



EVALUATION OF PRESCRIPTION PATTERN AND QUALITY OF LIFE IN ACNE IN TERTIARY CARE HOSPITAL IN NORTH INDIAN POPULATION

Dr. Nalini Negi^{*1}, Dr. Sumir Kumar², Sourabh Kosey¹ and Vir Vikram Sharma³

¹ISFCP Moga, Punjab, India 146001.

²Department of Skin and Veneral Disease, Guru Govind Singh Medical College and Hospital & Research Centre, Baba Farid University of Health Sciences, Faridkot, Punjab.

³Dayanand Medical College, Ludhiana, Punjab.

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Corresponding author: Dr. Nalini Negi

ISFCP Moga, Punjab, India 146001.

ABSTRACT

The aim of this study was to evaluate the prescription pattern and Quality of Life of patients and severity of the disease by using Cardiff Acne Disability Index and Global Acne Grading System score respectively. A cross-sectional study was conducted in North India with 150 samples of patients included into the study. The prescription pattern comprehends the information about the prescribed drugs and also their dosing pattern for different indications that are currently being used in clinical practice. The prescription pattern varies according to the severity of the disease. The cases in the study diagnosed were mostly of acne vulgaris (96.7%), followed by acne conglobata (1.3%), acne rosacea (1.3%) and acne fulminans (0.7%). It was noted that oral Isotretinoin was the drug of choice for the treatment of moderate and severe forms and antibiotics included into the therapy were minocycline, clindamycin, azithromycin and erythromycin for mild and severe forms. There was not a strong degree of association between therapy and improvement in Cardiff Acne Disability Index and Global Acne Grading System but by observing overall Cardiff Acne Disability Index improvement it can be estimated that the prescription practice used for therapy enhances Quality of Life of the patient.

KEYWORDS: Quality of Life, Cardiff Acne, Global Acne, Isotretinoin.

1. INTRODUCTION

Acne is a stereotype skin disorder that occurs by means of abnormal hyperkeratinization and increase in the production of sebum by the sebaceous gland.^[1] It is the term that was procured from Greek word acne that connotes a very peculiar meaning: prime of Life. It can be demonstrated as a well-disposed condition or it may be very well considered to be a condition leading to pleomorphism that is utmost palpable between ages of 12-24, affecting 85% of population significantly.^[2] There are various factors closely associated with acne including anxiety, perturbation, shame, depression and more often decreased self-confidence. Due to these animus conditions people may psychologically become propositional to suicide.^[3] This disease condition primarily affects the pilosebaceous follicles. The main causation of the disease includes the four pathogenic factors namely sebum production, follicular hyperkeratinization, microbial colonization of the

pilosebaceous unit by *Propionibacterium acnes* and the release of inflammatory mediators into the follicle.^[4]

Some of the pathological skin surface features like increased sebum excretion, alteration of lipid and oxidant/antioxidant ratio are liable features for acne formation.^[5] An effusive study acclaimed that between twins taken into the study, the one with higher fatty acid level in sebum secretion was an indicative factor for higher prevalence of acne than the other without it.^[6] The patients diagnosed with acne contain low levels of linoleic acid in surface lipids of skin.^[7] The concentration of sebum and skin surface composition are greatly affected by *Propionibacterium acnes*. It has been exclaimed now that inflammatory condition is oftentimes seen in pathophysiology of acne rather than hyperkeratinization. The cause of the escalating inflammation of acne is the activation of toll-like receptor (TLR) on the membranes of inflammatory cells. The sebum that is produced by the sebaceous gland gets

partially regulated by Peroxisome proliferator-activated receptors that promptly stimulate the formation of oxidized lipids in sebum. As the acne lesions get recovered there occurs a decrement in Matrix metalloproteinases (MMPs) present in sebum.^[8] There are various grading systems for the evaluation of severity of acne. Tutakne et al. in 2003, recommended that acne must be graded as 1 to 4 depending on the severity of skin lesions as follows.

Grade 1: Comedones, occasional papules.

Grade 2: Papules, comedones, few pustules.

Grade 3: Predominant pustules, nodules, abscesses.

Grade 4: Mainly cysts, abscesses, widespread scarring.^[9]

According to American Academy of Dermatology a Consensus Conference categorized severity of acne.^[10]

The consensus classified the grading system of acne vulgaris in mild, moderate, severe and very severe forms.

