Corneal Blindness in Asia: A Systematic Review and Meta-Analysis to Identify Challenges and Opportunities

Tu M. Tran, MSc, Huong Duong, MD,†‡ Clemence Bonnet, MD,†§ Ashkan Kashanchi, BS,¶ Arjun Buckshey, MD,† and Anthony J. Aldave, MD†*

Purpose: To describe the causes and prevalence of moderate-to-severe visual impairment (MSVI) and blindness from corneal diseases, as well as corneal transplantation across Asia.

Methods: A meta-analysis of the published literature to identify population-based surveys conducted from 2008 to 2019 in 22 Asian countries regarding the prevalence and causes of MSVI and blindness from corneal disease, and a review of national corneal transplant data and eye bank statistics.

Results: A total of 5307 records were screened to identify 57 reports that were used to estimate a prevalence of MSVI and blindness caused by corneal diseases in Asia of 0.38% (95% confidence interval, 0.29%–0.48%). The most frequent corneal diseases were infectious keratitis, trauma, and pseudophakic bullous keratopathy. As expected, these represented the most common indications for corneal transplantation, although the percentages in each country differed based on the level of economic development, with pseudophakic bullous keratopathy being the most common indication in countries with higher gross national income per capita. Despite this, endothelial keratoplasty is not the most commonly performed form of corneal transplantation in any Asian country and represents only a small percentage of keratoplasty procedures performed in most countries.

Conclusions: The prevalence of MSVI and blindness from corneal disease in Asia is approximately 0.4%, with a nearly 20-fold difference in the national prevalence across the region. The indications for keratoplasty, reflective of the causes of corneal dysfunction, also vary, more so according to the gross national income than to geographic location, and only a few Asian countries have rates of corneal transplantation above international means.

Key Words: corneal blindness, Asia, epidemiology, eye care services, corneal surgeon training, eye bank, corneal transplant

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Of the 7.33 billion people alive in 2015, an estimated 36 million were blind and 217 million people had moderate-to-severe visual impairment (MSVI).[1] Blindness and visual impairment affect not only the quality of life of the affected individual but also educational attainment, economic, and employment opportunities, and increases the risk of all-cause mortality.[2] Corneal diseases in adults greater than 50 years is one of the leading causes of MSVI and blindness. The 2015 prevalence estimated globally was 4.2 million with most, 2.6 million, living in East, South, and Southeast Asia.[3,4]

Fifty-four percent of the world's population live in East, South, and Southeast Asia,[5] wherein the annual Gross Domestic Product (GDP) growth projected to year 2024 will be the highest globally at 4.6% to 7.3%,[6] a promising indicator that there will be expanded resources for the improvement of eye care delivery systems in these populations. The prevalence and causes of MSVI and blindness due to cornea conditions have been estimated at regional levels using the data generated by country-level rapid assessments of avoidable blindness surveys.[3] These country-level and regional estimates are critical in improving global policy and volume-based assessments, for example, VISION2020 targets, promotion of eye health within national governments, and coordination among international nongovernmental organizations. Country-specific estimates for corneal diseases causing MSVI and blindness have not been pooled specifically for Asia. However, these data are critical to determine the burden of corneal disease in a region, and thus, the need for the development of corneal recovery and distribution (both domestic and international) programs. In addition, this information is necessary to determine the number of corneal transplant surgeons and the types of keratoplasty procedures that they will need to be able to perform. This will not only facilitate planning of service delivery at the national level but also promote existing and new international tissue-sharing collaborations, especially important for countries that are not able to meet the domestic demand for corneal tissue.[7] Therefore, we aim to evaluate the prevalence and causes of MSVI and blindness due to corneal diseases in Asia, determine what is being done regarding the number and types of keratoplasty procedures being performed, discuss challenges to reducing the burden of vision loss secondary to

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From the *Department of Ophthalmology and Visual Neurosciences, University of Minnesota Medical School, Minneapolis, MN; †Stein Eye Institute, David Geffen School of Medicine at UCLA, Los Angeles, CA; ‡Department of Medicine, Division of Ophthalmology, University of Medicine and Pharmacy at Ho Chi Minh City, Ho Chi Minh City, Vietnam; §Cornea Department, Cochin Hospital, Paris Descartes University, Paris, France; and ¶Department of Ophthalmology, Saint Louis University School of Medicine, St. Louis, MO.
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Correspondence: Anthony J. Aldave, MD, Department of Ophthalmology, Stein Eye Institute, 100 Stein Plaza, UCLA, Los Angeles, CA 90095-7003 (e-mail: aldave@jsei.ucla.edu).

corneal diseases, and propose potential solutions based on ongoing initiatives in selected Asian countries.

MATERIALS AND METHODS

Search Methods and Data Acquisition

Two investigators (H.D. and T.M.T.) independently performed a literature search using a combination of search terms (cornea, blind, epidemiology, prevalence, keratoplasty, keratitis, and medical subject headings) and the following publicly accessible databases: PubMed, EMBASE, IAPB.org Web site, Rapid Assessment of Avoidable Blindness repository (http://raabdata.info/repository/), Google/Google Scholar, and ophthalmology journals not indexed in PubMed or EMBASE (see Table 1, Supplemental Digital Content 1, http://links.lww.com/ICO/B26). Cross references were attempted by locating studies cited by a particular study report and accessing the supplement table for epidemiologic data used by the Global Burden of Disease Vision Loss Expert Group.[3] If journal articles were not available for a specific country, the International Agency for the Prevention of Blindness Web site and the rapid assessment of avoidable blindness repository were accessed for original reports. Data on corneal procurement and transplantation were obtained by the authors from colleagues who have access to such data from internal reporting. National Eye Bank associations and Ministry of Health Web sites were used to access annual reports when needed and available.

