Original Article

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# Relationship Between Lithium Dose, Serum Concentration and Duration of Lithium Therapy with Cutaneous Side-effects in Bipolar Affective Disorder Patients

Psychiatry/Mental Health Section

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## ABSTRACT

**Introduction:** Lithium has been used in the treatment of mood disorders for more than five decades. Despite a few studies focusing on the relationship between the dose of lithium, serum lithium levels, duration of therapy, and cutaneous side-effects, results remain inconclusive. Lithium is known to cause multiple cutaneous side-effects like acneiform eruptions, psoriasiform eruption, seborrheic dermatitis, and follicular keratitis.

**Aim:** To evaluate the relationship between cutaneous side-effects of lithium with the serum lithium levels, dosage and duration of lithium therapy in bipolar affective disorder patients.

**Materials and Methods:** An ambispective observational study conducted among 52 bipolar affective disorder patients on lithium therapy recruited by convenient sampling methods from both Inpatients and Outpatient Psychiatry Units of PSG Institute of medical sciences and research, Coimbatore, Tamil Nadu, India, June 2014 to August 2014. The patients with bipolar affective disorder who are either newly started on lithium or already on lithium therapy were included in the study. They were followed-up to assess the effect of lithium dosage, duration of lithium and serum lithium level with skin lesions, once a month for six months and once in two months for one year. Kaplan-Meier survival analysis was done with varying lithium dosages and serum lithium levels. Association between the lithium dose and serum lithium levels with the cutaneous side-effects were calculated using the survival analysis with the p-value of <0.01.

**Results:** Out of the total, 59.6 % of the participants were in the age group less than 40 years and 34.6 % were in the age group 40-60 years. There was almost equal distribution of males and females, 51.9% and 48.1%, respectively. Overall, 38.46% participants had cutaneous lesions. Various lithium dosage and serum lithium levels did not correlate statistically with skin reactions upto one year. Survival analysis at the end of 10 years revealed that participants with higher dosage and serum levels had higher prevalence of skin lesions (40% vs 4%: 47.1% vs 6.6% respectively, p-value <0.001). The cumulative proportion of skin lesions at the end of three, five, seven and 10 years for higher dose (>800 mg/day) was 38%, 46.9%, 52.2%, 59% and for higher lithium levels (>0.8 mEq/L) was 41%, 58.2%, 65.2%, 73.9%.

**Conclusion:** The patients who were treated with lower dosage and who had lower serum lithium level had reduced risk for cutaneous lesions. Lithium continued to exert its mood stabilisation property even when the serum level was maintained less than 0.8 mEq/L. This resulted in better compliance.

**Keywords:** Adverse-effect, Mood disorder, Mood stabiliser, Management

## INTRODUCTION

Lithium remains the cheaper, effective, and gold standard treatment for bipolar affective disorder for more than five decades. Lithium has narrow therapeutic index that is a low ratio between dose (serum levels) and its associated toxicity [1]. Lithium has adverse effects on kidneys, thyroid gland, and parathyroid glands, necessitating the monitoring of these organ functions through periodic blood tests. In most cases, lithium associated cutaneous side-effects are relatively mild but severe cutaneous involvement like psoriasis are observed in measurable percentage (1.8-6%) of lithium treated patients. Recognition of these cutaneous side-effects is necessary and neglect of which might result in non adherence to medication. Perlick et al, showed average of 40% non adherence due to side-effects with lithium therapy [2].

The reported prevalence of the cutaneous side-effects with lithium varies from 3% to 45% in different studies. Lithium is known to cause multiple cutaneous side-effects like acneiform eruptions, psoriasiform eruption., seborrheic dermatitis, and follicular keratitis. Other cutaneous manifestations include mucosal and vaginal ulceration, oedema, purpura, lupus erythematosis like syndrome, urticaria, pre-tibial ulceration, dermatitis herpetiformis, eczema, exfoliative dermatitis, folliculitis, alopecia, allergic vasculitis, hidradenitis suppurativa, lichenoid stomatitis, exacerbation of Darrier's disease, palmoplantar hyperkeratosis with icthyosiform features, increased growth of wart, mycosis fungoidosis and hair loss [3-8].

