Original Article

Prevalence and Spectrum of Eye Disorders Among Patients With Rheumatoid Arthritis and Systemic Lupus Erythematosus in a Tertiary Hospital in Northern Nigeria

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Abstract

Purpose: The aim of this study was to determine the spectrum of eye disorders in patients with rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE). **Materials and Methods:** A cross-sectional hospital-based study was conducted among 100 consecutive patients with RA and SLE. A semi-structured questionnaire was used to obtain details of patients' sociodemographics, type of rheumatic disease, and prescribed medications. Each patient had a detailed examination of the anterior and posterior segments of the eye. Refraction, intraocular pressure measurement, Schirmer's test, tear breakup time, gonioscopy, and dilated fundoscopy were also done. Fundus photograph, central visual field assessment, and optical coherence tomography were done as necessary. Analysis was done with the Statistical Package for Social Sciences (SPSS) version 25. Statistical significance was set at $P < 0.05$. **Results:** A total of 100 patients consisting of 74 RA and 26 SLE patients were evaluated. The female: male ratio was 4.3: 1 for RA, and all SLE patients were females. The prevalence of eye disorders was 42% in all patients; it was 41.9% and 42.3% among RA and SLE patients, respectively. The most common eye disorders were dry eye (38), refractive errors (18), and cataract (16). The mean age of RA patients with eye disorders (52.19 ± 16.17 years) was significantly higher than those without eye disorders (42.30 ± 13.14 years) ($P = 0.005$). **Conclusion:** Eye disorders are common in RA and SLE. Comprehensive eye examination should be done on all RA and SLE patients at diagnosis and before commencement of medications, and patients should be referred promptly for evaluation when they have eye complaints.

Keywords: *Eye disorders, prevalence, RA, SLE*

Introduction

Rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE) form part of a spectrum of rheumatic diseases, a varied group of chronic disorders, usually of an unknown aetiology that is associated with the presence of chronic inflammation, involving structures of the musculoskeletal system, blood vessels, and other tissues.[1] Ophthalmic manifestations are common[2,3] and may have diagnostic and prognostic implications.[4] Some ophthalmic manifestations present before systemic manifestations of the disease, others present during the active stage of the disease, whereas some of them are due to prolonged disease and/or medications used.[3,5] Some ophthalmic manifestations of rheumatic diseases such as peripheral ulcerative keratitis (PUK) and optic neuropathy could be potentially blinding.[6] Whereas other ophthalmic manifestations such as severe vaso-occlusive retinopathy may be an indication of threat to life itself.[7]

The prevalence of ophthalmic manifestation of rheumatic diseases has been reported to be between 10% and 33% with higher values in certain countries.[8] Typically, both RA and SLE have articular features, however, being systemic conditions, a wide range of extra articular manifestations involving many systems including the eye is common.[2] The most frequent extra-articular manifestations of RA are ocular, seen in almost 40% of the patients[9]; whereas ophthalmic manifestations affect over 30% of SLE patients.[10,11] Ophthalmic manifestations, which are pointers of active disease process and indicators of severe and potentially life-threatening systemic involvement,[7] have received little attention with very few studies done in Sub-Saharan Africa.[12,13] There is therefore the need to determine the spectrum of eye disorders in RA and SLE patients in Sub-Saharan Africa.

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Materials and Methods

This hospital-based cross-sectional study was conducted between July and December 2020 in the Rheumatology and Eye Clinics of Ahmadu Bello University Teaching Hospital (ABUTH), Zaria. Ethical approval for the study was obtained from the Health Research Ethical Committee (HREC) of the Institution (ABUTHZ/HREC/W21/2019). The study observed the guidelines of the Helsinki Declaration on Human Research. Written informed consent for the study was obtained from each participating patient prior to examination/evaluation.

All consenting adult patients aged 18 years and above diagnosed with RA or SLE [using the 1987 American College of Rheumatology (ACR) Criteria for RA[14] and 1997 ACR criteria for SLE[15]] attending the rheumatology clinic irrespective of gender, duration or severity of the disease, and the presence or absence of ocular symptoms were invited to participate in the study. Patients with uncontrolled systemic conditions such as diabetes or hypertension, patients with infectious diseases accounting for, or predisposing to ocular findings, such as active tuberculosis and human immunodeficiency virus, and patients who did not give their consent were excluded from the study.

