

2019

Prevalencia de ojo seco en pacientes que acuden a la Clínica de Optometría de la FESI, UNAM

Pedro Navarro Luna

Centro de Diagnóstico de Alteraciones de Superficie Ocular, Iztacala, revistasaludvisual@lasalle.edu.co

Alicia Vázquez Mendoza

Iztacala UNAM, revistasaludvisual@lasalle.edu.co

Javier Alonso Trujillo

Iztacala UNAM, revistasaludvisual@lasalle.edu.co

Álvaro Édgar González Aragón Pineda

Iztacala UNAM, revistasaludvisual@lasalle.edu.co

Óscar Antonio Ramos Montes

Iztacala UNAM, revistasaludvisual@lasalle.edu.co

Follow this and additional works at: <https://ciencia.lasalle.edu.co/svo>

Citación recomendada

Navarro Luna P, Vázquez Mendoza A, Alonso Trujillo J, González Aragón Pineda ÁÉ y Ramos Montes ÓA. Prevalencia de ojo seco en pacientes que acuden a la Clínica de Optometría de la FESI, UNAM. *Cienc Tecnol Salud Vis Ocul*. 2019;(1): 11-18. doi: <https://doi.org/10.19052/sv.vol17.iss1.1>

This Artículo is brought to you for free and open access by the Revistas Unisalle at Ciencia Unisalle. It has been accepted for inclusion in Ciencia y Tecnología para la Salud Visual y Ocular by an authorized editor of Ciencia Unisalle. For more information, please contact ciencia@lasalle.edu.co.

Artículos originales

Prevalence of Dry Eye in Patients at the FESI Optometry Clinic, UNAM*

Prevalencia de ojo seco en pacientes que acuden a la Clínica de Optometría de la FESI, UNAM

PEDRO NAVARRO LUNA**
ALICIA VÁZQUEZ MENDOZA***
JAVIER ALONSO TRUJILLO****
ÁLVARO ÉDGAR GONZÁLEZ ARAGÓN PINEDA*****
ÓSCAR ANTONIO RAMOS MONTES*****

Received: 09-03-2018 / Accepted: 01-21-2019

ABSTRACT

Objective: To report the prevalence of dry eye and to determine the differences between young and adult patients attending the Optometry Clinic of the Iztacala School of Higher Education at Universidad Nacional Autónoma de México (UNAM). **Material and methods:** In 1957, patients between the ages of 15 and 65 assessed at the “Centro de Diagnóstico de Alteraciones de Superficie Ocular” of the Iztacala School of Higher Education of UNAM between August 2016 and August 2017. The patients answered the digital version of the Ocular Surface Disease Index (OSDI) diagnostic questionnaire and the mucin arborization pattern was evaluated using the Tear Ferning Test (TFT). **Results:** The mean prevalence of the diagnosis with a significant difference of positive $P < 0.05$ for Ferning (59.1%) and OSDI (63.8%). Using the Ferning technique in young patients (15 to 29 years), it was possible to assess a prevalence of dry eye of 51.9%; whereas in adults (30 to 65 years) it was 66.9%. Using the OSDI questionnaire, the prevalence was 60.1% in young people and 67.8% in adults; in addition, for each year of increase in age, the probability of having a dry eye increased by 1% with OSDI and 2% with Ferning. **Conclusions:** With this study, it was established, for the first time, that the young people who go to the optometry clinic of FES-Iztacala, a sector that had not been previously considered, also suffer from this disease.

Keywords: Dry eye, prevalence, Ferning test, ocular surface.

* La presente investigación no depende de ningún proyecto institucional o subvención económica. En ella tampoco existe conflicto de intereses con los autores.

** BA in Optometry, in charge of Centro de Diagnóstico de Alteraciones de Superficie Ocular, Iztacala.

*** PhD in Biomedical Sciences, Professor for the BA in Optometry Iztacala UNAM.

**** PhD in Education, Coordinator of the Methodology of Research and Research in Nursing modules at Iztacala UNAM.

***** PhD in Dental Public Health, Professor for the Doctor of Dental Surgery Program at Iztacala UNAM.

***** Specialist in Electron Microscopy, Director of the BA Program in Optometry at Iztacala UNAM.

Cómo citar este artículo: Navarro Luna P, Vázquez Mendoza A, Trujillo AJ, González Aragón Pineda A, Ramos Montes OA. Prevalence of Drey Eye in Patients at the FESI Optometry Clinic, UNAM. *Cienc Tecnol Salud Vis Ocul.* 2019;17(1): 11-18. <https://doi.org/10.19052/sv.vol17.iss1.1>



