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ORIGINAL ARTICLE

Burden of Systemic Lupus Erythematosus on Work Productivity and Daily Living Activity: A Cross-Sectional Study Among Malaysian Multi-Ethnic Cohort

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ABSTRACT

Objectives: This study aims to assess the self-reported work productivity and activity daily living (ADL) impairment among Malaysian patients with systemic lupus erythematosus (SLE) and to examine their associated factors.

Patients and methods: This cross-sectional study included 167 SLE patients (21 males, 146 females; mean age 38.2±9.8 years; range, 20 to 60 years) recruited from the outpatient Rheumatology and Nephrology clinics. Face-to-face interviews were conducted to record patients' socio-demographics (age, sex, ethnicity, marital status, and occupation) and SLE disease characteristics (system involvement, age onset, and presence of organ damage). Disease activity was assessed using the Systemic Lupus Erythematosus Disease Activity Index-2000 (SLEDAI-2K). Short form 36 (SF-36) was used to determine health-related quality of life (HRQoL) while Work Productivity and Activity Impairment (WPAI) questionnaire was used to assess the four domains of absenteeism, presenteeism, overall work productivity, and non-work related ADL impairment. Univariate analyses and multivariable regression analysis examined the association of demographic variables, SLE disease characteristics, and activity with reduced HRQoL and WPAI scores.

Results: The majority of the patients were Malays (59.3%), followed by Chinese (34.7%) and Indian (3.6%) patients. More than two-thirds of the patients reported some degree of impairment in their work productivity and ADL due to the disease. The absenteeism rate was 10.4% in the past one week and their indirect costs were 2,875.17 Malaysian ringgits (US $701.22) in the past seven days. Significant predictors of higher work productivity and ADL impairment scores were higher disease activity, more frequent SLE flares, lupus nephritis, and hematological involvement of SLE. Patients with higher work productivity and ADL impairment scores were also strongly associated with poor QoL. No ethnic disparities of work productivity and ADL impairment were found.

Conclusion: Systemic lupus erythematosus significantly affected the overall productivity in work and non-work related activity in our Malaysian multi-ethnic cohort and both impairments were significantly associated with poor QoL.

Keywords: Lupus, nephritis, productivity, work.

Systemic lupus erythematosus (SLE) is a chronic autoimmune disease which predominantly affects young individuals of prime working years.[1] There is no cure for this disease and its course is variable and unpredictable.[2] Disability and organ damage may ensue if the disease is not adequately controlled. Generally, the prevalence of SLE around the world is estimated between 30 to 300 individuals for every 100,000 people of the country. Malaysia is a multi-ethnic country and the reported prevalence of SLE was 43/100,000. In Kuala Lumpur, the capital city of Malaysia, the Chinese have the highest prevalence of SLE (57/100,000), followed by Malays (33/100,000) and Indians (14/100,000).[3]

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Apart from disease activity, the assessment of the quality of life (QoL) has been included as one of the important patient-reported outcome instruments and this has been strongly advocated by the Food and Drug Administration and the European Medicines Agency.[4,5] This is to enable a holistic approach in the management of SLE. Indeed, the disease has a profound deleterious impact towards QoL which does not correlate with disease activity and damage.[6] Extensive reports in the literature conclude that poor QoL in SLE is a result from a complex interaction between disease severity, psychosocial factors, and poor socio-economic characteristics.[7]

Another important detrimental consequence of SLE is functional and work productivity impairment as up to 50% of SLE patients were found to be incapable for employment.[8,9] Work productivity of those who are employed is also significantly impaired with reduced working hours[10] and high rate of absenteeism.[11] In the United States (US), it has been reported that absenteeism accounts for 2.3 sick days/month[12] among employed SLE patients compared to a 0.3 sick days/month in the general US population in 2016.[13] This has taken a significant economic toll due to the increase in the indirect costs of the disease.[12,14] Despite the substantial negative impact of SLE towards work productivity, it is not part of a routine assessment in SLE patients.

