



ORIGINAL RESEARCH PAPER

Psychiatry

A STUDY ASSESSING THE TREATMENT RESPONSE OF ESCITALOPRAM ON PSORIATIC SKIN LESIONS IN PSORIATIC PATIENTS WITH DEPRESSION AND ANXIETY

KEY WORDS: Psoriasis, Depression & Anxiety, Escitalopram, PASI.

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ABSTRACT

Background: Psoriasis is a chronic inflammatory skin disease affecting approximately 1.4-2% of the world's population, frequently associated with psychiatric co-morbidities including depression and anxiety. The brain-skin connection and shared inflammatory pathways suggest potential therapeutic benefits of antidepressants in managing both psychiatric symptoms and dermatological manifestations. We aimed to determine the treatment response of Escitalopram on psoriatic skin lesions in psoriatic patients with depression and anxiety, and to assess the correlation between severity of depression and anxiety with psoriatic skin lesions. **Methods:** This comparative study included 70 consecutive patients with psoriasis and co-morbid depression/anxiety. Participants were divided into two groups: case group (n=25) receiving Escitalopram with psychotherapy, and control group (n=45) receiving psychotherapy alone. Clinical assessments using Hamilton Depression Rating Scale (HAM-D), Hamilton Anxiety Rating Scale (HAM-A), and Psoriasis Area and Severity Index (PASI) were conducted at baseline and every 2 weeks for 8 weeks. **Results:** Both depression and anxiety showed significantly greater improvement in the case group compared to controls ($p<0.001^*$). HAM-D scores decreased from 25.88 ± 5.16 to 15.12 ± 4.17 in the case group versus 21.80 ± 6.04 to 20.93 ± 6.69 in controls. HAM-A scores improved from 35.72 ± 4.50 to 10.28 ± 3.03 in the case group versus 31.31 ± 4.86 to 25.31 ± 6.61 in controls ($p=0.000^*$). PASI scores showed improvement in both groups (case group: 12.85 ± 8.92 to 8.15 ± 7.14 ; control group: 10.79 ± 7.17 to 6.74 ± 5.14) however it wasn't statistically significant ($p=0.355$). Depression severity and psoriasis severity was statistically significant at baseline ($p<0.05$). **Conclusion:** Escitalopram was significantly efficacious in treating depression and anxiety in psoriatic patients, with rapid symptom improvement. The treatment however had no effect in reduction of PASI score of the psoriatic skin lesions.

INTRODUCTION

Psoriasis is a common psycho-cutaneous disease that affects approximately 1.4-2% of the world's population and 0.4-2.8% of the Indian population.^[1,2] It is a chronic inflammatory, papulo-squamous disease of the skin which causes red, scaly patches and is proliferative in nature with genetic, environmental factors and immune components playing a critical role.^[3,4,5] Skin is one of the largest organs in the body, both in surface area and weight (>10% of body mass) developing from the embryonic ectodermal layer acting as a protective layer between the internal milieu and the environmental stressors thus playing a vital role in maintaining the homeostasis of the body.^[6] The central nervous system of the body also develops from the same ectoderm as the skin leading to a strong brain-skin connection.^[7]

Skin has a fully functional peripheral equivalent of the hypothalamic-pituitary-adrenal (HPA) axis which includes elements like pro-opiomelanocortin (POMC), corticotropin releasing hormone (CRH), the CRH receptor-1 (CRH-R1), key enzymes of corticosteroid synthesis and synthesizes glucocorticoids.^[8,9] The communication between central neuroendocrine system and skin seems bidirectional, made possible by the skin's extensive vascularization and the several nerve endings.^[7] The complex skin immune system involves innate and adaptive immune cells, skin cells such as keratinocytes (KC) and melanocytes, and an intricate signaling network between all these cellular components that includes cytokines, autoantigens, chemokines.^[10]

Skin cells also have functional serotonergic and melatonergic systems.^[11]