Inclusion, Exclusion Criteria, and Assessment of Study Quality

Reports written in any language from 22 countries in Asia were considered. For burden of disease data, the inclusion criteria were as follows: (1) population-based with defined geographic coverage and cluster random sampling; (2) visual impairment for all causes reported with World Health Organization classification system preferred (MSVI defined as a presenting visual acuity $<6/18$ to $\geq 3/60$ in the better eye and blindness as a presenting visual acuity $<3/60$ in the better eye due to all causes and corneal diseases); (3) corneal disease diagnosed after examination by an ophthalmologist that could include opacities/scars due to any cause, infectious keratitis, keratopathy due to any cause, or phthisis bulbi secondary to corneal disease; and (4) enumerated respondents in surveys conducted between 2008 and 2018. Studies were excluded based on the following: (1) hospital or clinic-based sampling, (2) sampling exclusively of children from school-based cluster design, or (3) failure to report on corneal-specific causes of visual impairment.

Data Extraction and Statistical Analyses

For burden of disease data, extracted elements included the following: country, geographic areas enumerated, base population if available, sample size, response rate, and sample demographics (age range, mean, standard deviation, gender, rural/urban locality, literacy/education level, poverty/socioeconomic stratifications, and occupation). Age- and gender-standardized rates were used for the statistical analyses.

Of the 22 Asian countries, 12 had only 1 study report that was used to represent corneal disease burden, whereas the other 10 had 2 or more studies that enabled pooling of prevalence estimates. Because most studies enumerated individuals age 50 years and older, we used 40 years as a cutoff for case counts of corneal disease. Pooling of prevalence estimates by each country was achieved with *meta* command in STATA (StataCorp, College Station, TX) using a random effects model and double arcsine transformation to calculate standard errors.[8] A random effects model was deemed appropriate after using *metareg* regression function in STATA to rule out significant associations with study covariables, such as study period, response rate, and level of geographic representation (eg, subcity to nationwide). A mixed effects hierarchical regression model, where the country was the highest level and any subnational division was one level below, was fit to determine significant association ($P < 0.05$) with prevalence of visual impairment from corneal disease. Demographic variables, such as gross national income (GNI) per capita, age, gender, literacy rate, poverty rate, percent living in rural locality, agricultural employment, cataract surgical rate, and ophthalmologists per million population, were regressed on prevalence. The mean age of respondents in each survey, response rate, sample size, and underlying base population were used to adjust the model, and a stepwise elimination of significant covariables ($P < 0.05$) was performed. If the study's authors did not supply demographic statistics in their reports, World Bank, United Nations, International Agency for the Prevention of Blindness, and the country's national statistics office, such as the National Statistics Bureau of China, were used to acquire the data most relevant to the study period and specific administrative regions enumerated. The aforementioned statistical method for pooling prevalence proportions was used to determine the leading causes of corneal diseases using all known population-based studies focused on corneal diseases.

Separate from the systematic review, we combined data from the consortium study of Tan et al. with retrospective reviews from India, Nepal, and Vietnam to provide estimates of indications for and types of keratoplasty performed.[9–12] A generalized linear model was fit to the combined data set to determine significant associations ($P < 0.05$).

RESULTS

Search Results and Study Characteristics

For burden of disease data, a total of 5307 records were identified, of which 5173 were excluded after removing duplicates and screening abstracts and 86 excluded after full-text review using the previously described inclusion and exclusion criteria. However, 8 records were reincluded after careful consideration because there were no newer sources of data for these countries (Fig. 1). Ultimately, 57 reports were identified representing 67 population-based surveys from 22 countries contributing a combined sample

