

## CORRELATION BETWEEN SYSTEMIC LUPUS ERYTHEMATOSUS DISEASE ACTIVITY AND LUPUS RETINOPATHY USING MEX-SLEDAI SCORE

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### ABSTRACT

**Introduction:** Lupus retinopathy and posterior uveitis are complications due to systemic lupus erythematosus which can threaten the vision. The presence of posterior segment manifestation is suggestive of high disease activity. The aim of this study is to identify posterior segment manifestation (Lupus Retinopathy and Posterior Uveitis) in SLE patient and their correlation with SLE disease activity using The Mexican-SLEDAI (MEX-SLEDAI) score.

**Methods:** This was an analytical observational study with cross-sectional design, conducted from August to October 2020 and involved 114 SLE patients in Dr. Saiful Anwar General Hospital. We calculated MEX-SLEDAI score to assess SLE disease activity. All participant that met inclusion criteria underwent ophthalmology examinations using a portable slit-lamp, head indirect ophthalmoscope, and fundus finding were documented using portable fundus imaging.

**Result:** Lupus retinopathy (LR) presents in 25/114 (21.9%) and posterior uveitis (PU) occurs in 2/114 (1.8%) SLE patients. The mean age of patient with LR, PU, and without retinopathy were 32.92; 37.00; and 31.08 years respectively. The posterior segment findings were hemorrhages, cotton wool spots, hard exudates, and vasculitis reflecting vascular damage. The most common manifestation found in retina was cotton wool spot. The mean of MEX-SLEDAI score of SLE patient with LR ( $7.200 \pm 3.905$ ) and SLE patient with PU ( $3.500 \pm 2.121$ ) was higher than the mean of SLE patient without LR and PU ( $2.871 \pm 2.534$ ). There was a significant association between LR and MEX-SLEDAI score ( $p=0.000$ ,  $r=0.480$ ). An insignificant association between PU and MEX-SLEDAI score was found ( $p=0.353$ ,  $r=0.021$ ).

**Conclusion** There is a significance correlation between lupus retinopathy and SLE disease activity based on MEX-SLEDAI scores. The mean of MEX-SLEDAI score in SLE patients with lupus retinopathy was higher than SLE with posterior uveitis and SLE without posterior segment manifestations.

**Keywords:** Lupus retinopathy, Posterior Uveitis, Systemic Lupus Erythematosus Disease Activity, MEX-SLEDAI Score

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### INTRODUCTION

Systemic Lupus Erythematosus (SLE) is a chronic autoimmune inflammatory disease

lung, kidney, central nervous system, immune system, and eye. The incidence of ocular manifestations due to SLE varies from 20–34%.<sup>1,2</sup> This disease can lead to ocular manifestations through several mechanisms, which are immune complexes deposition in the vascular endothelium

with broad range of clinical manifestations, comprising skin and mucus, joint, blood, heart,

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of conjunctiva, sclera, choroid, corpus ciliaris, and retina, which in turn cause damages in these tissues.<sup>3</sup> Lupus retinopathy is the second most common manifestation with an incidence 3-29% after Sjogren Syndrome (88%). Posterior uveitis is still the least occurring clinical manifestation with a prevalence 1%.<sup>4</sup> Microangiopathy is a mild finding of lupus retinopathy with classic signs of cotton wool spots, microaneurysm, hard exudate, and haemorrhages. Meanwhile, vasculitis is the least occurring clinical manifestation with signs of vascular sheathing which can alter visual functions.<sup>5,6</sup>

The presence of lupus retinopathy and posterior uveitis is presumed to be an accurate guide indicating active SLE disease activity, so proper interventions can be made as soon as possible. Hussein *et al*<sup>8</sup> reported that the active disease of SLE using SLEDAI score significantly related to eye affection especially retinopathy. In this study we used MEX-SLEDAI score to assessed disease activity, to the best of the author's knowledge, no studies have been reported regarding the assessment of SLE using MEX-SLEDAI score on posterior segment ocular manifestation.

In this study we aimed to identify posterior segment manifestation (Lupus Retinopathy and Posterior Uvetis) in SLE patient and their correlation with SLE disease activity using MEX-SLEDAI score.