RESUMEN

Objetivo: estimar la prevalencia de ojo seco y determinar si existen diferencias entre pacientes jóvenes y adultos que acuden a la Clínica de Optometría de la Facultad de Estudios Superiores Iztacala, UNAM. **Materiales y métodos:** se seleccionaron 1957 pacientes de 15 a 65 años de edad evaluados en el Centro de Diagnóstico de Alteraciones de la Superficie Ocular de la Facultad de Estudios Superiores Iztacala de la Universidad Nacional Autónoma de México, de agosto del 2016 a agosto del 2017. Los pacientes resolvieron el cuestionario de diagnóstico en su versión digital OSDI y se les evaluó el patrón de arborización de mucinas mediante Test Lagrimal de Ferning (TFT). **Resultados:** la prevalencia del diagnóstico tiene una diferencia significativa de $P < 0.05$ positivo para Ferning (59.1 %) y para OSDI (63,8 %). Mediante la técnica de Ferning en pacientes jóvenes (15 a 29 años), se pudo valorar una prevalencia de ojo seco del 51,9%, mientras que en adultos (30 a 65 años) fue de 66,9%. Utilizando el cuestionario OSDI en jóvenes, la prevalencia es del 60 % y en adultos del 67,8 %; se encontró, además, que por cada año de incremento en la edad, la probabilidad de padecer ojo seco aumenta en 1 % mediante OSDI y en 2 % con Ferning. **Conclusiones:** con este estudio se estableció por primera vez que los jóvenes que asisten a consulta de la clínica de optometría de la FES-Iztacala —un sector que no se había considerado— también padecen esta enfermedad.

Palabras clave: ojo seco, prevalencia, test de Ferning, superficie ocular.

INTRODUCTION

Dry Eye (DE) is a disease caused by the combination of patient activities, environmental conditions, and alterations of one or more elements of the ocular surface. Its definition has changed over time and finally reached the current definition by the Tear Film and Ocular Surface Society's (TFOS) International Dry Eye Workshop II (DEWS II) in 2017:

The dry eye is a multifactorial disease of the ocular surface characterized by the loss of homeostasis of the tear film and accompanied by ocular symptoms, in which the instability and hyperosmolarity of the tear film, inflammation and damage of the ocular surface, and neurosensory abnormalities play an etiological role. (1)

Currently, the diagnosis of this disease depends on both the performance of diagnostic tests and the implementation of diagnostic questionnaires (2), in addition to the tendency to associate the disease with the aging process, demeriting the risk factors. Different questionnaires and diagnostic tests are used in different studies (14-20), but the ocular surface disease index (OSDI) is the best validated questionnaire, designed to provide a rapid assessment of the symptoms of ocular irritation

consistent with dry eye disease and their impact on vision-related functioning. However, it is necessary to supplement this information with the results of the diagnostic tests, such as the techniques that evaluate the quality of the ocular surface, namely the Tear Breakup Time (T-But), the Schirmer I Test (21-22), and the Tear Ferning Test (TFT) (23-26); the TFT depends on the composition of the tear sample, and it is a simple test for tear film quality at a gross biochemical level. The test results can be observed under a light or digital microscope and depending on the tear film composition.

The results show us that the standardized average age to suffer from dry eye is at 50 years or older (5), with a greater risk for women at 70% (6), related to hormonal processes such as menopause (7-10) or syndromes (11) such as Sjögren (12-13). For this reason, the relationship between these conditions should be reported in the prevalence of dry eye in our patient population between the ages of 15 and 65.

