Age Distribution of Various Corneal Diseases in China by Histopathological Examination of 3112 Surgical Specimens

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PURPOSE. To analyze the age distribution of corneal disease in China by histopathological examination.

METHODS. A retrospective histopathological analysis of the prevalence and age distribution of corneal disease was performed on corneal specimens from 3112 patients who underwent corneal surgery between 2001 and 2012 in the Henan Eye Institute.

RESULTS. Infectious keratitis (2212 specimens, 71.08%) was the most common corneal disease. The distribution of age groups was significantly higher after age 30 (16.29%), reaching a peak by age 40 (22.04%) and remaining high until age 59 (21.05%, $P < 0.01$). The highest age-specific percentage of corneal infection was between the ages of 50 and 59 (83.21%, $P < 0.01$). Noninfectious corneal diseases occurred mainly in the age range of 10 to 19 years (42.47%) and 20 to 29 years (40.78%). Between the ages of 10 and 19, the leading pathologic diagnosis was keratoconus, accounting for 21.29% of cases. In patients aged 80 and older, the most common noninfectious corneal diseases were Terrien-marginal degeneration (8.33%) and Mooren's ulcer (4.17%). The highest incidence of corneal tumor was seen between the ages of 0 and 9 years (65.83%) and age 80 and older (45.86%; $P < 0.01$).

CONCLUSIONS. The age distribution of corneal diseases in the Chinese population is distinct from other countries. The corneal diseases tend to increase in prevalence in middle age, especially for infectious corneal disease. The prevalence of corneal tumor is high in early and late life. Corneal degenerative disease occurs predominately in seniors.

Keywords: age, corneal disease, histopathology, infection, tumor

Corneal disease is one of the most prevalent eye diseases and also is a major contributor to vision loss and blindness. Studies from past decades on the epidemiology of corneal disease show that most published data about the incidence or natural history of corneal disease is likened to the factors of population and geographic variation.¹⁻³ In terms of the distribution of age with corneal disease, it is hard to find a large scale of investigations that focus on the study of the relevance of age to corneal disease, especially by histopathological analysis that can be used to identify infectious pathogens and establish differential diagnoses.¹⁻⁴ The report by Godeiro et al.⁵ described an epidemiology characteristic of corneal diseases from human corneal specimens in North America; however, the details of the age-related distribution of corneal disease was not included in the report. In addition, a histological analysis of these kinds of data in the Chinese population has not been published. In the current study, we sought to evaluate the relevance of epidemiology features of age to corneal diseases in Chinese individuals by the approach of histopathological analysis. A total of 3112 corneal specimens

were included in the study. All patients were seen at Henan Eye Institute between January 2000 and August 2012. To the best of our knowledge, this is the largest retrospective report of the relationship between age and corneal disease using histopathological analysis.

PATIENTS AND METHODS

Patients

The Institutional Review Board of the Henan Eye Institute approved our use of human corneal specimens. All procedures conformed to the Declaration of Helsinki for research involving human subjects.

The 3112 corneal specimens were collected for retrospective histological analysis after surgery, which included penetrating keratoplasty, anterior lamellar keratoplasty, and lamellar resection, as well as evisceration and enucleation. All surgeries were performed by corneal specialists at the Henan Eye Institute between January 2000 and August 2012.

TABLE 1. Distribution by Corneal Disease Type ($n = 3112$)

Corneal Disease	Number of Cases	%
Infectious corneal disease	2212	71.08
Noninfectious corneal disease	637	20.47
Tumor	263	8.45

Of the 3112 corneal disease cases, 2212 (71.08%) were infectious corneal disease, 637 (20.47%) were noninfectious corneal disease, and 263 (8.45%) were tumor.

Tissue Sample Processing

Corneal specimens were fixed in 10% buffered neutral formaldehyde and embedded in paraffin. Paraffin sections (3 μ m) were stained with hematoxylin and eosin for general histology analysis. Periodic acid-Schiff and Grocott-Gomori's methenamine silver staining were performed to identify hyphae and spores for fungal infection. Giemsa staining was used to identify bacterial infection.