Serotonin (5-hydroxytryptamine; 5-HT), a classical neurotransmitter with a fundamental role in the central nervous system, has been also shown to play an essential role in skin, acting as a mediator between this organ and the neuroendocrine system. Serotonin is known for the profound

effects it has both at the central and peripheral levels of the neuroendocrine system, being involved in the regulation of physiological states and behaviors, e.g., pain, appetite, mood and sleep.^[12] Interestingly, there is an increasing evidence that the serotonergic system is also a regulator of immune signaling. It exerts its actions via interactions with different receptors that belong to seven different families, 5-HT_{1R} to 5-HT_{7R}.^[13] Equally important is the role of the 5-HT transporter (5-HTT or SERT), which is mainly expressed in platelets and mediates both the release and the uptake of 5-HT.^[14]

In skin, 5-HT is involved in processes such as vasodilation, inflammation, immunomodulation and pruritogenic effects.^[15,16] Serotonin, along with stress mediators, also contributes to the effects of psychological stress on the disruption of skin homeostasis.^[18] Stress in turn is known to worsen psoriasis and delay wound healing in 30-40% of cases.^[17]

Psychological stress in humans is responsible for delayed barrier function recovery, increased concentrations of cortisol in plasma (which has a negative impact in wound healing), and activation of several inflammation and immune players (e.g., IL-1 β , IL-10, TNF- α).^[18] Additionally, it has been suggested that chronic stress contributes to skin aging.^[19] Psoriasis has a prolonged course which is usually associated with intermittent exacerbations and remissions. This never-ending cycle poses a great source of stress to the patients, both physically and mentally.^[17] Psychiatric comorbidities like depression and anxiety are 1.5 times more likely to develop in patients of psoriasis as compared to those without it.^[20,21] They develop poor self-esteem, poor perception of health, sexual dysfunction and suicidal ideation.^[17]

Depressive disorders (16%) were the second most commonly diagnosed psychiatric disorder in psoriasis in the study by Padma et al., in 2020, after anxiety disorders.^[22]

Patients of psoriasis with anxiety and depression had a

significantly higher score on PASI as noted by Lakshmy et al., in 2015 with 76.7% prevalence of anxiety and 78.9% prevalence of depression with equal preponderance in men and women.^[23]

The prevalence of depression in psoriasis patients was 18% as detected by Jain et al., in 2017 which was higher as compared to the general population (3-15%).^[24] A study by O'Leary et al., in 2004 showed that the magnitude of anxiety and depression in patients with psoriasis was higher than that in healthy individuals. But there was no association between severities of psoriasis with anxiety.^[25] Gaikwad et al., in 2006, studied 43 psoriasis patients and found that their disease affected the social functioning, leading to decreased work efficiency and subjective distress at work in more than half of the subjects. Around two third patients consented that psoriasis has affected their interpersonal relationship resulting in stress in home environment, 16% of the patients had anxiety and 18% had depression.^[26]

METHODOLOGY

STUDY SETTING AND STUDY DESIGN: It is a hospital based, prospective and observational study conducted in the Department of Psychiatry in patients diagnosed with psoriasis (from the Department of Dermatology) at a tertiary health care center in Navi Mumbai.

SAMPLE SIZE: Assuming a prevalence rate of 1.5% as per a study done by Bhosle et al., in 2006 in Navi Mumbai, India with a 95% confidence level and a 3% margin of error, the required sample size was 63 patients.^[1]

For estimation of sample size, the following formula has been used $n = (Z_{\alpha} \times P \times Q \times (1-P)) / d^2$

Where; Z_{α} = Value of standard normal variate corresponding to α level of significance
 P = Likely value of parameter
 $Q = 1 - P$
 d = Margin of errors which is a measure of precision

With the following assumptions, the sample size comes out to be 63 patients but to account for potential drop outs, the sample size was increased to 70 patients.

INCLUSION AND EXCLUSION CRITERIA:

This study included patients of psoriasis with comorbid depression/anxiety, aged 18-75 years and excluded patients with prior history of psychiatric disorders on medications, those with suicidal ideations and patients with intellectual disability.

PROCEDURE: Hospital Ethical Committee approval was obtained prior to study initiation. Written informed consent was obtained from all participants. All patients underwent detailed psychiatric history taking and mental status examination. Psychiatric diagnoses were made as per DSM-5 criteria. Depression and anxiety were assessed using Hamilton Depression Rating Scale (HAM-D) and Hamilton Anxiety Rating Scale (HAM-A) respectively. Psoriatic skin lesions were quantified using Psoriasis Area and Severity Index (PASI) scale by dermatologists. All patients were receiving dermatological treatment in the form of systemic therapy (immunosuppressants, anti-inflammatory agents, oral retinoids) and/or topical treatment.

