Epidemiology and the Estimated Burden of Microbial Keratitis on the Health Care System in Taiwan: A 14-Year Population-Based Study

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• PURPOSE: To investigate the epidemiologic characteristics of microbial keratitis and its overall burden on the health care system in Taiwan.
• DESIGN: Retrospective, population-based study.
• METHODS: We conducted a study using claims data in the Taiwan National Health Insurance Research Database in 2000-2013, employing diagnoses, drugs, and procedure codes to define diseases and procedures. Participants were classified into groups according to the requirement of hospitalization and surgical intervention. The main outcome measures were incidence, risk factors, predictive factors for hospitalization and surgical intervention, and health care expenditure.
• RESULTS: A total of 2,071 patients were included. The overall incidence significantly increased from 8.4 in 2000 to 20.2 per 100,000 person-years in 2013. The peak age range of incidence was between 18 and 40 years, but the peak age group for health care expenditures was those older than 65 years. A total of 704 patients (33.99%) had analyzable risk factors, of which the top 3 were diabetes mellitus (DM, 11.52%), eye trauma (10.55%), and dry eye (8.72%). Older patients, those using steroid and antiglaucoma agents, and those with ocular and systemic diseases were susceptible to further hospitalization and surgical intervention for the treatment of microbial keratitis.
• CONCLUSIONS: In Taiwan, DM, eye trauma, and dry eye were key predisposing factors for microbial keratitis. Older patients (>40 years) accounted for approximately 80% of health care expenditure for the management of infectious keratitis. Special care may be required for older patients with medication-related risk factors and ocular and systemic comorbidities because they are likely to have severe diseases leading to hospitalization and surgical interventions. (Am J Ophthalmol 2020;220:152–159. © 2020 Elsevier Inc. All rights reserved.)

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MICROBIAL KERATITIS IS A MAJOR CAUSE OF ocular morbidity, and it can lead to visual impairment. Previous studies have revealed that bacterial and fungal keratitis are the most common types of microbial keratitis.[1–3] Identified risk factors for infectious keratitis include contact lens wear, eye trauma, prior eye surgery, ocular surface diseases, topical steroid use, topical antiglaucoma agent use, and systemic diseases.[4–6] Microbial keratitis may require long-term, costly antimicrobial treatment, and it may require further hospitalization and surgical management if the infection is poorly controlled through medical therapy.[6,7] Thus, microbial keratitis not only negatively influences the patient's quality of life and economic productivity but also presents a heavy burden for national health care systems.[8] A report from the U.S. Centers for Disease Control and Prevention revealed that the annual cost of health care for keratitis reached $175 million during 2010.[9]

The epidemiology of microbial keratitis varies with geographic region.[10] Thus, the establishment of local information is essential for providing useful clinical guidelines to practicing ophthalmologists. In Taiwan, medical center–based studies have investigated various aspects of microbial keratitis,[5,11] but limited data are available on the epidemiologic characteristics of infectious keratitis in the general population. Single-center studies can provide detailed clinical characteristics including risk factors, clinical features, treatment outcomes, and microbiological data; however, because the results may have referral bias, they may not reflect the condition of the general population. Conversely, population-based studies can determine the incidence of the disease and estimate its burden on the health care system. In the present study, we aimed to investigate the epidemiologic characteristics of microbial keratitis and its overall burden on the health care system in Taiwan by using a population-based database.

METHODS

• DATA SOURCE: The National Health Insurance (NHI) program of Taiwan covers the health care services of more than 99% of Taiwan's population. The National Health Insurance Research Database (NHIRD), containing registration files and original claims data for

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reimbursement, is maintained by the National Health Research Institutes of Taiwan. The registration files in NHIRD included registry for beneficiaries, medical personnel, medical services, drug prescriptions, contracted beds, contracted specialty services, contracted medical facilities, board-certified specialists, and catastrophic illness patients. Patient information in the database is encrypted. Data for the present study were obtained from the Longitudinal Health Insurance Database (LHID), a subset of the NHIRD that contains the original claims data of 1 million randomly sampled beneficiaries from the NHI program. This study was conducted in accordance with the Declaration of Helsinki and was approved by the Institutional Research Ethics Board of Chang Gung Memorial Hospital, Taiwan (IRB number: 102-2147B).