METHODOLOGY

This study is Cross sectional descriptive. As for the population, the study was carried out at the "Centro de Diagnóstico de Alteraciones de la Superficie Ocular" of the Optometry Clinic of the

Iztacala School of Higher Education of Universidad Nacional Autónoma de México and included a total of 1957 patients evaluated with different diagnostic techniques. The study was conducted between August 2016 and August 2017. Patients in the age range of 15 to 65 years were chosen to participate, and they had to be healthy and not be subject to any ophthalmic topical treatment. In the diagnostic process, all the patients answered the OSDI questionnaire after being submitted to the TFT and, subsequently, the results were divided between the ages of 15 to 29 and 30 to 65, according to the provisions of the United Nations (UN) (35). They signed an informed consent based on the Declaration of Helsinki, and the study was approved by the Optometry Ethic Committee of FES Iztacala; the patients answered the OSDI questionnaire (2.0 *Yor 2013*, in its digital version in Spanish), validated for the evaluation of dry eye symptoms; this questionnaire consists of 12 questions divided into 3 sections. Normal results were considered equal to and less than 13 points, while results with a higher value were diagnosed as dry eye. The TFT was performed with a 0.5-10 μ l micropipette (Eppendorf), calibrated at 4 μ l, taking a tear sample from the ocular surface (without pressure on the eyelids) and placing it on a glass slide, left to dry for three minutes under controlled temperature and humidity conditions. The results were compared with standardized patterns according to the Rolando (27-29) scale in which patients were considered as unaltered in scale 2 and 1, while patients in scale 3 and 4 were diagnosed with dry eye.

These two diagnostic techniques were chosen because the questionnaire is a subjective technique, the results showing the degree of symptomatology of the patient, to which we add the results of an objective technique, both of which are then compared with a standardized scale (30-31). The diagnoses depend on universally standardized conditions (32-34). For the statistical analysis, the Statistical Package for the Social Sciences (SPSS) program was used. The descriptive analysis was carried out by submitting the representative sample to the

Pearson's chi-squared test in order to determine if there were differences between age groups and sex. A multivariate analysis was performed with logistic regression, and two models were adjusted for prevalence with Ferning and OSDI, using binary logistic regression, including age in qualitative form (years of age) and sex. The results were statistically significant, being considered with a confidence interval of 95% and determining a value of $p < 0.05$.

RESULTS

A sample of 1957 patients was taken (1260 = 64.4% women) with an average age of 34.3 years \pm 15.14 (Table 1), who were assessed at the Centro de Diagnóstico de Alteraciones de la Superficie Ocular.

TABLE 1. Percentage of the total population divided by gender and evaluated at the "Centro de Diagnóstico de Alteraciones de la Superficie Ocular"

AGE	WOMEN (%)	MEN (%)	TOTAL (%)	P*
15 – 29 years	587 (46.59)	430 (61.69)	1017 (51.97)	<0.001
30 – 65 years	673 (53.41)	267 (38.31)	940 (48.03)	
Total	1260 (100.00)	697 (100.00)	1957 (100.00)	

Source: Own work

Their evaluation determined that there is a prevalence of dry eye of 59.1% using the objective test (TFT) and of 63.8% with the subjective test (OSDI), with a confidence interval of 95%. Thus, the results were statistically different ($p = < 0.05$) (Table 2). The TFT results showed that young patients have a prevalence of dry eye of 51.9%, similar to adult patients, with 66.9%. However, OSDI results show a prevalence in young people of 60.0% compared to adults (67.8%); both were statistically different ($p = < 0.001$), which shows a higher percentage when it comes to OSDI. The results were higher in both tests for adults (Table 3).

After adjusting the logistic model for TFT, it was found that for each year of increase in age the probability of suffering dry eye was increased by 2% (OR = 1.02, CI 95%, 1.02 - 1.03, $p < 0.001$), while for OSDI the increase is 1% (OR = 1.01, CI 95%, 1.00 - 1.01, $p < 0.001$).

TABLE 2. Diagnosis of patients evaluated through the Tear Ferning Test and the OSDI questionnaire divided by gender

	PATIENTS	WOMEN (%)	MEN (%)	TOTAL (%)	P*
Ferning	Healthy	508 (40.32)	292 (41.89)	800 (40.88)	0.497
	Dry eye	752 (59.68)	405 (58.11)	1157 (59.12)	
	Total	1260 (100.00)	697 (100.00)	1957 (100.00)	
OSDI	Healthy	446 (35.40)	262 (37.59)	708 (36.18)	0.334
	Dry eye	814 (64.60)	435 (62.41)	1249 (63.82)	
	Total	1260 (100.00)	697 (100.00)	1957 (100.00)	

Source: Own work

TABLE 3. Diagnosis of patients evaluated through the TFT and the OSDI questionnaire divided by age

