ORIGINAL RESERACH

The Columbia University JOURNAL of GLOBAL HEALTH

The burden of vision loss due to Diabetic Retinopathy in Asia from 1990-2021: findings from the Global Burden of Disease Study 2021

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ABSTRACT

Background and Objectives:
Diabetic Retinopathy (DR) has become the leading cause of vision impairment (VI) worldwide. Leveraging the most recent data and analytical techniques from the Global Burden of Diseases, Injuries, and Risk Factors Study (GBD), we produced comprehensive estimates of VI due to DR in Asia. These estimates were segmented by location, age, and gender for the period between 1990 and 2021. Furthermore, we projected the burden of DR up to 2050.

Methods:
We analyzed data from the GBD 2021 to assess the prevalence and Years Lived with Disability (YLDs) due to DR in Asia, examining age structure, trends over time, and gender differences. The study included an analysis of DR-induced VI severity across Asian countries. The Estimated Annual Percentage Change (EAPC) was calculated to illustrate trends at regional and national levels. Bayesian age-period-cohort (BAPC) analysis was used to project future prevalence trends up to 2050.

Results:
From 1990 to 2021, the age-standardized prevalence rate (ASR) and YLDs rate of DR in Asia significantly increased, with higher rates consistently observed in women ($p>0.05$). The elderly experienced a greater burden, with increasing rates of VI and YLDs with age. Moderate vision impairment (MVI) constituted the majority of DR-related ASR in Asia. There were notable differences in the burden of DR among Asian countries. In 2021, Mauritius, Seychelles, Malaysia, and Brunei had the highest ASR, while Bangladesh, Bhutan, Mongolia, and Japan had the lowest. Cambodia exhibited the fastest growth, whereas Singapore and Pakistan showed a decline. Most Asian countries have a Sociodemographic Index (SDI) at low-medium to medium levels, and correspondingly low ASR. According to BAPC projections, by 2050, the YLDs rate for DR in Asia will decrease to 3.92 for males and 4.96 for females.

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Conclusion:
Over the past 30 years, the burden of DR in Asia has increased, with persistent gender disparities and substantial variation among countries. This study displayed the importance of DR prevention, particularly for women and the elderly. BAPC projections suggested a decreasing trend in YLDs rate due to DR over the next 30 years.

KEY WORDS Diabetic Retinopathy; the Burden of Disease; GBD Study; Asia

INTRODUCTION

In recent years, the burden of diabetes mellitus (DM) has gradually increased globally, and it is estimated that by 2050, the prevalence numbers of DM will exceed 1.31 billion (Ong et al., 2023). As one of the microvascular complications of DM, diabetic retinopathy (DR) is the leading cause of vision loss and blindness among the working-age population (Cheung, Mitchell, & Wong, 2010; Sabanayagam, Yip, Ting, Tan, & Wong, 2016).

Approximately 30-40% of DM patients develop DR (Yau et al., 2012). In 2020, 1.07 million people were blind due to DR, and nearly 3.28 million suffered from severe vision loss (Curran et al., 2024). Studies have indicated that blood glucose levels and the duration of DM were risk factors for DR among DM patients (Song, Yu, Chan, Theodoratou, & Rudan, 2018).

According to the latest data, Asia accounts for approximately 59.3% of the global population (https://www.unfpa.org/data/world-population-dashboard). Many countries in Asia are experiencing an increase in the aging population, resulting in Asia bearing the highest burden of DR worldwide (Tan & Wong, 2023). The significant disparities in wealth and population characteristics across Asian countries, including differences in genetics, climate, culture, dietary habits, and economic conditions, may contribute to the variations in DR burden among these countries (Kang et al., 2022; Wan, Wang, & Zhang, 2021).

This study sought to examine the trends over time, gender disparities, and age-related patterns in the prevalence and Years Lived with Disability (YLDs) due to Diabetic Retinopathy (DR) in Asia from 1990 to 2021. Additionally, we performed a comparative analysis of gender differences and the severity of vision impairment (VI) across various Asian countries to identify the risk factors influencing the DR burden. Finally, we projected the future burden of DR up to the year 2050.

MATERIALS AND METHODS

Data Sources

The research on Global Burden of Disease Study (GBD) in 2021 was a comprehensive scientific study that estimated the worldwide impact of 369 diseases and injuries from 1990 to 2021, categorized by gender, location, age, and region (Diseases & Injuries, 2024). Visual impairment associated with DM, as defned by the GBD study, was caused only by DR. The data on the prevalence and YLDs of DR from 1990 to 2021 were collected from the Global Health Data Exchange query tool (https://ghdx.healthdata.org/gbd-2021). Prevalence refers to the total number of cases among a particular population at a specific time. YLD is the product of the prevalence of a sequela and its corresponding disability weight (Salomon et al., 2015). The calculation method has been reported in previous studies (Vos et al., 2020). The population prediction data for 2020-2050 was obtained from the United Nations (https://population.un.org/websitewpp//Download//Stan). The GBD world population age standard data came from an appendix table in the Lancet (Schumacher et al., 2024).