A great number of studies on work and health-related QoL (HRQoL) impairment have targeted predominantly Caucasian populations[6,11,15-19] and very scarce data are available from Asian patients including Malays despite more severe disease with high renal involvement.[20] Thus, examining the magnitude of the disease burden and risk factors is needed to increase our understanding of the disease and provide further evidence as well as to increase the awareness of employers, social welfare and policy-makers to collaborate with health-care institutions in improving the overall management of SLE by addressing worksite modification and compensatory strategies. Therefore, in this study, we aimed to assess the self-reported work productivity and activity daily living (ADL) impairment among Malaysian patients with SLE and to examine their associated factors.

PATIENTS AND METHODS

This cross-sectional study included 167 consecutive SLE patients (21 males, 146 females; mean age 38.2±9.8 years; range, 20 to 60 years) attending the outpatient Nephrology and Rheumatology clinics of Universiti Kebangsaan Malaysia Medical Centre (UKMMC) between March 2017 and July 2017. All patients fulfilled the 1997 revised American College of Rheumatology (ACR)[21] or Systemic Lupus International Collaborating Clinics (SLICC) 2012 classifications criteria of SLE.[22] All included patients were employed at the time of the study to be assessed on work productivity. The study protocol was approved by the Universiti Kebangsaan Malaysia Research Ethics Committee. A written informed consent was obtained from each patient. The study was conducted in accordance with the principles of the Declaration of Helsinki.

Information on demographic characteristics including age, sex, ethnicity, marital status, income and educational levels was obtained from medical records and clinical interviews. Meanwhile, information on disease characteristics (age at diagnosis, duration of disease, organ or system involvement) was obtained from medical records and electronic prescriptions.

Patients' socio-economic characteristics were recorded as education level (primary, secondary, tertiary or above) and marital status (single/widow/separate/divorced or married). In this study, lower education level was defined as patients who received formal education up to secondary education, which is equivalent to the duration of a formal education of ≤11 years.[23] Patients were also asked to state their employment and their type of work was further categorized as non-professionals and professionals. Professional occupation was defined according to the Malaysian Standard Classification of Occupation 2008, which included manager and sub-sectors professionals. Meanwhile, non-professionals referred to clerical support workers, sales and services workers, and technical or skilled labor workers.[24] Their monthly incomes were also recorded.

Disease activity was measured using the Systemic Lupus Erythematosus Disease Activity Index-2000 (SLEDAI-2K).[25] This is a validated

disease activity index with higher scores indicating greater degree of disease activity. The cumulative of SLE flare frequency was determined from the medical records and it was defined as any new increase in disease activity in one or more organ systems involving new or worse clinical signs and symptoms and/or laboratory measurements which required an increase in the steroid dose or addition of non-steroidal antiinflammatory drugs, hydroxychloroquine or other immunosuppressive therapy.[26]

The organ damage severity was measured using the SLICC/ACR Damage Index. This was designed and validated to capture non-reversible organ damage which was not related to the active disease, lasting for at least six months.

Patients' HRQoL was assessed using the Medical Outcomes Study Short Form 36 (SF-36) questionnaire.[27] This questionnaire was validated and is reliable to be used in SLE patients[28] and among the Malaysian population.[29] It is a self-administered questionnaire consisting of eight scaled scores that cover the whole aspect of well-being: physical functioning, role limitation due to physical problems, bodily pain, general health perception, vitality, social functioning, role limitation due to emotional problems, and mental health. Each scale is directly transformed into a 0-100 scale on the assumption that each question carries equal weight. The total average HRQoL scores from the eight domains were also calculated with lower scores indicating more severe disability.

Face-to-face interviews were conducted to assess patients' work productivity. Work Productivity and Activity Impairment (WPAI) questionnaire was used, which was validated[30] and used in several diseases including SLE.[18] The WPAI questionnaire contains six question items that measure work impairment due to SLE during the prior seven days of study visit (Table 1). The six items are then formulated into four primary outcomes which include *(i)* absenteeism (defined as the number of hours a patient missed from work due to their health over the past seven days, *(ii)* presenteeism (defined as percentage impairment of productivity during working; Q5/10), *(iii)* overall work productivity impairment (combination of absenteeism and presenteeism domains; Q2/ (Q2+Q4)+([1-Q2/(Q2+Q4])×(Q5/10) and *(iv)* daily activity impairment (defined as percentage of impairment in activity outside of work; Q6/10). WPAI of each domain was expressed as percentage (0 to 100), with higher percentage corresponding to greater impairment. Total WPAI scores were also calculated by adding all the scores from the four domains. Indirect costs of absenteeism over the past seven days were estimated using the ''lost wages method''.[31] Therefore, the total indirect costs were calculated by multiplying the average hourly salary of the patients with the total hours of missing from workplace for the past seven days.

