Original Article

The Correlation of Global Burden of Vision Impairment and Ambient Atmospheric Fine Particulate Matter

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Abstract

Purpose: To assess the correlation between the worldwide burden of vision impairment (VI) and fine particulate matter (PM) 2.5.

Methods: In this retrospective cross-sectional study, global and national prevalence and disability-adjusted lost year (DALY) numbers and rates of total VI, glaucoma, cataract, and age-related macular degeneration (AMD) were obtained from the Global Burden of Disease database. The global and national levels of PM2.5 levels were also extracted. The main outcome measures were the correlation of PM2.5 levels with total VI and three ocular diseases in different age, sex, and socioeconomic subgroups.

Results: In 2019, the worldwide prevalence of total VI and exposure level of PM2.5 was 9.6% (95% uncertainty interval: 8.0–11.3) and 42.5 μg/m^3, respectively. The national age-standardized prevalence rates of total VI ($r_p = 0.52$, $P < 0.001$), glaucoma ($r_p = 0.65$, $P < 0.001$), AMD ($r_p = 0.67$, $P < 0.001$), and cataract ($r_p = 0.44$, $P < 0.001$) have a positive correlation with PM2.5 levels. In addition, the national age-standardized DALY rates of total VI ($r_p = 0.62$, $P < 0.001$), glaucoma ($r_p = 0.62$, $P < 0.001$), AMD ($r_p = 0.54$, $P < 0.001$), and cataract ($r_p = 0.45$, $P < 0.001$) significantly correlated with PM2.5 levels. The correlations remained significant in different age, sex, and sociodemographic subgroups.

Conclusion: National prevalence rates of VI and three major ocular diseases correlate significantly with PM2.5 exposure levels, worldwide.

Keywords: Age-related macular degeneration, Air pollution, Blindness, Cataract, Fine particulate matter, Glaucoma, Global burden of disease, Particulate matter 2.5, Vision impairment

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Introduction

Air pollution is a global health problem. Based on the World Health Organization (WHO), air pollution levels have passed the upper limit in more than 90% of cities in low- and middle-income countries.[1] In 2019, air pollution led to 6.7 million deaths globally, among them 4.1 million deaths were related to ambient particulate air pollution.[2]

Among all air pollutants, long-term exposure to particulate matter (PM) is a strong predictor of human health.[3] The PMs are a mixture of suspended solid particles or liquid droplets of varying composition in the atmosphere that originate from organic or inorganic sources. The smaller the particle, the more its ability to pass the barriers of the respiratory system, access other internal organs, and cause damages.[4,5] Fine PM (PM2.5) is the air pollutant that poses the greatest risk to health, globally. Chua *et al.*[4] have shown more adverse effects of fine PM (PM2.5 with aerodynamic diameter ≤2.5 μm) compared with coarse PM (PM2.5–10 μm). Rome longitudinal study showed a 4% increased risk of all-cause mortality per 10 μg/m^3 increase in PM2.5 exposure.[6] Respiratory, cardiovascular, neurologic, metabolic, and even

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depressive disorders are also strongly associated with PM2.5 exposure level.[3,7-10]

The eye is in direct contact with the external environment. Exposure to air pollutants, especially PM2.5, impacts anterior eye disease, allergic conjunctivitis, and dry eye.[11,12] Moreover, it is hypothesized that PM2.5 induces some vascular and inflammatory mechanisms in intraocular tissues.[7,13-15] An association between retinal vessel disability and national levels of PM2.5 has been proposed.[16,17] Nevertheless, the studies on the effect of PM2.5 on ocular health remain scarce. Few previous studies identified that PM2.5 exposure levels can exacerbate some common ocular diseases such as glaucoma,[18-20] cataract,[21] and age-related macular degeneration (AMD).[22] However, these studies are limited to specific ocular diseases (e.g., glaucoma and AMD) or specific countries (e.g. UK and Taiwan). Moreover, no previous study evaluated the correlation of national PM2.5 levels with the global prevalence of vision impairment (VI) and blindness. Therefore, the aim of the current study is to investigate the correlation of the global prevalence of VI with PM2.5 levels and to evaluate whether the prevalence rate of total VI and the three most common ocular diseases (glaucoma, cataract, and AMD) varies in different countries with different PM2.5 exposure levels. We also evaluate the burden of these ocular diseases in various countries using national disability-adjusted lost year (DALY) rate.

