



**POLYMORPHOUS LIGHT ERUPTION AND ITS ASSOCIATION WITH HYPOTHYROIDISM AND AUTOIMMUNE THYROIDITIS – A COMPARATIVE CROSS-SECTIONAL STUDY**

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**ABSTRACT**

**BACKGROUND** In many parts of the world, polymorphous light eruption (PLE) is the commonest cause of photosensitivity. Previous studies have suggested the association of PLE with multiple autoimmune diseases. Few studies are available suggesting the association of PLE with autoimmune thyroiditis. We have undertaken this study to confirm such an association and to predict which cases of PLE are likely to have hypothyroidism and autoimmune thyroiditis.

**METHODS** This was a cross-sectional study with comparative group with 75 PLE cases and 75 controls. Thyroid function test (TFT) was done for all subjects and, if found abnormal, anti-thyroid peroxidase (TPO) antibodies were tested. The studied parameters were compared using Pearson's chi-squared test for significance.

**RESULTS** The male to female ratio was 1:2.1. Hypothyroidism and autoimmune thyroiditis were significantly present in PLE cases. PLE lesions with papular morphology, persistent and recurrent PLE, positive family history and associated other autoimmune diseases were significantly associated with autoimmune thyroiditis.

**CONCLUSION** PLE is significantly associated with hypothyroidism and autoimmune thyroiditis. Hence we suggest screening of PLE patients for hypothyroidism and, if required, for autoimmune thyroiditis for early diagnosis and treatment.

**KEYWORDS :** Polymorphous light eruption, hypothyroidism, autoimmune thyroiditis

**INTRODUCTION**

Polymorphous light eruption (PLE) is the most common idiopathic photodermatosis.<sup>1</sup> Though the exact etiology is unknown, it is postulated to be an abnormal delayed hypersensitivity reaction to undetermined self-antigens.<sup>2</sup> The age and sex predilection are similar to many other autoimmune disorders, with females of 20 to 40 years being commonly affected.<sup>3</sup> Common cutaneous manifestations of hypothyroidism include coarse, dry skin and diffuse alopecia.<sup>4</sup> When hypothyroidism is due to autoimmunity, additional autoimmune associations such as vitiligo, alopecia areata, chronic urticaria, immunobullous disorders and connective tissue diseases have been reported.<sup>5</sup> Autoimmune thyroiditis is a disorder characterized by autoantibodies against thyroid peroxidase and thyroglobulin. This study aims to determine the association between PLE and autoimmune thyroiditis and to determine the association between various clinico-epidemiological features of PLE and autoimmune thyroiditis.

**MATERIALS AND METHODS**

This was a cross-sectional study with comparative group conducted at a tertiary care teaching hospital in Puducherry from November 2018 to May 2020. After obtaining clearance from the institutional research and ethics committee, 75 cases with PLE and equal number of age- and sex-matched controls without PLE were enrolled for the study. The control group were either bystanders of the patient or other volunteering patients from the OPD. A detailed history followed by clinical examination will be done and a clinical diagnosis of PLE will be made by the following criteria:<sup>6</sup> Rash that appears following sun exposure on exposed parts of the body with latency period of 30 minutes to several hours – maximum up to 3 days – that may be pruritic and that heals without scarring within a few days to 2 weeks of subsequent sunlight avoidance. The rash can be any of the following types: papular, plaque, papulovesicular, vesicobullous, hemorrhagic, plaque, micropapular (pinpoint), strophula (insect-bite like), purpuric/haemorrhagic, erythema

multiforme-like and sine eruptions.

Pregnant and lactating women, patients on topical or systemic corticosteroids and photosensitizing drugs were excluded from the study. Thyroid function tests (TFT) were done from the blood samples of all 150 subjects. Those with normal TFT were classified as euthyroid and those with abnormal TFT were classified either as hypothyroidism or hyperthyroidism depending on their hormone levels. Subjects with abnormal TFT were further tested for the presence of anti-thyroid peroxidase (TPO) antibodies. The studied parameters were compared using Pearson's chi-square test for significance. For comparison of probability, p value of < 0.05 was taken as statistically significant difference.

