%, 51-75%, and >75%) for intergroup comparison. Written informed consent was obtained from all participants.

Results: The mean patient age was 21.30±4.93 years, with a female predominance (male: female ratio 1:1.2). Most patients had Fitz-Patrick Skin Type-V (64.7%) compared to Type-IV (35.3%). Baseline GAGS scores were comparable between groups (p=0.612). Notably, post-treatment GAGS scores were significantly lower in the azithromycin group (p<0.001), demonstrated by a greater mean change (19.33±3.03 vs. 17.70±2.99; p<0.001) and per cent reduction (81.87±8.74 vs. 75.97±11.12%; p<0.001) compared to doxycycline. Additionally, 75.3% of patients achieved an excellent reduction in GAGS score, with a significantly higher proportion observed in the azithromycin group (87.4% vs. 63.2%; p<0.001). Similar significant differences were observed across subgroups based on age, gender, and skin type.

Conclusion: This study suggests that azithromycin demonstrates superior efficacy to doxycycline for acne vulgaris management, regardless of patient demographics or skin type. Its established better safety profile further supports its potential as a preferred therapeutic option in future dermatological practice.

Keywords: Acne Vulgaris, Azithromycin, Doxycycline, Percent Reduction in GAGS Score

Authors' Contribution:

^{1,2}Conception; Literature research; manuscript design and drafting; ^{3,4}Critical analysis and manuscript review; ^{5,6}Data analysis; Manuscript Editing.

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Introduction

Acne vulgaris is a common chronic inflammatory skin condition affecting millions worldwide, primarily adolescents and young adults. It manifests as a complex interplay of multiple factors involving sebaceous gland hyperactivity, follicular hyperkeratinisation, colonization by

Propionibacterium acnes bacteria, and inflammation.¹ These processes collectively lead to the formation of comedones, papules, pustules, nodules, and cysts, which characterize acne lesions. Notably, it impacts around 85% of individuals aged 12-24 years, highlighting its significant occurrence during adolescence and young adulthood. Moreover, approximately 50% of patients aged 20-

29 years continue to experience the burden of acne, indicating its persistent impact beyond the teenage years.^{2,3} Extensive research has linked acne to heightened rates of anxiety, depression, and even suicidal ideation, underscoring the urgent need for effective management and intervention strategies. Notably, acne often manifests earlier in females compared to males, and its prevalence remains strikingly high, affecting approximately 85% of the adolescent population.⁴ The pathophysiology of acne vulgaris begins with increased sebum production, driven primarily by hormonal fluctuations during puberty and exacerbated by genetic predisposition. Excessive sebum production combines with abnormal follicular keratinization, resulting in the formation of microcomedones. These microcomedones progress to inflammatory lesions under the influence of *P. acnes* bacteria, which colonize the pilosebaceous unit and trigger an inflammatory response mediated by proinflammatory cytokines.⁵ Therapeutic options include topical agents such as retinoids, benzoyl peroxide, and antibiotics to reduce sebum production, unclog pores, and inhibit bacterial growth. Systemic treatments like oral antibiotics, hormonal therapies, and isotretinoin may be prescribed for more severe cases or when topical treatments fail to achieve adequate control.⁶ However, acne management often necessitates a multifaceted approach tailored to the individual's specific needs, considering factors such as acne severity, skin type, and treatment response.⁷ Oral Azithromycin, a nitrogen-containing macrolide, exerts its therapeutic effects in acne vulgaris through its potent anti-inflammatory and antibacterial properties. By reversibly binding to the 50S ribosomal subunit within bacterial cells, it inhibits protein synthesis, impeding bacterial proliferation. Remarkably, its high lipid solubility and ion trapping capability result in tissue concentrations exceeding plasma levels by over 50 times, enhancing its efficacy.⁸ On the other hand, Oral Doxycycline, a widely prescribed antibiotic for

