What We Know About the Epidemiology of Dry Eye Disease in Japan

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Submitted: December 6, 2017
Accepted: February 13, 2018

Citation: Uchino M. What we know about the epidemiology of dry eye disease in Japan. Invest Ophthalmol Vis Sci. 2018;59:DES1–DES6. https://doi.org/10.1167/iovs.17-23491

The aim of this paper is to propose a systematic review on the prevalence of dry eye disease (DED) and its economic burden in Japan and other countries. A systematic review was performed of data gathered from a PubMed search between 2002 and 2017, using the following key words: “dry eye,” “prevalence,” “epidemiology,” and “risk factors.” There have been several cross-sectional studies evaluating the epidemiological aspect of DED in Japan; two population-based studies, two cross-sectional studies on visual display terminal (VDT) users, and one study focusing on high school students. One study calculated the direct cost of DED, and two calculated the indirect cost using a work productivity assessment to evaluate the economic burden. The prevalence of DED in the Japanese population was relatively high in all studies compared to reports from other countries. In Japan, the annual health plan cost per patient was estimated to be $323 (US). Work productivity loss per patient associated with definite DED was estimated to be between $741 and $6160. To conclude, it was found that DED is prevalent across generations in the Japanese population, and costs related to the disease lead to considerable economic burden.

Keywords: dry eye disease, prevalence, risk factor, economic burden, epidemiology

MATERIALS AND METHODS

For the purpose of this report, a search of published, peer-reviewed literature was conducted using PubMed in November 2017 for articles that reported the prevalence of DED. The following key words were used to search articles published between 2002 and 2017: “dry eye,” “prevalence,” “epidemiology,” and “risk factors.” Observational studies with a minimum of 100 subjects were included. Studies were excluded if no variance in the measure of prevalence was available in the manuscript. Studies focusing on a particular type of DED, such as ocular graft-versus-host disease or Stevens-Johnson syndrome, were also excluded.

RECENT PROGRESS AROUND THE WORLD

In the Dry Eye Workshop (DEWS) II, the epidemiology committee summarized the available data regarding the prevalence, incidence, and risk factors of DED. In the report, they used PubMed data from the last 10 years and performed a meta-analysis to determine the prevalence of DED. The Women’s Health Study Questionnaire (WHSQ) revealed that the prevalence varies from 4.3% in American men to 21.6% in Asian women. The DEWS committee also showed that in Southeast Asia the prevalence is as high as 20.0% to 52.4%. Studies from Spain and the United States using similar definitions showed a prevalence of 18.4% and 14.5%, respectively.

The majority of studies revealed that the prevalence of DED in women is 1.35 to 1.74 times higher than that in men. Most studies showed individuals over 40 years of age were at a higher risk than those younger than 40. Although there is heterogeneity among the studies, it is clear that symptomatic DED is more common among women, older individuals, and the Asian population.

Incidence of disease describes the rate of new or incident cases of a disease over a period of time. To the author’s knowledge there are only two papers on the incidence of DED in the world. The Beaver Dam Eye Study reported that incidence in the Caucasian population is 13.3% over a 5-year period, and the Twins UK Study showed the incidence to be 4.4% in a 2-year period. To the author’s knowledge, there are no published studies available to compare the incidence of DED within the Asian population.

RECENT PROGRESS IN JAPAN: PREVALENCE AND RISK FACTORS OF DED IN JAPAN

Population-Based Studies

There have been two population-based studies evaluating the prevalence of DED in Japan (Table 1). In 2006, Uchino et al. examined 113 pensioners (50 men, 63 women; mean age, 67.5 ± 5.7 years) living in Chiba city, located next to Tokyo. The diagnostic criteria included positive ocular surface staining with fluorescein or rose bengal and Schirmer values less than or equal to 5 mm or tear film breakup time (TBUT) equal to or less than 5 seconds. Using this criteria, the positive DED was 73.5%; the 95% confidence interval (CI) was (65.3%–81.6%); TBUT less than 5 seconds was 79.6% (95% CI = 72.2%–87.1%); Schirmer less than 5 mm was 39.8% (95% CI = 30.8%–48.9%); fluorescein staining was 77.0% (95% CI = 69.2%–84.8%). This study did not include a validated questionnaire, which makes it difficult to compare it with studies from other countries.