• **STUDY DESIGN AND IDENTIFICATION OF MICROBIAL KERATITIS:** We conducted a retrospective cohort study from January 1, 2000, through December 31, 2013, using data from the LHID. Owing to absence of a specific diagnostic code for microbial keratitis, we established strict inclusion criteria combined with diagnoses, prescriptions, and clinic visits or hospitalizations to identify patients with a high possibility of having microbial keratitis. Cases that met the following criteria were included: (1) diagnosis of corneal ulcer according to the International Classification of Diseases, 9th Revision, Clinical Modification codes (ICD-9-CM code); (2) at least 2 clinic visits during 1 week[12] after the diagnosis of microbial keratitis or admission to a department of ophthalmology with a primary diagnosis of microbial keratitis; and (3) use of antibiotic or antifungal medication. All patients were included only once; recurrent episodes were not considered in this study.

• **DEMOGRAPHICS AND RISK FACTORS:** Demographic data including age, sex, and level of urbanization were collected. Urbanization was categorized into 7 grades according to the geographic location and level of urbanization; grade A was the most urbanized, and grade G was the least urbanized. The urbanization grades are defined by previous researchers based on the urbanization index developed by the National Health Research Institute, Taiwan. This index was derived from an analysis using data on 5 indicators: population density, percentage of population with college or greater educational levels, percentage of population aged more than 65 years, percentage of population working in agriculture, and density of physicians per 100,000 people.[13]

Risk factors for microbial keratitis were determined before the diagnosis of microbial keratitis. Identified risk factors, namely contact lens wear; eye trauma; prior eye surgery; ocular surface diseases that could damage the corneal epithelium such as dry eye, blepharitis, dacryocystitis, dacryoadenitis, and neurotrophic keratoconjunctivitis;[14] topical/systemic steroid use; topical antiglaucoma agent use; autoimmune diseases; diabetes mellitus (DM); malignancy; and malnutrition, were collected according to the ICD-9-CM disease and procedure codes (Supplementary Table A; Supplemental Material available at AJO.com). Because contact lens wear does not have a specific code, we used a combination of the diagnostic codes for corneal disorder due to contact lens and refractive error. Chronic topical use of corticosteroids or antiglaucoma agents was defined as the use of the medications for more than 3 months, with use within 1 month before the diagnosis of microbial keratitis.

Patients with hospitalization for infectious keratitis as the primary diagnosis were classified as the inpatient (IPD) group. This group was compared with the outpatient (OPD) group, which comprised patients who received treatment for microbial keratitis at a local clinic or ophthalmology outpatient department. Corneal surgical interventions performed within 3 months after the diagnosis of microbial keratitis were considered disease-related surgical treatments. Associated therapeutic and destructive surgeries included corneal transplantation, tarsorrhaphy, amniotic membrane graft, corneal gluing, evisceration, and enucleation.

• **ANTIMICROBIAL TREATMENT FOR MICROBIAL KERATITIS:** Data concerning topical antibiotic and antifungal treatments for microbial keratitis were collected according to the Anatomical Therapeutic Chemical codes.[15] Fortified and commercial antibiotic eye drops for bacterial keratitis consisted of vancomycin, tobramycin, gentamicin, cefazolin, ceftazidime, ciprofloxacin, norfloxacin, ofloxacin, and levofloxacin. Oral and topical antifungals for fungal keratitis included oral ketoconazole, fluconazole, voriconazole, itraconazole, clotrimazole, miconazole, and flucytosine and topical natamycin, amphotericin B, voriconazole, and fluconazole. We calculated the percentage of antibiotics and antifungal medications in 4 levels of the health care system in Taiwan: local clinic, district hospital, regional hospital, and medical center.