Histopathological Examination

All of the stained corneal sections were reviewed by two ocular pathologists under light microscopy. Histological changes in all layers of the cornea were observed. The presence of fungal infection was confirmed by the existence of hyphae and spores. Bacterial infection was confirmed by the existence of bacterium under oil immersion microscope and Giemsa staining. *Acanthamoeba* keratitis was confirmed by the existence of *Acanthamoeba* cysts or trophozoites. Diagnosis of viral infection was based on the finding of a mixed infiltrate composed of chronic inflammatory cells, including lymphocytes, neutrophils, and mononuclear phagocytes. Corneal dystrophy, degeneration, and tumor were diagnosed according to the standards described by Yanoff and Sassani.⁶

Statistical Analysis

We used χ^2 analysis to test for statistical significance among various groups. All data were weighted to reflect the age distribution of the population from age 0 to 80 and older.

RESULTS

Histopathologic review of the 3112 corneal specimens showed that the highest prevalence of corneal disease was infection (2212 specimens, 71.08%; Table 1), and the second most common was noninfectious corneal disease (637 specimens,

20.47%) followed by corneal tumor (263 specimens, 8.45%). The prevalence of any corneal disease by age was low in early and later life stages. Of the corneal disease patients, fewer than 8% were aged 20 or younger (5.85% for those aged 0–9 and 7.04% for those aged 10–19), only 4.53% were aged 70 to 79 years, and only 1% were 80 and older. Most of the patients with corneal disease were aged between 30 and 59 years, with 16.29% at 30 to 39 years, peaking at 22.04% for ages 40 to 49, and remained high at ages 50 to 59 (21.05%). Statistical analysis showed that the distribution of corneal disease across age groups was significant (Table 2).

Of the 3112 corneal specimens, 2212 (71.08%) were found to have infectious corneal disease (Table 1). The most common infectious corneal disease was fungal keratitis (1242, 56.15%), followed by virus infection (238, 10.76%), bacterial infection (166, 7.5%), *Acanthamoeba* infection (23, 1.04%), and combined fungal and bacterial infection (29, 1.31%; Table 3). The age-specific prevalence of infectious corneal disease is shown in Table 4. Infectious corneal disease occurred in patients as young as 1 year old and in those 80 or older. The observed prevalence of infectious corneal disease rose from 17.58% among those aged 0 to 9 years to 54.96% among those aged 20 to 29 and to 81.49% among those aged 40 to 49 years. The highest prevalence of corneal infection (83.21%) was among patients between 50 and 59 years of age. Although the prevalence was somewhat reduced after age 69, it remained substantially high (68.09% for age 70–79). In comparing the prevalence of corneal infection among the various age groups, the differences were significant (Table 4; $P < 0.001$).

Of 2212 corneal specimens found to exhibit infectious diseases, 1242 (56.15%) were determined to be fungal keratitis, of which 922 (74.24%) occurred in patients aged 30 to 59 years (Table 4). The peak age for fungal keratitis ranged from 40 to 49 years (51.5%). The prevalence of fungal keratitis gradually reduced to 28.37% in those 70 to 79 and 16.67% in those aged 80 or older. In the youngest patients (ages 0–9), the rate of fungal keratitis (4.95%) was much lower than that of the groups older than 70 years ($P < 0.001$).

Bacterial infection was found in 166 (7.5%) corneal specimens of 2212 infected cases (Table 3). The prevalence of bacterial infection increased from 4.95% for patients aged 0 to 9 years to 6.31% by age 30 to 39. Of note, the prevalence of bacterial infection rose to 8.89% among patients aged 60 to 69 years and reached its peak (11.35%) among those aged 70 to 79 years.