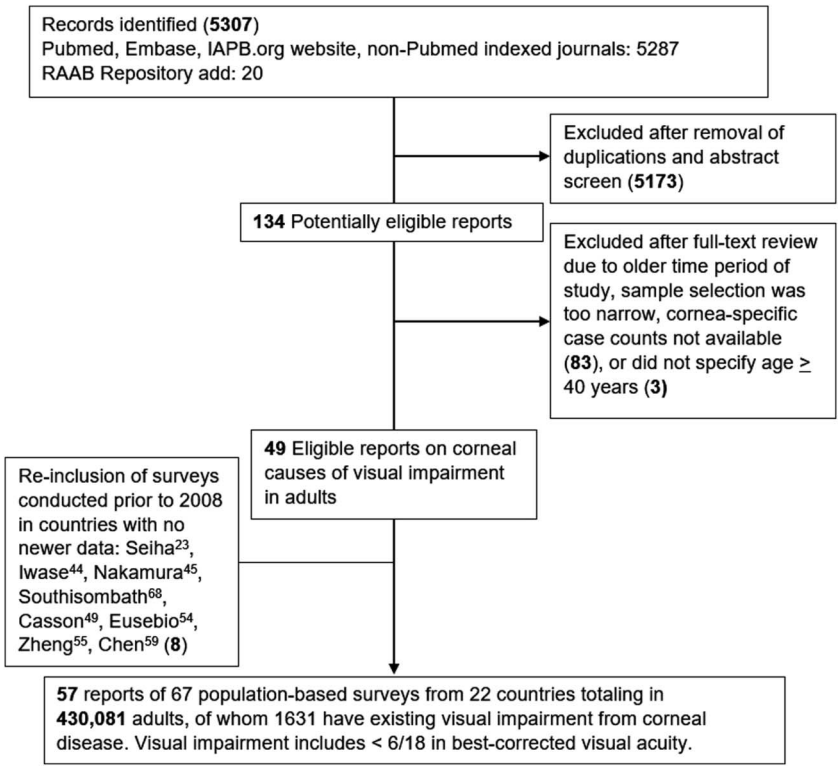

FIGURE 1. Systematic review process (PRISMA diagram). Visual impairment: <6/18 Snellen best corrected visual acuity in the better seeing eye. RAAB, rapid assessment of avoidable blindness.

of 430,081 adults age 40 years and older[13–40] (see Table 2, Supplemental Digital Content 2, http://links.lww.com/ICO/B27).[41–68] Among these adults, 1631 had moderate visual impairment or worse from corneal-specific causes. Twelve studies were designed to cover their respective countries, in which the largest study sample size was 168,673 individuals.[30] Three studies were intended and powered to determine the prevalence of corneal diseases.[30,33,38] To understand the relative frequencies of specific corneal diseases, 4 additional studies from China and India were included[69–72]; however, their data were not used in the pooled prevalence meta-analysis because these surveys were carried out before 2008. Strict application of the inclusion and exclusion criteria in the databasing and analysis was applied to yield comparable cross-country estimates in the adult population greater than 50 years. Restricting burden of disease data to those surveyed between January 2008 and December 2018 provides the most current estimates of prevalence. Incorporating data before 2008 and penalizing prevalence estimates increases the within-country pooled prevalence proportion in all but 3 countries. Data from Mongolia were too outdated for inclusion (surveyed in 1992) and would have resulted in an overestimate of the pooled prevalence among all countries.[48]

Prevalence and Causes of Vision Impairment and Blindness Due to Corneal Diseases

The prevalence of MSVI and blindness due to corneal diseases in Asia was estimated at 0.38% [95% confidence interval (CI), 0.30–0.46]. Calculation of the country-specific prevalence of MSVI and blindness due to corneal disease demonstrated the highest prevalence in India (0.88%; 95% CI, 0.38–1.57) and the lowest in Sri Lanka (0.05%; 95% CI, 0.00–0.11) (Fig. 2). In 7 countries, corneal diseases accounted for over 10% of the total MSVI and blindness (Fig. 3).

Five studies from China and 2 from India, consisting of a combined sample size of 235,643 individuals, were designed to determine the specific causes of corneal diseases in each country.[30,33,38,69–72] Inclusive of all levels of visual impairment, the most common cause in each country was infectious keratitis, accounting for 61.7% in China and 45.1% in India, followed by trauma (20.3% in China, 23.5% in India) and pseudophakic bullous keratopathy (PBK; 3.1% in China and 11.8% in India) (Fig. 4).

Age was the most important risk factor for MSVI and blindness due to corneal disease in Asia, with an increase of 0.39% in prevalence with each 1.0% increase in the proportion of the population greater than 60 years (Table 1). Although each of the other population level factors evaluated also reached statistical significance, their impact on prevalence of MSVI and blindness due to corneal disease was at least an order of magnitude less. A 1.0% increase in the percentage of the population that is women corresponded to a 0.05% increase in the prevalence of MSVI and blindness due to corneal disease, similar to the 0.04% increase in the prevalence of MSVI and blindness due to corneal disease associated with a 1% increase in the prevalence of all causes of MSVI and blindness in the population. Other variables, such as poverty rate, rural locality and literacy rate, were minimally impactful on the prevalence of MSVI and blindness due to corneal disease. The cataract surgical rate per 1000 individuals, an accepted and commonly used proxy for ophthalmic surgical capacity, had an anticipated

