







# Dry Eye Disease in the Middle East and Northern Africa: A Position Paper on the Current State and Unmet Needs

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**Abstract:** In the Middle East and Northern Africa (MENA), dry eye disease (DED) is often misdiagnosed or overlooked. This review summarizes a series of conversations with ophthalmologists in the region around a variety of climatic, lifestyle, and iatrogenic factors that contribute to specific features of DED in the MENA region. These considerations are further classified by patient lifestyle and surgical choices. All statements are based on discussions and formal voting to achieve consensus over three meetings. Overall, a deeper understanding of the disease characteristics of DED specific to MENA can better guide local eyecare practitioners on appropriate management and follow-up care. Additionally, population-based studies and patient and physician education on ocular surface diseases, together with the use of culturally appropriate and language-specific questionnaires can help ease the public health burden of DED in this region.

**Keywords:** ocular surface, regional clinical practice, epidemiology, treatment, patient outcomes

## Introduction

Dry eye disease (DED) is a common disease of the ocular surface that can significantly impact patient-related quality of life. In 2017, the Tear Film and Ocular Surface Society International Dry Eye Workshop 2 (TFOS DEWS II) report redefined DED as “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”. Overall, the TFOS DEWS II initiative indicates that dry eye disease is a global public health problem.<sup>1</sup> Global epidemiologic data suggest that the prevalence of DED varies significantly, with a range of 5% to 50%.<sup>1</sup> Extrapolation of the global prevalence rates indicates an estimated population of 400 million to 3.7 billion patients with DED worldwide.<sup>2</sup> Approximately 25% of patients who refer to eye clinics report DED-related symptoms.<sup>3</sup>

While most patients perceive DED merely as a discomfort, one third perceive it as a disease or even a handicap.<sup>4</sup> Among patients with DED, the most common symptoms include irritated, itchy, and dry eyes, with stinging/burning, foreign body sensation, grittiness, tearing, and blurred vision. DED presents a substantial socioeconomic burden worldwide. Cost estimates for DED range between \$300 and \$1100 per patient annually in European countries, with additional costs due to decreased work productivity.<sup>5</sup>

DED is also a significant clinical problem that is often overlooked or misdiagnosed in developing countries and/or emerging economies, especially in the Middle East and Northern Africa (MENA). Additionally, there is a relative scarcity of epidemiologic data and peer-reviewed publications on DED originating from this region.<sup>6–10</sup> The lack of

uniformity in existing publications limits reasonable estimates of the prevalence and burden of DED in the region.<sup>6–10</sup> Given the geographic size of area and population living in the region, there is an emergent need to establish a uniform approach for the management of DED for healthcare providers in MENA.

Countries such as Egypt, Algeria, and Tunisia in North Africa, and Lebanon, Saudi Arabia, and the United Arab Emirates in the Middle East have country-specific differences in the epidemiology of DED, including prevalence and associated risk factors. Such region-specific differences in DED-related factors need to be highlighted to provide local eyecare practitioners with a better understanding of managing DED in MENA.

Hence, a group of experts held a series of three meetings to discuss: 1) the epidemiological features of DED in MENA, 2) the different diagnostic modalities, 3) treatment options, 4) therapeutic strategies, and 5) perioperative management. This paper provides a practical and adapted approach for ophthalmologists in MENA to improve diagnostic modalities and ensure appropriate management and follow-up of DED.

## Approach for Achieving Consensus

The expert panel of six regional physicians and a chairperson from outside MENA met in three virtual meetings. Consensus on all statements and discussion was reached through voting, alignment, and written agreement.

## Etiology of Dry Eye Disease

Several comprehensive reviews on the pathogenesis of DED have been published,<sup>11–13</sup> and the reader is referred to them for detailed information. Dry eye disease is generally categorized as having evaporative, aqueous deficient, or mixed etiology,<sup>14</sup> with about 70% of cases having evaporative causes.<sup>15</sup> Both evaporative and aqueous deficient types of DED have multifactorial etiologies that ultimately results in loss of tear film homeostasis along with inflammation and ocular tissue damage, further exacerbating tear film dysfunction.<sup>14</sup> The primary cause of evaporative DED is believed to be meibomian gland dysfunction (MGD), which is present in at least 86% of DED cases.<sup>16</sup> Decreased lipids production in MGD reduces the tear film lipid layer thickness (LLT), which can lead to more rapid tear film evaporation and tear film instability.<sup>17–20</sup> Tear film instability can also result from decreased tear production secondary to dysfunction in pathways that stimulate the lacrimal glands or defects in the lacrimal gland itself.<sup>21</sup> The both the loss of tear film stability and increased tear osmolarity stimulate increased levels of inflammatory cells (CD4 and CD8 T cells) and enhanced production and secretion of a large number of pro-inflammatory cytokines and chemokines, including interleukin (IL)-1 $\beta$ , IL-6, IL-8, tumor necrosis factor- $\alpha$ , CCL3, CCL4, and CCL5.<sup>12,22</sup> These inflammatory cells, cytokines, and chemokines induce epithelial damage and further tear dysregulation, resulting in a cycle of DED pathogenesis.<sup>12</sup>

## Epidemiology of Dry Eye Globally and in MENA

Epidemiological studies report a wide range of DED prevalences based on disease definition, method of diagnosis, population surveyed, and how data are analyzed. A study that combined systematic literature in combination with Bayesian analysis reported that the prevalence of DED was 27.76% across Asia, 22.70% in Europe, 25.93% across the Middle East, 9.04% in Australia, 47.52% across Africa, 5.5% in North America, 12.80% across South America, and 32.00% in India.<sup>23</sup> Another systematic review published 2 years earlier found similar trends in the regional prevalences of DED: high DED rates in Africa, moderate rates in Asia and Europe, and lower rates in North America.<sup>24</sup> Several factors have been suggested as potential reasons for regional differences in the prevalence of DED, including climate, weather parameters, environmental exposures, and socioeconomic considerations.<sup>24,25</sup> However, validating clear relationships between these factors and DED prevalence is difficult because of the very large number of potential confounders.

Additional studies focusing specifically on DED in MENA have indicated by-country prevalences ranging from 6.8% to 69%.<sup>8–10,26</sup> One systematic review indicated that the estimated prevalence of DED in Saudi Arabia ranged from 32.1% to 62.4%, and from 6.8% to 28% in Egypt.<sup>26</sup> Prevalences for countries having only a single estimate indicated DED values of 69% for Palestine (West Bank), 52% for Jordan, 27.2% for Iraq, 10% for United Arab Emirates, 28.5% for Tunisia, 36.4% for Lebanon, and 40% for Libya.<sup>26</sup> Additional sources have indicated a DED prevalence of 15% for Israel,<sup>27</sup> 65.2% for Syria,<sup>28</sup> and 52.8% for Turkey.<sup>29</sup>

Taken together, the varied outcomes reported in the above-mentioned studies indicate that the overall prevalence of DED in MENA is not clearly established. Additionally, because of differences in the diagnostics, criteria, and methodologies used, it is tenuous at best to draw any specific conclusions from DED data in MENA. Furthermore, to the best of our knowledge, no international multicenter epidemiological studies have been conducted in the region, and current data are specific to studies performed in individual countries.