moderate to severe acne vulgaris, exhibits both antibacterial and anti-inflammatory actions. Through reversible binding to the 30S subunit of bacterial ribosomes, it disrupts the attachment of aminoacyl tRNA, thus halting the translation process and ultimately inhibiting bacterial protein synthesis.⁹ These mechanisms underline the therapeutic efficacy of both medications in managing acne vulgaris, offering promising treatment options for patients. While both drugs are effective in managing acne, the choice between them depends on various factors such as the severity of acne, patient preferences, and the potential for side effects or drug interactions.¹⁰ The effectiveness, tolerance, safety, side effect profile, and cost of many medicines remain poor despite the availability of several treatments, standard guidelines, and recommendations. As far as the candidates are aware, there is currently just one study conducted in Pakistan that compares the efficacy of azithromycin and doxycycline as therapy options for moderate to severe cases of acne vulgaris. The purpose of this study is to demonstrate how acne vulgaris treatment can be impacted by cost and clinical outcome. This research will contribute to closing the knowledge gap. If successful, this might be a helpful addition to acne treatment options.

Methodology

After obtaining approval from the Hospital Ethical Committee, a total of 190 individuals (95 patients in each group) who met the inclusion criteria were recruited for the study. The study was performed at Federal Medical and Dental College and PIMS, SZABMU. For our study, a sample size of 190 cases (95 cases in each group) was determined based on an 80% power of test and a 5% level of significance. We considered the expected percentage reduction in the mean severity index to be 81.08% in the oral azithromycin group and 64.66% in the oral doxycycline group among patients with acne vulgaris. Enrolled patients provided written

informed consent. A comprehensive medical history was obtained, and a thorough physical examination was conducted to exclude any related medical conditions. This study included both male and female patients between the ages of 14 and 30 who had moderate acne vulgaris on their face only. The study excluded patients with a history of drug sensitivity, medical conditions including endocrine or gastrointestinal disorders, smoking, and hyperandrogenism manifestations in females. Additionally, those with underlying hormonal imbalances causing acne, such as polycystic ovarian disease, drug-induced acne, or contraindications to oral azithromycin or doxycycline, were excluded. Patients who had received acne treatment within the preceding six weeks or undergone facial surgery within the last year were also excluded. Patients were allocated into two groups using a lottery approach. Group A received azithromycin 500 mg daily before meals for four consecutive days each month over a span of 12 weeks. Conversely, Group B received doxycycline 100 mg daily after meals for the same duration of 12 weeks. Patients were monitored 12 weeks later to assess the efficacy of each medication. The effectiveness of the treatment was evaluated based on the resolution of certain acne vulgaris lesions, including whiteheads, blackheads, red spots, and red bumps. The degree of improvement was calculated as a percentage, with categories ranging from excellent (more than 75% improvement), good (51-75% improvement), fair (25-50% improvement), to poor (less than 25% improvement). Every patient in both groups underwent clinical assessment every 4 weeks for a total of 12 weeks. The GAGS score was computed at the initiation of treatment and thereafter one month following the final session. The calculation of the percentage reduction was performed. A single resident (candidate) conducted all the pre and post treatment assessments, whereas a single consultant dermatologist with five years of expertise carried out all the treatment sessions. This approach was adopted to minimize

bias. Exclusion was used to adjust for confounding variables. The candidate recorded all this information in the enclosed proforma.

The collected data underwent analysis using SPSS version 20.0. Numerical variables such as age, baseline and follow-up GAGS score, as well as the change and percentage reduction in GAGS score, were presented as mean \pm SD. Categorical variables including gender, skin type, and treatment efficacy (categorized as poor, fair, good, and excellent) were presented as frequency and percentage. Chi-square tests were utilized to compare treatment efficacy between groups, with a significance level set at p-value \leq 0.05. Data were further stratified by age, gender, and skin type to address potential effect modifiers, and post-stratification chi-square tests were conducted with a significance level of p-value \leq 0.05.

Results

The age of the patients ranged from 14 years to 30 years with a mean of 21.30 ± 4.93 years. There were 85 (44.7%) male and 105 (55.3%) female patients with a male to female ratio of 1:1.2. The majority (n=123, 64.7%) of the patients had Fitz-Patrick Type-V skin phototype while 67 (35.3%) patients had Type-IV phototype skin. GAGS score ranged from 19 to 28 with a mean of 23.50 ± 2.71 as shown in Table I.