• **EPIDEMIOLOGY AND STATISTICAL ANALYSIS:** The annual incidence rate and cost of microbial keratitis were calculated according to the data from the NHIRD. The annual incidence rate was the number of new cases identified in 1 year divided by the alive population in the year. The average health care expenditures were determined on the basis of health expenditures for patients with microbial keratitis divided by the number of patients with the disease. Curve estimation regression was used to analyze the trends of incidence and cost. Clinical characteristics of age, sex, and urbanization were analyzed using χ^2 tests and independent Student t tests. Predictive factors associated with hospitalization or surgical interventions were analyzed using logistic regression. All statistical analyses were performed using the SPSS software package (SPSS, Inc, Chicago, Illinois, USA). Results with $P < .05$ were considered statistically significant.

TABLE 1. Demographics of Microbial Keratitis Outpatient and Inpatient Groups

Characteristic	Total (N = 2,071)	OPD Group (N = 1,740)	IPD Group (N = 331)	*P* Value
Age, years				
Mean ± SD	42.72 ± 21.65	40.85 ± 20.91	52.54± 22.81	<.001[a]
<18 years, n (%)	224 (10.82)	196 (11.26)	28 (8.36)	<.001[a]
18-40 years, n (%)	834 (40.27)	754 (43.33)	80 (23.88)	
41-65 years, n (%)	601 (29.02)	497 (28.56)	104 (31.42)	
>65 years, n (%)	412 (19.89)	293 (16.84)	119 (35.95)	
Sex, n (%)				
Male	950 (45.87)	776 (44.60)	174 (52.57)	.008[a]
Female	1121 (54.13)	964 (55.40)	157 (47.43)	
Grades of urbanization, n (%)				
A (Most urbanized)	600 (28.97)	526 (30.23)	74 (22.39)	.007[a]
B	603 (29.12)	513 (29.48)	90 (27.19)	
C	315 (15.21)	263 (15.11)	52 (15.71)	
D	306 (14.78)	248 (14.25)	58 (17.52)	
E	57 (2.75)	43 (2.47)	14 (4.23)	
F	88 (4.25)	68 (3.91)	20 (6.04)	
G (Least urbanized)	102 (4.93)	79 (4.54)	23 (6.95)	

IPD = inpatient; OPD = outpatient.
[a]Compare OPD and IPD group using independent *t* test, *P* value < .05.

RESULTS

• **STUDY POPULATION:** The initial sample comprised 39,344 records with ICD-9-CM codes 370.00 through 370.06. Patients with incomplete personal information, NHI enrollment after 2013, or failure to meet the inclusion criteria were excluded. Finally, 2,071 patients were enrolled in this study. The patients were further classified into OPD (1,740 patients) and IPD groups (331 patients) (Supplementary Figure A; Supplemental Material available at AJO.com).

• **DEMOGRAPHICS:** Table 1 lists the demographics of the patients with microbial keratitis. The sample included 1,121 women (54.13%) and 950 men (45.87%). Female patients (55.40%) predominated in the OPD group, whereas male patients (52.57%) were more common in the IPD group. The mean age of the patients was 42.72 ± 21.65 years. Patients in the OPD group (mean age: 40.85 ± 20.91 years) were younger than those in the IPD group (mean age: 52.54 ± 22.81). The majority of patients with microbial keratitis were aged between 18 and 40 years (n = 834, 40.27%), followed by 41-65 years (n = 601, 29.02%), older than 65 years (n = 412, 19.89%), and younger than 18 years (n = 224, 10.82%). Patients in the IPD group lived in less urbanized areas than those in the OPD group did (*P* = .007).

• **INCIDENCE:** During the 14-year study period from 2000 through 2013, the annual incidence of microbial keratitis in Taiwan significantly increased from 8.3 to 20.2 per 100,000 person-years. Figure 1 illustrates the annual incidence of microbial keratitis stratified by age. The peak age range for the incidence of microbial keratitis was 18-40 years (Supplementary Figure B; Supplemental Material available at AJO.com). The incidence of OPD-treated microbial keratitis was significantly higher than IPD-treated keratitis (Supplementary Figure C; Supplemental Material available at AJO.com).