Patients were divided into two groups based on their willingness to start antidepressant medication. The case group (n=25) received Tablet Escitalopram starting from 5 mg/day and titrated up to 10-15 mg/day as per clinical assessment, along with psychotherapy and counselling. The control group (n=45) received only psychotherapy and counselling. HAM-D, HAM-A and PASI scores were recorded at baseline and every 2 weeks for 8 weeks.

Statistical analysis Data was described in terms of range; mean $\pm$ standard deviation ($\pm$ SD), frequencies (number of

cases) and relative frequencies (percentages) as appropriate. Comparison of quantitative variables between the study groups was done using Student t-test for independent samples. Pearson Correlation was used to find relationship between severity of depression [HAM-D] and that of anxiety [HAM-A] with the PASI score. For comparing categorical data, Chi square (χ^2) test was performed. A probability value (p value) less than 0.05 was considered statistically significant. All statistical calculations were done using (Statistical Package for the Social Science) SPSS 21 version (SPSS Inc., Chicago, IL, USA) statistical program for Microsoft Windows.

RESULTS

The study included 70 patients of psoriasis with psychiatric comorbidities, 25 patients (35.7%) in the case group and 45 patients (64.3%) in the control group.

Out of 70 patients, 35.7% patients were diagnosed with Persistent depressive disorder with major depressive disorder, 60.1% had major depressive disorder and 4.2% had generalised anxiety disorder.

Table 1: Demographic and Clinical data of Psoriatic Patients (n=70)

Variable	Number	Percentage
Sex		
Female	36	51%
Male	34	49%
Religion		
Hindu	54	77%
Muslim	14	20%
Christian	2	3%
Occupation		
Semi-skilled	33	47%
Arithmetic skilled	13	19%
Skilled worker	8	11%
Semi-professional	7	10%
Unemployed	5	7%
Professional	2	3%
Unskilled	2	3%
Marital Status		
Married	58	83%
Unmarried	9	13%
Widower	2	3%
Separated	1	1%
Substance Use		
Nil	49	70%
Family History of Psoriasis		
None	66	94%
Positive	4	6%
Psoriasis Type		
Chronic Plaque Psoriasis	44	63%
Palmoplantar Psoriasis	18	26%
Guttate Psoriasis	2	3%
Psoriatic Arthritis	2	3%
Pustular Psoriasis	2	3%
Erythrodermic Psoriasis	1	1%
Psoriasis Vulgaris	1	1%

As seen in Table 1, majority of patients had chronic plaque psoriasis (63%), were married (83%), and belonged to semi-skilled occupation category (47%). There were no statistical significant differences between both the case and control groups in terms of sex, religion, occupation, marital status, substance use, family history of psoriasis, psoriasis type, or psychiatric diagnosis (Chi square test, $p > 0.05$).

Table 2: Comparison of Baseline Characteristics Between Psoriasis (Control & Case Groups)

Variable	Control Group (n=45)	Case Group (n=25)	t-value	p-value
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	Mean	SD	Mean	SD		
Age (years)	39.09	12.23	45.83	14.22	-2.061	0.043*
Psoriasis Duration (years)	3.38	3.29	6.19	7.85	-2.101	0.039*

*p<0.05 = statistically significant

As seen in Table 2, we observed that the mean age of patients in the control group was 39.09 years (± 12.23 years) whereas

that of the case was 45.83 years (± 14.22 years) suggesting they were older in the case group. The difference was statistically significant, ($p<0.05$). It is also important to note that the mean duration of psoriasis in the case group was 6.19 years compared to that in the control group which was 3.38 years, with SD of 7.85 and 3.29 years, respectively. This difference was statistically significant, with $p<0.05$.

This implies that the patients in the age group with mean of 45 years and duration of 6 years were forthcoming for pharmacotherapy for depression and anxiety.