## METHOD

This was an analytical observational study with cross-sectional design. This study involved outpatients at the Rheumatology clinic of dr. Saiful Anwar General Hospital starting from August to October 2020. All patients who fulfilled the 2019 EULAR/ACR classification for the SLE criteria, aged  $\geq 17$  years, and female were included. Patients with diabetes mellitus, primary hypertension, other rheumatologic diseases, and refractive media opacity were exclude. Informed consent is given to each research participant. This study has been

approved by the committee of medical research ethics of dr. Saiful Anwar General Hospital- Malang (400 / 077 / K.3 / 302 /2020).

Clinical examinations were carried out meticulously by conducting SLE activity index assessment by means of MEX-SLEDAI score. The patients were classified according to MEX-SLEDAI score which divided into, remission (0–1), mild activities (2–5), moderate (6–9), high (10–13), and very high ( $>14$ ).

Afterwards, all of the participants underwent eye examination which consists of portable slit-lamp (*NIDEK*) for the anterior segment, fundus examination using head indirect ophthalmoscope (*Keller Binocular Indirect Ophthalmoscope*) for the posterior segment. and fundus finding were documented using portable fundus imaging (*NIDEK*).

Statistical Analysis: All data analyses were performed using IBM SPSS Version 20. Kruskal Wallis and Mann Whitney test were used to compare the MEX-SLEDAI score in SLE patients with lupus retinopathy and posterior uveitis. While the correlation between MEX-SLEDAI score with lupus retinopathy and posterior uveitis ware analyzed using *Eta Coefficient* test. A value of  $p < 0.05$  was considered statistically significant. All data are presented as mean  $\pm$  SD.

## RESULT

There were 114 SLE patients included in this study. The mean age at the ophthalmological examination of SLE patients without lupus retinopathy and posterior uveitis is  $31.08 \pm 12.19$  years,  $32.92 \pm 10.46$  years for SLE patients with lupus retinopathy, and  $37.00 \pm 15.56$  years for SLE patients with posterior uveitis. The duration of SLE in patients without lupus retinopathy and posterior uveitis is  $49.93 \pm 40.23$  months,  $60.44 \pm 53.33$  months for SLE patients with lupus retinopathy, and  $36.50 \pm 50.20$  months for SLE patients with posterior uveitis.

Table 1. Demographic and Clinical Characteristic in Systemic Lupus Erythematosus Systemic Patients.

Characteristics	SLE Patients with LR	SLE Patients with PU	SLE Patients without LR and PU
	Mean $\pm$ SD	Mean $\pm$ SD	Mean $\pm$ SD
Age when diagnosed with SLE (years)	27.96 $\pm$ 8.68	34.00 $\pm$ 19.8	27.08 $\pm$ 12.07
Age when undergoing eye examination (years)	32.92 $\pm$ 10.46	37.00 $\pm$ 15.56	31.08 $\pm$ 12.19
Duration of SLE (months)	60.44 $\pm$ 53.33	36.50 $\pm$ 50.20	49.93 $\pm$ 40.23
Types of ocular manifestation (n, %)	25 (21.9%)	2 (1.8%)	87 (76.3%)
Laterality			
- Unilateral	22 (88%)	1 (50%)	-
- Bilateral	3 (12%)	1 (50%)	
MEX - SLEDAI	7.200 $\pm$ 3.905	3.500 $\pm$ 2.121	2.871 $\pm$ 2.534
MEX SLEDAI (n, %)			
Remission (0-1)	2 (1.75%)	0	32 (28.07%)
Mild activity (2-5)	3 (2.63%)	2 (1.75%)	31 (27.19%)
Moderate activity (6-9)	15 (13.16%)	0	24 (21.05%)
High activity (10-13)	3 (2.63%)	0	0
Very high activity ( $\geq$ 14)	2 (1.75%)	0	0
Therapy (n, %)			
- Therapy (-)			0
- Methylprednisolone (MP), single dose < 6mg			3 (2.63%)
- Methylprednisolone (MP), single dose 7-24 mg			4(3.51%)
- MP + chloroquine			21 (18.42%)
- MP + immunosuppressant			18 (15.79%)
- MP + chloroquine + immunosuppressant			32 (28.07%)
- Immunosuppressant + chloroquine			17 (14.91%)
- Immunosuppressant			11 (9.65%)
- Chloroquine			8 (7.02%)

SLE : Systemic Lupus Erythematosus, LR : Lupus Retinopathy, PU : Posterior Uveitis

Lupus retinopathy was found in 25 of the 114 patients (21.9%), and posterior uveitis was identified in 2 of the 114 patients (1.8%). Cotton-wool spots are the most often discovered findings in the retina of 15 patients, 6 patients had intraretinal hemorrhage, 11 patients showed hard exudates, and vasculitis lesion was found in 2 patients, which are ghost vessel and perivascular exudate.