• **PREDISPOSING FACTORS:** Because of the extremely low coding rate of "corneal disorder due to contact lens" (ICD-9-CM code 371.82), we could not put contact lens wear into analysis. Among the patients with analyzable predisposing factors (n = 704, 33.99%), the most common risk factor for microbial keratitis was DM (11.52%), eye trauma (10.57%) and dry eye (8.74%) (Table 2). Eye trauma was the most common risk factor among children and young adults (aged equal to or younger than 40 years), whereas DM was mostly observed in older patients (aged older than 40 years; Supplementary Table B; Supplemental Material available at AJO.com).

• **TREATMENT:** Medical therapy is the first-line treatment of microbial keratitis. In our analysis, antibiotics were more largely prescribed (85.6%) than antifungal medications (14.4%). The most widely administered antibiotic across all levels of the health care system from 2000 through 2013 was ciprofloxacin (86.20% in local clinics, 67.09% in local hospitals, 62.88% in regional hospitals, and 48.69% in medical centers). Antifungal medications were most commonly prescribed in medical centers; the most

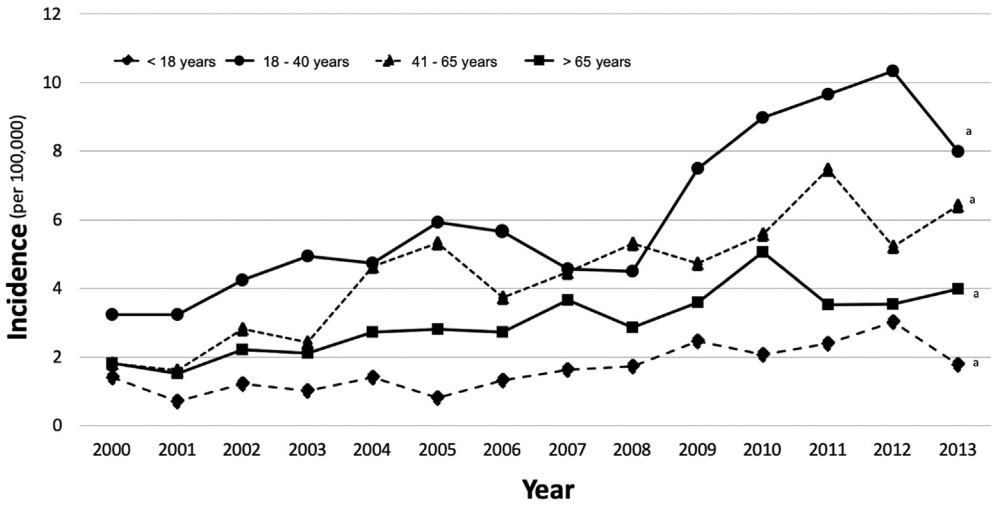

FIGURE 1. Annual incidence of microbial keratitis stratified by age (2000-2013). The trend of annual incidence was calculated by curve estimation regression. [a]$P < .0001$.

commonly administered antifungal medication was amphotericin B, followed by natamycin.

The average number of visits to a local clinic or outpatient clinic was 3.5 ± 2.5 per disease episode. The average hospital stay was 13.6 ± 12.8 days. Patients with topical and systemic steroid use (odds ratio [OR] = 2.8, $P < .001$, and OR = 2.0, $P = .014$, respectively), topical use of antiglaucoma agents (OR = 3.0, $P = .001$), and DM (OR = 1.5, $P = .025$) were more likely to be hospitalized (Table 3).

