International Journal of Research in Dermatology
Badabagni P et al. Int J Res Dermatol. 2022 Jan;8(1):8-14
http://www.ijord.com

DOI: https://dx.doi.org/10.18203/issn.2455-4529.IntJResDermatol20214443

Original Research Article

Efficacy and safety of adalimumab in treating patients with moderate to severe plaque psoriasis: a retrospective study

Purnachandra Badabagni[1], Birudala Ramadevi[2], Jahnavi Sambangi[1]*

[1]Department of Dermatology, ESIC Medical College and Hospital, Hyderabad, India
[2]Department of Dermatology, Kamineni Academy of Medical Sciences and Research Centre, Hyderabad, India

Received: 13 October 2021
Revised: 28 October 2021
Accepted: 29 October 2021

***Correspondence:**
Dr. Jahnavi Sambangi,
E-mail: janusmile9@gmail.com

ABSTRACT

Background: Psoriasis is a disease of systemic inflammation with multiple organ ramifications. It is a chronic, painful, non-communicable, immune-mediated, genetic disease-causing disfiguration and disability, for which there is no cure and with great negative impact on patients' quality of life (QoL). Aim and objective was to assess the efficacy and safety of adalimumab (ADA) in moderate to severe plaque psoriasis.
Methods: A hospital based, analytical retrospective observational study was conducted among patients aged 18 years and above, irrespective of gender and who received adalimumab treatment for moderate-to-severe plaque psoriasis and attended the outpatient clinic of dermatology at a tertiary care hospital for a period of 12 months. Efficacy was evaluated in all patients at 4, 12 and at last visit by calculating PASI (psoriasis area and severity index) relative to pre-treatment visit (baseline 0 week) as there was no comparative group. Safety was assessed by recording of side effects if any. Data was entered in MS excel 2019 and statistical analysis was done using SPSS 23 demo version.
Results: The mean PASI score at 0 week was 24.4±3.26, this when compared to PASI score at 4 weeks (11.2±4.08), at 12 weeks (3.2±2.40), at 52 weeks (0.5±0.96) had shown an extreme statistically significant difference. Side effects reported were urticaria, diarrhea, upper respiratory tract infections.
Conclusions: Adalimumab was very effective for chronic psoriasis, when given at high loading dose followed by maintenance dose every other week with minimal side effects.

Keywords: Adalimumab, Biologics, Efficacy, Psoriasis, PASI, Safety

INTRODUCTION

Psoriasis is a chronic, non-communicable, immune-mediated, painful, genetic disease-causing disfiguration and disability, for which there is no cure and with great negative impact on QoL.[1,2] The worldwide prevalence of psoriasis was estimated to be between 1-3 p.c., respectively.[3] The global age-standardized prevalence rate of psoriasis vulgaris during the year 2017 was 811 per 100,000 population (approximately 0.84 p.c. of world population), with an increase in incidence of psoriasis from 92 per 100,000 in 1990 to 99 in 2017.[4]

It is a disease of systemic inflammation with multiple organ ramifications.[5] It predominantly involves the skin and nails, it is also associated with co-morbidities like psoriatic arthritis, cardiovascular disease, diabetes, elevated risk of non-Hodgkin lymphoma and cutaneous T-cell lymphoma and psychiatric illness (depression, anxiety).[5] Skin lesions appear as localized or generalized, symmetrical, sharply demarcated, red papules and plaques and usually covered with white or silver scales, that cause itching, stinging and pain.[5] About 1.3-34.7 p.c. of the patients with psoriasis develop chronic, inflammatory arthritis that leads to joint deformations and disability, also called psoriatic arthritis.[6,7] Nail changes

develop among 4.2-69 p.c. of the patients suffering from psoriasis develop nail changes.[8]

