

A systematic review on prevalence, risk factors, clinical diagnosis and medical management of dry eye disease in the Arab population



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Background: Dry eye (DE) is a multifactorial disorder that can influence tear production, functional visual acuity and ultimately increase the osmolarity of the tear film. The prevalence of DE ranges from 7% to 33% across the world. However, to the best of our knowledge, the prevalence range of DE in Arab countries is not precisely documented in the literature.

Aim: The aim of this article was to determine the prevalence range of DE, investigate the major risk factors of DE and identify the clinical diagnosis and medical management of DE.

Method: In this study, only English language articles from 2017 to 2020 were selected. There were 52 articles on prevalence, risk factors, clinical diagnosis and medical management of DE in the Arab population.

Results: The prevalence of DE in the Arab population varies in reports, from 10% in the United Arab Emirates (Dubai) to 69% in Palestine (West Bank). Gender difference (DE more in women), wearing of contact lenses, diabetes mellitus and glaucoma were all known to intensify the symptoms of DE. Lastly, there are two approaches to reduce DE in the Arab population, namely, pharmacologic and non-pharmacologic methods.

Conclusion: The prevalence of DE in the Arab population was relatively high. In addition, the ocular surface disease index is one of the most common tools for the diagnosis of DE, whilst tear break-up time test is the common clinical test used in the Arab reports. Lastly, the most common treatment for DE is artificial tears.

Keywords: dry eye; artificial tears; contact lenses; glaucoma; Arab population.

Background

Dry eye (DE) is known as a multifactorial disease of the tears and ocular surface that results in symptoms such as discomfort and visual disturbance. In addition, profile tear film (TF) instability with possible damage to the ocular surface, which is characterised by increased osmolarity of the TF and inflammation of the ocular surface, is also observed.^{1,2} More so, researchers have postulated that DE is a specific pathology caused by diverse aetiologies.^{3,4} According to Farrand et al.,⁵ the pathology condition is also termed keratoconjunctivitis sicca (KCS) or dysfunctional tear syndrome (DTS) that results in a significant burden for both patients and ophthalmologists. Previous data have shown that the prevalence of DE ranges from 7% to 33% across the world.^{6,7} Researchers likewise suggested that the rates of DE vary widely from one population to another because of different definitions, race diversity, types of clinical diagnostic test used, lifestyle, specific regions and age range.^{8,9,10,11} Therefore, the exact percentage of DE is not accurately estimated worldwide.¹² Cases with positive DE signs and clinical symptoms often result in impairment militating against achieving a productive lifestyle, social living and even standard level of education.^{13,14}

Gender (more particularly women), advancing age, wearing of contact lenses (CLs), refractive surgery, smoking, visual display terminal (VDT) or extended smartphone use, watching TV and diabetes mellitus (DM) are known to be risk factors of DE that have been identified in extensive previous reports.^{6,7,10,11,15,16} Postmenopausal oestrogen therapy, vitamins A and D deficiency, antihistamines, eye diseases such as pterygium, blinking disorders and different educational and socio-economic status also exaggerate DE symptoms.^{17,18,19,20,21} Consequently, the treatment of this condition remains fairly problematic because of the lack of correlation between clinical symptoms and clinical diagnostic tests.^{16,22}

Previous studies have reported that the prevalence of DE ranges from 8.7% to 32% in the Middle East.^{23,24} However, to the best of our knowledge, the prevalence range of DE in Arab countries is not currently available in the literature. Thus, the present study is the first to perform a systematic review to investigate the prevalence, risk factors, clinical diagnosis, influencing factors and medical management of DE disease specifically in Arab countries within four seasons, namely, less rainfall, cold temperature in winter, hot temperature and high humidity in summer.

