ORIGINAL RESEARCH



Prospective, Multicenter, Cross-Sectional Survey on Dry Eye Disease in Japan

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ABSTRACT

Introduction: Dry eye disease (DED) is commonly encountered in eye clinics and hospitals, and it is therefore very important to understand DED prevalence in outpatients.

Methods: A multicenter, hospital-based crosssectional study was conducted among outpatients in Japan to ascertain DED prevalence and relationships between DED and patient profiles, including eye disease, DED diagnosis history, and surgical history. DED was diagnosed according to diagnostic criteria of the Asia Dry Eye Society. Patient self-assessment of DED-

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K. Kakinoki Kakinoki Eye Clinic, Tokyo, Japan related subjective symptoms was conducted using the 5-Item Dry Eye Questionnaire (DEQ-5). Tear break-up time was evaluated in subjective symptom-positive patients.

Results: The prevalence of DED was 55.7% in 990 patients (mean age 69.1 ± 13.4 years), DED was commonly experienced in combination with other ocular diseases. In revisiting patients, 15.2% had not previously been diagnosed as DED, and their total DEQ-5 scores were higher than those of patients who had undergone DED treatment.

Conclusion: This study revealed that more than half of the outpatients had DED. Among revisiting patients, there were many "hidden" DED patients who had not been diagnosed with DED in the past. There is a high likelihood of finding DED comorbidity in patients with other eye diseases in eye clinics and hospitals.

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Keywords: Comorbidity; Cutoff value; Dry eye disease; Hidden dry eye disease patient; Newly diagnosed patient; Prevalence of dry eye disease; Symptom

Key Summary Points

Why carry out this study?

Dry eye disease (DED) is commonly encountered in eye clinics and hospitals and it is therefore very important to understand the DED prevalence in outpatients.

We investigated the DED prevalence in outpatients of eye clinics and an eye hospital in Japan.

In addition, the relationships between DED and background information of the patients, including other eye diseases, DED diagnosis history and surgical history were examined.

What was learned from the study?

More than half of the outpatients had DED.

The patients with allergic conjunctivitis and patients after vitreoretinal surgery had the highest prevalence of DED.

Among revisiting patients, there were many hidden DED patients who had not been diagnosed with DED in the past.

INTRODUCTION

Dry eye disease (DED) is defined by the Asia Dry Eye Society as follows: DED is a multifactorial disease characterized by unstable tear film, causing subjective symptoms such as dryness and eye discomfort and/or accompanied by ocular surface damage [1]. Unstable tear film impairs visual function [2, 3], affecting the quality of vision and/or life in DED patients [4]. Also, work productivity was reduced in the DED group in comparison with the non-DED group [5]. As DED influences the daily life of the patients and is associated with work productivity loss, patients should be accurately diagnosed and treated.

Many epidemiological reports with respect to DED have been published worldwide, showing the prevalence of DED ranging from 6.8 to 61.57% [6–14]. This broad range in prevalence may be attributed to differences in race, age, and gender proportions in the study population, and the diagnostic criteria also impact the results. Regarding the racial differences, Hispanic and Asian women have more severe DED symptoms than Caucasians [14].

DED is associated with other eye diseases and treatments, for example, glaucoma. In patients with normal tension glaucoma (NTG) who prostaglandin topically received analog monotherapy for 1 year or longer, the ocular surface disease index and fluorescein keratoconjunctival staining score were significantly higher than those in normal subjects [15]. In cataract patients with no complications before cataract surgery, the incidence of DED 7 days after phacoemulsification was 9.8% [16]. It is known that short tear break-up time (TBUT)type DED is a major subtype, as is the aqueousdeficient type in Japan [17, 18], and this subtype is associated with allergic conjunctivitis [19]. Some subjective symptoms in allergic conjunctivitis overlap with those in DED. This may lead to misdiagnosis of DED, and for DED cases to be overlooked. Taken together, it is important to pay attention to the symptoms and medical history of eye diseases and treatments in the diagnosis of eve disease. Some dry eve prevalence surveys have been conducted in eye clinic outpatients [8, 13, 20-22]; however, there has been no study to examine the DED prevalence in patients with other eye diseases and history of eye surgery. Also, there has been no study to examine the "hidden" DED patient who had not been diagnosed with DED.