The second study was conducted in Koumi town, located in a rural mountain area 100 km north of Tokyo. The study...
TABLE 1. Summary of Prevalence Study Among Japanese Population

<table>
<thead>
<tr>
<th>Authors</th>
<th>Number</th>
<th>Age (Mean ± SD)</th>
<th>Prevalence (%)</th>
<th>Diagnostic Tool</th>
</tr>
</thead>
<tbody>
<tr>
<td>Population-based study, Uchino et al.12</td>
<td>113</td>
<td>≥60 (67.5 ± 5.7)</td>
<td>46.9%</td>
<td>Positive dry eye: Schirmer test &lt; 5 mm or TBUT &gt; 5 seconds; questionnaires/WHSQ</td>
</tr>
<tr>
<td>Uchino et al.3</td>
<td>3294</td>
<td>≥60</td>
<td>26.9%</td>
<td>Ocular surface staining with fluorescein or rose bengal and TBUT &lt; 5 s</td>
</tr>
<tr>
<td>Uchino et al.13</td>
<td>672</td>
<td>15–18</td>
<td>11.5%</td>
<td>Boys 21.0 (20.1–21.8); Girls 24.4 (23.9–25.0); questionnaire/WHSQ</td>
</tr>
<tr>
<td>Uchino et al.14</td>
<td>672</td>
<td>22–65 (43.3 ± 9.1)</td>
<td>26.9%</td>
<td>Boys 21.0 (20.1–21.8); Girls 24.4 (23.9–25.0); questionnaire/WHSQ</td>
</tr>
<tr>
<td>High school students, Uchino et al.16</td>
<td>3435</td>
<td>15–18</td>
<td>11.5%</td>
<td>Boys 21.0 (20.1–21.8); Girls 24.4 (23.9–25.0); questionnaire/WHSQ</td>
</tr>
</tbody>
</table>

M, male; F, female; TBUT, tear film break-up time.

VDT Users

There have been two studies evaluating the prevalence of DED among VDT users.13,14 Unfortunately, the two studies use different criteria for the diagnosis of DED, preventing an accurate comparison. In 2008, the WHSQ revealed that female VDT workers were 1.8 times more likely to complain of severe dry eye symptoms than were male VDT workers. There was no significant association between age and prevalence of severe DED symptoms. A significant trend was noted between the duration of VDT work and the expression of severe symptoms (P < 0.001). On the other hand, the type of VDT work, the position of a personal computer (PC) relative to the user’s eyes, and use of a PC glare filter or air conditioner did not influence the severity of DED symptoms. Although not statistically significant, the prevalence of severe DED symptoms was higher in smokers than in nonsmokers. However, severe symptoms were not related to heavy smoker status (OR, 0.98; 95% CI, 0.73–1.33). CL wearers were significantly (P > 0.001) more likely to report severe symptoms of DED (OR, 3.61; 95% CI = 2.13–6.10), and myocardial infarction or angina (OR, 2.04; 95% CI = 1.51–4.62).

The second study involved 672 VDT workers employed by a pharmaceutical company.14 A revised version of the Japanese diagnostic criteria was implemented. The diagnostic criteria required (1) presence of dry eye symptoms; (2) presence of a qualitative or quantitative disturbance of the tear film in one or both eyes (Schirmer test ≤ 5 mm or TBUT ≤ 5 seconds); and (3) presence of conjunctivocorneal epithelial damage (total staining score ≥ 3 points) in one or both eyes. The presence of all three criteria was necessary for a definite diagnosis of DED. Subjects showing the presence of two of the three criteria were diagnosed with probable DED, while those with one or no positive criteria were diagnosed as non-DED.15 Using these criteria, the study reported that the prevalence of definite DED was 8.0% (95% CI = 5.5%–11.3%) in men and 18.7% (95% CI = 13.4%–25.1%) in women. Probable DED was prevalent among the population, as almost half of the subjects (52.1% of men, 95% CI = 46.9%–57.3% and 57.8% of women, 95% CI = 50.3%–64.9%) had two of the three criteria. Female gender, age, and population included 3294 subjects over 40 years of age who were in the residential registry of Koumi town. This study implemented the WHSQ to analyze the prevalence world-wide. The WHSQ consists of three questions developed and validated by Schaumberg et al.: (1) How often do your eyes feel dry? (2) How often do your eyes feel irritated? (3) Have you ever been diagnosed by a clinician as having dry eye syndrome? Possible answers to the first two questions were “constantly,” “often,” “sometimes,” or “never,” and those to the last question were “yes” or “no.” The completed questionnaires were used to identify individuals with severe symptoms of DED (both ocular dryness and irritation, either constantly or often) and/or clinically diagnosed DED as reported by the participants. The study revealed that severe symptoms of DED were experienced by 11.5% (95% CI = 9.7%–13.4%) of men and 7.9% (95% CI = 6.6%–9.5%) of women. The percentage of women with a composite outcome of clinically diagnosed DED and severe symptoms (21.6%; 95% CI = 19.5–23.9) was higher than that of men (12.5%; 95% CI = 10.7–14.5; P < 0.001). The risks for DED were also evaluated. For men, risk factors included a low body mass index (odds ratio [OR, 2.07; 95% CI = 0.98–4.39], contact lens (CL) use (OR, 3.84; 95% CI = 1.46–10.10), and hypertension (OR, 1.39; 95% CI = 0.94–2.06). For women, risk factors included use of a VDT (OR, 2.33; 95% CI = 1.12–4.85), CL use (OR, 3.61; 95% CI = 2.13–6.10), and myocardial infarction or angina (OR, 2.04; 95% CI = 1.51–4.62).
VDT usage of over 8 hours were identified as risk factors for definite and probable DED.