The side-effects of lithium are dose-dependent and it co-relates with the serum lithium levels. Nice guidelines and Delphi survey recommends the therapeutic serum levels should be 0.60-0.80 mmol/L [9,10]. Whereas the serum lithium level below 0.6 mmol/L is found to be ineffective. Studies have also reported that no therapeutic advantage was noted when the serum lithium level is above 1.2 meq/L and it may result in more significant side-effects which can lead to poor compliance [11,12].

Heng MC, have observed acneiform eruptions in several patients with serum lithium levels in the range of 1.5-2. 5 mEq/L [13]. Rao AV et al., observed that lithium-induced cutaneous side-effects like acne and hair loss occurred mostly within the therapeutic range [14]. Few observed that longer the duration of lithium therapy, more is the chance of developing side-effects [15].

Most of the literature available measured only the prevalence of lithium induced cutaneaous side-effects, so this prospective study was planned with the rationale to find out the association of cutaneous side-effects with the dose, duration, and serum lithium levels in bipolar affective disorder patients. Whether regular monitoring, early diagnosis and management of lithium induced skin

lesions, will help in avoiding the issue of non compliance and further worsening of mood symptoms. Hence, the present study aimed to evaluate the relationship between cutaneous side-effects of lithium and with the serum lithium levels, dosage and duration of lithium therapy in bipolar affective disorder patients.

## MATERIALS AND METHODS

An ambispective observational study was conducted among 52 bipolar affective disorder patients on lithium therapy at the PSG Institute of Medical Sciences and Research, Coimbatore, Tamil Nadu, India. The study was conducted on the in- and out-patients attending the Psychiatry unit of the study institute, from June 2014 to August 2014. The study was approved by Institutional Human Ethics Committee with the reference number 14/147.

**Sample size calculation:** Sample size was calculated by unconsidering 45% as prevalence of the skin lesions. Thus, the sample size was found to the 177, based on the following formula [16]:

$N= 4PQ/d^2$, where

P= Prevalence

Q= 100-P

d= Allowable error (15-20% of P)

Participants were selected through convenient sampling from Outpatient and Inpatient setting of the hospital.

**Inclusion criteria:** Male and female aged 18-65 years with the primary diagnosis of bipolar affective disorder diagnosed based on International Classification of Diseases-10 (ICD-10) Criteria [17], who were newly started on lithium and already on lithium therapy for a duration of 10 years were eligible for the study. Participants who were newly started on lithium were recruited for prospectively studying the occurrence of skin lesion in the first year of the lithium therapy and participants who were on long-term therapy were included to study the association between the duration of treatment and the occurrence of skin lesion. Patients treated with antipsychotic medications like olanzapine with mean dosage of 15 mg and quetiapine with mean dosage of 300 mg at therapeutic dosages along with lithium were also included in the study.

**Exclusion criteria:** Patient on other mood stabilisers, on medications already known to cause cutaneous reactions, patients with thyroid disorder and acute or chronic kidney disease were excluded from the study. Diuretics, Angiotensin-I Converting Enzyme (ACE) inhibitors and Non Steroidal Anti-inflammatory Drugs (NSAIDs) which reduces excretion of lithium leading to toxicity were excluded from the study.

### Procedure

Patients with bipolar affective disorder diagnosed by a qualified psychiatrist based on the ICD-10 criteria were included in the study after subjecting them to selection criteria [17]. The study protocol was explained to the participants, and a written informed consent was obtained from the patient. If patient could not consent, it was obtained from the family member and later from the patient when he/she could consent.

Initial assessment was done using semi-structured proforma by the principal investigator. It included details on dosage of lithium, serum lithium levels, duration of lithium therapy, details of skin lesions and its relationship to treatment. Based on a retrospective cross-sectional study [17]:

- The dose of lithium was divided arbitrarily into: <800 mg, 800-1200 mg, and >1200 mg.
- Duration of lithium <6 months, 6 months to 1 year and >1 year.
- Serum lithium levels into subtherapeutic levels (<0.8 meq/L), therapeutic levels (0.8 to 1.2 meq/L) and supratherapeutic levels (>1.2 meq/L).

Then participants were examined by the dermatologist at baseline for the diagnosis of pre-existing skin lesion and to determine if the lesion was related to the usage of lithium.