The purpose of this study was to ascertain DED prevalence in outpatients of eye clinics

and an eye hospital in Japan. In addition, the relationships between DED and background information of the patients, including other eye diseases, DED diagnosis history, surgical history, and other characteristics was examined.

METHODS

Study Design

This study was a multicenter, hospital-based cross-sectional study carried out at 6 eye clinics [Fujita Eve Clinic (Tokushima, Japan), Sakka Eve Clinic (Fukuoka, Japan), Kasai Eye Clinic (Tokyo, Japan), Kakinoki Eye Clinic (Tokyo, Japan), Abe Eye Clinic (Oita, Japan), Sapporo Kato Eye Clinic (Hokkaido, Japan)] and one eye hospital [(Heisei Eye Hospital (Miyagi, Japan)]. All patients were given a full explanation about this study and provided written informed consent. This study followed the tenets of the Declaration of Helsinki. The Ethics Committee of Medical Corporation TOUKEIKAI Kitamachi Clinic (Tokyo, Japan), approved the protocol prospectively (ethical approval No. STS06238, date: 18 December 2018). The study was registered with UMIN-CTR (http://www.umin.ac.jp/, Identification no. UMIN000035506).

Patients

This study was conducted among outpatients who visited the study sites. The outpatients were over 20 years of age and were consecutively enrolled. The recruitment of subjects was conducted from January to April 2019. Outpatients who could not perform fluorescein staining for safety reasons, such as hypersensitivity, were excluded from the study. Also, patients wearing contact lenses on a visiting day of the study were excluded. The sample size of this study was calculated to include a sufficient number of patients (50 patients) with allergic conjunctivitis which had been reported to be associated with DED. Assuming the prevalence of allergic conjunctivitis of 5% and a combination with dry eye of 20%, the sample size was determined to be 1000 patients.

Patient Background

The patients' background information was collected from their medical records. Data collected were on sex, age, first visit/return visit, DED treatment, daily contact lens wearing, eye diseases on the study day, DED diagnosis history in the past 2 years, and eye surgery history in the past 1 year. All their information on multiple eye diseases and surgery history were also collected.

Questionnaire for DED-Related Subjective Symptoms

DED-related symptoms were evaluated using the 5-Item Dry Eye Questionnaire (DEQ-5, including eye discomfort, dryness, and watery eyes), which was translated into Japanese [23]. In addition, the presence or absence of the following 12 symptoms associated with DED was also confirmed at the same time as evaluation using DEQ-5: eye fatigue, eye pain, eye discharge, foreign body sensation, watery eyes, blurred vision, itchy eye, heaviness, red eye, eye discomfort, dryness, and photophobia [24]. The criterion for dry eye screening was DEQ-5 total score ≥ 6 as symptom-positive.

Ocular Surface Examination

In subjects with DED-related symptoms, the ocular surface was examined using a fluorescein examination test paper (Ayumi Pharmaceutical, Tokyo, Japan). A fluorescein strip moistened with saline was applied to the rim of the lower evelid and staining was performed with a minimal amount of dye. The TBUT was measured three times consecutively, and the average value was evaluated as ≤ 5 s or > 5 s. The fluorescein staining score (FSS) of the cornea and conjunctiva was then evaluated in three areas (temporal bulbar conjunctiva, nasal bulbar conjunctiva, and cornea), scored on a 0- to 3-point scale (from 0, no damage, to 3, damage over the entire area), and then totaled (maximum = 9 points). Total score was evaluated as < 3 or > 3.

Diagnostic Criteria and Definition of DED

The Asia Dry Eye Society criteria were used to diagnose DED, and subjects who met both DED symptom-positive status (DEQ-5 total score ≥ 6) and TBUT ≤ 5 s were diagnosed as DED [1]. Also, patients who had a DED history in the past 2 years were defined as DED. The newly diagnosed DED patients who had not been diagnosed with DED in the past 2 years were defined as hidden DED patients.