1. Mild acne, the presence of comedones as well as few to several papules-pustules;
2. Moderate acne, differentiated by several papules, pustules and few to several nodules;
3. Severe acne, characterized by numerous or extensive papules-pustules, or both, along with many nodules; and
4. Very severe forms of acne, including the most destructive conditions of the disease, such as acne conglobata, acne fulminans and the follicular occlusion triad.^[11]

Many researches are being preceded on pathophysiology of acne where every day new therapeutic evidences are explored. By means of severe conditions of acne the therapeutic approach for the disease may be influenced and better analysis of the ailment is done with appropriate medications. There are various therapeutic considerations for the disease like oral antibiotics, hormonal therapy and isotretinoin. The type of treatment to be conferred to the patient is implemented in accord with the condition of the patient.^[12] A group of dermatologists with clinical dexterity in acne vulgaris founded a Global Alliance to improve outcomes in acne that promises the rational use of antimicrobials in therapies that is provided for acne though there is still a resistance found to antimicrobials.^[13] Isotretinoin is administered in monotherapy as a drug of choice for moderate and severe forms of acne which gives more effective results when given in combination which depends upon the intensity of the disease that aims at predominant mechanisms of acne pathogenesis.^[14]

2. MATERIALS AND METHODS

A cross sectional study was performed in patients with various forms of acne with patient inclusion of above 12 years of age in the Dermatology Departments of north India. The duration of the study commenced was of six months, from October 2015 to March 2016. Quality of Life of the patients was measured by using Cardiff Acne Disability Index questionnaire and the severity of acne successfully judged by Global Acne Grading System

score. Assessment of Cardiff Acne Disability Index summons a five item questionnaire. The questions of Cardiff Acne Disability Index questionnaire were as follows.

Question 1 ("As a result of having acne, during the last month have you been aggressive, frustrated, or embarrassed?"), Question 2 ("Do you think that having acne during the last month interfered with your daily social Life, social events or relationships with members of the opposite sex?"), Question 3 ("During the last month, have you avoided public changing facilities or wearing swimming costumes because of your acne?"), Question 4 ("How would you describe your feelings about the appearance of your skin over the last month?") and Question 5 ("Please indicate how bad you think your acne is now"). Question 1 and Question 4 were indicative of emotional feeling of patients, Question 2 specified social Life of patients, Question 3 measured feeling of public isolation of patients and Question 5 estimated the recognised severity of patients. There were 4 answers to each question. The scoring of the answers was done from 0~4. The score of each question was summed up to give the Cardiff Acne Disability Index score that ensues a maximum score of 15 and a minimum score of 0.

The severity of acne was measured using the Global Acne Grading System (Global Acne Grading System). In this Grading system the counting of acne lesions was done on dividing the area into six regions that were vulnerable to acne location and factor. Forehead, right and left cheek were given a factor 2, nose and chin were given 1 and chest and upper back were given a 3. The grading was done as follows: for comedones = 1, papules = 2, pustules = 3 and nodules = 4. The score for each region is calculated as Factor \times Grade (0-4) is the product of severity score multiplied by the area factor. Then the total score was obtained by summing up of all six regional scores. The minimum score obtained was 1 and maximum score was 44. The scores were graded as follows; 1~18 considered as mild, 19~30 as moderate, and >31 as severe. The cumulated data were analysed using IBM SPSS version 20. There were continuous data demonstrated as means and standard deviations and examined by using Student's t test with the level of significance was at $p < 0.05$.

3. RESULTS

In the study it has been observed that among the 150 patients taken into the study 78 (52%) were males 72 (48%) were females among which majority were students (61.3%) and housewives (17.3%). According to the residential profile it was the patient from rural areas (61.3%) were more in number than in urban areas (38.7%). Higher number of unmarried patients i.e. 72% shows that acne is more prevalent in them than in married ones (28%). The cases of acne vulgaris were found to be more (96.7%), than other etiologies like acne conglobata (1.3%), acne rosacea (1.3%) and acne fulminans (0.7%) (Fig. 1).

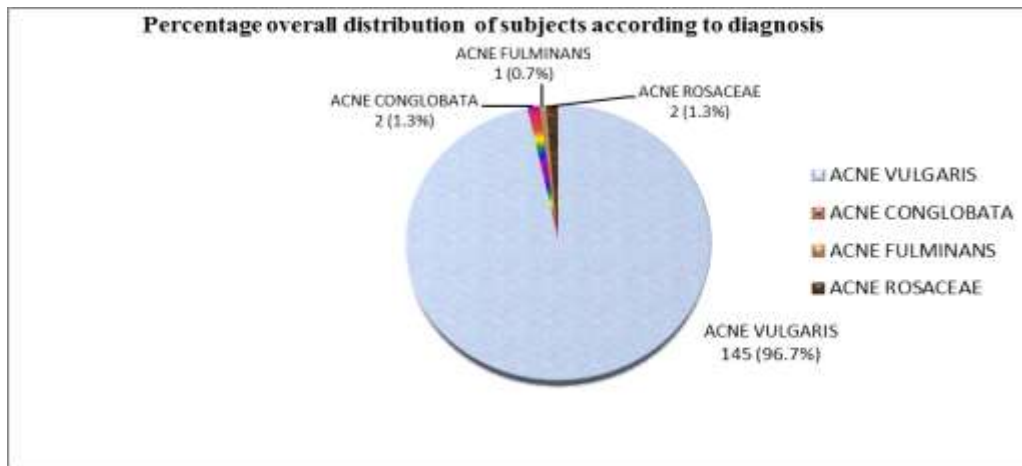


Fig. A. 1: Percentage overall distribution of patient according to diagnosis.