Methodology

In this study, all search keywords were carried out with Boolean operators (OR/AND). Main keywords such as prevalence OR incidence OR rate OR frequency OR proportion OR epidemiology OR distribution OR major risk OR influencing factors OR symptoms OR questionnaires OR signs OR clinical tests and DE disease OR syndrome OR disorder were searched on Google Scholar and PubMed databases from June 2017 to June 2020. Furthermore, other search terms included treatment OR management and DTS OR xerophthalmia OR KCS OR keratitis sicca and pharmacologic OR non-pharmacologic approaches and in Arab countries (Saudi Arabia OR Palestine OR Kuwait OR Egypt OR Algeria OR Bahrain) in this investigation (see Figure 1). Admittedly, the information about the prevalence, risk factors, clinical diagnosis and medical management of DE in the Arab population were not available in the Cochrane, KoreaMed and Elsevier databases. This could be one of the limitations of this study. Another possible drawback of this systematic review is that only English language articles published from 2017 to 2020 were selected. The DE started to be referred to as a multifactorial disorder in 2017.² However, meta-analysis reports conducted by Jüni et al.²⁵ and Egger et al.²⁶ postulated a higher quality of the methodology issues in the English

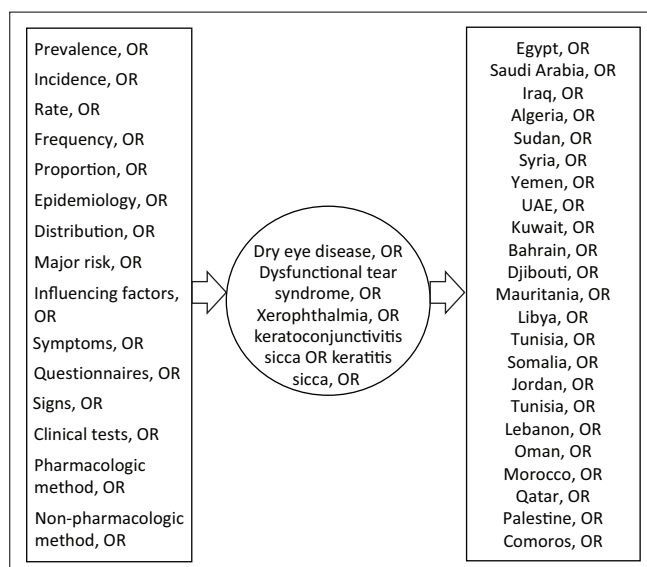


FIGURE 1: Search mode: Main keywords.

language reviews compared with non-English language publications. The same group of authors also found that English language journals had larger sample sizes and highly reliable outcomes than for other language articles. Case series, case reports and control studies including the TF biochemistry, immunological picture of primary Sjogren's syndrome (SS), homeostasis of the TF, ocular surface inflammation and graft disease were excluded. Then, the following data were extracted from the articles or abstracts that met our inclusion criteria: year of publication, name of first investigator and co-workers, study design, country or area of study, range age or mean age, crude prevalence (%), diagnostic criteria, risk factors and medical management. This enhances and helps to generalise the results of the study and improve internal validity. There were 52 articles and/or abstracts for DE disease in the Arab population in the different databases. However, there were very scarce cohort follow-up reports that aim to identify the treatment of DE disease and variation in the time of measurement of tear break-up time (TBUT) test and tear meniscus height. This is also a limitation of the study. All systematic reviews had a potential drawback, which is the tendency for publishing the manuscript's positive results. This is another limitation of the study. The flow chart of this study is presented in Figure 2.

Ethical consideration

This article followed all ethical standards for research without direct contact with human or animal subjects.