Statistical Analysis

All statistical analyses were performed using SAS v.9.4 (SAS Institute, Cary, NC, USA) or IBM SPSS Statistics 25.0 (IBM, Armonk, NY, USA), and other tests by RPM (Tokyo, Japan) and KONDO Photo Process (Osaka, Japan). Welch's t test was performed for comparisons between two groups. Receiver operating characteristics (ROC) analysis was used to calculate the cutoff values of the number symptoms among the 12 DED-related subjective symptoms between patients who met the DED diagnostic criteria and patients who did not. p values less than 0.05 were considered significant.

RESULTS

Characteristics of the Study Subjects

In this study, 1011 outpatients were enrolled. Among them, 990 subjects, who completed the DEQ-5 and underwent the prescribed TBUT measurement, were analyzed. The characteristics of the study patients are summarized in Table 1. The number of patients over the age of 60 accounted for more than 80% of this population. More than half of the patients were women, and most were return visitors.

Prevalence of DED, Proportion of DED Patients with Epithelial Disorder

Figure 1 shows the prevalence of DED in outpatients of eye clinics and an eye hospital in Japan. The prevalence of DED (Asia Dry Eye Table 1 Demographics of the study patients

0 1	7.1			
Background factors	Total	%		
Number of patients analyzed	990	100.0		
Sex				
Male	384	38.8		
Female	606	61.2		
Age (years)				
Mean \pm SD	69.1 ± 13.4			
Median	71.0			
Min/max	20/96			
Age group (years)				
20–29	18	1.8		
30–39	32	3.2		
40-49	43	4.3		
50-59	83	8.4		
60–69	233	23.5		
70–79	391	39.5		
80 or over	190	19.2		
First visit/return visit				
First visit	77	7.8		
Return visit	913	92.2		
Daily contact lenses wearing				
Wearing	51	5.2		
No wearing	939	94.8		

SD standard deviation

Society diagnostic criteria positive, or with DED history in the past 2 years) was 55.7% in this study. The prevalence of DED with Asia Dry Eye Society diagnostic criteria positive only was 37.0% overall (data not shown). The prevalence of DED in first-visiting patients was lower than that of revisiting patients.

Table 2 shows the proportion with epithelial disorder. DED patients without epithelial disorder (FSS score < 3) accounted for more than 80%. The scores were similar between the first visit and the return visit.

Total (n=990) First visit (n=77) Return visit (n=913) 44.3% 55.7% 61.0% 39.0% 42.9% 57.1% • Dry eye disease patients • Non-dry eye disease patients

Fig. 1 Prevalence of dry eye disease in outpatients of eye clinics and an eye hospital in Japan. *Blue* dry eye disease: patients who had been diagnosed with dry eye disease in

the past 2 years or with tear break-up time < 5 s and with a total score of 5-Item Dry Eye Questionnaire > 6; gray non-dry eye disease: patients other than the above

	Total		First visit		Return visit	
	n	%	n	%	n	%
DED paties	nts					
Total	551	100.0	30	100.0	521	100.0
FSS < 3	449	81.5	24	80.0	425	81.6
$FSS \ge 3$	86	15.6	6	20.0	80	15.4

DED patient dry eye disease patients who had been diagnosed with dry eye disease in the past 2 years or with tear break-up time ≤ 5 s and with a total score of 5-Item Dry Eye Questionnaire ≥ 6

Prevalence of DED for Each Patient Background Characteristic

Table 3 shows the prevalence of DED in patients with other eye diseases or after eye surgery. The patients with allergic conjunctivitis and patients after vitreoretinal surgery had the highest prevalence of DED. The prevalence of DED also exceeded 50% in many other patient background characteristics.

