Original Article

DOI: 10.7860/JCDR/2022/52221.16604

Prevalence and Association of Meibomian Gland Dysfunction with Dry Eye Severity from a Tertiary Care Rural Hospital in Central Gujarat: A Cross-sectional Study

Ophthalmology Section

DEVANSHI SMIT MEHTA[1], SONAL DHRUVPAL SISODIYA[2], HARSHA CHETAN JANI[3]

ABSTRACT

Introduction: Meibomian glands are holocrine meibum secreting glands driving out the oil from the orifice. It forms the outermost lipid layer of the tear film which prevents overflow of tears because of its hydrophobic properties and reduces their evaporation. The deficiency of oily layer of the tear film leads to evaporative dry eyes and ocular surface diseases. As Meibomian Gland Dysfunction (MGD) is one of the major causes of evaporative dry eye, with the help of this study, prevalence and association of MGD and dry eye can be evaluated and treated.

Aim: To find out the prevalence and association of MGD and dry eye as well as asymptomatic individuals having MGD and dry eye in 30 to 80 years age group in the region of central Gujarat, Western India.

Materials and Methods: This cross-sectional study was conducted in the Outpatient Department (OPD) of a rural tertiary care hospital in central Gujarat, India between February 2020 to February 2021, after taking approval from Institutional Ethics Committee. Study included 389 subjects representing rural population of Anand, Gujarat, India. Subjects were asked for symptoms of dry eye according to Ocular Surface Disease Index (OSDI) questionnaire and severity of symptoms was assessed. Comprehensive ophthalmic examination including Best Corrected Visual Acuity (BCVA), Schirmer's test, slit lamp examination including conjunctival and corneal surface staining, Tear Film Break Up Time (TBUT), evaluation of meibomian gland orifices, lid margin anatomy, meibum expressibility, quality of meibum, meibomian gland dropouts were done. On the basis of these parameters, diagnosis and grading of MGD and dry eye was done. Subgroups were made according to age, gender, co-morbidities (diabetes mellitus, hypertension, thyroid disease), cases of any refractive eye surgery, pseudophakic eyes, use of systemic drugs, hormonal pills, topical antiglaucoma drugs and use of contact lens. Data analysis was done by descriptive statistics (using Stata software 14.2 version). Analysis of Variance (ANOVA) were used to assess the association and Pearson test was applied to assess the correlation of MGD scores and dry eye severity with age.

Results: Overall prevalence of MGD and dry eye were 97.4% and 88.82% respectively. Out of total 389 subjects, 219 (56.3%) participants were asymptomatic. Age was significantly correlated with MGD and dry eye severity. Higher MGD scores were found with increase with dry eye severity. Highest MGD scores were observed when the tear break up time was ≤5 seconds.

Conclusion: The prevalence of MGD and dry eye was high in the region of central Gujarat, India. MGD leads to deficiency of oily layer of the tear film leading to evaporative dry eyes and ocular surface diseases.

Keywords: Meibum, Ocular surface disease index questionnaire, Tear film break up time

INTRODUCTION

Meibomian glands are holocrine meibum secreting glands driving out the oil from the orifice into the marginal lipid reservoir and forms the outermost lipid layer of the tear film [1]. Lipid layer of tear film prevents overflow of tears because of its hydrophobic properties and retard their evaporation [2]. MGD leads to deficiency of oily layer of the tear film leading to evaporative dry eyes and ocular surface diseases [3]. MGD is the major cause for evaporative dry eye disease. MGD has been reported to contribute 60% of all cases of dry eye diseases with worldwide prevalence of 3.5% to nearly 70% [4,5]. Prevalence of dry eye diseases ranges from 5-50% worldwide [6,7].

According to the rate of secretion, MGD is classified as: 1) Low delivery states with meibomian gland hyposecretion or obstruction 2) High delivery states with meibomian gland hypersecretion [2]. In low delivery state MGD, the underlying pathophysiology is epithelial hyperkeratinisation leading to duct obstruction, meibumstasis, cystic dilation, and eventually causing disuse acinar atrophy and gland dropout [8]. The acinar epithelial cells of meibomian gland atrophy with age, lead to reduction in lipid production and altered meibum composition [2,9]. As per human and mouse model studies, increase in age leads to decreased meibocyte differentiation, meibocyte cell renewal, meibomian gland size and increased in inflammatory cell infiltration [10,11]. Regulation of meibocyte differentiation and lipid biosynthesis require nuclear receptor protein Peroxisome Proliferator-Activated Receptor gamma (PPARγ), which contributes to meibomian glands formation and its function [12]. With increasing age, down regulation of PPARγ occurs causing gland atrophy and a hyposecretory state of meibomian glands [10].