**RESULTS**

The male to female ratio was 1:2.1 with mean age of 31.13 ± 10.42 years and 31.54 ± 11.33 years in cases and controls, respectively. Abnormal TFT showing hypothyroidism (Table 1) was present in 19 cases (25.33%) and 5 controls (6.66%) and this difference was found to be statistically significant (p = 0.002). None of the subjects in either group had hyperthyroidism.

**Table 1 Comparison of Hypothyroidism in cases and controls**

| Group | Cases          | Count          | Hypothyroidism |         | Total   | P value |
|-------|----------------|----------------|----------------|---------|---------|---------|
|       |                |                | Present        | Absent  |         |         |
|       | Cases          | Count          | 19             | 56      | 75      | 0.002   |
|       |                | % within Group | 25.33%         | 74.66%  | 100.00% |         |
|       | Controls       | Count          | 5              | 70      | 75      |         |
|       |                | % within Group | 6.66%          | 93.33%  | 100.00% |         |
| Total | Count          | 24             | 126            | 150     |         |         |
|       | % Within Group | 16.00%         | 84.00%         | 100.00% |         |         |

**Table 2 Comparison of anti-TPO antibodies (Ab) in cases and controls**

| Group | Cases    | Count          | Anti-TPO Ab |         | Total | P value |
|-------|----------|----------------|-------------|---------|-------|---------|
|       |          |                | Present     | Absent  |       |         |
|       |          | 9              | 66          | 75      | 0.002 |         |
|       |          | % within Group | 12.00%      | 88.00%  |       | 100.00% |
|       | Controls | 0              | 75          | 75      |       |         |
|       |          | % within Group | 0.00%       | 100.00% |       | 100.00% |
| Total |          | 9              | 141         | 150     |       |         |
|       |          | % Within Group | 6.00%       | 94.00%  |       | 100.00% |

Anti-TPO antibodies (Table 2) were present in 9 cases (12%) whereas none of the controls had anti-TPO antibodies, which was statistically significant (p = 0.002). Hypothyroidism was newly detected in 8 PLE cases (10.67%) and 2 controls (2.67%) and this difference was statistically significant (p = 0.04). There were 11 known cases of hypothyroidism in PLE group and 3 known cases of hypothyroidism in control group and all of them were on L-thyroxine supplementation.

It was found that PLE lesions which were recurrent, persisting beyond 2 weeks, having positive family history of PLE and co-existent urticaria or vitiligo had significant associations with autoimmune thyroiditis (Table 3). Similarly, papular PLE and lesions occurring in 3 or more sites were significantly associated with autoimmune thyroiditis (Table 4 & Table 5) (Figure 1).

**Table 3 Comparison of clinical history and associated diseases in anti-TPO Ab positive group and euthyroid group**

| History and associated diseases   |         | PLE cases with anti-TPO Ab |        | PLE cases with euthyroidism |        | P value |
|-----------------------------------|---------|----------------------------|--------|-----------------------------|--------|---------|
|                                   |         | %                          | Count  | %                           | Count  |         |
| Recurrence of PLE                 | Present | 9                          | 64.28% | 5                           | 35.71% | <0.0001 |
|                                   | Absent  | 0                          | 0.00%  | 51                          | 100.0% |         |
| Family history of PLE             | Present | 3                          | 60.0%  | 2                           | 40.0%  | 0.002   |
|                                   | Absent  | 6                          | 10.0%  | 54                          | 90.0%  |         |
| Family history of thyroid disease | Present | 2                          | 33.33% | 4                           | 66.66% | 0.147   |
|                                   | Absent  | 7                          | 11.86% | 52                          | 88.13% |         |
| Persistence of PLE beyond 2 weeks | Present | 5                          | 35.71% | 9                           | 64.28% | 0.007   |
|                                   | Absent  | 4                          | 7.84%  | 47                          | 92.15% |         |
| Urticaria                         | Present | 4                          | 80.0%  | 1                           | 20.0%  | <0.0001 |
|                                   | Absent  | 5                          | 8.33%  | 55                          | 91.66% |         |
| Vitiligo                          | Present | 2                          | 100.0% | 0                           | 0.0%   | <0.0001 |
|                                   | Absent  | 7                          | 11.11% | 56                          | 88.88% |         |
| Diabetes                          | Present | 1                          | 14.28% | 6                           | 85.71% | 0.972   |
|                                   | Absent  | 8                          | 13.79% | 50                          | 86.20% |         |

