INTRODUCTION

Early renowned physicians described "LUPUS" which is derived from the Latin word which means "WOLF" depicting its nature of destruction.¹ The ulcerated skin lesions typical of this disease signify this feature as it "bites, eats away and destroys". Lupus erythematosus (LE) was identified only as a cutaneous disease, until a century ago when emphasis was transferred from the integument to include visceral manifestations. At the beginning of this century blood vessels and connective tissues distributed throughout the body came to be implicated in the pathogenesis, which lead to the concept of “multisystem malady”.² In 1942 Klimperer et al were struck by the many morphological features that were common to diseases like scleroderma, rheumatoid arthritis, PAN, and classified them as collagenosis.³ The discovery of auto antibodies to various cellular components of different tissue in these diseases has of late given place to the concept of "autoimmune diseases".

Aim of the study

To study the incidence precipitating and exacerbating factors, relevant laboratory abnormalities, associated disorders, histopathological and immunofluorescence patterns of various spectrum of SLE.
METHODS

Study population

It is a prospective cohort study done at Government General Hospital, Chennai, Tamil Nadu, India, during the period August 2007 to September 2009.

100 cases of systemic lupus erythematosus who either fulfilled ARA criteria (or) ANA positivity were included in the study, from the patients attending the Skin and Rheumatology department, Govt. General Hospital.

A detailed history regarding the onset, progress, precipitating (or) exacerbating factors, recurrence, number, size, morphology, distribution and sequelae of the lesions was obtained. Symptoms related to cutaneous lesions and internal systems were noted in all cases. In all female patients detailed menstrual and obstetric history was taken to look for anti-phospholipid syndrome. Detailed laboratory investigations including biopsy were done.

Then depending on the above information conclusions and discussions were formulated. All these patients were followed up for 2 years and the patients were categorized according to their clinical features into the following groups.

Sample and diagnostic procedures

Chronic cutaneous lupus erythematosus (CCLE)

It include (a) Discoid LE (DLE) characterised by well-defined erythematous plaques with thick adherent scales and keratotic plugging, peripheral hyperpigmentation and central hyper, hypopigmentation, atrophy, telangiectasia, and scarring. It was subdivided into localised type, when lesions were restricted to head and neck and disseminated type (DDLE) when lesions were present elsewhere also and (b) Lupus erythematosus panniculitis, characterised by well defined, firm, non-tender, subcutaneous plaques with normal (or) indrawn overlying skin and with (or) without ulceration. Presence of DLE lesion elsewhere was taken as confirmatory evidence for the diagnosis.

Subacute cutaneous lupus erythematosus (SCLE)

It characterized by annular (or) polycyclic erythematous plaques with superficial scales (or) psoriasiform lesions without scarring.

Acute cutaneous lupus erythematosus (ACLE)

It characterised by acute erythema with edema and confined mostly to the malar area (or) other sun exposed areas. The lesions are sometimes generalised with morbilliform (or) exanthematous eruptions and are characteristically associated with other cutaneous lesions and systemic manifestations.

The morphological description given above was taken as “classical form” for each specific group.

Biopsy of the skin lesions was done in all patients to confirm the clinical diagnosis of LE. The characteristic and diagnostic histopathological findings in LE are, 1) hydropic degeneration of the basal cells of the epidermis (or) the follicles, 2) patchy lymphohistiocytic infiltrate both independently and around the blood vessels and appendages, 3) degenerative changes in connective tissues like hyalinization, edema, mucin and fibrinoid change.

In addition to the above findings the presence of following histopathological features were taken as suggestive evidence for specific clinical type.

DLE- Hyperkeratosis, keratotic plugging both follicular and extrafollicular, epidermal atrophy, inflammatory infiltrate extending up to the deeper dermis and mucin deposits.

SCLE- Absence (or) minimal keratotic plugging, no epidermal atrophy, vesicular changes in active borders, focal hydropic degeneration of basal cells and sparse inflammatory infiltrate confined to the upper third of the dermis, dermal edema, extravasation of RBC’s and dermal fibrinoid deposits.