Figure 2,3 infers that patients with lupus retinopathy and posterior uveitis have higher mean of MEX-SLEDAI score than patients without lupus retinopathy and posterior uveitis. The mean of

MEX-SLEDAI score for patients without lupus retinopathy and posterior uveitis, patients with posterior uveitis, and patients with lupus retinopathy is 2.871  $\pm$  2.534, 7.200  $\pm$  3.905, 3.500  $\pm$  2.121, respectively. Significant difference was found in MEX-SLEDAI score between patients with lupus retinopathy and patients without lupus retinopathy and posterior uveitis ( $p = 0.000$ ), whereas no significant difference was found between patients with posterior uveitis and patients without lupus retinopathy and posterior uveitis ( $p = 0.961$ ).

This study carried out correlation test using *Eta Coefficient* to evaluate the association between

posterior segment manifestation with MEX SLEDAI score. There were significant correlation between LR patients with MEX-SLEDAI score ( $p = 0.000$ ,  $r=0.480$ ), and no significant correlation between PU patient with MEX-SLEDAI score ( $p = 0.353$ ,  $r=0.021$ ).

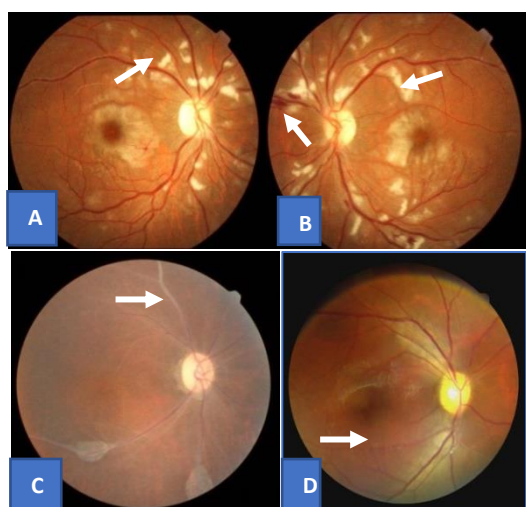


Figure 1. Posterior segment image in SLE patients with Lupus Retinopathy and Posterior Uveitis. (A,B) SLE patient with Lupus Retinopathy; cotton wool spot and haemorrhage (white arrow), (C) SLE patient with Posterior Uveitis; ghost vessel can be seen. (D) SLE patient with Posterior Uveitis; perivascular exudate (white arrow).

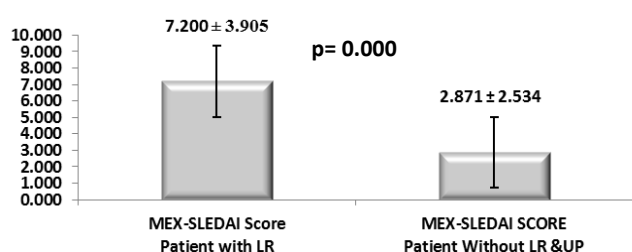


Figure 2. The Mean of MEX-SLEDAI score in SLE patients with lupus retinopathy is higher than that of SLE patients without retinal abnormality. (LR : Lupus Retinopathy, PU: Posterior Uveitis)

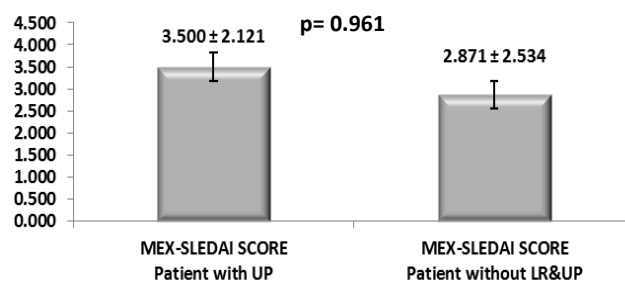


Figure 3. The mean of MEX-SLEDAI score in SLE patients with posterior uveitis is higher than that of SLE patients without retinal abnormality. (LR: Lupus Retinopathy, PU : Posterior Uveitis)