According to the GBD study, Moderate vision impairment (MVI) was defined as visual acuity (VA) ≥6/60 and <6/18 based on the Snellen chart, Severe vision impairment (SVI) was VA ≥3/60 and <6/60, and blindness was VA < 3/60 or <10% visual field around central fixation.

Asian Countries

All data about Asia came from the GBD website, including four Asia regions: East Asia, South Asia, Southeast Asia, and Central Asia. East Asia, as defined by GBD, includes China, Japan, South Korea, Taiwan, and North Korea. South Asia includes Bangladesh, Bhutan, India, Nepal and Pakistan. Southeast Asia included Brunei, Cambodia, Indonesia, Laos, Malaysia, Maldives, Mauritius, Myanmar, the Philippines, Seychelles, Singapore, Sri Lanka, Thailand, Timor-Leste, and Vietnam. Central Asia includes Armenia, Azerbaijan, Georgia, Kazakhstan,

Kyrgyzstan, Mongolia, Tajikistan, Turkmenistan and Uzbekistan. High-income Asia-Pacifici countries were considered to be Brunei, Japan, the Republic of Korea, and Singapore.

Sociodemographic Index

Sociodemographic Index (SDI) was widely quoted as an indicator of overall development(Diseases & Injuries, 2024). The SDI value changes between 0 ~ 1. The greater the value, the better the social and economic development. According to SDI, regions were divided into 5 parts, including high SDI (> 0.81), medium-high SDI (0.70-0.81), medium SDI (0.61-0.69), low-medium SDI (0.46-0.60), and low SDI (<0.46).

Statistical Analysis

Firstly, we obtained the prevalence and YLDs of DR in Asia and Asian countries from 1990 to 2021 and calculated the estimated annual percentage change (EAPC) to show the trends. The methods for calculating EAPC were previously described in detail (Ou et al., 2022). Secondly, we analyzed the gender differences, visual impairment differences and age trends of diabetic retinopathy in Asia through Rstudio. Finally, the Bayesian age-period-cohort analysis (BAPC) was used to predict the prevalence trend in diabetic retinopathy over the next 30 years. All data analyses were performed in IBM SPSS 24.0 Statistical software (IBM Corporation, Chicago, IL). A p value of $p < 0.05$ was considered statistically significant.

RESULTS

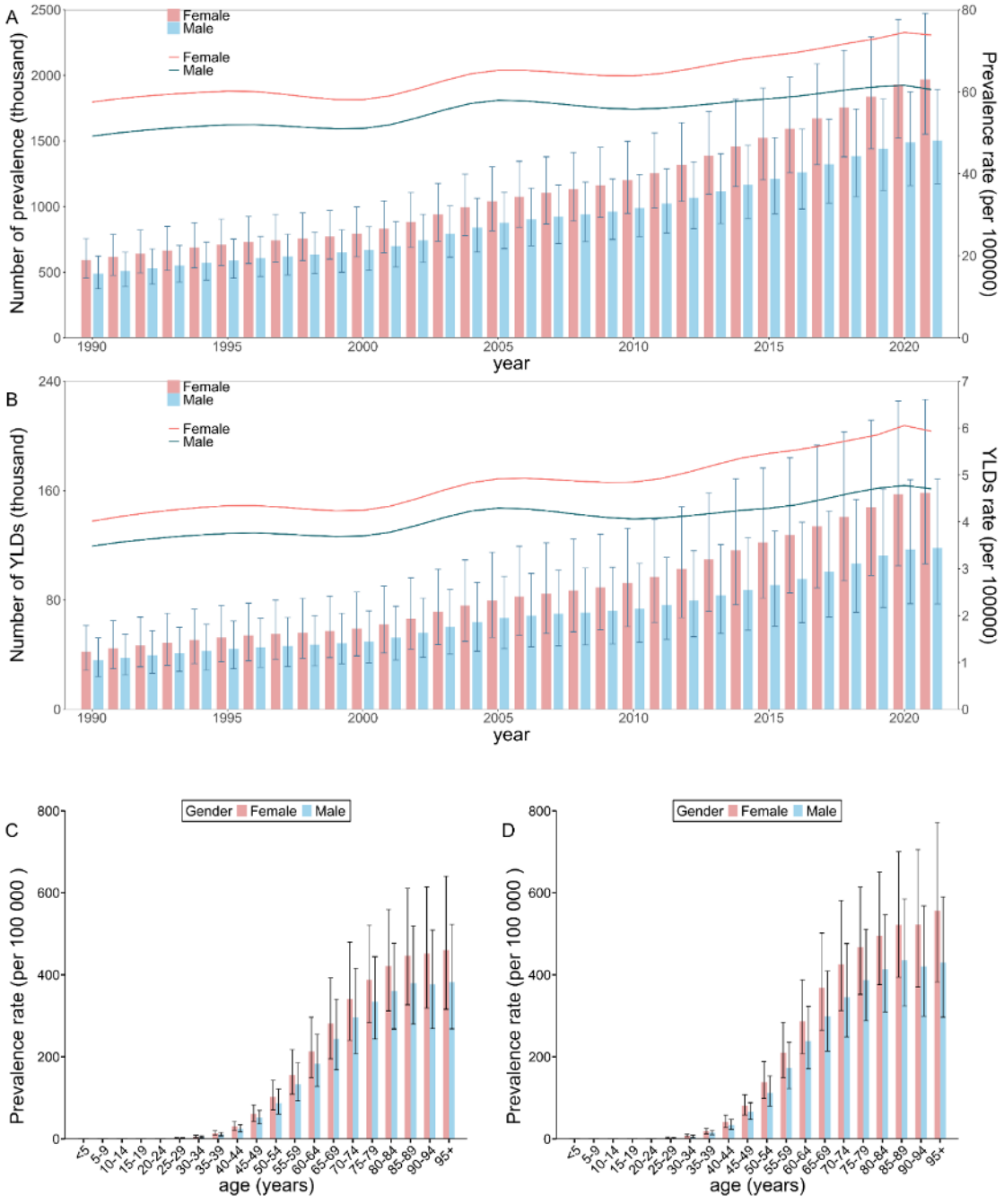
Overall IBD Burden and Time Trends in Asia

