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ISSN: 2663-9491 e-ISSN: 2789-6897

ORIGINAL ARTICLE

Pattern, Frequency, and Predictors of Comorbidity Among Patients with Cutaneous Lupus Erythematosus: A Hospital-Based Study in Bangladesh

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Received: 20 October 2026
Accepted: 06 November 2026
Published Online: 16 November 2026

Published by:
Gopalganj Medical College, Gopalganj, Bangladesh

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DOI: 10.5281/zenodo.24269533

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ABSTRACT

Background: *Cutaneous lupus erythematosus (CLE) may occur alone or with systemic lupus erythematosus (SLE), but data on its comorbidity burden in South Asia are scarce.* ***Objective:*** *To describe the frequency and pattern of physical and mental comorbidities in patients with CLE in Bangladesh, quantify burden with the Charlson Comorbidity Index (CCI), estimate multimorbidity prevalence, and explore associated factors.* ***Methods & Materials:*** *This descriptive cross-sectional study was conducted at Chittagong Medical College Hospital from January to December 2023. Consecutive adults with CLE, with or without SLE, were enrolled. Data came from interviews, record review, examination and laboratory tests. Disease activity was measured with the CLASI, depression and anxiety with the Hospital Anxiety and Depression Scale (HADS), and overall burden with the CCI. Multimorbidity was defined as two or more comorbidities. Associations were explored with chi-square, Student's t and Mann-Whitney U tests; no multivariable modelling was done.* ***Results:*** *Of 100 patients assessed, 96 were analysed (mean age 32.5 ± 11.6 years; 91.7% female; 86.5% with systemic manifestations; 11 with primary CLE). Multimorbidity affected 66 patients (68.8%), a single comorbidity 23 (24.0%), and none 7 (7.3%). Common conditions were secondary infection (66.7%), depression (54.2%), anxiety (39.6%), lupus nephritis (25.0%), thyroid dysfunction (22.9%), diabetes (19.8%), hypertension (18.8%), ischemic heart disease (13.5%), dyslipidemia (10.4%) and chronic kidney disease (7.3%). The mean CCI was 3.25 ± 1.62. Multimorbidity was not significantly associated with any sociodemographic or clinical variable examined (all p>0.05).* ***Conclusion:*** *Physical and mental comorbidity was substantial and multimorbidity common in this tertiary-care cohort. Exploratory analyses found no correlates, which may reflect limited power. Larger multicentre prospective studies with multivariable modelling are needed.*

Keywords: *cutaneous lupus erythematosus; multimorbidity; comorbidity; Charlson Comorbidity Index; depression; anxiety; Bangladesh*

(The Insight 2026; 9(3): 1034-1042)

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INTRODUCTION

Cutaneous lupus erythematosus (CLE) is a chronic, relapsing autoimmune skin disease, conventionally divided into acute, subacute and chronic subtypes [1]. It may be skin-limited or coexist with systemic lupus erythematosus (SLE), and some skin-limited cases progress to systemic disease; reported progression ranges from 0% to 42% in adults, depending on population, criteria and follow-up [2].

Lupus is accompanied by many coexisting conditions. Multimorbidity, the presence of two or more chronic conditions, treats these as equally relevant to the patient [3]. In a United States population-based cohort, about four in five patients with established SLE had multimorbidity [4], and a Cretan registry showed high physical and mental burden [5]. As survival improves, chronic conditions increasingly shape long-term outcome [6].

Evidence for CLE is thinner. Danish nationwide cohorts found more cardiovascular events (hazard ratio 1.31) [7], depression (hazard ratio 2.07) [8] and cancer [9] in CLE than in the general population. A United States population-based study, available as a conference abstract, reported multimorbidity in 79.5% of patients with CLE versus 65.7% of controls [10]; it enrolled older patients (mean age 59.4 years), excluded concomitant SLE and used diagnostic codes, so its findings may not transfer to younger patients elsewhere.

Comorbidity in CLE has not been examined systematically in Bangladesh, where clinical and histopathological features have been described [11]. Studies from South Africa suggest that infections, including tuberculosis, weigh heavily in lupus in low-resource settings [12,13]. A hospital-based Bangladeshi study is relevant because tertiary centres such as Chittagong Medical College Hospital receive referred patients with the most complex disease, so the comorbidity found there indicates the care needs that specialist services must be ready to meet. It also provides baseline data in a setting with high rates of infectious disease, rural residence and limited

ISSN: 2663-9491 e-ISSN: 2789-6897

screening, where patterns may differ from those in high-income countries. We therefore aimed to describe the frequency and pattern of physical and mental comorbidity in patients with CLE at a tertiary hospital in Chattogram, quantify burden with the CCI, estimate multimorbidity prevalence, and explore whether sociodemographic and clinical characteristics were associated with multimorbidity.

