ASIAN JOURNAL OF PHARMACEUTICAL AND CLINICAL RESEARCH

INNOVARE ACADEMIC SCIENCES
Knowledge to Innovation

Vol 17, Issue 12, 2024

Online - 2455-3891
Print - 0974-2441

Research Article

EVALUATION OF EFFICACY AND SAFETY OF AZITHROMYCIN AND DOXYCYCLINE IN TREATMENT OF ACNE VULGARIS WITH DIFFERENT LEVELS OF SERUM TESTOSTERONE: A PROSPECTIVE, RANDOMIZED, CONTROLLED, COST-EFFECTIVE, COMPARATIVE STUDY

PADMAJA MEKALA[1], ROOPALI SOMANI[1], USHARANI PINGALI[1], VIJAYALAKSHMI SRIPATHI PANDITHARADHYULA[2], IMRAN KHAN[1]*

[1]Department of Clinical Pharmacology and Therapeutics, Nizam's Institute of Medical Sciences, Hyderabad, Telangana, India. [2]Department of Dermatology, Aster Prime Hospital, Hyderabad, Telangana, India.
***Corresponding author: Imran Khan; Email: imran.khan1705@gmail.com**

Received: 09 September 2024, Revised and Accepted: 25 October 2024

ABSTRACT

Objectives: The objectives of this study are to compare the therapeutic efficacy, safety, quality of life (QoL), and cost-effectiveness of azithromycin and doxycycline in patients with acne vulgaris and the correlation of serum testosterone levels with the severity of acne.

Methods: A prospective, randomized, open-label study was conducted at a tertiary care hospital in South India, according to the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use Guideline for Good Clinical Practice principles. After institutional ethics committee approval, 100 patients aged 15–40 with moderate-to-severe acne were enrolled, excluding those with a history of gastritis, drug hypersensitivity, pregnancy, or under 12 years old. Participants were randomized to receive either oral azithromycin 500 mg daily for three consecutive days each week for 4 weeks, or doxycycline 100 mg daily for 28 days, along with topical treatments. Efficacy was measured by the type and number of acne lesions, graded according to standardized criteria. QoL was assessed using the Cardiff Acne Disability Index (CADI). Serum testosterone levels were correlated with acne severity.

Results: Of the 96 patients (42 males, 54 females) who completed the study, 49 were in the azithromycin group and 47 in the doxycycline group. The mean age was 23.5 years in the azithromycin group and 22.1 years in the doxycycline group. Significant reductions in acne severity and number of lesions were observed in both groups ($p<0.0001$), with azithromycin showing superior improvement ($p<0.01$). At baseline, most patients had Grade 3 or 4 acne, which improved significantly post-treatment. QoL improvements were also significant in both groups, with mean CADI scores reducing from around 8 to below 4 ($p<0.0001$). A weak positive correlation ($r=0.24$) was found between serum testosterone levels and acne severity. Adverse events were mild and did not necessitate discontinuation. To achieve a 1 unit decrease in CADI, azithromycin treatment costed an additional rupees of 264.5 over doxycycline.

Conclusion: Azithromycin and doxycycline are effective treatments for moderate-to-severe acne vulgaris, with significant improvements in clinical and QoL outcomes. While azithromycin offers better clinical efficacy, doxycycline provides a more cost-effective option. Further studies could explore long-term outcomes and the impact of hormonal variations on treatment efficacy.

Keywords: Acne vulgaris, Azithromycin, Doxycycline, Cost-effectiveness.

© 2024 The Authors. Published by Innovare Academic Sciences Pvt Ltd. This is an open access article under the CC BY license (http://creativecommons.org/licenses/by/4.0/) DOI: http://dx.doi.org/10.22159/ajpcr.2024v17i12.52618. Journal homepage: https://innovareacademics.in/journals/index.php/ajpcr

INTRODUCTION

Acne vulgaris is a chronic condition affecting more than 85% of adolescents. It is a chronic inflammatory disease of pilosebaceous unit which frequently affects the cosmetically important areas of the body such as the face, back, chest, neck, and upper arms. Acne vulgaris develops earlier in females than in males, which may reflect the onset of puberty in females. Teenagers are the most common suffers of acne, purely because of the hormonal shifts that are associated with puberty. Current figures indicate nearly 85% of people will develop some type of acne at some point between the ages of 12 and 25 years [1]. Although males tend to severe acne, females tend to have persistent disease. The severity of the disease varies markedly from one individual to the other depending upon the interplay of various factors involved in the development of acne vulgaris [2].