From 1990 to 2021, the burden of DR in Asia showed an overall increasing trend. The number of prevalence rose from 1,079,707.0 cases (95% UI: 828,237.5, 1,379,166.0) to 3,471,854.7 cases (95% UI: 2,729,341.2, 4,354,562.2) (Fig.S1A), and YLDs increased from 77,996.6 (95% UI: 52,462.4, 113,689.4) to 276,460.0 (95% UI: 182,713.5, 396,365.9) (Fig.S1B). The age-standardized prevalence rate (ASR) in Asia increased from 53.5 (95% UI: 41.6, 68.3) per 100,000 in 1990 to 67.5 (95% UI: 53.4, 84.7) per 100,000 in 2021, with a peak of 61.7 (95% UI: 48.7, 77.8) per 100,000 in 2005 (Fig.S1C). Similarly, the age-standardized YLDs rose from 3.8 (95% UI: 2.5, 5.4) per 100,000 in 1990 to 5.3 (95% UI: 3.6, 7.6) per 100,000 in 2021 (Fig.S1D). Statistical results from four continents indicated that Asia was the highest prevalence and YLDs numbers, with intermediate ASR and age-standardized YLDs rate. America had the highest ASR and YLDs rate, while Europe retained the lowest.

Gender Disparity of DR Burden in Asia

From 1990 to 2021, prevalence numbers, YLDs numbers, the ASR, and age-standardized YLDs rate for DR in Asia were higher in females than in males ($p < 0.05$) (Fig.1). In 2021, the amount of prevalence in Asia was 1,968,513.3 cases (95% UI: 1,552,533.1, 2,473,196.4) among females, while 1,503,341.4 cases (95% UI: 1,174,463.2, 1,893,907.0) among males. The ASR for females was 73.9 (95% UI: 58.5, 92.5) per 100,000, and for males, it was 60.6 (95% UI: 47.7, 76.1) per 100,000 (Fig. 1A). Taking age 5 as the age group, the ASR of females was higher than that of males for each age group in both 1990 and 2021 (Fig.1C and Fig.1D). Analyzing the trends in each age group from 1990 to 2021 in 5-year intervals, it was observed that the ASR of DR was 0 before the age of 20. Between the ages of 20 and 44, the increase in ASR was relatively gradual, while the increase was more rapid between the ages of 45 and 89. The rate of increase slowed down between the ages of 89 and 95+, reaching a peak at 95+ years (Fig.S2). Additionally, Fig.S2 showed a year-by-year increase in ASR.

Fig.1 Trends of prevalence(A) and YLDs(B) numbers and ASR of DR for males and females in Asia from 1990 to 2021. B. Trends of YLDs numbers and age-standardized YLDs rate of DR for males and females in Asia from 1990 to 2021. Age-specific trends of ASR of DR for males and females in Asia in 1990(C) and 2021(D).