METHODS & MATERIALS

Design, setting and participants

This descriptive cross-sectional, hospital-based study was conducted at Chittagong Medical College Hospital (CMCH), Chattogram, from January to December 2023. Patients were recruited consecutively from the dermatology, medicine, nephrology and rheumatology services. Eligible patients were aged 18 years or older with CLE, either primary or with a diagnosis of SLE (or four or more American College of Rheumatology criteria for SLE). The diagnosis was validated by record review, physician assessment and skin photographs, and skin biopsy with direct immunofluorescence was used where clinically indicated. Patients who did not consent or had difficulty communicating were excluded. The sample therefore includes CLE with or without systemic lupus; only 11 patients had primary CLE.

Sample size

The sample size was calculated for a single proportion ($n = Z^2pq/d^2$) using the multimorbidity prevalence of 79.5% reported by Hocaoglu et al. [10], rounded to 80%, with 95% confidence and precision of 10% of p (d=0.08). This gave 96.04, rounded to 96. The calculation targeted prevalence and was not designed to power the association analyses.

Data collection and variables

A pretested structured case record form was used. Sociodemographic, disease and treatment data came from face-to-face interview and record review. Clinical and dermatological examination, anthropometry and blood pressure measurement were performed, and venous blood was tested at the CMCH laboratory (antinuclear and anti-double-stranded DNA antibodies, complete blood count, creatinine, alanine aminotransferase, glucose, thyroid-stimulating hormone, lipids, complement and anti-phospholipid antibodies), with urine, imaging, skin and renal biopsy as clinically indicated. Comorbidity was assessed from patient report during interview together with medical record and hospital data. Socioeconomic class followed the modified Kuppuswamy scale [14]. CLE was classified as acute, subacute or chronic [1], and as localized (above the neck) or generalized (extending below the neck).

Disease activity was measured with the CLASI activity score [15], classified as mild (0 to 9), moderate (10 to 20) or severe (21 to 70) [16]. Study definitions were: hypertension, blood pressure above 140/90 mmHg on at least two visits or antihypertensive treatment; diabetes mellitus, fasting glucose above 7 mmol/L (126 mg/dL) on two measurements or treatment; chronic kidney disease, estimated glomerular filtration rate below 60 for over three months or chronic alterations on structural and urinary assessment; hepatic disease, chronic hepatitis B or C, steatohepatitis or cirrhosis; cardiovascular disease, a history of coronary revascularization, myocardial infarction, angina or stroke; neoplastic disease, any past or present neoplasia diagnosed by a registered physician; and obesity, BMI of 30.0 kg/m^2 or above or waist circumference of 90 cm (men) or 80 cm (women). Multimorbidity was two or more comorbidities, and participants were classed as having none, one, or multimorbidity.

Charlson Comorbidity Index and HADS

The CCI [17] was scored using the weights adapted by Deyo et al. [18], from one point (for example myocardial infarction, heart failure, chronic pulmonary disease, mild liver disease, diabetes without organ damage) to six points (metastatic cancer, HIV infection). The connective tissue disease item was modified to include disorders other than SLE, mainly anti-phospholipid syndrome and Sjogren syndrome. Hypertension, tuberculosis, serious infection, avascular necrosis and osteoporosis were documented but are not part of the classical index and were not assumed to contribute to the score. Depression and anxiety were assessed with the 14-item HADS [19], which has seven-item depression and anxiety subscales (each 0 to 21); the thesis took scores above 8 to indicate possible mood disorder and 10 to delimit pathology.

Statistical analysis

Data were analysed in SPSS. Continuous variables were summarized as mean ± SD, or median and interquartile range if not normally distributed; categorical variables as frequencies and percentages. Patients with multimorbidity were compared with those without (none or one comorbidity) using Student's t-test, the Mann-Whitney U test or the chi-square test, as appropriate. Significance was set at $p<0.05$. No multivariable regression, adjusted modelling, confidence intervals or effect sizes were produced.

Ethics

The Ethical Review Committee of Chittagong Medical College approved the study, and CMCH administration granted permission. Participants received an information letter, gave written informed consent, and were identified only by code. Interviews and examinations were conducted in private.