## Impact on Quality of Life

Quality of life can be significantly impaired in patients with DED in MENA. DED affects vision-related daily life activities such as reading, using computers or other digital devices, watching television, and driving. Professional activities and work productivity are negatively impacted by DED, with the most pronounced effect noted among Saudi Arabian office workers.<sup>30</sup>

Multiple studies have reported depression and anxiety resulting from impaired quality of life due to DED.<sup>31,32</sup> One questionnaire-based study reported that 42% of 476 patients with DED in Saudi Arabia were diagnosed with depression.<sup>33</sup> The authors concluded that DED was a possible risk factor for developing depression, including more severe forms of depression. Additionally, depression among DED patients is reported to be significantly more prevalent among females and young adults, compared to older adults.<sup>33</sup> Another study from Saudi Arabia reported that DED might also impact quality of sleep among patients.<sup>34</sup>

## Specific Risk Factors for DED in MENA

A listing of the numerous risk factors for DED more broadly is provided in [Table 1](#). Consistent with studies in other regions, studies conducted in Saudi Arabia and Lebanon indicate that aging and female sex are risk factors for DED.<sup>7-9</sup> Autoimmune diseases, such as Sjögren syndrome, rheumatoid arthritis, and thyroid disease are also major risk factors for DED.<sup>35,36</sup> However, factors specific to the MENA region include environment, lifestyle, and demographics.

## Environmental Factors

Environmental conditions in MENA vary widely, with significant differences in climates, ranging from mountainous to coastal regions, sandy deserts, and polluted megalopolises. The arid climate is a hallmark of MENA, leading to increased time spent indoors in air-conditioned (AC) environments.<sup>40</sup> AC, especially with prolonged duration of exposure, is a known risk factor for DED; one analysis of participant activity logs (N=35) reported that a mean of 4.9 hours of AC exposure was linked to dry eye symptoms.<sup>41,42</sup> Additionally, dry, sandy air in desert regions or salty air in windy coastal areas may cause or exacerbate DED symptoms. Pollution, which is also associated with DED, is of particular concern in MENA's megalopolises, including Cairo<sup>43</sup> and Beirut.<sup>44</sup> High exposure to ultraviolet light and living in a hot, dry, windy, or dusty environment, which is common in MENA, may give rise to pterygium, a fibrovascular proliferative lesion of the

**Table 1** Risk Factors for Dry Eye Disease

<ul style="list-style-type: none"> <li>● Age</li> <li>● Gender</li> <li>● Race</li> <li>● Ethnicity (Hispanic)</li> <li>● Hispanic ethnicity</li> <li>● Menopause</li> <li>● Meibomian gland dysfunction</li> <li>● Connective tissue disease</li> <li>● Sarcoidosis</li> <li>● Sjögren syndrome</li> <li>● Androgen deficiency</li> </ul>	<ul style="list-style-type: none"> <li>● Systemic lupus erythematosus</li> <li>● Thyroid disease</li> <li>● Psychiatric conditions</li> <li>● Acne</li> <li>● Rheumatoid arthritis</li> <li>● Rosacea</li> <li>● Pterygium</li> <li>● Diabetes</li> <li>● Allergic conjunctivitis</li> <li>● Computer use</li> <li>● Contact lens wear</li> <li>● Hematopoietic stem cell transplantation</li> </ul>	<ul style="list-style-type: none"> <li>● Environmental conditions (pollution, low humidity, and sick building syndrome)</li> <li>● Viral infection</li> <li>● Refractive surgery</li> <li>● Smoking</li> <li>● Alcohol</li> <li>● Pregnancy</li> <li>● Low fatty acid intake</li> <li>● Estrogen replacement therapy</li> </ul>
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**Notes:** Data from these studies.<sup>37-39</sup>

bulbar conjunctiva that extends over the corneal surface.<sup>45</sup> These lesions may be associated with decreased visual acuity,<sup>45</sup> increased corneal irregularity,<sup>46</sup> and eye redness.<sup>47</sup> Based on symptoms and abnormal Schirmer test results, there is a high prevalence of DED in patients with primary and recurrent pterygium.<sup>48</sup>

## Iatrogenic Risk Factors

Contact lens (CL) wear is prevalent in MENA, especially among young adults, and much of it is unsupervised, including the use of cosmetic CLs. CL-related dry eye is recognized as a specific entity<sup>49</sup> and could be aggravated by exposure to AC. In a Saudi Arabian study, up to one third of CL wearers reported significant DED symptoms.<sup>50</sup> Although published data are unavailable in some MENA countries—especially Egypt and Lebanon—the volume of corneal refractive and cataract surgeries is constantly increasing. These surgical procedures can result in corneal nerve damage (especially laser in situ keratomileusis) and may cause or exacerbate dry eye symptoms during the initial 6 months following surgery.<sup>49,51,52</sup> Fortunately, this complication is generally transient and can be treated with artificial tear substitutes.<sup>53</sup>

Use of specific medications has been associated with increased risk for developing DED (Table 2).<sup>37,54,55</sup> For example, the long-term use of glaucoma medications can trigger or exacerbate DED, especially in patients using one or more topical formulations containing preservatives, such as benzalkonium chloride (BAK).<sup>49</sup> A Tunisian study of 120 patients with glaucoma on topical therapy found that 90% of patients reported some form of DED.<sup>56</sup> Another Tunisian study of 155 medically-managed patients with glaucoma reported that the main risk factors for DED were advanced age, duration of glaucoma treatment, use of multiple therapies, and the use of antiglaucoma medications containing BAK.<sup>57</sup> Although specific data are lacking for MENA, generally, DED can also be caused by estrogen-containing hormone replacement therapies, antihistamines, and psychotropic drugs, many of which reduce lacrimal secretion.<sup>49</sup> Caffeine may also be associated with increased risk for DED,<sup>58</sup> but the available data are not yet consistent enough to draw a firm conclusion.<sup>7,59</sup>

## Lifestyle

There is widespread use of digital devices in MENA. Prolonged use of video display terminals (VDTs) and computers reduces blink rates and increases the proportion of incomplete blinks, leading to computer vision syndrome, which is highly prevalent but often misdiagnosed in MENA. Computer vision syndrome is a combination of oculomotor/vergence system abnormalities, tear film instability, and ocular inflammation, which can lead to DED.<sup>61,62</sup>

Smoking is another significant risk factor for DED in Saudi Arabia and Egypt, but not in Dubai.<sup>63</sup> Shisha cafés are very popular in some MENA countries, such as Egypt, and smoke from hookah sessions may be damaging to the ocular surface. Previous studies indicate that, in a 20- to 80-minute hookah session, users may smoke the equivalent of 100 or more cigarettes.<sup>64</sup> In addition, the use of charcoal as a heating source in Shisha cafés generates large amounts of carbon monoxide and polycyclic aromatic hydrocarbons, which are irritating to the ocular surface. These data suggest that frequent visits to Shisha cafés could promote DED. However, a study from Dubai did not find an association between exposure to smoking/shisha and DED.<sup>10</sup>

