Correlation Of Prevalence Of Dry Eye In Post Menopausal Females With Serum Vitamin-D And Insulin Level

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Abstract

Various studies have found that prevalence of dry eye disease increases with age especially in females, which leads to deterioration of the quality of life. Various factors have been studied and correlated with the increase prevalence of dry eye in these females . This study is aimed to study those factors like serum vitamin d and insulin and find out whether these factors are correlated with the increase prevalence of dry eye disease in these females. METHODS: 188 post-menopausal females with age 40 and above were studied with exclusion criteria of Age less than 40 years, Pre-existing ocular surface diseases like chemical burns, vernal Keratoconjunctivitis etc , Ocular surgery or trauma in the past 6 months, Ocular infection or contact lens use within past 3 months, Chronic ocular allergy, Topical medications, Systemic diseases or medications and Diabetic females on insulin therapy. Dry eye was diagnosed using Schirmer's test and TBUT. RESULTS: As per Schirmer's test prevalence was 51.06% and As per TBUT it was 50.53%. there was statistically significant positive correlation found between Vitamin -D and Dry eye (p-value <0.001). Insulin and dry eye disease had a positive correlation as per Schirmer's test (p-value 0.016) While as per TBUT the correlation of dry eye disease with insulin was statistically insignificant. CONCLUSION: This study concludes that there is increased prevalence of dry eye disease in females in the post-menopausal age group with majority exhibiting mild dry eye disease. Vitamin-D deficiency and post-menopausal females with decreased insulin levels are strongly correlated with the increased prevalence of dry eye disease in these females indicating their potential role in disease pathogenesis.

Keywords: *dry eye; post-menopausal females; vitamin d; insulin; Schirmer's; TBUT*

Introduction

Dry eye is a multifactorial disease of the ocular surface characterized by a loss of homeostasis of the tear film, and accompanied by ocular symptoms, in which tear film instability and hyperosmolarity, ocular surface inflammation and damage, and neurosensory abnormalities play etiological roles. Globally prevalence of dry eye disease was 5-50%. (DRY EYE WORKSHOP II, 2017).

Tear film compromises of three layers 1. Lipid layer 2. Aqueous layer 3. Mucous layer

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Classification of dry eye disease

   1) Aqueous deficient dry eye

      (A) Sjogren syndrome dry eye a. Primary b. Secondary

      (B) Non-Sjogren syndrome dry eye

         1) Primary lacrimal gland deficiencies

         2) Secondary lacrimal gland deficiencies

         3) Obstruction of the lacrimal gland ducts

         4) Reflex hypo secretion - a. reflex sensory block b. reflex motor block

         5) Systemic drugs – Antihistamines, Beta Blockers, Antispasmodics

   2) Evaporative dry eye

      A. Intrinsic – Meibomian gland dysfunction, Disorders of lid aperture, Low blink rate

      B. Extrinsic - Vitamin A deficiency, Topical drugs preservatives, Contact lens wear, Ocular surface disease; Allergy

Dry eye is divided into three categories depending on the severity:

MILD: Schirmer's test I 7-10 mm and TBUT 7-10 seconds.

 MODERATE: Schirmer's test I 5-7 mm and TBUT 5-7 seconds.

SEVERE: Schirmer's test I <5 mm and TBUT <5 seconds

1. **Investigations For The Assessment Of Dry Eye**

 • TEAR FILM BREAK-UP TIME (TBUT): The tear film is examined under the broad beam of light using the cobalt blue filter of the slit lamp after patient is advised to blink by prior instillation of 2% fluorescein or its impregnated strip moistened with normal saline. Tear break up time is measured which is the interval between the last blink and the appearance of the first randomly distributed dry spot or line. A break up time of less than 10 seconds is suspicious.

 • SCHIRMER'S TEST: The Schirmer's test is used for the assessment of aqueous tear production. It measures the amount of wetting of no. 41 Whatman filter paper which is 5 mm wide and 35 mm long. The test can be performed with or without topical anaesthesia.

 When the topical anaesthesia is used it is called as Schirmer's 2 test and it measures the basic secretion only. When it is done without topical anaesthesia it is called as Schirmer's 1 and it measures maximum basic as well as reflex secretion.

Fluorescein clearance test, Tear constituent measurement, Phenol red thread test and Impression cytology are the other tests used for the diagnosis of dry eye.

Various studies have found that dry eye disease prevalence increases with age especially in females which leads to deterioration of the quality of life of these females. Various factors have been studied and correlated with the increase prevalence of dry eye in these females . this study is aimed to study those factors like serum vitamin d and insulin and find out whether these factors are correlated with the increase prevalence of dry eye disease in these females.