One hundred and fifty (7.2%) patients with severe infection required additional surgical interventions, including corneal transplantation (36.7% of the patients), amniotic membrane grafting (22.3%), tarsorrhaphy (19.2%), evisceration (17.5%), enucleation (2.6%), and corneal gluing (1.7%). Patients with history of eye trauma (OR = 2.0, $P = .003$), prior eye surgery (OR = 3.4, $P = .005$), dry eye (OR = 3.3, $P < .001$), blepharitis (OR = 2.8, $P = .001$), topical steroid use (OR = 7.3, $P < .001$), systemic steroid use (OR = 4.0, $P < .001$), topical antiglaucoma agent use (OR = 6.1, $P < .001$), rheumatoid arthritis (OR = 2.0, $P = .01$), DM (OR = 3.0, $P < .001$), and malignancy (OR = 3.5, $P < .001$) exhibited higher risks of receiving surgical interventions for microbial keratitis (Table 3).

TABLE 2. Predisposing Factors for Microbial Keratitis

Predisposing Factors[a,b]	N (%)
History of eye trauma	219 (10.57)
Prior eye surgery	34 (1.64)
Ocular surface disease	
Dry eye	181 (8.74)
Blepharitis	82 (3.96)
Dacryocystitis and dacryoadenitis	9 (0.43)
Neurotrophic keratoconjunctivitis	2 (0.10)
Medication-related factors	
Systemic steroids	62 (2.99)
Topical steroids	93 (4.49)
Antiglaucoma agents	39 (1.88)
Systemic conditions	
Rheumatoid arthritis	140 (6.76)
HIV infection	2 (0.10)
Diabetes mellitus	239 (11.52)
Malignancy	94 (4.54)
Systemic lupus erythematosus	14 (0.68)
Malnutrition	10 (0.48)

HIV = human immunodeficiency virus.
[a]There were 704 patients (33.99%) with risk factors in total.
[b]Contact lens use could not be analyzed because of extremely low coding rates rather than a true reflection of low contact lens use in this population.

• **HEALTH CARE EXPENDITURE:** During 2000 through 2013, the average outpatient expenditure for microbial keratitis was NT$2,397.84 ± 4,900.86 (US$71.94 ± 147.03; average exchange rate during 2000 through 2013 of 1 NTD = 0.03 USD), whereas the equivalent inpatient expenditure was NT$34,261.20 ± 40,906.62 (US$1,027 ± 1,227.20). The average annual expenditure for microbial keratitis in Taiwan was NT$1,350,513 ± 1,039.07 (US$40,515 ± 31.17). The patients aged above 65 years spent the largest proportion of the health care expenditure (43.1%), followed by patients aged between 41 and 65 years (35.1%), young adults aged between 18 and 40 years (16.8%) and children below 18 years old (5.0%) (Figure 2).

TABLE 3. Risk Factors for Hospitalization and Surgical Intervention in Microbial Keratitis

	Hospitalization			Surgical Intervention		
Risk Factors[a]	Odds Ratio	95% CI	*P* Value[b]	Odds Ratio	95% CI	*P* Value[b]
Eye trauma	1.158	0.801-1.673	.4359	1.960	1.259-3.049	.0029
Prior eye surgery	1.129	0.464-2.748	.7895	3.408	1.459-7.961	.0046
Ocular surface disease						
Dry eye	1.191	0.801-1.772	.3877	3.348	2.198-5.100	<.0001
Blepharitis	0.808	0.423-1.542	.5182	2.783	1.526-5.057	.0008
Dacryocystitis and dacryoadenitis	0.656	0.082-5.263	.6915	1.593	0.198-12.824	.6615
Neurotrophic keratoconjunctivitis	5.270	0.329-84.460	.2403	-	-	-
Medication-related factors						
Systemic steroids	2.039	1.152-3.609	.0144	3.985	2.144-7.0409	<.0001
Topical steroids	2.797	1.786-4.379	<.0001	7.308	4.558-11.717	<.0001
Anti-glaucoma agents	3.030	1.558-5.892	.0011	6.053	3.001-12.207	<.0001
Systemic conditions						
Rheumatoid arthritis	1.036	0.652-1.647	.8802	1.995	1.180-3.373	.01
HIV infection	-	-	-	12.793	0.796-205.555	.0720
Diabetes mellitus	1.469	1.049-2.057	.0252	3.011	2.033-4.461	<.0001
Malignancy	1.547	0.938-2.551	.0874	3.541	2.077-6.037	<.0001
Systemic lupus erythematosus	2.950	0.982-8.858	.0538	3.518	0.971-12.748	.0555
Malnutrition	2.265	0.583-8.803	.2378	1.417	0.17-11.250	.7415

HIV = human immunodeficiency virus.