High School Students

Using the WHSQ, one study conducted a survey to determine the prevalence of DED among high school students. The study involved 3433 students from five private high schools, including 2848 boys and 585 girls. The prevalence of severe DED symptoms was 24.4% (95% CI = 23.9–25.0) among female high school students and 21.0% (95% CI = 20.1–21.8) among male high school students. One significant finding was that girls are 1.2 times more likely to complain of severe dry eye symptoms than boys (P < 0.001). In total, 4.5% (95% CI = 3.9–4.6) of boys and 8.0% (95% CI = 7.4–8.4%) of girls were diagnosed with DED. CL use was associated with a significantly higher prevalence of severe dry eye symptoms in boys (OR, 4.14; 95% CI = 3.42–5.00; P < 0.001) and girls (OR, 4.68; 95% CI = 3.02–7.26; P < 0.001). Almost twice as many girls as boys had a history of clinically diagnosed DED (Table 1). Subjects of both sexes who use soft CLs were associated with a significantly higher prevalence of clinically diagnosed DED (boys: OR, 4.21; 95% CI = 2.85–6.22; P < 0.001) (girls: OR, 4.88; 95% CI = 2.31–10.55; P < 0.001). In addition, the study revealed that hard CL use was also associated with a significantly higher prevalence in boys (OR, 4.63; 95% CI = 1.36–15.81; P < 0.001) and girls (OR, 2.51; 95% CI = 0.51–12.24; P < 0.001). The WHSQ has also been used to evaluate the prevalence of DED among high school students in the Chinese population. The prevalence of severe DED symptoms was 23.1% (95% CI = 21.3–25.1), and the prevalence of diagnosed DED was 5.0% (95% CI = 2.8–3.2). Interestingly, the prevalence was similar to that of the population over 40 years of age in the Koumi Study. This study showed that DED is not only associated with the aged but is also prevalent among the young population.

Comparing the Prevalence of DED in Japan to Other Parts of the World

Prevalence of DED Based on the WHS Criteria

Table 2 shows a summary of the prevalence of DED according to the WHSQ, as well as signs and symptoms. Seven studies have reported rates of the disease based on severe symptoms of dryness and irritation and/or a physician’s diagnosis of dry eye as reported by the participant. Most of the studies are from Asia, including Japan, and two are from the United States. Based on the WHSQ, the overall prevalence of DED ranged between 14.4% and 24.4%. Studies using the Korean National Health and Nutrition Examination Survey (KNHANES) reported the highest prevalence of diagnosed DED in both men and women. The prevalence among KNHANES participants was 16.0% for men and 20.6% for women over 40 years of age. In the WHS conducted in the United States, Schumberg et al. showed the prevalence to be 6.7% in women. The WHS clearly showed in one study that the Asian/Pacific Islander and Hispanic ethnicity can be risk factors for development of DED. They stated the reason was unclear, however, suggesting several factors such as a higher prevalence of other health problems causing side effects or a lack of knowledge regarding the availability of treatments.

