

## A Study of Dry Eye Disorder in Elderly Persons of Western Rajasthan

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### Abstract

**Introduction:** Dry eye syndrome is one of the most frequently encountered ocular condition and is a common cause of discomfort especially in the elderly population. It has a multifactorial etiology, which, in most cases, is always chronic and progressive.

**Material and Methods:** This study was conducted from January 2015 to December 2015 and total 108 patients of more than 50 years age group were enrolled. It was a non randomized observational study in which all patients attending outdoor of department of Ophthalmology at MDM Hospital, Jodhpur with features of dry eyes syndrome were enrolled after receiving informed written consent.

**Results:** Dry eye was more common in females (63.89%) in comparison to males (36.11%). Seventy eight percent of patients suffering from dry eye were above 60 years of age. 67.59% of dry eye patients were from rural areas. Most frequent complaint in patients suffering from dry eye was feeling of grittiness and soreness in eyes (80.56%). Next most frequent complaint was redness of eyes in 68.52% of cases followed by burning sensation in eyes (66.67%). Dry climatic condition was present for 100 percent of patients. Evidences suggestive of meibomian gland dysfunction were present in 63.89% of patients. History of cataract surgery by phacoemulsification and diabetes were present in 49.07% and 44.44% of patients respectively. Among symptomatic females, 34.26% patients were postmenopausal.

**Conclusions:** Dry eye disorders are more common in elderly females. Most frequent complaint in patients suffering from dry eye was feeling of grittiness, redness and burning sensation in eyes. Dry climatic conditions, meibomian gland dysfunction, previous eye surgery, diabetes mellitus, long term antihistaminics and topical anti glaucoma drugs were most important risk factors for causing dry eyes in our study.

**Keywords:** Dry eye syndrome, ocular surface, Meibomian gland dysfunction

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Dry eye syndrome is one of the most frequently encountered ocular condition and is a common cause of discomfort that can seriously

affect a patient's quality of life, especially in the elderly population.<sup>1</sup> It has a multifactorial etiology which in most cases, is always chronic and progressive. The tear film, cornea, conjunctiva, lacrimal glands and lids work together in a close anatomic and functional relationship as a functional unit to provide an efficient system recognized as the ocular surface. Dry eye is recognized as a consequence of disruption of lacrimal functional unit which consists of lacrimal glands, ocular surface including cornea, conjunctiva, eyelids, meibomian glands, ocular nerves, and goblet cells.<sup>2</sup>

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The tear film is composed of three main layers innermost mucin, middle aqueous and outermost lipid layer. Dry eyes can be divided into two groups: aqueous production deficient dry eye disease and evaporative dry eye disease. Insufficient tears cause damage to the interpalpebral ocular surface and are associated with symptoms of discomfort.

The prevalence of dry eye syndrome increases with age and affects a significant percentage of the population, especially those older than 50 years of age.<sup>3</sup> It is more common in women than in men.<sup>4</sup>

Tear deficient dry eye due to poor production of tears by the tear glands is found in older patients, in postmenopausal women and in patients with autoimmune diseases like primary Sjögren's syndrome and rheumatoid arthritis.<sup>5</sup> Rosacea, blepharitis, and MGD (meibomian gland dysfunction) are major causes of evaporative dry eyes. Patients with disease of the tear gland such as vitamin A deficiency, trachoma, sarcoidosis and lymphoma can also cause dry eye.<sup>6</sup> Other causes are allergies, chemical burns, thermal burns and immunological conditions such as mucous membrane pemphigoid.

The International Dry Eye Workshop (2007) defined dry eye as a multifactorial disease of the tears and ocular surface that results in symptoms of discomfort, visual disturbance and tear film instability with potential damage to the ocular surface. The main symptom of dry eyes is dry and gritty feeling in the eyes.<sup>7,8</sup> The additional symptoms include burning or itching in the eyes, foreign body sensation, excess tearing, pain and redness of the eyes and photophobia in some cases.<sup>7,8</sup> Sometimes it is also associated with a stringy discharge and blurred, changing vision. Symptoms are found to worsen in dry weathers with low humidity and higher temperatures.<sup>9</sup> DES is associated with decreased ability to perform certain activities such as reading, driving and computer related work, which requires visual attention.