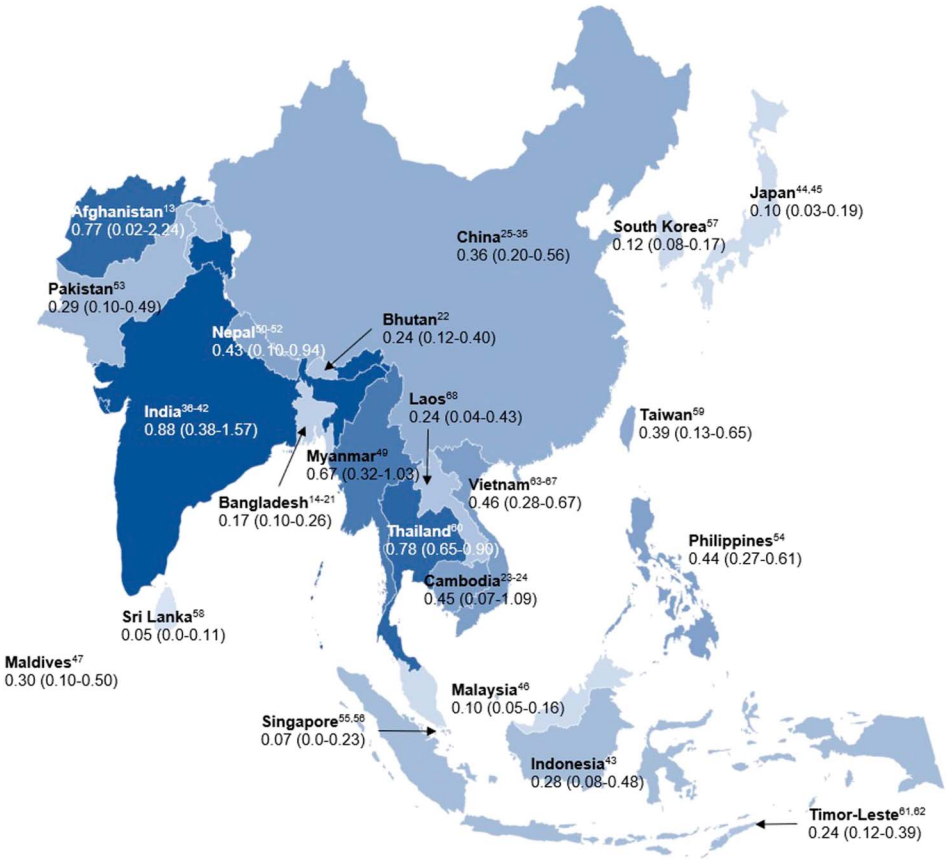

FIGURE 2. Prevalence of MSVI and blindness due to corneal diseases in 22 Asian countries [displayed as % (95% CI)]. (The full color version of this figure is available online at www.corneajrnl.com).

inverse relationship with prevalence of MSVI and blindness due to corneal disease. Surprisingly, agricultural work, which is commonly associated with infectious keratitis due to ocular vegetative trauma, also demonstrated an inverse relationship with the prevalence of MSVI and blindness due to corneal disease, with a decrease of 0.01% in prevalence with each 1.0% increase in the percentage of the population employed in agriculture. Of note, 2 variables were eliminated from our regression model: annual number of corneal transplants per capita and ophthalmologists per capita because they did not reach significance in univariate regression analysis ($P = 0.476$ and $P = 0.194$, respectively).

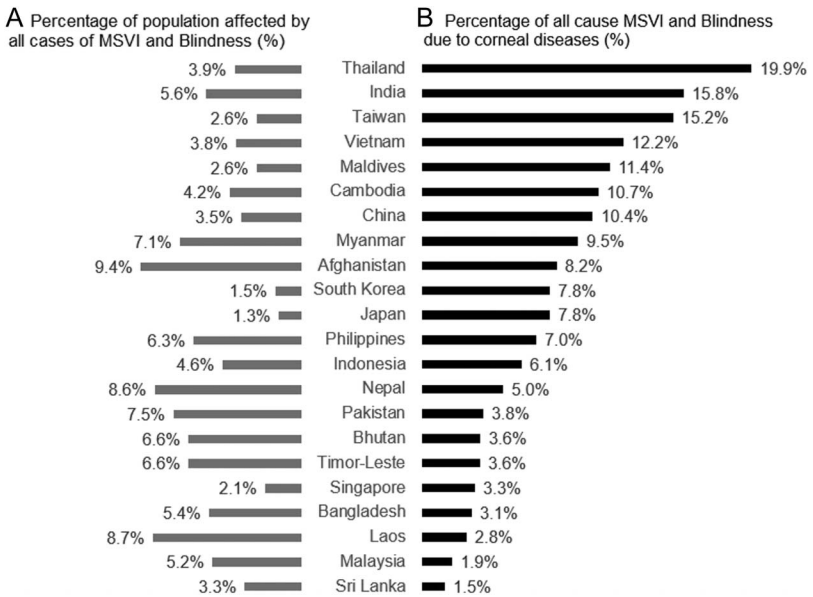

FIGURE 3. Percentage of population affected by all causes of MSVI and blindness and percentage of all cause MSVI and blindness due to corneal diseases in 22 Asian countries.