Androgen and estrogen receptors are present within meibomian glands, and meibocytes contain the enzymes necessary for the intracrine synthesis and metabolism of these hormones [2]. Androgens regulate the expression of thousands of genes in meibomian glands involving pathways of lipid dynamics and PPAR signaling [13]. MGD is seen in individuals who are on anti-androgen agents, with complete androgen insensitivity syndrome, and Sjogren's syndrome [2]. Exogenous factors responsible for MGD are use of systemic medications like 13-cis-retinoid acid and epinephrine, topical antiglaucoma medications, use of contact lenses and low humidity [14-17]. Dietary intake of oral omega-3 fatty acids reduce dry eye signs and symptoms by decreasing inflammation in MGD [18].

Common symptoms of MGD are foreign body sensation, eye ache, burning, watering, asthenopia, blurring of vision, itching, secretions, photophobia [19]. Many a times patients are asymptomatic and MGD is diagnosed on clinical examination [20-22]. Assessment of dry eye is done by blink rate and blink interval, Tear Meniscus Height (TMH), tear film osmolarity, TBUT, ocular surface staining, and Schirmer's test. Specialised tests for MGD evaluation are meibography, interferometry and in-vivo confocal laser microscopy [23]. Management guidelines for MGD is as per American Academy of Ophthalmology [24].

As MGD is the major cause of dry eye, with diagnosing and treating MGD, clinicians can prevent ocular surface disorders as well as reduce the economic burden to patients and to the whole country by cutting off the expense of artificial tears, which are prescribed for dry eye without treating the cause of dry eye. The study was done to reveal the asymptomatic and symptomatic patients having MGD and dry eyes and to establish their association.

In the Indian scenario, most of the studies are related to dry eyes but very less are related to MGD. Few have been providing data from West Bengal and Northern India but no such study has ever been done in the Western part of the country. Thus, the aim of the study was to find out the prevalence and association of MGD and dry eye as well as asymptomatic individuals having MGD and dry eye in 30 to 80 years age group in the region of central Gujarat, Western India.

MATERIALS AND METHODS

This cross-sectional study was conducted in Ophthalmology OPD of a rural tertiary care hospital in central Gujarat, India after taking approval from 'Institutional Ethics Committee-2' in its 117th meeting, held at H.M. Patel Centre for Medical Care and Education, Karamsad, on 31/01/2020, (number 105/2020) between February 2020 to February 2021. Total 389 participants were included in the study from the general ophthalmology OPD. The participants were selected by convenient sampling after taking written and informed consent from them.

Inclusion criteria: Patients between the age group of 30-80 years who came to the Ophthalmology Department were included in the study.

Exclusion criteria: Patients having other causes of dry eye such as Sjogren syndrome, cicatricial pemphigoid, chemical injuries were excluded from the study.

A brief demographic history for patient identification, personal and past history including the use of topical medication, systemic drugs, hormonal pills, co-morbidities such as diabetes mellitus, hypertension, thyroid disease, refractive surgeries, cataract surgeries, or use of contact lens wear was asked for the risk factor association.

Questionnaire

The participants were asked for ocular symptoms of dry eye as per Ocular Surface Disease Index (OSDI) questionnaire developed by the Outcomes Research Group at Allergan Inc (Irvine, Calif), (*written permission from Allergan pharmaceuticals was taken for using the same) and severity of dry eye was assessed [25]. The 12-items of the OSDI questionnaire were graded on scale of 0-4, where 0 indicates none of the time; 1-some of the time; 2-half of the time 3-most of the time; 4-all of the time. The total OSDI score was then calculated on the basis of the following formula:

OSDI=[(sum of sores for all questions answered)×100]

[(total number of questions answered)×4]

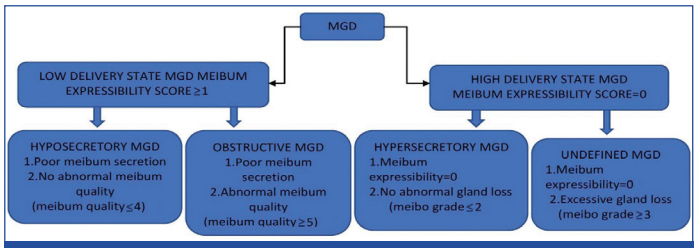
The OSDI is scored on a scale of 0-100 with 0-12 representing normal, 13-22 mild dry eye disease, 23-32 moderate dry eye disease, and ≥33 severe dry eye disease, higher scores suggesting greater disability [26].

Ocular examination included BCVA using the Snellen's chart, Schirmer's test, assessment of anterior segment on slit lamp examination with 2% fluorescein dye to assess conjunctival and corneal surface staining and TBUT. Dry eye severity was assessed by dry eye severity grading scheme [24].

Evaluation of meibomian gland morphology was done on the basis of lid margin anatomy, meibomian gland orifices, meibum expressibility, quality of meibum, meibomian gland dropouts and scored between 0-3.

MG score was (0-12) for each eyelid=Lid Margin anatomy+MG Expressibility+Meibum quality score+Meibomian gland dropouts score [24]. Since the total MGD score for one eyelid is 0-12, so for one eye (including upper lid+lower lid) it was (0-24).