Using a standard normal deviate of 1.96 (95% confidence interval), prevalence of 46% from a previous study,[8,9] a study population of less than 10,000, and an attrition rate of 10%, a minimum sample size of 100 patients was estimated. The convenience sampling technique was used to select study participants. Participants were enrolled into the study as they presented to the clinic. Each week, all new and follow-up patients with RA and SLE attending the Rheumatology Clinic were enrolled into the study and assigned a unique study identification number. Extra care was taken to avoid duplication of participants.

A semi-structured pre-tested interviewer-administered questionnaire was used to collect patients' biodata and sociodemographic characteristics, present and past ocular history, medical history of systemic disease, and family history of rheumatic disease. The type of rheumatic disease, disease duration, and details of medications patient was on were also obtained from patient's hospital medical records. Patients had a complete ophthalmic examination in the following sequence: visual acuity testing, refraction, colour vision test, central vision test, testing for dry eye using tear breakup time (TBUT) and Schirmer's test, anterior segment examination, applanation tonometry, gonioscopy, and then dilated fundal examination with +78D lens.

Visual acuity testing

Visual acuity was tested separately for each eye using a Snellen's chart (E-chart for non-literate patients) at 6 m. A pin hole was used where necessary and spectacles if available. Near vision testing was done using a handheld Snellen near vision chart at 40 cm.

Colour vision test

Colour vision test was conducted in a well-lit room with the Ishihara test plates. The plates were held 75 cm from the patient at right angle to the line of vision. Each patient was tested with 17 plates. Normal literate patients are expected to identify the number on each plate within 3 s, whereas normal non-literate patients are expected to trace the winding lines within 10 s. Correct identification or tracing of 10 plates or more indicates normal colour vision, whereas defective colour vision is identification of 7 plates or less.

Central vision test

Central vision was tested using the standard Amsler's chart. The patient was seated comfortably in a well-illuminated room. The procedure was explained to the patient. Each eye was tested separately. Patients were instructed to wear their near reading correction or were provided with one if necessary. The Amsler's chart was held 30 cm away from the eye to be tested, while the other eye was occluded. The patient was instructed to focus on the dot in the centre of the grid. The patient was then asked to report any lines that are blurred, wavy, distorted, or missing. The absence of any defects was considered normal.

Refraction

Refraction was carried out on patients with a visual acuity of 6/9 or worse by the optometrist. The procedure was explained to the patient. At a working distance of 66 cm, each eye was refracted using a streak retinoscope. Objective refraction followed by subjective refinement was done. The prescription was recorded and given to the patient to fix spectacles.

Applanation tonometry

The procedure was explained to each patient. The prism head of Perkins applanation tonometer (Clement Clark International, Model MK2) was sterilized with 0.5% sodium hypochlorite solution. A drop (or more, if required) of the topical anaesthetic agent was instilled into each eye with a drop of 2% fluorescein. The patient was seated comfortably and instructed to look straight ahead at a target. With the forehead rest of the tonometer in position, and the prism head in contact with the centre of the cornea, the intraocular pressure was measured by turning the thumb wheel. The measurement was taken at the point when the inner edges of the semi-circles met (by observing through the finder eye piece).

Testing for dry eye (using Schirmer's strip and tear breakup time)

Schirmer's test

The procedure was explained to the patient. A drop of topical anaesthetic agent was instilled into each eye. Excess tears were wiped off using cotton wool. Schirmer's strip (folded at the 5 mm at the upper end) was gently placed at the junction between the inner two-thirds and outer one-third of the lower eye lid. The patient was instructed to gently close the eyes.

The strip was removed after 5 min and the amount of wetting read off the strip. Wetting of less than 6 mm was taken as abnormal.[16]

Tear breakup time

The procedure was explained to each patient. A drop of 2% fluorescein was instilled into the eye to be examined. The patient was instructed to blink several times to ensure even distribution of fluorescein. Using a slit lamp biomicroscope with a cobalt blue filter, the patient was instructed to look straight ahead without blinking. The TBUT is the number of seconds (measured with a stop watch) between the last blink and the appearance of the first dry spot in the tear film. A TBUT of 10 s or more was taken as normal.[16]

Gonioscopy

The procedure was explained to each patient. The Goldmann 4 mirror gonioscopy lens was sterilized with 0.5% sodium hypochlorite solution, rinsed with clean water, and dried with cotton wool. A drop of topical anaesthetic agent was instilled into the eye to be examined. The patient was seated comfortably at the slit lamp, and the gonioscopy lens was gently applied on the eye. The patient was instructed to look straight ahead. The anterior chamber angles visualized were graded using Schaffer's grading system.

