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An Age Based Differential Response of Dry Eye Disease on Topical Lubrication

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Abstract

Background: To compare the OSDI (Ocular Surface Disease Index), SIT (Schirmer I Test), FBUT (Fluorescein Break Up Time), and FLCS (Fluorescence Staining) scores of dry eye patients at various ages.

Materials and Methods: A randomized controlled trial was conducted at Mayo Hospital, Lahore from September 2020 to September 2021 and 90 eyes from 90 patients with mild to moderate dry eye were incorporated split into three groups: young (20-39 years, n = 29), middle-aged (40-59 years, n = 30), and elderly (> 60 years, n = 31). Patients received a 28-day course of local physical therapy along with topical medications that lubricated the ocular surface and encouraged repair. At 7, 14, and 28 days, patients were checked in. Examinations were done on the OSDI, SIT, FBUT, and FLCS scores.

Results: The OSDI scores in three groups varied at each time point (all P 0.001); however, no group's score varied across time points. A time effect was discovered (F = 80.87, P 0.001), and SIT were different between the three groups (F = 350.61, P 0.001). Middle-aged and elderly groups had lower SIT at 14 and 28 days' post-treatment than young group (all P 0.001). SIT was lower in the elder group at 7, 14, and 28 days (all P 0.001). For all time points, the FLCS score was lower at 28 days (P 0.001).

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Conclusion: Patients with dry eyes are prescribed a 28-day course of topical medications that lubricate the ocular surface and promote corneal repair, along with local physical therapy. These medications have been shown to increase tear production, film stability, and corneal integrity. Age has an impact on how mild to modest dry eye is treated, with tear secretion being the most crucial component.

INTRODUCTION

Today, dry eye is understood to be an ocular surface disease characterized by tear film homeostasis loss, ocular symptoms, tear film instability and hyperosmolarity, inflammation, and ocular surface damage [1]. In order to maintain the ocular surface in its normal state, a healthy tear film is maintained by the coordinated regulation of various components of the ocular surface tissue, which is essential to maintaining the ocular surface in its normal state. Whenever the chain breaks, it compromises the tear film's structural integrity and possibly even its functionality, which will manifest as dry eye [2, 3]. There are several methods, including the Schirmer I test (SIT), the ocular surface disease index (OSDI) score, the fluorescein break up time (FBUT), and the corneal fluorescence staining (FLCS) score [2, 4]. As the population ages, it is predicted that the burden of dry eye, an age-related degenerative condition, will increase on public health globally [5-7]. However, more research is required to determine whether there are differences between the indicators and symptoms of dry eye individuals of various ages before and after therapies [8]. Although results are inconsistent and systematic stratified studies are advised, the Dry Eye Workshop II Epidemiological Report (DEWS II) shows differences between the sexes in the indications of dry eye with age [30-49]. To compare the OSDI score, SIT score, FBUT score, and FLCS rating of dry eye patients at various ages before and after hospitalization, patients were separated into three groups in this study based on age.

MATERIALS AND METHODS

Patients

A randomized controlled trial was conducted at Mayo Hospital Lahore included 90 eyes from 90 people who had mild to moderate dry eye who attended our outpatient clinic between September 2020 and September 2021. Ethical approval was taken from Ethical Review Committee of Mayo Hospital, Lahore which followed the Declaration of Helsinki, and all patients provided written informed consent. Except for dry eye, all patients had complete fundus examinations and slit lamp examinations to rule out other ocular surface diseases and fundus diseases.

In order to qualify, patients had to meet the following criteria: (1) they had symptoms such as blurred vision, dry eyes, and foreign body sensation that could be classified as mild to moderate dry eye; (2) they had not received any other dry eye remedy within the previous month; and (3) they were between the ages of 18 and 78 and did not have any mental or psychological maladies. Patients with other ophthalmic diseases who require local or systemic use of other drugs that may affect tear secretion were excluded, as were those who had previous chemical burns, eye surgery, or contact lenses; (3) those who have conditions affecting the normal metabolism of drugs, such as eyelid insufficiency, conjunctival sac relaxation, ectropion, or blepharospasm; (4) those who were pregnant or nursing, or who were taking hormone-related drugs; (6) those who have immune-related conditions like Sjögren's syndrome, Stevens-Johnson syndrome, abnormal thyroid function, and other severe conditions like tumour diseases.