Acne represents a spectrum of disease with severity ranging from a couple of blackheads to fulminant acne [1]. It is characterized by seborrhoea, open and closed comedones, papules, pustules, and in more severe cases nodules, pseudocysts, and scarring [2]. Acne has four main pathogenetic mechanisms–androgen-induced increased sebum production, follicular hyperkeratinisation, colonization of hair follicles by *Propionibacterium acne*, and the inflammation [2,3].

Acne is associated with greater psychological burdens such as depression, anxiety, and low self-esteem. Acne vulgaris remains one of the most common conditions affecting humanity and measurement of its impact on patient's quality of life (QoL) is important using validated measures along with an objective assessment of acne status [4,5]. Measurement of QoL is done commonly with questionnaires such as Dermatology Life Quality Index, Acne Disability Index (ADI), and Cardiff ADI (CADI) [6-8].

There are many topical and systemic modalities for acne treatment. *P. acne* is highly sensitive to a number of anti-microbial agents of different classes, including macrolides, tetracyclines, penicillins, clindamycin, aminoglycosides, cephalosporins, trimethoprim, and sulfonamide [9]. The effectiveness of drugs targeting *P. acne* is largely based on their potential to achieve sufficient concentration in the pilosebaceous follicles. Azithromycin and doxycycline are used routinely in clinical practice.

Azithromycin is a macrolide anti-biotic useful for the treatment of acne vulgaris. Azithromycin because of its specific pharmacokinetic characteristics (including fast and ample penetration into tissues, long half-life, safety, and few side-effects compared to other standard anti-biotics, the possibility of pulse therapy and higher tolerance profile as against other routine anti-acne treatments and non-interference with the p=450 complex in the liver) it might be an appropriate alternative for routine anti-biotics [10,11]. Doxycycline is a semisynthetic, second-generation, and broad-spectrum tetracycline derived from oxytetracycline [12,13]. There is a consensus that oral anti-biotic therapy should not exceed 3–4 months and that a minimum duration of 6 weeks is commonly required to see clinical improvement [14,15]. Hence, we want to evaluate the efficacy and safety of azithromycin and doxycycline in the treatment of acne with different levels of serum testosterone. We also planned to measure the QoL and to establish cost-effectiveness of these treatments.

METHODS

This was a prospective, randomized, open-label study conducted at a tertiary care center in south India according to the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use Guideline for Good Clinical Practice principles. The study was started after obtaining approval from the institutional ethics committee. Written informed consent was taken from all participants. Inclusion criteria were patients aged between 15 and 40 years of either sex with moderate to severe acne. Exclusion criteria were patients with a history of gastritis, H/o hypersensitivity to study drugs, pregnant and lactating females, and patients under the age of 12 years. Assent form was obtained from adolescents aged between 15 and 18 years apart from consent from the parents. A thorough dermatological examination was performed for the type, number, and site of lesions. Baseline serum testosterone levels were measured before starting the treatment. The selected patients were randomized to receive either oral azithromycin 500 mg given once daily orally for 3 consecutive days in a week for 4 weeks or doxycycline 100 mg given once daily orally for a period of 28 days. Randomization was done using random tables. All the patients were given topical treatment with acnesol gel and acne moist cream. The efficacy and QoL measurements were taken before and after the treatment. Patients were asked to come for follow-up at the end of 2nd and 4th week of treatment. Patients were enquired for adverse effects and compliance with the treatment at each visit. A cost analysis of each treatment was done at the end of the study.