Severity was demonstrated by Global Acne Grading System score which showed that more number of patients were moderately affected (82.7%), severely affected (12%) and mildly affected (5.3%). Overall Quality of Life affected was analyzed with the help of Cardiff Acne Disability Index questionnaire in which mean score was 6.29 (S.D.:1.84). Fifth question in the questionnaire with mean score 1.35(S.D.: 0.55) indicated that most of the patient found acne to be a major problem. According to mean score 1.34(S.D.: 0.58) of fourth question some of the patients were more concerned with their physical appearance. Third question with a mean score of 1.30(S.D.: 0.61) indicated that patients were occasionally concerned about condition of their disease publicly. Mean score of emotionally impaired Quality of Life of patients 1.25 (S.D.: 0.50). According to mean score of first and second question, patients were a little concerned emotionally about their social Life. Overall data distribution in frequency percentages is shown in Table A.1.

Table A.1: Overall Distribution [Mean (Percentage)].

Age(Years)	21.85 [SD: 5.16]
Weight(Kilograms)	56.75 [SD: 10.81]
Occupation:	
Businessman	8(5.3)
Driver	4(2.3)
Farmer	8(5.3)
Housewife	26(17.3)
Job	6(4.0)
Shopkeeper	3(2.0)
Student	92(61.3)
Worker	3(2.0)
Location:	
Rural	92(61.3)
Urban	58(38.7)
Gender:	
Male	78(52.0)
Female	72(48.0)
Literacy:	
Illiterate	8(5.3)
<tenth	10(6.7)

Tenth	14(9.3)
Twelfth	68(45.3)
Graduate	50(33.3)
Addiction:	
None	128(85.3)
Alcoholic	10(6.7)
Smoker	7(4.7)
Both	5(3.3)
Marital:	
Unmarried	108(72)
Married	42(28)
Diagnosis:	
Acne vulgaris	145(96.7)
Acne conglobata	2(1.3)
Acne fulminans	1(0.7)
Acne rosaceae	2(1.3)
Global acne grading system:	
Mild	8(5.3)
Moderate	124(82.7)
Severe	18(12.0)
Cardiff acne disability index score:	6.29[SD: 1.84]
Emotional PRECADI	1.25[SD: 0.50]
Social PRECADI	1.23[SD: 0.54]
Isolation PRECADI	1.30[SD: 0.61]
Feeling PRECADI	1.34[SD: 0.58]
Problem PRECADI	1.35[SD: 0.55]
Therapy:	
Antibiotics	43(28.7)
Isotretinoin	56(37.3)
Antibiotics with isotretinoin	51(34.0)

According to overall Cardiff Acne Disability Index scores Quality of Life impairment was more in females 6.36 (95% CI: 5.91-6.81) than in males 6.22 (95% CI: 5.82-6.62). On concerning the severity of disease it was obtained that the Quality of Life was more impaired in acne conglobata 7.50 (95% CI: 1.15-13.85), in acne rosaceae 6.50 (95% CI: 0.15-12.85), and very less affected in acne vulgaris 6.41 (95% CI: 6.14-6.69). There was only one case of acne fulminans showing varying result so it was omitted. The Quality of Life of alcoholic and smoker was severely affected indicating Cardiff

Acne Disability Index score 8.00 (95% CI: 5.68-10.32), than in smokers 6.29 (95% CI: 4.38-8.19), less impaired in alcoholic 6.20 (95% CI: 4.90-7.50), and non-alcoholic and non-smokers 6.23 (95% CI: 5.91-6.55). The Quality of life of the married patients 6.55 (95% CI: 6.03-7.06) was impaired more than the unmarried ones 6.19 (95% CI: 5.82-6.55).

When the comparison was made according to the literacy the students that were below high school less than 16

years of age had their Quality of life highly impaired 6.60 (95% CI: 6.03-7.06) which was found to be more than the students of 12th class above or the adolescents that was 6.43 (95% CI: 6.00-6.85), than in illiterate 6.38 (95% CI: 4.97-7.78) and less in the patients who were graduate or the adults 6.18 (95% CI: 5.64-5.72) and least in students in 10th class 5.71 (95% CI: 4.95-6.48). The patient in the urban areas have Quality of life more impaired 6.38 (95% CI: 5.85-6.91) than in rural areas 6.23 (95% CI: 5.87-6.59) represented in Table A.2.

Table A.2: Cardiff acne disability index distribution among different factors.

	Overall Cadi Mean(SD)	95% Confidence Interval for Mean	
		Lower bound	Upper bound
Gender:			
Male	6.22(1.77)	5.82	6.62
Female	6.36(1.92)	5.91	6.81
Diagnosis:			
Acne vulgaris	6.11(1.76)	5.80	6.42
Acne conglobata	7.43(2.50)	5.11	9.75
Acne fulminans	10.00(1.00)	7.52	12.48
Acne rosacea	6.50(1.66)	4.45	8.55
Acneiform eruptions	6.71(0.95)	5.83	7.59
Addiction:			
None	6.23(1.82)	5.91	6.55
Alcoholic	6.20(1.80)	4.90	7.50
Smoker	6.29(2.05)	4.38	8.19
Alcoholic and smoker	8.00(1.87)	5.68	10.32
Marital:			
Married	6.55(1.65)	6.03	7.06
Unmarried	6.19(1.91)	5.82	6.55
Literacy:			
Illiterate	6.38(1.68)	4.97	7.78
<tenth	6.60(2.75)	4.63	8.57
Tenth	5.71(1.32)	4.95	6.48
Twelfth	6.43(1.76)	6.00	6.85
Graduate	6.18(1.91)	5.64	6.72
Location:			
Rural	6.23(1.73)	5.87	6.59
Urban	6.38(2.02)	5.85	6.91