If a patient had two eyes that both met the inclusion requirements, the right eye was chosen as the study eye and one eye from each patient was chosen for the study. In accordance with their ages, the patients were divided into three categories.

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Patients in the young group were between the ages of 20 and 39, representing 29 cases and 29 eyes; patients in the middle-aged group were between the ages of 40 and 59, representing 30 cases and 30 eyes; and patients in the elderly group were between the ages of 60 and over, with a total of 31 cases and 31 eyes. To finish their OSDI score, SIT score, FBUT score, and corneal FLCS score at day 0, all patients underwent an examination by the same ophthalmologist.

Therapeutic method

The same ophthalmic nurse massaged all patients' meibomian glands once a week for four weeks in a row. The therapeutic method has previously been described [9]. Furthermore, for 28 days, patients in each group were given poly-ethylene glycol eye drops and vitamin A palmitate ophthalmic gel. Levofloxacin eye drops and gatifloxacin ophthalmic gel were applied to the affected eye after each massage. This was done three times a day and once a night. After three days of continuous use, these two drugs were discontinued. The same physician administered eye drops in accordance with standard procedure. Seven days, fourteen days, and 28 days after intervention, patients were observed.

Observational index

The same ophthalmologist evaluated all patients to accomplish their OSDI score, SIT, FBUT, and corneal FLCS rating. All 12 correctly answered questions, with scores ranging from 0 to 100, are included in the OSDI score [10]. For SIT, take a 5 mm x 35 mm standard filter paper strip fold one end for 5 mm, and let the other end hang innately before inserting it into the space where the middle and outer third of the lower eyelid meet. After five minutes, the filter paper was detached, and dry eyes can be identified by the wetted length of the filter paper in the rolled up position being less than 10 mm [11].

For FBUT, the patient's lower eyelid conjunctival sac was first moistened with chloramphenicol eye drops, and then the fluorescein test strip was placed there. The slit lamp microscope's cobalt blue light was chosen for analysis; the stopwatch was used for timing, and the patient blinking repeatedly and gazing forward. For three days straight, the patient's eyes were opened after the last blink, and the interval between that point and the occurrence of the first randomly distributed dry spot on the cornea was noted. A dry eye can be identified by an average time of less than 10 seconds [11].

The slit lamp microscope's cobalt blue light was chosen for observation; the stopwatch was used for timing, and the patient blinking repeatedly and gazing forward. The time between when the patient started opening his eyes after the last blink and when a random dry spot appeared was recorded three times in a row. Dry eyes can be identified by an average time of less than 10 seconds [11].

The fluorescein test strip was placed in the lower third of the patient's conjunctival sac using a drop of chloramphenicol eye drops to infiltrate the tip. After three to four blinks, the cornea was examined with a slit lamp using cobalt blue light to determine whether it was stained. The cornea was scored using a scale of 0 to 3 points, with 0 representing no staining, 1 representing punctate staining, 2 representing spotty staining, and 3 representing ulcers, filaments, and filament fusion [12].

Statistical Analysis

SPSS version 23.0 was used to conduct the analysis (IBM Corp.). Values are shown as both the mean and standard deviation or as numbers (percentage). For comparing categorical data between clusters, the chi-square test had been used, while multiple methods had been used to analyze continuous variables. These methods included the one-way analysis of variance (ANOVA). Using a two-way

ANOVA, we tested the significance of the OSDI, SIT, FBUT, and FLCS scores before the Bonferroni test. A statistically significant variation was deemed to exist when P 0.05 was obtained.

RESULTS

Before intervention, there had been no significantly different in gender, dry eye length of time, diabetes background, smoking record, OSDI score, SIT, FBUT, or FLCS score between the three groups (P > 0.05). (Table 1).

Table 1 Basic information

Variables	Young group (n= 29)	Middle-age group (n = 30)	Elder group (n = 31)	P Value
Male, n (%)	14(48.28)	14(46.67)	16(51.61)	**0.925**
Dry eye duration (month) (means ± SD)	4.37 ± 2.73	4.28 ± 2.30	4.56 ± 2.80	**0.912**
Diabetes history, n (%)	05(17.24)	8(26.67)	7(22.58)	**0.683**
Smoking history, n (%)	08(27.59)	6(20)	6(19.35)	**0.783**
OSDI Score (means±SD)	26.00±5.47	26.10±5.55	25.84±5.24	**0.979**
SIT (mm/5min) (means ± SD)	04.59 ± 01.24	04.50 ± 01.17	4.42 ± 1.29	**0.872**
FBUT (s) (means ± SD)	04.31 ± 01.34	04.13 ± 01.55	4.00 ± 1.39	**0.682**
FLCS score (means±SD)	03.10 ± 1.94	03.23 ± 1.87	3.45 ± 1.71	**0.794**

The OSDI is an index of ocular surface disease; SIT is the Schirmer I test; FBUT is the fluorescein breakup time; and FLCS is the corneal fluorescence staining.