ACLE- Increased degree of hydropic degeneration of basal cells, sparse dermal cellular infiltrate and upper dermal edema and rarely epidermal necrosis(Fig 8).

All case selected were examined clinically to rule out any systemic manifestations. Depending upon the systemic symptoms patients were investigated in detail pertaining to the system suspected to be involved.

CBC, platelet count, urine for albumin, sugar and deposits, RFT, LFT, CRP, VDRL, RF, CXR, and ECG were done to all patients. APL antibodies were done in all suspected patients. Patients with symptoms suggestive of renal problems and vasculitis were investigated for C3 and C4 levels. Renal biopsy was also done for few patients as suggested by nephrologist. Doppler was done for lower limb vessels for patients with gangrene and leg ulcer. Direct immunofluorescence and indirect immunofluorescence (IDIF) were done in few patients.

With all the above methodologies and investigation, results were formulated and conclusions were drawn.

Statistical analysis

The data analysis was performed using descriptive statistics including median, frequency and frequency percentage. Comparisons are made using chi square test
using standard equates. Results were reported with 
$p\leq 0.05$ as the accept level of significance.

**RESULTS**

ACLE lesions were seen in 50% followed by CCLE and SCLE patients 46% and 4% respectively (Table 1). Sunlight was the most common precipitating factors [55%] followed by physical exertion and infections [11.11%].

Among the mucocutaneous lesions, 47.91% presented with photosensitivity followed by 26.08% and 21.73% presented with non-scarring alopecia (Table 3) and oral ulcer respectively. 45% of patients presented only with mucocutaneous problems initially, 40.47% of the patients primarily presented with systemic problems. 14.53% of patients presented initially with both systemic and mucocutaneous problems.

<table>
<thead>
<tr>
<th>LE specific skin lesions</th>
<th>LE non specific skin lesions</th>
<th>Both</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total number of cases</td>
<td>CCLE</td>
<td>SCLE</td>
</tr>
<tr>
<td></td>
<td>19 (19.11%)</td>
<td>13 (13.04%)</td>
</tr>
</tbody>
</table>

In patients with systemic problems as initial presentation 45.45% had fever and 35.71% had arthralgia (Figure 1). Photosensitivity was seen in almost all patients in SCLE spectrum [99.85%], 41.17% CCLE patients had photosensitivity.

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**Histopathology**

Majority of study patients showed features suggestive specific for LE.

In ACLE patients, other than the common features 56% of them had sparse inflammatory infiltrate, 16% had upper dermal edema.

In patients with SCLE, focal liquefactive degeneration was most common [66.66%), followed by upper dermal infiltrate [66.66%] and upper dermal edema [33.33%].

In DLE patients, more than dermal edema, keratotic plugging [51%], colloid bodies [50%], dense and deep dermal infiltrate [51%], periappendageal infiltrate [48%], more melanophages [33%], perivascular infiltrate [29%] were observed.

**Table 1: Initial clinical presentation.**

<table>
<thead>
<tr>
<th>Lesions</th>
<th>Percentage (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diffuse non scarring alopecia</td>
<td>48.88</td>
</tr>
<tr>
<td>Nail changes</td>
<td>22.22</td>
</tr>
<tr>
<td>Mucosal lesions</td>
<td>22.22</td>
</tr>
<tr>
<td>Icthyosis</td>
<td>8.88</td>
</tr>
<tr>
<td>Vasculitis</td>
<td></td>
</tr>
<tr>
<td>Urticarial vasculitis</td>
<td>4.44</td>
</tr>
<tr>
<td>Purpura</td>
<td>4.44</td>
</tr>
<tr>
<td>Leg ulcer</td>
<td>2.22</td>
</tr>
<tr>
<td>Gangrene</td>
<td>2.22</td>
</tr>
<tr>
<td>Acanthosisnigricans</td>
<td>4.44</td>
</tr>
<tr>
<td>LE/LP overlap</td>
<td>2.22</td>
</tr>
<tr>
<td>Anetoderma</td>
<td>2.22</td>
</tr>
</tbody>
</table>