There was significant improvement in Quality of Life impairment and in severity of disease as demonstrated by percentage improvement in Cardiff Acne Disability

Index (50.17%) and Global Acne Grading System score (29.71%); $p < 0.0001$. (Table A.3) and (Fig. A.2).

Table A.3: Percentage improvement in cardiff acne disability index and global acne grading system scores.

	Mean difference	T	Sig. (2-tailed)	95% Confidence Interval of the differences	
				Lower	Upper
Percentage improvement in CADI score	50.17	43.582	<0.0001	47.9020	52.4520
Percentage improvement in GAGS score	29.71	30.273	<0.0001	27.7759	31.6551

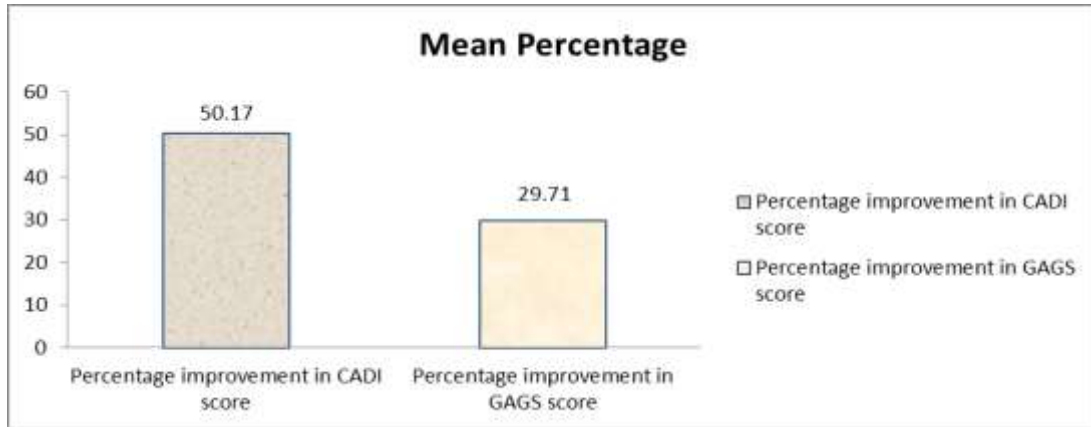


Fig. A.2: Percentage distribution of overall Cardiff Acne Disability Index and Global Acne Grading System Scores.

Patients prescribed with antibiotics as a primary agent (n=43) have a mean improvement in Cardiff Acne Disability Index Score [3.28(S.D.: 1.27)] from mean pre follow up score [6.74(S.D.: 1.85)] to mean post follow up score [3.47 (S.D.: 1.45)] having percentage improvement [32.47% (S.D.: 8.23)]; p=0.030, same as with isotretinoin (n=56) with mean improvement in Cardiff Acne Disability Index score [3.04 (S.D.: 1.27)] from mean pre follow up score [5.84(S.D.: 1.69)] to mean post follow up score [2.93 (S.D.: 1.14)] having

percentage improvement [32.47 (S.D.: 8.46)]; p=0.040. On the administration of antibiotic in combination with isotretinoin (n=51) mean improvement in Cardiff Acne Disability Index score [3.17(S.D.: 1.09)] from mean pre follow up score [6.48(S.D.: 2.01)] to mean post follow up score [3.31(S.D.:1.81)] having percentage improvement [33.35 (S.D.:8.25)]; p=0.052. (Table A.4) and (Fig. A.3) and improvement in CADI scores after providing therapy by various agents is very well described in Fig. A.4.

Table A.4: Therapy effect on cardiff acne disability index score.

Therapy	Number of cases (N)	Precadi score [Mean (SD)]	Postcadi score [Mean (SD)]	Improvement in cadi score [Mean (SD)]	Percentage improvement in cadi score [Mean (%) (SD)]	F	Significance
Antibiotic	43	6.74(1.85)	3.47(1.45)	3.28(1.27)	32.47(8.23)	4.806	0.030
Isotretinoin	56	5.84(1.69)	2.93(1.14)	3.04(1.27)	32.47(8.46)	4.290	0.040
Antibiotic and isotretinoin	54	6.48(2.01)	3.31(1.81)	3.17(1.09)	33.35(8.25)	3.840	0.052