The OSDI score was not statistically distinct between the factions, as shown in Table 2, and there was a considerable time effect (F = 427.21, P 0.001) that was discovered. Time and collaboration was also significant (F = 7.01, P 0.001). At each time point before and after intervention, there were significant statistical variations between the three groups in terms of within-group comparisons (all P 0.001).

Table 2: OSDI score among three groups.

Variables (means±SD)	Young group (n = 29)	Middle-age group (n = 30)	Elder group (n = 31)	Mixed ANONA (P value)		
				Group effect	Time effect	Interaction effect
Before treatment	26.07±5.47	26.10±5.55	25.84± 5.24	0.057	< 0.001	**0.001**
7 days after treatment	23.31±4.98	20.30±4.47	21.32 ± 4.20*			
14 days after treatment	19.10±4.14*	15.97±3.82*#	17.74 ± 3.68*			
28 days after treatment	14.97±3.91*#&	10.67± 2.92*#&	13.26 ± 3.74*#&			

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OSDI, ocular surface disease index
*P < 0.05, compared with OSDI score before treatment
#P < 0.05, compared with OSDI score 7 days after treatment
&P < 0.05, compared with OSDI score 14 days after treatment

An important time impact was also discovered (F = 80.87, P 0.001), as well as a statistically significant difference in SIT between the three groups (F = 350.61, P 0.001). Groups and time interacted significantly (F = 10.70, P 0.001) in this study. Both the middle-aged group and the elder group's SIT at 14 and 28 days post-treatment were lower than those of the young group (all P 0.001). Elderly patients had lower SIT at 7, 14, and 28 days post-treatment (all P 0.001) than middle-aged patients. There had been statistically significant variations between the three clusters at each time point before and after treatment in terms of within-group comparisons (all P 0.001) (Table 3).

Table 3: SIT among three groups.

Variables (means±SD)	**Young group (n = 29)**	**Middle-age group (n = 30)**	**Elder group (n = 31)**	**Mixed ANONA (P value)**		
				Group effect	**Time effect**	Interaction effect
Before treatment	4.59±1.24	4.50±1.17	4.42±1.29	< 0.001	< 0.001	**< 0.001**
7 days after treatment	6.55±1.40	6.10±1.52	5.10±1.51*			
14 days after treatment	8.41±1.94*	7.40±1.83*#	6.23±1.56*			
28 days after treatment	9.72±1.77*#&	8.10±1.45*#&	6.97±1.45*#&			

SIT, Schirmer I test
*P < 0.05, compared with SIT before treatment
#P < 0.05, compared with SIT 7 days after treatment
&P < 0.05, compared with SIT 14 days after treatment
aP<0.05, compared with young group
bP<0.05, compared with middle-age group

According to Table 4, there was no statistically significant difference in FUBT between the groups (F = 2.66, P = 0.08), but there was a significant time effect (F = 56.63, P 0.001). Additionally, there was an important interface between time and groups (F = 4.58, P 0.001). In neither the middle-aged group nor the elder group, there were any appreciable differences between FUBT at 28 days after treatment and FUBT at 14 days after treatment. It is observed that other time points, prior to and after procedure, also showed statistically significant variations between the three groups (all P 0.001).

Table 4: FUBT among three groups.