The diagnosis of dry eye syndrome can be made by physical examination and performing diagnostic tests like tear film breakup time (TBUT), Schirmer test and epithelial staining and can be graded into 4 grades.<sup>10</sup>

## Materials and Methods

The study was conducted from January 2015 to December 2015 and total 108 patients of more than 50 years age group were enrolled. It was non randomized observational study in which all patients attending outdoor of department of Ophthalmology at MDM Hospital, Jodhpur with features of dry eyes syndrome were enrolled.

Exclusion criteria:

1. Active eye infection/inflammation.
2. Those who refused for consent.

Informed consent was obtained from each participant. Age, gender, demographic details, detailed history and detailed eye examination were recorded. Tear film status was examined using Schirmer test and tear film break up time was recorded.

The time required for the tear film to break up following a blink is called TBUT. The normal time for tear film breakup is 15–20 sec. A fluorescein strip is moistened with saline and applied to the inferior cul-de-sac. After several blinks, the tear film is examined using a broad-beam of slit lamp with a blue filter for the appearance of the first dry spots on the cornea. TBUT values of less than 5–10 seconds indicate tear film instability.<sup>11</sup>

Schirmer test quantitatively measures the tear production by the lacrimal gland during fixed time period.<sup>12</sup> The basic test is performed by instilling topical anaesthetic and then placing a thin strip of filter paper in the inferior cul-de-sac.<sup>13</sup> The patient's eyes are closed for 5 minutes and the amount of tears that wets the paper is measured in terms of length of wet strip and wetting of <15 mm after 5 minutes is considered abnormal.<sup>14</sup>

## Dry eye severity grading system<sup>10</sup>

Severity level	Grade 1	Grade 2	Grade 3	Grade 4
1. <b>Discomfort (severity &amp; frequency)</b>	Mild, episodic; occurs under environmental stress	Moderate, episodic or chronic; occurs with or without stress	Severe, frequent or constant; occurs without stress	Severe or disabling, constant
2. <b>Visual symptoms</b>	None or episodic mild fatigue	Annoying or activity-limiting, episodic	Annoying, chronic or constant, activity-limiting	Constant and possibly disabling

3.	<b>Conjunctival injection</b>	None to mild	None to mild	+/-	+/>+
4.	<b>Conjunctival staining</b>	None to mild	Variable	Moderate to marked	Marked
5.	<b>Corneal staining (severity &amp; location)</b>	None to mild	Variable	Marked central	Severe punctate erosions
6.	<b>Corneal and tear signs</b>	None to mild	Mild debris, decreased meniscus	Filamentary keratitis, mucus clumping, increased tear debris	Filamentary keratitis, mucus clumping, increased tear debris, ulceration
7.	<b>Lid &amp; meibomian glands</b>	MGD variably present	MGD variably present	MGD frequent	Trichiasis, keratinization, symblepharon
8.	<b>Tear breakup time</b>	Variable	≤ 10 s	≤ 5 s	Immediate
9.	<b>Schirmer score</b>	Variable	≤ 10 mm/5 min	≤ 5 mm/5 min	≤ 2 mm/5 min

## Results

**Table 1.** Age and sex wise distribution

Age	Male	Female	Total
50- 55	04	02	06 (05.55%)
55 – 60	06	12	18 (16.66%)
60 – 65	14	18	32 (29.63%)
65 -70	08	36	44 (40.74%)
>70	07	01	08 (07.40%)
Total	39 (36.11%)	69 (63.89%)	108 (100%)

Table 1 shows age and sex wise distribution of dry eye patients. Dry eye was more common in females (63.89%) in comparison to males (36.11%). 77.78% of patients suffering from dry eye were above 60 years of age. 40.74% of patients were of 65-70 years of age group. Only 22.22% of patients suffering from dry eyes were less than 60 years age group.

Dry eye conditions are more common in patients residing in rural areas. In our study 67.59% of dry eye patients were from rural areas. Rest 32.41% patients were from urban background.

**Table 2.** Grades of dry eye

Grade	Male	Female	Total
Grade 1	18	38	<b>56 (51.85%)</b>
Grade 2	15	23	<b>38 (35.19%)</b>
Grade 3	04	05	<b>09 (08.33%)</b>
Grade 4	02	03	<b>05 (04.63%)</b>
<b>Total</b>	<b>39</b>	<b>69</b>	<b>108</b>

Grade 1 dry eye was present in 51.85% of patients. Grade 2 dry eye was present in 35.19% of patients, 8.33% patients had grade 3 dry eye and rest of 4.63% patients had grade 4 dry eye.