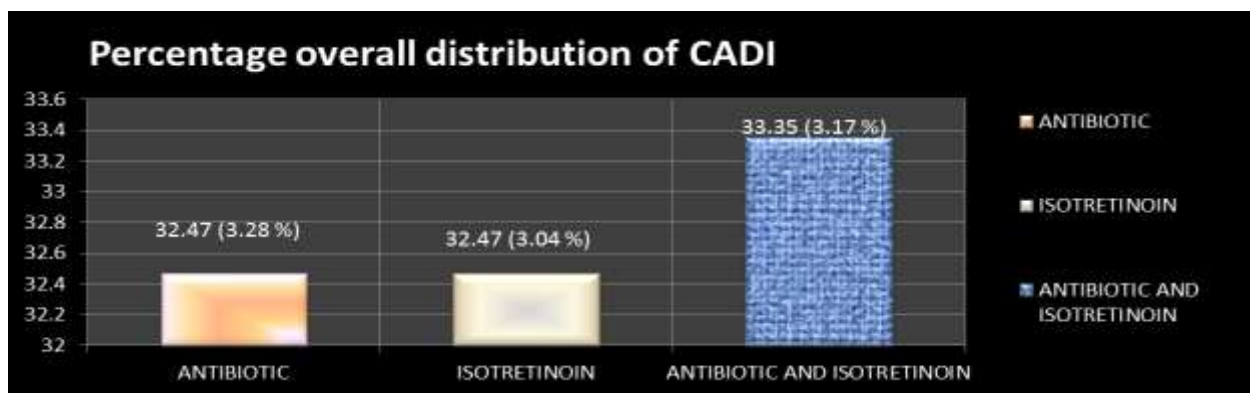


Fig. A.3: Percentage overall distribution of Cardiff Acne Disability Index improvement in patient according to therapy.

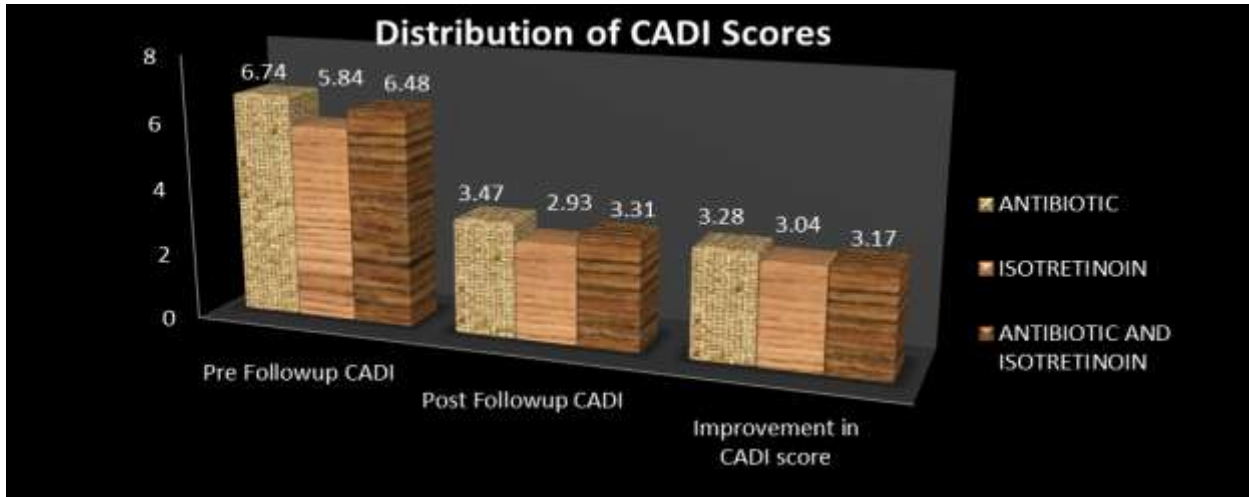


Fig. A.4: Distribution of Cardiff Acne Disability Index Scores among different therapies.

Patients prescribed with isotretinoin as a primary agent (n=56) mean improvement in Global Acne Grading System Score [7.41 (S.D.: 3.22)] from mean pre follow up score 24.63[S.D.: 7.21] to mean post follow up score [17.21(S.D.: 6.11)] with percentage improvement [39.24(S.D.: 7.25)]; p=0.174, combination of antibiotic and isotretinoin (n=51) with mean improvement in Global Acne Grading System Score [7.16(S.D.: 3.96)] from mean pre follow up score [23.87(S.D.: 7.51)] to mean post follow up score (16.70(S.D.: 6.45)] with

percentage improvement [38.93(S.D.: 7.08)]; p=0.181 and on the administration of antibiotic (n=43) mean improvement in Global Acne Grading System score [6.51(S.D.: 3.48)] from mean pre follow up score [23.16(S.D.: 8.05)] to mean post follow up score [16.65(S.D.: 6.96)] with percentage improvement [37.98(S.D.: 7.05)]; p=0.275.(Table A.5) and (Fig. A.5) and improvement in CADI scores after providing therapy by various agents is very well described in Fig. A.6.

Table A.5: Therapy effect in global acne grading system score.