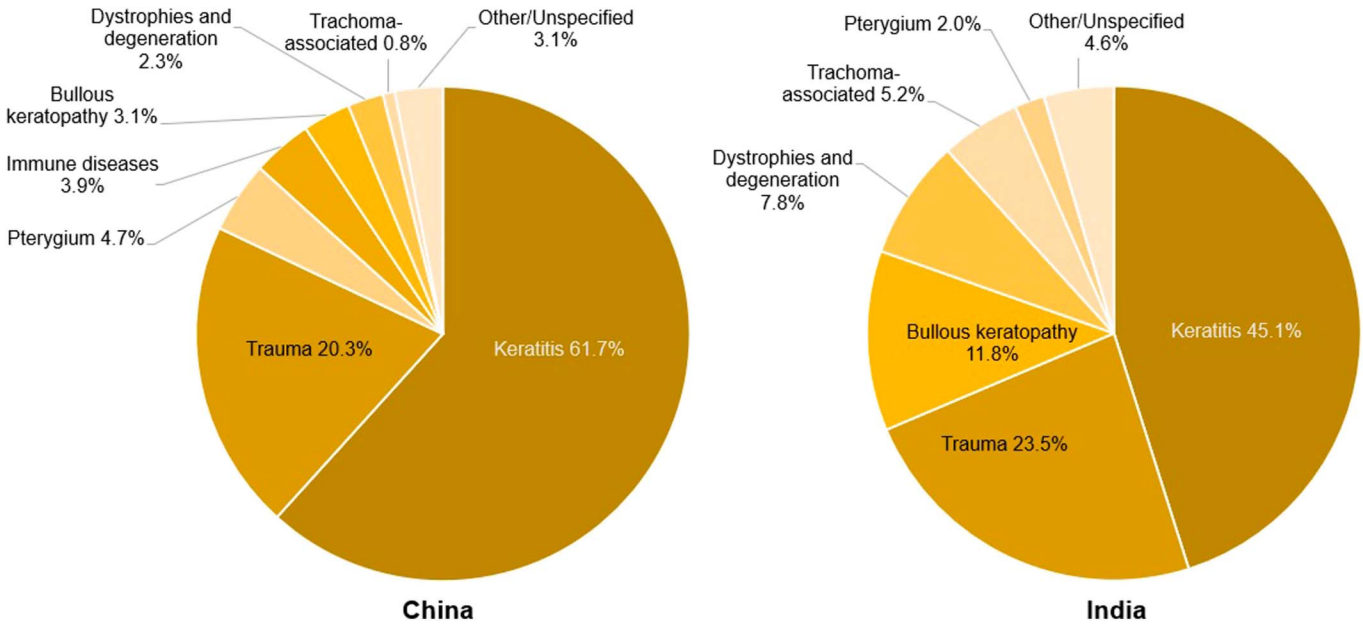

FIGURE 4. Diagnostic categories of corneal diseases in China and India causing MSVI and blindness. (The full color version of this figure is available online at www.corneajrnl.com).

Domestic Corneal Procurement and Corneal Transplant Volumes

Per capita rates of domestic corneal procurement (excluding imported tissue) and corneal transplantation throughout Asia are presented in Table 2, with most data taken from a 2016 publication by Gain et al[7] that reported the 2012 rates. The top 3 countries in annual corneal procurement are Sri Lanka (20 per 100,000 individuals), India (5 per 100,000 individuals), and Singapore (3.5 per 100,000 individuals); half of the countries for which data are available (8/16) report fewer than 1 cornea recovered per 100,000 population per year. For countries for which the corneal procurement data are not available (Afghanistan, Bhutan, Cambodia, Indonesia, Maldives, and Timor-Leste) because the corneal transplantation rate is <0.5 per 100,000 population per year in each country (unknown for Maldives), the rate of corneal procurement is almost certainly fewer than 1 per 100,000 individuals. In comparison, the corneal procurement rate in the United States in 2018 was 40.8 per 100,000.[76] The top countries in corneal transplantation are Singapore (8 per 100,000 individuals), Sri Lanka (7.5 per 100,000 individuals), and Taiwan and Japan (both 2.5 per 100,000 individuals); most countries for which data are available (13/21) report fewer than 1 cornea transplanted per 100,000 population per year. In comparison, the corneal transplantation rate in the United States in 2018 was 1.57 per 100,000.[76] Taking into consideration the rates of domestic corneal procurement and corneal transplantation, Sri Lanka, Nepal, and the Philippines are the only Asian countries currently exporting corneal tissue, and together with India, are the only countries with strong enough growth trajectory in rates of domestic recovery to conceivably meet domestic demand in the near future. Without knowing the number of individuals in each country in need of a corneal transplant at present, or the number of individuals who are added to the waiting list each year, it is difficult to determine what the country-specific corneal procurement or transplantation rates would need to be to adequately address MSVI and blindness due to corneal disease. However, using the burden data would likely lead to an overestimate because not all of the MSVI and blindness

TABLE 1. Population Level Factors Associated With Increasing Prevalence of MSVI and Blindness due to Corneal Diseases

Variables	β (95% CI)	Z Test Statistic	*P*
Age greater than 60 years (per 1% increase in the population)	39.32 (39.23 to 39.42)	804.0	<0.001
Female sex (per 1% increase in the population)	4.62 (4.69 to 4.56)	142.6	<0.001
Prevalence of all causes of MSVI and blindness (per 1% increase in the population)	3.85 (3.82 to 3.87)	295.2	<0.001
Poverty rate (per 1% increase in the population)	0.77 (0.74 to 0.79)	67.0	<0.001
Rural locality (per 1% increase in the population)	0.04 (0.03 to 0.05)	12.9	<0.001
Literacy rate (per 1% increase in the population)	−0.08 (−0.10 to −0.06)	−8.0	<0.001
Cataract surgical rate (per increase of 1 per 100)	−0.87 (−0.87 to −0.86)	−277.5	<0.001
Employment in agriculture (per 1% increase in the population)	−0.96 (−0.97 to −0.94)	−97.6	<0.001

TABLE 2. Corneas Transplanted (CT) and Procured (CP) Annually (Per 100,000 Individuals)