Distribution of DR burden for VI severity in 2021

From 1990 to 2021, the majority of the ASR in Asia was attributed to MVI, followed by blindness, with SVI being the least (Fig.2A). All four indicators showed an increasing trend over the years. In terms of YLDs rate, blindness accounted for the largest proportion, with MVI and SVI being roughly equivalent (Fig.2B). The YLDs rate due to blindness showed the most significant variation over the years, while MVI and SVI remained relatively stable.

In 2021, across all age groups in Asia, the ASR for VI severity was higher in females than in males (Fig.2C). For both males and females, MVI had the highest proportion, followed by blindness, with SVI having the smallest proportion (Fig.2C). In terms of YLDs rate, blindness accounted for the largest proportion across all age groups, with MVI and SVI being approximately equal (Fig.2D).

Fig.2 Distribution for VI severity of ASR(A) and YLDs rate(B) in 2021. Distribution for VI severity of ASR(C) and YLDs rate(D) for all ages for males and females in 2021.

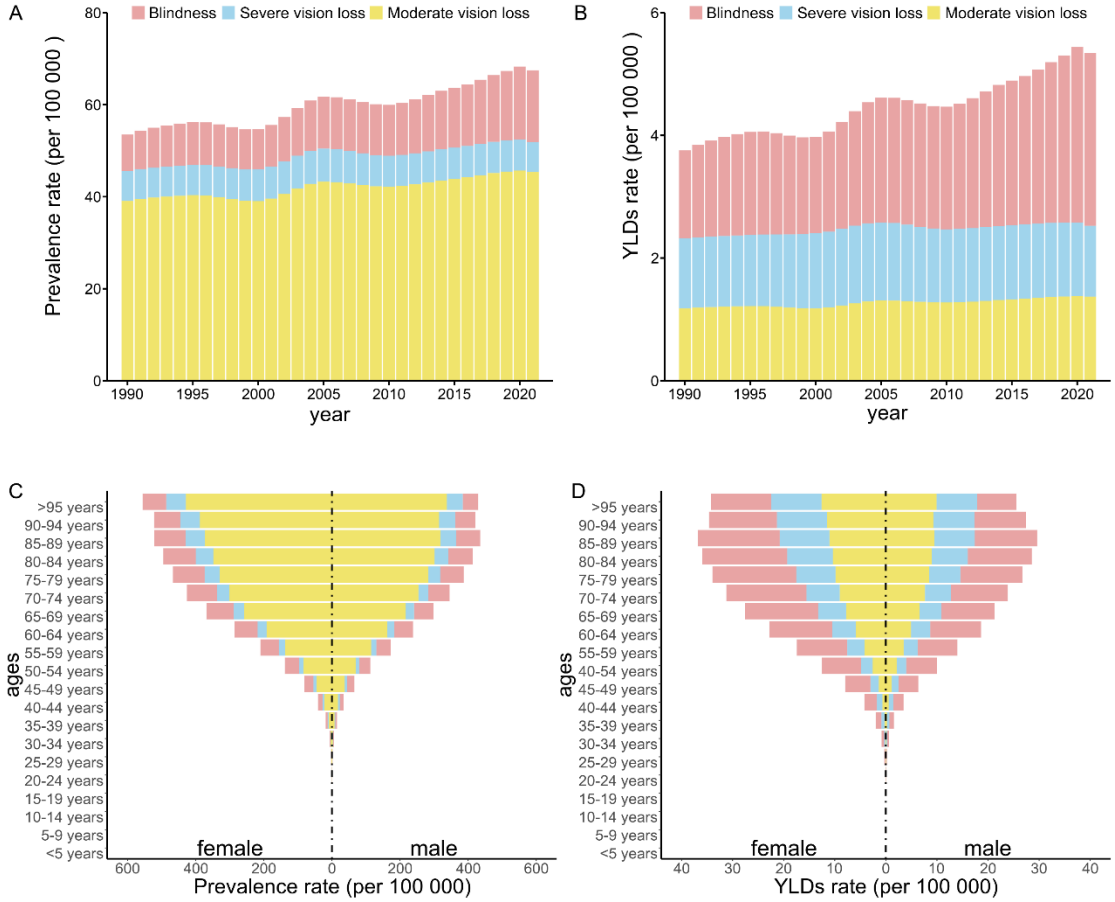
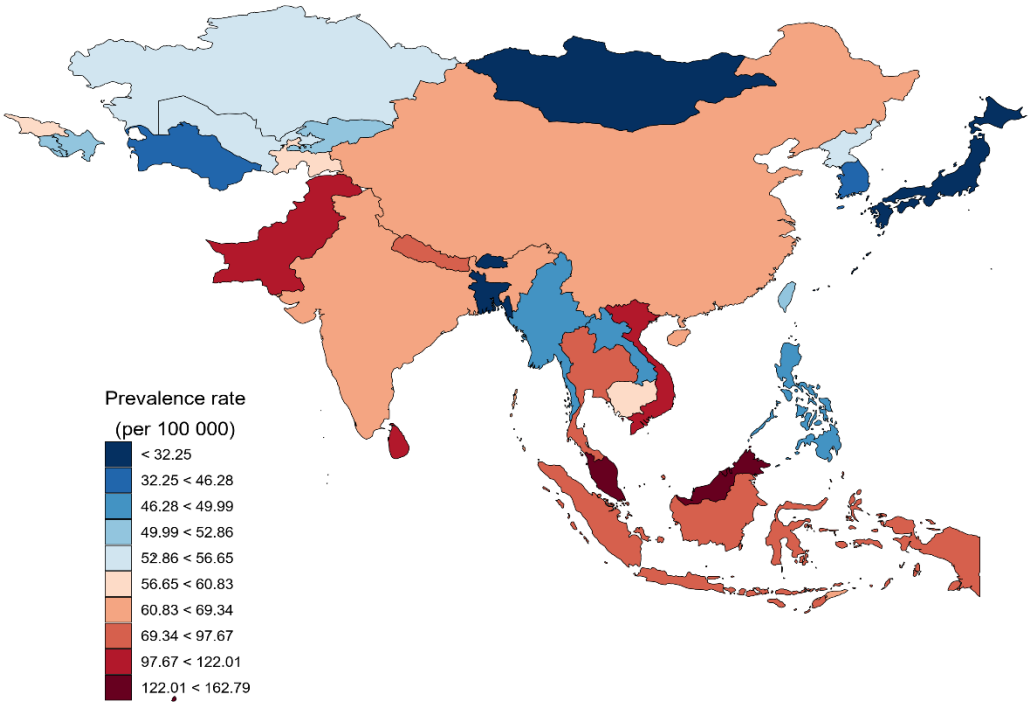