Dash (-) indicates low number to be analyzed.

[a]Contact lens use could not be analyzed because of extremely low coding rates rather than a true reflection of low contact lens use in this population.

[b]Comparison using logistic regression.

DISCUSSION

THIS IS THE FIRST 14-YEAR POPULATION-BASED STUDY investigating the epidemiologic characteristics and health care cost of microbial keratitis in Taiwan. The present study revealed 3 principal findings. First, the peak incidence of microbial keratitis was in patients aged 18-40 years. Second, approximately 80% of health care expenditures were spent for patients aged older than 40 years. Third, DM is both a crucial predisposing factor for microbial keratitis and a predictive factor for its severity.

• **DEMOGRAPHICS AND INCIDENCE:** The patients in this study were younger (average age of 43 years) than those in previous single-center studies (average age of approximately 50 years) in Taiwan.[5,11] Female patients were more common overall, but the IPD group included more male patients than female. Because the previous domestic studies were restricted to medical centers, the present study can reflect the generalized characteristics of microbial keratitis in Taiwan.

The present study demonstrated an increase in the incidence of microbial keratitis from 8.3 per 100,000 person-years in 2000 to 20.2 per 100,000 person-years in 2013. Previous population-based studies have indicated this incidence rate varies between different areas, even in the same country. A study of patients in Minnesota, USA, reported an incidence rate of 11 per 100,000 person-years,[16] whereas another study in northern California, USA, reported an incidence rate of 27.6 per 100,000 person-years.[17] A study of patients in Portsmouth, UK, revealed an incidence rate of 40.3-52.1 per 100,000 person-years.[18] Generally speaking, the incidence of microbial keratitis is higher in Asian countries than in western countries. In southern India, the incidence of microbial keratitis was 113 per 100,000 person-years.[19] The rate was even higher in Nepal, with an incidence of 799 per 100,000 person-years.[20] However, the incidence of microbial keratitis in the present study cannot be compared with those revealed in previous studies because of differences in the populations, study designs, and study durations.

• **PREDISPOSING FACTORS:** Previous single-center studies conducted in Taiwan reported that contact lens wear was the leading risk factor for microbial keratitis during the preceding 2 decades,[11,17,21] which could be explained by the high prevalence of myopia and the popularity of contact lens use by young people in Taiwan. The statistical data of the Ministry of Economic Affairs demonstrated the increasing domestic sales volume of soft contact lenses during the study period (Supplementary Figure D; Supplemental Material available at AJO.