Of the 2212 infectious corneal disease cases, 238 cases (10.76%) were caused by virus (Table 3). The lowest rate (1.10%) of viral infection was found among patients aged 0 to 9 years. The prevalence rose sharply to 11.42% among those

TABLE 2. Distribution of Corneal Disease by Age Group ($n = 3112$)

Age Group, y	Total n (%)	Infectious Corneal Disease		Noninfectious Corneal Disease		Tumor	
		n	%	n	%	n	%
0–9	182 (5.85)	32	17.58	31	17.03	119	65.38
10–19	219 (7.04)	86	39.27	93	42.47	40	18.26
20–29	282 (9.06)	155	54.96	115	40.78	12	4.26
30–39	507 (16.29)	404	79.68	100	19.72	3	0.59
40–49	686 (22.04)	559	81.49	117	17.06	10	1.46
50–59	655 (21.05)	545	83.21	92	14.05	18	2.75
60–69	416 (13.37)	326	78.37	64	15.38	26	6.25
70–79	141 (4.53)	96	68.09	21	14.89	24	17.02
80+	24 (0.77)	9	37.50	4	16.67	11	45.83
χ^2 P value	<0.001	<0.001		<0.001		<0.001	

Of the 3112 corneal disease cases, 182 (5.85%) were in patients aged 0 to 9 years and 686 (22.04%) were 40 to 49 years. Of the 219 corneal disease cases in the 10- to 19-year age group, 86 (39.27%) were infectious, 93 (42.47%) were noninfectious, and 40 (18.26%) were tumor.

TABLE 3. Prevalence of Infectious Corneal Disease

Corneal Infection	Number of Cases	%
Fungus	1242	56.15
Unidentified	514	23.24
Virus	238	10.76
Bacteria	166	7.50
<i>Acanthamoeba</i>	23	1.04
Fungus combined with bacteria	29	1.31
Total	2212	100.00

Of the 2212 cases with infectious corneal disease, 56.15% were fungus, 23.24% were unidentified, 10.76% were virus, 7.5% were bacterial, 1.04% were *Acanthamoeba*, and 1.31% were fungal combined with bacteria.

aged 10 to 19 years and remained between 7.09% and 9.62% from age 20 to age 79. By age 80 and older, the prevalence of viral infection dropped to 4.17%. The differences in the prevalence of viral infection among various age groups were significant (Table 4; $P < 0.020$).

The lowest prevalence of corneal infection found in the current study was *Acanthamoeba* (23 cases, 1.04%; Table 3). From age 20 to 69, the prevalence of *Acanthamoeba* infection was less than 2%. The highest rate (4.17%) of *Acanthamoeba* infection was observed in patients aged 80 or older, with a significant difference as compared with other age groups (Table 4; $P < 0.04$).

Notably, there were 514 (23.24%) cases diagnosed as unidentified corneal infection (Table 3). The lowest prevalence of unidentified corneal infection was among those aged 0 to 9 years (12, 6.59%; Table 4). The prevalence of unidentified infection increased in those aged 10 or older, reaching a peak (20.43%) among those aged 60 to 69 years ($P < 0.001$). In the remaining age groups, the variation in the prevalence of unidentified corneal infection was not significant (Table 4).

Noninfectious corneal diseases (637) accounted for 20.47% of the total cases of corneal disease included in the study (Table 1). The most common noninfectious corneal disease was corneal leucoma (22.61%), followed by keratoconus (15.38%), Terrien-marginal degeneration (9.11%), corneal dystrophy (7.85%), and chemical burn (7.38%; Table 5). The largest portion of noninfectious corneal disease occurred in the age range of 10 to 29 years, including 42.47% among those aged 10 to 19 years and 40.78% among patients aged 20 to 29 years, showing a significant difference as compared with other age groups (Table 6; $P < 0.01$). Corneal degeneration (3.90%), chemical burn (3.55%), and corneal dystrophy (3.19%) all occurred among those aged 20 to 29 years (Table 6; $P < 0.01$). Other common noninfectious corneal diseases, such as staphyloma (1.83%), keratoconus (21.29%), and corneal

TABLE 5. Prevalence of Noninfectious Corneal Diseases

Noninfectious Corneal Disease	Number of Cases	%
Bullous keratitis	30	4.71
Corneal degeneration	42	6.59
Chemical burn	47	7.38
Corneal dystrophy	50	7.85
Foreign body	4	0.63
Corneal melting	4	0.63
Neovascularization	16	2.51
Corneal opacity after keratoplasty	39	6.12
Perforating injury	11	1.73
Staphyloma	16	2.51
Keratoconus	98	15.38
Mooren's ulcer	50	7.85
Terrien-marginal degeneration	58	9.11
Thermal burn	28	4.40
Corneal leucoma	144	22.61
Total	637	100.00

Of the 637 cases with noninfectious corneal disease, 22.61% were corneal leucoma, 15.38% were keratoconus, and 9.11% were Terrien-marginal degeneration.

leucoma (10.96%) occurred in younger age groups (ages 10–19). The highest incidence of perforating injury (1.65%) was observed among those aged 0 to 9 years. In contrast, Mooren's ulcer (4.17%) and Terrien marginal degeneration (8.33%) occurred in those aged 80 and older (Table 6; $P = 0.08, 0.18$, respectively).