Fig.3 The distribution of ASR levels in Asia in 2021.



Asian countries of DR burden

In 2021, Mauritius, Seychelles, Malaysia, and Brunei had the highest ASR for DR in Asia. Conversely, Bangladesh, Bhutan, Mongolia, and Japan had the lowest ASR(Fig.3).

In this study, the burden of DR exhibited varying increasing rates across different Asian countries and regions (Table.S1). Cambodia showed the fastest growth with an annual increase of 3.57% (95% CI: 3.15, 4.00), followed by Seychelles at 3.36% (95% CI: 3.17, 3.56) and Mauritius at 3.21% (95% CI: 2.78, 3.64). In contrast, Singapore (EAPC = −0.71, 95% CI: −0.8, −0.62) and Pakistan (EAPC = −0.45, 95% CI: −0.71, −0.20) showed a decline in ASR.

Leading causes of VI in Asia in 1990 and 2021

From 1990 to 2021, in the rankings of causes of VI by ASR for DR, Vietnam showed the most significant improvement, rising from 9th to 5th. Most countries saw an increase in their DR rankings, with only Singapore's ranking decreasing (from 7th to 6th) (Fig.S3A and Fig.S3C). In 2021, the DR ranking for most countries was around 8th place, with Brunei Darussalam, Mauritius, Seychelles, Taiwan, and Vietnam ranked at 5th (Fig.S3C). Regarding YLDs rate for DR from 1990 to 2021, the ranking of DR in Asian countries showed an upward trend, with Vietnam's ranking rising most significantly (from 9th to 5th) (Fig.S3 B and Fig.S3D).

Gender Disparity and VI severity in Asian countries

In most Asian countries, the ASR for females was higher than for males, with the exception of 11 Southeast Asian countries: Cambodia, Indonesia, Laos, Malaysia, Mauritius, Myanmar, the Philippines, Seychelles, Sri Lanka, Timor-Leste, and Vietnam (Fig.S4). In most countries, MVI accounts for the largest proportion of VI. However, in Cambodia, Mauritius, and Seychelles, blindness has the highest proportion. In Brunei, India, Malaysia, and Myanmar, the proportions of MVI and blindness are comparable.

ASR of DR by SDI

As shown in Fig.4, most Asian countries had a low-medium and medium Socio-demographic Index (SDI), and their ASR was relatively low. Countries with a medium-high SDI had higher ASR, while those with a high SDI

had lower ASR. For example, Bangladesh represented the low-medium SDI with Asia's lowest ASR of DR. Pakistan, which has the same SDI as Bangladesh, had an ASR four times higher than that of Bangladesh. Brunei and Japan served as examples among high SDI countries: Brunei's DR ASR was ranked 4th out of 34, whereas Japan was ranked 30th out of 34. With a medium-high SDI, China had ASR and YLDs rate at mid-levels, with its ASR ranking 13th out of 34 in Asia.