Variables (means±SD)	Young group (n = 29)	Middle-age group (n = 30)	Elder group (n = 31)	Mixed ANONA (P value)		
				Group effect	Time effect	Interaction effect
Before treatment	4.31±1.34	4.13±1.55	4.00±1.39	0.076	< 0.001	**< 0.001**
7 days after treatment	5.21±1.61	4.83±1.68*	4.42±2.01*			
14 days after treatment	5.86±1.87*	5.33±1.69*#	5.00±1.93*			
28 days after treatment	6.93±1.83*#&	5.73±2.02*#&	5.13±1.98*#&			

FBUT, fluorescein break up time
*P < 0.05, compared with FBUT before treatment
#P < 0.05, compared with FBUT 7 days after treatment
&P < 0.05, compared with FBUT 14 days after treatment

Table 5 demonstrates that there was no statistically significant difference in FLCS score between the groups (F = 1.23, P = 0.30), and that there was a significant time effect (F = 49.625, P 0.001). Time and group interactions were not significant (F = 1.533, P = 0.170). Regarding differences within groups, the FLCS score was lower at 28 days post-treatment than it was at 7, 14, and 28 days post-treatment (all P 0.001).

Table 5: The FLCS score among three groups.

Variables (means±SD)	Young group (n = 29)	Middle-age group (n = 30)	Elder group (n = 31)	Mixed ANONA (P value)		
				Group effect	Time effect	Interaction effect
Before treatment	3.1 ± 1.94	3.23 ± 1.87	3.45 ± 1.71	0.299	< 0.001	**0.170**
7 days after treatment	2.76 ± 1.90	3.07 ± 1.43	3.13 ± 1.78*			
14 days after treatment	2.41 ± 1.78*	2.73 ± 1.78*#	2.94 ± 1.71*			
28 days after treatment	1.10 ± 0.82*#&	1.70 ± 1.32*#&	2.32 ± 1.50*#&			

FLCS, corneal fluorescence staining
*P < 0.05, compared with FLCS score before treatment
#P < 0.05, compared with FLCS score 7 days after treatment
&P < 0.05, compared with FLCS score 14 days after treatment

DISCUSSION

According to subsequent observational studies, the pervasiveness of dry eye has risen exponentially, and there is a significant correlation between continuing to increase age and associated symptoms, diagnostic markers of dry eye, aqueous tear inadequacy, and meibomian gland impotence [13, 14]. Because of this, dry eye is regarded as a multifactorial, age-related debilitating disease that worsens with incremental long term exposure to numerous environmental and biological considerations, resulting in hormonal modulation, neurosen- sory pathways, ocular modifications in infection, and tear film homeostasis [15, 16]. The percentage of patients with dry eyes will rise as the older population grows and as people live longer. As a result, we must better comprehend age-related dry eye in order to enhance the status quo and guidance therapeutic interventions [17].

The OSDI scores, SIT, FBUT, and FLCS scores of the OSDI scores in three groups at 28 days after therapy had been considerably better than those at the start of therapy and at 7 days following treatment, indicating that protracted intervention of dry eyes yields improved outcome.

At each time point both before and after hospitalisation, there had been statistically significant differences between the three groups. Concerning that the accumulated exposure due to advancements in science and technology and risk choices may vary by age bracket, the OSDI scores for the middle-aged group at each time point were, overall, lower than those of the other two groups, though this difference was not statistically significant [18]. Furthermore, ocular nerve responsiveness and feedback sensitivity decline with age.

The most accurate method of measuring tear production is the SIT, and patients' signs of ocular surface distress and visual appeal can be directly improved by an uptick in tear production. SIT was lower in the older group in this investigation at 7, 14, and 28 days after therapy than in the middle-aged group. When compared to patients over 60 years of age, the recovery from tear insufficiency is more prominent and rapid in clients under 60 [18]. The research postulates that the cause is that sex sex hormones may control tear output by stabilising the ocular surface surroundings through their impacts, and that as people age, their hormone levels slowly decrease, which also influences tear output to some degree [19, 20]. Observations of the tear secretion test suggest that hormone replacement therapy has a positive effect on lacrimal efflux, and that this impact is age-related [21]. In terms of age-related variations in the clinical effectiveness of dry eye, in the particular instance of SIT, tear secretion glands and their neural connections constitute tear specific functions, and anomalies in some of these units can result in dysfunction. The standard lacrimal gland is made up of 80% acinar cells, which hold and excretes tear aspects. The category of acinar modifications from orginally being serous to serous-mucinous acinus, and then steadily to mucinous acinus as a result of age, according to an animal study [22]. Along with inordinate structural failure, mast cell infiltration, periductal fibrosis, acinar atrophy, and chronic inflammation, the lacrimal gland also experiences these conditions as it ages. In mice from 3 to 5 months old, 20 to 24 months old, the capacity of the acini to synthesise and excretes proteins steadily declined or vanished [23]. These morphological and secretory changes also explain age-related decreases in tear production.