2. **Material And Methods**

The present study was conducted in the Upgraded Department of Ophthalmology at government medical college Jammu over a period of one year ranging from August 2023 to July 2024. 188 (376 eyes) post-menopausal women

who attained natural menopause with age more than or equal to 40 years were included in the study on the basis of p=39.5 with 7% absolute precision, alpha=0.05, beta= 0.2.

Following patients were excluded from the study: Age less than 40 years , Pre-existing ocular surface diseases like chemical burns, vernal Keratoconjunctivitis etc , Ocular surgery or trauma in the past 6 months , Ocular infection or contact lens use within past 3 months, Chronic ocular allergy, Topical medications, Systemic diseases or medications and Diabetic females on insulin therapy.

Following tests were performed for the assessment of dry eye:

• Tear film breakup time: 2% Fluorescein dye was instilled using impregnated strip and tear film w a s examined using the cobalt blue filter of the slit lamp after the patient was advised to blink. Tear break up time was measured which is the interval between the last blink and the appearance of the first randomly distributed dry spot 24 or line and noted in seconds.

• Schirmer's test I: The Schirmer's test was done using the no. 41 Whatman filter paper. The test was performed without topical anaesthesia. The filter paper was folded 5 mm and inserted at the junction of the middle and lateral third of the lower lid and then the patient was asked to gently close the eyes. After 5 minutes the filter paper was removed and the amount of wetting was measured.

BIOCHEMICAL INVESTIGATIONS Included serum 25- OH Vitamin D, and Insulin.

NORMAL REFERENCE RANGE Vitamin-D : 20-60 ng/ml Insulin: 1-300 µU/mL

3. **Results**

Table 1. Prevalence of dry eye disease.

test	Total eyes studied(Tn)	No. of dry eyes	Prevalence pn/Tn*100	95%confidence interval for prevalence
Schirmer's test	376	192	51.06	(46.03 – 56.08)
TBUT	376	190	50.53	(45.50 – 55.55)

In the present study, out of 376 eyes studied, 192 eyes were diagnosed with dry eye disease as per Schirmer's test which corresponds to the prevalence of 51.06% with 95% confidence interval of 46.03-56.08. As per TBUT , 190 eyes were diagnosed with dry eye disease out of total 376 eyes which corresponds to the prevalence of 50.53% with 95% confidence interval of 45.50-55.55.

Table 2. Distribution of Vitamin-D among the patients studied.

Hormone	Hormone level	Frequency	Percentage
	Normal	81	43.1
	Deficient	72	38.3
	excess	35	18.6
	Total	188	100.0

81(43.1%) patients had normal levels of Vitamin-D, 72(38.3%) patients had deficiency of vitamin-D and 35(18.6%) had their vitamin-D in more than normal range.

Table 3. Distribution of Insulin among the patients studied

Hormone	level	frequency	percentage
	Normal	167	88.8
	Deficient	21	11.2
	Total	188	100.0

Majority of the patients 167(88.8%) had their insulin levels in the normal range and 21(11.2%) patients had levels in the deficient range. While none was having excess of insulin.

Table 4. Correlation of different variables with dry eye disease as per TBUT test.

	N	TBUT(R/E)		TBUT(L/E)	
		Pearson correlation	P-value	Pearson correlation	P-value
AGE	188	0.041	0.581	0.06	0.412
VITAMIN-D	188	.412	<0.001	.478	<0.001
INSULIN	188	0.094	0.201	0.113	0.123

Table 5. Correlation of different variables with dry eye disease as per Schirmer's test.

	N	Schirmer's(R/E)		Schiermer's(L/E)	
		Pearson correlation	P-value	Pearson correlation	P-value
AGE	188	-0.055	0.45	-0.021	0.78
VITAMIN-D	188	.304	<0.001	.346	<0.001
INSULIN	188	.176	0.016	.174	0.017

There was statistically significant positive correlation found between Vitamin -D and Dry eye disease as per Schirmer's test and TBUT . Results showed that Vitamin-D deficiency is strongly correlated with increased prevalence of dry eye disease. Insulin and dry eye disease had a positive correlation as per Schirmer's test with p value of 0.016 for right eye and 0.017 for left eye. Less amount of insulin in post-menopausal women is correlated with increased prevalence of dry eye disease. While as per TBUT the correlation of dry eye disease with insulin was statistically insignificant.