Table 3: Comparison of HAM-D Scores and their differences between Case and Control Groups

Time Point	Case Group (n=25) Mean $\pm$ SD	Control Group (n=45) Mean $\pm$ SD	t-value	p value	Case group Difference Mean $\pm$ SD	Control group Difference Mean $\pm$ SD	t- value	p value
Baseline	25.88 $\pm$ 5.16	21.80 $\pm$ 6.04	-2.849	0.006*				
1st Follow-up (2 weeks)	23.24 $\pm$ 5.10	20.42 $\pm$ 5.96	-1.992	0.050*	2.64 $\pm$ 0.81	1.38 $\pm$ 1.48	-3.937	0.000**
2nd Follow-up (4 weeks)	20.24 $\pm$ 4.82	20.20 $\pm$ 6.12	-0.028	0.978	5.64 $\pm$ 1.15	1.60 $\pm$ 2.77	-6.957	0.000**
3rd Follow-up (6 weeks)	17.40 $\pm$ 4.30	19.98 $\pm$ 6.11	1.864	0.067	8.48 $\pm$ 1.78	1.82 $\pm$ 3.28	-9.395	0.000**
4th Follow-up (8 weeks)	15.12 $\pm$ 4.17	20.93 $\pm$ 6.69	3.935	0.000**	10.76 $\pm$ 2.11	0.87 $\pm$ 3.80	-12.009	0.000**

*p<0.05 = statistically significant; **p $\leq$ 0.001 = statistically highly significant

higher in the case group compared to controls ($p=0.006$), indicating more severe depression in patients who opted for pharmacotherapy.

Depression Severity Assessment

As seen in Table 3, for depression assessment, HAM-D scores showed significant improvement in the case group from baseline (25.88 $\pm$ 5.16) to 4th follow-up (15.12 $\pm$ 4.17) compared to controls (21.80 $\pm$ 6.04 to 20.93 $\pm$ 6.69, $p<0.001$). The baseline HAM-D scores were significantly

The rate of improvement was significantly faster in the case group at each follow-up. At the 1st follow-up, the case group improved by 2.64 $\pm$ 0.81 points versus 1.38 $\pm$ 1.48 points in controls ($p=0.000$ **). By the 4th follow-up, the case group showed improvement of 10.76 $\pm$ 2.11 points compared to only 0.87 $\pm$ 3.80 points in controls ($p=0.000$ **).

Table 4: Comparison of HAM-A Scores Between Case and Control Groups

Time Point	Case Group (n=25) Mean $\pm$ SD	Control Group (n=45) Mean $\pm$ SD	t-value	p value	Case group Difference Mean $\pm$ SD	Control group Difference Mean $\pm$ SD	t value	p value
Baseline	35.72 $\pm$ 4.50	31.31 $\pm$ 4.86	-3.735	0.000*				
1st Follow-up (2 weeks)	28.56 $\pm$ 3.36	30.13 $\pm$ 5.46	1.307	0.196	7.16 $\pm$ 2.37	1.18 $\pm$ 3.43	-7.745	0.000*
2nd Follow-up (4 weeks)	22.84 $\pm$ 3.40	27.56 $\pm$ 6.1	3.563	0.001*	12.88 $\pm$ 3.14	3.76 $\pm$ 4.17	-9.534	0.000*
3rd Follow-up (6 weeks)	16.08 $\pm$ 4.02	26.13 $\pm$ 6.16	7.331	0.000*	19.64 $\pm$ 3.28	5.18 $\pm$ 4.38	-14.400	0.000*
4th Follow-up (8 weeks)	10.28 $\pm$ 3.03	25.31 $\pm$ 6.61	10.735	0.000*	25.44 $\pm$ 4.59	6.00 $\pm$ 4.98	-16.076	0.000*

*p<0.05 = statistically significant; **p $\leq$ 0.001 = statistically highly significant

Anxiety Severity Assessment

Similarly, anxiety scores (HAM-A) improved significantly more in the case group (35.72 $\pm$ 4.50 to 10.28 $\pm$ 3.03) compared to controls (31.31 $\pm$ 4.86 to 25.31 $\pm$ 6.61, $p=0.000$ *). The baseline HAM-A scores were significantly higher in the case group ($p=0.000$ *).