Therapy	Number of cases (N)	Pre gags score [Mean (S.D.)]	Post gags score [Mean (S.D.)]	Improvement in gags score [Mean (S.D.)]	Percentage improvement in gags score [Mean (S.D.)]	Significance
Antibiotic	43	23.16 (8.05)	16.65 (6.96)	6.51 (3.48)	37.98 (7.05)	0.275
Isotretinoin	56	24.63 (7.21)	17.21 (6.11)	7.41 (3.22)	39.24 (7.25)	0.174
Antibiotic and Isotretinoin	51	23.87 (7.51)	16.70 (6.45)	7.16 (3.96)	38.93 (7.08)	0.181

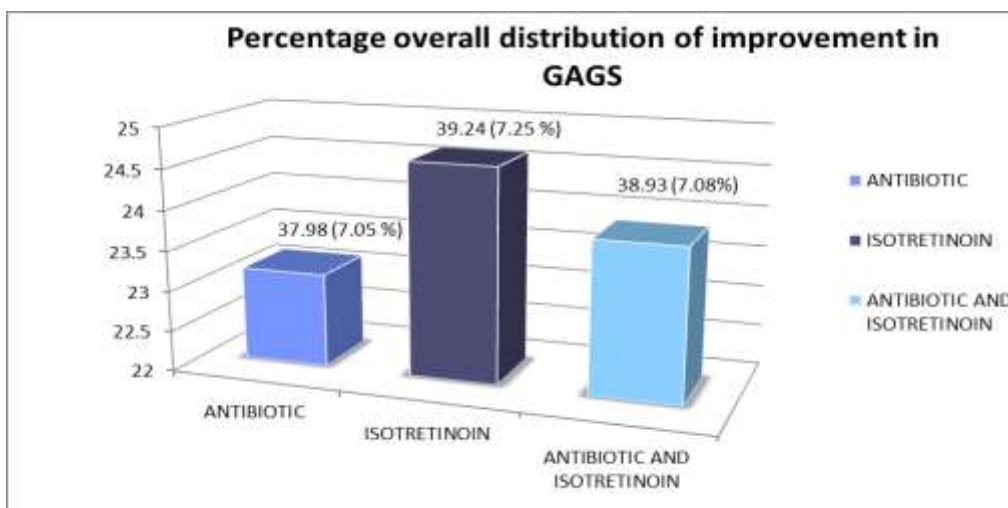


Fig. A.5: Percentage overall distribution of Global Acne Grading System improvement in patient according to therapy.

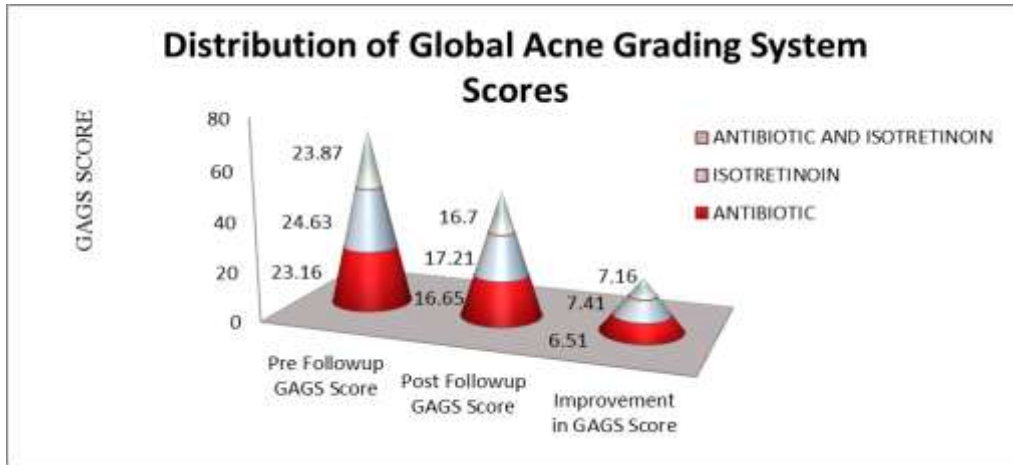


Fig. A.6: Distribution of Global Acne Grading System Scores among different therapies.

Medications were prescribed on the basis of the severity of the disease and the use of antibiotics and isotretinoin was mostly considered in the prescription pattern and among the antibiotics minocycline was mostly prescribed into the therapy by the physician. Then clindamycin, azithromycin, erythromycin and clarithromycin were followed as per the motif into the remedial treatment. Mostly antibiotics were prescribed for mild non inflammatory comedal form, isotretinoin for inflammatory papules or pustules of moderate form and antibiotics combined with isotretinoin mostly preferred for severe form of the disease. Azelaic acid, benzoyl peroxide, and topical retinoid were the adjuvants into the therapy. It is very well described by the table the administration of medications according to the prescription pattern (Table A.6) and graphically represented. (Fig. 7).

Table A.6: Prescription pattern of Acne.