Psoriasis causes great physical, emotional, social burden and significant QoL impairment.[9-13] Disfiguration, disability and marked loss of productivity are common challenges for people with psoriasis.[14,15] There were significantly higher rates of depression, leading to negative impact for individuals and society.[16] Despite of different treatment options availability to treat moderate-to-severe psoriasis, epidemiological studies reported a low rates of systemic treatments usage and patient satisfaction.[17,18] Due to low systemic treatment usage, low patient satisfaction, high side-effects and toxicities, the major focus in psoriasis research was the development of biologic therapies which dramatically changed the treatment and management of psoriasis.[19] There were various biological factors available as of 2018 that included two tumor necrosis factor (TNF)-α inhibitors infliximab (IFX) and adalimumab (ADA); one anti-interleukin (IL)-12/23p40 antibody ustekinumab (UST); three IL-17 inhibitors secukinumab, ixekizumab (IXE) and brodalumab; and one anti-IL-23p19 antibody guselkumab.[1] ADA is the first recombinant fully human monoclonal antibody used for the treatment of psoriasis that inhibited TNF.[20]

Evidence-based guidelines and Canadian psoriasis expert panel have integrated biologics in the management of patients with moderate-to-severe psoriasis.[21] Various cytokines were implicated in pathogenesis of psoriasis, among which TNF-α is a major proinflammatory cytokine.[22] ADA, an anti-TNF-α IgG1 antibody was approved by USFDA for the treatment of moderate-to-severe plaque psoriasis and psoriatic arthritis. This anti-TNF-α IgG1 antibody blocked the TNF-α activity by inhibiting its interaction with p55 and p75 TNF-α receptors with high efficacy and tolerability.[22]

ADA efficacy in the treatment of moderate-to-severe psoriasis was evaluated by clinical trials using PASI-75 or PASI-90 response rate (the proportion of patients who achieve ≥75% or ≥90% improvement with respect to their baseline PASI.[23]

Aim and objective

The aim and objective was to assess the efficacy and safety of ADA in moderate to severe plaque psoriasis.

METHODS

A hospital based, analytical retrospective observational study was conducted among patients aged 18 years and above, irrespective of gender and who received ADA treatment for moderate-to-severe plaque psoriasis and attended the outpatient clinic of dermatology in Employees' State Insurance Corporation medical college and hospital, Sanathnagar, Hyderabad, Telangana state. Pregnant women, lactating mothers, severely immunocompromised, patients with other active infections were excluded from the study. The study was conducted for a period of 12 months (1 October 2020 to 30 September 2021). IEC approval was obtained. A written informed consent was obtained from the patients before including their details in the study. A detailed history taken and reports of conducted screening procedures (included chest X-ray, screening for hepatitis B, C, HIV and tuberculin skin testing) were also verified. A sample size was calculated considering an α-error of 0.05; β-error of 0.2; an expected mean difference of the outcome between the two groups was 5.6 and an expected standard deviation of difference of the outcome between the two groups of 4.5; using the formula,

$$n \geq \frac{2\,(Z_{1-\alpha/2}+Z_{1-\beta})^2}{\left(\delta_{difference}/\sigma_{difference}\right)^2} + \frac{(Z_{1-\alpha/2})^2}{2}.$$

The calculated sample size (n) was ≥13, in the present study about twenty-five patients were included.

All the patients received ADA 80 mg at week 0 followed by 40 mg every other week starting from first week after initial dose. Efficacy was evaluated in all patients at 4, 12 and at last visit by calculating PASI relative to pre-treatment visit (baseline) as there was no comparative group. The comparison of PASI score was performed through time, baseline (0 week) in relation to 4, 12, 52 weeks.