Statistical analysis

Data were analyzed using the IBM SPSS version 23.0 software (IBM Corp., Armonk, NY, USA). Variables and data were reported using descriptive statistics. Spearman's correlation analyses were performed to determine the correlation between continuous variables with the percentage of the four different productivity impairment WPAI

Table 1. Work productivity and activity impairment questionnaire

Question	Items
1	Current employment (Yes or No)
2	Hours work missed due to health problems related to SLE
3	Hours work missed for other reasons (eg: vacation, holidays, appointments)
4	Total hours actually worked
5	The degree that SLE affects productivity while working (0-10 points scale, where 0 is the lowest degree)
6	The degree that SLE impacts regular activities (0-10 points scale, where 0 is the lowest degree).

SLE: Systemic lupus erythematosus.

domains. Meanwhile, for categorical variables, Student's t-test or Mann-Whitney U test was used to determine their associations with the WPAI scores. A *p* value <0.05 was considered statistically significant. In this study, a multivariable linear regression analysis was performed to determine the independent factors of lower work productivity ad ADL impairment.

RESULTS

Patients' disease duration was 13.1±6.7 years. Majority had tertiary education (74.8%, n=125) and half of them were in non-professional type of employment (n=90, 53.9%). More than two-thirds of the patients had musculoskeletal manifestation of SLE (n=143, 85.6%) while 71.9% of them had renal involvement. Up to 50% of them had mucocutaneous and hematological manifestations.

All domains of the HRQoL were impaired, with the most affected being role limitation on physical health (mean score 65.2±38.8) and the least affected being pain (mean score 81.2±17.6). Table 2 illustrates the baseline socio-demographic, disease characteristics and the mean scores of the SF-36 domains among the SLE patients.

Table 2. Baseline socio-demographic, disease characteristics and HRQoL domains of SLE patients

Variables	n	%	Mean±SD
Age (year)			38.2±9.8
Disease duration (year)			13.1±6.7
Sex			
Male	21	12.6	
Female	146	87.4	
Ethnicity			
Malay	99	59.3	
Chinese	58	34.7	
Indian	6	3.6	
Others	4	2.4	
Marital status			
Married	110	65.9	
Single/divorcee/widow	57	34.1	
Education level			
Primary	6	3.6	
Secondary	36	21.6	
Tertiary and above	125	74.8	
Employment			
Professional	77	46.1	
Non-professional	90	53.9	
Systemic lupus erythematosus system involvement			
Musculoskeletal	143	85.6	
Renal	120	71.9	
Mucocutaneous	88	52.7	
Hematology	87	52.1	
Neuropsychiatric	11	12.6	
Short Form 36 domain			
Physical functioning			78.9±20.9
Role limitation on physical health			65.2±38.8
Pain			81.2±17.6
General health			74.4±21.1
Role limitation on emotional			65.6±39.2
Energy			75.2±80.0
Emotional well-being			77.3±17.5
Social functioning			80.8±16.8

SD: Standard deviation.

A total of 17 patients (10.4%) reported missed work (absenteeism) due to health problems in the past one week and their median hours of missing work was four (interquartile range 5) hours/week. The total indirect cost of absenteeism for the past seven days was 2,875.17 Malaysian ringgits (US$701.22). No significant associations were found between the various socio-demographics, disease characteristics and activity with absenteeism reported for the week prior to the study.

Table 3. Spearman's correlations of factors associated with overall work productivity and daily activity impairment scores