Hidden DED Patients at Return Visit

Figure 2 shows the proportion of DED patients who had not previously been diagnosed among revisiting patients. In revisiting patients, 15.2% were the newly diagnosed DED patients who had not been diagnosed with DED in the past 2 years (hidden DED patients). The hidden DED patients had the highest proportion of allergic conjunctivitis, but the condition was uniformly present across all patient background characteristics.

Subjective Symptoms and TBUT Between DED Patients with Treatment and Hidden DED Patients

Table 4 shows the total score of DEQ-5 and the number of symptoms among 12 DED-related subjective symptoms in the revisiting patients with DED treatment and the hidden DED patients. In the background of all patients except allergic conjunctivitis patients, the total DEQ-5 scores of the patients with DED treatment were significantly lower than those of the hidden DED patients (p < 0.001, Welch's *t* test). The number of subjective symptoms in patients with DED treatment was also significantly lower in comparison with that of hidden DED patients (p < 0.001, Welch's *t* test).

Patient background	Total	Total		Non-DED patients		DED patients	
	n	%	n	%	n	%	
Allergic conjunctivitis	158	100.0	48	30.4	110	69.6	
Glaucoma	242	100.0	103	42.6	139	57.4	
Retinal disease	186	100.0	80	43.0	106	57.0	
Cataract	265	100.0	146	55.1	119	44.9	
After cataract surgery	174	100.0	73	42.0	101	58.0	
After vitreoretinal surgery	23	100.0	7	30.4	16	69.6	

Table 3 Dry eye disease prevalence in patients with other eye diseases or after eye surgery

DED patients dry eye disease patients who had been diagnosed with dry eye disease in the past 2 years or with tear break-up time ≤ 5 s and with a total score of 5-Item Dry Eye Questionnaire ≥ 6 , Non-DED patients non-dry eye disease patients other than the above, after cataract surgery and vitreoretinal surgery more than a month had passed after surgery

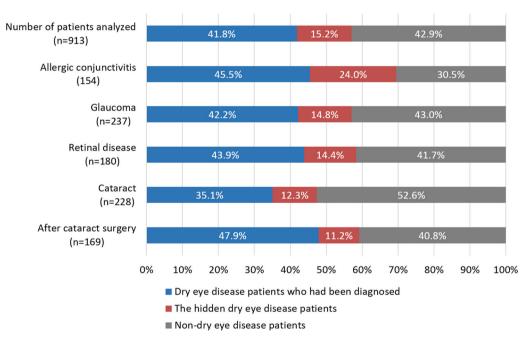


Fig. 2 Proportion of dry eye disease patients who had not been diagnosed previously among revisiting patients. *Blue* dry eye disease patients who had been diagnosed with dry eye disease in the past 2 years; *red* dry eye disease patients

Table 5 shows the proportion of patients with TBUT \leq 5 s in the revisiting patients with DED treatment and the hidden DED patients. The proportion of patients with TBUT \leq 5 s among the hidden DED patients was not included in the 95% CI of the treatment group.

who had not been diagnosed with dry eye disease in the past 2 years; *gray* non-dry eye disease patients, *After cataract surgery* more than a month had passed since surgery

Distribution of 12 DED-Related Subjective Symptoms in DED and Non-DED Patients

Table 6 shows the differences in the 12 DEDrelated subjective symptom distributions in DED and non-DED patients, in which DED was