The improvement in anxiety was remarkable in the case group. At the 1st follow-up, the case group improved by 7.16 $\pm$ 2.37 points versus 1.18 $\pm$ 3.43 points in controls ($p=0.000$ *). By the 4th follow-up, the case group showed dramatic improvement of 25.44 $\pm$ 4.59 points compared to only 6.00 $\pm$ 4.98 points in controls ($p=0.000$ *).

Table 5: Pearson Correlation Between HAM-D and HAM-A Scores and PASI Scores

Time Point	PASI	Pearson Correlation (r)	p-value
HAM-D (Baseline)	PASI-B	0.254	0.034*
HAM-D (1st Follow-up)	PASI-1	0.221	0.066
HAM-D (2nd Follow-up)	PASI-2	0.202	0.093
HAM-D (3rd Follow-up)	PASI-3	0.150	0.215
HAM-D (4th Follow-up)	PASI-4	0.157	0.196
HAM-A (Baseline)	PASI-B	0.108	0.372
HAM-A (1st Follow-up)	PASI-1	-0.027	0.822
HAM-A (2nd Follow-up)	PASI-2	-0.027	0.823
HAM-A (3rd Follow-up)	PASI-3	-0.088	0.471
HAM-A (4th Follow-up)	PASI-4	-0.087	0.474

*p<0.05 = statistically significant

CORRELATION ANALYSIS

As noted in table 5, a statistically significant correlation was found between depression severity and psoriasis severity only at baseline ($r=0.254$, $p=0.034$) and not at subsequent follow ups. Interestingly, no significant correlation was observed between anxiety severity (HAM-A) and psoriasis severity (PASI) at baseline or at any follow up ($p>0.05$).

Table 6: Comparison of treatment response of Escitalopram on Psoriatic lesions (PASI Score) in control vs case groups.

Taking Escitalopram	NO (CONTROLS) Mean + SD	YES (CASES) Mean+SD	t value	p-value
PASI (B)	10.79 $\pm$ 7.17	12.85 $\pm$ 8.92	-1.057	0.294
PASI (1)	9.66 $\pm$ 6.55	11.46 $\pm$ 8.25	-1.001	0.320
PASI (2)	8.72 $\pm$ 6.08	10.20 $\pm$ 7.84	-0.882	0.381
PASI (3)	7.59 $\pm$ 5.46	8.99 $\pm$ 7.37	-0.902	0.370
PASI (4)	6.74 $\pm$ 5.14	8.15 $\pm$ 7.14	-0.953	0.344

*p<0.05 = statistically significant

As observed in table 6, the mean of baseline PASI score in the case group is 12.85 with SD 8.92 that went down on the 4th follow-up to 8.15 with SD 7.14. In the control group, mean of PASI at baseline was 10.79 with a SD of 7.17. It went down to a mean of 6.74 with SD 5.14 at the 4th visit after 8 weeks. The difference in the PASI scores in the two groups was not statistically significant.

When analyzed separately by treatment group, only the case group showed stronger correlations between depression and psoriasis severity, though these did not reach statistical

significance probably due to smaller sample size. (t test, $p < 0.05$)

DISCUSSION

In our study, we assessed the treatment response of an antidepressant, Escitalopram, on the skin lesions of psoriasis patients with depression and anxiety, in the Indian population. Literature review till date has shown limited studies in India advocating the use of anti depressants in psoriatic patients and all demographic and clinical parameters thus making comparison with others difficult. We found one study by A Mitra in 2001 who used Fluoxetine as an adjunct with PUVA in 10 psoriatic patients vs placebo in the rest 10, however psychopathology was not assessed in the study. Patients on Fluoxetine responded with reduction in pruritus but it was not statistically significant. We found a similar international study conducted by D'Erme et al., in 2014 in Florence using Escitalopram in psoriatic lesions.^[27]

In the two groups of our study, the demographic parameters were of comparable value, thus, making the comparison easier, between cases and control.

Patients of our study in the case group were significantly older (45.83 ± 14.22 years) compared to controls (39.09 ± 12.23 years, $p = 0.043$) and the mean duration of psoriasis in the case group was 6.19 years compared to that in the control group which was 3.38 years with SD of 7.85 and 3.29 years, respectively. This suggests that middle aged patients with longer duration of psoriasis opted for pharmacotherapy with Escitalopram.