**Table 4 Comparison of morphology of PLE in anti-TPO Ab positive group and euthyroid group**

| Morphology of PLE   |         | PLE cases with anti-TPO Ab |        | PLE cases with euthyroidism |        | P value |
|---------------------|---------|----------------------------|--------|-----------------------------|--------|---------|
|                     |         | %                          | Count  | %                           | Count  |         |
| Papule              | Present | 6                          | 31.57% | 13                          | 68.42% | 0.008   |
|                     | Absent  | 3                          | 6.52%  | 43                          | 93.47% |         |
| Plaque              | Present | 1                          | 9.09%  | 10                          | 90.90% | 0.616   |
|                     | Absent  | 8                          | 14.81% | 46                          | 85.18% |         |
| Macule              | Present | 0                          | 0.0%   | 16                          | 100.0% | 0.065   |
|                     | Absent  | 9                          | 18.36% | 40                          | 81.63% |         |
| Papule with vesicle | Present | 0                          | 0.0%   | 3                           | 100.0% | 0.477   |
|                     | Absent  | 9                          | 14.51% | 53                          | 85.48% |         |
| Papule with plaque  | Present | 1                          | 11.11% | 8                           | 88.88% | 0.798   |
|                     | Absent  | 8                          | 14.28% | 48                          | 85.71% |         |
| Papule with macule  | Present | 1                          | 14.28% | 6                           | 85.71% | 0.972   |
|                     | Absent  | 8                          | 13.79% | 50                          | 86.20% |         |

**Table 5 Comparison of sites of PLE diseases in anti-TPO Ab positive group and euthyroid group**

| Sites of PLE        |         | PLE cases with anti-TPO Ab |        | PLE cases with euthyroidism |        | P value |
|---------------------|---------|----------------------------|--------|-----------------------------|--------|---------|
|                     |         | %                          | Count  | %                           | Count  |         |
| Single site lesion  | Present | 4                          | 6.89%  | 54                          | 93.10% | <0.0001 |
|                     | Absent  | 5                          | 71.42% | 2                           | 28.57% |         |
| Two sites lesions   | Present | 2                          | 50.0%  | 2                           | 50.0%  | 0.031   |
|                     | Absent  | 7                          | 11.47% | 54                          | 88.52% |         |
| Three sites lesions | Present | 1                          | 100.0% | 0                           | 0.0%   | 0.012   |
|                     | Absent  | 8                          | 12.50% | 56                          | 87.50% |         |
| Four sites lesions  | Present | 2                          | 100.0% | 0                           | 0.0%   | <0.0001 |
|                     | Absent  | 7                          | 11.11% | 56                          | 88.88% |         |

**Figure 1 Extensive PLE lesions in more than 3 sites associated with hypothyroidism and positive anti-TPO antibodies in a female patient**



**DISCUSSION**

The association between PLE and hypothyroidism have been suggested in a few studies (Table 6). In our study, abnormal TFT was present in 25.33% of PLE cases and 6.66% of controls, and the difference was statistically significant. Similar study conducted by Sharma L et al.7 with 100 cases and controls revealed that abnormal TFT was present in 25% of cases and 7% of controls, which was statistically significant. Overall recurrences, family history of PLE and associated vitiligo were comparable in both studies (Table 7).