## DISCUSSION

The mean age of patients with and without retinopathy is  $28.24 \pm 1.43$  years and  $25.84 \pm 0.48$  years, respectively and all of the participants in this study are women. Systemic Lupus Erythematosus commonly affects women during the childbearing years, sex hormones all strongly suggest a role for estrogens in the initiation and possibly maintenance of the disease.<sup>7</sup> Ushiyama et al.<sup>8</sup> reported that the mean onset age of SLE on patients with and without retinopathy is 34.2 and 31.9 years, respectively and all of the participants in the study are women.

Retinopathy is one of the important manifestation of SLE, the frequency of the findings varies depending on the patient population being studied and systemic disease activity. According to Hussein et al<sup>9</sup> study in Egyptian which suggested that the incidence of lupus retinopathy is 24% (24/100) which is similar to our study, reveals that the incidence of lupus retinopathy is 21.9% (25/114).

Autoimmune process can affect the retina and choroid in two ways: direct, by immune complex-mediated vasculitis; and indirect, by secondary hypertension influenced by the kidney.<sup>11</sup> There are 3 direct retinal damages caused by SLE, which are: microangiopathy, severe vaso-occlusion, and vasculitis. Ocular manifestations due to SLE, particularly lupus retinopathy, are caused by autoimmune dysregulation activity where immune complex is a crucial contributor for the occurrence

of lupus retinopathy. Immune complex deposition in the retinal blood vessel walls leads to inflammatory reaction which will induce nerve cell death and infarction on retinal nerve fiber layer. In our study, cotton-wool spots are findings in the retina that are most commonly found, which are in 15 patients, whereas 6 patients were found with intraretinal hemorrhage, and 11 patients with hard exudates. This is similar to a study by Franz et al<sup>12</sup> which reported that cotton-wool spots are the most frequently found formations, amounting to 13 out of 21 (61.9%) SLE patients. Classic findings on retina are in the form of cotton-wool spots, microaneurysm, hard exudate, and intraretinal hemorrhage which are usually associated with good visual prognosis.<sup>13</sup>

Posterior uveitis in SLE patients is a rarely-occurring complication with an incidence of 1.4%.<sup>8</sup> In studies with smaller samples, the prevalence of posterior uveitis can reach 2-8%. Retinal vasculitis is a part of retinal vasculopathy which causes inflammation the retinal arteriole or venule, thus are likely to decrease vision. It is usually found in acute phase.<sup>14</sup> The deposition of immune complexes in the retinal and choroidal blood vessel walls plays a role in vasculitis. In other situations, immune complexes or pathogenic autoantibody interact with platelets on the surface of endothelial cells and may result in vaso-occlusion.<sup>15</sup> Our study found the incidence of posterior uveitis at 1.8% (2/114), with features of ghost vessels and perivascular exudate present in each patient. This is comparable to a study conducted by Ossamu et al<sup>8</sup> where the incidence of posterior uveitis was 1.4% (1/69) and to a study by Hussein et al.<sup>9</sup> where the incidence was 3% (3/100).

Retinopathy in SLE can be an indication for high SLE activities. In our study we used MEX-SLEDAI score to measure disease activity. The MEX-SLEDAI was less expensive to administer, easy to apply and no studies have been reported regarding the assessment of SLE disease activity using MEX-

SLEDAI on posterior segment manifestation. Tolba et al<sup>16</sup> reported that in 30 active SLE patients, 40% of whom have retinopathy and significantly-correlating SLEDAI score (have a relationship). In our study, the mean MEX-SLEDAI score was found higher in SLE patients with lupus retinopathy compared to the non-retinopathy ( $7.200 \pm 3.905$ ,  $2.871 \pm 2.534$ , respectively) and we came to the conclusion that there was a significant relationship between lupus retinopathy and the MEX-SLEDAI score. In SLE patients with posterior uveitis, the mean MEX-SLEDAI score was found to be higher than SLE patients without posterior uveitis ( $3.500 \pm 2.121$ ,  $2.871 \pm 2.534$ , respectively), though this relationship was not significant. This condition is probably due to the number of patients with positive posterior uveitis was much fewer, i.e. 2 out of 114 SLE patients.