	PATIENTS	YOUNG (%)	ADULT (%)	TOTAL (%)	P*
Ferning	Healthy	489 (48.09)	311 (33.09)	800 (40.88)	<0.001
	Dry eye	528 (51.91)	629 (66.91)	1157 (59.12)	
	Total	1017 (100.00)	940 (100.00)	1957 (100.00)	
OSDI	Healthy	406 (39.93)	302 (32.13)	708 (36.18)	<0.001
	Dry eye	611 (60.07)	638 (67.87)	1249 (63.82)	
	Total	1017 (100.00)	940 (100.00)	1957 (100.00)	

Source: Own work

DISCUSSION

The presence of dry eye increases with age (from the age of 40) and is related to the decrease in tear production, which triggers the gradual increase in symptoms (6). It is suggested that the patient's symptoms may or not affect the diagnosis of dry eye and its classification, combined with the results of the clinical tests (31). Therefore, implementing different objective techniques, such as the TFT, Tear Break Up Time (T-But), Schirmer I (ST I), Schirmer II (ST II), Phenol Thread Network, Green Lisamine, Demodex identification, together with subjective techniques, such as diagnostic questionnaires (OSDI or Mc Monnies), is fundamental to make a good diagnosis of ocular surface alterations. As such, the reason for choosing the OSDI questionnaire and the TFT is that the results of the stability tests of the tear film are highly variable and, therefore, decreasing the stimuli on the ocular surface allows greater reliability in the results (50).

Subjective tests can always have some type of error (40), due to the fact that there are variables inherent to patients (41), which cannot be controlled either (42), and it should also be considered that objective tests are capable of generating a tear reflex (43). This alters the results of the tests (44), which could mean that the fewer invasive techniques are performed, the more reliable the result will be. The correlation between symptoms and the clinical signs of dry eye indicate that they may or may not be related, which does not mean that one technique is more useful than another, but that both techniques (objective and subjective) should be used to be able to generate a reliable diagnosis.

In Mexico, a study was carried out by the Ministry of Health through the Mexican Institute of Social Security (IMSS) in November 2011 (3). In the study, a sector of the population ranging between 15 and 35 years of age was evaluated, determining that different reading activities in electronic devices (e.g., computer, cell phone, tablets, etc.)

are a risk factor for dry eye because they limit the number of blinks per minute, generating different symptoms, such as burning, tearing, redness and itching, which contributes to the development of the dry eye disease. In addition, different studies around the world indicate that the symptomatology is greater as age increases (4), depending on the patient's line of work. A few studies on the prevalence of this disease have been carried out in different areas of the country, such as in Monterrey, Nuevo Leon, in 2016, where a study was conducted at a university using only the OSDI diagnostic questionnaire, with which they established a prevalence of the disease of 70.4% in a young population (21 to 23 years of age). In that same year, during a study conducted in a hospital in downtown Mexico City, the OSDI questionnaire and the Dry Eye Questionnaire-5 determined a prevalence of dry eye of 43% and 30%, respectively. The work was carried out in a population of 338 patients from 16 to 85 years of age, and the analysis of the data shows that, based on age range, the prevalence of dry eye is greater than 25% in patients between 15 and 35 years and greater than 35% after 46 years of age.

The use of objective and subjective techniques for diagnosing alterations of the ocular surface (36-37) has been studied; considering that, the greater the number of techniques used in the same patient, the more complex the relationship of the results are (38), due to their variability, and therefore the techniques whose results are more reliable should be chosen. The Ferning Test was used because it is an easy technique to perform, and the results depend on the observation of the chemical effect where hyperosmolarity is essential to determine the degree of dry eye. Therefore, its results are reliable and, combined with the results provided by the OSDI questionnaire, a complete analysis of the information can be performed, where we can determine the patient's tear quality as a whole according to their symptoms (39). When observing the results of young people by gender, we can see that women with objective and subjective tests have a lower prevalence of dry eye (50.4%–58.7%)

compared to adult patients (67.7%–69.6%), which supports the theory that the different hormonal processes that take place during aging generate different alterations in the elements of the ocular surface, culminating with dry eye disease (7-10). Young women compared to men in the same age range have a lower prevalence of the disease using both techniques.

With the results of the prevalence of dry eye in both sectors of the population (young and adult), the visual health professional will be able to deduce, during their clinical practice, that patients who appear in their office may suffer from this disease, and therefore they should be able to perform different evaluation techniques (45). Specific tests should be used to reduce the variability of the results, due to the low repetitiveness of the invasive tests (46). It is also important to consider that saturating the ocular surface with different techniques can generate an alteration in the results, as a consequence of the production of basal and reflex tearing (47). Therefore, using one or two techniques of ocular surface evaluation for diagnosis may be sufficient for an accurate diagnosis of dry eye, as our results show.