RESULTS

Participants and sociodemographic profile

Of 100 patients assessed, four declined and 96 were analysed. Mean age was 32.5 ± 11.6 years (range 17.0 to 76.0), with 41.7% aged 20 to 29 years. Women made up 91.7% (88 patients). Most lived in rural areas (67, 69.8%), were married (79, 82.3%) and were housewives (66, 68.8%). About half (49, 51.0%) had education above primary up to secondary level, and 43.8% belonged to the upper lower socioeconomic class (**Table I**).

Clinical characteristics and laboratory findings

Mean age at onset was 28.7 ± 11.1 years. Disease duration was under 5 years in 68.8%. Generalized disease affected 77 patients (80.2%) and systemic manifestations 83 (86.5%). Common presenting features were photosensitivity (81.3%), joint pain (79.2%), pruritus (79.2%), oral ulcer (74.0%), fever (72.9%) and malar rash (72.9%). The mean CLASI activity score was 13.8 ± 10.3; activity was mild in 44.8%, moderate in 33.3% and severe in 21.9%. Hydroxychloroquine was used by 78.1% and prednisolone by 44.8%; 8.3% took no systemic immunosuppressant (**Table I**). Antinuclear antibodies were positive in 75.0% and anti-double-stranded DNA in 46.9%; anemia was present in 34.4%, hypocomplementemia in 10.4%, anti-phospholipid antibodies in 5.2%, and abnormal urinalysis in 49.0%. Renal biopsy was recorded for 8 patients (8.3%). Serum creatinine was abnormal in 8 patients (8.3%), alanine aminotransferase was raised in 10 (10.4%), chest radiography was abnormal in 13 (13.5%), and 24-hour urinary protein exceeded 0.5 g in 23 patients. Other dermatological conditions such as paronychia, erythema multiforme, scarring alopecia, vitiligo, Stevens-Johnson syndrome and toxic epidermal necrolysis each affected one or two patients.

Physical, dermatological and infectious comorbidity

Lupus nephritis affected 24 patients (25.0%), thyroid dysfunction 22 (22.9%; 19 hypothyroidism, 3 hyperthyroidism), diabetes mellitus 19 (19.8%), hypertension 18 (18.8%), ischemic heart disease 13 (13.5%), dyslipidemia 10 (10.4%) and chronic kidney disease 7 (7.3%) (**Table II**, **Figure 1**). All lupus nephritis and chronic kidney disease cases were previously known, whereas most cases of thyroid dysfunction (18 of 22), diabetes (13 of 19), hypertension (13 of 18), ischemic heart disease (12 of 13) and dyslipidemia (9 of 10) were newly identified during the study assessment. Raynaud phenomenon (10, 10.4%), scleroderma (5, 5.2%), interstitial lung disease (3, 3.1%), osteoporosis (4, 4.2%) and malignancy (2, 2.1%; one squamous and one basal cell carcinoma) were less frequent. Secondary infection was recorded in 64 patients (66.7%), scabies in 17 (17.7%), candidiasis in 11 (11.5%), and tuberculosis-related diagnoses five times.

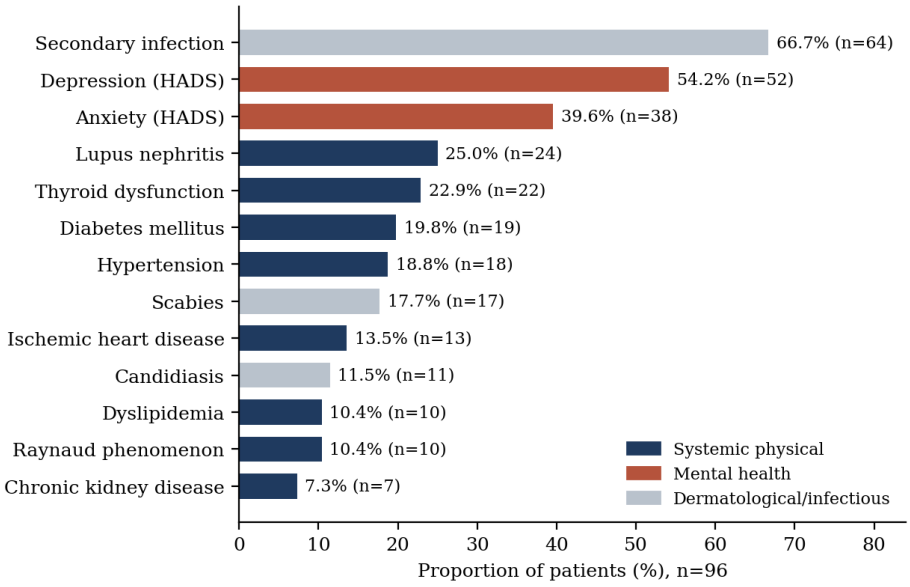


Figure 1: Frequency of the main comorbidities among patients with cutaneous lupus erythematosus (n=96). HADS, Hospital Anxiety and Depression Scale