Efficacy was measured by type and number of lesions of acne. Depending on the type of lesions acne was graded as Grade 1-comedones, occasional papules, Grade 2-papules, comedones, few pustules, Grade 3-predominant pustules, nodules, abscesse, and Grade 4-mainly cysts, abscesses, widespread scarring. Depending on the number of lesions (according to the Hayashi acne grading criteria for acne severity), acne was graded as mild: 0–5, 6–20 moderate, 21–50 severe, and >50 very severe [16].

QoL was assessed using CADI. CADI was measured at baseline and after 4th week. CADI is a five-item patient-reported questionnaire. The five questions were related to feeling of aggression, frustration, interference with social life, avoidance of public changing facilities, self-image, and an indication of how bad the acne was. Each question had four responses and each response carried either 0, 1, 2, or 3 points. The final score ranges from 0 to 15. Scores were graded as low (0–4), medium (5–9), and high (10–15). High scores indicated a high impairment of QoL. CADI identified the area of concern in patients with acne. Testosterone levels were correlated with baseline severity (No. of lesions) of all patients.

Statistical analysis

Data were expressed as mean±standard deviation and categorical data in percentage. $p<0.05$ was considered statistically significant. The differences in the efficacy parameters within groups before and after treatment were assessed using student's paired t-test. The differences in the study parameters between the groups were assessed using unpaired t-test. The differences in the grade of acne between and within groups (baseline and 4 weeks) were compared using the Chi-square test. A sample size of 100 patients was required to randomize 50 patients into each group to get statistically significant. The association between serum testosterone level and severity of acne was assessed using Pearson correlation. The power of the study was kept at 80%.

RESULTS

A total of 96 patients were included in the final analysis. Four patients were lost to follow-up. There were 49 patients in the azithromycin group and 47 in the doxycycline group. The baseline characteristic between the groups is presented in Table 1.

There was a significant reduction ($p=0.0001$) in the grades of lesions at the end of 4 weeks in both the study groups compared to baseline. Majority of patients at baseline had Grade 3 acne in Group A and Grade 4 in Group B. At the end of 4 weeks, the acne severity reduced in both the groups with majority of patients in Group A having Grade 1 and Group B having Grade 2 as depicted in Table 2.

A highly significant reduction ($p<0.001$) was found in the number of lesions after the treatment in both the study groups compared to baseline. The mean number of lesions at baseline was 44.4±15.6 in Group A and 45.3±8.5 in Group B. At the end of 4 weeks, the mean number of lesions in Group A was 15.6±8.3 and in Group B was 19±7 (Fig. 1). Group A showed significant reduction ($p<0.01$) in the number of lesions than Group B. The number of patients with different severities before and after treatment were given in Table 3.

CADI scores

There was a significant improvement ($p<0.001$) in CADI score at the end of the study in both the study groups compared to baseline. The mean CADI score at baseline was 8±3.2 in Group A and 8.2±2.6 in Group B. At the end of treatment, the mean CADI score was 3.6±1.6 in Group A and 3.8±1.5 in Group B indicating mild impairment in the QoL in both the groups. The mean CADI scores and number of patients with different CADI scores before and after treatment were given in Table 4. No significant change was found in CADI scores compared between the groups.

Correlation with testosterone levels

The mean free testosterone levels were correlated with baseline severity (No. of lesions) of all 96 patients. We found a significant ($p<0.05$) weak positive correlation ($r=0.24$) between testosterone level and the severity of lesions (Fig. 2). At baseline, the mean testosterone level in Group A was 2.6±3.1 pg/mL and in Group B was 3.5±2.8 pg/mL. We assessed the correlation between the severity of lesions and testosterone levels in each study group. There was a significant ($p<0.01$) weak positive correlation ($r=0.34$) in Group B and no correlation was found with Group A.

All the adverse events were reported to the pharmacovigilance unit of the institution. There were no serious adverse drug reactions (ADRs) reported during the study period. The reported adverse events were mild and did not warrant discontinuation from the study. Two subjects in the azithromycin group and five subjects in the doxycycline group complained of gastritis in 2nd week and 4+ week, which was unrelated to the study drug.

