Prevalence of inflammatory eye disease in patients with Systemic Lupus Erythematosus: a systematic review of the literature.

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The importance of the eye in SLE

- Systemic Lupus Erythematosus (SLE) is a multisystem autoimmune inflammatory disorder affecting many organs including the eye
- Ocular involvement is estimated in one-third of SLE patients (1) occurring as a result of active disease, damage, a consequence of therapy or other co-morbidities e.g. Sjorgren's syndrome
- **The British Isles Lupus Assessment Group (BILAG) index** is a well-validated, comprehensive tool for the assessment of SLE disease activity (2)
- It lists thirteen ocular manifestations of active SLE, which, when severe can pose significant risk of visual loss (see figure 1)

The epidemiological data thus far…

- The incidence and prevalence of SLE in patients with ophthalmic pathologies is relatively well-studied.
- Much less, however, is known about the incidence and prevalence of these manifestations in patients with an antecedent diagnosis of SLE.

The aim of this systematic review was to determine the incidence and prevalence of disease-activity related ophthalmic conditions in patients with SLE.

Methods:

We performed a systematic review of articles with the following inclusion criteria:

1) Cohort, cross-sectional and case-control original research
2) English language only
3) Diagnosis of SLE diagnosed with classification criteria
4) SLE diagnosis predated eye disease onset

Outcomes:

1) Incidence rates and ratios, incidence proportions and odd ratios of ophthalmic pathologies listed in BILAG

Study search and data extraction

- Databases searched: Ovid MEDLINE and Ovid EMBASE
- Two independent searchers (NJ,JW). NJ extracted data whilst JW error checked for bias.
- Two independent researchers assessed for bias

OPHTHALMIC

65. Orbital inflammation/myositis/proptosis
66. Keratitis - severe
67. Keratitis - mild
68. Anterior uveitis
69. Posterior uveitis/retinal vasculitis - severe
70. Posterior uveitis/retinal vasculitis - mild
71. Episcleritis
72. Scleritis - severe
73. Scleritis - mild
74. Retinal/choroidal vaso-occlusive disease
75. Isolated cotton-wool spots (cytoid bodies)
76. Optic neuritis
77. Anterior ischaemic optic neuropathy

Figure 1: A snapshot of BILAG-2004 showing the ophthalmic features

Results

- 22 eligible studies
- Studies were heterogenous
- 13/22 were deemed at high risk of bias
- See Table 1 showing individual outcomes

Discussion points:

1) **Low prevalence of ocular manifestations** – with all but one study reporting prevalence of <5%
2) **Paucity of data** – no data for 5 of the 11 outcomes - the remaining incident data was taken from two studies conducted in the 1980s.
3) **Possible underreporting** – since only 14 of 22 studies mentioned assessment by an ophthalmologist, increasing the chances of underreporting
4) **Predominance of data from North America and Europe** – studies originating from Africa were underrepresented which is important particularly since complications are often reported as severer in Black African and Caribbean patients. (3)

Table 1: **Summary of the incidence and prevalence for each of the ophthalmic BILAG outcomes observed across relevant studies.**
Numbers in () brackets indicate the number of studies reporting the demographic.

	Outcome	Epidemiology	No of Studies	Risk of Bias	Publication Dates	Geographic Location	SLE group Sample sizes	Average ages (range in years)	%Female (range)	Incidence/ Prevalence
ANTERIOR SEGMENT PATHOLOGIES	Orbital inflammation/myositis/proptosis	Incidence	No studies retrieved							
		Prevalence	No studies retrieved							
	Episcleritis	Incidence	No studies retrieved							
		Prevalence	5	High - 4; Medium - 1	1967-2018	Nepal, USA, Egypt	24-179	13-26.6 (3)	80-96 (4)	0-4.2%
	Scleritis	Incidence	No studies retrieved							
		Prevalence	2	Medium - 2	2015-2018	USA, Italy	98-179	33 (1)	92 (1)	0-2.0%
	Keratitis	Incidence	No studies retrieved							
		Prevalence	2	Medium - 2	2015-2018	USA, Italy	78-179	33 (1)	92 (1)	0.56-4.1%
	Anterior Uveitis	Incidence	1	High	1989	Greece	112	Not stated	Not stated	2.7% over 7 years
		Prevalence	5	High - 3; Medium - 1; Low - 1	1998-2018	Brazil, Cameroon, USA, Singapore, Saudi Arabia	52-852	11.3-32.9 (4)	87-94 (4)	0-2.9%
POSTERIOR SEGMENT PATHOLOGIES	Posterior Uveitis	Incidence	No studies retrieved							
		Prevalence	2	Low - 1; Medium -1	2015-2017	Brazil, USA	179-852	12.5 (1)	92 (1)	0-0.59%
	Retinal Vasculitis	Incidence	1	High - 1	1988	Canada	550	Not stated	Not stated	0.36% over 15 years
		Prevalence	4	High -3; Medium - 1	2000-2018	Nepal, Japan, India, Egypt	40-437	13-41 (4)	80-95 (4)	0-2.9%
	Retinal Vaso-occlusive Disease	Incidence	1	High - 1	1988	Canada	550	Not stated	Not stated	
		Prevalence	7	High - 4; Medium - 3; Low - 1	1998-2018	Singapore, China, Spain, Egypt, Saudi Arabia, Italy, Nepal	40-5298	11-36 (7)	80-95 (7)	0-7.3%
	Isolated Cotton-wool Spots	Incidence	1	High -1	1988	Canada	550	Not stated	Not stated	3.6% over 15 years
		Prevalence	5	High - 3, Medium - 1; Low - 1	1999-2018	China, Japan, Nepal, Spain, Egypt	40-5298	13-40.7 (4)	80-95 (4)	0-2.4%
	Optic Neuritis	Incidence	1	High -1	1989	Greece	112	Not stated	Not stated	0.89% over 7 years
		Prevalence	3	High - 2; Medium -1	2011-2018	Nepal, Egypt, Greece	40-370	13-32 (3)	80-94 (3)	0-2.3%
	Anterior Ischaemic Optic Neuropathy	Incidence	1	High -1	1988	Canada	550	Not stated	Not stated	0.36% over 15 years
		Prevalence	2	Medium - 2	1999-2015	USA, Spain	82-179	36 (1)	94 (1)	0-1.2%

Key Messages:

1) The prevalence of SLE activity related ophthalmic manifestations is low.
2) Clinicians should nonetheless remain vigilant in certain groups of SLE patients due to associated morbidity.
3) Further research is needed to elucidate incidence of activity-related eye disease in modern SLE cohorts.

References:

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3) Drenkard C, Lim SS. Update on lupus epidemiology: advancing health disparities research through the study of minority populations. Current opinion in rheumatology. 2019 Nov;31(6):689.

For references of the articles obtained through the systematic review please contact jessicawalker@doctors.org.uk