Among the 3112 cases included in the study, the most common corneal tumor was corneal dermoid (58.17%), followed by carcinoma in situ (10.65%), squamous cell hyperplasia of cornea (6.46%), nevus (5.70%), and atypical hyperplasia (5.32%; Table 7). There was a distinct age distribution for corneal tumors. Of the 263 cases with corneal tumors, 119 (45.2%) cases were found among patients aged 0 to 9 years; the rest of the corneal tumors (144 cases, 54.8%) were observed among those aged 10 and older (Table 8; $P < 0.02$). The age-specific incidence of corneal tumor dropped sharply from 65.38% (ages 0–9) to 4.26% (ages 20–29); however, the incidence rose again at age 70 (17.02%) and subsequently increased to 45.83% by age 80 and older (Table 8; $P < 0.001$). Most corneal tumors were corneal dermoid tumors (62.61%), which occurred among patients aged 0 to 9 (Table 8; $P < 0.001$). Other corneal tumors, such as atypical hyperplasia (2.84%), occurred in patients aged 70 to 79; carcinoma in situ (25%), corneal squamous cell (12.5%), and squamous cell papilloma (8.33%) occurred in patients aged 80 and older (Table 8; $P < 0.001$).

TABLE 4. Distribution of Corneal Infectious Disease by Age Group

Corneal Infection	Age Group, n (%)									P
	0–9	10–19	20–29	30–39	40–49	50–59	60–69	70–79	80+	
Fungal	9 (4.95)	34 (15.53)	76 (26.95)	234 (46.2)	353 (51.5)	335 (51.2)	157 (37.7)	40 (28.37)	4 (16.67)	0.001
Unidentified	12 (6.59)	23 (10.5)	43 (15.25)	87 (17.16)	106 (15.5)	127 (19.4)	85 (20.43)	28 (19.86)	3 (12.5)	0.001
Virus	2 (1.10)	25 (11.42)	20 (7.09)	39 (7.69)	54 (7.87)	47 (7.18)	40 (9.62)	10 (7.09)	1 (4.17)	0.02
Bacterial	9 (4.95)	4 (1.83)	9 (3.19)	32 (6.31)	36 (5.25)	23 (3.51)	37 (8.89)	16 (11.35)	0	0.001
<i>Acanthamoeba</i>	0	0	4 (1.42)	8 (1.58)	5 (0.73)	4 (0.61)	1 (0.24)	0	1 (4.17)	0.04
Fungal and bacterial combined	0	0	3 (1.06)	4 (0.79)	5 (0.79)	9 (1.37)	6 (1.44)	2 (1.42)	0	0.50
Total	32 (17.58)	86 (39.27)	155 (55.0)	404 (79.7)	559 (81.5)	545 (83.2)	326 (78.4)	96 (68.09)	9 (37.5)	0.001

P is the χ^2 P value, n is the number of cases in each group, and % is the percentage of cases in each group among the whole group.