	WPAI productivity scores			WPAI daily activity		
	Mean±SD	r_s	*p*	Mean±SD	r_s	*p*
Age (year)		-0.04	0.57		-0.001	0.99
Age onset (year)		-0.03	0.74		-0.03	0.67
Disease duration (year)		-0.06	0.45		0.02	0.37
SLEDAI-2K score		0.22	0.006*		0.20	0.01*
SLE flare frequency		0.22	0.006*		0.26	0.001*
SLICC ACR damage index		0.03	0.69		0.06	0.49
Sex			0.84			0.43
Male	21.3±17.5			17.6±16.6		
Female	20.3±19.5			20.8±17.5		
Ethnicity			0.12			0.46
Malay	23.5±21.5			22.3±19.4		
Chinese	15.5±14.5			17.4±15.5		
Indian	23.0±17.9			22.0±14.8		
Others	17.0±18.7			20.4±17.8		
Marital status			0.08			0.21
Married	22.3±21.3			21.7±18.9		
Single	16.8±13.8			18.0±15.3		
Education level			0.99			0.35
Low	20.5±15.8			22.7±16.2		
High	20.5±20.3			19.7±18.4		
Type of work			0.61			0.92
Professional	19.6±18.7			20.3±19.1		
Non-professional	21.2±19.8			20.6±16.8		
SLE manifestation						
Lupus nephritis			0.02*			0.04*
Yes	22.6±20.9			22.2±18.9		
No	15.0±12.6			15.9±14.1		
Hematological			<0.001*			0.001*
Yes	26.6±22.5			25.1±20.4		
No	15.1±13.2			15.7±13.1		
Musculoskeletal			0.63			0.71
Yes	20.8±19.4			19.1±19.8		
No	18.7±18.4			20.6±17.6		
Mucocutaneous			0.02*			0.12
Yes	17.2±17.1			18.4±15.6		
No	24.1±20.7			22.7±19.8		
Average SF-36 scores			0.93 <0.001*			0.85 <0.001*

WPAI: Work Productivity and Activity Impairment; SD: Standard deviation; SLEDAI-2K: Systemic Lupus Erythematosus Disease Activity Index-2000; SLE: Systemic lupus erythematosus; SLICC ACR: Systemic Lupus International Collaborating Clinics American College of Rheumatology; SF-36: Short Form 36; * Significant *p* at <0.05.

Table 4. Multiple linear regression analysis of predictors of higher work impairment and non-work related activity daily living impairment scores

WPAI scores	Factors	Regression coefficient (β)	SE (β)	95% CI of OR	*p*
Work productivity	SLE flare frequency	0.82	0.08	-0.76 to 2.38	0.31
	Hematology	4.07	0.10	-1.74 to 9.74	0.17
	Mucocutaneous	-4.44	-0.12	-9.81 to 0.33	0.10
	Lupus nephritis	3.84	0.09	-2.38 to 10.05	0.22
	SLEDAI-2K score	-0.15	-0.03	-0.97 to 0.69	0.72
	Average SF-36 score	-0.41	-0.41	-0.55 to -0.22	<0.01*
ADL impairment scores	SLE flare frequency	1.43	0.14	0.06 to 2.79	0.04*
	Average SF-36 scores	-0.42	-0.45	-0.54 to -0.29	<0.01*
	Hematology	3.95	0.11	-1.22 to 9.11	0.13
	Lupus nephritis	1.77	0.61	-3.97 to 7.52	0.58
	SLEDAI-2K score	0.02	0.003	-0.76 to 0.79	0.98

WPAI: Work Productivity and Activity Impairment; SE: Standard error; CI: Confidence interval; OR: Odds ratio; SLE: Systemic lupus erythematosus; SLEDAI-2K: Systemic Lupus Erythematosus Disease Activity Index-2000; SF-36: Short Form 36; ADL: Activity daily living.

A total of 76.6% (n=128) reported some degree of impairment (score >0) while working (presenteeism) with their average impairment scores of 17.8±18.2. Meanwhile, a total of 80.8% (n=135) reported work productivity impairment (absenteeism + presenteeism) with their average scores of 20.5±19. A total of 142 patients (85.0%) reported ADL impairment with their mean impairment scores of 20.4±17.8.

Higher work productivity and ADL impairment scores were significantly correlated with SLEDAI-2K score, flare frequency, lupus nephritis (LN) and hematological manifestations of SLE. Presence of mucocutaneous involvement in SLE was significantly associated with lower work productivity impairment score (Table 3).

Multiple linear regression analysis, which included all the significant factors above, revealed that lower average HRQoL was significantly associated with higher work productivity and ADL impairment scores. In addition, frequent SLE flare was associated with impairment in ADL (Table 4).