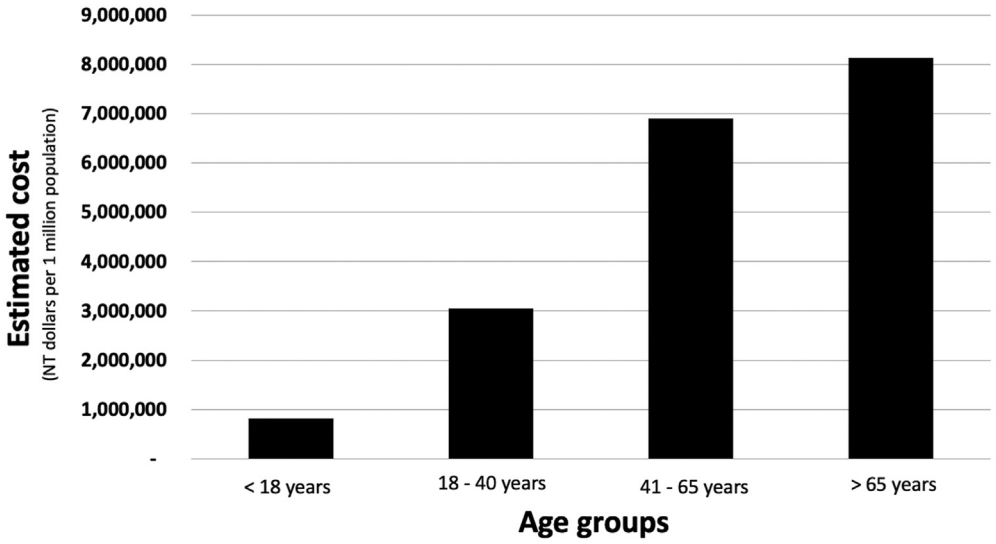

FIGURE 2. Estimated overall cost of microbial keratitis stratified by age (2000-2013). The patients aged above 65 years spent the largest proportion of the health care expenditure (43.1%, NT$ 6,682,529 in total), followed by patients aged between 41 and 65 years (35.1%, NT$ 5,447,672 in total), young adults aged between 18 and 40 years (16.8%, NT$ 2,599,610 in total), and children below 18 years old (5.0%, NT$ 782,881 in total).

com).[22] However, in the present study, we could not analyze soft contact lens use as a risk factor owing to incomplete data in the Taiwan NHIRD. Generally speaking, contact lens use is not routinely coded in our clinical practice. Taking the previous study conducted in our hospital[5] as an example, the diagnosis of corneal ulcers and information about contact lens use were collected separately; corneal ulcers were coded in the ICD-9-CM format, whereas contact lens use was recorded as text in patients' medical charts. In this study, we revealed that the peak incidence of microbial keratitis is between the ages of 18 and 40 years, but 84.77% of patients in this group did not have analyzable risk factors. Therefore, we believe that the extremely low number of contact lens–associated corneal disease in the present study may be a result of low medical coding rate, not a reflection of the real condition in Taiwan.

This study revealed that DM is a crucial risk factor for microbial keratitis. DM patients have been shown to have higher infection rates than nondiabetic counterparts.[23] A study revealed hyperglycemia inhibits humoral effector recruitment and complement-mediated opsonization and phagocytosis in response to bacteria.[24] Besides, microvascular injury due to hyperglycemia may lead to impaired blood supply and may increase risk for infection.[23] Previous studies have also reported that DM is a risk factor for microbial keratitis[25,26] and even that it is associated with the severity of microbial keratitis.[27,28] DM can cause alterations in the corneal nerves, including a reduction of corneal nerve fiber density, length, and branch density,[29] as well as alterations in the corneal epithelial basal cells and basement membrane, leading to corneal epitheliopathy and adhesion disorders.[30,31] DM-related damage to the corneal barrier function and impaired epithelial healing can increase susceptibility to infection.

Furthermore, the present study revealed that topical use of antiglaucoma agents is not only a predisposing factor for infectious keratitis but also a risk factor for severe microbial keratitis requiring hospitalization and surgical intervention. Although topical use of antiglaucoma agents was described as a risk factor for microbial keratitis in a previous study,[14] the information was limited. The relationship between antiglaucoma agents and the ocular surface has been discussed extensively, and the preservatives in antiglaucoma agents, such as benzalkonium chloride, have been reported to play a role.[32] Compromise of the ocular surface caused by antiglaucoma agents may increase the risk of infection.

• DISEASE SEVERITY: HOSPITALIZATION AND SURGERY: This study used 2 surrogate measures to indicate the disease severity, namely hospitalization and surgical interventions. Approximately one-sixth of patients were hospitalized. During the 14-year period, the number of outpatients with microbial keratitis in Taiwan increased significantly; however, the number of inpatients decreased. This trend may be associated with the approval of fluoroquinolone ophthalmic solution,[33] which can be used to treat mild infectious keratitis in outpatient clinics and in the community. Moreover, education and media have increased awareness of microbial keratitis among contact lens and orthokeratology lens wearers; early diagnosis may prevent deterioration of corneal infections, which can lead to hospitalization.