Parameters	Characteristics	Participants (n=190)
Age	Mean \pm SD	21.30 \pm 4.93
	\leq 20 years	101 (53.2%)
	>20 years	89 (46.8%)
Gender	Male	85 (44.7%)
	Female	105 (55.3%)
Skin Phototype	Fitz-Patrick IV	67 (35.3%)
	Fitz-Patrick V	123 (64.7%)
Baseline GAGS score	Mean \pm SD	23.50 \pm 2.71

Parameters	Characteristics	Azithromycin (n=95)	Doxycycline (n=95)	P-value
Age	Mean±SD	21.40±4.95	21.20±4.94	0.781
	≤20 years	51 (53.7%)	50 (52.6%)	0.884
	>20 years	44 (46.3%)	45 (47.4%)	
Gender	Male	43 (45.3%)	42 (44.2%)	0.884
	Female	52 (54.7%)	53 (55.8%)	
Skin Phototype	Fitz-Patrick IV	34 (35.8%)	33 (34.7%)	0.879
	Fitz-Patrick V	61 (64.2%)	62 (65.3%)	
Baseline GAGS score	Mean±SD	23.60±2.64	23.40±2.79	0.612

GAGS Score	Azithromycin n (n=95)	Doxycycline (n=95)	P-value
Baseline	23.60±2.64	23.40±2.79	0.612
Follow-up	4.27±2.09	5.70±2.90	<0.001*
Mean Change	19.33±3.03	17.70±2.99	<0.001*
Percent Reduction	81.87±8.74	75.97±11.12	<0.001*

Both the study groups were comparable in terms of mean age (p-value=0.781), mean baseline GAGS score (p-value=0.612) and distribution of various groups based on patient's age (p-value=0.884), gender (p-value=0.884) and skin phototype (p-value=0.879) as shown in Table II. The follow-up GAGS score was significantly lower in patients receiving azithromycin as compared to doxycycline (4.27±2.1 vs. 5.70±2.90; p-value<0.001). There was

significantly greater mean change (19.33±3.03 vs. 17.70±2.99; p-value<0.001) and percent reduction (81.87±8.74 vs. 75.97±11.12%; p-value<0.001) in baseline GAGS score in patients receiving azithromycin as compared to doxycycline as shown in Table III. 143 (75.3%) patients showed excellent reduction in baseline GAGS score while good reduction was noted in 47 (24.7%) patients. The frequency of excellent reduction in baseline GAGS score was significantly higher among patients receiving azithromycin (87.4% vs. 63.2%; p-value<0.001) as compared to doxycycline as shown in Table IV.

Efficacy	Azithromycin (n=95)	Doxycycline (n=95)	P-value
Excellent (>75% reduction)	83 (87.4%)	60 (63.2%)	<0.001*
Good (51-75% reduction)	12 (12.6%)	35 (36.8%)	
Total	95 (100%)	95 (100%)	

Table V: Comparison of Efficacy (Various Grades of Percent Reduction in GAGS Score) between the Study Groups across Age, gender & Fitz-Patrick skin type				
Age	Efficacy	Azithromycin (n=95)	Doxycycline (n=95)	P-value
≤20 years (n=101)	Excellent	45 (88.2%)	33 (66.0%)	0.008*
	Good	6 (11.8%)	17 (34.0%)	
	Total	51 (100.0%)	50 (100.0%)	
>20 years (n=89)	Excellent	38 (86.4%)	27 (60.0%)	0.005*
	Good	6 (13.6%)	18 (40.0%)	
	Total	44 (100.0%)	45 (100.0%)	
Male (n=85)	Excellent	37 (86.0%)	27 (64.3%)	0.020*
	Good	6 (14.0%)	15 (35.7%)	
	Total	43 (100.0%)	42 (100.0%)	
Female (n=105)	Excellent	46 (88.5%)	33 (62.3%)	0.002*
	Good	6 (11.5%)	20 (37.7%)	
	Total	52 (100.0%)	53 (100.0%)	
Fitz-Patrick IV (n=67)	Excellent	29 (85.3%)	20 (60.6%)	0.023*
	Good	5 (14.7%)	13 (39.4%)	
	Total	34 (100.0%)	33 (100.0%)	
Fitz-Patrick V (n=123)	Excellent	54 (88.5%)	40 (64.5%)	0.002*
	Good	7 (11.5%)	22 (35.5%)	
	Total	61 (100.0%)	62 (100.0%)	