**Table 2: Spectrum of LE specific skin lesions.**

<table>
<thead>
<tr>
<th>LE specific skin lesions</th>
<th>Percentage (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Malar rash</td>
<td>68</td>
</tr>
<tr>
<td>Butterfly rash</td>
<td>4</td>
</tr>
<tr>
<td>Maculopapular rash</td>
<td>24</td>
</tr>
<tr>
<td>Bullous lesions</td>
<td>4</td>
</tr>
<tr>
<td>Annular</td>
<td>33.33</td>
</tr>
<tr>
<td>Papulosquamous lesions</td>
<td>66.66</td>
</tr>
<tr>
<td>Localised</td>
<td>64.70</td>
</tr>
<tr>
<td>Generalised</td>
<td>35.29</td>
</tr>
<tr>
<td>Verrucous</td>
<td>5.88</td>
</tr>
<tr>
<td>LEP</td>
<td>5.88</td>
</tr>
</tbody>
</table>

**Table 3: Spectrum of LE nonspecific skin lesions.**
Patients with urticarial vasculitis, LEP, LE/LP overlap all of them showed features classical of their own histopathological entity.

**Laboratory findings**

In our study raised ESR, anemia and leucopenia was observed in 63.34%, 42%, and 15.55% patients respectively (Figure 2).

**Figure 2: Laboratory criteria of ARA in various spectrums of SLE.**

Abnormal 24 hrs urine protein excretion was seen in 33% and grade III lupus nephritis was observed in 50% in our study.

False positive VDRL was seen in 18% of patients and thrombocytopenia in 4.45%.

ANA was done for all the patients and was positive in 94% of the patients.

**DISCUSSION**

In this study, among the total 52,369 new patients attending skin op GGH, Chennai, during the study period of August 2007 to September 2009, total number of patients with SLE was 100. The incidence of SLE in our study is 0.08% as compared to incidence of 0.01 to 0.12% in literature. The incidence of 46.5%, 38.8%, 12.7%, and 2% of ACLE, CCLE, SCLE, LEP respectively, which is comparable with our study of 47.94%, 39.92%, 8.48% and 2.86% of ACLE, CCLE, SCLE, LEP respectively as shown in literature.

Burning sensation and erythema were the most common symptoms among patients, which is 63.63% & 42.42% respectively. Photosensitivity was the most common symptom in SCLE patients and pain is the most common symptom in LEP patient as documented in literature.

Photosensitivity was observed in 52% in study done PGI and 54.4% in study done in Iran, which is comparable with our study of 55%.

In a Chinese study, 44.52% presented only with mucocutaneous symptoms as primary complaints which is consistent with our study of 45%.

An Indian study done in Kerala observed primary presenting complaints as photosensitivity in 78% of his study patients, non scarring alopecia in 60%, malar rash in 57%, which is comparable with our study of 80%, 57.77% and 60% respectively.

In a study done in China showed arthritis as primary presenting complaint in 44% while an Indian study showed it as 66% which is comparatively high than our study of 34%. Fever was primary presenting complaint in 56.6% of patients in the literature which is high compared to our study of 45.44%.

Photosensitivity as a symptom is seen in 76% of ACLE patients, 62% of SCLE patients and 42% of CCLE patients as per literature. In our study it was 88%, 100% and 43% of ACLE, SCLE and CCLE patients respectively.

Photosensitivity is the most common ARA skin criteria associated with other ARA criteria as given in the literature. Photosensitivity is most commonly associated with 36.65% of hematological criteria and 21.5% of immunological criteria.

In 16 patients with DLE, 73.64% had lesions localised to the head and neck, 26.46% had disseminated type. This is compatible with an Indian study which observed 18.17% had DLE lesions over the scalp which is nearer to our study of 17.7%.

In our study majority of ACLE patients had mucosal involvement followed by SCLE and ACLE as described in Iranic study. A study done in India documented oral involvement in 64% in his study as compared to 62% observed in our study. Among the mucosa, palate was
involved in 83.30% of patients, lips in 25% and gingiva in 3.57% (Figure 4).