Thus, the total MGD score for both eyes was between 0-48. MGD was classified according to Novel classification as per [Table/Fig-1] [27-29].



[Table/Fig-1]: Showing Novel classification of MGD [27-29].

STATISTICAL ANALYSIS

The study was analysed using Stata software (version 14.2). Descriptive statistics mean, standard deviation and frequency and percentage were used to present socio-demographic and clinical profile of the study participants. MGD with age was correlated through Pearson correlation. The dry eye severity assessment according to OSDI and MGD scores were depicted using mean (standard deviation) as well as frequency and percentage after applying relevant classification rules. The association between dry eye severity and MGD scores, MGD classification and others were assessed using ANOVA for association depending on type of variables involved.

RESULTS

In present study, 389 subjects of both eyes (778 eyes) were included, of which 758 eyes showed changes of MGD with 97.4% prevalence of MGD. Out of 758 eyes with MGD, 378 had right eye MGD and 380 had left eye MGD. The mean age of the study population was 53±12.54 years. The total number of males were 230 and females were 159. Among male subjects, 447 eyes (222 right eye+225 left eye) had MGD and in females, 311 eyes (156 right eye+155 left eye) had MGD.

On correlating the age with MGD scores, a significant correlation was observed. MGD scores increased with increasing age [Table/Fig-2]. On correlating the age with dry eye severity scoring and grading, a significant positive correlation was observed, suggesting significant increase in dry eye severity with age [Table/Fig-3,4]. Few old patients did not know their age correctly and as the study was carried over for few days, some patients were not carried over and hence the denominator was changed.

No significant difference between males and females among MGD score was observed (p-value >0.05) [Table/Fig-5].

Variable		Age	MGD scores Right eye	MGD scores Left eye
Age (n=385)	Pearson correlation	1	0.573	0.589
	Sig. (2-tailed)#		<0.001	<0.001

[Table/Fig-2]: Correlation of MGD and age.
*The data for 4 old patients is missing, since they did not know their age
#Pearson correlation coefficient test; p-value <0.05 considered significant

Variable		OSDI score
Age (n=385)	Pearson correlation	0.166
	Significance (2-tailed)	0.001

[Table/Fig-3]: Correlation of age and OSDI score.
*The data for 4 old patients is missing, since they did not know their age
Pearson correlation coefficient test

Variable		Age	Right eye dry eye severity score	Left eye dry eye severity score
Age (n=385)	Pearson correlation	1	0.295	0.299
	Significant (2-tailed)		<0.001	<0.001

[Table/Fig-4]: Correlation of age and dry eye severity score.
*The data for 4 old patients is missing, since they did not know their age
Pearson correlation coefficient test; p-value <0.05 considered significant

Eye	Sex	N	Mean	Standard deviation	p-value
MGD right eye	Male	222	9.69	5.71	0.96
	Female	156	9.72	5.69	
MGD left eye	Male	225	9.82	5.68	0.87
	Female	155	9.72	5.61	

[Table/Fig-5]: Mean MGD scores in males and females.
Independent sample t test

Out of 389 participants, 356 participants (91.5%) had dry eye. There was no significant difference between dry eye severity and gender. Out of all the participants, 170 (43.70%) had symptoms of dry eyes and 219 (56.3%) were asymptomatic. Mean MGD score among asymptomatic participants was 17.06±11.08 and among symptomatic participants was 25.47±10.71. The p-value was <0.001, suggestive of higher scores of MGD among symptomatic participants [Table/Fig-6]. A total of 213 right eyes among 378 right eyes and 216 left eyes among 380 left eyes were asymptomatic with MGD.

Dry eye severity according to OSDI questionnaire	Frequency of participants	MGD scores	Standard deviation	p-value
Normal (Asymptomatic)	219	17.06	11.08	<0.001
Mild dry eye	79	20.26	10.87	
Moderate dry eye	80	23.65	10.56	
Severe dry eye	11	32.50	4.99	
Total	389	19.42	11.28	

[Table/Fig-6]: MGD scores among asymptomatic (normal) individuals and symptomatic (mild, moderate, severe dry eye).
Analysis of variance (ANOVA) test; p-value <0.05 considered significant

The TBUT is the most reliable variable in dry eye severity scoring, clinical evaluation of dry eye showed results in [Table/Fig-7]. [Table/Fig-6] is based on symptomatic evaluation of dry eye according to OSDI Questionnaire (on the basis of patient's history) and [Table/Fig-7] is related to dry eye severity score (ocular examination). The difference in the frequency means that there were patients who did not have symptoms of dry eye but actually, they were having dry eye on the basis of examination.

Tear film break up time right eye	Sex		Total n (%)
	Male	Female	
Variable (No dry eye)	20	13	33 (8.5)
≤10 (Mild dry eye)	81	39	120 (30.9)
≤5 (Moderate dry eye)	116	95	211 (54.3)
Immediate (Severe dry eye)	13	12	25 (6.44)
Total	230	159	389
Tear film break up time left eye	**Sex**		**Total n (%)**
	Male	**Female**	
Variable (No dry eye)	21	13	34 (8.7)
≤10 (Mild dry eye)	76	42	118 (30.3)
≤5 (Moderate dry eye)	122	92	214 (55.0)
Immediate (Severe dry eye)	11	12	23 (5.9)
Total	230	159	389

[Table/Fig-7]: Dry eye grading according to TFBUT(Tear Film Break Up Time) in male and female.