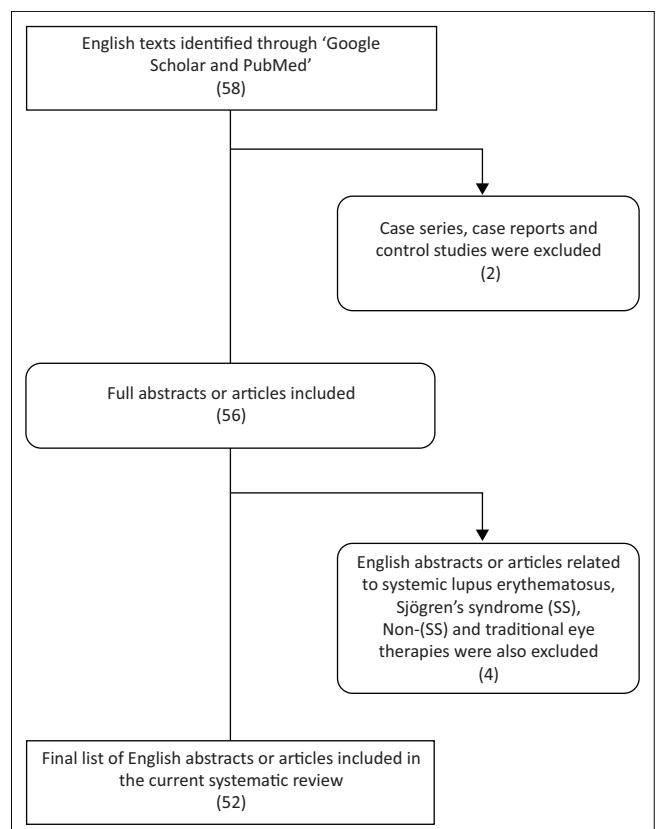


FIGURE 2: Flow chart of the current systematic review.

Results

Prevalence of dry eye

The latest development is a prevalence study of DE in Riyadh district based on a prospective study by utilising the McMonnies' DE questionnaire.¹² A similar study reported that the overall prevalence of DE was 35.9% in cases ≥ 40 years of age (Table 1). Another study, which observed the frequency of DE in the Northern Region of Saudi Arabia, was performed by Alswilem et al.¹⁹ Their sample consisted of 384 teenagers, which was investigated at 3 months for data collection. The rate of DE in the report was assessed by a predesigned questionnaire. Their results showed that approximately 36.5% of the teenager participants had clinical symptoms. A less recent report that also postulated to determine the prevalence of clinical symptoms associated with risk factors in the King Abdulaziz Specialist Hospital (Taif) was adopted by Alzahrani et al.²⁰ In that report, the identified risk factors impacting ocular surface disease index (OSDI) included arthritis, hypercholesterolaemia and Lasik surgery. The frequency of DE symptoms in Al-Ahsa, Saudi Arabia was 32.1%, with a higher percentage in subjects > 56 years of age and more predominant in women compared with men, and with the highest percentage amongst smokers and diabetic patients.²³ Likewise, Alharbi and co-workers revealed a higher frequency of DE in coastal population of eastern province, Saudi Arabia (62.4%) compared with the previous clinical report.²³ The same group used the OSDI to assess DE disease.²⁷

Furthermore, in a cross-sectional study of DE cases in Egypt, the prevalence of DE disease was 6.8%.²⁸ It was carried out in Behira, Egypt, with an average age of 40 years for participants. Another clinic-based study by Rashwan et al. demonstrated that the percentage of DE was 12.8% in the Al-Zahraa University Hospital in Egypt.²⁹ In addition, Iqbal et al. found the prevalence of DE subjectively in those with computer

vision syndrome (CVS).³⁰ The same group of researchers demonstrated that the rate of DE was 28% amongst the medical students in Sohag University, Egypt. More recently, Shanti et al. postulated that 69% of subjects in northern West Bank of Palestine had positive DE symptoms and signs.³¹ Their investigation of DE was performed in 769 subjects recruited through a random sampling method. Similarly, the prevalence of DE disease was reported to be as high as 52% in a study of DE in Jordan involving 802 participants based on DE questionnaires.³⁶

According to Younis et al., 27.2% of patients with rheumatoid arthritis had DE symptoms.³² Ali et al.³³ found that the overall prevalence of DE symptoms was 10% in 120 Dubai households in UAE. One such report was by Zbiba et al. who looked at the DE disease and its relationship with Acanthamoeba keratitis (AK) amongst the patients of Taher Maamouri Hospital in Tunisia. They found four DE syndrome cases out of 14 AK.³⁴

One such report was by Omran et al. who looked at the DE disease and its relationship with pterygium amongst the patients of Benghazi eye hospital in Libya.¹⁷ They evaluated 35 subjects aged 26 years and older and found using Schirmer's tear test (STT) that the prevalence of DE was 40%. In a clinical study of an asymptomatic DE in the Lebanese population, with subjects older than 18 years, the prevalence was found to be 36.4%.³⁵ The symptomatic DE assessment by the OSDI questionnaire was adopted in some studies.