PASI was calculated as follows: the body was divided into four sections (head (H) (10% of a person's skin); arms (A) (20%); trunk (T) (30%); legs (L) (40%)). Each of these areas was scored by itself and then the four scores were combined into the final PASI. For each section, the percent of area of skin involved was estimated and then transformed into a grade from 0 to 6: (1) 0% of involved area; (2) <10% of involved area; (3) 10-29% of involved area; (4) 30-49% of involved area; (5) 50-69% of involved area; (6) 70-89% of involved area; (7) 90-100% of involved area. Within each area, the severity was estimated by three clinical signs: erythema (redness), induration (thickness) and desquamation (scaling). Severity parameters were measured on a scale of 0 to 4, from none to maximum. The sum of all three severity parameters was then calculated for each section of skin, multiplied by the area score for that area and weight of respective section (0.1 for H, 0.2 for A, 0.3 for body and 0.4 for L).

Data recorded included age, gender, type of psoriasis, age at diagnosis of psoriasis, details of previous treatments, response to treatment as PASI (75, 90, 100), duration of therapy, discontinuation of drug, reasons for discontinuation.

Safety was assessed by recording of side effects (allergic reactions, injection site reactions, upper respiratory tract infections, any symptoms of reactivation of TB or hepatitis B).

Statistical methods

Collected data was entered into MS excel 2019 and analyzed using SPSS 23 demo version. Continuous variables were expressed as mean and standard deviations, while categorical variables were expressed as proportions and percentages. Paired t test (also called before and after test) and ANOVA were used for analysing the continuous data wherever necessary at 95% confidence limit ($p<0.05$).

RESULTS

In the present study twenty five patients who received ADA treatment for moderate to severe psoriasis were included, about 76 p.c. were males and 24 p.c. were females and majority of the males and females were in 30-40 years age group (Table 1). The mean age of the patients was 39.5±9.42 years, the mean weight of the patients was 68.5±9.01 kilograms, the mean height of the patients was 166.6±10.3 centimeters and the mean BMI of the patients was 24.7±2.89 kilograms per square meter (Table 2).

Table 1: Distribution of patients based on gender and age.

Gender		Age (in years)					Total
		18-30	31-40	41-50	51-60	>60	
Male	N (%)	5 (26.3)	6 (31.6)	4 (21.1)	4 (21.1)	0 (0)	19 (76)
Female	N (%)	0 (0)	3 (50.0)	3 (50.0)	0 (0)	0 (0)	6 (24)

Table 2: Characteristics of the study population before starting ADA.

Variables		Findings
Gender (%)	Male	19 (76)
	Female	06 (24)
Age (in years)	Mean (SD)	39.5 (9.42)
Weight (in kg)	Mean (SD)	68.52 (9.01)
Height	Mean (SD)	166.6 (10.3)
BMI	Mean (SD)	24.7 (2.89)
Psoriasis type (%)	Chronic plaque psoriasis	21 (84)
	Chronic plaque psoriasis with arthritis	4 (16)
Family history	Present	06 (24)
	Absent	19 (76)
Co-morbidities	Nil	19 (76)
	Diabetes	05 (20)
	Hypertension	01 (4)
Duration of illness (years) (%)	1	08 (32)
	2	04 (16)
	3	02 (8)
	4	01 (4)
	5	05 (20)
	6	05 (20)
	≥7	
Biologic (%)	Naïve	04 (16)
	Non-naïve	21 (84)
Previous treatments (topical) (%)	Steroids	13 (52)
	Coal tar	01 (4)
Previous treatments (oral) (%)	Methotrexate	11 (44)
Phototherapy (%)	PUVA	03 (12)

Table 3: Comparison between PASI scores at various weeks after ADA treatment initiation.

PASI score (weeks) at various levels	PASI score (mean±SD)	t	df	P value
0 and 4	24. 416±3.26 and 11.236±4.08	14.990	24	0.0001
0 and 12	24. 416±3.26 and 3.236±2.40	31.348	24	0.0001
0 and 52	24. 416±3.26 and 0.560±0.96	37.198	24	0.0001
4 and 12	11.236±4.08 and 3.236±2.40	11.717	24	0.0001

Continued.