**Table 2** Medications That Increase Risk for DED

<ul style="list-style-type: none"> <li>● Antihistamines</li> <li>● Anti-anxiety medications</li> <li>● Antidepressants</li> <li>● Treatments for benign prostatic hyperplasia</li> <li>● Calcium channel blockers</li> <li>● Cholesterol-lowering medications</li> <li>● Alpha-agonists (epinephrine)</li> <li>● Glaucoma medications</li> <li>● Angiotensin receptor blockers</li> </ul>	<ul style="list-style-type: none"> <li>● Isotretinoin</li> <li>● Anticholinergics</li> <li>● Diuretics</li> <li>● <math>\beta</math>-blockers</li> <li>● Taxanes</li> <li>● Aromatase inhibitors</li> <li>● Checkpoint inhibitors</li> <li>● Epidermal growth factor receptor inhibitors</li> <li>● Aspirin</li> </ul>	<ul style="list-style-type: none"> <li>● Acetaminophen</li> <li>● Benzodiazepines</li> <li>● Multivitamins</li> <li>● Hormones delivered to women as contraceptives or treatments for infertility</li> <li>● Fibroblast growth factor inhibitors</li> <li>● Belantamab mafodotin</li> <li>● Preservatives in ophthalmic preparations</li> </ul>
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**Notes:** Data from these studies.<sup>37,54,55,58,60</sup>

**Abbreviation:** DED, dry eye disease.

## Dietary Habits

Many clinicians recommend and many patients take omega-3 fatty acid dietary supplements to reduce inflammation. However, the efficacy of omega-3 fatty acid supplementation in improving the signs and symptoms of DED remains controversial.<sup>65</sup> For instance, the DREAM study concluded that patients with DED who received omega-3 fatty acid supplementation did not show a significant improvement in symptoms compared to a similar cohort that received olive oil as placebo.<sup>66</sup> It is possible, however, that omega-9 fatty acids, which are present in olive oil, could improve DED signs and symptoms similar to omega-3 fatty acids.<sup>67</sup> A meta-analysis of randomized clinical trials of omega-3 fatty acids concluded that they can be effective for treating DED.<sup>68</sup> However, there are currently no available data on omega-3 intake and DED in MENA.

A separate meta-analysis suggested that vitamin D deficiency was associated with worsening of dry eye symptoms and reduced tear production in patients with DED,<sup>62</sup> vitamin D deficiency is highly prevalent in Lebanon. In a study with 446 participants, up to 71.9% of the study population had vitamin D deficiencies.<sup>69</sup> Hence, vitamin D deficiency may be another MENA-specific factor predisposing patients to DED.

## Inflammation and Infections

Trachoma is fortunately no longer as prevalent as it used to be in MENA. However, in some regions where the prevalence used to be high (notably, remote rural regions of Tunisia<sup>70</sup>), a significant number of patients suffer from the sequelae of trachomatous infections, which can cause severe meibomian gland dysfunction (MGD) and aqueous deficiency.<sup>71</sup>

Vernal keratoconjunctivitis (VKC) is another common inflammatory DED risk factor in MENA. VKC exacerbates the problem of DED via two pathways: the pathophysiology of the disease itself, where the ocular surface is involved in an inflammatory reaction that slowly destroys the accessory lacrimal apparatus and goblet cells, and the chronic use of topical anti-inflammatory and antihistamine agents that contain preservatives that further contribute to ocular surface damage.

## Unmet Needs in DED Epidemiological Research in MENA

There is a significant need for epidemiological, population-based studies of DED in MENA. In particular, studies that are more realistic and based on questionnaires that are standardized across different countries to identify regional specificities in DED prevalence and treatment are needed. There is a need to determine proactive public health measures to decrease the burden of DED in MENA.

## Diagnostic Procedures in DED

### Patient Interview

An expert panel agreed that a detailed patient history is crucial to identify DED and its risk factors in MENA. This includes daily living activities and occupation, focusing on environmental, systemic, and ocular risk factors, assessing DED symptoms and their consequences in daily life and socio-professional productivity. According to the expert panel, three DED symptoms seem more specific to the MENA region, as follows:

- Light sensitivity, the most commonly-reported symptom in two studies from MENA (Jordan and Lebanon)<sup>8,72</sup>
- Difficulty opening eyes upon waking due to overnight air conditioning
- Fluctuating vision or blurred vision caused by tear film instability, which may be exacerbated by environmental conditions

The panel recommends that validated symptom questionnaires, such as the Dry Eye Questionnaire 5 (DEQ-5),<sup>73</sup> Ocular Surface Disease Index (OSDI),<sup>74</sup> and Standard Patient Evaluation of Eye Dryness (SPEED),<sup>75</sup> are helpful in evaluating symptoms and the impact of these symptoms on vision and daily life. These questionnaires are critical for monitoring DED progression and response to treatments and should be used at the beginning of the consultation. Among the validated DED symptom questionnaires, only OSDI is available in Arabic. The OSDI is a useful tool for assessing the severity of DED. Patients are considered positive for DED if their total OSDI score is  $\geq 13$ , with further subdivisions into

mild (score 13–22), moderate (score 23–32), and severe (score 33–101). The panel also suggested that a visual analogue scale of DED symptoms may provide a quick and reliable assessment of disease severity and patient burden.<sup>76</sup>

## Clinical Examination

Clinical evaluation of patients who may have DED should be stepwise, beginning with a careful inspection of the facial and eyelid skin to detect associated skin diseases such as acne rosacea. The blink rate dynamics should also be assessed, as reduced blinking rates or partial blinking are frequently observed in patients with DED. Decreased blink rates can result from a variety of factors, including computer vision syndrome and Parkinson disease.<sup>77,78</sup> These phenomena increase ocular surface exposure and tear film evaporation and reduce meibomian gland drainage.<sup>79</sup>

Slit lamp examination should first include a careful assessment of the eyelid margins to detect anterior and posterior blepharitis and eyelash abnormalities. The ocular surface should be examined before fluorescein instillation to observe lid-parallel conjunctival folds (LIPCOF), which are helpful in diagnosing dry eye.<sup>80</sup> The presence of foamy tears on the eyelid margins, also called saponification of tears, is an indirect indicator of meibomian gland deficiency.

Slit lamp examination should be followed by evaluating: i) tear film stability, which can be considered compromised if tear break-up time (TBUT) is shorter than 10 seconds and may indicate an evaporative component of DED; and ii) tear secretion, using either tear meniscus height (TMH) or the Schirmer I test. A TMH <0.3 mm or Schirmer I test <10 mm/5 min indicate an aqueous deficient component of dry eye.<sup>81</sup>

Tarsal conjunctiva should be examined for papillae, follicles, or fibrotic scars to exclude any differential diagnoses or co-existing conditions, such as allergic conjunctivitis or sequelae from trachomatous or viral conjunctivitis. Pterygium has been described in association with DED in many countries, including MENA. Pterygium is more prevalent in Algeria (18%) than Saudi Arabia (0.074%),<sup>82</sup> and it may exacerbate dry eye symptoms in affected patients.<sup>83</sup> DED may occur in young patients with VKC, though the diagnosis of both conditions is challenging due to overlapping symptoms.