In conclusion, our comparison using the same diagnostic criteria shows Asian ethnicity to be a risk factor for DED. Japanese are also included in this population. Further studies are needed to investigate the possibility of environmental differences affecting the prevalence of DED.

Prevalence of DED Based on Symptoms and Signs

Besides the studies in Japan, five population-based studies have analyzed a combination of symptoms and signs, with an overall prevalence ranging from 8.7% to 30.1%. It is difficult to compare the studies because most of them use different criteria. The reports from China and England used similar diagnostic criteria based on symptoms reported often or constantly, and either one or two clinical signs, including a TBUT equal to or less than 10 seconds, a Schirmer test score equal to or less than 5 mm, a fluorescein staining score equal to or greater than 1 point, and a rose bengal staining score equal to or greater than 3 points. The inclusion criteria ensured the studies evaluated a wide age range of randomly sampled participants. The prevalence reported in the study from China was three times higher than that of the study from Spain (China: 30.1%, 95% CI = 27.4–32.8, compared with Spain: 11.8%, 95% CI = 6.9–13.3). The prevalence of definite DED diagnosis was also higher among the Chinese compared with that of the Japanese population.

Economic Burden of DED

An increased number of studies have estimated the burden of cost related to DED. The economic burden caused by DED can be divided into two categories: direct costs such as medical fees and the purchase of medications and indirect costs such as reduced employment rates, absence from work (absenteeism), and lost work days resulting from adversely affected performance (presenteeism). In 2012, Mizuno et al. estimated the total annual direct cost of DED treatment using 118 dry eye patients aged 20 years or older who visited any of the 15 participating medical care facilities (Table 3). The annual direct cost was estimated using outpatient medical records and survey questionnaires obtained from the patients. The annual cost of prescription drugs per patient was evaluated to be $323 ± $219 per year. The clinical cost was evaluated to be $165 ± $101 per year. The study also evaluated other direct costs, including the cost of punctual plug treatment, which was evaluated to be $530 ± $384 per year. Indirect costs were estimated using workplace productivity losses, which were evaluated using the Japanese version of the Work Limitations Questionnaire (Sompo Japan Healthcare Services, Inc., Tokyo, Japan). The questionnaire, consisting of 25 items, is a validated self-report survey for assessing the impact of health problems on at-work performance and productivity.

Yamada et al. measured work productivity loss using an online survey of 396 individuals over 20 years of age (258 men and 138 women, mean age 43.4 ± 13.0 years). They divided DED patients into four groups according to their diagnostic status and subjective symptoms of dry eye: a definite dry eye group; a marginal dry eye group; a self-reported dry eye group; and a control group. The degrees of work performance loss were 5.6% in the definite dry eye group, 4.37% in the marginal dry eye group, 6.06% in the self-reported dry eye group, and 4.27% in the control group. The survey revealed a significant loss-of-work productivity in the self-reported dry eye group compared with the control group (P < 0.05). The annual cost of work productivity loss associated with dry eye was estimated to be $741 per person. Uchino et al. also estimated the economic burden of DED among 553 VDT workers (366 men and 187 women). Using the Japanese clinical evaluation diagnostic criteria, Uchino concluded that individuals in a non-DED group demonstrated a loss-of-work productivity of 3.56%; those with probable DED demonstrated a loss of 4.06%; and those with definite DED demonstrated a loss of 4.82%. The results showed significantly worse performance and productivity among those with definite DED (P = 0.014, trend test).
<table>
<thead>
<tr>
<th>Diagnostic Tool</th>
<th>Authors</th>
<th>Population</th>
<th>Prevalence, Symptoms</th>
<th>Authors</th>
<th>Country</th>
<th>Population</th>
<th>Prevalence, Symptoms</th>
<th>Prevalence, Physician Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>WHSQ</td>
<td>Uchino et al., 2008</td>
<td>VDT workers</td>
<td>Men 26.9 [25.9-28.7]; Women 48.0 [44.3-49.5]</td>
<td>Men 10.1 [8.4-10.2]; Women 21.5 [18.7-22.9]</td>
<td>Schaumberg et al., 2003</td>
<td>USA</td>
<td>Longitudinal Physicians Health Studies I (n = 18,596) and II (n = 6848)</td>
<td>6.8 [6.5-7.1]</td>
</tr>
<tr>
<td></td>
<td>Uchino et al., 2008</td>
<td>Japanese high school students</td>
<td>Boys 21 [20.1-21.8]; Girls 24.4 [23.9-25.0]</td>
<td>Boys 4.5 [3.9-4.6]; Girls 8.0 [7.4-8.4]</td>
<td>Zhang et al., 2012</td>
<td>China</td>
<td>High school students</td>
<td>23.1 [21.3-25.1]</td>
</tr>
<tr>
<td></td>
<td>Uchino et al., 2012</td>
<td>Pensioners of Chiba city</td>
<td>Positive dry eye 73.5 [65.3-81.6]; TBUT &lt; 5 s 79.6 [72.2-87.1]; Schirmer &lt; 5 mm 39.8 [30.8-48.9]; Fluorescein staining over 1 point 77.0 [69.2-84.8]</td>
<td>Tian et al., 2009</td>
<td>China</td>
<td>Population-based Jiangning District, Shanghai</td>
<td>50.1 [27.4-32.8]; men 24.1 [20.3-28.4]; women 33.8 [30.3-37.5]</td>
<td></td>
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<tr>
<td></td>
<td>Uchino et al., 2012</td>
<td>VDT workers</td>
<td>Men definite 8.0/probable 52.1 Women Definite 18.7/probable 57.8</td>
<td>Hashemi et al., 2014</td>
<td>Iran</td>
<td>Population-based Shroud</td>
<td>11.0 [8.6-13.3]; men 9.0 [5.3-12.6]; women 11.9 [8.8-15.1]</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Uchino et al., 2013</td>
<td>VDT workers</td>
<td>Men definite 8.0/probable 52.1 Women Definite 18.7/probable 57.8</td>
<td>Vehof et al., 2014</td>
<td>England</td>
<td>Adult twins registry at St. Thomas’ Hospital</td>
<td>8.7 [6.9-10.6]</td>
<td></td>
</tr>
</tbody>
</table>