Cost-effectiveness

Per patient medicine cost as per protocol was Rs. 336/- in Group A and Rs. 190/- in Group B. Total medicine cost per group was 336 × 49 patients=Rs. 16,464/- in Group A and 190 × 47=Rs. 8930/- in Group B. Topical treatment was received by both the groups. In Group A

Table 1: Baseline characteristic between the study groups

Characteristic	Group A (n=49)	Group B (n=47)	p-value
Age (mean±SD)	23.5±5.7	22.1±4.7	0.19
Gender (M: F)	15:34	27:20	0.008

SD: Standard deviation

Table 2: Grades of acne at baseline and 4 weeks in the groups

Grade	Group A (n=49) azithromycin			Group B (n=47) doxycycline			p-value between groups at 4 weeks*
	Baseline (%)	4 weeks (%)	p-value within group from baseline to 4 weeks*	Baseline (%)	4 weeks (%)	p-value within group from baseline to 4 weeks*	
1	1 (2)	29 (59.2)	0.0001	1 (2)	14 (29.8)	0.0001	0.03
2	10 (20.4)	19 (38.8)		10 (21.3)	28 (59.6)		
3	19 (38.8)	1 (2)		12 (25.5)	5 (10.6)		
4	19 (38.8)	0		24 (51.1)	0		

*Chi-square test

Table 3: Severity of acne in at baseline and 4 weeks in the groups

No. of lesions	Group A (n=49) azithromycin			Group B (n=47) doxycycline			p-value between groups at 4 weeks*
	Baseline (%)	4 weeks (%)	p-value within group from baseline to 4 weeks *	Baseline (%)	4 weeks (%)	p-value within group from baseline to 4 weeks	
Mild (0–5)	0	12 (24.5)	0.0001	0	1 (2)	0.0001	0.0011
Moderate (6–20)	6 (12.2)	22 (44.9)		1 (2)	18 (38.3)		
Severe (21–50)	23 (47)	15 (30.6)		21 (44.7)	28 (59.6)		
Very severe (>50)	20 (40.8)	0		25 (53.2)	0		

*Chi-square test

Table 4: CADI score in the study groups

CADI severity score	Group A (n=49) azithromycin			Group B (n=47) doxycycline			p-value between groups at 4 weeks*
	Baseline (%)	4 weeks (%)	p-value within group from baseline to 4 weeks*	Baseline (%)	4 weeks (%)	p-value within group from baseline to 4 weeks*	
Low (0–4)	9 (18.4)	36 (73.5)	0.0001	5 (10.2)	33 (70.2)	0.0001	0.821
Medium (5–9)	25 (51)	13 (26.5)		26 (55.3)	14 (29.8)		
Severe (10–15)	15 (30.6)	0		16 (34)	0		

* Chi square test. CADI: Cardiff acne disability index

Table 5: Total treatment expenditure of study patients

Parameter	Group A (Azithro)	Group B (Doxy)
Medicine cost (Rs)	16,464	8,930
Expenditure of ADRs (Rs)	420	1050
Total Cost (Rs)	16,884	9,980
Per patient cost	344.6	212.34
Mean CADI reduction	4.5	4
ICER	264.5	

ADR: Adverse drug reaction, CADI: Cardiff acne disability index, ICER: Incremental cost effectiveness ratio