Depression, anxiety, CCI and multimorbidity

By HADS, 52 patients (54.2%) had depression and 38 (39.6%) had anxiety. The mean CCI was 3.25 ± 1.62; only 2 patients scored 0, 74 (77.1%) scored 2 to 5, and scores ranged up to 8 (*Table III, Figure 2*). Sixty-six patients (68.8%) had multimorbidity, 23 (24.0%) a single comorbidity, and 7 (7.3%) none.

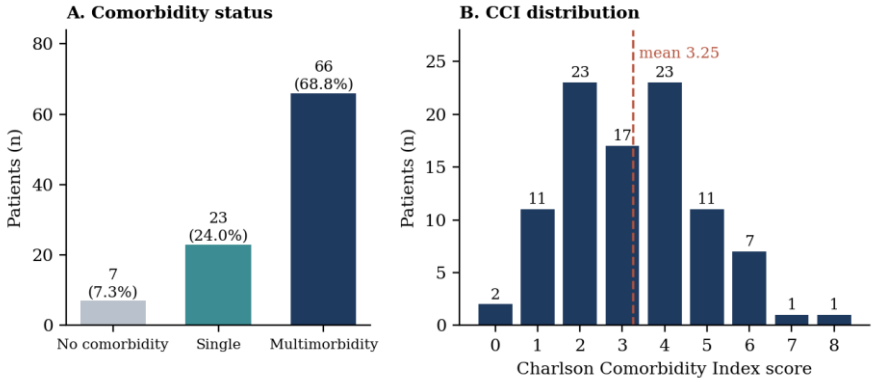


Figure 2: (A) Comorbidity status and (B) distribution of Charlson Comorbidity Index scores among 96 patients with cutaneous lupus erythematosus

Factors explored in relation to multimorbidity

Patients with multimorbidity were on average 33.8 ± 15.9 years old versus 29.7 ± 7.5 years in those without (p=0.106). Multimorbidity was not significantly associated with sex (p=0.690), education (p=0.174), residence (p=0.142), marital status (p=0.449), occupation (p=0.317) or socioeconomic class (p=0.890) (*Table IV*). Median age at onset was 26.0 years (interquartile range 20.0 to 36.0) with multimorbidity and 27.0 (19.0 to 32.5) without (p=0.624). No significant association was seen with disease duration (p=0.315), CLE type (p=0.091), systemic manifestations (p=0.546) or disease activity (p=0.814) (*Table V, Figure 3*). Overall, the exploratory bivariate analyses did not identify statistically significant sociodemographic or clinical correlates of multimorbidity.

ISSN: 2663-9491 e-ISSN: 2789-6897

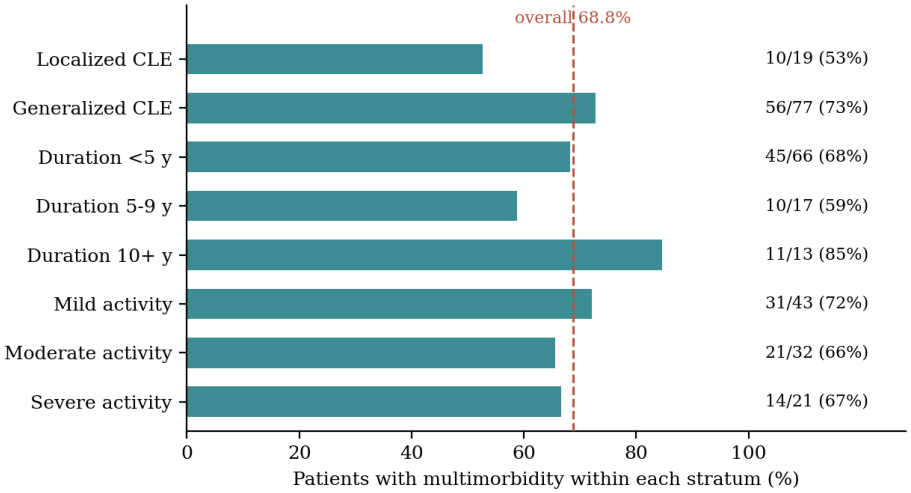


Figure 3: Proportion of patients with multimorbidity within clinical strata

Table I: Sociodemographic and clinical characteristics of patients with cutaneous lupus erythematosus (*n*=96)