Follow-up assessments were done every month for the first six months from baseline and thereafter every two months for the next six months, based on the findings by Ummar S et al., who showed that cutaneous lesions emerge within the initial 6 months [15]. During each follow-up patients were examined for the presence of skin lesions and its relationship with the dose of lithium, duration of lithium and the serum lithium levels. A dermatologist's opinion was sought for all the patients who developed cutaneous lesions in the follow-up. If the patient had missed a follow-up, they were contacted over phone and enquired for the presence of any skin lesions and the current dose, duration, and serum lithium level both from the patient and the caregiver. Five patients were lost to follow-up (not reported the results of lithium levels).

Total 52 patients were recruited for the study. Ten patients dropped out till the end of the study. Five patients for poor compliance, One patient for lithium toxicity (immediately 1 week after initiating lithium). One patient due to persistent vomiting (at 4$^{th}$ month follow-up), one patient developed severe hair fall (at 4$^{th}$ month follow-up). One patient dropped out at the end of 5$^{th}$ month due to unaffordability to do routine serum lithium level and hence changed to other mood stabiliser. One patient's diagnosis was changed to schizophrenia; hence the treating therapist had stopped her medication.

## STATISTICAL ANALYSIS

Statistical analysis was done using Statistical Package for Social Sciences (SPSS) version 19.0 for windows. Association of the cutaneous lesions with dosage, serum lithium level and duration in all follow-ups was calculated using the Chi-square test with statistical significance of p-value ≤0.05. Association of the cutaneous lesion with lithium dose, serum lithium level, and duration was done using the independent Student's t-test. Kaplan-Meier survival analysis was performed to estimate the proportion of skin lesions with lithium dosage and serum lithium levels. Survival analysis was planned for patients with long-term duration of treatment with lithium. Based on the survival function output table, percentage was calculated. Right censoring was done based on information available in case sheets, whereas left censoring was done based on periodic follow-up and attrition. Relapse and remission were not captured but the increase or decrease in dosing was considered in statistical analysis as individual data points.

## RESULTS

In this study, 59.6 % of the participants were in the age group less than 40 years and 34.6 % were in the age group 40-60 years. There was almost equal distribution of males and females, 51.9% and 48.1% respectively. 94.2% of the participants belonged to upper middle socio-economic class and 5.8% belonged to the lower middle class as per modified Kuppuswamy classification of socio-economic class [18] [Table/Fig-1].

Overall, 38.46% participants had cutaneous lesions out of which 19.2% had acneiform skin eruptions, 7.6% had hair fall and 1.9% had combined acne and hyperpigmentation, acne and hair fall and acne with seborrheic dermatitis. Prevalence of lithium induced skin lesions was 32.6% in the participants with >800 mg (n=41) of lithium therapy [Table/Fig-2]. Prevalence of Lithium induced skin lesion was 9.45% (2/11) in the participants with the dose <800 mg (n=11).

There was no significant association between occurrence of skin lesions and dose of lithium [Table/Fig-3] and serum lithium levels between the three groups during all the follow-ups at one year [Table/Fig-4]. There was no association between prevalence of skin infection and duration of drug intake in all the visits except third follow-up [Table/Fig-5].

An event-based analysis is done to understand the lithium induced skin reaction with the dose of lithium. On analysing the association

between the lithium dose and the skin reactions at ten years showed 4% of the participants who were on <800 mg of lithium got skin reactions compared to 40% of those who took dose more than 800 mg the results are statistically significant [Table/Fig-6].

| Variables | Number of patients (%) |
|---|---|
| **Mean age (year)** | **36.65±12.8** |
| **Age (years)** | |
| <40 | 59.6% |
| 40-60 | 34.6% |
| >60 | 5.8% |
| **Gender** | |
| Female | 48.1% |
| Male | 51.9% |
| **Socio-economic Status** | |
| Upper middle | 94.2% |
| Lower middle | 5.8% |