TABLE 6. Age Distribution in Noninfectious Corneal Disease

Noninfectious Diseases	Age Group, <i>n</i> (%)									<i>P</i>
	0–9	10–19	20–29	30–39	40–49	50–59	60–69	70–79	80+	
Bullous keratitis	1 (0.55)	0	0	4 (0.79)	4 (0.58)	5 (0.76)	10 (2.4)	5 (3.55)	1 (4.17)	0.001
Corneal degeneration	2 (1.1)	2 (0.91)	11 (3.9)	4 (0.79)	4 (0.58)	10 (1.53)	8 (1.92)	1 (0.71)	0	0.009
Chemical burn	0	4 (1.83)	10 (3.55)	10 (1.97)	19 (2.77)	2 (0.31)	2 (0.48)	0	0	0.001
Corneal dystrophy	4 (2.2)	5 (2.28)	9 (3.19)	8 (1.58)	9 (1.31)	7 (1.07)	7 (1.68)	1 (0.71)	0	0.41
Foreign body	0	0	2 (0.71)	2 (0.39)	0	0	0	0	0	0.11
Corneal melting	0	0	0	1 (0.2)	1 (0.15)	0	2 (0.48)	0	0	0.63
Neovascularization	1 (0.55)	1 (0.46)	1 (0.35)	6 (1.18)	4 (0.58)	3 (0.46)	0	0	0	0.46
Corneal opacity after keratoplasty	2 (1.1)	0	4 (1.42)	4 (0.79)	9 (1.31)	12 (1.83)	6 (1.44)	2 (1.42)	0	0.55
Perforating injury	3 (1.65)	1 (0.46)	0	3 (0.59)	1 (0.15)	1 (0.15)	1 (0.24)	1 (0.71)	0	0.12
Staphyloma	1 (0.55)	4 (1.83)	4 (1.42)	1 (0.2)	4 (0.58)	2 (0.31)	0	0	0	0.04
Keratoconus	1 (0.55)	48 (21.29)	32 (11.35)	8 (1.58)	5 (0.73)	2 (0.31)	2 (0.48)	0	0	0.001
Mooren's ulcer	0	0	4 (1.42)	9 (1.78)	18 (2.62)	8 (1.22)	6 (1.44)	4 (2.84)	1 (4.17)	0.08
Terrien-marginal degeneration	2 (1.1)	2 (0.91)	7 (2.48)	5 (0.99)	12 (1.75)	16 (2.44)	9 (2.16)	3 (2.13)	2 (8.33)	0.18
Thermal burn	0	2 (0.91)	7 (2.48)	10 (1.97)	4 (0.58)	4 (0.61)	1 (0.24)	0	0	0.18
Corneal leucoma	14 (7.69)	24 (10.96)	24 (8.51)	25 (4.93)	23 (3.35)	20 (3.05)	10 (2.4)	4 (2.84)	0	0.007
Total	31 (17.03)	93 (42.47)	115 (40.78)	100 (19.72)	117 (17.06)	92 (14.05)	64 (15.38)	21 (14.89)	4 (16.67)	<0.01

P is the χ^2 *P* value, *n* is the number of cases in each group, and % is the percentage of cases in each group among the whole group.

DISCUSSION

Corneal disease is one of leading causes of blindness in the world. This report summarizes the prevalence and age distribution of corneal diseases in a large patient population in Henan, a Chinese province with more than 100 million inhabitants. The epidemiological tendencies of corneal disease may vary among different age groups^{2–4,7–9}; therefore, information gathered by a comprehensive study is important for establishing appropriate diagnostic and therapeutic strategies. We reported the prevalence of corneal disease and age-related distribution of corneal diseases in 3112 specimens by retrospective histopathologic analysis.

Our data were derived from specimens collected over a period of 10 years in the Henan Eye Institute. We found the most common corneal disease (71.08%) was infectious keratitis, followed by noninfectious corneal disease (20.47%) and corneal tumor (8.45%). Most corneal infection was caused by fungus, virus, bacteria, and then protozoa in the current study. As others have noted, the significantly increased incidence of fungal keratitis may be due to the abuse of antibiotics and corticosteroids and ocular trauma with