Characteristic	n (%) or mean ± SD
Sociodemographic	
Age, years, mean ± SD (range)	32.5 ± 11.6 (17.0 to 76.0)
Age <20 years	8 (8.3)
Age 20 to 29 years	40 (41.7)
Age 30 to 39 years	24 (25.0)
Age 40 to 49 years	15 (15.6)
Age 50 to 59 years	5 (5.2)
Age 60 years or more	4 (4.2)
Sex: female / male	88 (91.7) / 8 (8.3)
Residence: rural / urban	67 (69.8) / 29 (30.2)
Education: no formal / primary or below	10 (10.4) / 26 (27.1)
Education: above primary to secondary / higher secondary or above	49 (51.0) / 11 (11.5)
Marital status: married / unmarried	79 (82.3) / 17 (17.7)
Occupation: housewife / service / other	66 (68.8) / 14 (14.6) / 16 (16.7)
Socioeconomic class: upper or lower middle / upper lower / lower	28 (29.2) / 42 (43.8) / 26 (27.1)
Clinical	
Age at onset, years, mean ± SD (range)	28.7 ± 11.1 (14.0 to 65.0)
Disease duration: <5 / 5 to 9 / 10 or more years	66 (68.8) / 17 (17.7) / 13 (13.5)
CLE type: localized / generalized	19 (19.8) / 77 (80.2)
Systemic manifestations present	83 (86.5)
Primary CLE (no systemic lupus)	11 (11.5)
Family history of CLE or SLE	4 (4.2)
CLASI activity score, mean ± SD (range)	13.8 ± 10.3 (0 to 42)
Mild (0 to 9)	43 (44.8)
Moderate (10 to 20)	32 (33.3)
Severe (21 to 70)	21 (21.9)
Body mass index, kg/m^2, mean (range)	22.7 (12.0 to 35.4)
Current systemic treatment	
Hydroxychloroquine	75 (78.1)
Prednisolone	43 (44.8)
Methotrexate / azathioprine	6 (6.3) / 6 (6.3)
Mycophenolate mofetil / intravenous cyclophosphamide	5 (5.2) / 3 (3.1)
No systemic immunosuppressant	8 (8.3)

CLE, cutaneous lupus erythematosus; CLASI, Cutaneous Lupus Erythematosus Disease Area and Severity Index; SD, standard deviation; SLE, systemic lupus erythematosus.

Percentages were calculated from the reported counts with a denominator of 96. Patients could receive more than one drug.

ISSN: 2663-9491 e-ISSN: 2789-6897

Table II: Frequency and distribution of major systemic, mental, dermatological and infectious comorbidities among patients with cutaneous lupus erythematosus (*n*=96)

Comorbidity	n	%	Previously known	Newly identified
Systemic physical comorbidities				
Lupus nephritis	24	25.0	24	0
Thyroid dysfunction*	22	22.9	4	18
Diabetes mellitus	19	19.8	6	13
Hypertension	18	18.8	5	13
Ischemic heart disease	13	13.5	1	12
Dyslipidemia	10	10.4	1	9
Chronic kidney disease	7	7.3	7	0
Mental health (HADS)				
Depression	52	54.2	NR	NR
Anxiety	38	39.6	NR	NR
Dermatological and infectious				
Secondary infection	64	66.7	NR	NR
Scabies	17	17.7	NR	NR
Candidiasis	11	11.5	NR	NR
Tuberculosis-related diagnoses†	5	5.2	NR	NR
Rheumatological and connective tissue overlap				
Raynaud phenomenon	10	10.4	NR	NR
Scleroderma	5	5.2	NR	NR
Progressive systemic sclerosis	2	2.1	NR	NR
Other organ systems				
Interstitial lung disease	3	3.1	NR	NR
Pulmonary hypertension	2	2.1	NR	NR
Chronic obstructive pulmonary disease	2	2.1	NR	NR
Myelitis	2	2.1	NR	NR
Osteoporosis	4	4.2	NR	NR
Malignancy‡	2	2.1	NR	NR

HADS, Hospital Anxiety and Depression Scale; NR, not reported in the source data. Percentages use a denominator of 96, and one patient may have more than one condition.
** Nineteen patients had hypothyroidism and three had hyperthyroidism. † Tuberculous lymphadenitis (2), pulmonary tuberculosis (2) and intestinal tuberculosis (1), counted as diagnoses. ‡ One squamous cell carcinoma and one basal cell carcinoma.*

Previously known and newly identified are the terms for the source labels old case and new case; newly identified refers to conditions first recorded during the study assessment.