Clinical diagnosis of dry eye

Routinely, dry eye questionnaires (DEQs) are employed for examining the natural history of the disease and in population-based studies.³ Ocular symptoms are the major concern for patients with DE,¹ which signifies the importance of the application of the appropriately validated

TABLE 1: Summary of Arab studies on the prevalence of dry eyes from 2017 to 2020.

Authors	Sample size (n)	Country/area	Age range (years)	Mode of diagnosis of DEs	Crude prevalence (%)	Associated with old age	Associated with female gender
Yasir et al. ¹²	400	Saudi Arabia (Riyadh)	≥ 40	McMonnies symptom questionnaire	35.9	NS	S
Alswilem et al. ²⁰	384	Saudi Arabia (Arar)	≥ 15	Predesigned questionnaire	36.5	NS	NS
Alzahrani et al. ²¹	482	Saudi Arabia (Taif)	6–86	OSDI questionnaire	41.7	S	NS
Alshamrani et al. ²³	1224	Saudi Arabia (Al-Ahsa)	16–78	Six-item questionnaire	32.1	S	S
Alharbi et al. ²⁷	384	Saudi Arabia (Eastern province)	6–40	OSDI questionnaire	62.4	S	NS
Mourad et al. ²⁸	6252	Egypt (Beheira)	1–88	FL/S and TBUT	6.8	N/A	N/A
Rashwan et al. ²⁹	500	Egypt (Cairo)	14–81	TBUT, STT, STT and MGD	22.8	N/A	N/A
Iqbal et al. ³⁰	100	Egypt (Sohag)	18–24	CVS questionnaire	28	N/A	N/A
Shanti et al. ³¹	769	Palestine (West Bank)	18–90	OSDI, FL/S, TBUT and STT	69	S	S
Haddad et al. ³⁶	802	Jordan (Irbid)	18–80	Presence of one or more dry eye symptoms	52	NS	S
Younis et al. ³²	103	Iraq (Bagdad)	23–60	Presence of one or more dry eye symptoms, STT	27.2	NS	NS
Ali et al. ³³	770	UAE	≥ 20	One or more symptoms often or most time	10	N/A	N/A
Zbiba et al. ³⁴	230	Tunisia	≥ 20	FL/S, TBUT	28.5	N/A	N/A
Sherry et al. ³⁵	602	Lebanon	≥ 18	OSDI	36.4	S	NS
Omran et al. ¹⁷	35	Libya (Benghaz)	≥ 26	STT-1 and TBUT	40	N/A	S

OSDI, ocular surface disease index; TBUT, tear break up time test; STT, Schirmer's tear test; FL/S, fluorescein staining; S, statistically significant association; NS, statically insignificant association; DEs, dry eyes; MGD, meibomian gland dysfunction; CVS, computer vision syndrome; N/A, not applicable.

questionnaires in defining the issue.² Several DEQs have been included in Arab studies, such as the OSDI questionnaire, six-item questionnaire and CVS questionnaire.^{21,23,27,30,31,32,33,35,36} However, the OSDI is one of the most common tools for the diagnosis of DE syndrome and other ocular surface diseases, such as allergic conjunctivitis and blepharitis,³⁷ in the Arab population. This questionnaire consists of 12 items that evaluate three subscales of DE consisting of experiencing symptoms of ocular irritation in the eyes, change in functional quality of vision and environmental factor stimuli of DE.¹

Meanwhile, it was also reported that a number of clinical tests could be applied to diagnose DE in the Arab population reports. Examples include the TBUT, STT, meibomian gland dysfunction (MGD), tear meniscus height, lid-to-globe apposition, blink abnormalities, lissamine green staining, rose Bengal staining and the corneal/conjunctival fluorescein staining.^{17,28,29,31,32,34,38} However, the most common clinical test used in the Arab reports is the TBUT. The period from the last blink to the appearance of random dark spots and streaks in tears was recorded as TBUT.