Using FBUT, which is reproducible, less upsetting to the physician, and yields precise, accurate findings, patients' tear film consistency can be assessed. As a result, clinical practise uses it frequently. Because all patients in this study had their FBUT

measurements taken by the same doctor in the same setting, external factors like the size of their eye slit, the moisture of their surroundings, and the amount of fluorescein staining were not taken into account. Young group FUBT at 28 days after therapy were greater than the other two groups, despite not being substantially distinct.

The age of 33 to 38 years old, between 33 and 38 years old, may be the ideal prognostic cut-off age for tear film destabilisation and hyperosmolarity. High osmotic pressure may be associated with lower FBUT in elderly dry eye clients, and patients under the age of 40 recover tear film stabilisation more quickly and dramatically than those over the age of 40. For the evaluation of corneal destruction, the corneal FLCS is a frequently used clinical technique. A more advanced stage of dry eye is thought to be indicated by corneal and conjunctival staining on the ocular surface, which denotes affected corneal, conjunctival, and lid margin epithelial integrity [14, 18, 24].

Three groups of people experienced markedly decreased FLCS at 28 days post-treatment than at other times. The delayed onset of this injury necessitates long therapy because adjustments in tear film homeostasis in dry eyes may boost the drying risk due to tear film upheaval and inordinate water loss through an inflammatory cascade provoked by tear film hyper-osmolarity, causing harm to the ocular surface epithelium and eye movements with diminished stickiness and rising abrasion [16, 27, 28].

This study's constraints included a small sample size and a narrow follow-up period. Furthermore, there are no appropriate biochemical predictors in this research. Another drawback of the research is the lack of a significant difference in baseline OSDI between clusters. This study did not examine patients' blepharitis as a potential co-founding factor. Because of the study's small sample size, it is possible that there is not a high incidence of dry eye in women.

As a result, there will be more extensive and ongoing study in the future. Due to the 2019 novel coronavirus, every patient in each of the three age groups wore masks throughout the study period (COVID-19). But the well-known condition known as "Mask Associated Dry Eye (MADE)" wasn't covered in greater depth.

CONCLUSION

Patients with dry eyes are given a 28-day course of topical medications that lubricate the ocular surface and promote repair along with local physical therapy. These medications can relieve symptoms, encourage tear production, enhance tear film stability, and aid in the restoration of corneal and ocular surface integration. A persistent therapy is required for this chronic, long-term eye disease. Patients with light to moderate dry eye are impacted by age, and tear production is the most major factor. To safeguard the ocular surface, dry eye should be identified and treated as soon as possible.

REFERENCES

1. Craig JP, Nichols KK, Akpek EK, Caffery B, Dua HS, Joo CK, Liu Z, Nelson JD, Nichols JJ, Tsubota K, et al. TFOS DEWS II Definition and Classification Report. Ocul Surf. 2017;15(3):276–83.
2. Willcox MDP, Argüeso P, Georgiev GA, Holopainen JM, Laurie GW, Millar TJ, Papas EB, Rolland JP, Schmidt TA, Stahl U, et al. TFOS DEWS II Tear Film Report. Ocul Surf. 2017;15(3):366–403.
3. Chuang J, Shih KC, Chan TC, Wan KH, Jhanji V, Tong L. Preoperative optimiza- tion of ocular surface disease before cataract surgery. J Cataract Refract Surg. 2017;43(12):1596–607.
4. Chapter ADEAC. Expert consensus on dry eye in China: definition and clas- sification. Chin J Ophthalmol. 2020;56(6):418–22.
5. Stapleton F, Alves M, Bunya VY, Jalbert I, Lekhanont K, Malet F, Na KS, Scha- umberg D, Uchino M, Vehof J, et al.