PASI score (weeks) at various levels	PASI score (mean±SD)	t	df	P value
4 and 52	11.236±4.08 and 0.560±0.97	13.763	24	0.0001
12 and 52	3.236±2.40 and 0.560±0.97	8.244	24	0.0001

Table 4: PASI score in relation to biologics.

PASI score at various intervals (weeks)	Biologic	N	Mean	Std. deviation	F	P value
0	Naive	4	25.7750	2.29837	0.818	0.375
	Non-naive	21	24.1571	3.40067		
4	Naive	4	14.1750	1.61323	2.631	0.118
	Non-naive	21	10.6762	4.19356		
12	Naive	4	4.0500	2.81129	0.537	0.471
	Non-naive	21	3.0810	2.36085		
52	Naive	4	0.6500	1.30000	0.040	0.844
	Non-naive	21	0.5429	0.92713		

Table 5: Pre-treatment characteristics of biologic naive and non-biologic naive patients.

Variables	Biologic naive	Non-naive	P value
Age (mean±SD)	35±7.52	40.38±9.65	0.35
Weight (mean±SD)	73±7.51	67.66±9.16	0.28
Height (mean±SD)	164.75±8.26	167.04±10.8	0.67
BMI (mean±SD)	26.8±1.3	24.28±2.94	0.20

Table 6: Distribution of patients based on side effects.

Side effects	Number of patients (%)
Urticaria	2 (8)
Diarrhoea	1 (4)
Upper respiratory tract infections (URTIs)	1 (4)

Table 7: Comparison of various studies in relation to PASI.

Study	Study design	Treatment protocol	Baseline mean PASI	PASI 75 achievement (%)
Present study	Retrospective	80 mg loading, followed by 40 mg every other week	24.4	96
Armesto et al[3]	Retrospective	80 mg loading, followed by 40 mg every other week	15.9	95
DiLernia et al[24]	Retrospective COHORT	(15-30 kg) 20 mg loading, followed by 20 mg eow. (≥30 kg) 40 mg loading, followed by 40 mg eow.	14.7	55.5
Menter et al[25]	12-week, randomized, double-blind, placebo-controlled	80 mg loading followed by 40 mg every other week	16.7	-

Table 8: Side effects comparison in various studies.

Study	Side effects
Present study	Urticaria, diarrhoea, URTIs
DiLernia et al[25]	Recurrent pharyngo-tonsillitis; recurrent bacterial skin infections; increased weight gain
Armesto et al[3]	Increase in serum aminotransferases; weight gain; raise in serum cholesterol and triglycerides.