Medical management of dry eye

Dry eye disorder (DED) is reduced in the Arab population by many approaches, such as pharmacologic and non-pharmacologic methods.^{16,19,39} There are several pharmacologic methods, which include tear supplementation, tear retention, tear stimulation and anti-inflammatory agents.⁴⁰ On the other hand, there are many possible non-pharmacologic approaches regarding the management of DE pathology. These include avoidance of exacerbating factors and eyelid hygiene.^{41,42,43}

Many tear supplements can be applied to manage the DE syndrome, but the most common treatment of DE in Arab populations includes artificial tears.⁴⁴ Asbell⁴⁵ found that the use of artificial tears in mild to moderate DE disease was effective. Patients with moderate to severe disease often

combine artificial tears with other forms of treatments.⁴⁶ The autologous serum tear secreted by the patient has also been used in the management of severe DE syndrome.⁴⁷

There are four approaches for tear retention, namely, punctal plugs, moisture spectacles/goggles, therapeutic CLs and tarsorrhaphy.^{48,49} Whilst tear stimulation, for instance, oral cholinergic agents such as pilocarpine or cevimeline (used off-label for aqueous-deficient DED).^{50,51}

Another form of treatment is the use of anti-inflammatory agents. The anti-inflammatory agents can be divided into three main medications, which include topical corticosteroids, oral tetracyclines and topical cyclosporine.^{39,52} On the other hand, other therapies such as nutritional supplements (essential fatty acids), mucolytics (topical acetylcysteine, used off-label in DED with filamentary keratitis) and topical vitamin A (off-label and controversial, but possibly useful in severe DED with squamous metaplasia or ocular surface keratinisation) have also been explored.^{52,53,54}

Discussion

There is high prevalence of DED in the Arab studies compared with other parts of the world. This might be because of the high percentage of rheumatoid arthritis, DM and the use of age-related systemic and topical medications in the elderly population.^{21,23,27,31,35}

Alzahrani et al.²¹ and several other researchers (Sherry et al.³⁵; Shanti et al.³¹) have reported a significant association between TF harm and increase in age (see Table 2). This may be because of the high percentage of rheumatoid arthritis, DM and the use of age-related systemic and topical medications, which may lead to deterioration of TF intact.^{5,12} Furthermore, gender is another factor that has been documented to influence TF profile.^{6,7} Arab data found altered rate of tear production in women as compared to men, particularly after

TABLE 2: Risk factors associated with dry eyes amongst the Arab population from 2017 to 2020.

Risk factors	References
Increase in age	Alzahrani et al. ²¹ ; Alshamrani et al. ²³ ; Alharbi et al. ²⁷ ; Shanti et al. ³¹ ; Sherry et al. ³⁵
Female gender	Yasir et al. ¹² ; Alshamrani et al. ²³ ; Shanti et al. ³¹ ; Haddad et al. ³⁶ ; Shadia et al. ⁵⁸
CLs uses	Alswilem et al. ²⁰ ; Sharief ³⁷
Refractive operations and cataract operation	Alswilem et al. ²⁰ ; Alzahrani et al. ²³ ; Sharief ³⁷ ; Kalakattawi et al. ⁵⁹
Glaucoma, medications, topical glaucoma eye drops and biological drugs	Yasir et al. ¹² ; Younis and Al-Quzweeni ³²
Using antidepressants drug and/or multivitamins supplements	Alharbi et al. ²⁷
Acanthamoeba keratitis, pterygium, blepharitis, spring catarrh, MGD, allergic conjunctivitis and keratoconus	Omran et al. ¹⁷ ; Alswilem et al. ²⁰ ; Zbiba et al. ³⁴ ; Sharief ³⁷ ; Awad et al. ⁶⁰ ; El Sawy et al. ⁶¹
Rheumatoid arthritis, thyroid diseases and high total cholesterol levels	Alzahrani et al. ²¹ ; Alharbi et al. ²⁷ ; Younis ³² ; Abusharaha et al. ⁶² ; ALANAZI ⁶³
Diabetes mellitus	Alshamrani et al. ²³ ; Alzahrani et al. ²¹ ; Alharbi et al. ²⁷ ; Masmali et al. ⁶⁴ ; Kamel et al. ⁶⁵ ; El Sawy et al. ⁶¹ ; Kalakattawi et al. ⁵⁹ ; Elnour et al. ⁶⁶ ; Masmali et al. ⁶⁴
Hypertension, dyslipidaemia and obesity	Safaa Bashir et al. ⁶⁷ ; Alghamdi ⁶⁸
Wider usage of the computer or smartphone or ATM	Baabdullah et al. ¹¹ ; Iqbal et al. ³⁰ ; Ghufuran et al. ⁵⁶ ; Al Tawil et al. ⁵⁷ ; Kalakattawi et al. ⁵⁹ ; Ahmed et al. ⁶⁹
Smoking or passive smoking and high body mass index	Sherry et al. ³⁵ ; Khalil et al. ⁷⁰ ; Alanazi et al. ⁷¹ ; Alanazi ⁷²
Vitamin A deficiency and vitamin D deficiency	Alanazi et al. ¹⁹ ; Sharief ³⁷ ; Elagamy ⁷³
Tropical regions and drive for long distances	Kalakattawi et al. ⁵⁹
Degree of refractive error and occupation	Sharief ³⁷ ; Ahmed et al. ³⁸
Obstructive sleep apnoea and impact on CCT	Kalakattawi et al. ⁵⁹ ; Alharthi et al. ⁷⁴ ; Ali et al. ⁷⁵ ; Elnour et al. ⁶⁶
Indoor/outdoor occupation and urban area	Yasir et al. ¹² ; Alharbi et al. ²⁷ ; Sharief ³⁷ ; Fagehi et al. ⁷⁶