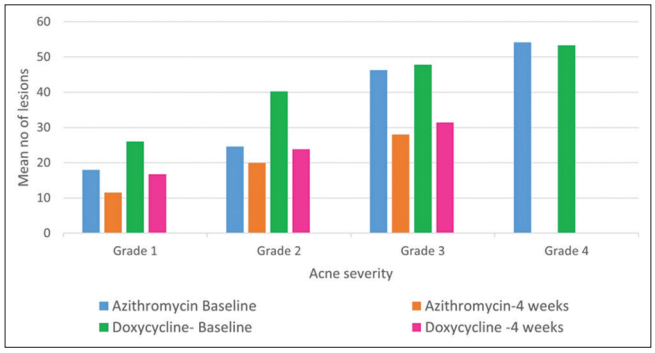

Fig. 1: Mean number of lesions in study groups

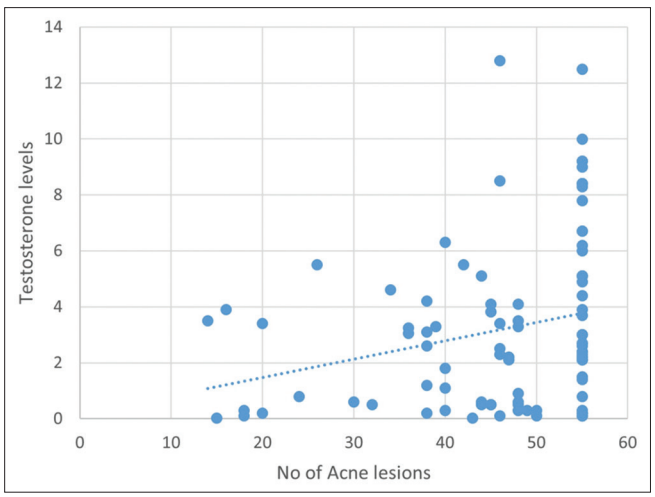

Fig. 2: Correlation of testosterone levels to number of lesions at baseline (n=96)

number of ADRs were 2 and 5 in Group B. Treatment cost of ADRs and total treatment costs were given in Table 5. The Incremental Cost effectiveness ratio (ICER) was calculated and to achieve a 1 unit increase in CADI score, an additional amount of Rs. 264.5/- for azithromycin treatment over doxycycline was calculated.

DISCUSSION

In the present study, azithromycin was found to be significantly more effective in reducing the severity and grade of acne as compared to

doxycycline. Testosterone levels were weakly correlated with the severity of acne at baseline.

In the present study, acne was more commonly seen in females which is similar to the study by Adityan and Thappa [17] and most of the patients had Grade 3 or 4 (Pustules, nodules, and abscesses) severity of acne. Although azithromycin was found to be more effective in reducing the grading and severity of acne, there was no difference between the groups in the improvement of QoL as measured by CADI scores. Previous studies across different regions showed similar results [18,19].

A meta-analysis by Kim *et al*. [20], which compared the efficacy of azithromycin and doxycycline in 6 randomized control trials analyzing 906 patients of moderate-to-severe acne vulgaris, showed azithromycin and doxycycline to be equipotent in both efficacy and QoL measures, however, doxycycline arm had more adverse events. This difference in results could be attributed to the varying doses of azithromycin used in the trials included in the meta-analysis which ranged from 4 days a month to twice weekly and the efficacy was assessed using QoL measures and investigator assessment as opposed to grading and severity of acne.

The CADI is a questionnaire that measures the impact of acne on teenagers and young adults. However, no studies have yet calculated the smallest CADI score change required for the patient to have experienced a positive benefit from treatment [21]. In the present study, at the end of treatment, the mean CADI score was below 4, in more than 70% of the patients in both the study groups indicating mild impairment of QoL, with the domain of feelings most affected, whereas in the previous study conducted by Yap it was 59.5% [22]. Another study by Gupta [23] showed 73.03% of patients in mild impairment of QoL which is in alignment with our results. Facial and physical appearance are important to most of the adolescents and even the presence of minimal acne can have adverse impact on QoL which could explain the mild impairment of QoL in our study and the previous studies.

In the present study, testosterone levels were estimated and correlated with acne severity only at baseline. However, only weak positive correlation between testosterone levels and severity of acne was demonstrated. These findings are in line with previous studies,where although testosterone levels are increased in acne patients although they do not correlate with severity of acne [24,25]. Henze *et al*. have attributed this discordance to the overactivity of 5α-reductase in the pilosebaceous unit as it reduces testosterone to 5α dihydrotestosterone which has more potent activity as compared to testosterone in the pilosebaceous glands [26].

In terms of ICER, the present demonstrated that a 1 unit decrease in CADI score with azithromycin, costed an additional Rs. 264.5 as compared to doxycycline treatment.