Fluorescein staining is crucial to assess corneal and conjunctival damage. Staining occurs when the integrity of the corneal epithelium is compromised due to a disruption in superficial cell tight junctions or defective glycocalyx. The staining can be visualized with a yellow filter. The use of semi-quantitative staining scales, such as the Oxford score, is helpful as a somewhat objective measure and facilitates follow-up.<sup>81</sup> Lissamine green is a vital dye that stains corneal epithelial cells only if the cell membrane is damaged, irrespective of the presence of mucin.<sup>81</sup> However, lissamine green is not readily available, and the panel agreed that fluorescein is sufficient for daily practice. Meibomian gland expression should be routinely performed at the end of the examination to avoid interference with the previous steps of the clinical assessment.

## Ancillary Investigations

Among the multiple imaging techniques available to quantify and assess the ocular surface, the expert panel agreed that infrared meibography is a valuable noninvasive tool to visualize meibomian gland anatomy, quantify meibomian gland loss, and further guide DED treatment.<sup>81</sup> Other tools, such as tear film interferometry, tear osmolarity, matrix metalloproteinase 9 (MMP-9),<sup>84</sup> aberrometry, and meniscometry can also be helpful<sup>81</sup> but are primarily only available in specialized centers.

In addition to imaging the ocular surface, assessments of the tear film itself are critical in for evaluating patients with suspected DED.<sup>85</sup> These assessments each capture information on tear film characteristics key to DED. TBUT, the time that elapses between a complete blink and the appearance of the first break in the tear film, assesses tear film evaporation rates.<sup>81</sup> During a TBUT assessment, instilling sodium fluorescein stain can help the tear film be more visible. Alternatively, non-invasive breakup time assessments involve observing the specular reflection of an illuminated grid pattern from the tear film.<sup>81</sup> To evaluate tear film production, the Schirmer test uses standardized strips of filter paper placed in the temporal inferior cul-de-sac. After 5 minutes, the length of wetting on the paper is measured, with values <10 mm indicating meaningfully reduced tear production.<sup>81,86</sup> Interferometry permits determination of the tear film's LLT, which appears thinner in patients with DED versus healthy controls.<sup>87</sup> Additionally, tear film hyperosmolarity, a defining characteristic of DED, is often assessed via electrical impedance.<sup>87</sup>

## The Remaining Challenge in DED Diagnosis in MENA

One significant challenge of identifying and treating DED in MENA is the lack of awareness of this disease among non-ophthalmic practitioners and general ophthalmologists. DED is often misdiagnosed as allergic conjunctivitis in MENA, so it should be classified in terms of pathophysiology and severity, using both signs and symptoms.<sup>88</sup> Additionally, many systemic diseases are associated with DED (eg, Sjögren syndrome, rheumatoid arthritis, systemic lupus erythematosus, thyroid conditions; Table 1), which may complicate DED diagnosis and its treatment.<sup>38</sup>

Additionally, MENA has very few ocular surface and corneal specialists, so ocular surface diseases are often managed by general ophthalmologists. For example, there are about 500 ophthalmologists in Lebanon, with only 35 ocular surface and corneal specialists.<sup>71</sup> Another major gap in MENA is the lack of validated questionnaires adapted to the local languages for more standardized data collection and proper scoring and analyses. We recommend a minimal diagnostic assessment tool to improve the diagnosis and management of DED in MENA (Table 3). To facilitate the diagnosis and treatment of DED in MENA, therefore, education on the ocular surface can be improved among general ophthalmologists, and minimal diagnostic procedures should be standardized.

## Therapeutic Tools

DED treatment should aim to address the major cause of DED in each patient (ie, aqueous deficiency or hyper-evaporation). The main factors influencing disease management are the severity of the disease, the underlying etiology, and the response to treatment. However, other factors may influence the selection of treatment, such as access to reimbursement, cost of treatment, patient adherence, socioeconomic status, distance from the treatment center, and age.<sup>89</sup> DED management and treatment recommendations should be done in stages, but therapies must be tailored to individual patient profiles and needs.<sup>90</sup>

## Tear Substitutes

Tear replacement with tear substitutes (TSs; also known as artificial tears) is the mainstay of DED treatment. Many different classes and formulations are available, including drops, gels, ointments, and lubricants, mainly as over-the-counter (OTC)

**Table 3** Minimal Diagnostic Assessment Tool for Patients Seeking Care for Dry Eye Disease

Lifestyle/Risk Factors	Medical History	Symptom Assessments	Clinical Examination
<ul style="list-style-type: none"> <li>Exposure to:               <ul style="list-style-type: none"> <li>- AC</li> <li>- Video display terminals</li> <li>- Pollution</li> </ul> </li> <li>Smoking (active or passive)</li> <li>Certain dietary habits</li> </ul>	Systemic: <ul style="list-style-type: none"> <li>Autoimmune disease (eg, rheumatoid arthritis, Sjögren syndrome)</li> <li>Skin disease (eg, acne rosacea, seborrheic dermatitis)</li> <li>Thyroid disease</li> <li>Atopy</li> <li>Hormone therapy (estrogen-containing hormonal replacement therapy)</li> <li>Antihistamines</li> <li>Psychotropic treatments</li> </ul> Ophthalmological: <ul style="list-style-type: none"> <li>Contact lens wear</li> <li>Corneal refractive surgery</li> <li>Cataract surgery</li> <li>Glaucoma medications</li> <li>Pterygium</li> <li>Allergic conjunctivitis</li> </ul>	Quantitative assessments using visual analogue scales, ideally with validated questionnaires such as: <ul style="list-style-type: none"> <li>OSDI</li> <li>SPEED</li> <li>DEQ-5</li> </ul>	<ul style="list-style-type: none"> <li>Eyelid statics and dynamics (blinking)</li> <li>Eyelid margins and meibomian glands</li> <li>Tear break-up time</li> <li>Ocular surface staining using fluorescein (ideally scored with the Oxford scheme)</li> <li>Schirmer test</li> <li>Tear osmolarity</li> </ul>

**Abbreviations:** AC, air conditioning; DEQ-5, Dry Eye Questionnaire 5; OSDI, Ocular Surface Disease Index; SPEED, Standardized Patient Evaluation of Eye Dryness.

products, and their availability differs significantly among MENA countries.<sup>90</sup> The main types of ingredients used in the composition of TSs are viscosity-enhancing agents (eg, hyaluronic acid [HA]), osmoprotectants, lipids, antioxidants, and vitamins.<sup>91</sup>