**Signs and symptoms**
- Positive dry eye
- TBUT < 5 s
- Schirmer < 5 mm
- Fluorescein staining over 1 point
- Population-based Jiangning District, Shanghai
- Population-based Shroud
- Adult twins registry at St. Thomas’ Hospital
The estimated cost of annual work productivity losses per person was $6160 in the definite DED group and $2444 in the probable DED group when measured by total production. Based on the average annual wage at the participating company, the estimated cost of annual work productivity loss was $1178 per employee with definite DED and $467 per employee with probable DED. These studies indicate that DED has a significant impact on work productivity in Japan.

**FUTURE DIRECTIONS**

This report has summarized the results of published population-based studies on the prevalence of DED and its economic burden in the Japanese population. Since the definition of the disease varies between studies, an exact comparison between studies was difficult to establish. We need a standard, worldwide definition to be utilized in epidemiologic studies. The Asia Dry Eye Society revised the definition for DED in 2012. This revision simplified the diagnostic criteria as well as emphasized the importance of tear film stability and symptoms. Implementing these simple diagnostic criteria might be effective in documenting a worldwide comparison.

In addition, the measurements of dry eye signs are often difficult to repeat. The improvement of technique is needed to standardize and obtain accurate measurements of DED signs. In Japan, there is limited data available regarding the prevalence of DED and its risk among individuals younger than 40. Further studies are needed to evaluate the prevalence among younger generations. Furthermore, the incidence and the natural history of DED in Japan remain unknown. Both areas require more investigation and larger longitudinal studies. In addition, the economic burden of DED, especially the burden related to absenteeism, remains unknown. Since the prevalence of DED within the Japanese population is high and the use of VDTs has increased dramatically, we need to pay closer attention to the burden of DED. Japan has a health care system with unified prices in all prefectures. Cost analyses, which enable us to give recommendations regarding resource allocation, should be calculated using unified prices in the near future. This analysis might enable us to save costs through improved quality of life, improved productivity and reduction in health care utilization costs through effective disease treatment.

In conclusion, we found the prevalence of DED is relatively high in Japan and worldwide. Improved awareness among the public, as well as among practitioners, is essential for better eye health and to improve the general health of the population.

**Acknowledgments**

Funding of the publication fee and administration was provided by the Dry Eye Society, Tokyo, Japan. The Dry Eye Society had no role in the contents or writing of the manuscript.

Disclosure: M. Uchino, None

**References**