Slit lamp biomicroscopy and dilated fundoscopic examination with +78D fundus lens

The procedure was explained to each patient. A detailed anterior segment examination was carried out on each eye. A drop of dilating agent (0.5% tropicamide + 2.5% phenylephrine) was instilled. When required, additional drops were instilled to achieve adequate dilatation. With an adequately dilated eye, the patient was seated comfortably at the slit lamp. Each eye was examined for the presence of posterior segment changes such as cotton wool spots, retinal haemorrhages, perivascular sheathing, retinal exudates, arteriolar attenuation, venous tortuosity, neovascularization, papillitis, pallor and cupping of the optic nerve head, and macular changes. Findings were recorded. Patients with abnormal findings had one or more investigations of central visual fields, anterior segment photography, fundus photography, central visual fields using Optopol PTS 920 machine, and optical coherence tomography (OCT) using Zeiss Stratus OCT, Model 3000.

Operational definitions

Dry eye was defined as TBUT of less than 10 s and/or Schirmer's test of less than 6 mm.[16]

Refractive error

was considered significant when spherical correction was −0.50DS (myopia), +1.00DS (hyperopia), and 0.5DC (astigmatism).

Cataract was defined as a clouding or loss of transparency of the lens of the eye.

Corneal opacity was defined as loss of transparency of the whole or part of the cornea due to scarring.

Episclertis was defined as inflammation of the loose connective tissue layer (episcleral tissue) overlying the scleral stroma.

Uveitis was defined as inflammation of the uveal tissue (iris, ciliary body, and choroid) either singly or in combination.

Maculopathy was defined as any disease affecting the macular area like age-related macular degeneration.

Lateral rectus (*LR*) *palsy* was defined as the inability to fully abduct the eye due to paralysis of the abducens nerve (sixth cranial nerve).

Data handling/statistical analysis

Data were checked for consistency and completeness and entered into Statistical Package for Social Sciences (SPSS) version 25 (IBM Corp., Armonk, NY, USA) and analysed.

For descriptive statistics, frequencies and percentages were used for qualitative variables, whereas mean and standard deviation were used for quantitative variables. These variables were categorized where necessary and presented in tables and graphs. At the bivariate level, χ^2 test, Fisher's exact test, or *t*-test was used as appropriate to compare for association between variables, and statistical significance was assessed at *P*-value < 0.05.

Results

A total of 100 patients, 74 of which had RA and 26 SLE, were recruited for the study. Of the recruited patients, 86 (86%) were females and 14 (14%) were males.

The demographic characteristics of the patients are shown in Table 1. The majority of the study participants are females, of Hausa ethnic group, and had tertiary education. The most frequent age group affected was 21–40 years, followed by the age group 41–60 years.

Table 2 shows that all the SLE patients were females, with a mean age of 37.08 ± 13.71, whereas most of the RA patients were females giving a female-to-male ratio of 4.3: 1 and a mean age of 46.45 ± 15.19.

Thirty-six (48.6%) of RA and 18 (69.2%) of SLE patients were Hausas. The majority of the patients in the RA group had tertiary education, whereas those in the SLE group had secondary education. These observed differences were not statistically significant [Table 2].

The prevalence and distribution of eye disorders in RA and SLE patients is shown in Table 3, in which 42 (42%) of the patients had eye disorders.

The prevalence of eye disorders, mean age, and gender variation among RA patients are as shown in Table 4; 31 (41.9%) patients with RA had eye disorders. The mean age of those with eye disorders (52.19 ± 16.17 years) was significantly higher than those without eye disorders (42.30 ± 13.14 years) [Table 4].