**[Table/Fig-1]:** Socio-demographic details.

| Skin lesions | Cumulative prevalence | Prevalence with dose <800 mg | Prevalence with dose >800 mg |
|---|---|---|---|
| Acneiform eruption | 10 (19.2%) | 1 (1.9%) | 9 (17.3%) |
| Hair fall | 4 ( 7.6%) | 1 (1.9%) | 3 (5.7%) |
| Seborrheic dermatitis | 1 (1.9%) | 0 | 1 (1.9%) |
| Hyperpigmentation | 1 ( 1.9%) | 0 | 1 (1.9%) |
| Acne and hyperpigmentation | 1 (1.9%) | 0 | 1 (1.9%) |
| Lithium induced ulcer | 1 (1.9%) | 0 | 1 (1.9%) |
| Acne and hair fall | 1 (1.9%) | 1 (1.9%) | |
| Acne and seborrheic dermatitis | 1 (1.9%) | 0 | 1 (1.9%) |

**[Table/Fig-2]:** Prevalence of lithium induced skin lesions (N=52).

An event-based analysis is done to understand the lithium induced skin reaction with the serum lithiumlevel. On analysing the association between serum lithium levels and skin reaction at ten years, the study population was divided in to two groups <0.8 meq/L and >0.8 meq/L based on the serum lithium level since there were only two participants above the level >1.2 meq/L of lithium. It showed 6.6% of the participants whose serum lithium levels were less than the recommended therapeutic range for the treatment of the bipolar disorder (0.8 mEq/L) got skin reactions compared to 47.1% of those whose serum lithium levels were more than the recommended therapeutic range (0.8 mEq/L). The results were statistically significant [Table/Fig-7].

The dose response relationship was studied using survival analysis. Patients newly started on lithium and already on lithium therapy for more than 10 years were subjected to survival analysis. Out of 52 participants, 16 patients were newly started on lithium and 36 patients were already on lithium therapy for more than 10 years. The drug dose response for ten years was assessed using case records in addition to a follow-up of one year. Overall, 21.1% had lithium induced skin reactions in the study population. At the end of one year 12.2% of the study population had cutaneous skin lesion. The proportion of skin lesions at the end of three, five, seven and 10 years are 31.7%, 42.9%, 47.7%, 54.2% respectively from survival analysis [Table/Fig-8].

Kaplan-Meier survival analysis for varying lithium doses at 10 years showed that there is no lithium induced skin reaction up to one and a half years. The proportion of skin lesion at the end of three years is 20% and after five years is 40% for dose less than 800 mg of lithium. For those who were on lithium more than 800 mg, 19.7% of the study population had skin lesion at the end of one year. The proportion of skin lesions at the end of three, five, seven and ten years are 38%, 46.9%, 52.2%, 59% respectively. [Table/Fig-9] clearly shows that the proportion of skin reactions are higher in dose more than 800 mg compared to lower doses.

Kaplan-Meier survival analysis for varying serum lithium levels at 10 years follow-up determined the proportion of skin lesion at the end of three year is 9.6% and five years is 23.5% for serum lithium levels less than 0.8 mEq/L. For those who had serum lithium levels more than 0.8 mEq/L, 22.8% of the study population had cutaneous skin lesion at the end of one year. The proportion of skin lesions at the end of three, five, seven and 10 years are 41%, 58.2%, 65.2% and 73.9% respectively. The proportion of skin reactions are higher with serum lithium levels more than 0.8 mEq/L [Table/Fig-10]. Relapse and remission were not captured but the increase or decrease in dosing was considered in statistical analysis as individual data points.

## DISCUSSION

The effectiveness of lithium for bipolar disorder was well established since 1950's. Concerns about toxicity and side-effects limited initial acceptance of lithium use but its use increased gradually over the last 50 years. Cutaneous side-effects are consistently found to be the most common side-effects associated with Lithium with the prevalence rate of 38.46 % in this study which is similar to the study done by Chann HH et al., and Sarantidis D and Waters B, which is 34% and 45% respectively [3,19].

Skin reactions observed in this study are acneiform eruptions, hair fall, seborrheic dermatitis, Lithium induced ulcers and hyperpigmentation. Acneiform eruption and hair fall were the most common cutaneous lesion seen in our study. In this study acne form eruption and hair fall was found to commonly occur with the higher dosage of lithium which is in contrary with the case report done by pendota Swetha P et al., where the lesion was reported to develop at the lower the dose of lithium [20,21].