Projection to 2050

As shown in Fig.5, the YLDs rate for both males and females is projected to decrease from 2022 to 2050. According to our predictions, by 2050, the YLDs rate will decline to 3.92 for males and to 4.96 for females .

Fig.4 ASR (A) and YLDs rate(B) of DR by SDI in Asian

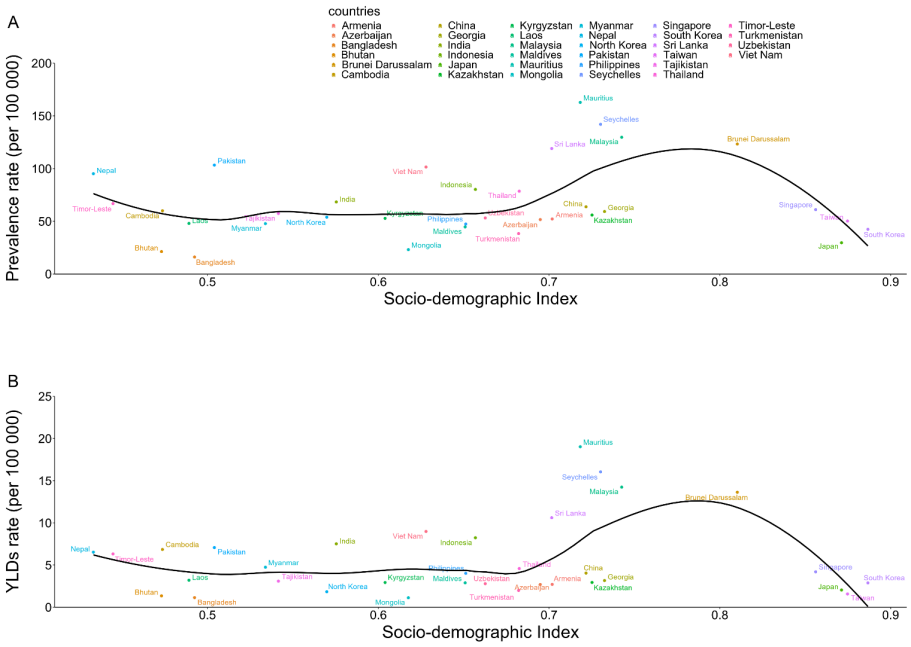
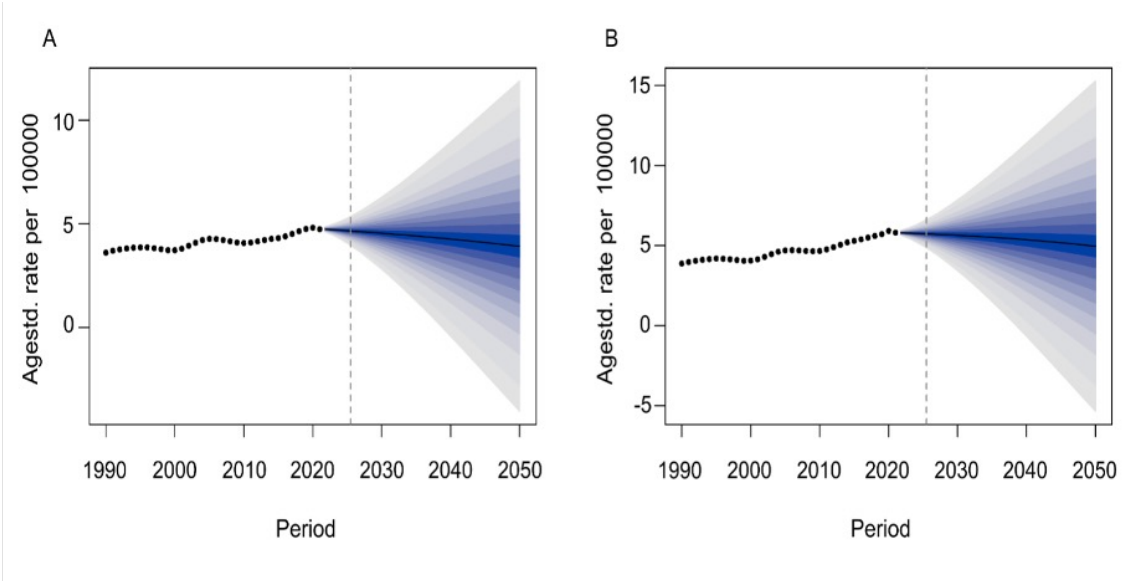


Fig.5 Trends of YLDs rate of DR for males (A) and females (B) in Asia in 2022-2050.