The limitation of this study was conducted by means of cross-sectional design, so we were not able to consolidate all of the samples in regard to their disease onset, degree of severity, and the duration of experiencing SLE. However, by discovering the relationship between posterior segment ocular manifestations and SLE activities, further studies are needed with prospective cohort design that involve larger samples and longer research period by considering the duration, the disease's severity degree, the involvement of systemic organs, and laboratory results.

## CONCLUSION

There is a significance correlation between lupus retinopathy and SLE disease activity based on MEX-SLEDAI scores. The mean of MEX-SLEDAI score in SLE patients with lupus retinopathy was higher than SLE with posterior uveitis and SLE without posterior segment manifestations.

## ACKNOWLEDGEMENT

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## REFERENCE

1. Palejwala, Neal V., Harpreet S. Walia, and Steven Yeh. "Ocular manifestations of systemic lupus erythematosus: a review of the literature." *Autoimmune Diseases* 2012 (2012).
2. Lahita RG. The clinical presentation of systemic lupus erythematosus. In:Lahita RG, Tsokos G, Buyon J, Koike T. Editors. Systemic Lupus erythematosus, 5th ed. San Diego. Elsevier; 2011: 525-540
3. Bajwa A and Foster SC, Ocular Manifestations of Systemic Lupus Erythematosus, *J Clin Cell Immunol* 2014, 5:1
4. Davies, John B, RAO, Prabakar Kumar. Ocular manifestations of systemic lupus erythematosus. *Current opinion in ophthalmology*, 2008, 19.6: 512-518.
5. Garcia D, Erkan D. Diagnosis and management of the antiphospholipid syndrome. *New England Journal of Medicine*. 2018 May 24;378(21):2010-21.
6. Zink J M, Singh-Parikshak R, Johnson CS, et al. Hypopyon uveitis associated with systemic lupus erythematosus and anti phospholipid antibody syndrome. *Graefes Arch Clin Exp Ophthalmol* 2005;243:386–8.
7. Eliza FC, Lisa RS. Pregnancy and Autoimmune Disease, Reproductive and Hormonal Issues. Dubois. Edisi ke-9. (2019), Elsevier Inc.;2019. h. 499-548.
8. Ushiyama, Osamu, et al. Retinal disease in patients with systemic lupus erythematosus. *Annals of the rheumatic diseases* 59.9 (2000): 705-708.
9. Hussein DA, El Bakry SA, Morshedy NA, Ibrahim SE, Mohammed MA. Ocular manifestations in Egyptian systemic lupus erythematosus patients and their relation with disease activity and anti-phospholipid antibodies. *The Egyptian Rheumatologist*. 2018 Jul 1;40(3):179-82.
10. L. Ostanek, M. Modrzejewska, D. Bobrowska-Snarska, M. Brzosko Ocular manifestations in patients with systemic lupus erythematosus and antiphospholipid syndrome *Pol Arch Med Wewn*, 117 (Suppl) (2007), pp. 18-23
11. Seth, Gaurav, et al. Lupus retinopathy: a marker of active systemic lupus erythematosus. *Rheumatology international* 38.8 (2018): 1495-1501.
12. Franz, M. C., and C. Idefonso. "Retinopathy in systemic lupus erythematosus." *Philipp J Ophthalmol* 34.2 (2009): 66-69.
13. Silpa-archa S, Lee JJ, Foster CS. Ocular manifestations in systemic lupus erythematosus. *British Journal of Ophthalmology*. 2016 Jan 1;100(1):135-41.
14. Butendieck, Ronald R., et al. Systemic lupus erythematosus-associated retinal vasculitis. *The Journal of rheumatology* 39.5 (2012): 1095-1096.
15. Nag, Tapas C., and Shashi Wadhwa. Vascular changes of the retina and choroid in systemic lupus erythematosus: pathology and pathogenesis. *Current Neurovascular Research* 3.2 (2006): 159-168.
16. Tolba DA, El Fayoumi DM, Abdel aziz MS, Nabih MH. Fluorescine angiographic findings in patients with active systemic lupus erythematosus. *Ocular Immunol Inflamm* 2016.



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