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TFOS DEWS II Epidemiology Report. Ocul Surf. 2017;15(3):334–65.
6. Kawashima M. Systemic Health and Dry Eye. Investig Ophthalmol Vis Sci. 2018;59(14):Des138–des142.
7. Farrand KF, Fridman M, Stillman I, Schaumberg DA. Prevalence of Diagnosed Dry Eye Disease in the United States Among Adults Aged 18 Years and Older. Am J Ophthalmol. 2017;182:90–8.
8. Ding J, Sullivan DA. Aging and dry eye disease. Exp Gerontol. 2012;47(7):483–90.
9. Liu Z. Expert consensus on dry eye in China: treatment. Chinese Journal of Ophthalmology, 56(12):7.
10. Zheng B, Liu XJ, Sun YF, Su JZ, Zhao Y, Xie Z, Yu GY. Development and valida- tion of the Chinese version of dry eye related quality of life scale. Health Qual Life Outcomes. 2017;15(1):145.
11. Chapter ADEAC. Expert consensus on dry eye in China: examination and diagnosis. Chin J Ophthalmol. 2020;56(10):714–47.
12. Zhang Y, Yi G, Ke X, Li S, Zhang Z, Chen X. Effects of Demodex mites on ocular surface function in patients with Meibomian gland dysfunction. Int J Ophthalmol. 2019;19(7):4.
13. Rico-Del-Viejo L, Lorente-Velázquez A, Hernández-Verdejo JL, García-Mata R, Benítez-Del-Castillo JM, Madrid-Costa D. The effect of ageing on the ocular surface parameters. Contact lens & anterior eye: the journal of the British Contact Lens Association. 2018;41(1):5–12.
14. Wang MTM, Craig JP. Natural history of dry eye disease: Perspectives from inter-ethnic comparison studies. Ocul Surf. 2019;17(3):424–33.
15. Knop E, Knop N, Millar T, Obata H, Sullivan DA: The international workshop on meibomian gland dysfunction: Report of the subcommittee on anatomy, physiology, and pathophysiology of the meibomian gland. Investigative ophthalmology & visual science 2011, 52(4):1938–1978.
16. Bron AJ, de Paiva CS, Chauhan SK, Bonini S, Gabison EE, Jain S, Knop E, Mar- koulli M, Ogawa Y, Perez V, et al. TFOS DEWS II pathophysiology report. Ocul Surf. 2017;15(3):438–510.
17. Pflugfelder SC. Prevalence, burden, and pharmacoeconomics of dry eye disease. Am J Manag Care. 2008;14(3 Suppl):102–6.
18. Wang MTM, Muntz A, Lim J, Kim JS, Lacerda L, Arora A, Craig JP. Ageing and the natural history of dry eye disease: A prospective registry-based cross- sectional study. Ocul Surf. 2020;18(4):736–41.
19. Wickham LA, Gao J, Toda I, Rocha EM, Ono M, Sullivan DA. Identification of androgen, estrogen and progesterone receptor mRNAs in the eye. Acta Ophthalmol Scand. 2000;78(2):146–53.
20. Gupta PD, Johar K, Sr., Nagpal K, Vasavada AR. Sex hormone receptors in the human eye. Surv Ophthalmol. 2005;50(3):274–84.
21. Feng Y, Feng G, Peng S, Li H. The effects of hormone replacement therapy on dry eye syndromes evaluated by Schirmer test depend on patient age. Con- tact lens & anterior eye: the journal of the British Contact Lens Association. 2016;39(2):124–7.
22. Vais VB, Vangeli IM, Bakeeva LE. Ultrastructural changes in ageing lacrimal gland in Wistar rats. Bull Exp Biol Med. 2014;157(2):268–72.
23. Li J, Ma J, Hu M, Yu J, Zhao Y. Assessment of tear film lipid layer thickness in patients with Meibomian gland dysfunction at different ages. BMC Ophthal- mol. 2020;20(1):394.
24. Wang MTM, Dean SJ, Xue AL, Craig JP. Comparative performance of lid wiper epitheliopathy and corneal staining in detecting dry eye disease. Clin Exp Ophthalmol. 2019;47(4):546–8.
25. Uchino M, Dogru M, Yagi Y, Goto E, Tomita M, Kon T, Saiki M, Matsumoto Y, Uchino Y, Yokoi N. The features of dry eye disease in a Japanese elderly population. Optom Vis Sci. 2006;83(11):797–802.
26. Mathers WD, Lane JA, Zimmerman MB. Tear film changes associated with normal aging. Cornea. 1996;15(3):229–34.
27. Yu J, Asche CV, Fairchild CJ. The economic burden of dry eye disease in the United States: a decision tree analysis. Cornea. 2011;30(4):379–87.
28. Korb DR, Herman JP, Blackie CA, Scaffidi RC, Greiner JV, Exford JM, Finnemore VM. Prevalence of lid wiper epitheliopathy in subjects with dry eye signs and symptoms. Cornea. 2010;29(4):377–83.
29. Craig JP, Muntz A, Wang MTM, Luensmann D, Tan J, Trave Huarte S, Xue AL, Jones L, Willcox MDP, Wolffsohn JS. Developing evidence-based guidance for the treatment of dry eye disease with artificial tear supplements: A six-month multicentre, double-masked randomised controlled trial. Ocul Surf. 2021;20:62–9.
30. Khan MI, Ashfaq F, Alsayegh AA, Hamouda A, Khatoon F, Altamimi TN, et al. Advanced glycation end product signaling and