In countries such as France, Germany, Italy, Spain, Sweden, and the United Kingdom, it has been reported that dry eye syndrome produces an average net cost in treatment for the patient between \$ 273,000 and \$ 1,100,000 every year. In that sense, and considering that dry eye occurs in patients over 40 years of age, we could say that the maintenance time of this disease is about four decades. Considering this, as well as the results obtained in this study, in Mexico, a 19-year-old patient with a dry eye diagnosis should follow a treatment of at least 60 years. Therefore, they must generate preventive measures, such as reporting the consequences of the use of electronic devices for prolonged periods, because they reduce the number of blinks per minute (51), avoiding a well-hydrated corneal surface, which are habits that are mostly observed in young people (52); they must also create control measures in order

to prevent the disease and improve the health conditions of the Mexican population.

CONCLUSIONS

Dry eye is a disease whose prevalence has historically been associated with one sector of the population. However, with this study, we establish that young people, a vulnerable sector of the population that was recently taken into consideration, may also suffer from this disease.

The results show similar values for both techniques (Table 3), which represents a relationship between the symptomatology of the patient and the characteristics of the tear observed, supported by the bibliography, which indicates that an alteration in the ocular surface will cause the symptomatology to increase. It is worth mentioning that women have more symptoms than men when they are adults, something that should be evaluated in depth in another study.

The analysis of the results for both techniques shows a prevalence of the disease for the general population of 59.1% using the objective test (TFT) and of 63.8% with the subjective test (OSDI). The results in terms of quality vary depending on age and sex; women will have a greater number of alterations in the results compared to adult men. These results are reversed when it comes to young people, something that would be supported by previously published studies, which have shown that changes in sex hormones affect the conjunctival epithelium, triggering the dry eye syndrome (48-49).

As a complement to the analysis, it is observed that the symptomatology also changes depending on the age and sex; in fact, adult patients show greater symptoms as compared to young ones, which is evident in the case of women. However, this circumstance changes when we talk about symptomatology in young people, since it is at this point that men show more symptoms.

REFERENCES

1. Bron AJ., de Paiva CS, Chauhan SK, Bonini S, Gabison E E, Jain S., Uchino Y. TFOS DEWS II pathophysiology report. *Ocul Surf.* 2017;15(3):438-510. <https://doi.org/10.1016/j.jtos.2017.05.011>
2. Nichols KK, Nichols JJ, Mitchell GL. The reliability and validity of McMonnies dry eye index. *Cornea.* 2004;23(4):365-371. https://journals.lww.com/cornea-jrnl/Fulltext/2004/05000/The_Reliability_and_Validity_of_McMonnies_Dry_Eye.10.aspx
3. Presidencia de la República. Uso prolongado de la computadora, una de las causas del ojo seco. Internet [Consultado 4 Feb 2018]. <http://calderon.presidencia.gob.mx/2011/11/uso-prolongado-de-la-computadora-una-de-las-causas-del-sindrome-del-ojo-seco/>
4. Schaumberg DA, Sullivan DA, Buring JE, Dana MR. Prevalence of dry eye syndrome among US women. *Am J Ophthalmol.* 2003;136(2):318-326. [https://doi.org/10.1016/S0002-9394\(03\)00218-6](https://doi.org/10.1016/S0002-9394(03)00218-6)
5. Schaumberg DA, Dana R, Buring JE, Sullivan DA. Prevalence of dry eye disease among US men: estimates from the Physicians' Health Studies. *Arch Ophthalmol.* 2009;127(6):763-768. <https://doi.org/10.1001/archophthalmol.2009.103>
6. McCarty CA, Bansal AK, Livingston PM, Stanislavsky YL, Taylor HR. The epidemiology of dry eye in Melbourne, Australia. *Ophthalmology.* 1998;105(6):1114-1119. [https://doi.org/10.1016/S0161-6420\(98\)96016-X](https://doi.org/10.1016/S0161-6420(98)96016-X)
7. Erdem U, Ozdegirmenci O, Sobaci E, Sobaci G, Göktolga U, Dagli S. Dry eye in post-menopausal women using hormone replacement therapy. *Maturitas.* 2007;56(3):257-262. <https://doi.org/10.1016/j.maturitas.2006.08.007>
8. Gipson IK, Spurr-Michaud SJ, Senchyna M, Ritter IIR, Schaumberg D. Comparison of mucin levels at the ocular surface of postmenopausal women with and without a history of dry eye. *Cornea.* 2011;30(12):1346. <https://doi.org/10.1097/ICO.0b013e31820d852a>
9. Golebiowski B, Badarudin N, Eden J, You J, Hampel U, Stapleton F. Does endogenous serum oestrogen play a role in meibomian gland dysfunction in postmenopausal women with dry eye? *Br J Ophthalmol.* 2017;101(2):218-222. <https://doi.org/10.1136/bjophth.almol-2016-308473>
10. Scuderi G, Contestabile MT, Gagliano C, Iacovello D, Scuderi L, Avitabile T. Effects of phytoestrogen supplementation in postmenopausal women with dry eye syndrome: a randomized clinical trial. *Can J Ophthalmol.* 2012;47(6):489-492. <https://doi.org/10.1016/j.cjco.2012.08.019>
11. Guedry J, Roujeau JC, Binaghi M, Soubrane G, Muraine M. Risk factors for the development of ocular complications of Stevens-Johnson syndrome and toxic epidermal necrolysis. *Arch Dermatol.*