In present study 107 eyes were pseudophakic. Data analysis showed a significant comparison, suggesting increased prevalence of MGD and dry eyes among pseudophakic eyes but, the age was confounding factor as cataract surgeries are done in elderly individuals [Table/Fig-8].

Eye	Pseudophakic right eye	N	Mean	Standard deviation	p-value
MGD right eye	No	327	9.19	5.76	<0.001
	Yes	51	12.96	3.94	
MGD left eye	**Pseudophakic left eye**	**N**	**Mean**	**Standard deviation**	**p-value**
	No	324	9.23	5.69	<0.001
	Yes	56	13.02	4.19	

[Table/Fig-8]: Comparison of MGD scores in pseudophakic right and left eye.
Independent sample t test; p-value <0.05 considered significant

A total of 45 (11.6%) participants of the study were using topical antiglaucoma drugs. A significant difference in MGD scores with the use of topical antiglaucoma drugs (p value=0.02), while dry eye severity score showed no significant difference with use of topical antiglaucoma drugs (p-value=0.27) [Table/Fig-9].

Score	Use of antiglaucoma medication	N	Mean MGD score	Standard deviation	p-value
OSDI score	No	342	10.34	10.67	0.27
	Yes	45	12.21	10.47	
Total MGD score	No	334	18.92	11.42	0.02
	Yes	42	23.31	9.48	

[Table/Fig-9]: Comparison of MGD and dry eye scores among antiglaucoma medication users and non users.
Independent sample t test; 2 participants were on some drops but no documentation was available. Hence not documented. That is for OSDI score tabulation, the authors had only 387 out of 389 participants. For MGD score tabulation, the data for only 376 participants were available, out of 389 participants-Data not available for some patients

In present study, 89 participants had hypertension (HTN), 66 participants had Diabetes Mellitus (DM), and 34 participants had hypertension and diabetes mellitus both. Subjects with diabetes mellitus and hypertension along with MGD showed p-value of 0.001 and <0.001 respectively and dry eyes showed p-value of 0.04 and 0.02 respectively [Table/Fig-10,11].

Score	History of DM	N	Mean	Std. Deviation	p-value
OSDI score	No	321	9.94	10.24	0.04
	Yes	66	13.29	12.18	
Total MGD score	No	315	18.58	11.21	0.001
	Yes	61	23.67	10.88	

[Table/Fig-10]: Comparison of MGD and dry eye scores among diabetics.
Independent sample t test
2 participants were not sure about their history of diabetes. Thus, the authors had only 387 out of 389 participants for Diabetic x OSDI score tabulation. For MGD score tabulation X diabetic, the data for only 376 participants were available, out of 389 participants-Data not available for some patients

Score	History of HTN	N	Mean	Std. Deviation	p-value
OSDI score	No	298	9.80	10.9	0.02
	Yes	89	12.87	11.51	
Total MGD score	No	290	18.28	11.28	<0.001
	Yes	86	23.22	10.54	

[Table/Fig-11]: Comparison of MGD and dry eye scores among hypertensives.
Independent sample t-test.
2 participants were not sure about their history of hypertension. So, the authors had only 387 out of 389 participants for Hypertensives x OSDI score tabulation. For MGD score tabulation X hypertensives, the data for only 376 participants were available, out of 389 participants-Data not available for some patients

Statistical analysis of thyroid disease as a risk factor for MGD and Dry eyes was not done (not reliable) because of small sample size (10 participants).

Total 29 participants were using different systemic drugs out of which 19 were on systemic beta blockers, seven were on systemic

antipsychotics and three were on other drugs. Data analysis showed no correlation between use of systemic drugs: beta blockers, antipsychotic and others to MGD prevalence and dry eye severity.

Sample size for statistical analysis for contact lens wearers (two participants), hormonal pill users (nine participants), Eyes with Refractive surgery done in past (10 eyes) was very less in number so association between those with MGD and dry eyes was not done.

As the symptoms of dry eyes increases (according to OSDI questionnaire), scores of MGD also increases in right eye and left eye with p-value <0.001, suggesting significant association of dry eye and MGD [Table/Fig-12].