metabolic complications: Dietary approach. World Journal of Diabetes [Internet]. 2023 Jul 15;14(7):995–1012. Available from: http://dx.doi.org/10.4239/wjd.v14.i7.995

31. Aladel A, Khatoon F, Khan MI, Alsheweir A, Almutairi MG, Almutairi SO, et al. Evaluation of miRNA-143 and miRNA-145 Expression and Their Association with Vitamin-D Status Among Obese and Non-Obese Type-2 Diabetic Patients. Journal of Multidisciplinary Healthcare [Internet]. 2022 Dec;Volume 15:2979–90. Available from: http://dx.doi.org/10.2147/jmdh.s391996

32. Kumar R, Khan MI, Ashfaq F, Alsayegh AA, Khatoon F, Altamimi TN, et al. Hesperidin Supplementation Improves Altered PON -1, LDL Oxidation, Inflammatory Response and Hepatic Function in an Experimental Rat Model of Hyperlipidemia. Indian Journal of Clinical Biochemistry [Internet]. 2023 Jun 20; Available from: http://dx.doi.org/10.1007/s12291-023-01140-5

33. Ashfaq F, Aljaadi AM, Salaka AS, Noorwali EA, Khatoon F, Khan MI. Comparison of TCN-2 (776C>G) Gene Polymorphism and Vitamin B12 Status with Different Body Mass Index among Saudi Adults. Life [Internet]. 2023 May 15;13(5):1185. Available from: http://dx.doi.org/10.3390/life13051185

34. Mughal h, Abdullah m, Jamil a, Malik a, Rasheed s, Khatoon f. Efficacy of methotrexate alone or with low-dose prednisone in alopecia areata totalis. Biological and Clinical Sciences Research Journal [Internet]. 2023 Jun 23;2023(1):332. Available from: http://dx.doi.org/10.54112/bcsrj.v2023i1.332

35. SIDDIQUI E, ABBASI M, KHOSA M, MOHSIN R, JABEEN N, SIDDIQUE U, et al. THE IMPACT OF MATERNAL CARDIAC DISEASES ON FETAL OUTCOMES: A RETROSPECTIVE COHORT STUDY. Biological and Clinical Sciences Research Journal [Internet]. 2023 Jun 16;2023(1):315. Available from: http://dx.doi.org/10.54112/bcsrj.v2023i1.315

36. Altamimi T, Balouch F. Mini Review; Role of Changes in SARS-CoV-2 Spike Protein and Its Human Interaction. Egyptian Academic Journal of Biological Sciences C, Physiology and Molecular Biology [Internet]. 2023 Jun 9;15(1):503–7. Available from: http://dx.doi.org/10.21608/eajbsc.2023.303781

37. Ali S, Saeed SJ, Zahid S, Rashid I, Khatoon F, Altamimi TN. Impact of Evaluation of Tumour Grade by Core Needle Biopsy on Clinical Risk Assessment and Patient Selection for Adjuvant Systemic Treatment in Breast Cancer. Pakistan Journal of Medical and Health Sciences [Internet]. 2023 Mar 15;17(2):817–9. Available from: http://dx.doi.org/10.53350/pjmhs2023172817

38. **Khan MI, Hashmi MO, Abid SUH, Khan B, Iqbal H, Khatoon F. Mid-Term Clinical and Echocardiographic Outcomes of Percutaneous Transvenous Mitral Commissurotomy in Patients with Rheumatic Mitral Stenosis. Pakistan Journal of Medical and Health Sciences [Internet]. 2023 Mar 15;17(2):793–5. Available from:** http://dx.doi.org/10.53350/pjmhs2023172793