Methods

In this study, the Global Burden of Disease (GBD) 2019 data were extracted from the Global Health Data Exchange (GHDx) enrolled by the Institute for Health Metrics and Evaluation. GHDx provides a publicly available resource for the prevalence of 364 diseases and injuries including eye diseases across 204 countries/territories in 2019.[23]

GHDx defines VI as visual acuity (VA) <6/12 and VA <3/60, respectively.[24] We used data of "vision loss and blindness" and three subgroups (glaucoma, cataract, and AMD), in all ages, and age-standardized format as well as in two ages (50–69 years [middle age] and 70 years ≤ [elderly]) and sex (male and female) subgroups. Two indicators were assessed in this study including prevalence and DALY. DALY is a measure of overall disease burden, expressed as the number of years lost due to ill-health, disability, or early death. The rate was calculated by accounting for population size (prevalence per 100,000 populations). Age-standardized rate per 100,000 inhabitants was produced by the direct standardization method, with the world population developed for GBD. For all estimates, 95% uncertainty intervals (UI) were considered.

The human development index (HDI) has been used to assess the socioeconomic level across countries by considering years of school education, expected years of school education, life expectancy, and gross national income.[25] The HDI parameter is calculated in a range of 0–1, with higher values showing more socioeconomic development. The countries have been grouped into four socioeconomic classes: low (0–0.549), medium (0.550–0.699), and high to very high (0.700–1.000) HDI. The data on national levels of HDI in 2019 came from the Human Development Report (http://hdr.undp.org/en/data) published by the United Nations Development Program.

The PM2.5 concentrations were defined as the mean annual concentration of fine suspended particles of <2.5 μm in diameters in a country (μg/m^3), which is expressed as annual averages. The countries have been divided into low and high PM2.5 exposure by considering 10 μg/m^3 as the cut-off value which has been specified by the WHO's air quality guidelines for long-term exposure.[26] The country-level PM2.5 in 2019 was available in the open database of the Organization for Economic Co-operation and Development (https://data.oecd.org/air/air-pollution-exposure.htm).

Statistical analyses were performed using SPSS software version 24 (SPSS Inc., Chicago, IL, USA). The correlation between VI and PM2.5 concentrations was evaluated by the Pearson correlation test in total and age, sex, and HDI subgroups. Countries with high and low PM2.5 exposure were compared using an independent sample *t*-test. Results were considered statistically significant at $P < 0.05$.

Results

The global level of PM2.5 exposure has increased 13.4% from 1990 to 2015 although there were two reduction points in 1995 and 2005 [Figure 1 and Table 1]. It has a trend of reduction after 2015 which was 8.6%. In 2019, the global PM2.5 exposure was 42.5 μg/m^3. More than 80% (82.4%, 168/204) of countries had high national levels of PM2.5 exposure, whereas others (17.6%, 36/204) were classified as low levels of exposure. India, Nepal, and Niger had the highest exposure concentration, whereas Finland, Sweden, and Estonia had the lowest exposure [Table 2].

The crude number of prevalence rates and DALY rates of total VI had an increasing trend since 1990–2019 [Figures 2, 3 and

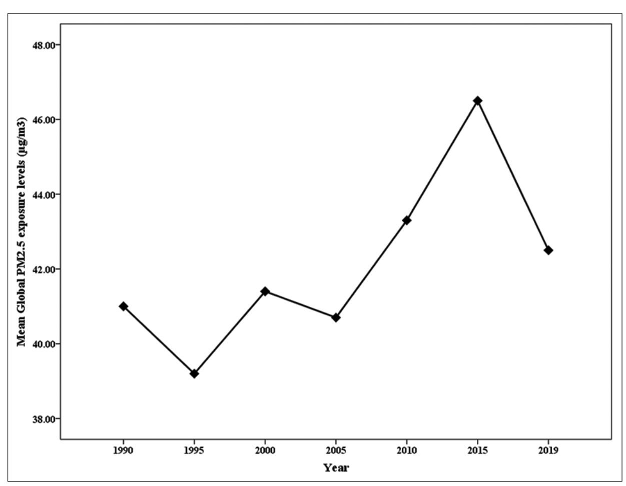

Figure 1: The global particulate matter 2.5 exposure levels since 1990–2019

Table 1: The global particulate matter 2.5 exposure level, prevalence rates, and disability-adjusted lost year rates of vision impairment since 1990–2019