	CT	CP	Year	Source(s) of Data
Afghanistan	<0.5	NA	2012	Published literature[7]
Bangladesh	0.3	0.03	2017	Published literature[73]
Bhutan	<0.5	NA	2012	Published literature[7]
Cambodia	<0.5	NA	2012	Published literature[7]
China	<0.5	0.38	2007, 2012	Published literature[7,74]
India	2.3	5.0	2017	National Eye Bank of India
Indonesia	<0.5	NA	2018	Lions Eye Bank Jakarta
Japan	2.5	1.5	2012	Published literature[7]
Laos	0	0	2012	Published literature[7]
Malaysia	0.8	0.29	2015	Malaysia Transplant Society
Maldives	NA	NA		
Myanmar	<0.5	0.28	2012, 2016	Published literature[7,75]
Nepal	1.0	1.3	2012	Published literature[7]
Pakistan	0.5	0.09	2012	Published literature[7]
Philippines	0.4	1.5	2012, 2015	Published literature,[7] Santa Lucia International Eye Bank of Manila
Singapore	8.0	3.5	2012	Published literature[7]
South Korea	1.1	0.5	2012	Published literature[7]
Sri Lanka	7.5	20.0	2012	Published literature[7]
Taiwan	2.5	1.3	2012	Published literature[7]
Thailand	1.3	1.0	2012	Published literature,[7] Thai Red Cross Eye Bank
Timor-Leste	<0.5	NA	2012	Published literature[7]
Vietnam	<0.5	0.05	2012, 2018	Published literature,[7] Vietnam National Institute of Ophthalmology Eye Bank

due to corneal disease could be successfully managed by corneal transplantation.

Indications for and Types of Keratoplasty

The indications for and types of keratoplasty performed in 11 countries with comparable data are presented in Table 3. The 3 most frequent indications for corneal transplantation were infectious keratitis (23.1%), PBK (21.3%), and corneal opacities (15.4%). Despite the fact that PBK was the second most common indication for keratoplasty, less than 5% of the corneal transplant procedures were endothelial keratoplasties in half of the 14 surveys conducted in 11 Asian countries. Although it is acknowledged that most data reported in these surveys are from 2011 to 2012 and the percentage of corneal transplant procedures that are endothelial keratoplasties has increased since in some Asian countries,[77] it is likely still far lower in most Asian countries than in the United States, where endothelial keratoplasty surpassed penetrating keratoplasty to become the most commonly performed form of corneal transplantation in 2011. Endothelial keratoplasty accounts for more than 25% of the corneal transplants in only 2 Asian countries, Singapore and Japan, which have the highest and third highest GNI per capita in Asia, respectively. The association between the percentage of keratoplasty procedures that are endothelial keratoplasty and the GNI per capita in each Asian country was in fact found to be significant ($P < 0.001$) and is true for the United States as well, where 62% of the corneal transplants performed in 2018 were endothelial keratoplasties.[76] To assess whether ophthalmic surgical capacity was associated with keratoplasty indication or type, a surrogate measure, cataract surgical rate, was used, which showed no significant relationship to either ($P = 0.738$).

DISCUSSION

Burden of MSVI and Blindness Due to Corneal Disease in Asia

The epidemiology and prevalence of corneal diseases in Asia and the rate of domestic corneal recovery and corneal transplantation are highly variable among countries in the region. Therefore, we report country-level estimates of the burden of corneal MSVI and blindness and the national corneal recovery and transplantation volumes, including the indications for and types of corneal transplantation. We anticipate that these data will inform the delivery of preventive interventions, ophthalmic clinical services, the need for developing or expanding donor corneal recovery programs, and highlight the need for corneal surgeon training. Among all countries, having a large population greater than 60 years is the leading factor associated with increased burden of corneal disease; this should not however diminish the importance of visually impairing corneal diseases with early onset affecting individuals in their most productive years of life, such as keratoconus.[78] The association of female sex with an increase in the prevalence of MSVI and blindness due to corneal diseases is consistent with previous reports of sex inequities regarding vision impairment and corneal disease in Asia, with women having a 69% higher odds of being blind due to cataract in India,[79] a significantly higher prevalence of corneal opacity in rural India,[38] and a significantly higher prevalence of infectious keratitis in China.[30]

In China and India, infectious keratitis and trauma are the most common causes of MSVI and blindness due to corneal diseases and are recognized as important public health problems in most developing countries in Asia.[3,80] Corneal transplantation remains the primary sight restoring procedure for the management of corneal visual impairment, with an estimated 2 million people in China and 7 million people in India awaiting a corneal transplant.[7] Although the number of corneal transplants performed each year in India has more than doubled in the past 10 years, from approximately 13,000 in 2007 to 30,800 in 2017 (written communication, Samar Basak, MD, DNB, FRCS), only a small percentage of individuals who need a corneal transplant receive one. Thus, the burden of corneal blindness in India and throughout Asia remains significant. Strategies to address this burden should include a multipronged approach, including increasing the supply of donor corneas for transplantation through the use of domestically recovered tissue and imported tissue, changing the one donor-one recipient paradigm, using alternatives to traditional cadaveric human donor corneas, and expanding corneal surgeon training.