Eye	Dry eye severity according to OSDI questionnaire	Frequency of participants	MGD scores	Standard deviation	p-value
Right eye	Normal	213	8.52	5.58	<0.001
	Mild dry eye	77	10.02	5.55	
	Moderate dry eye	80	11.92	5.29	
	Severe dry eye	8	16.25	2.49	
Left eye	Normal	216	8.63	5.56	<0.001
	Mild dry eye	77	10.26	5.44	
	Moderate dry eye	79	11.83	5.28	
	Severe dry eye	8	16.25	2.49	

[Table/Fig-12]: Association of OSDI with MGD right eye and MGD left eye.
Analysis of variance (ANOVA) test; p-value <0.05 considered significant

As the TBUT increases, scores of MGD also increases in right eye and left eye with p-value <0.001 suggesting significant association of dry eye and MGD, as TBUT is the most reliable variable in dry eye severity scoring and MGD is the major cause of evaporative dry eye. [Table/Fig-13,14] [3].

Tear film break up time (seconds)	N	Mean of MGD score	Standard deviation
Variable (No dry eye)	33	4.09	4.94
≤10 (Mild dry eye)	117	8.86	5.61
≤5 (Moderate dry eye)	204	11.00	5.22
Immediate (Severe dry eye)	24	10.46	5.87
Total	378	9.70	5.69

[Table/Fig-13]: TBUT with MGD right eye (p<0.001).
Analysis of variance (ANOVA) test

Tear film break up time (seconds)	N	Mean of MGD score	Standard deviation
Variable (No dry eye)	34	4.35	5.24
≤10 (Mild dry eye)	115	9.07	5.56
≤5 (Moderate dry eye)	210	11.01	5.21
Immediate (Severe dry eye)	21	10.09	5.49
Total	380	9.78	5.65

[Table/Fig-14]: TBUT with MGD left eye p<0.01.
Analysis of variance (ANOVA) test

According to Novel Classification, 290 eyes had hypersecretory MGD, 460 eyes had hyposecretory MGD, eight eyes had obstructive MGD.

DISCUSSION

Dry eye is one the most common causes of ophthalmic consultation. International Dry Eye Workshop defined dry eye as '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.' One diagnostic classification scheme divides dry eye into aqueous deficiency dry eye and evaporative dry eye [3].

The MGD is defined as a chronic, diffuse abnormality of the meibomian glands, commonly characterised by terminal duct obstruction and/or qualitative/quantitative changes in the glandular secretion, which may result in alteration of the tear film, clinical apparent inflammation, ocular surface disease, and symptoms of eye irritation [28]. The present study included 389 participants (778 eyes) between 30-80 years of age. Mean age of the study population was 53±12.54 years. The study results showed that the prevalence of MGD increased with age (p-value is <0.001). Similar results were found in different studies done in different region of India and in the world. In Central Indian study, the mean age of the MGD subjects was 53.3±15.2 years among the study population of 570 and the risk of total MGD increased with age [21]. In North western Spain, among 619 participants, the mean age was 63.4±14.5 years and the prevalence of MGD increased with age [20]. Similar mean age of the subjects was noted in Beijing study, Japan, Austrian dry eye clinic study, Singapore eye study, Bankok study and Western Indian study [4,30-34]. However the mean age of study population was higher in korea dry eye study; among 657 individuals, with mean±SD age 72.0±5.9 years [35] and in Taiwan eye study with mean age 72.2 years [22].

The prevalence of MGD was 97.4% in the present study which was higher in comparison with other studies, however the authors could not conclude any reason for high MGD prevalence. Studies done in West Bengal, India and Japan had 31.7% and 32.9% MGD prevalence respectively, while study in central India, Singapore, Taiwan, Bangkok, Austria had 55.6%, 56.3%, 60.8%, 63.6%, 70.3% MGD prevalence, respectively [21,22,30-33,36]. World wide prevalence of MGD ranges from 3.5% (among Whites) to 70% (among Asian population) [37]. In present study 219 (56.3%) subjects were asymptomatic and 170 (43.7%) were symptomatic. Mean MGD score among asymptomatic subjects was 17.06±11.08 and among symptomatic subjects was 22.49±10.83. [Table/Fig-15] shows the prevalence of symptomatic and asymptomatic MGD subjects across the world [4,20-22,33].

Study	Symptomatic MGD	Asymptomatic MGD
North western Spain [20]	8.6%	21.9%
Central India study [21]	26.1%	73.9%
Beijing eye study [4]	411 (21%)	1546 (79%)
Bangkok study [33]	34.0% reported >/=1 symptoms of dry eye	9.4%
Taiwan [22]	33.7%	66.1%
Present study	170 (43.7%)	219 (56.3%)

[Table/Fig-15]: Prevalence of symptomatic and asymptomatic MGD subjects in Spain, central India, Bangkok, Beijing and Taiwan.

Clinical dogma has long suggested that severity of dry eye becomes more common with age and some evidence suggests age related decrease in tear production [3,38]. In present study dry eye symptoms and dry eye test severity increased with increasing age. Similar results were found in Indonesia dry eye study [39] while in Bangkok study age association was found in dry eye test analysis with p-value <0.05 but not in dry eye symptoms analysis with p-value 0.691 [33].