Year	PM2.5 exposure (μg/m³)	Crude prevalence rate (per 100,000 population)				Crude DALY rate (per 100,000 population)				Age-standardized prevalence rate (per 100,000 population)				Age-standardized DALY rate (per 100,000 population)			
		Blindness	Glaucoma	AMD	Cataract	Blindness	Glaucoma	AMD	Cataract	Blindness	Glaucoma	AMD	Cataract	Blindness	Glaucoma	AMD	Cataract
1990	41.00	6601.33	72.56	66.94	791.36	232.56	8.27	5.55	812.91	8427.74	111.92	98.78	1150.56	303.48	12.78	8.29	93.17
1995	39.20	7097.00	72.05	71.09	812.76	239.74	8.14	6.07	779.41	8750.01	105.59	100.01	1126.69	301.65	11.95	8.61	90.31
2000	41.40	7421.99	76.71	73.48	934.68	252.43	8.45	5.95	826.59	8778.62	105.67	97.80	1221.63	304.70	11.68	8.01	94.52
2005	40.70	7768.22	79.42	80.22	1009.57	259.25	8.50	6.28	824.14	8732.79	101.90	100.02	1234.66	297.38	10.95	7.90	92.10
2010	43.30	8199.04	81.83	83.71	1088.76	268.20	8.69	6.45	818.28	8684.11	96.37	96.22	1232.25	289.70	10.26	7.47	89.38
2015	46.50	8738.66	89.40	91.19	1220.25	280.21	9.15	6.85	834.19	8677.21	95.43	95.21	1266.85	283.26	9.81	7.20	88.12
2019	42.50	9226.73	96.59	100.71	1253.93	291.56	9.67	7.29	775.38	8686.88	94.68	96.76	1207.88	278.22	9.52	7.05	82.94

PM: Particulate matter, DALY: Disability adjusted lost year, AMD: Age-related macular degeneration

Table 1]. However, the age-standardized rates of prevalence and DALY remained stable and decreased, respectively [Figures 2, 3 and Table 1]. Similar patterns were observed in glaucoma, cataracts, and AMD [Table 1]. In 2019, the prevalence of total VI was 9.6% (95% UI: 8.0–11.3) worldwide, including 1.3% (95% UI: 1.1–1.5) for cataracts, 0.1% (95% UI: 0.09–0.12) for glaucoma, and 0.1% (95% UI: 0.09–0.12) for AMD.

Globally, the crude prevalence rates ($r_p = -0.07$, $P = 0.33$) and crude DALY rates ($r_p = -0.08$, $P = 0.29$) of total VI did not correlate with national levels of PM2.5 exposure [Table 3]. Similarly, the crude prevalence rates of AMD ($r_p = -0.06$, $P = 0.38$) and cataract ($r_p = -0.11$, $P = 0.11$) did not have a significant correlation with PM2.5 exposure although crude prevalence rates of glaucoma showed statistically significant but weak correlation ($r_p = -0.19$, $P = 0.006$). Crude DALY rates of glaucoma ($r_p = -0.17$, $P = 0.02$) and AMD ($r_p = -0.18$, $P = 0.01$) also correlated significantly with PM2.5 levels.

After adjusting the countries for their age groups, there were positive significant correlations of national PM2.5 exposure levels with age-standardized prevalence rates of total VI ($r_p = 0.52$, $P < 0.001$) [Figure 4], glaucoma ($r_p = 0.65$, $P < 0.001$), AMD ($r_p = 0.67$, $P < 0.001$), and cataract ($r_p = 0.44$, $P < 0.001$). National age-standardized DALY rates of total VI ($r_p = 0.62$, $P < 0.001$), glaucoma ($r_p = 0.62$, $P < 0.001$), AMD ($r_p = 0.54$, $P < 0.001$), and cataract ($r_p = 0.45$, $P < 0.001$) also had significant positive correlations with the national PM2.5 levels. Moreover, the national age-standardized prevalence rates and age-standardized DALY rates of countries with high PM2.5 levels were significantly higher than countries with low PM2.5 levels [Table 4].

The significant positive correlations of national PM2.5 levels with prevalence rates and DALY rates of total VI, glaucoma, AMD, and cataract were observed in middle age (people aged 50–69 years), elderly (people ≥70 years), females, males, and countries with various HDI levels [Table 3].

