Research Paper

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Characteristics of Patients With Systemic Lupus Erythematosus Currently on Remission, With Active Disease But Not Experiencing Flare, And Those Experiencing Flares in Clinical Practices in Europe

Medical Science

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Siva Narayanan | MS MHS SVP and Global Head, Global Evidence, Value and Access

Ipsos Healthcare | 2020 K Street Washington, DC, 20006, USA

ABSTRACT

Assessing the characteristics of patients with Systemic Lupus Erythematosus (SLE) currently on Remission (Group-1), currently with active disease but not experiencing a flare (Group-2) and those who are experiencing flares (Group-3) could help portray SLE burden. A multi-center chart review of adult SLE patients was conducted among rheumatologists/internal medicine physicians in UK/France/Germany/Italy/Spain (EU5) to collect data on disease characteristics and treatment patterns. 747 SLE patient charts were abstracted; 25.7%/56.2%/18.1% were Groups 1/2/3 respectively; 23.4%/32.1%/55.6% in Groups 1/2/3 respectively had >=1 hospitalization in past 12mo. Patients with serum hypocomplementemia and impairment to perform every-day activities, work/keep employment or interact with family/friends were higher among Groups 3/2 and they had higher SELENA-SLEDAI score vs. Group 1. Clinical and humanistic burden varied based on patient disease status, with highest burden observed among those experiencing flares. Appropriate interventions aimed at decreasing disease activity and flares could prove beneficial to alleviate SLE disease burden.

INTRODUCTION

Systemic lupus erythematosus (Lupus, SLE) is a chronic autoimmune disease which affects multiple organ systems, including musculoskeletal, renal, neuropsychiatric, and hematologic manifestations. (Oglesby 2013) SLE patients typically experience multiple organ manifestations. [Meacock 2013] SLE is a complex disease with important genetic factors. Due to lack of effective treatments and the difficulty in developing new drugs in the SLE area, disease burden remains high. (Eisenberg 2009)

SLE is characterized by periods of fluctuating disease activity, ranging from a period of minimal disease activity to a period of 'flare'. (Meacock 2013) Flares have been shown to impact SLE disease burden, encompassing clinical (e.g., organ damage), economic (e.g., higher healthcare resource use such as hospitalizations) and humanistic attributes (e.g., lower health-related quality of life). (Narayanan 2013; Pollard 2015; Zhu 2009; Zhu 2011) Even varying degrees of disease activity shy of a flare imposes burden on the patient. (Kan 2013, Steiman 2012) The variability of SLE symptoms causes problems in disease assessment in everyday practice. Data suggest that all the most widely used indices for assessing disease severity are acceptable for use, although further efforts are required to establish a consensus on definition of remission in SLE. (Mosca 2006)

Identifying SLE patients currently experiencing disease remission (or quiescent disease), those with active disease (but no flare) and those experiencing a disease flare may help discriminate patient needs based on their disease status/burden and thereby better inform future strategies for optimal disease management and therapeutic interventions.

MATERIAL AND METHODS

The study was a multi-country, multi-center retrospective medical chart review of adult (16-89 years old) SLE patients, conducted among rheumatologists in the big-5 European countries (EU5), namely, the UK, France, Germany, Italy and Spain. Physicians of rheumatology and internal medicine specialty were sampled in each of the countries using online physician panels to attain a geographically representative sample in respective regions. Invitations to participate in our research were sent to a random set of physicians in the existing online physician panels. The physicians representing both hospital-based and private practices in each geography, personally responsible for choosing and prescribing treatment for patients with SLE, and treating a minimum of 15 SLE patients per month and having 3-35 years of clinical practice experience were screened for study participation. Each physician reported de-identified anonymous data on patients who were recently treated with a biologic as part of usual care. Up to 5 patient charts were randomly selected by each physician from a sample of prospective patients visiting their respective center/practice during the study screening period in 1Q2014, if the patient(s) had persistent active or relapse remitting disease and was being managed as part of usual care.