In the year of 2018, a dry eye study done in Western India (same tertiary care hospital in central Gujarat) showed 54.3% prevalence of dry eye [34]. Due to COVID-19 pandemic, use of digital devices has been increased leading to digital eye strain which can be the cause for increased prevalence of dry eye. The prevalence of digital eye strain ranges from 25-93%, as reported in different studies [40-43]. The prevalence of dry eye in West Bengal was 26% [36]. A population based study in Korea showed the prevalence as 30.3% dry eye [35]. Similar findings were found in Indonesia study in 1058 participants (mean age 37±13 years), where prevalence of dry eye was 27.3% [39].

In the present study, there was no significant difference in MGD between both the gender. However, a study done in Spain showed higher prevalence of MGD in males than in females (p-value=0.003) [20]. Similarly, Central India study and Singapore study showed

higher prevalence of MGD in males than in females [21,32]. In Beijing eye study dry eye symptoms were significantly associated with female gender [4]. In West Bengal study and Korean study dry eye diseases were significantly higher in females than in male [35,36]. Contrary to this findings , in Indonesia study dry eye prevalence was 1.4 times higher in males than in females [39].

Studies done in Beijing and Taiwan had evaluated TBUT. The TBUT was <10 seconds in 54.7% and 79.3% subjects respectively and 6.5% and 33.4% subjects showed positive fluorescein staining of cornea respectively [4,22]. While in present study, 691 (88.82%) eyes had TBUT <10s [Table/Fig-13,14]. In present study, out of 389 subjects (778 eyes); 639 eyes cases showed schirmer's test >10 mm, suggesting these eyes have evaporative dry eyes with normal aqueous production. This finding was similar to that of Norwegian Dry Eye Clinic Study in 2019 which showed no significant difference in value of schirmer's test in different grades of MGD [44]. With contrary to this finding Taiwan study showed Schirmer's test ≤5 mm in 58.4% [22] while in current study only eight eyes (1.03 %) showed Schirmer's test ≤5 mm.

Present study also evaluated the risk factors association for MGD and Dry eyes like co-morbidities (diabetes mellitus, hypertension, thyroid disease), use of systemic drugs, use of hormonal pills, use of topical antiglaucoma agents, use of contact lens, cases of any refractive eye surgery or pseudophakic eyes. Participants having diabetes mellitus, hypertension had increased MGD scores and dry eye severity. In Spain study, asymptomatic MGD was associated with diabetes and cardiovascular disease while symptomatic MGD was associated with Rosacea and Rheumatoid arthritis [20]. In Beijing eye study, 1957 subjects were assessed for dry eye symptoms and many associations including diabetes mellitus, p-value of 0.007, was suggestive of dry eye to be more prevalent among diabetic patients [4]. A study done in Western India, 67% prevalence of dry eye was found in diabetics, 95% dry eye was found in participants having MGD, 72% prevalence of dry eye was found in topical antiglaucoma medication users [34]. According to Novel Classification, 290 eyes had hypersecretory MGD, 460 eyes had hyposecretory MGD and 8 eyes had obstructive MGD in the present study, while in Norwegian dry eye clinic study 78 eyes had hypersecretory MGD, 66 eyes had hyposecretory MGD, 254 eyes had obstructive MGD and 49 eyes had undefined MGD [44].

Limitation(s)

Single centre study and lack of use of infrared meibography are the limitations of the present study. As higher prevalence of MGD is observed in this study, it is essential to draw clinician's attention towards all dry eye patients. Instead of treating dry eye patients, MGD should be looked for, in all patients of dry eye and needs to be managed accordingly. As it was a single centre study, multicentric study should be carried out, so that MGD diagnosis can be made and management guidelines should be implemented nation wise by higher authorities accordingly.

CONCLUSION(S)

Higher MGD scores is associated with increase in dry eye severity suggestive of MGD as contributory factor for dry eyes, to which clinician's attention must be drawn as most of them miss the diagnosis and treat the dry eyes without treating the cause. In present study with good clinical history and examination, asymptomatic patients with MGD and dry eye were also identified. The also study reflected the major burden of MGD and dry eye disease in this region. MGD need to be diagnosed properly, as treating dry eye without treating MGD can lead to lots of financial burden to the patients without gaining much benefits.

Acknowledgement

Authors would like to acknowledge Mr. Ajay Phatak for his help in the statistical analysis of the data.