In terms of the prevalence of skin lesions with the dose of lithium therapy, prevalence was high with therapeutic dosage during the one year of follow-up, this is consistent with the previous study by Ummar S et al., which revealed that as the dose of lithium increased,

| Follow-up | Less than 800 mg n (%) | 800-1200 mg n (%) | More than 1200 mg n (%) | p-value (Chi-square test) |
|---|---|---|---|---|
| Baseline assessment | 2/20 (10%) | 8/26 (30.8%) | 2/6 (33.3%) | 0.207 |
| Follow-up 1 | 1/14 (7.1%) | 4/27 (14.8%) | 3/8 (37.5%) | 0.171 |
| Follow-up 2 | 1/12 (8.3%) | 4/27 (14.8%) | 3/8 (37.5%) | 0.338 |
| Follow-up 3 | 2/10 (20.0%) | 5/26 (19.2%) | 4/9 (44.4%) | 0.156 |
| Follow-up 4 | 1/7 (14.3%) | 4/25 (16%) | 3/8 (37.5%) | 0.530 |
| Follow-up 5 | 1/7 (14.3%) | 5/24 (20.8%) | 1/7 (14.3%) | 0.923 |
| Follow-up 6 | 1/7 (14.3%) | 6/23 (26.1%) | 1/7 (14.3%) | 0.801 |
| Follow-up 7 | 1/7 (14.3%) | 6/22 (27.3%) | 2/8 (25%) | 0.845 |
| Follow-up 8 | 2/16 (12.5%) | 3/17 (17.6%) | 2/4 (50%) | 0.353 |
| Follow-up 9 | 1/7 (14.3%) | 3/22 (13.6%) | 1/8 (12.5%) | 0.983 |

**[Table/Fig-3]:** Relationship between prevalence of Lithium induced skin reaction and various doses of Lithium during 1 year of follow-up: *p-value <0.05 was considered significant.

| Follow-ups | <0.8 mEq/L n (%) | 0.8-1.2 mEq/L n (%) | >1.2 mEq/L n (%) | p-value (Chi-square test) |
|---|---|---|---|---|
| Initial Assessment | 3/25 (12.0%) | 8/20 (40.8%) | 1/7 (14.3%) | 0.072 |
| Follow-up 1 | 2/21 (9.5%) | 5/23 (21.7%) | 1/5 (20%) | 0.534 |
| Follow-up 2 | 2/20 (10%) | 6/23 (26.1%) | 0/5 (0%) | 0.211 |
| Follow-up 3 | 4/19 (21.1%) | 6/22 (27.3%) | 2/5 (40%) | 0.681 |
| Follow-up 4 | 1/16 (6.3%) | 6/20 (30%) | 1/4 (25%) | 0.319 |
| Follow-up 5 | 1/15 (6.7%) | 4/19 (21.1%) | 2/4 (50%) | 0.219 |
| Follow-up 6 | 2/15 (13.3%) | 3/17 (17.6%) | 3/5 (60%) | 0.139 |
| Follow-up 7 | 3/16 (18.8%) | 3/17 (17.6%) | 3/4 (75%) | 0.082 |
| Follow-up 8 | 2/16 (12.5%) | 3/17 (17.6%) | 2/4 (50%) | 0.353 |
| Follow-up 9 | 1/16 (6.3%) | 3/17 (17.6%) | 1/4 (25%) | 0.657 |

**[Table/Fig-4]:** Relationship between prevalence of lithium induced skin reaction and various serum lithium levels during 1 year of follow-up: *p-value <0.05 was considered significant.

| Follow-up | <6 months n (%) | 6 months-1 year n (%) | >1 year n (%) | p-value (Chi-square test) |
|---|---|---|---|---|
| Initial | 3/16 (18.8%) | 1/5 (20%) | 8/31 (25.8%) | 0.850 |
| Follow-up 1 | 3/15 (28.6%) | 1/4 (25%) | 4/30 (13.3%) | 0.754 |
| Follow-up 2 | 4/14 (28.6%) | 1/5 (20%) | 3/29 (10.3%) | 0.316 |
| Follow-up 3 | 4/13 (30.8%) | 3/4 (75%) | 5/29 (17.2%) | 0.043 |
| Follow-up 4 | 5/14 (35.7%) | 0/1 (0%) | 3/25 (12%) | 0.293 |
| Follow-up 5 | 2/12 (16.7%) | 0/1 (0%) | 5/25 (20.0%) | 0.914 |
| Follow-up 6 | 3/11 (27.3%) | 0/1 (0%) | 5/25 (20%) | 0.848 |
| Follow-up 7 | 3/11 (27.3%) | 0/1 (0%) | 6/25 (24%) | 0.873 |
| Follow-up 8 | 3/11 (27.3%) | 0/1 (0%) | 4/25 (16%) | 0.772 |
| Follow-up 9 | 2/11(18.2%) | 0/1 (0%) | 3/25 12% | 0.902 |