Our study had 51% females and 49% males, and out of the 70 patients, 83% were married and 13% were unmarried. The most common type of psoriasis found was chronic plaque psoriasis amounting to 63%.

A study by Lakshmy et al., in 2015 showed the mean age of the study sample was 41.91 years. The study also found that there is a higher cumulative probability for patients with longer duration of psoriasis to have a severe grade of depression/anxiety. The majority patients in that study were males (56.7%) and were married (87.8%) and the most frequently diagnosed type of psoriasis was psoriasis vulgaris (75.6%).^[23]

Our study demonstrated significant efficacy of Escitalopram in treating depression and anxiety in psoriatic patients, with marked symptom reduction (mean difference, $p = 0.0000^*$) which was statistically significant in case group as compared to control group. A study done by D'Erme et al., in 2014, in Florence also found a similar reduction in the HAM-D and HAM-A scores in the case group. However, they had assessed patients only on 2 follow-ups, at the end of 3 months and 6 months from baseline unlike our study where patients were assessed every 2 weekly for 8 weeks.

We noted that PASI scores reduced significantly from baseline to 4th follow up within both groups, however the difference was not statistically significant. This highlights the efficacy of combined pharmacotherapy with psychotherapy and psychotherapy alone in skin lesions of both case and control groups. This finding is consistent with a study done by D'Erme et al., suggesting potential indirect benefits of SSRI therapy on psoriatic lesions through stress reduction and improved psychological well-being.^[27]

The significant correlation between depression severity and psoriasis severity at baseline ($r = 0.254$, $p = 0.034$) supports previous findings by Lakshmy et al., in 2015 confirming the bidirectional relationship between psychiatric symptoms and dermatological manifestations.^[23] The persistence of this correlation throughout the study period suggests an ongoing relationship between mood and skin disease severity.

However, no significant correlation was found between anxiety severity and psoriasis severity.

The Swedish population-based study by Thorslund et al., in 2013 demonstrated that SSRI exposure was associated with reduced need for systemic psoriasis treatments, supporting potential protective effects of antidepressants in psoriasis management.^[14] The lack of direct statistical significance in PASI improvement between groups may reflect the complex pathophysiology of psoriasis and the multifactorial nature of treatment response. Additionally, as noted by Carlin et al., in 2004, PASI scores may not linearly reflect disease severity, particularly for smaller affected areas that significantly impact quality of life.^[28]

The study reinforces the importance of addressing psychiatric comorbidities in psoriasis through integrated care approaches, as psychological factors often represent stronger determinants of disability than dermatological severity alone.

This study demonstrated that Escitalopram significantly improved depression and anxiety symptoms in psoriatic patients when combined with psychotherapy, showing superior efficacy compared to psychotherapy alone. Both HAM-D and HAM-A scores showed statistically significant and rapid improvement in the treatment group at every follow-up over the 8 weeks study period. The dramatic improvement in anxiety symptoms, with all treated patients achieving mild anxiety status, was particularly noteworthy.

A significant correlation was established between depression severity and psoriasis severity at baseline ($r = 0.254$, $p = 0.034$), supporting the bidirectional relationship between psychiatric and dermatological manifestations. Patients who opted for pharmacotherapy had more severe baseline depression and anxiety scores and longer disease duration, suggesting that symptom severity influences treatment acceptance.

While no statistically significant difference was observed in PASI score improvement between groups, both groups showed meaningful clinical improvement (case group 41.6%, control group 38.61%). This suggests that addressing psychiatric comorbidities through either psychotherapy alone or combined treatment approaches can benefit skin manifestations, likely through stress reduction and improved coping mechanisms.

CONCLUSION

Our study highlights the importance of a consultation liaison between dermatologists and psychiatrists and the implementation of a holistic treatment approach that addresses both dermatological and psychiatric aspects of psoriasis. The need of the hour for early identification of psychiatric symptoms in psoriatic patients is to offer a holistic approach to treatment, providing pharmacotherapy in addition to psychotherapy and counselling. This will not only benefit the psoriatic patients in improving their quality of life but also boost up their morale and mental well-being

Further studies, with a longer follow-up period and a larger sample size are advocated for better evaluation of the effects of SSRI therapy on psoriatic skin lesions.

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