When compared, similar significant difference was noted between the groups across various subgroups based on age, gender and skin type as shown in Tables V.

Discussion

Acne is a widespread skin issue, affecting millions globally, causing physical and psychological distress. Factors like sebum overproduction, bacteria,

inflammation, and hormonal imbalances contribute to its development. Genetics, hormones, stress, and certain medications increase the risk. Treatments range from topical and oral medications to lifestyle adjustments like stress reduction and diet changes. Antibiotics, like tetracyclines and macrolides, reduce acne-causing bacteria, with recent studies favoring azithromycin over doxycycline due to better treatment outcomes. This prompts further investigation due to conflicting evidence and limited local research.¹¹ The mean age of patients with acne vulgaris in our study, 21.30±4.93 years, aligns well with findings from previous research. Vidyadhar et al. (2017)¹² reported a mean age of 19.3±1.8 years, Saizuddin et al. (2017)¹³ observed a mean age of 22.4±5.2 years among Bangladeshi acne patients, and Aryal et al. (2018)¹⁴ found a comparable mean age of 20.1±2.1 years in Nepal. These consistent findings across diverse populations indicate a consistent age distribution pattern among individuals affected by acne vulgaris. Our study identified a female predominance among acne patients, with a male-to-female ratio of 1:1.2. This observation is consistent with findings reported by Aryal et al. (2018) found a male-to-female ratio of 1:1.6 among acne patients in Nepal.¹⁴ Additionally, this study revealed that the majority (64.7%) of acne patients exhibited Fitzpatrick Type-V skin phototype, while 35.3% had Type-IV phototype skin. Sheth et al. (2018), also noted similar male-to-female ratios of 1:1.2 and 1:1.5 among acne patients.¹⁵ This distribution closely mirrors findings reported by Budamakuntla et al., among Indian patients with dermatological disorders, where they observed incidences of 36.7% and 63.3% for Type-IV and Type-V skin, respectively.¹⁶ In our study, we observed that the frequency of efficacy was significantly higher among patients receiving azithromycin (87.4% vs. 63.2%; p-value < 0.001) compared to doxycycline. Similarly, Sultan et al. (2020) reported a significantly higher efficacy rate with azithromycin compared to doxycycline (90.0% vs. 34.3%; p-value < 0.001).¹⁷ Our study's findings are consistent with

those of Moravvej et al. (2012) in an Iranian population. In their study, they randomly allocated 60 patients to either the azithromycin (n=30) or doxycycline (n=30) group. They reported that azithromycin was more efficacious than the conventional practice of doxycycline, with efficacy rates of 90.0% and 83.3%, respectively (p-value=0.45).¹⁸ While Ali et al. reported a reduction of up to 81.08% in the azithromycin group and up to 64.66% in the doxycycline group after 2 months of treatment, our findings showed a significantly greater reduction in baseline GAGS score among patients receiving azithromycin compared to doxycycline (87.4% vs. 63.2%; p-value<0.001).¹⁹ These results are consistent with our study's findings, further strengthening the evidence supporting the superior efficacy of azithromycin over doxycycline in the treatment of acne vulgaris. This consistency across different studies and populations underscores the robustness and reliability of our findings, suggesting that azithromycin may indeed be a preferable treatment option for acne compared to doxycycline. Our findings align with those of Arooba et al. (2022), who also reported a significantly higher frequency of excellent reduction in GAGS score among patients receiving azithromycin compared to doxycycline. Specifically, our study revealed that 87.4% of patients treated with azithromycin experienced excellent reduction, whereas only 63.2% of those treated with doxycycline. Similarly, Arooba et al. found that 48.7% of patients in the doxycycline group had an excellent response, compared to 23.0% in the azithromycin group, with a statistically significant difference (p-value 0.000001).²⁰ Additionally, our results corroborate with those of Iqbal et al. (2006), who reported a significant difference in efficacy between azithromycin and doxycycline groups. They found that 83.3% of patients treated with azithromycin experienced effectiveness, whereas 86.7% of those treated with doxycycline did, with a p-value of 0.001.²¹ In comparison to Mudassir et al. (2023), our study