TABLE 3. Indications for and Types of Keratoplasty Performed in 11 Asian Countries

			Preoperative Indications (%)							Types of Keratoplasty (%)			
Country-Region	**CSR**	**GNI Per Capita**	**IK**	**CD**	**CO, scars**	**KCN**	**PBK**	**RT**	**Other**	**PK**	**EK**	**LK**	**Other**
China-Shandong (2011–12)	1402	8250	Data unavailable							63.0	1.0	36.0	0.0
China-Tongren (2011–12)	1402	8250	20.9	8.5	15.9	12.8	7.0	0.0	34.9	68.0	4.0	28.0	0.0
Hong Kong (2011–12)	1402	43,240	2.0	12.2	18.7	4.1	31.3	13.8	17.9	66.0	21.0	13.0	0.0
India (2011–12)	4830	1670	39.0	11.0	18.0	4.0	15.0	11.0	2.0	89.0	3.0	7.0	1.0
India (2013–14)	4830	1670	43.9	6.7	4.9	5.5	13.6	10.6	14.8	80.6	12.4	6.3	0.7
Japan (2011–12)	10,198	37,930	19.0	4.2	0.0	6.5	37.6	17.2	15.5	47.0	43.0	6.0	4.0
Nepal (2005–10)	4364	730	40.9	1.7	26.8	0.0	9.0	11.3	10.3	86.8	2.9	7.1	3.2
Philippines (2011–12)	1485	3580	20.5	3.6	10.5	3.3	38.3	9.1	14.7	96.0	2.0	0.0	2.0
Singapore (2011–12)	2627	51,880	4.5	16.1	3.5	9.8	32.2	14.1	19.9	28.0	44.0	28.0	0.0
South Korea (2011–12)	7950	27,600	11.6	0.0	16.9	4.8	20.3	21.7	24.7	78.0	9.0	13.0	0.0
Sri Lanka (2011–12)	5386	3850	25.0	0.0	15.0	20.0	14.0	10.0	16.0	66.0	11.0	20.0	3.0
Taiwan (2011–12)	5350	23,325	0.0	0.0	25.6	2.6	37.6	23.1	11.1	75.0	21.0	4.0	0.0
Thailand (2011–12)	3102	5640	25.4	14.3	20.6	2.9	15.8	12.4	8.6	94.0	0.5	5.0	0.5
Vietnam (2002–13)	2435	2060	48.2	10.5	24.0	1.9	5.2	8.1	2.1	93.5	2.0	4.5	0.0
Unweighted means			23.1	6.8	15.4	6.0	21.3	12.5	14.8				

CD, corneal dystrophy; CO, corneal opacity; CSR, cataract surgical rate; EK, endothelial keratoplasty; IK, infectious keratitis; KCN, keratoconus; LK, lamellar keratoplasty; PK, penetrating keratoplasty; RT, repeat transplant.

One of the limitations of this study was the lack of representation of children and adults younger than 40 years in the pooled prevalence estimates of MSVI and blindness due to corneal disease because of limited data availability (see Table 3, Supplemental Digital Content 3, http://links.lww.com/ICO/B28). Although population-based surveys that met our inclusion criteria were available from each of the 22 Asian countries for individuals 50 years and older, such surveys for individuals 40 years and younger were available from only 3 countries (4 studies from China, 2 from India, and 1 from Bangladesh).[42,81–86] Because comparable data were lacking for the other 19 countries, we decided to limit the scope of this study to capture most epidemiologic surveys, which examined adults older than 40 years. Because the causes of MSVI and blindness due to corneal disease in these 7 studies including individuals 40 years and younger were not specified beyond "corneal opacity" and "cornea disease," it is not possible to determine whether the most frequent causes of MSVI and blindness due to corneal disease in these individuals are the same as those in individuals 50 years and older. Another limitation of this study was the combining of the prevalence of MSVI and blindness due to corneal disease into one prevalence proportion. This was performed to harmonize the prevalence proportions because some studies, notably the national survey from South Korea,[57] only provided data on MSVI and blindness combined.

Increasing the Supply of Donor Corneas for Transplantation

One of the strategies to tackle the issue of donor corneal shortage and increase the supply of donor corneas for transplantation is through tissue importation. In 2018, 27,913 corneas recovered in the United States were exported internationally, representing approximately one-third of all corneas distributed by the US eye banks for transplantation, with 11,883 exported to Asian countries.[76] However, because the United States, Sri Lanka, and Italy are the only countries with a surplus of domestically recovered corneas, importing donor corneal tissue will never sufficiently address the significant burden of corneal visual impairment in Asia.[7]

Although the number of corneas exported from the United States to Asia each year is reflective of the fact that domestic corneal recovery programs in nearly all Asian countries are insufficient to meet the countries' needs, local recovery programs have been successfully implemented in several Asian countries and serve as models that may be replicated in other countries in the region. Since the founding of the International Eye Bank in Sri Lanka in 1961, over 120,000 corneas have been distributed for domestic and international use, and nearly 1.3 million Sri Lankans have been registered as donors, providing evidence of the effectiveness of donor registries, even in predominantly Buddhist countries, such as Sri Lanka.[7] In the Philippines, an organ donation law passed in 1995 contained a presumed consent provision for coroners' cases. In the same year, the Santa Lucia International Eye Bank of Manila opened, and more than 16,000 corneas have subsequently been distributed for transplantation (written communication, Ma. Dominga B. Padilla, MD). In India, many of the largest eye banks are converting to hospital-based cornea retrieval programs, using trained eye-donation counselors and professional eye bank managers. This has resulted in a 250% increase in the number of corneas recovered over an 11-year period from approximately 27,000 in 2006 to 67,000 in 2017 (written communication, Samar Basak, MD, DNB, FRCS). As an example, Asia's largest eye bank, the Ramayamma International Eye Bank in Hyderabad, India, has demonstrated a greater than 400-fold increase in the annual corneal procurement from 1989 (20) to 2018 (more than 8000), attributed primarily to

the introduction of the hospital-based cornea retrieval programs in 1991.[77]