Surgical interventions were indicated for cases with failure of medical treatment. Fewer than 10% of patients

required additional surgery in the present study. Two referral center–based studies in Taiwan revealed higher rates of surgical interventions (27.7%[34] and 31.2%[5]). The patients referred to tertiary hospitals had more severe disease and may have had a higher demand for surgical interventions. Among patients treated surgically, 20.1% received destructive operations including evisceration and enucleation; the percentage was higher than those of previous studies.[5,34]

In this study, we determined the potential factors associated with disease severity requiring hospitalization or surgical interventions. DM was independently associated with hospitalization (OR 1.47, 95% confidence interval [CI] 1.05-2.06) and need for further surgical intervention (OR 3.0, 95% CI 2.03-4.46). Besides, chronic use of topical and systemic steroid as well as topical antiglaucoma agents were also related to hospitalization and need for further operation. Local risk factors such as eye trauma (OR 2.0, 95% CI 1.26-3.05), previous ocular surgery (OR 3.4, 95% CI 1.46-7.96), dry eye (OR 3.3, 95% CI 2.20-5.10), and blepharitis (OR 2.8, 95% CI 1.53-5.06) were linked with need for surgical interventions.

• **HEALTH CARE EXPENDITURE:** Health care expenditure depended on the disease severity. Although the incidence rate was higher among younger adults, older adults represented the larger proportion of health care cost. Older adults have more comorbidities and poorer immunity than their younger counterparts. This increases their disease severity and can result in hospitalization and surgical interventions.

• **LIMITATIONS:** This study had several limitations. First, the incidence of microbial keratitis may have been underestimated owing to our strict inclusion criteria. To exclude mild and sterile keratitis, we used a combination of diagnostic codes for corneal ulcers and omitted cases with only 1 clinic visit. Patients with microbial keratitis whose prescriptions were not covered by insurance were also excluded. Second, expenditures owing to microbial keratitis may also have been underestimated. We only included hospitalized patients with a primary diagnosis of microbial keratitis, thus overlooking microbial keratitis patients with other primary diseases. Third, contact lens wearers were difficult to directly identify in the Taiwanese health care system data because of the low coding rate of contact lens–related disease; this may have prevented us from revealing the importance of contact lens wear among patients with microbial keratitis. Therefore, we collected domestic sales data of contact lenses during this period and investigated previous related studies in Taiwan to indirectly demonstrate the positive relationship between microbial keratitis and contact lens use. Fourth, diagnostic codes may have been inconsistent with patients' clinical charts. Nevertheless, to verify the Taiwan NHI system, the Taiwan National Health Administration frequently assesses consistency between claims data and medical charts and evaluates whether patients have received a standard protocol of examinations to confirm their diagnoses. Therefore, the diagnoses in our database were of high accuracy. Fifth, owing to the absence of microbiological data in the NHIRD, the definite diagnosis of microbial keratitis was not possible. However, we adopted strict inclusion criteria to accurately enroll patients with microbial keratitis. Finally, bilateral microbial keratitis cannot be excluded from this study; but bilateral cases were so few that they had negligible impact on the overall results.

The strengths of the current study were its large sample size and comprehensive data, representing the whole of the Taiwanese population because of the wide coverage of the dataset. This study demonstrated a real trend in the incidence because we used the same method for all years, thus averaging periods of under- and overdiagnosis. The epidemiologic data of microbial keratitis in this study may be useful for ophthalmologists in clinical practice and research in Taiwan.

This is the first population-based report on microbial keratitis in Taiwan, and it provides useful generalized information about the demographics and estimated burden of infectious keratitis in Taiwan during the preceding decade. DM is a crucial risk factor for microbial keratitis. Despite the increasing prevalence of infectious keratitis among younger patients, older adults consumed the larger share of health care expenditure. This study revealed that older patients who use steroids and those with ocular and systemic comorbidities are more likely to have more severe disease characteristics. Therefore, ophthalmologists should perform careful evaluation of such patients.

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