**Table 3.** Symptoms at presentation

Symptoms	Males	Females	Total
Burning sensation in the eyes	27	45	72 (66.67%)
Feeling of dryness in the eyes	11	19	30 (27.78%)
Feeling of grittiness and soreness in the eyes	29	58	87 (80.56%)
Eye sensitivity to wind (eyes water more in the wind)	18	04	22 (20.37%)
Redness of eyes	25	49	74 (68.52%)
Eye fatigue, even after reading for a relatively short period	16	06	22 (20.37%)
Photophobia - sensitivity to light	17	21	38 (35.19%)
Discomfort when wearing contact lenses	0	0	0
Tearing	09	13	22 (20.37%)
Blurred vision - usually worse towards the end of the day	05	07	12 (11.11%)
Eyelids stick together when awake	19	26	45 (41.67%)

Most frequent complaint in patients suffering from dry eye was feeling of grittiness and soreness in eyes (80.56%). Next most frequent complaint was redness of eyes in 68.52% of cases. 66.67% patients reported burning sensation in eyes. Stickiness of eyes on waking up in morning was reported in 41.67% of patients.

Sensitivity to light was present in 35.19% of patients suffering from dry eyes. Feeling of dryness in eyes was reported only in 27.78% of patients. Excessive tearing (reflex), eye fatigue and eye

sensitivity to wind was reported in 20.37% of patients. Blurred vision was reported only in 11.11% of patients.

**Table 4.** Risk factors for dry eye

Risk factors	Males	Females	Total
Dry climatic conditions	39	69	108 (100%)
Sjogren syndrome (Connective tissue disorders)	04	11	15 (13.89%)
Diabetes mellitus	18	30	48 (44.44%)
Allergic disorders	12	21	33 (30.56%)
HIV infection	01	00	01 (00.92%)
Vitamin A deficiency	00	00	00
Trachoma	04	11	15 (13.89%)
Facial nerve palsy	00	00	00
Immunological diseases of skin and eyes like SJS, pemphigoid, etc	01	04	05 (04.63%)
Chemical injury of eyes	03	01	04 (03.70%)
Meibomian gland dysfunction	21	48	69 (63.89%)
Lid abnormalities	05	02	07 (06.48%)
Proptosis	00	00	00
Computer users (>6 hours per day)	00	00	00
Drivers (>6 hours per day)	03	00	03 (02.78%)
Prolonged TV watching (>6 hours per day)	00	00	00
Menopause	00	37	37 (34.26%)
Ocular Trauma	00	00	00
Post Cataract Surgery (Phacoemulsification)	21	32	53 (49.07%)
Large incision ECCE	02	01	03 (02.78%)
Laser surgery	0	1	01 (00.92%)
Systemic chemotherapy	00	00	00
Radiation therapy	00	00	00
Penetrating keratoplasty	02	01	03 (02.78%)
Cigarette smoking	27	02	29 (26.85%)
<b>Medications</b>			
Antihistamines (long term)	10	15	25 (23.15%)
Isotretinoin therapy	00	00	00
Tricyclic antidepressants	00	00	00

Diuretics	07	04	11 (10.19%)
Beta-blockers topical	08	06	14 (12.96%)
Beta-blockers systemic	09	04	13 (12.04%)
Alcohol	13	00	13 (12.04%)

Dry climatic condition was present for 100 percent of patients. Evidences suggestive of meibomian gland dysfunction were present in 63.89% of patients. History of cataract surgery by phacoemulsification was present in 49.07% of patients. The possible explanation for this are age related factors which are responsible for both the disorders (cataract and dry eye). Forty four percent of patients suffering from dry eye were diabetics, 34.26% patients were postmenopausal females and 30.56% of the patients had history of coexisting allergic disorder. History suggestive of cigarette smoking was present in 26.85% of patients. Twenty three percent patients were on long term antihistaminics.

History and clinical features suggestive of Sjogren syndrome were present in 13.89% of patients. History of medications like topical beta blockers, systemic beta blockers and diuretic ingestion were present in 12.96%, 12.04% and 10.19% of patients respectively. History of regular alcohol consumption was present in 12.04% of patients. Lid abnormalities were present in 6.48% of dry eye cases.