**Figure 4: ACLE patient with butterfly rash, crusting of lips and conjunctivitis.**

Morphology and sequelae of lesions were classical in the majority of the patients, in all the three spectrum as described in literature. In DLE patients majority of them had plaque like lesions which ended with scarring as described in literature. Few of the patients also had verrucous lesion, follicular plugging lesion in the ear which is also described in literature. In our study two third of SCLE patients had papulosquamous lesions and one third had annular lesions (Figure 3), both these types of lesions did not end in scarring as described in the literature.

**Figure 5: Squamous cell carcinoma in a case of LE/LP overlap.**

As per Gilliam classification of specific and non-specific lesions, specific skin lesions are comparatively common than non-specific skin lesions in our study.

In Kerala study, malar rash was seen in 28%, butterfly rash was seen in 26% of patients and maculopapular rash was seen in 20%. In our study malar rash, butterfly rash and maculopapular rash were seen in 37%, 35%, 18% respectively. Though only few presented with LE specific skin lesions initially, in due course of follow up, majority of them developed LE specific skin lesions.

**Figure 6: Lupus erythmatosus panniculitis over abdomen.**

Madras study showed facial erythema in 80% which is observed as 82% in our study. Out of 25 patients with ACLE 24% had butterfly rash, which is consistent with literature. Literature documents malar rash in 80% of patients which is observed as 76.52% in our study. An Japanese study observed bullous SLE in 10% of their patients which is high compared to our study of 2.22%.

Various review studies showed diffuse non scarring alopecia in 86%of patients, which comparable to our study patients with 85%. It was observed that the severity of hair loss was proportional to the disease activity, as also observed by the above same study. Nail changes documented in our study included ragged cuticle in 42%, paronychia in 25%, nail dystrophy in 16%, melanonychia in 6% and beau’s lines in 11%. In our study among the above findings ragged cuticle was seen in most of the patients.

Non-specific mucosal lesions are seen in 26% of patients in literature, but in our study it was 22.22%. As per literature vasculitis presented as urticaria in 10% of patients, as purpura in 8%, as leg ulcer in 10%, and as gangrene (Figure 7) in10% of patients, but in our study it was 4.44%, 4.44%, 2.22% and 2.22% respectively which is very low. Among the 2 patients with urticarial vasculitis 1 patient had renal involvement and low complement levels which states that the urticaria may be due to immune complex mediation. Association of hypocomplementemia was documented with lupus.
nephritis and urticaria in literature.\textsuperscript{7,9} Patients with leg ulcer, was also associated with urticarial vasculitis. LE/LP overlap was seen in 1 patient, who turned into SCC later, which is a rare documentation in literature.\textsuperscript{9}

By literature observations fever and arthralgia in 92.67\% and 22.4\% respectively which is comparable with our study of 92.42\% and 22.4\%\textsuperscript{7,9}. As per studies done in Kerala and RadhaMadhavan Madras, lupus nephritis is observed in 35\% as compared to 33.33\% in our study.\textsuperscript{6,10} RadhaMadhavan studies showed renal symptoms as initial complaints in 7.4\% but in our study it was 4.04\%.\textsuperscript{10} Respiratory problems were seen 26\% in Nazarinia Iranian study which is comparatively higher than our study of 8.88\%.\textsuperscript{5} Radhamadavan observed 25\% of neuropsychiatric manifestations in their patients which is nearer to our observation of 26.52\%.\textsuperscript{10} Among 12 patients with neuropsychiatric manifestations 4.32\% had seizures and 40\% had psychiatric problems like depression, anxiety neurosis and obsessive compulsive neurosis. Lymphadenopathy was documented as 50\% in literature but in our study it was 11.11\%.\textsuperscript{7,9}

\textbf{HPE}

Classical common histopathological features documented in literature were same in our study.\textsuperscript{13} Other uncommon literature findings like atrophic epidermis, vesicular changes in active borders, fibrinoid deposits were not encountered in our study.