- 2012;145(2):157-162. <https://doi.org/10.1001/archdermatol.2009.540>
12. Fox RI, Howell FV, Bone RC, Michelson PE. Primary Sjogren syndrome: clinical and immunopathologic features. *Semin Arthritis Rheum*. 1984;14(2):77-105. [https://doi.org/10.1016/0049-0172\(84\)90001-5](https://doi.org/10.1016/0049-0172(84)90001-5)
 13. Vitale S, Goodman LA, Reed GF, Smith JA. Comparison of the NEI-VFQ and OSDI questionnaires in patients with Sjögren's syndrome-related dry eye. *Health Qual Life Outcomes*. 2004;2(1):44. <https://doi.org/10.1186/1477-7525-2-44>
 14. Sullivan BD, Crews LA, Sönmez B, Maria F, Cormert E, Charoenrook V, Lemp MA. Clinical utility of objective tests for dry eye disease: variability over time and implications for clinical trials and disease management. *Cornea*. 2012;31(9):1000-1008. <https://doi.org/10.1097/ICO.0b013e318242fd60>
 15. Lee JS, Yoon TJ, Kim KH. Clinical effect of Restasis eye drops in mild dry eye syndrome. *Journal of the Korean Ophthalmological Society*. 2009;50(10):1489-1494. <https://doi.org/10.3341/jkos.2009.50.10.1489>
 16. Li M, Gong L, Sun X, Chapin WJ. Anxiety and depression in patients with dry eye syndrome. *Curr Eye Res*. 2011;36(1):1-7. <https://doi.org/10.3109/02713683.2010.519850>
 17. Torricelli AA, Novaes P, Matsuda M, Braga A, Saldiva PH, Alves MR, Monteiro ML. Correlation between signs and symptoms of ocular surface dysfunction and tear osmolarity with ambient levels of air pollution in a large metropolitan area. *Cornea*. 2013;32(4):e11-e15. <https://doi.org/10.1097/ICO.0b013e31825e845d>
 18. Pult H, Riede-Pult BH. A new modified fluorescein strip: Its repeatability and usefulness in tear film break-up time analysis. *Cont Lens Anterior Eye*. 2012;35(1):35-38. <https://doi.org/10.1016/j.clae.2011.07.005>
 19. Kurtul BE, Özer PA, Aydinli MS. The association of vitamin D deficiency with tear break-up time and Schirmer testing in non-Sjögren dry eye. *Eye*. 2015;29(8):1081. <https://doi.org/10.1038/eye.2015.96>
 20. Gupta N, Prasad I, Himashree G, D'Souza P. Prevalence of dry eye at high altitude: a case controlled comparative study. *High Alt Med Biol*. 2008;9(4):327-334. <https://doi.org/10.1089/ham.2007.1055>
 21. Kallarackal GU, Ansari EA, Amos N, Martin JC, Lane C, Camilleri JP. A comparative study to assess the clinical use of Fluorescein Meniscus Time (FMT) with Tear Break up Time (TBUT) and Schirmer's tests (ST) in the diagnosis of dry eyes. *Eye*. 2002;16(5):594. <https://doi.org/10.1038/sj.eye.6700177>
 22. Isreb MA, Greiner JV, Korb DR, Glonek T, Mody SS, Finnemore VM, Reddy CV. Correlation of lipid layer thickness measurements with fluorescein tear film break-up time and Schirmer's test. *Eye*. 2003;17(1):79. <https://doi.org/10.1038/sj.eye.6700224>