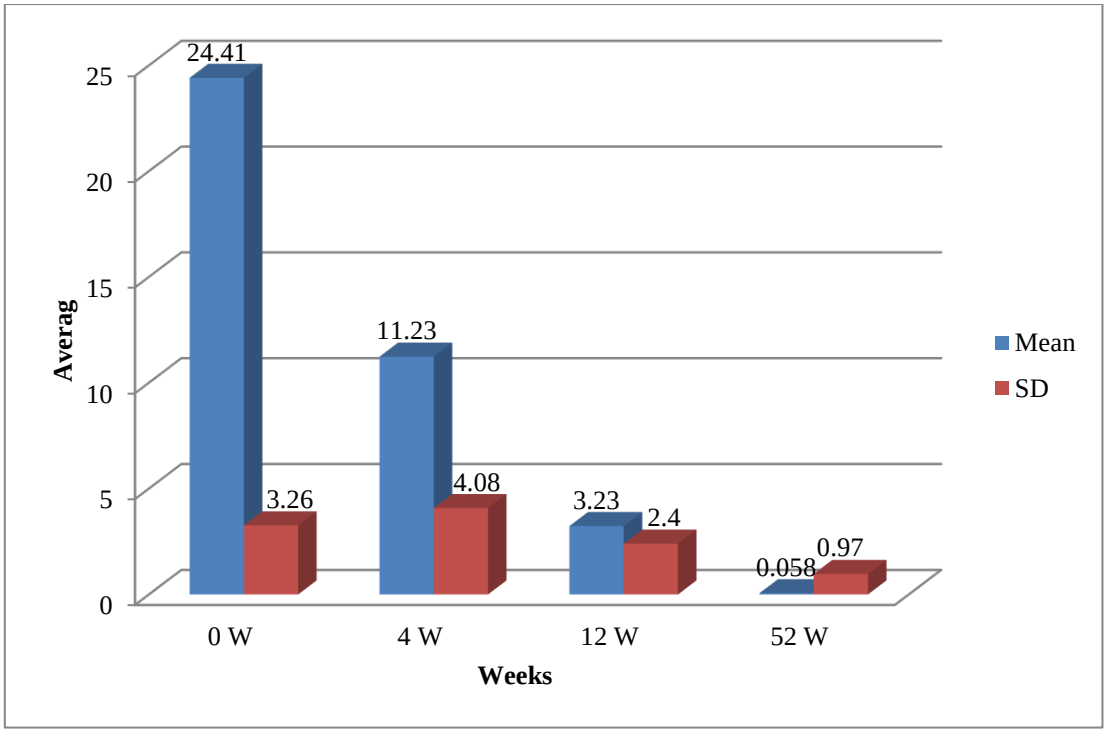

Figure 1: PASI score wise distribution in weeks.

Among the patients 84 p.c. were diagnosed as chronic plaque psoriasis and 16 p.c. were diagnosed as chronic plaque psoriasis with arthritis. There was a positive family history of psoriasis among 24 p.c. of the patients. About 20 p.c. of the patients were diabetics and 4 p.c. of the patients were hypertensives. Previous treatment with topical steroids, topical coal tar and oral methotrexate was present among 52 p.c., 4 p.c. and 44 p.c. of the patients. About 12 p.c. oof the patients had undergone psoralen and ultraviolet A radiation (PUVA) therapy (Table 2).

To understand the efficacy of ADA, PASI score was considered at 0, 4, 12, 52 weeks. The comparison of PASI score was done through time, baseline (0 week) in relation to 4, 12, 52 weeks, as there was no comparative group. The mean PASI score at 0 week was 24.4±3.26, this when compared to PASI score at 4 weeks (11.2±4.08), at 12 weeks (3.2±2.40), at 52 weeks (0.5±0.96) had shown an extreme statistically significant difference with $p<0.001$ using one sample t test (Table 3). Later, mean PASI score at 4 week (11.2±4.08) was considered as baseline, this when compared to PASI score at 12 weeks (3.2±2.40), at 52 weeks (0.5±0.96) had shown an extreme statistically significant difference with $p<0.001$ (Table 3). Finally, mean PASI score at 12 week (3.2±2.40) was considered as baseline, this when compared to PASI score at 52 weeks (0.5±0.96) had shown an extreme statistically significant difference with $p<0.001$ (Table 3) (Figure 1).

About 16 p.c. of the patients were in biologic naïve group and 84 p.c. were in non-naïve group, when PASI score at 0, 4, 12, 52 weeks was compared to biologic using statistical test ANOVA, there was no statistically significant difference (Table 4). Age, weight, height and BMI when compared with biologic naïve and non-naïve groups, had reported no statistical significance (Table 5).

To understand the safety of ADA side effects were studied, 8 p.c. of the patients had urticaria followed by 4 p.c. (each) were with diarrhea and URTIs (Table 6).