TSs have widely different properties in terms of composition, water-binding capacity, ocular surface residency time, viscosity, osmolarity/osmolality, and pH. Each of these properties may affect a drop's overall effect, use, and tolerability, ultimately influencing their ability to protect and restore the damaged ocular surface.<sup>92</sup> To determine the suitability of a TS for treating DED, it is important to assess its physical properties. TSs with moderately high viscosity and a near-physiological pH provide good tear distribution and ocular comfort; however, very high viscosity formulations may be uncomfortable for the patient.<sup>93–95</sup> Polymers, such as hyaluronic acid or carboxymethyl cellulose sodium, are sometimes included in TSs. Polymers tend to have similar effects on DED signs and symptoms despite any molecular differences,<sup>96</sup> but TS formulations containing multiple polymers been shown to improve tear film characteristics.<sup>95</sup>

### Viscosity-Enhancing Agents

Carboxymethylcellulose (CMC) is a common viscosity-enhancing agent used in TSs<sup>91</sup> that is beneficial for patients with mild to moderate DED; it improves corneal surface wettability and tear film integrity.<sup>97</sup> Other viscosity-enhancing agents used in TSs include hydroxypropyl methylcellulose (HPMC), carbomers, HA, polyvinyl alcohol, povidone, dextran, and hydroxypropyl-guar (HP-guar). These agents have mucoadhesive and mucomimetic properties and play a protective role on the ocular surface. Carbomers increase the viscosity and thickness of tears and decrease drag during blinking. They also improve hydration and alleviate irritation due to dry eye. Many TSs include HA, a natural component of the tear film that is also present in the outer cornea and vitreous.<sup>98</sup>

HA has water-binding, lubricating, and antioxidant properties on the ocular surface,<sup>2</sup> and HA-based TSs—at an optimal concentration of 0.2%—have epithelium-healing properties,<sup>99</sup> reduce squamous metaplasia, and improve goblet cell and epithelial cell morphology.<sup>98</sup> In ophthalmic formulations, HA concentrations range between 0.1% and 0.4%, which are considered safe and effective for treating DED. There are some gaps in the literature regarding the optimal concentration, drop frequency, and molecular weight of HA, and potential differences exist in optimizing treatment for different severities and subtypes of DED.<sup>2</sup> HA concentrations of 0.1% and 0.2% resulted in improved TBUT and ocular surface staining compared to placebo drops,<sup>2</sup> and patients subjectively preferred 0.2% HA over 0.1% HA.<sup>2</sup> Generally, TSs with 0.1% and 0.2% HA produce symptom relief, greater patient comfort, and improved objective and subjective measures of dry eye.<sup>2</sup> Some have postulated that improved Schirmer test scores reported in the literature could be due to the resolution of ocular inflammation by HA, leading to improved lacrimal gland function.<sup>2</sup> Studies of higher HA concentrations (>0.2%) reported longer tear film stability and transient visual blur that resolved within 5 minutes of administration.<sup>2,100</sup>

Previous studies have investigated low (60 kDa) to high (3000 kDa) molecular weight HA.<sup>2,100</sup> Higher molecular weight HA has antiangiogenic, anti-inflammatory, and immunosuppressive properties,<sup>2</sup> whereas low molecular weight HA can be pro-inflammatory.

HA is considered a non-Newtonian fluid that changes its viscosity against shear stress, such as blinking, mimicking the normal tear film.<sup>101</sup> This non-Newtonian behavior allows HA to have thicker viscosity when the eye is open, increasing its ocular surface residence time, thereby reducing evaporation. During blinks, however, the viscosity of HA decreases, reducing the amount of the molecule that is washed out from the ocular surface and preventing friction-related ocular tissue damage.<sup>101</sup> Additionally, differences in physiochemical properties of various HA molecules result in variant-specific rheological properties that could be optimized for particular clinical situations. In patients with elevated ocular surface inflammation and epithelial damage, for example, high molecular weight HA—with higher viscosity at low shear stress—may be more appropriate than a lower molecular weight, less viscous HA molecule.<sup>101</sup> Once inflammation and epithelial damage has resolved, patients can be transitioned to a lower-viscosity HA to maintain a stable tear film quality.<sup>101</sup>

HA receptors are present in the cornea and may be involved in the wound-healing properties of this substance.<sup>99</sup> HA stimulates corneal epithelial repair both *in vitro* and *in vivo* in a concentration-dependent manner.<sup>99</sup> A study by Camilleri et al of denuded rabbit corneas found that 0.2% HA stimulated corneal epithelial migration for different ranges of molecular weight of HA.<sup>99</sup>



Lipid-based TSs may substitute for a deficient lipid layer and are indicated in evaporative or mixed DED with both aqueous-deficient and evaporative components. Lipid-based TSs can reduce dry eye symptoms, decrease evaporation, increase tear film stability, and mitigate the effect of ocular surface lesions.<sup>102–104</sup>

### Osmoprotectants

Hyperosmolarity induced by DED causes apoptosis of corneal and conjunctival epithelial cells. Osmoprotectants such as L-carnitine, erythritol, betaine, sorbitol, glycerin, and trehalose have been used in some TS formulations to help prevent apoptosis, with positive experimental and clinical results.<sup>91</sup>

Ectoin is a bacteria-derived extremolyte with the ability to protect proteins and biological membranes from damage caused by extreme environmental conditions such as heat, ultraviolet light, high osmolarity, or desiccation. Ectoin is used as a primary treatment in many DED cases or as an adjuvant with other TSs. Ectoin seems to be effective in alleviating the symptoms of DED as well as VKC, but clinical data are limited.<sup>105</sup>

### Topical Vitamins

Dexpanthenol is a provitamin and an alcohol analog of vitamin B5 (pantothenic acid). In vitro studies indicate that dexpanthenol promotes corneal and conjunctival epithelial healing,<sup>106,107</sup> and a randomized controlled trial (RCT) reported that dexpanthenol improved disturbances in corneal epithelium permeability in patients with DED.<sup>108</sup>

Vitamin B12 (cyanocobalamin) eye drops have proven effective at improving both corneal epithelial healing and nerve regeneration in an animal model of DED.<sup>109</sup> Sodium hyaluronate eye drops containing vitamin B12 are commonly used for improving the corneal epithelium.<sup>110</sup>

Vitamin A increases the expression of conjunctival mucins, promotes corneal and conjunctival wound healing, and reduces corneal keratinization. Several studies confirmed the efficacy of topical vitamin A (either as an ointment or eye drop) for reducing the signs and symptoms of DED.<sup>107</sup>

### Preserved Vs Preservative-Free, and Multidose Vs Unidose DED Treatments

Preservative-free eye drops are preferable in the treatment of DED, but in cases of very mild dryness with only occasional use of lubricants, some preservatives might be clinically acceptable.