Therapy	No. of patients	Percentage
Antibiotics:		
Minocycline	44	29.33 %
Clindamycin	41	27.33 %
Azithromycin	20	13.33 %
Erythromycin	12	8.00%
Clarithromycin	10	6.66%
Oral retinoid:		
Isotretinoin	107	71.33 %
Topical retinoid:		
Adapalene	42	28 %
Tretinoin	11	7.33 %
Azelaic acid:		
	65	43.33 %
Benzoyl peroxide:		
	94	62.66 %

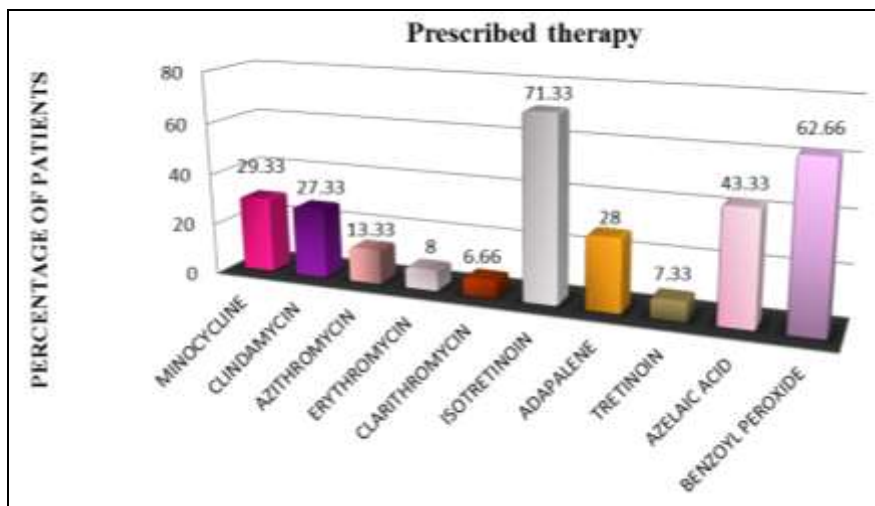


Fig 7. Percentage distribution of prescription pattern in acne.

4. DISCUSSION

In our study the mean Cardiff Acne Disability Index score obtained was 6.29 when compared to a study conducted in Iran with a Cardiff Acne Disability Index score of 5.97 the result was found to be analogous to our study. The repercussion that acne had on the Quality of Life was found to be very severe in 1.4%, severe in

16.8%, and moderate in 33.6% indicating Quality of Life was moderately impaired in most of the patients which was similar to findings of our study i.e. 72.7% moderately, 18% mildly and 9.3% severely affected with no case of very severe form. But the results reported were varying in different countries.^[15] In some of the studies conducted in Iraq and Odisha have shown that

females were more prone to acne.^[16,17] A study by Kameran also gave an evidence of the occurrence of disease mostly below 20 years of age which was very similar to our study while another study conducted in Malaysia expressed that males were affected predominantly. One difference directed from a study was that acne found to be more prevalent in urban population while it was more prevalent in rural population according to our study.^[18]

In our study the Cardiff Acne Disability Index score ranged from 3-12 which was consistent with our study held in Iran with scores ranging 2-14.^[19] The higher the Cardiff Acne Disability Index score is commonsensical to be indicative of the greater effect on the Quality of Life. As demonstrated by mean Cardiff Acne Disability Index score the Quality of Life mostly seemed to be worsen in case of the severity of acne. Another study in Iran presented the effect of acne on Quality of Life of the patients in 51.8% of subjects. The results of our study show clear impact of acne on patients' Quality of Life. In accord with the questions of Cardiff Acne Disability Index the main consideration was on the social Life, emotional conditions including feelings viz frustration or embarrassment, inhibition of changing facilities publicly and the severity of acne. A large number of patients found acne to be a major problem and a very less number of patients were concerned emotionally about their social Life.

Overall Quality of Life of patients was perused with the help of Cardiff Acne Disability Index questionnaire. The five questions of the questionnaire indicated the increased or decreased Quality of Life. The fifth question in the questionnaire gives a sign of acne to be a problem specified by the mean score of 1.35 (S.D.: 0.55). According to the mean score of fourth question 1.34 (S.D.: 0.58) it was indicated that some of the patients were more bothered regarding their physical appearance. Third question with a mean score of 1.30 (S.D.: 0.61) was an evocative of the condition of their disease publicly. According to mean score of first and second question 1.25 (S.D.: 0.50) and 1.23 (S.D.: 0.54) respectively it was seen that patients were not so much concerned emotionally about their social life.

Sophie et al. described the prescribing compartment into their study which included the use of isotretinoin and local antibiotics together for mild or moderate acne (Sophie Seite et al. 2015). Similar finding was observed in our study with the inclusion of isotretinoin and oral antibiotics into the therapy. (36%). Antibiotics as a monotherapy were mostly prescribed for mild forms of comedonal form of acne, (28.7%) while in moderate or severe forms of acne Isotretinoin was stipulated into the therapy (37.3%).

Two studies held in Malaysia and Saudi Arabia demonstrated the association of the Quality of Life with acne severity while in a study by Noorbala in Iran the

direct concurrence between the Quality of Life and acne severity was obtained.^[20,21,22] In our study there was not a very sturdy relationship between the Quality of Life and severity of the disease but it can be stated that a significant improvement was observed after the providence of the therapy that improved the Quality of Life to a far extent.