Patient background	Revisitir	ng patients with DED treatment	The hidden DED patients		p value
	n	Mean ± SD	n	Mean ± SD	
Total score of DEQ-5					
Number of patients analyzed	321	7.2 ± 5.0	139	9.6 ± 3.5	$p < 0.001^{**}$
Allergic conjunctivitis	64	8.9 ± 4.5	37	9.4 ± 3.6	p = 0.550
Glaucoma	82	6.7 ± 4.6	35	8.9 ± 2.7	$p = 0.002^*$
Retinal disease	67	5.6 ± 4.8	26	9.0 ± 2.8	$p < 0.001^{**}$
Cataract	70	6.5 ± 4.6	28	9.6 ± 3.6	$p < 0.001^{**}$
After cataract surgery	61	6.8 ± 5.3	19	10.1 ± 3.9	$p = 0.006^*$
Number of 12 DED-related sul	bjective sy	nptoms			
Number of patients analyzed	321	5.4 ± 3.0	139	6.8 ± 2.7	$p < 0.001^{**}$
Allergic conjunctivitis	64	7.2 ± 2.6	37	7.0 ± 2.4	p = 0.735
Glaucoma	82	5.4 ± 3.1	35	6.7 ± 2.3	$p = 0.015^*$
Retinal disease	67	4.6 ± 2.9	26	6.3 ± 2.6	$p = 0.009^*$
Cataract	70	4.8 ± 2.9	28	6.6 ± 2.5	$p = 0.003^*$
After cataract surgery	61	5.0 ± 3.0	19	7.3 ± 2.5	$p = 0.002^*$

Table 4 The comparison of subjective symptoms in revisiting patients with dry eye disease treatment and newly diagnoseddry eye disease patients

DEQ-5 5-Item Dry Eye Questionnaire, *DED* dry eye disease, *The hidden DED patients* the newly diagnosed DED patients who had not been diagnosed with DED in the past 2 years, *SD* standard deviation, after cataract surgery more than a month had passed since surgery

Welch's t test, *p < 0.05; **p < 0.001

Asia Dry Eye Society diagnostic criteria positive only. The subjective symptoms that had the most difference between DED and non-DED were dryness and eye discomfort, which were included in the DEQ-5. On the other hand, although watery eyes was one of the subjective symptoms included in the DEQ-5, it showed the smallest difference between DED and non-DED patients. Among the subjective symptoms not included in DEQ-5, those with large differences between DED and non-DED patients were eye fatigue and foreign-body sensation.

Figure 3 shows the patient distribution for 12 DED-related subjective symptoms in patients who met the DED diagnostic criteria and patients who did not, in which DED was Asia Dry Eye Society diagnostic criteria positive only. DED patients had more subjective symptoms than non-DED patients. The average number and standard deviation of symptoms in DED patients (n = 367) was 6.9 ± 2.4 , and that in non-DED (n = 623) was 3.55 ± 2.6 . The number of symptoms was were significantly different between DED and non-DED patients (p < 0.001, Welch's *t* test). The cutoff value of the number of symptoms among 12 DED-related subjective symptoms between DED and non-DED was 5 (area under the curve = 0.823, ROC analysis).

DISCUSSION

Prevalence of DED

In this multicenter, hospital-based cross-sectional study, we assessed the prevalence of DED in outpatients who were seen in six eye clinics and an eye hospital in Japan. Multiple DED

Patient background	Revisiting	g patients with I	The hidden DED patients		
	n	%	95% CI	n	%
Proportion of TBUT ≤ 5 s					
Number of patients analyzed	261	84.7	80.4, 88.4	139	100.0
Allergic conjunctivitis	55	85.9	75.9, 92.8	37	100.0
Glaucoma	64	81.0	71.3, 88.5	35	100.0
Retinal disease	50	80.6	69.5, 89.0	26	100.0
Cataract	60	87.0	77.5, 93.3	28	100.0
After cataract surgery	49	84.5	73.6, 92.0	19	100.0

Table 5 The proportion of tear break-up time in the revisiting patients with dry eye disease treatment and the newly diagnosed dry eye disease patients

TBUT tear break-up time, *CI* confidence interval, *DED* dry eye disease, *The hidden DED patients* the newly diagnosed DED patients who had not been diagnosed with DED in the past 2 years, after cataract surgery more than a month had passed since surgery

Table 6 Differences in the 12 dry eye disease-related subjective symptom distribution in dry eye disease and non-dry eyedisease patients