vegetative material.^{2,3} In reviewing our patient histories, we found that most of our cases diagnosed with fungal infection were related to agricultural work; therefore, fungal keratitis was largely associated with farms.^{10–12} China is a developing country in which farmers are still the largest part of the population overall. This fact may help to explain why the incidence of fungal keratitis is higher in China. From our study and other previously published reports, it is clear that the prevalence of fungal keratitis is closely related to the developmental status of the economy and medical care. In less-developed countries, the incidence of fungal keratitis is beyond 30%,^{11–13} whereas in developed countries, the corresponding incidence of fungal keratitis is between 6% and 20% of all microbial keratitis cases.^{11,14} The major risk factor for infectious keratitis in the United States and the United Kingdom is contact lens application.^{11,14} We noted that the age of the patients with corneal diseases varied from 1 to 80 years. The age groups with the most prevalent corneal disease were 40 to 49 years (686 cases, 22.04%), followed by 50 to 59 years (655 cases, 21.05%) and 30 to 39 years (507 cases, 16.29%). Among the 3112 specimens, 1848 (59.38%) were obtained from patients aged 30 to 59. These specimens showed a significantly different prevalence of corneal disease compared with specimens from other age groups ($P < 0.001$). The lowest prevalence of corneal disease was in those 80 and older, accounting for only 0.77%. Compared with the other age groups, the difference was significant ($P < 0.001$). Our results are different from a survey showing that the highest prevalence of corneal blindness is in individuals 50 to 94 years living in rural areas.¹⁵ The difference between previous publications and our data in peak age of corneal disease may reflect differences in geography, population, living conditions, and the methods of diagnosis. Importantly, the diagnosis of corneal diseases was established by corneal specialists and ocular pathologists in our study; therefore, the data are much more reliable. Our results suggest that more attention should be paid to eye care for the population of the age groups with a higher prevalence of corneal disease.

Our retrospective study found that the corneal infection rate increased with increasing age. The age range with the highest prevalence of corneal infection was 50 to 59,

TABLE 7. Prevalence of Various Corneal Tumors

Corneal Tumor	Number of Cases	%
Atypical hyperplasia	14	5.32
Carcinoma in situ	28	10.65
Melanoma	2	0.76
Nevus	15	5.70
Corneal squamous cell carcinoma	14	5.32
Corneal dermoid	153	58.17
Implanted cyst	3	1.14
Hemangioma of granulation tissue	4	1.52
Squamous cell hyperplasia of cornea	17	6.46
Squamous cell papilloma	13	4.94
Total	263	100.00

Of the 263 cases with corneal tumor, the following were the most prevalent: 58.17% were corneal dermoid, 10.65% were carcinoma in situ, and 6.46% were squamous cell hyperplasia of cornea.

TABLE 8. Distribution of Corneal Tumor by Age Group

Corneal Tumor	Age Group, n (%)									P
	0–9	10–19	20–29	30–39	40–49	50–59	60–69	70–79	80+	
Atypical hyperplasia	0	0	0	0	2 (0.29)	3 (0.46)	5 (1.2)	4 (2.84)	0	0.001
Carcinoma in situ	0	0	0	0	3 (0.44)	4 (0.61)	6 (1.44)	9 (6.38)	6 (25)	0.001
Melanoma	0	0	0	0	1 (0.15)	1 (0.15)	0	0	0	0.95
Nevus	2 (1.10)	6 (2.74)	1 (0.35)	1 (0.20)	2 (0.29)	2 (0.31)	0	1 (0.71)	0	0.001
Corneal squamous cell carcinoma	0	0	0	0	0	2 (0.31)	6 (1.44)	3 (2.13)	3 (12.50)	0.001
Corneal dermoid	114 (62.61)	31 (14.16)	8 (2.84)	0	0	0	0	0	0	0.001
Implanted cyst	1 (0.55)	0	2 (0.71)	0	0	0	0	0	0	0.06
Hemangioma of granulation tissue	0	0	0	1 (0.20)	1 (0.15)	0	2 (0.48)	0	0	0.39
Squamous cell hyperplasia of cornea	2 (1.10)	1 (0.46)	1 (0.35)	1 (0.20)	1 (0.15)	5 (0.76)	4 (0.96)	2 (1.42)	0	0.40
Squamous cell papilloma	0	2 (0.91)	0	0	0	1 (0.15)	3 (0.72)	5 (3.55)	2 (8.33)	0.001
Total	119 (65.38)	40 (18.26)	12 (4.26)	3 (0.59)	10 (1.46)	18 (2.75)	26 (6.25)	24 (17.02)	11 (45.83)	0.001

P is the χ^2 P value, n (%) is the age-specific number of cases and percent, where the denominator is the number of corneal cases in that age group (i.e., there were 119 [65.38%] of 182 tumor cases in the 0–9 age group).