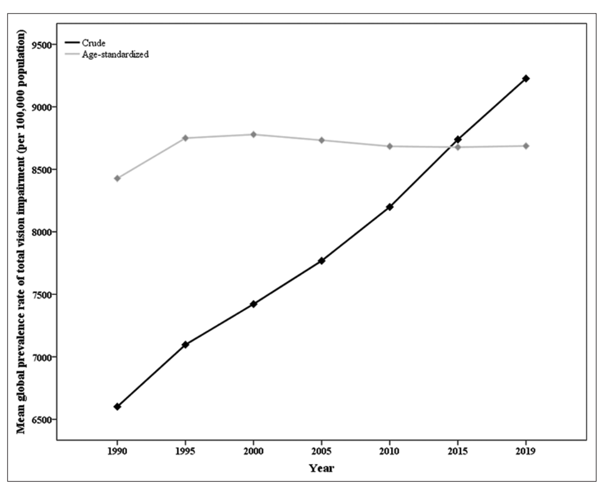

Figure 2: The global prevalence rate and age-standardized prevalence rate of total vision impairment since 1990–2019

Table 2: Ten countries with the highest and lowest national particulate matter 2.5 exposure levels and their age-standardized prevalence rates of vision impairment, worldwide in 2019

Rank	Country	PM2.5 exposure level	Age-standardized prevalence rate (rank* out of 204 countries)				Age-standardized DALY rate (rank* out of 204 countries)			
			Total blindness	Glaucoma	AMD	Cataract	Total blindness	Glaucoma	AMD	Cataract
					Highest exposure					
1	India	83.30	15,293.50 (195)	129.03 (122)	103.55 (145)	2653.81 (196)	525.44 (202)	12.23 (112)	8.16 (144)	195.06 (196)
2	Nepal	82.80	21,272.46 (204)	81.63 (72)	390.86 (204)	1651.48 (161)	478.28 (199)	7.72 (66)	20.71 (202)	100.21 (149)
3	Niger	80.10	15,408.46 (196)	298.90 (201)	147.30 (170)	1402.40 (138)	434.20 (191)	37.69 (201)	10.37 (162)	119.05 (179)
4	Qatar	77.10	6790.40 (44)	265.77 (183)	126.12 (159)	1547.04 (145)	287.43 (120)	32.58 (190)	7.80 (141)	88.46 (127)
5	Nigeria	70.50	12,869.54 (193)	309.09 (202)	282.25 (203)	2841.53 (200)	467.75 (196)	35.19 (196)	19.15 (201)	204.77 (198)
6	Egypt	67.90	7587.56 (73)	212.03 (163)	167.46 (185)	1789.96 (175)	330.49 (155)	23.54 (163)	12.90 (186)	112.09 (170)
7	Mauritania	66.50	10,562.69 (165)	259.72 (180)	177.75 (188)	1575.42 (151)	347.16 (163)	28.04 (178)	11.17 (169)	101.10 (150)
8	Cameroon	66.20	9959.03 (152)	245.18 (175)	167.51 (186)	1133.00 (118)	290.28 (127)	26.20 (171)	10.53 (164)	71.67 (114)
9	Saudi Arabia	64.10	8343.91 (102)	269.14 (186)	232.31 (200)	2372.55 (192)	464.76 (195)	30.69 (186)	21.02 (203)	172.16 (191)
10	Pakistan	63.90	12,421.42 (192)	121.82 (117)	182.37 (190)	3184.53 (203)	539.49 (203)	10.93 (97)	11.30 (171)	273.31 (203)
					Lowest exposure					
1	Finland	5.60	2568.52 (20)	53.56 (41)	79.91 (125)	354.33 (20)	104.08 (13)	6.15 (50)	7.49 (134)	18.14 (14)
2	Sweden	5.70	1938.30 (1)	47.26 (21)	68.89 (105)	277.03 (6)	86.85 (3)	5.87 (42)	7.44 (133)	17.16 (8)
3	Estonia	5.90	9391.39 (138)	32.57 (3)	15.50 (2)	356.17 (21)	180.54 (53)	2.91 (3)	1.21 (3)	21.30 (45)
4	Nauru	5.90	8248.49 (100)	88.96 (81)	34.84 (49)	1633.35 (160)	248.33 (88)	10.54 (92)	3.44 (63)	102.28 (154)
5	New Zealand	6.10	2577.80 (22)	54.04 (43)	40.44 (67)	371.32 (35)	104.63 (16)	5.56 (33)	4.25 (87)	21.54 (46)
6	Tuvalu	6.10	8352.20 (103)	94.73 (86)	36.13 (57)	1674.55 (166)	258.12 (94)	11.42 (103)	3.64 (69)	108.46 (162)
7	Cook Islands	6.30	7881.61 (87)	112.22 (112)	43.88 (69)	1689.48 (168)	260.65 (98)	14.30 (126)	4.97 (107)	110.45 (167)
8	American Samoa	6.40	8009.95 (93)	86.23 (76)	34.95 (51)	1617.19 (158)	240.50 (83)	10.08 (84)	3.48 (64)	98.34 (143)
9	Iceland	6.40	2361.21 (8)	64.32 (54)	132.08 (164)	348.52 (16)	108.34 (27)	8.15 (68)	14.43 (192)	19.94 (39)
10	Greenland	6.50	2246.60 (4)	53.70 (42)	30.63 (37)	289.69 (7)	91.06 (5)	6.30 (54)	3.26 (56)	20.13 (41)