DISCUSSION

The present study had descriptive data regarding efficacy of ADA in patients with moderate-to-severe psoriasis who attended at dermatology outpatient. The moderate-to-severe psoriasis treatment algorithm was reviewed by expert panels and it was proposed that biological agents to be positioned at the same level as conventional systematic therapy and phototherapy.[21]

In the course of this study, 12 weeks after the start of treatment with ADA 96 p.c. of the patients experienced 75 p.c. of reduction in PASI and 72 p.c. of patients achieved total clearance of skin psoriasis (PASI 100). In the study conducted by Armesto et al among 100 patients it was reported that 16 weeks after the treatment initiation of 95 p.c. of the patients experienced 75 p.c. improvement in PASI (PASI-75) and 40 p.c. achieved total skin psoriasis clearance (PASI 100).[3] In the study conducted by DiLernia et al among 54 patients it was reported that 16 weeks after the treatment initiation of 55.5 p.c. of the patients experienced a PASI-75 response,

29.6 p.c. of the patients experienced a PASI-90 response and 18.5 p.c. achieved PASI 100 (Table 7).[24]

In present study side effects reported were urticaria, diarrhoea, upper respiratory tract infections (URTIs) which were similar to DiLernia et al study (Table 8).[24]

Limitation

The limitation was that the drug was costly and results cannot be generalized as the sample size was small.

CONCLUSION

ADA was very effective for moderate to severe chronic plaque psoriasis, when given at high loading dose followed by maintenance dose every other week with minimal side effects. Novel biological drug ADA is effective compared to other drugs. Psoriatic arthritis is one disease causing morbidity with deformities. This drug brings down morbidity drastically not only in chronic plaque psoriasis but also in psoriatic arthritis. Quality of life was also improved significantly in patients treated with this drug. This drug was found to be safe in all age groups (>5 years) with periodic screening for infections. But this cannot be widely used because of its cost.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the institutional ethics committee

REFERENCES

1. Kamiya K, Karakawa M, Komine M, Kishimoto M, Sugai J, Ohtsuki M. Results of a retrospective study on the efficacy and safety of adalimumab 80 mg administrated every other week in patients with psoriasis at a single Japanese institution. J Dermatol. 2019;46(3):199-205.
2. Raychaudhuri SP, Raychaudhuri S, Bagchi D. Psoriasis and psoriatic arthritis: pathophysiology, therapeutic intervention, and complementary medicine. Angiogenesis and roles of adhesion molecules in psoriatic disease. Angiogenesis in Psoriasis. New Delhi: CRC Press; 2017.
3. Armesto S, Coto-Segura P, Mayorga J, Illaro A, Santos-Juanes J. Efficacy of adalimumab in the treatment of moderate-to-severe psoriasis: a retrospective study of 100 patients in daily practice. J Dermatol Treat. 2015;26(1):49-53.
4. AlQassimi S, AlBrashdi S, Galadari H, Hashim MJ. Global burden of psoriasis-comparison of regional and global epidemiology, 1990 to 2017. Int J Dermatol. 2020;59(5):566-71.
5. Kim WB, Jerome D, Yeung J. Diagnosis and management of psoriasis. Canadian Fam Phys. 2017;63(4):278-85.
6. Bedi TR. Clinical profile of psoriasis in North India. Indian J Dermatol Venereol Leprol. 1995;61:202-5.
7. Pariser D, Schenkel B, Carter C, Farahi K, Brown TM, Ellis CN, et al. A multicenter, non-interventional study to evaluate patient-reported experiences of living with psoriasis. J Dermatol Treat. 2016;27(1):19-26.
8. Reich K, Krüger K, Mössner R, Augustin M. Epidemiology and clinical pattern of psoriatic arthritis in Germany: a prospective interdisciplinary epidemiological study of 1511 patients with plaque-type psoriasis. Br J Dermatol. 2009;160(5):1040-7.
9. Fujii RK, Mould JF, Tang B, Brandt H, Pomerantz D, Chapnick J, et al. PSY46 burden of disease in patients with diagnosed psoriasis in Brazil: results from 2011 National health and wellness survey (NHWS). Value Health. 2012;15(4):107.
10. Kimball AB, Jacobson C, Weiss S, Vreeland MG, Wu Y. The psychosocial burden of psoriasis. Am J Clinic Dermatol. 2005;6(6):383-92.
11. DeKorte J, Mombers FM, Bos JD, Sprangers MA. Quality of life in patients with psoriasis: a systematic literature review. J Investigat Dermatol. 2004;9(2):140-7.
12. Augustin M, Krüger K, Radtke MA, Schwippl I, Reich K. Disease severity, quality of life and health care in plaque-type psoriasis: a multicenter cross-sectional study in Germany. Dermatology. 2008;216(4):366-72.
13. Tang MM, Chang CC, Chan LC, Heng A. Quality of life and cost of illness in patients with psoriasis in Malaysia: a multicenter study. Int J Dermatol. 2013;52(3):314-22.
14. Feldman SR, Goffe B, Rice G, Mitchell M, Kaur M, Robertson D, et al. The challenge of managing psoriasis: unmet medical needs and stakeholder perspectives. Am Health Drug Benefit. 2016;9(9):504.
15. Nguyen CM, Beroukhim K, Danesh MJ, Babikian A, Koo J. The psychosocial impact of acne, vitiligo, and psoriasis: a review. Clinic Cosmet Investigation Dermatol. 2016;9:383.
16. Pariser D, Schenkel B, Carter C, Farahi K, Brown TM, Ellis CN, et al. A multicenter, non-interventional study to evaluate patient-reported experiences of living with psoriasis. J Dermatolog Treat. 2016;27(1):19-26.
17. Krueger G, Koo J, Lebwohl M, Menter A, Stern RS, Rolstad T. The impact of psoriasis on quality of life: results of a 1998 National psoriasis foundation patient-membership survey. Arch Dermatol. 2001;137(3):280-4.
18. Patel V, Horn EJ, Lobosco SJ, Fox KM, Stevens SR, Lebwohl M. Psoriasis treatment patterns: results of a cross-sectional survey of dermatologists. J Am Aca Dermatol. 2008;58(6):964-9.
19. Boehncke WH, Prinz J, Gottlieb AB. Biologic therapies for psoriasis. A systematic review. J Rheumatol. 2006;33(7):1447-51.