accounting for 83.21% of all corneal disease in that age group followed by age ranges of 40 to 49, 30 to 39, 60 to 69, and 70 to 79. In patients aged 80 or older, only 37.5% of corneal disease was caused by infection. The differences in the prevalence of corneal infection among various age groups were significant ($P < 0.001$). There was a higher rate of corneal infection in older people compared with those aged 0 to 9 years. The susceptibility of seniors to infections is likely related to systemic and ocular characteristics, such as reduced systemic and local innate immunity to infection, reduced anti-infection factors from the lacrimal gland, fragility of the corneal epithelium, and reduced corneal sensitivity.^{16–19}

Our results showed that the highest prevalence of fungal infection was in the middle age group (40–59 years). The incidence of fungal infection in those aged 40 to 49 and 50 to 59 was 51.46% and 51.15%, respectively. Most of our patients with fungal infection were from farming areas, probably because the great majority of inhabitants from rural areas belong to a working class with a substantially high rate of exposure to fungal infection. Our results are different from the findings in India, where most fungal corneal infection occurred between the ages of 16 and 49.^{7,20}

In the current study, the second most common histopathologic diagnosis of corneal infection was herpetic keratitis. Ocular herpetic scar and recurrence of herpes keratitis (especially recurrent interstitial herpetic keratitis) are the most common reasons for corneal transplantation. Previous studies reported that herpetic keratitis was considered to be the most common corneal disease leading to corneal transplantation in developed countries in the 1990s, which is higher than that in our study.^{21,22}

The peak age for viral infection appeared to be the age range of 10 to 19 (11.42%) and then the infection sustained for rest of life. Possibly most of the virus infections were due to herpetic simplex virus, therefore the infection may last for life because of the latent infection establishment in trigeminal ganglion. Notably, a report from New Zealand demonstrated a higher prevalence of viral keratitis at age 54.²³ The differences between previous reports and our result may be related to the difference of age structure in the general population, living areas, and the standard of diagnosis.

Bacterial infection was the third most common corneal infection in the current study; 166 cases of bacterial keratitis

were found and accounted for 7.5% of all infectious keratitis, which is higher than that found in an epidemiological study in Canada (all of infectious keratitis 5.6%),⁵ but is lower than the reports by Bharathi et al.²⁴ from India (by epithelial cell scraping), which was 34.4% in all corneal infections. The difference of incidence of bacterial keratitis may due to different times the corneal specimens were collected, the geography, and population. The lower incidence of bacterial infection in China as compared with India may be due to improved living conditions, patient education, disease prevention, and the easy access to medical care, especially access to ophthalmologists for prompt treatment of infected corneas. The range of peak age for bacterial corneal infection was 70 to 79 (11.35%), followed by 60 to 69 (8.89%), suggesting that seniors are vulnerable to bacterial infection in the cornea.

Acanthamoeba keratitis was the fourth most common infectious keratitis in our series, accounting for 1.04% ($n = 23$). Bharathi et al.²⁴ from India reported that in 3183 eyes with infectious keratitis, 33 (1.04%) were diagnosed with *Acanthamoeba* keratitis.²⁴ The incidence of *Acanthamoeba* keratitis in the present study was similar to a report by Bharathi et al.²⁴ although a corneal scrap was used for the detection of infectious pathogens in their study. Among patients with infection, the highest incidence of *Acanthamoeba* corneal infection (4.17%) was seen in senior patients, aged 80 or older. Most likely a lowered immunity against bacterial or *Acanthamoeba* infections in later life is the major reason for this susceptibility to microbial infection.

In our retrospective study, we found 514 specimens (23.24%) with unidentified infectious keratitis. Godeiro et al.⁵ from Canada also reported that they were unable to determine the pathogenic organism in 45.6% of their keratitis cases by histopathologic examination of the infected corneas. There are a number of possible explanations as to why the cause of corneal infection could not be defined by the histopathologic methods. First, a fungal or bacterial infection could not be completely excluded even with a negative PAS or Giemsa staining because the hyphae or bacteria may be significantly decreased or absent after long-term application of antifungal or antibacterial treatment. Second, there was a possibility of a false-negative result. And third, the rate of missed diagnoses could occur in a clinical study.