REFERENCES

[1] 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. Invest Ophthalmol Vis Sci. 2011;52(4):1938-78.
[2] Bron AJ, Tripathi RC, Tripathi B. Wolff's Anatomy of the eye and orbit. Am J Ophthalmol. 1998;4(125):571-72.
[3] Cantor L, Rapuano C, McCannel C. Clinical approach to ocular surface disease, In: Basic and Clinical Science Course, Section 8-External Disease and Cornea, American Academy of Ophthalmology. 2019-2020: p.83.
[4] Jie Y, Xu L, Wu YY, Jonas JB. Prevalence of dry eye among adult Chinese in the Beijing Eye Study. Eye (Lond). 2009;23(3):688-93.
[5] McCarty CA, Bansal AK, Livingston PM, Stanislavsky YL, Taylor HR. The epidemiology of dry eye in Melbourne, Australia. Ophthalmol. 1998;105(6):1114-19.
[6] Stapleton F, Alves M, Bunya VY, Jalbert I, Lekhanont K, Malet F, et al. TFOS DEWS II epidemiology report. Ocul Surf. 2017;15(3):334-65.
[7] Chan TCY, Chow SSW, Wan KHN, Yuen HKL. Update on the association between dry eye disease and meibomian gland dysfunction. Hong Kong Med J. 2019;25(1):38-47. Doi: 10.12809/hkmj187331. Epub 2019 Jan 31.
[8] Jester JV, Parfitt GJ, Brown DJ. Meibomian gland dysfunction: Hyperkeratinization or atrophy?. BMC Ophthalmol. 2015;15:156.
[9] Liu S, Richards SM, Lo K, Hatton M, Fay A, Sullivan DA. Changes in gene expression in human meibomian gland dysfunction. Invest Ophthalmol Vis Sci. 2011;52(5):2727-40.
[10] Nien CJ, Massei S, Lin G, Hatton M, Fay A, Sullivan DA. Effects of age and dysfunction on human meibomian glands. Archives of Ophthalmology. 2011;129(4):462-69. [PubMed: 21482872].
[11] Jester JV, Potma E, Brown DJ. PPARγ Regulates mouse meibocyte differentiation and lipid synthesis. Ocul Surf. 2016;14(4):484-94.
[12] Call M, Fischesser K, Lunn M, Kao W. Notch regulation of PPAR-gamma and development of meibomian gland dysfunction. Invest Ophthalmol Vis Sci. 2013;54(15):924-24.
[13] Khandelwal P, Liu S, Sullivan DA. Androgen regulation of gene expression in human meibomian gland and conjunctival epithelial cells. Molecular Vision. 2012;18:1055-67.
[14] Samarawickrama C, Chew S, Watson S. Retinoic acid and the ocular surface. Survey of Ophthalmology. 2015;60(3):183-95.
[15] Jester JV, Nicolaides N, Kiss-Palvolgyi I, Smith RE. Meibomian gland dysfunction. II. The role of keratinization in a rabbit model of MGD. Invest Ophthalmol Vis Sci. 1989;30(5):936-45.
[16] Agnifili L, Fasanella V, Costagliola C, Ciabattoni C, Mastropasqua R, Frezzotti P, et al. In vivo confocal microscopy of meibomian glands in glaucoma. The Br J Ophthalmol. 2013;97(3):343-49.
[17] Larke JR. The eye in contact lens wear. London: Butterworth; 1985. p. 5-6.
[18] Liu Y, Kam WR, Sullivan DA. Influence of omega 3 and 6 fatty acids on human meibomian gland epithelial cells. Cornea. 2016;35(8):1122-26.
[19] Salmon JK, Jack JB. Dry eye In: Kanski's Clinical Ophthalmology, A Systematic Approach International ed. Elsevier Health Sciences; 2020:p.158.
[20] Viso E, Rodríguez-Ares MT, Abelenda D, Oubiña B, Gude F. Prevalence of asymptomatic and symptomatic meibomian gland dysfunction in the general population of Spain. Investigative Invest Ophthalmol Vis Sci. 2012;53(6):2601-06.
[21] Chatterjee S, Agrawal D, Sharma A. Meibomian gland dysfunction in a hospital-based population in Central India. Cornea. 2020;39(5):634-39.
[22] 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(6):1096-101.
[23] Sharma N, Maharana P, Sahay P, Singhal D. Urkude J. All India ophthalmologicaly society guidelines on Meibomian Gland Dysfunction, Cipla, All India Ophthalmological Society focus group meeting 29th July 2017:09-13.
[24] Cantor L, Rapuano C, McCannel C. Clinical approach to ocular surface disease, In: Basic and Clinical Science Course, Section 8-External Disease and Cornea, American Academy of Ophthalmology 2019-2020: p.87-97.
[25] Walt JG, Rowe MM, Stern KL. Evaluating the functional impact of dry eye: The ocular surface disease index [abstract]. Drug Inf J. 1997;311436.
[26] Grubbs Jr JR, Tolleson-Rinehart S, Huynh K, Davis RM. A review of quality of life measures in dry eye questionnaires. Cornea. 2014;33(2):215.
[27] Tomlinson A, Bron AJ, Korb DR, Amano S, Paugh JR, Pearce EI, et al. The international workshop on meibomian gland dysfunction: Report of the diagnosis subcommittee. Invest Ophthalmol Visual Sci. 2011;52(4):2006-49.
[28] Nelson JD, Shimazaki J, Benitez-del-Castillo JM, Craig JP, McCulley JP, Den S, et al. The international workshop on meibomian gland dysfunction: Report of the definition and classification subcommittee. Invest Ophthalmol Vis Sci. 2011;52(4):1930-37.
[29] Arita R, Itoh K, Maeda S, Maeda K, Furuta A, Fukuoka S, et al. Proposed diagnostic criteria for obstructive meibomian gland dysfunction. Ophthalmology. 2009;116(11):2058-63.e1.
[30] Arita R, Mizoguchi T, Kawashima M, Fukuoka S, Koh S, Shirakawa R, et al. Meibomian gland dysfunction and dry eye are similar but different based on a population-based study: The Hirado-Takushima study in Japan. Am J Ophthalmol. 2019;207:410-18. Doi: 10.1016/j.ajo.2019.02.024. Epub 2019 Mar 7.
[31] Rabensteiner DF, Aminfar H, Boldin I, Schwantzer G, Horwath-Winter J. The prevalence of meibomian gland dysfunction, tear film and ocular surface parameters in an Austrian dry eye clinic population. Acta Ophthalmol. 2018;96(6):e707-e711.