Table 1: Sociodemographic characteristics of all patients

Variables	Frequency (*n*=100)	%
Age mean ± SD (years)	44.01±15.32 (18–90)	
Age range (years)	18–90	
Age category (years)		
≤20	7	7.0
21–40	42	42.0
41–60	42	42.0
61–80	7	7.0
>80	2	2.0
Occupation		
Unemployed	32	32.0
Student	16	16.0
Civil servant	21	21.0
Business	12	12.0
Artisan	5	5.0
Others	14	14.0
Level of education		
No formal education	21	21.0
Primary	7	7.0
Secondary	27	27.0
Tertiary	45	45.0
Ethnicity		
Hausa	54	54.0
Fulani	15	15.0
Yoruba	6	6.0
Igbo	3	3.0
Others	22	22.0

The prevalence of eye disorders, mean age, and gender variation among SLE patients are as shown in Table 5; 11 (42.3%) patients with SLE had eye disorders. The mean age of patients with eye disorder was 40.18±15.97 years, whereas it was 34.80±11.85 years for those without eye disorder, but the difference was not statistically significant [Table 5].

Majority of the patients had dry eyes (38%), followed by refractive errors (18%) and cataracts (16%). The least findings were corneal opacities and LR palsy [Table 6]. The results show that there was no statistically significant difference in the pattern of eye disorders between RA and SLE patients except LR palsy ($P = 0.016$) [Table 6].

Discussion

This study assessed the prevalence and pattern of eye disorders among 100 consecutive patients with RA and SLE and found a prevalence of eye disorders of 42% (41.9% among RA patients and 42.3% in SLE patients).

This study found the female gender to be more affected as observed in other studies by Sen *et al.*,[2] Cho,[3] and Choudhary *et al.*[17] The finding of preponderance of female patients in RA (81.1%) and SLE (100%) is in keeping with the nature of autoimmune diseases. Varying explanations have been given to why the female gender is more affected; these include female reproductive hormones, genetic factors, and environmental exposures that may be culturally or

Table 2: Sociodemographic characteristics of RA and SLE patients

Variable	Rheumatic disease		χ^2/FET/*t*-test	*P*-value
	RA (*n*=74)	SLE (*n*=26)		
Age (years), mean±SD	46.45±15.19	37.08±13.71	2.771***	0.007*
Gender				
Female	60 (81.1)	26 (100.0)	5.720**	0.017*
Male	14 (18.9)	0		
Ethnicity				
Hausa	36 (48.6)	18 (69.2)	4.048**	0.373
Fulani	13 (17.6)	2 (7.7)		
Yoruba	4 (5.4)	2 (7.7)		
Igbo	3 (4.1)	0		
Others	18 (24.3)	4 (15.4)		
Educational level				
No formal education	19 (25.7)	2 (7.7)	7.861**	0.041*
Primary	5 (6.8)	2 (7.7)		
Secondary	15 (20.3)	12 (46.2)		
Tertiary	35 (47.3)	10 (38.5)		
Occupation				
Unemployed	23 (31.1)	9 (34.6)	3.388**	0.655
Student	10 (13.5)	6 (23.1)		
Civil servant	15 (20.3)	6 (23.1)		
Business	11 (14.9)	1 (3.8)		
Artisan	4 (5.4)	1 (3.8)		
Others	11 (14.9)	3 (11.5)		

*P-value significant at <0.05
**FET: Fisher's exact test
***t-test
****χ^2 test

occupationally determined.[2] Additionally, differences in health-seeking behaviour in female patients compared with males could also be a factor. Several studies have alluded to a better health-seeking behaviour among female patients compared with males.[18-20]

Most of the patients in this study were educated as 74.4% of RA and 92.3% of SLE patients had at least primary school education. This is similar to the findings of the study by Akintayo *et al.*,[12] in which 96% of the patients had at least primary education. This may be attributable to the studies being tertiary hospital-based and the higher likelihood of educated people to seek health care in such facilities.

The majority of the patients in this study were of Hausa ethnicity at 48.6% and 69.2% in RA and SLE, respectively. This may be due to Hausa being the predominant ethnic group in Zaria where the study was conducted. In comparison with the study by Akintayo *et al.*[12] in Southwestern Nigeria, where majority of the patients were of Yoruba ethnicity at 68% and only 2% were of the Hausa ethnicity, this observed difference may be due to the fact that the Yorubas are the predominant ethnic group in Southwestern Nigeria.