The unidentified corneal infection could be found in all age groups included in this study. Incidence of unidentified corneal infection increased starting from the age group 20 to 29 (15.25%) and sustained until age 70 to 79 (19.86%), with the peak of unidentified corneal infection in the age group 60 to 69 (20.43%). Again, the higher prevalence of corneal infection in the senior reflects the susceptibility to microbial infection.

The most common histopathologic finding in noninfectious corneal disease was corneal leucoma (after wound or infections), accounting for 22.61% of more than 637 specimens of noninfectious corneal disease, followed by keratoconus, Terrien-marginal keratitis, Fuch's corneal dystrophy, Mooren's ulcer, and chemical burn.

Of interest, the histopathologic finding in our study was that only 98 cases (15.38%) of keratoconus were demonstrated. A large investigation reported by Siganos et al.²⁵ from Greece showed that of the 2233 eyes included in their cases, 580 eyes (26%) were diagnosed with keratoconus. In a 10-year period of study in Canada, Sheldon et al.²⁶ showed one of the top five corneal diseases treated by corneal transplantation is keratoconus. The lower incidence of keratoconus in the present study may be related to racial difference and the relatively higher incidence of infectious corneal diseases in China.

We observed a strong association between age and noninfectious corneal diseases. Most cases of corneal degeneration, corneal dystrophy, staphyloma, keratoconus, and corneal leucoma occurred before age 30, whereas bullous keratitis, Mooren's ulcer, and Terrien marginal degeneration occurred predominately after the age of 80. Our findings are consistent with data from a previous epidemiological study by Edwards et al.,²³ who showed that most of the keratoconus diagnosed in New Zealand occurred by the age of 31.8. Staphyloma is usually caused by infection or traumatic corneal diseases in China rather than by genetic factors. The early occurrence of corneal leucoma may be related to the patients' poor self-protection and lack of eye care. The higher prevalence of degenerative corneal diseases, such as Mooren's ulcer and Terrien marginal degeneration, in seniors is more likely related to autoimmune response, which reflects abnormal homeostasis of immunosuppression systemically or locally in elderly persons.²⁷⁻²⁹

Our findings regarding the age distribution of Mooren's ulcer are consistent with the report by Srinivasan et al.³⁰ from India, which showed that most cases presenting with Mooren's ulcer were 65 years or older.

In our study, corneal tumor (8.45%) was the third most common corneal disease diagnosed by histopathology. The most common subtype of corneal tumor (58.17%) was dermoid. The incidence is far beyond other subtypes of corneal tumors, including carcinoma in situ (10.65%). The incidence of corneal dermoid was much higher than the incidence (29%) reported by Sunderraj et al.³¹ from India. Again our data suggest that the incidence of corneal disease is variable according to population and geographic differences.

In the present study, we found an association between age and prevalence of corneal tumor. The highest prevalence of tumor was in patients 0 to 9 years (65.38%), followed by those 80 or older (45.83%). From age 20 to 60, the prevalence of corneal tumor is relatively low. The most common corneal tumor in the younger age group (0-9 years) is corneal dermoid, accounting for 74.5% of the total for corneal dermoid in all age groups. In contrast, only 25.5% of corneal dermoid tumors were diagnosed in persons 10 or older. These findings agree with those reported by Watts et al.³² in Toronto, which showed that most corneal dermoid tumors occur during childhood. In our histopathologic analysis, the highest prevalence of malignant corneal tumors, such as carcinoma

in situ (25%), corneal squamous cell (12.50%), and squamous cell papilloma (8.33%) occurred in patients 80 or older.

In the current study, we found that the most common corneal diseases are corneal infections (especially fungus infection), followed by noninfectious corneal disease and corneal tumor. The highest prevalence of severe corneal disease requiring surgical intervention occurs in middle age and this age group is vulnerable to infectious corneal disease. The most common age for the occurrence of corneal tumor is in the first decade of life, whereas most degenerative corneal disease occurs in seniors. These data would be helpful in the establishment of the strategies of health care, especially eye disease treatment and blindness prevention.

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