Subjective symptom	Non-DED patients		DED patients		% difference
	n	%	n	%	
Number of patients analyzed	623	100.0	367	100.0	_
Dryness	143	23.0	269	73.3	50.3
Eye discomfort	216	34.7	298	81.2	46.5
Eye fatigue	280	44.9	293	79.8	34.9
Foreign-body sensation	167	26.8	223	60.8	34.0
Heaviness	113	18.1	182	49.6	31.5
Eye pain	87	14.0	149	40.6	26.6
Photophobia	271	43.5	254	69.2	25.7
Blurred vision	292	46.9	249	67.8	21.0
Red eye	123	19.7	145	39.5	19.8
Eye discharge	150	24.1	152	41.4	17.3
Itchy eye	199	31.9	176	48.0	16.0
Watery eyes	127	20.4	130	35.4	15.0

DED patients dry eye disease patients with tear break-up time ≤ 5 s and with a total score of 5-Item Dry Eye Questionnaire ≥ 6 , Non-DED patients non-dry eye disease patients other than the above

98 100 90 86 79 80 The number of patient 68 68 58 57 60 50 18 41 38 36 36 40 29 24 21 17 20 15 8 6 0 0 7 0 2 3 4 5 6 8 9 10 11 12 1 The number of 12 dry eye disease-related subjective symptoms that study patients had Non-dry eye disease patients Dry eye disease patients

Fig. 3 The patient distribution for 12 dry eye diseaserelated subjective symptoms in dry eye disease and non-dry eye disease patients. *Blue* dry eye disease patients: Patients with tear break-up time ≤ 5 s and with a total score of DEQ-5 ≥ 6 , n = 367; gray non-dry eye disease patients:

prevalence surveys for outpatients have been conducted in the past, and the DED prevalence reported 7.99-61.57% has been as [8, 13, 20-22]. The surveyed areas of these reports were Asia (Japan, China, India) and Africa (Nigeria). Among them, in the previous report in Japan [22], dry eye diagnosis was determined in terms of the presence or absence of dry eye treatment and necessity for eye drop treatment, and the prevalence rate was 26.3%. The prevalence of DED in the present study was 55.7% (Fig. 1), higher than in the previous surveys. The difference in reported prevalence may be attributable to the difference in DED criteria, or the timing of conduction of the survey, as the current study was conducted in the winter spring season. Ophthalmologists may to encounter dry eye patients very frequently among outpatients of eye clinics and hospitals in Japan, and need to be aware as to whether any patients have dry eye.

Hidden DED Patients

In this study, 15.2% of the revisiting outpatients were the hidden DED patients (Fig. 2).

Patients other than the above, n = 623. The 12 dry eye disease-related subjective symptoms were eye fatigue, eye pain, eye discharge, foreign body sensation, watery eyes, blurred vision, itchy eye, heaviness, red eye, eye discomfort, dryness, and photophobia

The hidden DED patients were found as a result of consecutively performing dry eye diagnosis in this study. The hidden DED patients were those patients who had a sufficient degree and frequency of subjective symptoms, as DEQ-5 total score ≥ 6 . It is an important problem that such obvious DED cases were missed among 10% of revisiting patients.

There may be multiple reasons why these patients were not recognized as DED. One of the reasons is the difficulty in differentiating DED from other eye diseases. Another is that the prioritization of the treatment of diseases with high blindness rates may have diminished awareness that an ophthalmologist would suspect these patients to have associated DED. Blindness by DED is very rare. However, DED is a disease that lowers the quality of life (QOL) as seriously as does angina [25], affects sleep [26], and reduces labor productivity [5]. Detection and treatment of DED can be expected to improve patients' QOL. In this study, the total DEQ-5 score and the number of 12 DED-related subjective symptoms of the patients with DED treatment was significantly lower than those of the hidden DED patients (p < 0.001, Welch's

t test; Table 4), and the proportion of patients with TBUT < 5 s was also lower. These results suggest that DED treatment for the hidden DED patients may improve their subjective symptoms and TBUT.