20. Wu JJ, Valdecantos WC. Adalimumab in chronic plaque psoriasis: a clinical guide. J Drug Dermatol. 2017;16(8):779-90.
21. Guenther L, Langley RG, Shear NH, Bissonnette R, Ho V, Lynde C, et al. Integrating biologic agents into management of moderate-to-severe psoriasis: a consensus of the Canadian Psoriasis Expert Panel. J Cutan Med Surg. 2004;8(5):321.
22. Chopra A, Mitra D, Agarwal R, Saraswat N, Chemburkar P, Sharma L. Real-life efficacy and safety of biosimilar adalimumab (ZRC-3197) in patients with plaque psoriasis: a tertiary care center experience. Indian Dermatol Online J. 2020;11(2):182.
23. Saurat JH, Stingl G, Dubertret L, Papp K, Langley RG, Ortonne JP, et al. Efficacy and safety results from the randomized controlled comparative study of adalimumab vs. methotrexate vs. placebo in patients with psoriasis (CHAMPION). Br J Dermatol. 2008;158(3):558-66.
24. DiLernia V, Bianchi L, Guerriero C, Stingeni L, Gisondi P, Filoni A, et al. Adalimumab in severe plaque psoriasis of childhood: a multi-center, retrospective real-life study up to 52 weeks observation. Dermatolog Ther. 2019;32(6):13091.
25. Menter A, Tyring SK, Gordon K, Kimball AB, Leonardi CL, Langley RG, et al. Adalimumab therapy for moderate to severe psoriasis: a randomized, controlled phase III trial. J Am Aca Dermatol. 2008;58(1):106-15.

Cite this article as: Badabagni P, Ramadevi B, Sambangi J. Efficacy and safety of adalimumab in treating patients with moderate to severe plaque psoriasis: a retrospective study. Int J Res Dermatol 2022;8:8-14.