*Ranking was performed from low to high levels. PM: Particulate matter, DALY: Disability-adjusted lost year, AMD: Age-related macular degeneration

Table 3: Correlation of national particulate matter 2.5 exposure level with national disability-adjusted lost year rates and prevalence rates of total blindness, glaucoma, age-related macular degeneration, and cataract in 204 countries, worldwide

Indices	Subgroups	Total VI	Glaucoma	AMD	Cataract
Prevalence rate	Crude	r_p=−0.07, P=0.33	r_p=−0.19, P=0.006	r_p=−0.06, P=0.38	r_p=−0.11, P=0.11
	Age standardized	r_p=0.52, P<0.001	r_p=0.65, P<0.001	r_p=0.67, P<0.001	r_p=0.44, P<0.001
	People aged 50–69 years	r_p=0.48, P<0.001	r_p=0.62, P<0.001	r_p=0.69, P<0.001	r_p=0.48, P<0.001
	People ≥70 years	r_p=0.40, P<0.001	r_p=0.63, P<0.001	r_p=0.58, P<0.001	r_p=0.40, P<0.001
	Female age-standardized	r_p=0.53, P<0.001	r_p=0.66, P<0.001	r_p=0.66, P<0.001	r_p=0.47, P<0.001
	Male age-standardized	r_p=0.50, P<0.001	r_p=0.63, P<0.001	r_p=0.68, P<0.001	r_p=0.42, P<0.001
	Low HDI	r_p=−0.02, P=0.91	r_p=0.44, P=0.01	r_p=0.54, P=0.001	r_p=0.47, P=0.006
	Medium HDI	r_p=0.45, P=0.005	r_p=0.05, P=0.79	r_p=0.64, P<0.001	r_p=0.26, P=0.12
	High to very high HDI	r_p=0.36, P<0.001	r_p=0.64, P<0.001	r_p=0.55, P<0.001	r_p=0.45, P<0.001
DALY rate	Crude	r_p=−0.08, P=0.29	r_p=−0.17, P=0.02	r_p=−0.18, P=0.01	r_p=−0.02, P=0.77
	Age-standardized	r_p=0.62, P<0.001	r_p=0.62, P<0.001	r_p=0.54, P<0.001	r_p=0.45, P<0.001
	People aged 50–69 years	r_p=0.60, P<0.001	r_p=0.55, P<0.001	r_p=0.59, P<0.001	r_p=0.45, P<0.001
	People ≥70 years	r_p=0.59, P<0.001	r_p=0.60, P<0.001	r_p=0.42, P<0.001	r_p=0.44, P<0.001
	Female age-standardized	r_p=0.64, P<0.001	r_p=0.61, P<0.001	r_p=0.53, P<0.001	r_p=0.48, P<0.001
	Male age-standardized	r_p=0.60, P<0.001	r_p=0.59, P<0.001	r_p=0.56, P<0.001	r_p=0.43, P<0.001
	Low HDI	r_p=0.39, P=0.03	r_p=0.42, P=0.02	r_p=0.39, P=0.03	r_p=0.36, P=0.04
	Medium HDI	r_p=0.45, P=0.006	r_p=−0.07, P=0.67	r_p=0.49, P=0.002	r_p=0.26, P=0.13
	High to very high HDI	r_p=0.52, P<0.001	r_p=0.61, P<0.001	r_p=0.41, P<0.001	r_p=0.40, P<0.001

