

Burden of Lupus Nephritis among Patients Managed in Routine Clinical Practices in Europe

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Subject: Immunology

Abstract: *Assessing the characteristics of patients with Lupus Nephritis (LN) in comparison to those without LN among patients with systemic lupus erythematosus (SLE) could help portray LN disease 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. 168 LN patients and 569 non-LN patients with SLE were analyzed. Among LN/Non-LN cohorts, % currently receiving care in in-patient setting was:14.9/8.8, % hospitalized ≥ 1 in the past-year was:49.4/29.7. Clinical burden (patients experiencing a flare, low C3/C4, higher SELENA-SLEDAI scores) and humanistic burden (diminished ability to perform every-day tasks, interact fully with family and friends, or work/keep employment) was higher among LN cohorts. Factors influencing the observed burden, including the therapeutic strategies used in these geographies warrant further investigation to manage LN optimally.*

Keywords: Lupus Nephritis, Burden, Flares, Hospitalizations, Europe

1. Introduction

Systemic lupus erythematosus (Lupus, SLE) is a chronic autoimmune disease which affects multiple organ systems [1]. Glomerulonephritis (or lupus nephritis; LN) caused by SLE is a common and severe SLE complication which is associated with significant mortality and morbidity, including adverse impact on daily activities and quality of life [1-4]. The incidence and prevalence of LN varies; the LN cumulative incidence is higher in people of Asian (55%), African (51%), and Hispanic (43%) ancestry compared with Caucasians (14%) [5]. Approximately 50% of patients with SLE will develop LN, which increases the risks for renal failure, cardiovascular disease and death [6-9].

Despite the significance of LN within the context of SLE, there is very little literature on current status of care management among the LN cohort, and especially in Europe. A retrospective observational cohort study was undertaken to identify the burden of LN among patients managed in routine clinical practices to highlight unmet needs and inform future strategies for optimal disease management.

2. Material and Methods

The study was a multi-country, multi-center retrospective medical chart review of adult 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 countries. Up to 5 SLE patient charts were selected by each physician from a

sample of prospective patients visiting their respective center/practice during the study screening period of Jan-March 2014, if the patient(s) had persistent active or relapse remitting disease and was being managed as part of usual care. The research methodology was reported elsewhere by Narayanan [2016] [10].

The electronic data collection form was used to collect the following data elements from medical charts of SLE patients treated with a biologic as part of usual care: 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 every-day tasks, patient ability to interact fully with family and friends, and patient ability to work/keep employment. Physicians further assessed the patient knowledge or interest in learning about their disease (on a scale of 1 (no knowledge about their disease or disinterested) to 7 (extremely knowledgeable/interested about their disease)) based on their most recent patient encounter. 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 LN and Non-LN cohort based on the documentation of diagnosis of LN in the patient charts. Descriptive statistics were utilized to analyze the data, comparing the two cohorts. 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.

Volume 5 Issue 5, May 2016

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3. Results

Physicians abstracted 168 LN and 569 non-LN patient charts in the EU5. The mean age of the LN cohort was higher than their non-LN counterparts (41.2yrs vs. 42.7yrs; $p < .05$); majority were female and Caucasian; approximately one-third and one-fifth of patients in both the cohorts had full-time and part-time employment respectively. A significantly higher proportion within LN cohort was either currently hospitalized or was hospitalized at least once in the past 12 months. LN cohort had significantly more number of organ manifestations, in comparison to their non-LN counterparts [Table 1].

Table 1: Patient Demographic and Clinical Characteristics

	LN Cohort (N=168)	Non-LN Cohort (N=579)
Age, mean years	41.2*	42.7
Female, %	82.7	79.4
Caucasian, %	82.7	88.8
Weight, kg	66.9	66.4
Employment status:		
Currently working full-time, %	32.1	35.9
Currently working part-time, %	19.0	21.9
Currently on sick-leave, %	9.5	7.9
Student, %	8.3	5.5
Hospitalizations:		
Currently hospitalized (in-patient status), %	14.9*	8.8
Hospitalized at least once in the past 12 months, %	49.4*	29.7
Number of organ manifestations, mean	3.9*	3.0
Organ Manifestations (top-5):		
Musculoskeletal (%)	85.1	90.8
Mucocutaneous (%)	85.1	84.8
Haematologic (%)	51.8	52.2
Renal (%)	100.0	5.9
Pulmonary (%)	16.7	16.2

*Significantly different from non-LN cohort at $p < 0.05$

Among the LN and non-LN cohorts, the frequency of clinic visits was 9.5 weeks and 10.6 weeks respectively. Renal biopsy was performed in 88% of LN cohort and 4% of Non-LN cohort. Significantly higher percentage of LN cohort were using immunosuppressants and steroids, in comparison to non-LN cohort, and they were more treatment experienced (having gone through 3 or more lines of treatment) [Table 2].

Table 2: Current treatment patterns

	LN Cohort (N=168)	Non-LN Cohort (N=579)
Class of drugs used:		
Steroids, %	82.1*	69.4
Antimalarials, %	67.3	62.0
Immuno-suppressants, %	71.4*	35.2
Line of treatment:		
1 st line, %	10.7	23.0
2 nd line, %	16.7	27.1
3 rd line, %	14.3	19.0
4 th line, %	20.2	14.2
5 th line, %	14.9	8.3
6 th + line, %	23.2	8.5

*Significantly different from non-LN cohort at $p < 0.05$

Clinical characteristics of LN cohort in comparison to non-LN cohort based on recent select laboratory measures

revealed a significantly higher disease burden among LN cohort; a significantly higher proportion of LN cohort had low C3 & C4 complement levels and a higher erythrocyte sedimentation rate [Table 3].