demonstrated a notable disparity in the efficacy outcomes between azithromycin and doxycycline groups. While Mudassar et al. found similar efficacy rates between the two groups (73.90% in the Azithromycin group and 78.26% in the Doxy group, p-value 0.625), our study revealed a significantly higher frequency of efficacy among patients receiving azithromycin compared to doxycycline (87.4% vs. 63.2%; p-value<0.001).²²

Conclusion

The study findings suggest that there is Azithromycin's superiority over doxycycline in managing acne vulgaris, regardless of patient demographics or skin type, coupled with its established better safety profile, which supports its preferred utilization in future dermatological practice.

Limitations: However, limitations of our study include its single-center design, potentially limiting generalizability, and the lack of long-term follow-up to assess sustained treatment efficacy and potential adverse effects.

Recommendations: Further multicenter randomized controlled trials with long-term follow-up are warranted to confirm the superiority of azithromycin over doxycycline

References

1. Nandy P, Shrivastava T, Shrivastava Sr T. Exploring the Multifaceted Impact of Acne on Quality of Life and Well-Being. *Cureus*. 2024 Jan 22;16(1): e52727. <https://doi.org/10.7759/cureus.52727>
2. Eichenfield DZ, Sprague J, Eichenfield LF. Management of acne vulgaris: a review. *J Am Med Assoc*. 2021;326(20):2055-67. <https://doi.org/10.1001/jama.2021.17633>
3. Jorgaqi E, Savo I, Koraqi A, Doci X, Cela R, Vasili E, et al. Efficacy of acne vulgaris treatment protocols according to its clinical forms. *Dermatol Ther*. 2020;33(4): e1361. <https://doi.org/10.1111/dth.13611>
4. Layton AM, Ravenscroft J. Adolescent acne vulgaris: current and emerging treatments. *Lancet Child Adol Health*. 2023;7(2):136-44. [https://doi.org/10.1016/s2352-4642\(22\)00314-5](https://doi.org/10.1016/s2352-4642(22)00314-5)
5. Vasam M, Korutla S, Bohara RA. Acne vulgaris: A review of the pathophysiology, treatment, and recent nanotechnology based advances. *Biochem Biophy Rep*. 2023;36(4):101578. <https://doi.org/10.1016%2Fj.bbrep.2023.101578>
6. Leung AK, Barankin B, Lam JM, Leong KF, Hon KL. Dermatology: how to manage acne vulgaris. *Drugs Context*. 2021; 10:6-8. <https://doi.org/10.7573%2Fdic.2021-8-6>
7. Thiboutot D, Dreno B, Sanders V, Rueda MJ, Gollnick H. Changes in the management of acne: 2009-2019. *J Am Acad Dermatol*. 2020;82(5):1268-9. <https://doi.org/10.1016/j.jaad.2019.04.012>
8. Heng AH, Chew FT. Systematic review of the epidemiology of acne vulgaris. *Sci Rep*. 2020;10(1):5754-57. <https://doi.org/10.1038/s41598-020-62715-3>
9. Hazarika N. Acne vulgaris: new evidence in pathogenesis and future treatment modalities. *J Dermatol Treat*. 2021;32(3):277-85. <https://doi.org/10.1038/s41598-020-62715-3>
10. Alsulaimani H, Kokandi A, Khawandanh S, Hamad R. Severity of acne vulgaris: comparison of two assessment methods. *Clin Cosmet Invest Dermatol*. 2020;43(5):711-6. <https://doi.org/10.1038/s41598-020-62715-3>
11. Mavranezouli I, Daly CH, Welton NJ, Deshpande S, Berg L, Bromham N, et al. A systematic review and network meta-analysis of topical pharmacological, oral pharmacological, physical and combined treatments for acne vulgaris. *Bri J Dermatol*. 2022;187(5):639-49. <https://doi.org/10.1111/bjd.21739>
12. Vidyadhar SR, Deka YT. Comparison of efficacy of oral azithromycin with oral minocycline in the treatment of acne vulgaris. *Clin Dermatol Rev* 2017;1(2):37-40. <https://doi.org/10.1179/joc.1998.10.6.469>
13. Saizuddin M, Hasan MS, Sen SK, Alfazzaman M, Rahman MM, Rahman MM, et al. A study on