**Table 6 Comparison of studies with association of hypothyroidism and autoimmune thyroiditis**

| S.No | Study Name                       | Study Type                          | Association with hypothyroidism | Association with Autoimmune Thyroiditis |
|------|----------------------------------|-------------------------------------|---------------------------------|---|
| 1    | Hasan T et al, 19988 (n = 94)    | Questionnaire-based follow-up study | Present                         | Commented but not confirmed             |
| 2    | Seetharam K et al, 20109 (n=152) | Case-Control                        | Significantly present           | Significantly present                   |

|   |                                  |                                   |                        |                       |
|---|----------------------------------|-----------------------------------|------------------------|-----------------------|
| 4 | Sharma L et al., 20147 (n = 200) | Case-Control                      | Significantl y present | Not commented         |
| 5 | Sharma P et al., 201710 (n = 90) | Prospective observational study   | Present                | Not commented         |
| 6 | Chadha C et al., 201811 (n = 70) | Case-Control                      | Significantl y present | Not commented         |
| 7 | Bains A et al., 201912 (n = 126) | Cross sectional descriptive study | Present                | Not commented         |
| 8 | Present study (n = 150)          | Comparative cross-sectional study | Significantl y present | Significantly present |

**Table 7 Comparison of clinico-epidemiological features of PLE with Sharma et study**

| S. No | clinico-epidemiological features of PLE | Sharma L et al study <sup>13</sup> (n=200) | Present study (n=150) |
|-------|---|--|-----------------------|
| 1     | Abnormal TFT                            | 25%  | 25.33%                |
| 2     | Recurrence                              | 24% (p >0.7)                               | 29.33%                |
| 3     | Family history of PLE                   | 10%  | 8%                    |
| 4     | Vitiligo                                | 2%   | 2.67%                 |

As per Sharma et al.,<sup>7</sup> the most common site of PLE lesions in patients with abnormal TFT was the neck (28.57%) followed by face (27.27%). Papular PLE was the most common morphology (27%) followed by plaques and macules (16% each). But these clinical and epidemiological features of PLE were not found related to abnormal TFT on statistical comparison. Tests for anti-TPO antibodies were not done in their study. Unlike their study, we found significant associations of certain clinico-epidemiological features of PLE with anti-TPO antibodies, which may help predict the presence of thyroid disorder in such PLE cases. In a long-term follow-up study by Hasan et al<sup>8</sup> with 94 PLE cases, they report that 8% had hypothyroidism or non-toxic goitre of probable autoimmune etiology, all of whom were females. The most common morphology of PLE was vesiculopapular variety (37.23%). They also could not find statistically significant differences in the clinical characteristics of PLE between patients with or without autoimmune diseases. In a study by Seetharam KA et al.<sup>9</sup> with 112 PLE cases and 40 controls, it was found that hypothyroidism was present in 25.9% of PLE cases and 7.5% of controls, which was statistically significant similar to our study. All 25.9% of hypothyroid PLE cases had anti-TPO antibodies. Other studies found association of PLE with hypothyroidism but did not comment on anti-TPO antibodies (Table 6). Hasan T et al.<sup>8</sup> have suggested that PLE is a slowly ameliorating disease with a tendency to develop autoimmune diseases. Our study helps substantiate their statement.

#### Limitations of the study

The diagnosis of PLE was made mostly on clinical grounds. Histopathological examination of PLE was limited to a few doubtful cases. ANA testing was not done. Other thyroid autoantibodies such as TSH receptor antibodies and anti-thyroglobulin antibodies were not tested. Anti-TPO antibodies can also be present in euthyroid population and as such were not tested.

#### CONCLUSION

PLE is the most common idiopathic photodermatosis, commonly affecting females of 20-40 years. The association between PLE and autoimmune diseases has been a matter of non-consensus and only a few studies are available in the

literature showing the association between PLE and autoimmune thyroiditis. Our study has found a significant association between PLE and hypothyroidism and autoimmune thyroiditis. Hence we suggest screening of all PLE patients for hypothyroidism and, if found hypothyroid, for autoimmune thyroiditis. Our study is also the first to find significant associations of autoimmune thyroiditis with recurring and persistent PLE, positive family history of PLE and PLE co-existing with other autoimmune diseases like urticaria or vitiligo. Such cases of PLE may therefore help to predict the presence of autoimmune thyroiditis. Euthyroid PLE patients may also benefit from long-term follow-up for developing autoimmune thyroiditis later in life.

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