Table III: Distribution of Charlson Comorbidity Index and overall multimorbidity status among patients with cutaneous lupus erythematosus (*n*=96)

Measure	n (%)
Charlson Comorbidity Index score	
0	2 (2.1)
1	11 (11.5)
2	23 (24.0)
3	17 (17.7)
4	23 (24.0)
5	11 (11.5)
6	7 (7.3)
7	1 (1.0)
8	1 (1.0)
Mean ± SD	3.25 ± 1.62
Comorbidity status	
No comorbidity	7 (7.3)
Single comorbidity	23 (24.0)
Multimorbidity (two or more)	66 (68.8)

SD, standard deviation. Score frequencies were taken from the frequency histogram of the study data. Percentages may not sum to 100 because of rounding.

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Table IV: Association of sociodemographic characteristics with multimorbidity

Variable	Multimorbidity present (n=66)	Multimorbidity absent (n=30)	p value
Age, years, mean ± SD	33.8 ± 15.9	29.7 ± 7.5	0.106†
Sex			
Female	61 (92.4)	27 (90.0)	0.690
Male	5 (7.6)	3 (10.0)	
Education			
No formal education	6 (9.1)	4 (13.3)	0.174
Primary or below	20 (30.3)	6 (20.0)	
Above primary to secondary	30 (45.5)	19 (63.3)	
Higher secondary or above	10 (15.2)	1 (3.3)	
Place of residence			
Rural	43 (65.2)	24 (80.0)	0.142
Urban	23 (34.8)	6 (20.0)	
Marital status			
Married	53 (80.3)	26 (86.7)	0.449
Unmarried	13 (19.7)	4 (13.3)	
Occupation			
Housewife	44 (66.7)	22 (73.3)	0.317
Service	12 (18.2)	2 (6.7)	
Others	10 (15.2)	6 (20.0)	
Socioeconomic class			
Upper middle and lower middle	20 (30.3)	8 (26.7)	0.890
Upper lower	29 (43.9)	13 (43.3)	
Lower	17 (25.8)	9 (30.0)	

Data are n (%) unless stated. Multimorbidity present: two or more comorbidities; absent: none or one. Chi-square test for categorical variables; † independent-samples test for age, as reported in the source.

The percentage for higher secondary education or above in the absent group was recalculated from 1 of 30 (3.3%).

Table V: Association of clinical characteristics with multimorbidity

Variable	Multimorbidity present (n=66)	Multimorbidity absent (n=30)	p value
Age at onset, years, median (IQR)	26.0 (20.0 to 36.0)	27.0 (19.0 to 32.5)	0.624‡
Duration of disease			
<5 years	45 (68.2)	21 (70.0)	0.315
5 to 9 years	10 (15.2)	7 (23.3)	
10 years or more	11 (16.7)	2 (6.7)	
Type of CLE			
Localized	10 (15.2)	9 (30.0)	0.091
Generalized	56 (84.8)	21 (70.0)	
Systemic manifestations			
Present	58 (87.9)§	25 (83.3)	0.546
Absent	8 (12.1)§	5 (16.7)	
Disease activity (CLASI)			
Mild	31 (47.0)	12 (40.0)	0.814
Moderate	21 (31.8)	11 (36.7)	
Severe	14 (21.2)	7 (23.3)	

Data are n (%) unless stated. IQR, interquartile range; CLE, cutaneous lupus erythematosus; CLASI, Cutaneous Lupus Erythematosus Disease Area and Severity Index. Chi-square test for categorical variables; ‡ Mann-Whitney U test.

§ Counts in the multimorbidity-present column were obtained by subtracting the multimorbidity-absent counts from the whole-sample totals (83 and 13), because the source table displayed the whole-sample totals in this column. The reported p value is unchanged. Percentage for generalized disease in the present group recalculated as 56 of 66 (84.8%).

DISCUSSION

In this hospital-based study of 96 patients with CLE, about two thirds had two or more comorbidities and only 7.3% had none. Secondary infection, depression, anxiety, lupus nephritis, thyroid dysfunction, diabetes and hypertension were the most frequent conditions, and the mean CCI was 3.25. No sociodemographic or clinical variable was significantly associated with multimorbidity. With a single centre and no comparison group, these findings describe burden and pattern in this population and do not show excess risk relative to people without CLE.