The mean age of all RA patients in this study was found to be 46.45 ± 15.19 years, which is similar to several other studies.[12,21,22] Patients with eye disorders had a significantly higher mean age of 52.19 ± 16.71 years when compared with those without eye disorders of 42.30 ± 13.14 years, similar to the findings of the study carried out by Akintayo *et al.*, in which patients with eye disorders had a mean age of 51.9 ± 13.5 years whereas those without eye disorders had a mean age of 44.0 ± 10.7 years. Older age and longer duration of the disease have been found to be predictors of eye disorders in patients with RA.[12]

The mean age of SLE patients studied was however lower than that of the RA patients at 37.08 ± 13.71 years with a range of 19–63 years, which is similar to what was found in the study by Hussein *et al.*[6] with an age range of 18–61 years. The mean age of those with and without eye disorders among SLE patients was found to be lower than that of RA patients in this study. This difference may be due to the early onset of SLE in Blacks.[23]

Table 3: Prevalence of eye disorders in all patients

Eye disorder	Frequency	Percentage
Absent	58	58.0
Present	42	42.0
Total	100	100.0

Table 4: Prevalence of eye disorders, mean age, and gender variation among RA patients

Variables	Eye disorder		χ^2/FET/*t*-test	*P*-value
	Absent (*n* = 43, 58.1%)	Present (*n* = 31, 41.9%)		
Age (years), mean±SD	42.30 ± 13.14	52.19 ± 16.17	2.900	0.005*
Gender				
Female	38 (88.4)	22 (71.0)	3.557	0.059
Male	5 (11.6)	9 (29.0)		

F:M ratio is 22:9 = 2.4:1, *t*-test = 2.900; **P*-value significant at <0.05; χ^2 = 3.557

Table 5: Prevalence of eye disorders, mean age, and gender variation among SLE patients

Variables	Eye disorder		*t*-test	*P*-value
	Absent (*n* = 15, 57.7%)	Present (*n* = 11, 42.3%)		
Age (years), mean±SD	34.80 ± 11.85	40.18 ± 15.97	0.988	0.333
Gender				
Female	15 (100.0)	11 (100.0)	—	—
Male	—	—		

F:M ratio is 11:0, *t*-test = 0.988

Table 6: Comparison of eye disorders among RA and SLE patients

Eye disorder	*n*	Rheumatic disease		χ^2	*P*-value
		RA	SLE		
Dry eye	38	29 (39.2)	9 (45)	0.171	0.679
Refractive errors	18	13 (17.5)	5 (25)	0.036	0.849
Corneal opacities	2	1 (1.4)	1 (5)	0.611	0.434
Cataract	16	14 (18.9)	2 (10)	1.804	0.179
Episcleritis	4	4 (5.4)	0	1.464	0.226
Uveitis	5	4 (5.4)	1 (5)	0.098	0.754
LR palsy	2	0	2 (10)	5.808	0.016*
Maculopathy	9	9 (12.2)	0	3.475	0.062

**P*-value significant at <0.05

The overall prevalence of eye disorders in this study was 42% (in both RA and SLE). However, the prevalence in RA patients was 41.9% similar to studies by Vignesh and Srinivasan[8,9] (39%) and Akintayo *et al.*[12] (46%). Other studies by Aboud *et al.*[21] and Zlatanović *et al.*[24] found a lower prevalence of 33.9% and 27.2%, respectively.

The prevalence of eye disorders in SLE in this study was found to be 42.3%. This value is close to that of a similar study by Sitaula *et al.*[4] with a prevalence of 46.6% but higher than that in the studies by Dammacco *et al.*[25] (29.6%) and El Shareef *et al.*[26] (34.6%). The study design may explain the differences in prevalence. The studies with lower prevalence were retrospective hospital-based and case–control studies, whereas this study was cross-sectional. Missed cases/records as well as limited number of cases and controls may account for the lower values obtained in these studies.[25,26]