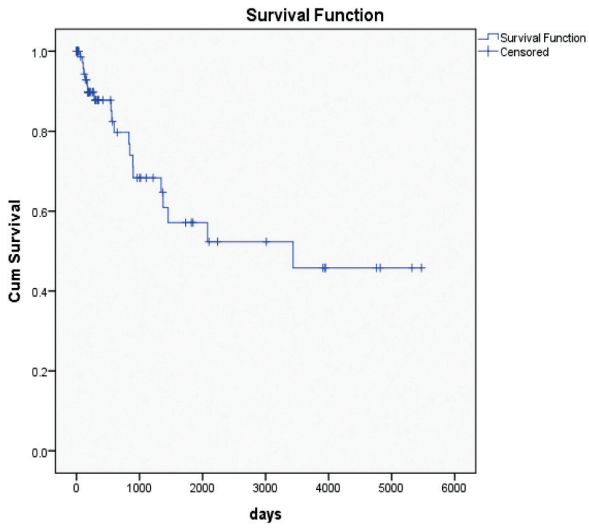
**[Table/Fig-5]:** Relationship between prevalence of Lithium induced skin reaction and various duration of lithium therapy during 1 year of follow-up.
*p-value <0.05 was considered significant.

| Dose of lithium | Lithium induced skin reaction | | | | $\chi^2$ | p-value |
|---|---|---|---|---|---|---|
| | Present | | Absent | | | |
| | Frequency | Percentage | Frequency | Percentage | | |
| <800 | 2 | 4 | 48 | 96 | 18.47 | <0.001 |
| >800 | 18 | 40 | 27 | 60 | | |

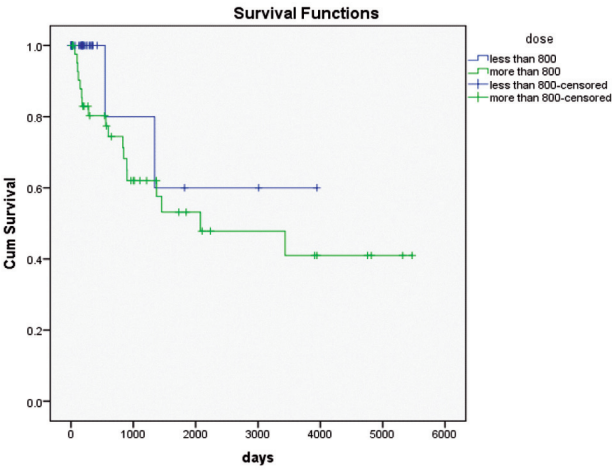
**[Table/Fig-6]:** Association between lithium dose and skin reaction at 10 years of follow-up.
Chi-square test, *p-value <0.05 was considered significant.
(An event-based analysis is done to understand the incidence of lithium induced skin lesion with the dose and the duration of lithium)

| Serum level of lithium | Lithium induced skin reaction | | | | $\chi^2$ | p-value |
|---|---|---|---|---|---|---|
| | Present | | Absent | | | |
| | Frequency | Percentage | Frequency | Percentage | | |
| <0.8 | 4 | 6.6 | 57 | 93.4 | 21.55 | <0.001 |
| >0.8 | 16 | 47.1 | 18 | 52.9 | | |

**[Table/Fig-7]:** Association between serum lithium levels and skin reaction at 10 years of follow-up.
Chi-square test, *p-value <0.05 was considered significant.
(An event-based analysis is done to understand the incidence of lithium induced skin lesion with the dose and the duration of lithium.)