Despite the possible harmful effects of preservatives on the ocular surface, it is important to remember that preservative-free preparations carry the potential risk of microbial contamination, and single-dose therapies should be discarded immediately after use. Additionally, cost assessment is important when choosing the best eye drops for each patient, considering that preservative-free eye drops are often more expensive. Ideally, all prescribed dry eye products should be supplied in unit-dose or preservative-free multidose bottles. Preservative-free alternatives should be recommended, especially for patients who require frequent daily instillation, such as patients with severe DED.<sup>90</sup>

Multidose containers are more cost-effective, convenient, and carry a better carbon footprint than single-dose containers. Unidose drops may be more expensive in some countries—though prices are similar across the Gulf region—and can be difficult to handle for some patients. The opened containers may be reused, though there is a risk of ocular complications. Additionally, unidose formulations have a relatively long shelf life, while opened multidose vials should be consumed within a given time, especially if preservative-free. For the best overall patient adherence and outcomes, patient preference must be considered when selecting a treatment program for DED.

### Topical Anti-Inflammatory/Immunomodulatory Agents

Inflammation is a core element of the TFOS DEWS II definition of DED. Ocular surface inflammation in DED is caused by damage induced by hyperosmolarity and desiccation, which are present to some degree in virtually all patients with DED. Anti-inflammatory and immunomodulatory agents are essential in treating DED to break the inflammatory cycle that induces and perpetuates ocular surface damage.<sup>84</sup>

### Steroids

Topical steroids such as loteprednol etabonate (LE), dexamethasone, prednisone, methylprednisolone, fluorometholone, and hydrocortisone are effective in breaking the inflammatory cycle in DED.<sup>111</sup> Topical steroids can be used to rapidly

decrease DED signs and symptoms, and in severe cases requiring ophthalmic cyclosporine, they can also help improve tolerance to cyclosporine.<sup>112,113</sup> Topical steroids may be prescribed for a short-term course to treat disease flares, but long-term use of topical corticosteroids is not recommended due to the risk of steroid-related side effects, such as increased intraocular pressure (IOP), severe steroid-induced glaucoma, and cataract formation. Steroids with more favorable safety profiles, such as LE, may offer better therapeutic options, with the potential for fewer steroid-related side effects.

Dexamethasone, prednisone, and methylprednisolone can pass through the cornea into the anterior chamber. These molecules are very effective in reducing DED signs and symptoms but are associated with high rates of steroid-induced ocular side effects. For this reason, their use should be restricted to controlling severe disease, in patients with a low steroid response or steroid nonresponders; even in these cases, only short-term therapy should be prescribed.

LE is a steroid therapy developed via retrometabolic drug design, modifying an inactive metabolite of prednisolone acetate, with the goals of preserving prednisolone acetate's anti-inflammatory effects while enabling rapid metabolism of inactive metabolites, thereby reducing the potential for steroid-related adverse events (AEs). LE effectively reduces the signs and symptoms of moderate to severe DED.<sup>114,115</sup> In a prospective, double-masked, multicenter RCT, 0.5% LE started 2 weeks before beginning long-term topical 0.05% cyclosporine provided more rapid improvements in Schirmer scores, ocular surface staining, and DED symptoms compared with topical cyclosporine or TSs alone. Additionally, LE induction therapy significantly improved topical cyclosporine tolerance and decreased the risk of having to stop cyclosporine therapy.<sup>112</sup> Additionally, LE therapy seemed to have a lower incidence of AEs such as increased IOP, steroid-induced glaucoma, ocular hypertension, and cataract formation. For these reasons, LE is the only steroid formulation that can be used for extended periods of time.<sup>114–116</sup>

Fluorometholone can reduce ocular surface signs in patients with DED and prevent worsening DED due to desiccating stress.<sup>117</sup>

Hydrocortisone at a low concentration (0.001%) does not reach the aqueous humor<sup>118</sup> and is effective at reducing the signs and symptoms of DED, with a very good safety profile.<sup>119</sup>

### Immunomodulatory Agents

Cyclosporine is an immunosuppressive agent that reduces T cell growth and activity.<sup>111</sup> Several studies, many of which evaluated patients with DED receiving 0.05% or 0.1% cyclosporine for up to 8 weeks, and meta-analyses support the efficacy of cyclosporine drops for DED.<sup>120–123</sup> While cyclosporine does not demonstrate the rapid anti-inflammatory effect of steroids, it is relatively safe and effective for treating both aqueous-deficient and evaporative DED/MGD.<sup>111</sup> Additionally, quality of life studies have concluded that topical cyclosporine can be a cost-effective treatment for DED compared to ocular lubricants. The Asclepius Panel recommended a DED treatment paradigm that starts with a steroid, such as LE, for immediate anti-inflammatory action, symptomatic relief, and disease control,<sup>123</sup> then at 2 weeks, adding cyclosporine while decreasing the steroid frequency, which can help encourage patient adherence.<sup>124</sup> Because cyclosporine and LE act on different steps of the inflammatory cascade, their concomitant use can have a synergistic effect.<sup>124</sup> Additionally, maintaining the steroid therapy throughout cyclosporine treatment can help alleviate cyclosporine-related stinging, a commonly reported AE.<sup>124</sup> Topical cyclosporines, however, are not available in some MENA countries.

Tacrolimus is a macrolide that modulates the immune response by inhibiting T and B cell activation.<sup>125,126</sup> Tacrolimus eye drops are effective for severe inflammatory aqueous-deficient DED cases, such as graft-versus-host disease, Sjögren syndrome,<sup>125</sup> and severe allergic disease.<sup>126</sup> Although multiple studies have reported conflicting data, tacrolimus may be more potent and faster acting than cyclosporine.<sup>127,128</sup> In MENA, tacrolimus is available in some countries as an in-house preparation, where it is mainly used for patients with refractory DED or who are intolerant of cyclosporine eye drops.

Lifitegrast is an integrin antagonist, engineered to act as a competitive antagonist to block binding between lymphocyte function-associated antigen 1 (LFA-1) and intercellular adhesion molecule 1 (ICAM-1), inhibiting T cell migration into target tissues, reducing cytokine release, and reducing further T cell recruitment.<sup>111</sup> Lifitegrast eye drops have been evaluated in 3 multicenter RCTs, including more than 1000 patients with moderate to severe DED. The outcomes indicate an improvement in the signs or symptoms (not both) with 2 weeks of treatment.<sup>129–131</sup> The 5% ophthalmic solution was

approved in July 2016 in the United States (US), approved in the United Arab Emirates (UAE) for about 3 years, and has recently been approved in Saudi Arabia.

Blood-derived eye drops, such as autologous or heterologous serum or platelet-rich plasma eye drops, contain a high concentration of proteins, particularly pro-healing molecules such as epithelial neurotrophins.<sup>111,132</sup> Blood-derived eye drops directly support corneal epithelial cell proliferation and migration, and they indirectly enhance epithelial viability by binding and neutralizing inflammatory cytokines. Blood-derived eye drops have shown efficacy for managing DED, improving signs and symptoms within a few weeks. However, because these treatments are resource-intensive, have limited availability, and can be associated with infectious complications, they are currently reserved for the most severe DED cases.