Other risk factors identified were immunological diseases of skin and eyes like SJS, pemphigoid, etc and chemical injuries to eyes in 4.63% and 3.70% of cases respectively. Driving more than 6 hours per day, penetrating keratoplasty and history of large incision ECCE were present in 2.78% of cases. Laser surgery and HIV infection was present in only 0.92% of cases.

### Discussion

The prevalence of dry eye is in the range of 5-30% in the population aged 50 years and older. We found that 77.78% of our patients suffering from dry eye were above 60 years of age. Dry eye is more common in older patients due to relative reduction in tear production and increased meibomian gland dysfunction with age.<sup>15-17</sup>

In present study dry eye syndrome was more common in females (63.89%) in comparison to males (36.11%). Recent epidemiological studies support the fact that there is a higher prevalence of dry eye among women.<sup>18</sup> The hormonal changes that

accompany menopause can also play an important role in the production of dry eye symptoms.<sup>19</sup>

The present study revealed that about 68% of our patients were from rural areas working in adverse environmental conditions for long hours. Sahai and colleagues also reported that dry eye conditions are more common in rural areas in comparisons to urban areas.<sup>20</sup> In rural areas, patients are exposed to excessive heat, sunlight, dust, wind and poor economic conditions as well as lack of awareness in this group of people prevents them from adopting protective equipment during work.

Grade 1 and grade 2 dry eyes were present in 51.85% and 35.19% of patients respectively. Only patients who had history of chemical injury or trachoma in past had grade 4 dry eyes (04.63%).

Most frequent complaint observed in present study amongst patients suffering from dry eye was feeling of grittiness and soreness in eyes (80.56%). Next most frequent complaints were redness of eyes in 68.52% and burning sensations in 66.67% of patients with stickiness of eyes on waking up in morning, Sensitivity to light and feeling of dryness was reported in 41.67%, 35.19% and 27.78% of patients respectively. Excessive tearing (reflex), eye fatigue and eye sensitivity to wind - each was reported in 20.37% of patients. Ohash and Solomen also observed that main symptom of dry eyes is dry and gritty feeling in the eyes and other symptoms including burning or itching in the eyes, foreign body sensation, excess tearing, pain and redness of the eyes and photophobia in some cases. Stringy discharge and blurred, changing vision was also reported in some of the patients.<sup>7,8</sup>

In the present study dry climatic condition was present for 100 percent of patients. Both relative humidity and temperature influence the overall thermal climate and its effect on the precorneal tear film and thus, dry eye symptoms. Kaercher and Bron also reported that symptoms of dry eyes are found to worsen in dry weather, with low humidity and higher temperatures.<sup>9</sup>

Around 64% of dry eye disease patients had evidences suggestive of meibomian gland dysfunction. Meibomian gland dysfunction is a chronic, diffuse abnormality of the meibomian glands, commonly characterized by terminal duct obstruction and/or qualitative/quantitative changes in the glandular secretion.<sup>21</sup> This may result in alteration of the tear film, symptoms of eye irritation, clinically apparent inflammation and ocular surface disease.<sup>21</sup> In a study by Nelson et al found meibomian gland dysfunction as the most common cause of evaporative dry eye.<sup>21</sup> Further,

aging is associated with the development of meibomian gland dysfunction, which in turn leads to tear film instability and evaporative dry eye.

In present study history of cataract surgery by phacoemulsification was present in 49.07% of patients. The possible explanation for this is the age related factors are responsible for both the disorders (cataract and dry eye). Previous eye surgery (such as corneal transplantation, extracapsular cataract procedures and refractive surgery), or long-term use of medications which create hypersensitivity or toxicity in the eye can predispose to dry eye. Ang et al reported that dry eye-associated symptoms, such as foreign body sensation and fatigue, frequently occur after cataract surgery.<sup>22</sup>

Forty four percent of dry eye patients were diabetic. This is consistent with a study conducted by Manaviat *et al.* in Iran where 54.3% of the type 2 diabetic patients suffered from dry eye syndrome.<sup>23</sup> In their study by Alves Mde et al reported that diabetic patients have tear secretion deficiency, peripheral neuropathy and hyperglycaemia that lead to corneal epitheliopathy and consequent hyperosmolarity which can be related to DES.<sup>24</sup>