 23. Masmali AM, Purslow C, Murphy PJ. The tear ferning test: a simple clinical technique to evaluate the ocular tear film. *Clin Exp Optom*. 2014;97(5):399-406. <https://doi.org/10.1111/cxo.12160>
 24. Horwath J, Ettinger K, Bachernegg M, Bodner E, Schmut O. Ocular ferning test—effect of temperature and humidity on tear ferning patterns. *Ophthalmologica*. 2001;215(2):102-107. <https://doi.org/10.1159/000050838>
 25. Mathers WD. Why the eye becomes dry: a cornea and lacrimal gland feedback model. *CLAO J*. 2000;26(3):159-165. <https://www.ncbi.nlm.nih.gov/pubmed/10946988>
 26. Evans KS, North RV, Purslow C. Tear ferning in contact lens wearers. *Ophthalmic Physiol Opt*. 2009;29(2):199-204. <https://doi.org/10.1111/j.1475-1313.2008.00626.x>
 27. Masmali AM, Purslow C, Murphy PJ. The tear ferning test: a simple clinical technique to evaluate the ocular tear film. *Clin Exp Optom*. 2014;97(5):399-406. <https://doi.org/10.1111/cxo.12160>
 28. Tatlipinar S, Gedik Ş, Ircek M, Orhan M, Erdener U. Ocular ferning during the menstrual cycle in healthy women. *Eur J Ophthalmol*. 2001;11(1):15-18. <https://doi.org/10.1177/112067210101100104>
 29. Mayorga MT. Diferencias en la variación del helechito lagrimal con el uso de lentes de contacto de hidrogel y de hidrogel de silicona. *Ciencia & Tecnología para la Salud Visual y Ocular*. 2010;8(2):73-79. <https://doi.org/10.19052/sv.816>
 30. Dougherty BE, Nichols JJ, Nichols KK. Rasch analysis of the ocular surface disease index (OSDI). *Invest Ophthalmol Vis Sci*. 2011;52(12):8630-8635. <https://doi.org/10.1167/iovs.11-8027>
 31. Begley CG, Chalmers RL, Abetz L, Venkataraman K, Mertzanis P, Caffery BA, Simpson T. The relationship between habitual patient-reported symptoms and clinical signs among patients with dry eye of varying severity. *Ocul Immunol Inflamm*. 2003;44(11):4753-4761. <https://doi.org/10.1167/iovs.03-0270>
 32. Özcura F, Aydin S, Helvacı MR. Ocular surface disease index for the diagnosis of dry eye syndrome. *Ocul Immunol Inflamm*. 2007;15(5):389-393. <https://doi.org/10.1080/09273940701486803>
 33. Korb DR. Survey of preferred tests for diagnosis of the tear film and dry eye. *Cornea*. 2000;19(4):483-486. <https://www.ncbi.nlm.nih.gov/pubmed/10928763>
 34. Norn M. Quantitative tear ferning. *Acta Ophthalmol Scand*. 1994;72(3):369-372. <https://doi.org/10.1111/j.1755-3768.1994.tb02775.x>
 35. ONU. Día Internacional de la Juventud. *Naciones Unidas*. [Consultado 21 Mayo 2018]. Available in: <http://www.un.org/es/events/youthday/>
 36. Pflugfelder SC, Tseng SC, Sanabria O, Kell H, Garcia CG, Felix C, Reis BL. Evaluation of subjective assessments and objective diagnostic tests for