[32] Siak JJ, Tong L, Wong WL, Cajucom-Uy H, Rosman M, Saw SM. Prevalence and risk factors of meibomian gland dysfunction: The Singapore Malay eye study. Cornea. 2012;31(11):1223-28. Doi: 10.1097/ICO.0b013e31823f0977.
[33] Lekhanont K, Rojanaporn D, Chuck RS, Vongthongsri A. Prevalence of dry eye in Bangkok,Thailand. Cornea. 2006;25(10):1162-67.
[34] Shah S, Jani H. Prevalence and associated factors of dry eye: Our experience in patients above 40 years of age at a Tertiary Care Center. Oman J Ophthalmol. 2015;8(3):151-56.
[35] Han SB, Hyon JY, Woo SJ, Lee JJ, Kim TH, Kim KW. Prevalence of dry eye disease in an elderly korean population. Arch Ophthalmol. 2011;129(5):633-38.
[36] Basak SK, Pal PP, Basak S, Bandyopadhyay A, Choudhury S, Sar S. Prevalence of dry eye diseases in hospital-based population in West Bengal, Eastern India. J Indian Med Assoc. 2012;110(11):789-94.
[37] Schein OD, Muñoz B, Tielsch JM, Bandeen-Roche K, West S. Prevalence of dry eye among the elderly. Am J Ophthalmol. 1997;124(6):723-28.
[38] Schaumberg DA, Sullivan DA, Dana MR. Epidemiology of dry eye syndrome. Adv Exp Med Biol. 2002;506:989-98.
[39] Lee AJ, Lee J, Saw SM, Gazzard G, Koh D, Widjaja D, et al. Prevalence and risk factors associated with dry eye symptoms: A population based study in Indonesia. Br J Ophthalmol. 2002;86(12):1347-51.
[40] Available from: https://government.economictimes.indiatimes.com/news/education/covid-19-pandemic-impact-and-strategies-foreducation-sector-in-india/75173099 [Last accessed on 2020 Oct 06].
[41] Portello JK, Rosenfield M, Bababekova Y, Estrada JM, Leon A. Computer-related visual symptoms in office workers. Ophthalmic Physiol Opt. 2012;32(5):375-82.
[42] Hagan S, Lory B. Prevalence of dry eye among computer users. Optom Vis Sci. 1998;75(10):712-13.
[43] Reddy SC, Low CK, Lim YP, Low LL, Mardina F, Nursaleha MP. Computer vision syndrome: A study of knowledge and practices in university students. Nepal J Ophthalmol. 2013;5(2):161-68.
[44] Xiao J, Adil MY, Chen X, Utheim ØA, Ræder S, Tønseth KA, et al. Functional and morphological evaluation of meibomian glands in the assessment of meibomian gland dysfunction subtype and severity. Am J Ophthalmol. 2020;209:160-67.

PARTICULARS OF CONTRIBUTORS:
1. Third Year Resident, Department of Ophthalmology, Pramukhswami Medical College, Bhaikaka University, Anand, Gujarat, India.
2. Associate Professor, Department of Ophthalmology, Pramukhswami Medical College, Bhaikaka University, Anand, Gujarat, India.
3. Professor, Department of Ophthalmology, Pramukhswami Medical College, Bhaikaka University, Anand, Gujarat, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Dr. Devanshi Smit Mehta,
12, Rajumugut Society, Opp. Vishwesh Towers, Near Naranpura Police Chowky,
Naranpura, Ahmedabad-380013, Gujarat, India.
E-mail : devanshipatel89@yahoo.com

PLAGIARISM CHECKING METHODS: [Jain H et al.]
- Plagiarism X-checker: Sep 04, 2021
- Manual Googling: Mar 16, 2022
- iThenticate Software: Jun 08, 2022 (11%)

ETYMOLOGY: Author Origin

AUTHOR DECLARATION:
- Financial or Other Competing Interests: None
- Was Ethics Committee Approval obtained for this study? Yes
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. NA

Date of Submission: **Sep 03, 2021**
Date of Peer Review: **Nov 23, 2021**
Date of Acceptance: **Mar 17, 2022**
Date of Publishing: **Jul 01, 2022**