The electronic data collection form was used to collect the following data elements from eligible patient charts: patient demographics, laboratory values, treatment patterns/dynamics and patient symptomatology pertaining to the different organ manifestations. Physicians also assessed the humanistic burden of the patient (on a scale of 1 (unable to perform) – 7 (does not have any problem performing)) based on clinical judgment and patient interaction by reporting patient ability to perform everyday tasks, patient ability to interact fully with family and friends, and patient ability to work/keep employment. Only de-identified anonymous data was collected from the patient charts by the treating physicians. This mode of data collection method met the criteria for local ethics review exemption per the respective physician/site requirements in the EU5.

The SLE patients were stratified into patients currently in remission (Group-1), currently with active disease but not experiencing a flare (Group-2), and those who were experiencing flares (Group-3), per physician clinical judgment. C3 & C4 complement test results were classified as 'low' if the values were <900 mg/L and <16 mg/dL respectively. Patients were classified as anti-ds-DNA positive if the laboratory results were >=30 IU/mL. Descriptive statistics were utilized to analyze the data, comparing the three patient groups. Statistical differences were assessed using chi-square tests for categorical variables or t-tests for continuous variables; p-values of <0.05 were considered significant in all analyses.

RESULTS AND DISCUSSIONS

Physicians abstracted 747 eligible SLE patient charts in the EU5 (UK: 156, France: 149, Germany: 148, Italy: 146, Spain: 148). Overall, 25.7% were classified to be in remission (Group-1) and 56.2% to be with active disease but not experiencing a flare (Group-2), while 18.1% were classified to be currently experiencing a flare. Patient distribution across these disease severity groups differed by country. (Table-1)

Table 1: Distribution of Patient Groups by Country

	Group-1: In Remission	Group-2: With active disease but not experiencing a flare	Group-3: Experiencing a flare
United Kingdom (N=156), %	28.8	42.3	28.8[F,G,I]
France (N=149), %	29.5	55.7	14.8
Germany (N=148), %	29.7	56.8	13.5
Italy (N=146), %	19.9	66.4[U]	13.7
Spain (N=148), %	20.3	60.8	18.9

Note: U,F,G,I – Significantly different from UK, France, Germany, Italy respectively at p<0.05, within the respective groups

Across the countries and patient groups, mean age of the SLE study cohort was 42.2 yrs, and 80.2% were female; 35.1% were currently (at the time of the study) in full-time employment, whereas 21.3% were in part-time employment and 8.3% were in sick leave. These employment characteristics varied slightly between the three patient groups, with a lower proportion of patients in full-time or part-time employment within the group experiencing a flare (Group-3), while more patients in Group-3 were in sick leave. A significantly higher proportion of patients in Group-3 were either currently hospitalized or were hospitalized at least once in the past 12 months. More patients in Gorup-3 had hematologic, renal or pulmonary organ manifestations due to their SLE disease, in comparison to patient Groups 1 & 2. (Table 2)

Table 2: Patient Demographic and Clinical Characteristics

	Group-1: In Remission (N=192)	Group-2: With active disease but not experiencing a flare (N=420)	Group-3: Experiencing a flare (N=135)
Age, mean	41.4	43.0	40.6
Female, %	81.8	80.2	77.8
Employment status:			
Currently working full-time, %	38.0	34.5	32.6
Currently working part-time, %	25.5	20.5	17.8
Currently on sick-leave, %	3.6	7.6	17.0*
Hospitalizations:			
Currently hospitalized (in-patient status), %	3.1	7.6	28.1*
Hospitalized at least once in the past 12 months, %	23.4	32.1	55.6*
Organ Manifestations (top-5):			
Musculoskeletal (%)	90.6	89.5	88.1
Mucocutaneous (%)	86.5	84.0	85.2
Haematologic (%)	45.8	53.8	55.6
Renal (%)	23.4	26.7	33.3
Pulmonary (%)	15.1	13.6	26.7*

***Significantly different from Groups 1 & 2 respectively at p<0.05**

Clinical characteristics of patients experiencing flares (Group-3) in comparison to those with active disease (Group-2) and those in remission (Group-1) based on select laboratory measures revealed a significantly higher disease burden among Group-3 patients; a significantly higher proportion of patients in Group-3 were anti-ds-DNA positive, a significantly higher proportion had low C3 & C4 complement levels and had a higher erythrocyte sedimentation rate. (Table 3)