- diagnosing tear-film disorders known to cause ocular irritation. *Cornea*. 1998;17(1):38-56. <https://doi.org/10.1097/00003226-199801000-00007>
37. Versura P, Profazio V, Campos EC. Performance of tear osmolarity compared to previous diagnostic tests for dry eye diseases. *Curr Eye Res*. 2010;35(7):553-564. <https://doi.org/10.3109/02713683.2010.484557>
 38. Versura P, Profazio V, Campos EC. Performance of tear osmolarity compared to previous diagnostic tests for dry eye diseases. *Curr Eye Res*. 2010;35(7):553-564. <https://doi.org/10.3109/02713683.2010.484557>
 39. Finis D, Pischel N, König C, Hayajneh J, Borrelli M, Schrader S, Geerling G. Comparison of the OSDI and SPEED questionnaires for the evaluation of dry eye disease in clinical routine. *Ophthalmologie*. 2014;111(11):1050-1056. <https://doi.org/10.1007/s00347-014-3042-z>
 40. Pakdel F, Gohari MR, Jazayeri AS, Amani A, Pirmarzdashti N, Aghaee H. Validation of farsi translation of the ocular surface disease index. *J Ophthalmic Vis Res*. 2017;12(3):301. https://doi.org/10.4103/jovr.jovr_92_16
 41. Garza M, Valencia M, Martínez B, Villarreal P, Marcos HG, Cortéz AL, Jasso A. Prevalence of ocular surface disease symptoms and risk factors in group of university students in Monterrey, Mexico. *J Ophthalmic Inflamm Infect*. 2016;6(1):44. <https://doi.org/10.1186/s12348-016-0114-z>
 42. Yun CM, Kang SY, Kim HM, Song JS. Prevalence of dry eye disease among university students. *Journal of the Korean Ophthalmological Society*. 2012;53(4):505-509. <https://doi.org/10.3341/jkos.2012.53.4.505>
 43. Tsubota K, Kaido M, Yagi Y, Fujihara T, Shimmura S. Diseases associated with ocular surface abnormalities: the importance of reflex tearing. *Br J Ophthalmol*. 1999;83(1):89-91. <https://doi.org/10.1136/bjo.83.1.89>
 44. Wolffsohn JS, Arita R, Chalmers R, Djalilian A, Dogru M, Dumbleton K, Sullivan BD. TFOS DEWS II diagnostic methodology report. *Ocul Surf*. 2017;15(3):539-574. <https://doi.org/10.1016/j.jtos.2017.05.001>
 45. Nichols KK, Mitchell GL, Zadnik K. The repeatability of clinical measurements of dry eye. *Cornea*. 2004;23(3):272-285. <https://doi.org/10.1097/00003226-200404000-00010>
 46. Farris RL, Stuchell RN, Mandel I. D. Basal and reflex human tear analysis: I. Physical measurements: osmolarity, basal volumes, and reflex flow rate. *Ophthalmology*. 1981;88(8):852-857. [https://doi.org/10.1016/S0161-6420\(81\)34939-2](https://doi.org/10.1016/S0161-6420(81)34939-2)
 47. Schaumberg DA., Uchino M, Christen WG, Semba RD, Buring JE, Li JZ. Patient reported differences in dry eye disease between men and women: impact, management, and patient satisfaction. *PloS One*. 2013;8(9):e76121. <https://doi.org/10.1371/journal.pone.0076121>
 48. Pelit A, Bağış T, Kayaselçuk F, Dursun D, Akova Y, Aydin P. Tear function tests and conjunctival impression cytology before and after hormone replacement therapy in postmenopausal women. *Eur J Ophthalmol*. 2003;13(4):337-342. <https://doi.org/10.1177/112067210301300402>
 49. Bartley EJ, Fillingim RB. Sex differences in pain: a brief review of clinical and experimental findings. *BJA*. 2013;111(1):52-58. <https://doi.org/10.1093/bja/aet127>
 50. Wolffsohn JS, Arita R, Chalmers R, Djalilian A, Dogru M, Dumbleton K, Sullivan BD. TFOS DEWS II diagnostic methodology report. *Ocul Surf*. 2017;15(3):539-574. <https://doi.org/10.1016/j.jtos.2017.05.011>
 51. Uchino M, Yokoi N, Uchino Y, Dogru M, Kawashima M, Komuro A, Tsubota K. Prevalence of dry eye disease and its risk factors in visual display terminal users: the Osaka study. *Am J Ophthalmol*. 2013;156(4):759-766. <https://doi.org/10.1016/j.ajo.2013.05.040>
 52. Park JS, Choi MJ, Ma JE, Moon JH, Moon HJ. Influence of cellular phone videos and games on dry eye syndrome in university students. *Journal of Korean Academy of Community Health Nursing*. 2014;25(1):12-23. <https://doi.org/10.12799/jkachn.2014.25.1.12>