We found that 34.26% patients of dry eyes were postmenopausal females. Wenderlein also found that dry eye is more common in postmenopausal females.<sup>25</sup> In our study 30.56% of the patients had history of coexisting allergic disorder. According to Gregg et al allergic ocular disorders and dry eyes can occur simultaneously or independently of each other and both can have similar symptoms.<sup>26</sup> Additionally, treatment of ocular allergy can lead to the exacerbation of dry eye symptoms.<sup>26</sup>

History suggestive of cigarette smoking was present in 26.85% of patients. Previous studies have also related an increased prevalence of dry eye among smokers.<sup>27</sup>

In our study 23.15% dry eye patients were on long term antihistaminics and 12.96% of patients were on topical antiglaucoma medications. Many components of eye drop formulations can induce a toxic response from the ocular surface. The most common offenders are preservatives such as benzalkonium chloride, which causes surface epithelial cell damage and punctate epithelial keratitis. This interferes with ocular surface wetting.<sup>28</sup>

History and clinical features suggestive of Sjögren syndrome were present in 13.89% of patients. Sjögren's syndrome is a long term autoimmune disease in which the moisture-producing glands of the body are affected.<sup>29</sup>

We found history of medications like topical beta blockers, systemic beta blockers and diuretic ingestion were present in 12.96%, 12.04% and 10.19% of patients respectively. History of regular alcohol consumption was present in 12.04% of patients.

Lid abnormalities were present in 6.48% of dry eye cases. Other risk factors identified were immunological diseases of skin and eyes like SJS or pemphigoid and chemical injuries to eyes in 4.63% and 3.70% of cases respectively.

## Conclusion

Dry eye disorders are prevalent, multifactorial disorders that are particularly frequent in elderly patients and women, especially menopausal and postmenopausal women. Dry eye disorders can be episodic with transient signs and symptoms or chronic with persistent signs and symptoms. It has a significant impact on visual function that can negatively impinge on the patient's quality of life and productivity. Dry eye conditions are more common in patients residing in rural areas.

Most frequent complaint in patients suffering from dry eye was feeling of grittiness, redness and burning sensation in eyes. Dry climatic conditions, meibomian gland dysfunction, previous eye surgery, diabetes mellitus, long term antihistaminics and topical anti glaucoma drugs were most important risk factor for causing dry eyes in our study. Trachoma and Chemical Injury of eye were responsible for severe form of dry eyes.