Table 3: Select Laboratory & Disease Severity Measures

	LN Cohort (N=168)	Non-LN Cohort (N=579)
Serum complement level - C3: % low (<900 mg/L) (n)	66.3* (160)	48.1 (528)
Serum complement level - C4: % low (<16 mg/dL) (n)	60.2* (161)	50.0 (524)
Erythrocyte Sedimentation Rate (ESR): mean mm/h (n)	40.2 (140)	36.8 (481)
SELENA-SLEDAI score, mean (n)	11.5* (49)	8.5 (152)

Note: SELENA-SLEDAI: Safety of Estrogens in Lupus Erythematosus National Assessment - SLE Disease Activity Index.

*Significantly different from non-LN cohort at $p < 0.05$

Latest SELENA-SLEDAI score as documented in the patient charts was significantly higher among LN cohort [Table 3]. Correspondingly, the percentage of patients experiencing a flare was 23% and 17% respectively among LN and non-LN cohorts. Patient burden in terms of diminished ability to work (or keep employment), interact with family/friends or perform everyday tasks were lower among LN cohort (as indicated by lower mean scores) in comparison to non-LN cohort [Table 4].

Table 4: Humanistic burden ratings

	LN Cohort (N=168)	Non-LN Cohort (N=579)
Ability to work/keep employment, mean (n)	4.5* (160)	5.0 (565)
Ability to interact fully with family and friends, mean (n)	5.4 (166)	5.6 (578)
Ability to perform everyday tasks, mean (n)	5.0* (168)	5.3 (579)

Note: Response scale for the 3 items were: 1 (unable to perform) - 7 (does not have any problem performing).

*Significantly different non-LN cohort at $p < 0.05$

On a scale of 1 (no knowledge about their disease or disinterested) to 7 (extremely knowledgeable/interested about their disease), physicians rated the LN and non-LN cohorts to be comparable (mean scores: 4.9 (LN) vs. 5.1 (non-LN)). Proportion of patients for whom their physicians gave a score of 7 was 10.7% among LN cohort in comparison to 14.3% among non-LN cohort.

4. Discussion

In this study, the clinical burden among LN cohort was high, as depicted by the higher SELENA-SLEDAI score and higher prevalence of patients with low C3 & C4 complement levels. A larger percentage of LN cohort were experiencing a flare at the time of study evaluation and had a higher healthcare resource utilization, in terms of hospitalization (either at the time of study (via receipt of care at in-patient settings) or at any time within the past 12 months) and frequent physician office visits. This increased healthcare resource utilization among SLE patients with renal manifestations, and especially, the LN

cohort in comparison to the Non-LN SLE cohort was consistent with past research reports [11-14]. This study further portrayed the diminished ability to work or keep employment among LN cohort in comparison to their non-LN counterparts. This is directionally consistent with the loss of productivity, absenteeism and short-term disability among patients with LN reported by Carls et al [2009] [11].

LN thus imposes significant clinical and economic burden to the patients with the condition and to the society at large [15]. The humanistic burden, in terms of diminished ability to carry out daily tasks/activities and participate in psychosocial activities, is high among LN cohort. Appropriate therapeutic management of this condition could alleviate this burden. Current recommendations for management of LN include use of glucocorticoids in combination with immunosuppressive treatment to control disease, with specific treatment guidelines dependent on sub-classification of disease [3,7]. The ultimate goals of treatment are long-term preservation of renal function, prevention of flares, avoidance of treatment-related side-effects and improved quality of life and survival [7]. In this study cohort, immunosuppressant's and steroids were predominantly used, aligned with international treatment guidelines. Past research has revealed that up to 70% of LN patients may be resistant to immunosuppressive regimens [16]; prevalence and impact of resistant/refractory disease in this study cohort is unknown. However, the observation that the LN cohort in this study was a lot more treatment experienced, with more than half of them gone through 3 or more lines of prior treatments, assumes significance and warrants further scrutiny.

EULAR recommends that LN treatment must be based on shared decision between patient and doctor [7]. For this to happen, patients must possess adequate knowledge of their disease/condition. In this study cohort, physicians had rated both the LN and non-LN cohorts to be similarly knowledgeable / interested about their disease. Prevalence of higher disease burden observed among the LN cohort did not seem to have influenced their interest in the disease any more than what was observed among their non-LN SLE counterparts. Relevant and consistent communication from the physicians may help facilitate active patient engagement.

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.

5. Conclusion

Clinical burden, humanistic burden and select healthcare resource use was higher among LN cohort, in comparison to the non-LN SLE cohort in the EU5 region. Factors influencing the observed burden, including the therapeutic strategies used in these geographies, warrant further investigation to manage LN optimally.

Acknowledgements

Author would like to acknowledge the contributions from Yao Lu and Richard Hutchings for their research support efforts.

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Author Profile



Siva has over 18 yrs of experience in developing product value propositions through market/customer focus, research excellence, and brand strategy support. He is a proven leader and team builder with business and clinical backgrounds. Siva built a strong career in HEOR and Market Access within Pharmaceutical industry through tenures at Human Genome Sciences (GSK), Merck & Co., Boehringer-Ingelheim and BMS, covering several therapeutic areas and markets. Within healthcare provider sector, Siva has in-depth experience in Long Term Care (LTC) segment, through his tenure at Beverly Enterprises covering the clinical and strategic evaluations across a spectrum of LTC services. In the consulting arena, Siva held a position of Senior Vice President leading Global Treatment Performance Optimization/HEOR Business Unit at TNS (now, part of Kantar) and currently serves as Senior Vice President at Ipsos to lead Global Evidence, Value and Access division/COE, helping clients generate and/or communicate evidence to support their product value propositions.