- factors influencing acne among the medical students of Bangladesh. *Med Today*. 2017;29(2):30-2.
<http://dx.doi.org/10.3329/medtoday.v29i2.34623>
14. Aryal E, Shrestha S, Shrestha P, Pokhrel G, Bhattarai S. Psychological impact of acne vulgaris in basic science medical students in Nepal. *Nepal J Dermatol Venereol Leprol* 2018;16(1):30-4.
<http://dx.doi.org/10.3126/njdvl.v16i1.19401>
 15. Sheth SK, Mundada A, Gokhale N, Mahajan P. Comparison of oral levofloxacin and minocycline in treatment of inflammatory acne vulgaris: a randomized control trial. *Indian J Drugs Dermatol*. 2018;4(1):7-12.
http://dx.doi.org/10.4103/ijdd.ijdd_21_17
 16. Budamakuntla L, Loganathan E, Suresh DH, Shanmagun S. A randomized, open-label, comparative study of tranexamic acid microinjections and tranexamic acid with microneedling in patients with melasma. *J Cutan Aesthet Surg* 2013; 6:139-43.
<https://doi.org/10.4103/0974-2077.118403>
 17. Sultan N, Dar M, Rehman Z. To compare the clinical effectiveness of azithromycin vs. doxycycline on the first follow-up visit of acne vulgaris patients. *J Dermat Cosmetol* 2020;4(3):72-6.
 18. Morawej H, Mousazadeh HA, Yousefi M, Givrad
 19. S. Efficacy of doxycycline versus azithromycin in the treatment of moderate facial acne vulgaris. *Iran J Dermatol* 2012;15(1):7- 10.
 20. Ali S, Parveen A. Safety and efficacy of oral azithromycin pulse versus doxycycline daily in treating acne vulgaris: a hospital based comparative study. *Int J Sci Res* 2021;10(4):1- 4.
 21. Arooba Z, Tariq H, Batool S, Tabassum N, Aman S. Comparison of efficacy of oral azithromycin pulse versus doxycycline daily in treatment of moderate acne vulgaris. *Ann King Edward Med Uni*. 2022;28(5):296-9.
[https://doi.org/10.21649/akemu.v28iSpecial%20Issue%20\(Jul,%20Sep\).5182](https://doi.org/10.21649/akemu.v28iSpecial%20Issue%20(Jul,%20Sep).5182)
 22. Iqbal F, Alam MA, Tahir M, Qasim M, Ansar M, Mustafa SH, et al. Efficacy of oral azithromycin and oral doxycycline in patients with acne vulgaris. *Pak J Physiol*. 2023;19(2):25- 7. Available from:
<https://pjp.pps.org.pk/index.php/PJP/article/view/1522>
 23. Mudassir M, Amar A, Raza N, Khokhar A, Siddiqui A, Ahmed N, et al. Comparison of monthly pulse of oral azithromycin with daily doxycycline in the treatment of moderate acne vulgaris. *Pak Armed Forces Med J*. 2021;71(Suppl-1): S268-72.
<https://doi.org/10.51253/pafmj.v71iSuppl-1.2926>