CONCLUSION

Although both azithromycin and doxycycline were effective in the treatment of acne, azithromycin was found to be more effective than doxycycline in reducing the acne lesions and improving the QoL, with less side effects.

ACKNOWLEDGMENT

Nil.

AUTHOR'S CONTRIBUTION

Dr. M Padmaja: Conceptualization of study, preparation of protocol, data collection, data analysis supervision throughout the study from idea to publication, manuscript writing, editing, and review. Dr. Roopali Somani: Study conception and design, data acquisition, data analysis, manuscript writing, editing, and review. Dr Usharani Pingali: Study conception and design, manuscript writing, editing, and review. Dr. Vijayalakshmi SP: Study conception and design, data acquisition, manuscript editing, and review. Dr. Imran Khan: Study conception and design, Data acquisition, data entry in case record form, data analysis, manuscript writing, editing, and review.

CONFLICT OF INTEREST

Nil.

AUTHOR FUNDING

Nil.

REFERENCES

1. Mahmood NF, Shipman AR. The age-old problem of acne. Int J Womens Dermatol. 2016 Dec 2;3(2):71-6. doi: 10.1016/j.ijwd.2016.11.002, PMID: 28560299; PMCID: PMC5440448
2. Simpson NB, Cunliffe WJ. Disorders of the sebaceous glands. In: Burns T, Breathnach S, Cox N, Griffiths C, editirs. Rook's Text Book of Dermatology. 7th ed., Vol. 43. United States: Blackwell Science; 2004. p. 1-7. doi: 10.1002/9780470750520.ch43
3. Harper JC. An update on the pathogenesis and management of acne vulgaris. J Am Acad Dermatol. 2004 Jul;51(1 Suppl):S36-8. doi: 10.1016/j.jaad.2004.01.023, PMID: 15243503
4. Koo J. The psychosocial impact of acne: Patients' perceptions. J Am Acad Dermatol. 1995 May;32(5 Pt 3):S26-30. doi: 10.1016/0190-9622(95)90417-4, PMID: 7738224
5. Thomas DR. Psychosocial effects of acne. J Cutan Med Surg. 2004;8(Suppl 4):3-5. doi: 10.1007/s10227-004-0752-x, PMID: 15778823
6. Walker N, Lewis-Jones MS. Quality of life and acne in Scottish adolescent schoolchildren: Use of the Children's Dermatology Life Quality Index (CDLQI) and the Cardiff Acne Disability Index (CADI). J Eur Acad Dermatol Venereol. 2006 Jan;20(1):45-50. doi: 10.1111/j.1468-3083.2005.01344.x, PMID: 16405607
7. Durai PC, Nair DG. Acne vulgaris and quality of life among young adults in South India. Indian J Dermatol. 2015 Jan-Feb;60(1):33-40. doi: 10.4103/0019-5154.147784, PMID: 25657394; PMCID: PMC4318060
8. Raju BP, Nagaraju U. Quality of life among adolescents with acne in a tertiary referral centre in Bangalore. J Evid Based Med Healthc. 2016;3(62):3345-9. doi: 10.18410/jebmh/2016/723
9. Kraft J, Freiman A. Management of acne. CMAJ. 2011 Apr 19;183(7):E430-5. doi: 10.1503/cmaj.090374, PMID: 21398228; PMCID: PMC3080563
10. Kardeh S, Saki N, Jowkar F, Kardeh B, Moein SA, Khorraminejad-Shirazi MH. Efficacy of azithromycin in treatment of acne vulgaris: A mini review. World J Plast Surg. 2019 May;8(2):127-34. doi: 10.29252/wjps.8.2.127, PMID: 31309049; PMCID: PMC6620802
11. Bardazzi F, Savoia F, Parente G, Tabanelli M, Balestri R, Spadola G, *et al*. Azithromycin: A new therapeutical strategy for acne in adolescents. Dermatol Online J. 2007 Oct 13;13(4):4, PMID: 18319001
12. Del Rosso JQ. Oral doxycycline in the management of acne vulgaris: Current perspectives on clinical use and recent findings with a new double-scored small tablet formulation. J Clin Aesthet Dermatol. 2015 May;8(5):19-26. PMID: 26029331; PMCID: PMC4445892
13. Rok J, Karkoszka M, Rzepka Z, Respondek M, Banach K, Beberok A, *et al*. Cytotoxic and proapoptotic effect of doxycycline - An *in vitro* study on the human skin melanoma cells. Toxicol *In Vitro*. 2020 Jun;65:104790. doi: 10.1016/j.tiv.2020.104790, Epub 2020 Feb 8. PMID: 32044399
14. Goh CL, Abad-Casintahan F, Aw DC, Baba R, Chan LC, Hung NT, *et al*. South-East Asia study alliance guidelines on the management of acne vulgaris in South-East Asian patients. J Dermatol. 2015 Oct;42(10):945-53. doi: 10.1111/1346-8138.12993, PMID: 26211507
15. Oon HH, Wong SN, Aw DC, Cheong WK, Goh CL, Tan HH. Acne management guidelines by the dermatological society of Singapore. J Clin Aesthet Dermatol. 2019 Jul;12(7):34-50, PMID: 31531161; PMCID: PMC6715335
16. Hayashi N, Akamatsu H, Kawashima M, Acne Study Group. Establishment of grading criteria for acne severity. J Dermatol. 2008;35:255-60. doi: 10.1111/j.1346-8138.2008.00462.x
17. Adityan B, Thappa DM. Profile of acne vulgaris--a hospital-based study from South India. Indian J Dermatol Venereol Leprol. 2009 May-Jun;75(3):272-8. doi: 10.4103/0378-6323.51244, PMID: 19439880
18. Arjel A, Pokhrel K, Sharma S. Efficacy of oral azithromycin versus