DISCUSSION

Systemic lupus erythematosus mainly affects young females during the career-building phase of life. Therefore, burden of the disease towards patients' work productivity[11,16,18,19,32] and QoL[6] is substantial. Despite the fact that the Asian population displays more severe SLE,[33] there is still a relative paucity of studies quantifying the socio-economic burden of the disease which may indirectly influence patients' QoL. SLE is known to reduce patient's ability to work and hence results in reduced productivity and working hours.[18,34] Similarly, our study demonstrated that up to two-thirds of our patients had some degree of impairments in their work productivity and ADL due to SLE.

The cumulative flare frequency was one of the factors associated with reduced work and ADL productivity among our cohort. This is consistent with the nature of the disease which runs through unpredictable courses with episodes of exacerbations. Therefore, prevention of disease flares is important to ensure that work productivity remains optimum as diminished productivity may lead to the risk of permanent disability.[35] Our study has revealed that greater disease activity was significantly correlated with higher work productivity and non-work related ADL impairment scores. Our findings concurred with a US cohort which consisted of predominantly African-American patients[16] and a SLE Latin

cohort from Argentina.[32] Other studies have failed to demonstrate similar associations;[8,17,32,36] however, they had variabilities in disease activity indices or instruments used.

We reported significant associations of renal and hematological involvement of work productivity and ADL impairment. Patients with SLE, particularly those with active LN, were demonstrated to be more likely to miss work compared to non-LN patients in a multi-ethnic Canadian study (Lupus Nephritis New Emerging Team (LuNNET) study cohort.).[15] In contrast, the afore-mentioned multi-ethnic US study (Georgians Organized Against Lupus [GOAL] cohort) also revealed that mucocutaneous and musculoskeletal involvement were found to have a significant detrimental impact on workplace productivity,[16] which was not observed in our cohort. This can be explained by the fact that the mucocutaneous and musculoskeletal manifestations in our patients were rather mild and not significantly associated with joint damage or deformity.[20] The GOAL cohort, which comprised of predominantly African-American patients, had more chronic cutaneous lupus erythematosus.[37]

Racial disparities in SLE disease manifestations and outcomes have been demonstrated in the multi-ethnic US study and our local populations.[20,38,39] Severe disease leads to higher burden as African-American patients were reported to have an increased risk of unemployment compared to Caucasians.[40] Although our earlier study demonstrated that Indian patients had more severe disease with significantly higher organ damage,[20] there were no significant inter-ethnic differences in work productivity and daily activity impairment. However, a small number of Indian patients in this current study may not be able to capture any significant disability; thus, future larger studies are needed to confirm this.

Our study also showed that both work and non-work related productivity impairments were significantly associated with poor QoL measured with SF-36. This finding concurred with the SLE cohort in Argentina[32] and rheumatoid arthritis populations.[41,42] However, due to the cross-sectional nature of this study, a causal relationship of poor QoL and work productivity could not be ascertained. The relationship between work and QoL is complex as various studies have demonstrated that under-employment had a negative impact towards both mental and physical health.[43,44] This is probably because of the fact that employment may influence patients' mental health through rewarding jobs and earnings as well as providing a distraction from symptoms.[45] Employment is also one of the platforms for social interaction and this may also contribute to better QoL.[46]

The one-week indirect cost of absenteeism in our study was equivalent to US$700. However, since the WPAI does not capture sufficient data such as worker replacement costs and actual productivity losses, the indirect cost calculated may be under-estimated. We also could not calculate the annual indirect cost of productivity lost due to the inadequate data in our study. The published reports on annual indirect cost of productivity loss among SLE patients varied, from US$2,239 to US$35,540 (year 2010 values), depending on the different costing methods.[47]

There are several limitations of this study. One was the exclusion of healthy controls, which prevented us from performing direct comparisons. Moreover, the study subjects were recruited from outpatient clinics and this may have caused under-reporting of the overall impairment as inpatients were not included. Apart from that, we did not examine the nature of the works as certain occupations that require higher physical demand are associated with workplace activity limitations.[11,36] Other possible factors that have potential roles in influencing QoL such as social support[48] and psychological well-being[49,50] were also not examined in our study. Furthermore, the information on reduced work productivity was based on patient-reported data, hence there was a potential recall bias.

In conclusion, we have revealed that the burden of SLE towards employment and non-work related daily activity was substantial among our multi-ethnic cohort prompting further evaluation of the socio-economic impact of the disease in our country.

Declaration of conflicting interests

The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

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