In the present study, the grading of dry eye as per Schirmer's test through which 188 right eyes were tested 64 (34%) eyes were diagnosed with mild dry eye disease, 29(15.4%) eyes as moderate dry eye disease, 4(2.1%) eyes as severe dry eye disease while 91(48.4%) eyes were having no dry eye disease. Mild dry eye disease was more prevalent than moderate and severe dry eye. Similar results were found for Schirmer's test left eye where, out of total 188 left eyes, 64 (34%) eyes had mild dry eye disease, 30(16%) eyes had moderate dry eye disease, 1(0.5%) eye had severe dry eye disease while 93 (49.5%) eyes were in normal range and had no dry eye. TBUT showed similar trends, 94(50%) right eyes and 92(48.9%) left eyes were normal and had no dry eye disease. 70(37.2%) right eyes and similar number of left eyes were having mild dry eye disease while 22(11.7%) right eyes and 25(13.3%) left eyes were diagnosed with moderate dry eye disease. 2(1.1%) right eyes and 1(0.5%) left eye had severe dry eye disease. As per TBUT also mild dry eye disease was more prevalent than moderate and severe dry eye.

4. **Discussion**

In our study, the prevalence of dry eye syndrome was found to be 51.06% (table 1). These findings are correlated to a study conducted by Gnanadurai JSC et al. (2019) where in the reported prevalence of dry eye in postmenopausal

women was 52%. In another study conducted by Kritika et al. (2023) Out of 150 post-menopausal women it was found that 83(55.3%) showed signs of dry eye disease and maximum women belong to >60 years age group. In a study conducted by Kumar GV et al. (2018) on 200 post-menopausal women with the mean age group of 51.66 years prevalence of dry eye disease was found to be 39.5%.

In our study maximum number of patients had mild dry eye disease as per Schirmer's test and TBUT followed by moderate dry eye and then severe dry eye disease. These findings are correlated with the study conducted by Kritika et al. (2023) wherein with Schirmer's test 45.7% (38) patients showed mild signs, 32.5% (27) had shown moderate signs and 21.6% (18) had severe signs of dry eye disease.

In our study, Statistically significant positive correlation was found between vitamin -D and dry eye as per Schirmer's test and TBUT with p-value of <0.001 for both the test. It is correlated with the study conducted by Jain N et al. (2022) to study the association between vitamin-D deficiency and dry eye syndrome in the Indian population and compared 60 subjects with vitamin-D deficiency (< 20 ng/dl) to 60 subjects with normal vitamin-D levels (equal to or greater than 20 ng/dl). They concluded a positive association between vitamin-D deficiency and dry eye disease. In another study conducted by Bhatt RB et al. (2023) to study vitamin-D3 deficiency as causative factor for dry eye in 60 subjects. They reported that the patients having dry eye had decreased vitamin-D3 levels. Vitamin-D3 level was positively correlated with Schirmer's test 1 and 2 and tear film break up time score. In a case control study conducted by Malik D et al. (2023) on postmenopausal women on hospital based population to study the correlation between serum Vitamin-D levels with (cases) and without (controls) Dry eye disease it was found that there was Significantly lower mean Vitamin-D levels found in cases with dry eye disease (14.36 ± 4.08 ng/ml) as compared to controls with no dry eye (19.19 ± 6.4 ng/ml) (P =0.001)

In current study, statistically significant positive correlation was found between insulin and dry eye as per Schirmer's test but the correlation was statistically insignificant as per TBUT .

There is not much literature available on evaluation of the role of insulin in the pathophysiology of dry eye. However, there are various studies which have evaluated the correlation of diabetes with dry eye disease. Hann LE et al. (1991) in their study stated that insulin has a synergistic action with androgens on lacrimal gland function. Manaviet et al. (2008) studied the prevalence of dry eye syndrome and diabetic retinopathy in type 2 diabetics (insulin dependent) in 199 subjects out of which 108 (54.3%) had dry eye syndrome. They concluded that diabetic patients have increased prevalence of dry eye syndrome and diabetic retinopathy & dry eye have a common association.

5.   Conclusion

This study concludes that there is increased prevalence of dry eye disease in females in the post-menopausal age group with majority exhibiting mild dry eye disease. Vitamin-D deficiency and post-menopausal females with decreased insulin levels are strongly correlated with the increased prevalence of dry eye disease in these females indicating their potential role in disease pathogenesis.

And further to find out the type of dry eye disease and to look for the specific cause tests like meibography to assess MG dropout, biomicroscopy to assess MG expressibility & meibum quality and tests like tear film osmolarity should be done so that cause targeted treatment can be started accordingly. Such data will help to improve the diagnostic and treatment modalities for dry 61 eye disease, prevent complications and improve the quality of life of women suffering from the same disease.

Our study only includes the patients attending eye OPD and a larger sample size is further required to establish the hormonal and metabolic factors contributing to increased prevalence of dry eye disease in post-menopausal females.

6.   Conflict of Interest

The authors declare that they have no conflict of interest.

7. **Funding Declaration**

8. **References**

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