doxycycline in the treatment of acne vulgaris. J Nepalgunj Med Coll. 2021 Aug 9;18(2):59-62. doi: 10.3126/jngmc.v18i2.38908

19. Amatya A, Chaudhary MK, Khan DK, Rajouria EA. A comparative study of azithromycin versus doxycycline in the treatment of acne vulgaris. Nepal J Dermatol Venereol Leprol. 2012 Jul 10;10(1):33-40. doi: 10.3126/njdvl.v10i1.6421
20. Kim JE, Park AY, Lee SY, Park YL, Whang KU, Kim HJ. Comparison of the efficacy of azithromycin versus doxycycline in acne vulgaris: A meta-analysis of randomized controlled trials. Ann Dermatol. 2018 Aug;30(4):417-26. doi: 10.5021/ad.2018.30.4.417, PMID: 30065581; PMCID: PMC6029975
21. Abdelrazik YT, Ali FM, Salek MS, Finlay AY. Clinical experience and psychometric properties of the Cardiff Acne Disability Index (CADI). Br J Dermatol. 2021 Oct;185(4):711-24. doi: 10.1111/bjd.20391, PMID: 33864247
22. Yap FB. Cardiff acne disability index in Sarawak, Malaysia. Ann Dermatol. 2012 May;24(2):158-61. doi: 10.5021/ad.2012.24.2.158, PMID: 22577265; PMCID: PMC3346905
23. Gupta PV, Garima R. Assessment of quality of life in patients of acne vulgaris pre and post treatment by using "Cardiff Acne Disability Index (CADI)". Int J Contemp Med. 2019;7(2):50-4.
24. Iftikhar U, Choudhry N. Serum levels of androgens in acne & their role in acne severity. Pak J Med Sci. 2019 Jan-Feb;35(1):146-50. doi: 10.12669/pjms.35.1.131, PMID: 30881413; PMCID: PMC6408631
25. Aizawa H, Nakada Y, Niimura M. Androgen status in adolescent women with acne vulgaris. J Dermatol. 1995 Jul;22(7):530-2. doi: 10.1111/j.1346-8138.1995.tb03440.x, PMID: 7560449
26. Henze C, Hinney B, Wuttke W. Incidence of increased androgen levels in patients suffering from acne. Dermatology. 1998;196(1):53-4. doi: 10.1159/000017867, PMID: 9557226