Overall multimorbidity burden

Multimorbidity prevalence (68.8%) was lower than in a United States population-based CLE study (79.5%) [10] and in established SLE (81.5%) [4], and higher than in new-onset SLE (57.0%) [4]. A Finnish study of incident SLE reported about three quarters with two or more comorbidities [20]. These figures are not directly comparable. The American studies used diagnostic codes with look-back periods and counted 44 or 57 conditions [4,10], whereas we combined interview, record review and examination for a narrower set. Their CLE cohort was also much older (mean 59.4 years versus 32.5) and excluded SLE, while 86.5% of our patients had systemic

manifestations. In Crete, over half of patients with SLE had three or more physical comorbidities and about one third had two or more mental comorbidities [5], and the authors of the American SLE study themselves attributed differences from that Cretan report to thresholds, the number of categories and recall bias [4]. In an Egyptian cohort of 902 patients with SLE, comorbidity was found in 75.5% [21]. Ascertainment, the number of conditions counted, age and disease spectrum therefore plausibly explain the differences, and the true burden in CLE from South Asia can only be judged against a matched control group.

The demographic and clinical profile of our cohort resembles earlier reports from the same hospital and from Bangladesh more widely [11]: patients were young, predominantly female, and most had CLASI activity in the mild or moderate range. This supports the view that the cohort is typical of patients attending this referral centre, although it is not representative of patients managed in the community.

Renal and cardiometabolic comorbidity

Lupus nephritis (25.0%) and chronic kidney disease (7.3%) are distinct: the first is an immune-mediated organ manifestation, the second a functional and structural definition with several possible causes. Only 8 patients had a renal biopsy, so we could not relate chronic kidney disease to nephritis. Given the high proportion with systemic features and the documented risk of progression from CLE to SLE [2], regular renal monitoring seems prudent.

Hypertension (18.8%), diabetes (19.8%), ischemic heart disease (13.5%) and dyslipidemia (10.4%) were present at a mean age of only 32.5 years. Hypertension was less frequent than in the older American SLE cohort (45.9%) [4]. A Danish study reported a 31% higher hazard of cardiovascular events in CLE than in the general population [7], but our design cannot address relative risk. Diabetes and prediabetes together affect over a quarter of Bangladeshi adults [22], so the burden here may partly reflect background prevalence. Dyslipidemia is a recognized comorbidity of SLE [23]; the low figure here may reflect limited testing or thresholds that were not fully described. That 12 of 13 ischemic heart disease cases were newly identified warrants caution, because the study definition of cardiovascular disease (revascularization, infarction, angina or stroke) does not map neatly onto that label. Inflammation, metabolic risk and glucocorticoid exposure (44.8% took prednisolone) are plausible contributors, but cross-sectional data cannot establish causality. Current recommendations favor hydroxychloroquine and minimizing glucocorticoids in SLE [24].

Thyroid disease

Thyroid dysfunction (22.9%, mostly hypothyroidism) was common, and 18 of 22 cases were newly identified. Hypothyroidism was more frequent in CLE than in matched controls in a population-based study [10], and in established SLE (20.9% versus 12.0%) [4]. Serum thyroid-stimulating hormone was abnormal in 20 patients (20.8%); the small difference from the 22 patients with a thyroid diagnosis may reflect previously diagnosed patients whose hormone levels were normal on treatment. Antithyroid antibodies were not measured, so we cannot comment on autoimmune mechanisms, and thyroid screening in this group is worth testing prospectively.

Infection

Secondary infection (66.7%), scabies (17.7%), candidiasis (11.5%) and tuberculosis-related diagnoses were prominent. Secondary infection was recorded among associated skin diseases and should not be equated with the serious infection defined in the Methods. Infection is a recognized part of lupus comorbidity: UK primary care data showed a heavier comorbidity burden in SLE than in controls [25], and South African reports describe a wide infectious spectrum including tuberculosis [12,13]. Immune dysregulation, immunosuppression and comorbid disease may contribute, but most of our patients took hydroxychloroquine and few took other immunosuppressants. In the South African studies, infection was a frequent comorbidity and a cause of hospital admission and death [12,13], which underlines why infection surveillance deserves attention in resource-limited settings. Scabies hints that living conditions and access to care may matter, though this is speculative and was not measured.

Depression and anxiety

More than half of patients had depression (54.2%) and 39.6% had anxiety by HADS. These proportions exceed the 25.4% depression recorded from diagnostic codes in an SLE cohort [4], but the HADS screens for symptoms and codes capture diagnoses, so the two are not equivalent. Danish data show a twofold hazard of depression in CLE [8], and a systematic review found wide variation in depression and anxiety prevalence in SLE, partly from differences in assessment [26]. Visible and scarring disease, chronicity, pain, stigma and socioeconomic strain are plausible contributors but were not tested, and the HADS cut-off strongly influences prevalence. The signal nonetheless supports routine mental health screening in CLE clinics.