Dry eye was found to be the most common eye disorder in both RA and SLE patients. The prevalence of dry eye in RA patients was found to be 39.2%, which is slightly higher than that of a study carried out in Southwest Nigeria by Akintayo *et al.*,[12] in which the prevalence was 30%. In other studies, the prevalence of dry eye in RA patients was between 17.6% and 50%.[10,21,24] This variation may be due to the different methodologies employed in the studies. The predominance of dry eye in most RA patients may be because ocular manifestations are commonly found in patients with advanced age, and dry eye disease is more common in older individuals. Patients with dry eye will therefore require supplementation of artificial tears for a lifetime.[12]

Dry eye was the most common manifestation among SLE patients with a frequency of 45%, similar to the findings of a study by Sitaula *et al.*,[4] with a prevalence of 41.5%. However, the study by Goginski *et al.*[27] in Brazil found a higher prevalence of 51.4%. This difference may be due to the different methods used in assessing dry eye. This study assessed dry eye using TBUT and Schirmer's test, whereas Goginski *et al.* used Schirmer's test and Ocular Surface Disease Index (OSDI) score.[22] The OSDI score being a subjective assessment tool may overestimate the presence of dry eye. Environmental factors such as hot, dry, and windy weather conditions and possibly genetic background of the studied population may also have contributed to the observed difference in the results obtained.[27]

The second most common eye disorder in RA patients was cataract with a prevalence of 18.9%. The study by Akintayo *et al.*[12] found a higher prevalence of 26%; this difference may be due to having more elderly patients in their study and a smaller sample size. The study by Vignesh and Srinivasan[9] with a much larger sample size found the cataract prevalence of 1% among RA patients. Individual and genetic susceptibility as well as advancing age are also known to play a role in the development of cataract. RA/SLE-induced inflammation and prolonged use of medication such as steroids are also known to predispose these patients to the development of cataract.

Cataract was also found to be common among SLE patients in this study with a prevalence of 10%. The frequency of cataract was reported to be in the range of 5–32% in some studies.[4] Cataracts have been associated with the use of corticosteroids; however, advancing age and duration of SLE along with individual and genetic susceptibility have been recognized as factors.[28]

Refractive errors constituted 17.5% and 25% of eye disorders among RA and SLE patients, respectively. These may be incidental findings as refractive errors are not known to be major eye disorders found in either RA or SLE. However, refractive changes may complicate scleritis in these patients even in the inactive phase[29]; we found no patient with active scleritis in this study.

Episcleritis was found to have a prevalence of 5.4% among RA patients in this study, which is similar to the study by Zlatanović *et al.*,[24] which showed a prevalence of 5%. However, Vignesh and Srinivasan[9] and Aboud *et al*.[21] found prevalences of 3% and 4.9%, respectively. No patients with SLE were found to have episcleritis. The inflammatory response in episcleritis is usually limited to the superficial episcleral vascular network.

The prevalences of uveitis were found to be 5.4% and 5% among RA and SLE patients, respectively. A study by Albidri *et al.*[22] in Iraq found a prevalence of uveitis of 1.9%. The higher value in this study may be due to the smaller sample size as well as the difference in geographical location of the studies.

Two patients (10%) with SLE had LR palsy whereas none with RA had, and this difference in prevalence was statistically significant. The prevalence of LR palsy among SLE patients varies between 2% and 7% in other studies.[30] The slightly higher prevalence in this study may be due to the small number of SLE patients studied. LR palsy (abducent nerve palsy) is a rare manifestation of SLE whose pathogenesis is unknown but is thought to be due to either inflammation related to cytokine production or vascular lesions (vasculitis).[22] Vision-threatening eye disorders such as PUK and retinal vasculitis were not observed in the patients studied. This may be due to patients being enrolled from the Rheumatology Clinic who are mostly on medications and have stable disease.

In conclusion, this study assessed the prevalence and pattern of eye disorders in RA and SLE patients and found that eye disorders were common among RA and SLE patients with a prevalence of 41.9% and 42.3%, respectively, with dry eye and cataracts being the most common eye disorders. It is recommended that comprehensive eye examination be done on all RA and SLE patients at diagnosis, before commencement of medications, and periodically during follow-ups. In addition, patients with eye complaints should also be referred promptly for evaluation by an ophthalmologist.

Limitations of the study include being a hospital-based study, and the results may not be a true reflection of the general population. The non-probability sampling technique used is also a limitation of the study.

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Conflicts of interest

There are no conflicts of interest.

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