CLs, contact lenses; MGD, meibomian gland dysfunction; CCT, central corneal thickness; ATM, automated teller machine.

menopause,^{31,36} probably because of lower levels of sex hormones, which support sufficient lacrimal gland production, meibomian gland function, goblet cells density and normal tear flow.^{31,55} More so, previous reports from Saudi Arabia (Taif and Arar) discovered that DE symptoms were significantly higher in cases with refractive operation as compared with non-refractive operation.^{21,23} On the same note, according to previous surveys, many ocular diseases such as blepharitis, glaucoma, MGD, keratoconus, spring catarrh, pterygium and allergic conjunctivitis have been identified as the risk factors of DED in the Arab population.^{12,16,17,37} In addition, numerous clinical reports have postulated a high frequency of clinical DE symptoms in patients applying topical glaucoma eye drops and biological drugs.^{12,32} Likewise, other reported risk factors associated with DTS in the Arab population include arthritis, DM, hypertension, vitamins A and D deficiency and thyroid disease.^{21,22,32,37} Khalil et al., Alanazi et al. and Sherry et al. have also postulated that DE symptoms significantly differed between smokers and non-smokers in Egypt, Saudi Arabia and Lebanon, respectively. Many reports have also shown a relationship between prolonged use of the computer or smartphone and intense symptoms.^{11,30,56,57} Risk factors of DE in the Arab countries are shown in Table 2.

Previous studies on the Arab population found a significant relationship between DE symptoms and positive clinical signs.^{17,29,31} This might be attributed to different DE surveys and types of clinical diagnostic tests used. For instance, Shanti et al.³¹ reported a strong association between intense symptoms and clinical diagnostic signs, whilst Yasir et al.¹² reported a lack of association between the self-reported symptoms and positive DE signs.

Conclusion

The prevalence of DE in the Arab population varies in reports, from 10% in UAE to 69% in Palestine. Increase in age, gender difference (more in females), wearing of CLs, refractive operation, glaucoma, blepharitis, MGD, pterygium, spring catarrh and allergic conjunctivitis were all known to be related to DE in the Arab population. In addition, topical glaucoma eye drops, biological drugs, arthritis, thyroid disease, hypertension, DM, smoking or passive smoking, computer or smartphone, watching television and continuous reading were also reported to influence the DED prevalence. Furthermore, OSDI is one of the most common tools for the diagnosis of DE syndrome in the Arab population, whilst the most common clinical test used in the Arab reports is the TBUT. Some previous reports have found a lack of association between DE symptoms and signs. However, other studies have found a strong association between them. For treatment, tear supplements can be applied to manage the DE syndrome, and the most common treatment of DE in Arab populations is the use of artificial tears.

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Competing interests

The authors declare that there are no financial or personal relationships that may have inappropriately influenced them in writing this article.

Authors' contributions

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Data availability statement

Data sharing is not applicable to this article.

Disclaimer

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