DISCUSSION

Diabetic retinopathy (DR) has become a leading cause of vision loss and blindness, and it was the only cause of blindness with an increasing prevalence from 1990 to 2020 (Steinmetz et al., 2021). Analyzing the prevalence and YLDs of DR, we comprehensively explored the changing trend of DR in time, gender, and age from 1990 to 2021. In addition, we analyzed the prevalence and its increase in Asian countries, as well as the gender differences and the ranking of DR in the leading causes of VI in Asian countries, and predicted the trend of DR to 2050.

Our results showed that the ASR of DR in Asia rose, peaking in 2005 and declined after. The change trend of YLDs rate was the same. Our analysis may be related to the following points. Firstly, in the early 21st century, the International Clinical Diabetic Retinopathy (ICDR) grading system and severity scale were widely adopted, leading to a global consensus on DR (Wilkinson et al., 2003), indicating that DR had gained widespread global attention. Secondly, in 2006, anti-vascular endothelial growth factor (anti-VEGF) drugs were approved for the treatment of neovascular age-related macular degeneration (AMD) (Ferrara, Damico, Shams, Lowman, & Kim, 2006). Numerous clinical trials for anti-VEGF drugs were conducted simultaneously, opening new avenues for DR treatment (Elman et al., 2010; Nguyen et al., 2012). Lastly, since 2000, blood glucose levels in DM patients have been effectively controlled, thereby reducing the risk of developing DR (Ford, 2011).

In this study, from 1990 to 2021, the burden of DR in Asia was higher in females than in males, consistent with findings from other studies (Khairallah et al., 2014; Li et al., 2020). Firstly the global average lifespan of women longer than that of males ((https://www.worldometers.info/demographics/life-expectancy); also, women bear a higher risk of disease (Candore et al., 2024). The global aging population exacerbated this phenomenon. Women tended to have a longer duration of diabetes mellitus (DM), resulting in a higher burden of DR compared to men. Secondly, estrogen could prevent retinal damage caused by DR through various pathways(Nuzzi, Scalabrin, Becco, & Panzica, 2018). Many research indicated that irregular menstrual cycles(Kiconco, Teede, Earnest, Loxton, & Joham, 2022), pregnancy(Complications, 2000), and early menopause (Appiah, Winters, & Hornung, 2014) could affect blood glucose control, leading to a higher burden of DR in women.

We found that as age increased, the ASR for DR also increased, peaking at 95+ years. The YLDs rate followed the same trend. Previous studies showed that the global prevalence of DM peaked at 24.4% between the ages of 75 and 79(Ong et al., 2023). The duration of DM was one of the most important risk factors for the occurrence of DR and to progress to proliferative DR (Bulum, Tomic, Vrabec, Brkljacic, & Ljubic, 2023). This indicated that the duration of DR extended beyond that of DM, which was consistent with the findings of this study.

In terms of the VI severity, MVI accounted for the most significant proportion of ASR in Asia, followed by blindness. For the YLDs rate in Asia, blindness accounted for the largest proportion, with MVI and SVI being similar, consistent with other research findings (Shan et al., 2021). Vision loss not only affects the quality of life for patients and their families but also increases economic burdens (Matza, Rousculp, Malley, Boye, & Oglesby, 2008). Early, regular screening and timely treatment are crucial for preventing blindness. However, less than half of DM patients adhered to recommended screening guidelines (Kuo et al., 2005). The unequal distribution of medical resources exacerbates this issue also. Previous studies indicated that poorer regions had fewer retinal specialists (Pandit et al., 2020). These factors contribute to the lack of timely treatment for many DR patients, accelerating the progression of DR and leading to blindness.

From 1990 to 2021, the ranking of DR as a leading cause of VI increased in most countries. This may be related to the World Health Organization's "Vision 2020" initiative. The WHO defined refractive errors and cataracts as avoidable causes of blindness and aimed to eliminate avoidable blindness by 2020 (Murray McGavin, 1998; Pararajasegaram, 1999). Although the target was not fully achieved, VI, due to cataracts and refractive errors, had decreased globally from 1999 to 2020 (Steinmetz et al., 2021). The increased detection of DR due to better visualization of the retina post-cataract surgery, along with factors such as aging populations and improved living standards, had collectively contributed to the higher ranking of DR.