## Inflammatory Modulation with Systemic and Topical Antibiotics

Systemic tetracycline, tetracycline analogues (eg, doxycycline, minocycline), and macrolides (eg, azithromycin) may decrease bacterial load across a range of tissues, including the ocular surface. By reducing the levels of bacteria that produce lipolytic exo-enzymes and lipases, for example, systemic antibiotics can positively impact the meibum for patients with MGD. Additionally, while systemic antibiotics are typically thought of in terms of their anti-bacterial effects, they also have anti-inflammatory properties, including at the ocular surface.<sup>111</sup>

Systemic tetracyclines, however, may cause gastrointestinal symptoms and photosensitivity, can interact with anticoagulant therapy, and are contraindicated during pregnancy and in children younger than 8 years old. Additionally, systemic macrolides can cause diarrhea, nausea, and vomiting.

To reduce systemic side effects, antibiotics can be used to treat ocular surface conditions via topical administration: topical azithromycin is effective in the management of MGD and evaporative DED.<sup>111</sup> Thus, the panel agreed that topical azithromycin is preferred in cases of isolated DED, and systemic antibiotics should be reserved for cases resistant to topical treatment and/or cases associated with other systemic features, such as acne rosacea, which require systemic treatment. Currently, there is no standardization on the optimal posology and modalities of prescription of these agents.

## Dietary and Lifestyle Factors

Many clinicians recommend, and many patients take, omega-3 fatty acid dietary supplements, which can have some anti-inflammatory activity. However, contradictory evidence has been published (as discussed above) of the effectiveness of omega-3 fatty acid supplementation in improving symptoms or signs of DED.<sup>65,133</sup> Currently, there are no data available on omega-3 intake and DED in MENA.

### Lifestyle Interventions

The panel agreed that eye care providers should advise their patients with DED to minimize time spent on digital devices and video display terminals and to reduce smoking and exposure to smoke, though clinical studies on associations between smoking and/or smoke exposure and DED are not conclusive.

Some case reports have described encouraging results for patients with DED who use moisture chamber goggles and air humidifiers. Currently, there are no RCTs that have investigated the therapeutic value of these devices, but we think that these could be a potential adjunct to prescription treatments, especially in conditions that may promote dry eye symptoms, such as AC.<sup>111</sup>

## Other Procedures

Lacrimal occlusion with punctal or canalicular plugs has been used to treat DED for decades. Punctal plugs typically are associated with a low rate of AEs, and they are effective for retaining the natural tear film and prolonging the effect of tear substitutes in DED. Their use is recommended in patients with aqueous deficient DED.<sup>111,134</sup> A wide variety of punctal plugs are available, with multiple options for plug designs, placement (ie, punctal vs canalicular), and resorbability. The indications for punctal plugs have expanded, now including numerous ocular surface diseases. Their use for managing evaporative DED, however, remains controversial, even though clinical data indicate that punctal plugs are effective in treating evaporative dry eye and improving meibomian gland status and lipid layer stability.<sup>111</sup> One caveat to

the use of punctal plugs in DED is that they should not be used in active inflammatory ocular surface disease as they reduce the ability of the ocular surface to flush out circulating toxins, exacerbating dry eye signs and symptoms.

Additional treatments that may help patients with more difficult-to-treat DED include bandage and scleral contact lenses and autologous serum eye drops.<sup>111</sup> Bandage contact lenses protect the cornea and decrease the abrasive effects of eyelids during blink. Bandage contact lenses can facilitate corneal tissue repair, decrease pain, stabilize the tear film, and restore normal epithelial cell turnover.<sup>135</sup> Scleral contact lenses also protect the ocular surface and maintain ocular surface hydration.<sup>135</sup> Autologous serum eye drops are used in a variety of ocular surface conditions—most importantly, DED, non-healing corneal epithelial defects, and neurotrophic keratopathy—and they are believed to contain multiple factors that stimulate ocular surface healing.<sup>136</sup> However, a meta-analysis of several clinical trials evaluating the effects of autologous tears found that they provide inconsistent benefit; additionally, there is a need for more standardized questionnaires and objective clinical tests to assess the value of autologous tears in the treatment of DED.<sup>137</sup>

### In-Office Treatments for MGD

As a first line of treatment, many eye care providers recommend improving eyelid hygiene, which can be achieved using eyelid-warming masks (eg, EyeBag, EyeBag Company Ltd, Halifax, West Yorkshire, UK; Therapearl Bausch + Lomb Inc, Rochester, NY, USA; and Eyegiene, Eyedetec Medical Inc, Danville, CA, USA), which facilitate meibum expression. Beyond these devices, a variety of in-office treatments are now available to treat MGD.

Thermal pulsation systems (TPSs) combine heat and mechanical compression of the meibomian glands. Commercially available systems include Lipiflow (Johnson and Johnson Inc, New Brunswick, NJ, USA), Ilux (Alcon Inc, Fort Worth, TX, USA), and Tearcare (Sight Sciences, Menlo Park, CA, USA). In patients with MGD, TPSs improve symptoms overall and enhance tear film stability.<sup>138</sup> Additionally, TPSs may provide more sustained improvements than traditional eyelid hygiene,<sup>138</sup> but the long-term efficacy of TPSs needs further evaluation.<sup>139</sup>

Intense pulse light (IPL) therapy delivers pulses of non-coherent light (500 to 1200 nm) to the eyelids to improve meibum expression.<sup>139</sup> A recent systematic review and meta-analysis concluded that, though IPL therapy alone is not superior to eyelid hygiene alone,<sup>140</sup> it may be an effective and relatively safe treatment for MGD when combined with meibomian gland expression. IPL therapy does not always provide consistent results, with its efficacy being influenced by the number and frequency of treatments.<sup>140</sup> Additionally, the efficacy of IPL therapy may decrease within 6 months after the last treatment.<sup>140</sup> Contraindications to the use of IPL therapy are epilepsy, pregnancy, metal implants, photosensitivity or photosensitizing treatments, and active infection. Additionally, IPL therapy may not be tolerated well on darker skin tones, hence limiting use in the MENA region.

Intraductal probing of meibomian glands with a microcannula is performed at the slit lamp and can offer symptomatic relief to patients with obstructive MGD.<sup>141</sup> It involves passing a 2-mm probe directly into the orifice of each meibomian gland, allowing meibum egress. Although intraductal probing is relatively safe, it can cause lid hemorrhage and may require re-treatments.<sup>139</sup>

Overall, currently available in-office procedures for DED can help alleviate dry eye signs and symptoms without a high rate of AEs, but their use in MENA is limited due to by-country availability and cost, resulting in a wide disparity in use across the region.