**[Table/Fig-8]:** Ten year Kaplan-Meier survival curve for occurrence of lithium induced skin lesions.



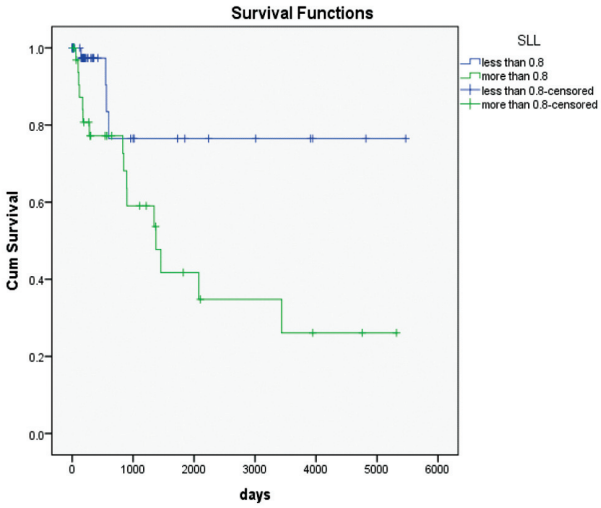

**[Table/Fig-9]:** Kaplan-Meier Survival analysis for varying lithium doses.

the frequency of skin lesions increased i.e. 50 % of the participants in the dose group above 1200 mg developed skin lesions [15].

Several case reports published, had described cases developing skin lesions, within the therapeutic range of lithium levels (0.5-1.5 mEq/L) [22]. Other than case reports, no studies were found correlating the dose and the lithium levels with the cutaneous side-effects. In the current study it was observed that the proportion skin lesion increased when measured at the end of five years compared to the 1 year follow-up in the participants with serum lithium level less than 0.8 mEq/L.

Observation regarding the cumulative prevalence of skin lesion with respect to the different doses and serum levels of lithium at the end of one year did not show any significant difference across the three groups, indicating no corelation between the dose and the serum levels of lithium to the occurrence of skin lesion. In present study when the data was subjected to survival analysis, we found significant association between the dose and serum level of lithium to the prevalence of skin lesion suggesting that patients on higher dose and high serum level for longer duration have increased risk for developing the cutaneous side-effects.

Kaplan-Meier survival analysis showed that significant proportion of lithium induced skin lesion (38%) developed within a period of three years (1000 days) in the above 800 mg dosage group compared to the 20% of the lesions in less than 800 mg dosage group. 59% of the skin lesions developed only when survival analysis was done for 10




**[Table/Fig-10]:** Kaplan-Meier survival analysis for varying serum lithium levels.

years. This showed that maintaining less than 800 mg is beneficial in reducing the proportion of occurrence of skin lesions [Table/Fig-9].

Kaplan-Meier survival analysis showed that significant proportion of skin leision (41%) developed within a period of 3 years (1000 days) in the serum level above 0.8 mEq/L group while 9.6% developed skin lesion in the <0.8 meq/L group. This showed that maintaining therapeutic levels <0.8 meq/L is beneficial in reducing the proportion of skin lesion [Table/Fig-10].

Previous study by Suganya Priyadharshini BS and Ummar IS also suggest that most skin reactions are reversible upon reduction or discontinuation of Lithium except for few serious skin lesions like psoriasis [22]. In the present study, no such cases were reported, and one patient with systemic lupus erythematosus had severe hair fall, which improved after stopping Lithium.

Previous studies by Suganya Priyadharshini BS and Ummar IS have shown that increase in dosage of lithium resulted in deterioration of skin lesions which improved after reducing the lithium dosage [22]. However, in this study, no reduction of the dosage of lithium was done and skin lesions subsided with subsequent dermatological treatment (topical applicant). Hence, continuing the same dosage of Lithium with concomitant dermatological treatment after the onset of skin lesion may be advisable.

### Limitation(s)

Since, the study had small sample size, the results cannot be generalised. Sampling bias and interviewer bias was observed due to convenient sampling method. The dropout rate was high (19%). The compliance was analysed only with the patient's own words.

## CONCLUSION(S)

The patients who were treated with lower dosage and who had lower serum lithium level had reduced risk for cutaneous lesions. Lithium continued to exert its mood stabilisation property even when the serum level was maintained less than 0.8 mEq/L. This resulted in better compliance.

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