Charlson Comorbidity Index

A mean CCI of 3.25, with only 2 patients scoring 0, indicates substantial index-based burden in a young cohort. The CCI was designed to predict mortality [17], was adapted for administrative data [18], and has been associated with mortality in SLE [27]. Its usefulness here is limited: hypertension, thyroid disease, tuberculosis, serious infection, osteoporosis, depression and anxiety are outside the classical index, and its connective tissue item was modified. That 2 patients had a CCI of 0 while 7 had no recorded comorbidity suggests the index and the comorbidity count drew on different item sets. The CCI should be read as a descriptive, study-specific summary rather than a prognostic estimate.

Absence of associations with multimorbidity

No sociodemographic or clinical variable was significantly associated with multimorbidity. This does not show that these factors have no effect. The sample was sized to estimate prevalence, not to detect group differences, the group without multimorbidity was small (n=30), and no confidence intervals were calculated, so modest associations could easily have been missed. Other explanations include the cross-sectional design, a fairly homogeneous population of young, mostly female, rural patients of lower socioeconomic class, tertiary referral, narrow measurement of comorbidity, lack of data on exposures such as cumulative glucocorticoid dose, no multivariable modelling and residual confounding. Other studies did find correlates: older age and higher BMI in established SLE, plus smoking in new-onset SLE [4], and links with severity and social factors in Crete [5]. In our data, patients with multimorbidity were somewhat older and more often had generalized disease or 10 or more years of duration (Figure 3), but none of these differences was significant and they are hypothesis-generating at most.

Clinical implications

The findings support proportionate, systematic comorbidity assessment in CLE, particularly with systemic features: blood pressure, glucose and lipids, thyroid function, urinalysis and renal function, cardiovascular risk, infection awareness including tuberculosis, and depression and anxiety screening. That most cardiometabolic and thyroid conditions were newly identified suggests screening may uncover unrecognized

disease, though cost-effectiveness is unknown. Integrated care across dermatology, rheumatology, nephrology and mental health may be appropriate [6]. For patients with CLE who are taking hydroxychloroquine or prednisolone, baseline and periodic screening for glucose intolerance, blood pressure and bone health may be particularly relevant, and current lupus guidance provides a framework for minimizing glucocorticoid exposure [24]. Screening for depression and anxiety, with a clear referral pathway, can be added at low cost during dermatology visits. These suggestions rest on descriptive data and need testing in prospective studies.

STRENGTHS & LIMITATIONS

Strengths include consecutive recruitment with few refusals (4 of 100), combined clinical, dermatological and laboratory assessment, use of established instruments (CLASI, HADS, CCI), joint assessment of physical and mental comorbidity, and, to our knowledge, some of the first comorbidity data for CLE in Bangladesh.

Limitations are as follows. There was no control group without CLE. Recruitment was hospital-based at one tertiary centre with a modest sample, limiting generalizability and power. The design was cross-sectional and mainly descriptive, precluding causal inference, and no multivariable modelling or confidence intervals were used. Some comorbidities were not assessed systematically, so osteoporosis and malignancy may be under-detected; few patients had bone densitometry despite corticosteroid exposure. The sample mixed primary CLE (n=11) with CLE plus systemic lupus, so results do not apply to skin-limited CLE. Some operational definitions differ in wording from current guideline conventions, which could cause minor misclassification. The CCI carried a study-specific modification, and the HADS case cut-off and multimorbidity item list need explicit specification. Because the survey relied partly on patient report and hospital records, recall bias and incomplete records may have led to under-ascertainment, especially for conditions that require specific tests. Finally, the association analyses compared 66 patients with 30, so even large differences in proportions might not have reached statistical significance. Multicentre evaluation would strengthen the evidence.

CONCLUSION

Patients with CLE in this tertiary-care cohort from Bangladesh had a substantial burden of physical and mental comorbidity, and multimorbidity was common (68.8%). The main burdens were lupus nephritis, thyroid disease, diabetes, hypertension, ischemic heart disease, dyslipidemia, chronic kidney disease, depression, anxiety and infection. No statistically significant association was found between multimorbidity and the sociodemographic or clinical variables measured, but limited power and the exploratory design mean a true association cannot be excluded. Findings come from one hospital and should not be extrapolated to national prevalence. Larger multicentre prospective studies with multivariable modelling are needed.

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