Table 3: Select Laboratory Measures

	Group-1: In Remission (N=192)	Group-2: With active disease but not experiencing a flare (N=420)	Group-3: Experiencing a flare (N=135)
Anti-ds-DNA: % positive (>=30 IU/mL) (n)	54.7 (169)	71.0^ (389)	78.5^ (122)
Serum complement level - C3: % low (<900 mg/L) (n)	33.3 (174)	53.9^ (386)	73.4* (128)
Serum complement level – C4: % low (<16 mg/dL) (n)	31.6 (171)	53.2^ (385)	77.5* (129)
Erythrocyte Sedimentation Rate (ESR): mean mm/h	28.7 (149)	37.2 (357)	50.1* (115)

***Significantly different from Groups 1 & 2 respectively at p<0.05**

^ Significantly different from Group 1 at p<0.05

Latest SELENA-SLEDAI score as documented in the patient charts was the highest for Group-3, at 15.38 (n=40), while the scores were relatively lower for Group 2 (8.57; n=113) and Group-1 (5.60; n=48). Conversely, patient burden in terms of ability to work, ability to interact with family/friends and ability to perform everyday tasks were lower among Groups 1 & 2 (as shown by higher scores) in comparison to Group 3. (Table 4)

Table 4: Humanistic burden ratings

	Group-1: In Remission (N=192)	Group-2: With active disease but not experiencing a flare (N=420)	Group-3: Experiencing a flare (N=135)
Ability to work/keep employment	5.8*	4.8^	3.9
Ability to interact fully with family and friends	6.2*	5.5^	4.9
Ability to perform everyday tasks	6.1*	5.2^	4.4

Note: Response scale for the 3 items were: 1 (unable to perform) – 7 (does not have any problem performing).
*Significantly different from Groups 2 & 3 respectively at p<0.05
^ Significantly different from Group 3 at p<0.05

SLE is a complex disease with no cure and the course of the disease is unpredictable, with frequent periods of increased symptoms (flares) alternating with remission (or quiescent disease). Annual flare rates reported in the literature vary, with 60-70% of patients reporting at least one flare, and the economic burden of disease has been shown to distinctly vary based on the severity of flares. (Petri 2009; Buyon 2005; Narayanan 2013) This study found one in five patients experiencing flares at the time of the study, with more than half of the patients with an active disease. Among those with flares (Group 3) and with active disease (Group 2) respectively, 56% and 32% were hospitalized within the past 12 months, indicating the clinical and economic burden associated with these patient groups.

Besides anti-DS-DNA, serum hypocomplementemia (as documented via low C3 and C4) has been regarded as a sensitive indicator of lupus activity (zonana-nacach 2000; Tseng 2006) and has been found reliable in disease prognostication. (Kasitanon 2006) In this study cohort, proportion of patients who were anti-ds-DNA positive or with hypocomplementemia were significantly higher in Group 3 in comparison to Group 2 and Group 1, further highlighting the SLE clinical burden. This was further substantiated by the differential score of SELENA-SLEDAI among these groups.

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Previous studies have shown flares, especially the musculoskeletal flares and associated joint pain, are a significant predictor of low health related quality of life. (Pollard 2015; Zhu 2010; Doria 2004) The significantly diminished abilities to perform everyday tasks, interact with family/friends and work/keep employment among Group 3 and Group 2 in relation to Group 1 in this study highlights the humanistic burden and diminished quality of life among SLE patients.

Although physicians were randomly recruited for this study, the findings represent only the participating physician practices, and may vary from those of non-participating physician practices. Nevertheless, the SLE clinical and humanistic burden varied across the countries based on patient disease status, with highest burden observed among those experiencing flares and the lowest among those in remission.

Tseng et al (2006) has shown the addition of prophylactic, moderate-dose corticosteroids to prevent severe disease flares in patients with serologically active but clinically stable SLE could be beneficial. Long-term exposure to corticosteroids may however result in accrual of organ damage. (Zonana-Nacach 2000; Gladman 2003) Van Vollenhoven et al (2011) has shown that in the low complement/anti-dsDNA positive subgroup of patients from BLISS trials, belimumab reduced severe flares and corticosteroid use while improving health-related quality of life.

It is critical that relevant interventions tailored to individual patient disease status and comorbidities are considered to alleviate SLE disease burden, especially those associated with active disease and flares.

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