39. **Khatoon f, mohammad alshammari sm, alshammari na, alshurtan ks, alshammari ns, alreshidi fs, et al. Perception, awareness and attitude towards varicose veins among employees working in prolonged sitting and standing postures in hail region, saudi arabia. Medical science [internet]. 2023 may 2;27(135):1–8. Available from:** http://dx.doi.org/10.54905/disssi/v27i135/e206ms2985

40. **Khan m, nouman m, hashim h, latif s, husain s, sattar s, et al. A correlation biomarker between bmi and lipid peroxidation in type 2 diabetes mellitus with and without other complications. Biological and clinical sciences research journal [internet]. 2023 Apr 21;2023(1):253. Available from:** http://dx.doi.org/10.54112/bcsrj.v2023i1.253

41. **Sohair A M Shommo, Firas S. Azzeh, Alsolami Ahmed Khatoon F Et Al, Prevalence Of Serum Vitamin Deficiency In Pakistan Of Chronic Fatigue Without Any Systemic Illness** 2023.Volume -12, Special Issue-13 (2023 Doi; 10.53555/Ecb/2023.12.Si13

42. Ahmed S , Mahmood T , Mudasir M, Khatoon F et al.The Worth Of Tranexamic Acid In The Controlling Of Non-Variceal Gastrointestinal

BleedingVolume -12, Special Issue-13 (2023) 10.53555/ecb/2023.12.Si13.1982023.25/11/2023

43. Gul S, mir n, Fatima k, tahir s, Younis ns, Khatoon F, et al. Catheter-related infections in hemodialysis: frequency and microbiological profile patients undergoing antimicrobial lock therapy with gentamicin for prophylaxis. Biological and Clinical Sciences Research Journal [Internet]. 2023 Apr 18;2023(1):247. Available from: http://dx.doi.org/10.54112/bcsrj.v2023i1.247

44. Alreshidi FF, Alshammari RF, Alenazi SH, Alshammry TE, Altamimi TN, Almughais ES, et al. Sciatica pain in Saudi population: Knowledge and attitude towards sciatica pain and treatment methods among the population of Hail in Saudi Arabia. Medical Science [Internet]. 2023 Mar 1;27(133). Available from: http://dx.doi.org/10.54905/disssi/v27i133/e142ms2906

45. Zahra A, Hassan SU, Hassan MS, Parveen N, Park JH, Iqbal N, Khatoon F, Atteya MR. Effect of physical activity and sedentary sitting time on psychological quality of life of people with and without disabilities; A survey from Saudi Arabia. Front Public Health. 2022 Sep. fpubh.2022.998890 PMID: 36225781; PMCID: PMC9548647.https://doi.org/10.3389/fpubh.2022.998890

46. Almughais, E. S., Abdullah Alshammari, K. A., Alshammari, H. H., Alreshidi, F. F., Alarfaj, R., Alshammari, R. F., Altamimi, T. N., Aboras, R., Almehmadi, S. A., & Balouch, F. K. (2023, February 5). "Assessment of knowledge and practice of Carpal tunnel syndrome among pregnant and non-pregnant women in Hail region, Saudi Arabia." Medical Science, 27(132), 1–8. https://doi.org/10.54905/disssi/v27i132/ee116ms2910

47. Khatoon, F., Alshammari, R. A., Batool, A., Elhaj, A. H., Alreshidi, F. F., Elhussein, G. E. M. O., Abdalla, R. A. H., Elhag, A. B. M., & Balouch, Z. (2022, October 30). Systematic Review on Implication for DNA Assisted Technology into Molecular Medicine and the useful is the application of Genome Wide Studies. Pakistan Journal of Medical & Health Sciences, 16(10), 217–220. https://doi.org/10.53350/pjmhs221610217

48. Khatoon, F. (2022, August 30). Association of Genetic and Reproductive Hormone with Infertility in Male. Progress in Medical Sciences, 1–11. https://doi.org/10.47363/pms/2022(6)175

49. Kausar, M. A., Shahid, S., Anwar, S., Kuddus, M., Khan, M. K. A., Khalifa, A. M., Khatoon, F., Alotaibi, A. D., Alkhodairy, S. F., Snoussi, M., & Arif, J. M. (2022, February 4). Identifying the alpha-glucosidase inhibitory potential of dietary phytochemicals against diabetes mellitus type 2 via molecular interactions and dynamics simulation. Cellular and Molecular Biology, 67(5), 16–26. https://do

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