Changing the One Donor–One Recipient Paradigm

Traditionally, a single donor cornea has been used to restore sight to a single recipient. However, with the widespread adoption of lamellar keratoplasty techniques, 1 donor corneal tissue can be used for 2 patients (such as for deep anterior lamellar keratoplasty and Descemet membrane endothelial keratoplasty), where permissible.[87] In addition, the lower rates of corneal transplant rejection associated with anterior and posterior lamellar keratoplasty techniques compared with penetrating keratoplasty translate to decreased rates of graft failure and the need for repeat keratoplasty.[88] Anterior lamellar keratoplasty also permits the use of corneal tissue with poorer endothelial quality, tissue that would otherwise be discarded or used only for tectonic keratoplasty, to be used for optical keratoplasty. Furthermore, ex vivo expansion of allogenic human corneal endothelial cells offers the potential to transplant expanded endothelial cells from a single donor to up to 45 recipients with an endothelial cell density of approximately 3000 cells/mm^2.[89]

Alternatives to Traditional Cadaveric Human Donor Corneas

Owing to the severe shortage of cadaveric donor corneal tissue in many countries in Asia, alternatives are emerging, including the use of decellularized porcine corneas in China,[90] clinical trials using biomaterials-enabled cornea regeneration in India,[91] and 3D bioprinting of corneal stroma,[92] also in clinical trials in India. Although obvious advantages of decellularized porcine corneas include the ample supply of the corneas, limitations include the fact that the decellularized xenografts carry a risk of immune rejection from incomplete decellularization, cross-species infection with unrecognized infectious agents, and at present, a cost that is similar to imported human corneas. Although bioengineered and 3D printed corneas avoid the risks associated with xenotransplantation, early results in humans have not been associated with the same level of success as observed in animal models because of the failure of the biomaterials to integrate into chronically diseased or aged tissues.[91] However, in a small observational study, a cell-free corneal implant comprising recombinant human collagen improved vision in half of treated individuals,[91] relieved discomfort, and promoted nerve regeneration, leading to optimism that it could one day be a useful substitute for cadaveric donor corneal tissue.

Expanding the Number and Training of Corneal Surgeons

Increasing the supply of donor corneal tissue and the use of emerging alternatives to cadaveric donor corneal tissue will not in and of itself decrease the burden of MSVI and blindness due to corneal disease in Asia because trained corneal surgeons are needed to transplant the donor cadaveric or bioengineered corneal tissues. It is estimated that there are approximately 500 fellowship-trained corneal surgeons in India, with the 70% who perform corneal transplants performing an average of 60 transplants per year (written communication, Samar Basak, MD, DNB, FRCS). The estimated corneal transplant capacity in India, assuming that all fellowship-trained corneal surgeons begin performing transplants, is therefore approximately 30,000 transplants per year. As previously noted, 30,800 corneal transplants were performed in India in 2017, indicating that increasing the supply of corneas further will likely not result in an increase in the number of corneal transplants performed; surgeon capacity must be increased. Although cornea fellowship training is available in India, it is not in most other countries in Asia, in which the lack of donor corneal tissue results in a lack of exposure to corneal transplantation in residency training and few opportunities to develop keratoplasty skills after the completion of training. Therefore, along with increasing the supply of donor corneas, addressing the burden of corneal MSVI and blindness necessitates the training of surgeons who have completed their formal ophthalmology training. Organizations such as the International Council of Ophthalmology and the Asia Cornea Society provide funding support for cornea fellowship training both in and outside of Asia, and nonprofit nongovernmental organizations such as Orbis, SightLife, Seva, and Visionaries International conduct keratoplasty skills transfer courses in a number of Asian countries.

CONCLUSION

In summary, approximately 70% of the global burden of MSVI and blindness due to corneal disease is in Asia, although the percentage of the population that is affected in each country varies greatly, correlated most closely with GNI. The most frequent causes of MSVI and blindness due to corneal diseases in Asia are infectious keratitis, trauma, and PBK, which also represent the most common indications for corneal transplantation. Although the rates of corneal transplantation and corneal procurement per capita in most Asian countries are below the international means, a few countries, notably Sri Lanka, have successful corneal recovery programs that have resulted in a low percentage of MSVI and blindness due to corneal disease. Local corneal recovery programs that utilize donor registries, such as in Sri Lanka, and hospital-based corneal retrieval programs, such as in India, can and should be adopted in other Asian countries to increase the supply of corneal tissue available for transplantation. However, the eventual increase in the supply of corneal tissue necessitates a similar increase in the number of trained corneal surgeons to decrease the burden of visual impairment from corneal disease in Asia.

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