Prevalence of DED for Each Patient Background Characteristic

DED is a multifactorial disease characterized by unstable tear film, and may be accompanied by ocular surface damage. Many eye diseases with ocular surface disorders are known besides DED. The ocular surface disorders may also be caused by eye treatments. It is conceivable that the mechanism by which these eye diseases and treatments cause ocular surface disorders coincides with the mechanism by which DED develops. The presence of other ocular surface diseases or topical treatments may exacerbate DED condition. For example, allergic conjunctivitis is an inflammatory disease of the conjunctiva in which a type I allergic reaction is involved, and is a disease accompanied by ocular findings such as subjective symptoms and hyperemia, and its relevance to dry eye has been reported [19]. In patients with NTG who topical prostaglandin received analog monotherapy for 1 year or longer, OSDI and fluorescein keratocorneal conjunctival staining scores were significantly higher than in normal subjects [15]. In patients after cataract surgery and retinal vitreous surgery, it has been reported that conjunctival goblet cell counts were lower [27, 28] and that TBUT was shortened [28, 29]. In the present study, DED patients were found among more than half of patients with allergic conjunctivitis, glaucoma, retinal disease, after cataract surgery, and after retinal vitrectomy (Table 3). More caution in regard to DED complications should be heeded for the patients with these patient background characteristics. The results of this study are considered to support the above published reports.

DED-Related Subjective Symptoms

The evaluation of DED subjective symptoms is an important step in DED diagnosis. There are great differences between individuals in the expression of subjective symptoms. Questionnaires make it possible to objectively evaluate subjective symptoms. In this study, we evaluated subjective symptoms with DEQ-5 and the presence or absence of 12 symptoms. The DEQ-5 is a very simple questionnaire, with only five questions. DEQ-5 made it possible to evaluate to the subjective symptoms of more than 1000 patients within a limited time of outpatient care, and to diagnose DED. The evaluation of 12 DED-related subjective symptoms was useful in studying the characteristics of subjective symptoms of DED patients. The results of this study revealed that, in DED diagnosis, it may be necessary to pay attention to subjective symptoms such as dryness, eye discomfort, eye fatigue, and foreign-body sensation (Table 6).

Limitations

This study had several limitations. There is an inherent selection bias since only patients visiting six eye clinics and one eye hospital were included, and therefore it is not truly an epidemiological study of the prevalence of DED in the general population. This is especially true since the study cohort included postoperative patients. This may explain the reason for the high prevalence relative to previous published studies. We selected the seven study sites from all over Japan. However, the possible existence of selection bias in the study site selection cannot be denied. The "history of DED in the past 2 years" criteria were not based on standardized diagnostic criteria across study sites. The "patients who had not been diagnosed with DED in the past 2 years" and those "diagnosed with DED in this study" may include patients who developed DED between the time of the last visit and the time of the present visit in this study. The present study was conducted from winter to spring; DED is a disease for which the prevalence is affected by the season. It is necessary to investigate the DED prevalence at other seasons or throughout the year. In this study, there were differences in the number of patients with other eye diseases and postoperative patients. By examining the prevalence of DED with the same number of these patients, it will be possible to examine the relationship with DED in more detail.

CONCLUSIONS

More than half of the outpatients had DED, and most DED cases were short TBUT-type dry eye. Patients with allergic conjunctivitis and patients after vitreoretinal surgery had the highest prevalence of DED. Among revisiting patients, there were many hidden DED patients who had not been diagnosed with DED in the past. There is a high likelihood of finding DED comorbidity in patients with other eye diseases in eye clinics and hospitals.

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Compliance with Ethics Guidelines. This study protocol was approved by The Ethics Committee of Medical Corporation TOUKEIKAI Kitamachi Clinic (Tokyo, Japan). This study was conducted in accordance with the guidelines of the World Medical Association Declaration of Helsinki, and Ethical Guidelines for Medical and Health Research involving Human Subjects in Japan. The subjects received a full explanation of the procedures and provided their written informed consent for participation prior to inclusion in the study. The study was registered in the public registration system (University Hospital Medical Information Network: UMIN (registries no. UMIN000035506)).

Data Availability. The data sets during and/ or analyzed during the current study are available from the corresponding author on reasonable request.

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