## References

- Moss SE, Klein R, Klein BE. Incidence of dry eye in an older population. *Arch Ophthalmol* 2004;122:369-373.
- Lang JC and Roehrs RE, Ophthalmic preparations in Remington: The Science and Practice of Pharmacy, Troy DB, (Ed.), vol. 1, pp. 850-854, Lippincott Williams Wilkins, Philadelphia, 21st edition, 2005. [http://scholar.google.com/scholar\\_lookup?title=Ophthalmic+preparations&author=J.+C.+Lang&author=R.+E.+Roehrs&publication\\_year=2005](http://scholar.google.com/scholar_lookup?title=Ophthalmic+preparations&author=J.+C.+Lang&author=R.+E.+Roehrs&publication_year=2005)
- Schaumberg DA, Dana R, Buring JE, and Sullivan DA. Prevalence of dry eye disease among US men: estimates from the physicians' health studies. *Archives of Ophthalmology*. 2009; 127:763:768.
- Schaumberg DA, Sullivan DA, Dana MR. Epidemiology of dry eye syndrome, *Advances in Experimental Medicine and Biology*. 2002; 506:989-998.
- Fujita M, Igarashi T, Kurai T, et al. Correlation between dry eye and rheumatoid arthritis activity, *Am J Ophthalmol*. 2005; 140(5):808-813.
- Guzey M, Ozardali I, Basar E, et al. A survey of trachoma: the histopathology and the mechanism of progressive cicatrization of eyelid tissues, *Ophthalmologica*, 2000; 214(4), 277-284.
- Ohashi Y, Ishida R, Kojima T, et al., Abnormal protein profiles in tears with dry eye syndrome, *Am J Ophthalmol.*, 2003; 136(2): 291-299.
- Solomon, D. Dursun, Z. Liu, Y. Xie, A. Macri, and S. C. Pflugfelder, Pro- and anti-inflammatory forms of interleukin-1 in the tear fluid and conjunctiva of patients with dry-eye disease, *Invest Ophthalmol Vis Sci.*, 2001; 42(10):2283-2292.
- Kaercher T, Bron A, Classification and diagnosis of dry eye in surgery for the dry eye, Geerling G, Brewitt H (Eds.). 2008; 41:36-53.
- Behrens A, Doyle JJ, Stern L, et al. Dysfunctional tear syndrome. A Delphi approach to treatment recommendations. *Cornea* 2006;25:90-7
- Abelson MB, Ousler GW III, Nally LA, et al. Alternative reference values for tear film break up time in normal and dry eye populations. *Advances in Experimental Medicine and Biology*. 2002; 506: 1121-1125.
- Pflugfelder SC, Solomon A, Stern ME, The diagnosis and management of dry eye: a twenty-five-year review, *Cornea*, 2000; 19(5):644-649.
- Yokoi N, Komuro A, Non-invasive methods of assessing the tear film, *Experimental Eye Research*. 2004; 78(3): 399-407.
- Tsubota K, Kaido M, Yagi Y, et al. Diseases associated with ocular surface abnormalities: the importance of reflex tearing, *British Journal of Ophthalmology*. 1999; 83(1):89-91.
- Shine WE, McCulley JP, Keratoconjunctivitis sicca associated with meibomian secretion polar lipid abnormality, *Archives of Ophthalmology*. 1998; 116(7):849-852.
- Mathers WD, Lane JA, Zimmerman MB. Tear film changes associated with normal aging. *Cornea* 1996; 15:229-34.
- Hom MM, Martinson JR, Knapp LL, Paugh JR. Prevalence of Meibomian gland dysfunction. *Optom Vis Sci* 1990; 67:710-2.
- Lin PY, Tsai SY, Cheng CY, Liu JH, Chou P, Hsu WM. Prevalence of dry eye among an elderly Chinese population in Taiwan: the Shihpai Eye Study. *Ophthalmology* 2003; 110:1096-101.
- Mathers WD, Stovall D, Lane JA, Zimmerman MB, Johnson S. Menopause and tear function: the influence of prolactin and sex hormones on human tear production. *Cornea* 1998; 17:353-8.

20. Sahai A, Malik P. Dry Eye: Prevalence and attributable risk factors in a hospital-based population. *Indian J Ophthalmol* 2005;53:87-91
21. Nelson JD, Shimazaki J, Benitez-del-Castillo JM, et al. The international workshop on meibomian gland dysfunction: report of the definition and classification subcommittee. *Invest Ophthalmol Vis Sci*. 2011;52(4):1930–1937.
22. Ang RT, Dartt DA, Tsubota K. Dry eye after refractive surgery. *Curr Opin Ophthalmol*. 2001; 12:318–322.
23. Manaviat MR, Rashidi M, Afkhami-Ardekani M, Shoja MR. Prevalence of dry eye syndrome and diabetic retinopathy in type 2 diabetic patients. *BMC Ophthalmol*. 2008; 8:10.
24. Alves Mde C, Carvalheira JB, Modulo CM, Rocha EM. Tear film and ocular surface changes in diabetes mellitus. *Arquivos brasileiros de oftalmologia*. 2008; 71(6 Suppl):96-103.
25. Wenderlein M, Mattes S. The “dry eye” phenomenon and ovarian function. Study of 700 women pre- and postmenopausal. *Zentralblatt fur Gynakologie*. 1996; 118(12): 643-649.
26. Gregg J, Berdy, Bo Hedqvist. Ocular Allergic Disorders and Dry Eye Disease: Associations, Diagnostic Dilemmas, and Management. *Acta Ophthalmol. Scand*. 2000; 78: 32–37
27. Klein BE, Klein R. Lifestyle exposures and eye diseases in adults. *Am J Ophthalmol*. 2007; 144: 961–969.
28. The definition and classification of dry eye disease: Report of the Definition and Classification Subcommittee of the International Dry Eye Workshop (2007) *Ocul Surf*. 2007; 5:75–92.
29. "What Is Sjögren's Syndrome? Fast Facts". NIAMS. November 2014.