## Therapeutic Strategies

A therapeutic strategy should follow the staged management and treatment recommendations for DED published in the TFOS DEWS II report,<sup>111</sup> compensating for patient specifics and the local availability of treatments. Table 4 summarizes the main steps adapted from the TFOS DEWS II management report<sup>111</sup> and the report from the management and treatment subcommittee, International Workshop on MGD.<sup>111,142</sup>

## Perioperative DED Management

### Corneal Refractive Surgery

Corneal refractive surgeries may induce or aggravate preexisting DED that is already prevalent among contact lens wearers seeking refractive surgery. DED can be exacerbated through various mechanisms, including corneal nerve

**Table 4** Staged Treatment of Dry Eye Disease, Adapted from the TFOS DEWS II Management report<sup>111</sup> and the Report on the Management and Treatment Subcommittee of the International Workshop on MGD.<sup>142</sup>

Stage 1	
Education	Patients should be given information about the condition, available treatments, and prognosis
Environmental and lifestyle modifications	- Decrease exposure to high temperature, low humidity, AC, smoke, pollution, dust - Reduce video display terminal use, take periodic breaks, perform blinking exercises, and reduce smoking
Address potential iatrogenic factors	Identify and, if possible, eliminate the use of offending topical and systemic medications
Eyelid hygiene	Manual, daily warm compress applications followed by eyelid massage
Tear supplementation	Eye lubricants containing HA and lipid-containing eye lubricants in patients with evaporative dry eye/ MGD
Stage 2: If stage 1 is insufficient, or if required by severity	
Tear supplementation and conservation	- Moderate-viscosity tear substitutes, ideally preservative-free - Consider punctal occlusion (specifically in case of aqueous deficiency), and moisture-chamber goggles
In-office treatments for MGD	Automated heat and pressure application on meibomian glands/ IPL therapy
Anti-inflammatory treatments	- Short-term topical steroids, topical cyclosporine (at least 6 months) - In case of MGD, consider immunomodulatory antibiotics; topical (azithromycin) or systemic (azithromycin, doxycycline)
Lid hygiene	Manual, daily, with warm compress applications followed by eyelid massage
Stage 3: If stage 2 is insufficient, or if required by severity	
Tear stimulation	Oral secretagogues (pilocarpine, cevimeline)
Blood-derived products	Autologous serum eye drops
Therapeutic contact lenses	Bandage lenses Scleral lenses
Stage 4: If stage 3 is insufficient, or if required by severity	
Anti-inflammatory treatments	Long-term topical steroids, cyclosporine, tacrolimus
Surgery	Amniotic membrane graft, tarsorrhaphy, punctal cautery

**Abbreviations:** AC, air conditioning; HA, hyaluronic acid; IPL, intense pulsed light; MGD, meibomian gland dysfunction; TFOS DEWS II, Tear Film and Ocular Surface Society International Dry Eye Workshop 2.

damage, surgical trauma, postoperative inflammation, and toxicity of perioperative eye drops.<sup>143</sup> Preoperative DED may cause topographical errors, which can be detrimental to the final refractive results. Postoperative DED may last up to 12 months and alter the quality of vision and the quality of life and is considered a major cause of dissatisfaction after refractive surgery. Therefore, every candidate for corneal refractive surgery should undergo a thorough preoperative evaluation of the ocular surface, including an assessment of risk factors, symptoms, and comprehensive clinical examination.

As there is often a mismatch between symptoms and signs in dry eyes, using several tests, such as questionnaires, slit-lamp examination, and tear film biomarkers (osmolarity and staining), could be extremely helpful for detecting as many patients with DED as possible.

If a patient with DED is determined to undergo refractive surgery, the dry eye should be treated before proceeding with surgery. Treatment options include TS, nutritional supplementation, topical cyclosporine, topical steroids, and punctal plugs.<sup>143</sup> The duration of preoperative treatment should be based on the status of the DED symptoms. The choice of the procedure should be based on DED status, as LASIK is considered a greater risk for postoperative DED

than surface ablation or small incision lenticule extraction (SMILE).<sup>144</sup> The panel agreed that preoperative optimization of the ocular surface decreases the incidence and severity of postoperative symptoms of the condition.<sup>145</sup>

## Cataract Surgery

Increased life expectancy in the general MENA population has resulted in a greater number of patients presenting for cataract surgery, as well as an increasing prevalence of DED signs and symptoms in the elderly. Low-grade and/or non-symptomatic DED is extremely common in cataract surgery candidates and can be exacerbated postoperatively. In the PHACO study, a prospective, multicenter, observational study of 136 patients who were scheduled to undergo cataract surgery, the majority of patients (62.9%) had a TBUT  $\leq 5$  seconds, 77% of eyes had positive corneal staining, and 50% of eyes had positive central corneal staining. Eighteen percent had a Schirmer score with anesthesia  $\leq 5$  mm.<sup>146</sup>

Additionally, DED can induce errors in IOL power calculation due to inaccurate keratometry measurements.<sup>147,148</sup> It can also falsely induce higher-order aberrations and irregular astigmatism, thus limiting the use of premium IOLs.

DED can impair the postoperative quality of vision and comfort, resulting in an unsatisfied patient and an unsatisfied surgeon. Hence, preoperative evaluation for DED for all cataract candidates is crucial to mitigate these risks.<sup>148</sup>

Preoperative evaluation should be standardized and include both an assessment of the symptoms and a comprehensive clinical examination of the ocular surface.<sup>149</sup> Preoperative treatment is adapted to the clinical findings and treatment should follow the same staged system outlined above.

Cataract surgery may exacerbate DED between 1 week and 3 months postoperatively. Hence, patients should be adequately treated with preservative-free eye drops, TS, and steroids with close postoperative follow-up. Non-steroidal eye drops should be avoided in patients with DED because there is an increased risk of corneal melting and perforation. Intraoperatively, exacerbation of dry eye may be mitigated by a short duration of surgery and reduced exposure to microscope lighting. It has been postulated that coating the cornea with an ophthalmic viscosurgical device instead of frequent balanced salt solution (BSS) instillation can protect the ocular surface and lower the incidence and severity of DED postoperatively.

## Conclusions

DED has specific epidemiologic features in MENA due to climatic, lifestyle, and iatrogenic factors. Management of DED should account for pathophysiology, patient lifestyle, and whether the patient may undergo LASIK or cataract surgery in the near future.

The initial patient history and, perhaps, language-specific and culturally appropriate DED questionnaires can serve as an appropriate first step in screening. The constellation of signs and symptoms in DED overlap across mild, moderate, and severe disease, and the outcomes of a thorough history-taking, along with the responses to questionnaires, may aid in determining appropriate management. The lack of availability of some diagnostic tests and therapeutic options in MENA limits our ability to propose specific criteria for diagnosis and management. Additionally, the education of ophthalmologists and general healthcare providers on ocular surface diseases remains a challenge in many regions in MENA.

As with any scientific article, the present document comes with limitations. As a consensus document, the statements herein are derived from a panel of experts. However, such panels are of limited size, and individual members inherently have personal biases. Achieving consensus on the statements in this article, however, ensures that they are not merely a single person's thought, but are ideas supported by multiple people, all of whom are experts in the area. Thus, while the n-value may be limited, the quality of each panel participant is very high,<sup>150</sup> and consensus documents are viewed throughout the scientific community as an important adjunct to formal treatment guidelines.<sup>151</sup>

The broader implications are that DED in the MENA region is likely much more common than the current literature indicates. Patient and physician education is a critical first step in addressing the public health burden of DED in the region. Furthermore, population-based studies in MENA on the epidemiology, diagnosis, and management of DED are warranted in the future.

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