There were significant differences in the burden of DR among Asian countries. Firstly, high BMI and dietary habits were the major risk factors for DM(Ong et al., 2023). The three countries in Asia with the highest ASR of DR, Mauritius, Seychelles and Malaysia, had modern lifestyles, which led to the prevalence of high-calorie diet and lack of exercise, as well as the increasing prevalence of overweight and obesity, which increased the prevalence of DR (Aly, Viswanathan, Mangroo, Gedeon, & Bovet, 2018; Bundhun, Rampadarath, Puchooa, & Jeewon, 2018; Lai, Palaniveloo, Mohd Sallehuddin, & Ganapathy, 2024). Moreover, the three countries in Asia

with the lowest ASR of DR, Bangladesh and Bhutan, had low-fat diets, resulting in lower prevalence rates (Al Hasan et al., 2020). As a high-income region in the Asia-Pacific, Japan had a healthy diet characterized by low salt and oil, effectively controlling the progression of DM (Shobako, Itoh, & Honda, 2024). Secondly, there was a certain relationship between SDI and the burden of DR. Areas with high SDI, such as Singapore, which has well-developed medical facilities, advanced public health systems and various policies to prevent and control the progression of DM, had the most significant reduction in ASR of DR (Chen et al., 2023). Areas with medium and high SDI, such as Sri Lanka, had an aging population structure, long life expectancy, and adequate medical resources, leading to an increased disease burden of chronic diseases. In addition, the process of urbanization may also affect the ASR of DR. The data showed that the urban population of Cambodia more than doubled from 19.7 in 2008 to 39.4 in 2019, while the ASR of DR In Cambodia has also increased the most("https://nis.gov.kh/nis/Census2019/Final%20General%20Population%20Census%202019-English.pdf").

Additionally, gender differences in DR burden varied among Asian countries. In 2021, except for 11 Southeast Asian countries (Cambodia, Indonesia, Laos, Malaysia, Mauritius, Myanmar, the Philippines, Seychelles, Sri Lanka, Timor-Leste, and Vietnam), the ASR for females was higher than for males in other Asian countries. This disparity may be related to the status of women. In Southeast Asia, men were typically the decision-makers for family healthcare, making it harder for women to access medical services compared to men, which led to a significant underestimation of DR prevalence in women(Khairallah et. al., 2014). Moreover, the higher the level of education, the more access one has to health knowledge and resources (Chung & Lim, 2020). Women in Southeast Asia generally had lower educational attainment than men, which limited their access to medical information and resources, contributing to the observed differences in DR prevalence.

This study predicted a downward trend in the DR burden over the next thirty years, consistent with previous research(Curran et al., 2024; Hashimoto et al., 2023). We considered this to be related to several factors. Firstly, advancements in medical technology have played a crucial role in preventing and controlling DR. Improved early detection methods, such as fundus photography and optical coherence tomography (OCT), could identify retinal lesions at the early stages of DR(Fujimoto & Swanson, 2016). Additionally, the application of artificial intelligence (AI) technology has made automated screening systems more accurate and efficient(Gulshan et al., 2016). Progress in treatment methods is also essential. For instance, anti-VEGF drug injections could effectively inhibit abnormal blood vessel growth, preventing and delaying the progression of retinal lesions(Wells et al., 2016). Improvements in surgical methods, such as laser photocoagulation and vitrectomy, provided effective treatment options for patients with advanced DR(Alasil & Waheed, 2014). Secondly, strengthened public health policies and preventive measures have significantly reduced the incidence of DR. Many countries have implemented screening programs that facilitate early detection, diagnosis, and treatment of DR(Muqit et al., 2019). Policies have been formulated to increase healthcare access, such as Thailand's universal healthcare coverage, which reached 99.8% of the population in 2013(Reutrakul & Deerochanawong, 2016). Moreover, lifestyle improvements are a key factor in reducing the incidence of DR. An increasing number of people recognize the importance of a healthy diet, adopting low-sugar and low-fat dietary habits, which helps in preventing diabetes and its complications.

This study has several limitations. Firstly, our research is constrained by the limitations of the GBD study methodology. The data used were estimated through stratified models from representative population-based studies, and the diagnosis criteria for DR may not be consistent across different regions. Therefore, the original data and statistical assumptions from these studies may introduce biases. Secondly, our data are sourced from the GBD 2021 database, and we have only accounted for the disease burden of DR without further distinguishing type 1 and type 2 diabetes. Additionally, it is challenging to identify the primary cause of blindness in patients with multiple complications.

CONCLUSION

In summary, the overall disease burden of diabetic retinopathy (DR) in Asia has been on an upward trend from 1990 to 2021. There was a persistent gender disparity, with females consistently showing higher rates than males. Among the VI severity, MVI was the most prevalent. Significant differences existed between Asian countries due to economic, dietary, and cultural factors. Predictive models suggest the YLDs rate will decline in the next 30 years. As the population ages, it is crucial to pay more attention to vision loss and blindness caused by DR. Adopting low-fat, low-sugar dietary habits and engaging in regular exercise are essential preventive measures. Additionally, countries should implement public policies to reduce the incidence of DR.

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