5. CONCLUSION

In the following study various facets were taken into consideration including the prescription pattern in various grades of acne depending upon the severity. It has been projected that oral Isotretinoin was the drug of choice majorly for the treatment of moderate and severe forms while minocycline, clindamycin, azithromycin, erythromycin and clindamycin arranged according to their use in a decreasing manner were the various antibiotics that were counted for mild and severe forms. Local administration therapy instantly being used in practice with Isotretinoin and antibiotics was adapalene and topical retinoids that were found beneficial for the improvement of the disease state. Other adjuvant topical therapies included azelaic acid and benzoyl peroxide. Upon the introduction of the Cardiff Acne Disability Index questionnaire, the Quality of Life of the patients was assessed and a significant improvement observed after the providence of the therapy which caused to a decrease in the severity of the disease. On spotting the Global Acne Grading System score after the therapy being initialised it was certain that there was a refinement in the condition of the disease.



Fig. 8: Patient with severe form of acne (Acne conglobata).

REFERENCES

1. Billman Jennifer D. Management of acne vulgaris: A Review, Pharm. D. Candidate, December 2009; 25(3).
2. Ray C, Trivedi P, Sharma V. Acne and its treatment lines. International Journal of Research in Pharmaceutical and Biosciences, 2013; 3(1): 1-16.

3. Kairavee D, Choksi V. Factors aggravating or precipitating acne, *National Journal of Community Medicine*, 2010; 1(1).
4. Ryu S, Han H.M, Song P.I, Armstrong C.A. and Park Y. PLoS One. Suppression of Propionibacterium acnes Infection and the Associated Inflammatory Response by the Antimicrobial Peptide P5 in Mice, 2015: 10(7).
5. Zouboulis CC. Acne and sebaceous gland function. *Clinics in Dermatology*, 2004; 22: 360–366.
6. Makrantonaki E, Ganceviciene R and Zouboulis C. An update on the role of the sebaceous gland in the pathogenesis of acne. *Dermatoendocrinology*, 2011; 3(1): 41–49.
7. Stewart ME. Sebaceous gland lipids. *Seminar Dermatology*, 1992; 11: 100–105.
8. Thiboutot D, Gollnick H, Bettoli V, et al. New insights into the management of acne: update from the Global Alliance to Improve Outcomes in Acne group. *Journal of American Academy of Dermatology*, 2009; 60(5 Suppl): S1–S50. Copyright Elsevier 2009.
9. Tutakne MA, Chari KVR. Acne, rosacea and perioral dermatitis. In: Valia RG, Valia AR, editors. *IADV Textbook and atlas of dermatology*, 2003; 689-710.
10. Titus S, and Hodge J. Diagnosis and Treatment of Acne, *Am Fam Physician*, 2012 Oct 15; 86(8): 734-740.
11. Feldman S, Careccia RE, Barham KL and Hancox J, M.D. Diagnosis and Treatment of Acne *American Family Physician*, 2004; 69(9): 2123-2130.
12. Arshdeep, Dipankar De. What's new in the management of acne? *Department of Dermatology, Venereology and Leprology*, 2013; 79: 279-87.
13. Mandekou LI, Delli F, Teknetzis A, Euthimiadou R, Karakatsanis G. Low-dose schema of isotretinoin in acne vulgaris. *State Hospital for Skin and Venereal Diseases, Thessaloniki, Greece. International Journal of Clinical Pharmacology Research*, 2003; 23(2-3): 41-46.
14. Rathi SK. Acne vulgaris treatment: the current scenario *Indian Journal of Dermatology*, 2011; 56(1): 7–13.
15. H. Safizadeh, Meymandy SS and Naeimi A. Quality of Life in Iranian Patients with Acne, 2012(2012): 1-4.
16. Ismail K, Ali KM. Quality of Life in patients with acne in Erbil city, *Health and Quality of Life Outcomes*, 2012: 60.
17. Patro N, Jena M, Panda M, Dash M. A Study on the Prescribing Pattern of Drugs for Acne in a Tertiary Care Teaching Hospital in Odisha. *Journal of Clinical and Diagnostic Research*, 2015; 9(3).
18. Samanthula H, Kodali M, Acne and Quality of Life- A Study from a Tertiary Care Centre in South India, *IOSR Journal of Dental and Medical Sciences*, 2013; 6(3): 59-62.
19. Aghaei S, Mazharinia N, Jafari P, Abbasfard Z. The Persian version of the Cardiff Acne Disability Index Reliability and validity study. *Saudi Med J.*, 2006; 27(1): 80-82.
20. Hanisah A, Omar K, Shah SA. Prevalence of acne and its impact on the Quality of Life in school-aged adolescents in Malaysia. *J Prim Health Care*, 2009; 1(1): 20-25.
21. Kokandi A. Evaluation of Acne Quality of Life and Clinical Severity in Acne Female Adults. *Dermatology Research and Practice*, 1-3.
22. Noorbala MT, Mozaffary B, Noorbala M. Prevalence of acne and its impact on the Quality of Life in high school-aged adolescents in Yazd, Iran *Journal of Pakistan Association of Dermatologists*, 2013; 23(2): 168-172.