Characteristic HPE (Figure 8) skin changes of LE specific skin lesion as in literature like hyperkeratosis liquefaction degeneration of basal cells peripendageal infiltrate, perivascular infiltrate is seen in majority of patients.\textsuperscript{7,9} Varying mosaicism of these features were seen in 3 major spectrum of LE specific skin disease.\textsuperscript{13}

It is described in literature that, follicular plugging, keratotic plugging, extensive basal cell degeneration, dense pigment incontinence, patchy inflammatory infiltrate around and independent of appendages and dense deep dermal infiltrate is seen more commonly in DLE than in SCC or ACLE.\textsuperscript{9,13} The above finding is consistent with our study like extensive basal cell degeneration in 100\%, follicular plugging is seen in 74\% of patients, keratotic plugging in 65\%, dense pigment incontinence in 82\%, dense deep dermal infiltrate in 70\% and periappendageal infiltrate in 68\% of patients.

Focal liquefaction degeneration of basal cells, dermal edema and sparse inflammatory infiltrate in upper dermis (as against the deep dermal infiltrate of DLE lesions) which are all common documentation in SCLE patients in literature, were also documented in our study. Other uncommon literature findings like atrophic epidermis, vesicular changes in active borders, extravasation of RBC’s and fibrinoid deposits were not encountered in our study.\textsuperscript{9,13}

As per literature reports hyperkeratosis is less striking in ACLE than in DLE and SCLE, this finding is consistent with our study.\textsuperscript{13} Upper dermal sparse inflammatory cell, and upper dermal edema, which is a common finding documented in literature, was frequently encountered in our study. Histopathological feature of bullous SLE is consistent with the literature. Severe forms of ACLE may have epidermal necrosis and the clinical lesion may resemble TEN. The above finding, which was a rare entity, has not been encountered in our study.

In patients with urticarial vasculitis, histopathological examination showed inflammatory infiltrate predominantly within and around small blood vessels mainly of neutrophils and also leukocytoclastosis. A case of LEP showed minimal atrophy of epidermis, inflammatory infiltrate cell collection in dermis and septallobular lymphohistiocytic infiltrate in subcutis. In patient with LE/LP overlap, hypertrophic DLE lesions histopathologically showed features of lichen planus, but ulcerative DLE lesions showed features of SCC like, individual cell keratinisation and keratin pearls (Figure 9). All the above findings documented in our study were also seen in literature.\textsuperscript{13}

\textbf{Laboratory findings}

Paul study showed raised ESR in 65.43\%, anemia in 42\% and leucopenia in 13\% in his patients, which is observed.
as 63.34%, 42%, and 15.55% respectively in our study. In Indian study 26.67% had abnormal 24 hrs urine protein excretion which is comparable to 33% in our study. Grade III lupus nephritis was observed in 49.7% of Nazarinia study as compared to our study of 50.4.

Figure 9: Squamous cell carcinoma with horn pearls which occurred over a DLE lesion.

False positive VDRL was seen in 23% as per literature but in our study it was 18%. Thrombocytopenia was seen in 12.22% Yokohari studies, which is 4.45% in our study.

ANA was done for all the patients. Paul and Nazarinia studies showed ANA positivity in of 93% and 94% respectively, which is almost correlating with our study of 9%.6

ANA positivity in literature in various spectrum like DLE, SCLE and CCLE are 30%-40%, 60% and 85% respectively.7,9 But in our study it was 70%, 100% and 100% in CCLE, SCLE and ACLE respectively.

CONCLUSION

The incidence of SLE varies with the western literature and an increase in incidence shows there is environmental and genetic factors’ role. The female preponderance shows that the hormonal influence is the key factor. Photosensitivity being the common symptom and sunlight being the common precipitating factor makes us conclude that there is environmental effect like increased ultraviolet light reaching the atmosphere due to ozone depletion. There is also association with other autoimmune disorders in few patients which states that autoimmune trigger may enhance the possibility. Hence suspected disease overlap with other disorders should be investigated in detail. ACLE patients have more common acute systemic involvement; hence these patients should be thoroughly examined clinically and investigated to reduce the morbidity and mortality. Though most of the SLE patients present initially with dermatological manifestations, it is highly necessary for even the asymptomatic patients to have periodic screening for other organs involved to reduce the morbidity and mortality.

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Ethical approval: The study was approved by the institutional ethics committee

REFERENCES