HDI: Human Development Index, DALY: Disability-adjusted lost year, AMD: Age-related macular degeneration, VI: Vision impairment

Table 4: Comparison of national age-standardized disability-adjusted lost year rates and age-standardized prevalence rates of total blindness, glaucoma, age-related macular degeneration, and cataract in 204 countries with low or high levels of national particulate matter 2.5 exposure (based on 10 μg/m³), worldwide

Indices	Subgroups	Low level of PM2.5 exposure, mean (SD)	High level of PM2.5 exposure, mean (SD)	*P**
Age-standardized prevalence rate	Total VI	5018.51 (2727.68)	8865.67 (3189.30)	<0.001
	Glaucoma	70.04 (23.07)	144.32 (82.33)	<0.001
	AMD	49.95 (32.04)	90.25 (63.62)	<0.001
	Cataract	776.32 (598.97)	1151.35 (717.43)	0.004
Age-standardized DALY rate	Total VI	163.57 (67.39)	283.31 (103.64)	<0.001
	Glaucoma	7.88 (2.95)	15.85 (10.05)	<0.001
	AMD	4.86 (3.37)	6.87 (4.61)	0.004
	Cataract	47.52 (38.80)	78.70 (55.58)	0.002

*Independent samples *t*-test. PM: Particulate matter, DALY: Disability-adjusted lost year, AMD: Age-related macular degeneration, SD: Standard deviation, VI: Vision impairment

Discussion

The current study identified that age-standardized prevalence and DALY rates of total VI, glaucoma, AMD, and cataracts have a significant correlation with national PM2.5 exposure levels in 2019. In other words, the age-standardized prevalence rates of VI and the three most common ocular diseases are increasing by rising the national levels of PM2.5 exposure, worldwide. Similar correlations were observed in middle-aged and elderly people as well as countries with various HDI levels.

Epidemiologic studies have found increased production of inflammatory cells and cytokine due to the exposure to fine particles that cause systemic inflammatory responses.[7,27] The air pollution-induced inflammatory response accelerates the oxidative process.[13] Moreover, PM2.5 can impair microvascular endothelium-dependent dilation and increase the hypercoagulative state.[14,28] Therefore, exposure to ambient air pollution, especially PM2.5, has been shown to increase the risk of dementia, cognitive impairment, and cardiovascular disease.[8,9] Inflammation and oxidative stress are also underlying pathophysiological mechanisms of some ocular diseases such as glaucoma and AMD.[29] Consequently, PM2.5 air pollutants may be an independent factor in developing or exacerbating of this ocular disease which is a potentially modifiable risk factor. VI is a general term consisting of many etiologic factors. As cataract, glaucoma, and AMD were the main causes of VI in general populations, second to refractive errors, we further focus on these ocular diseases.[30]

Risk factors of glaucoma are classified into external factors (environmental risk and socioeconomic development) and internal factors (age, family history, ethnicity, and high intraocular pressure [IOP]).[31,32] The prevalence of glaucoma

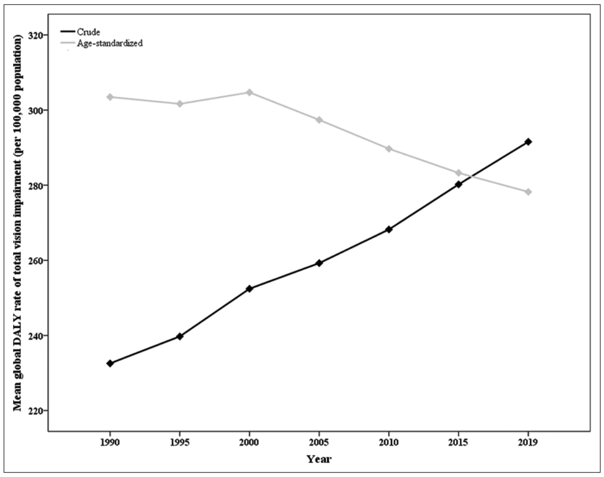

Figure 3: The global disability-adjusted lost year (DALY) rate and age-standardized DALY rate of total vision impairment since 1990–2019

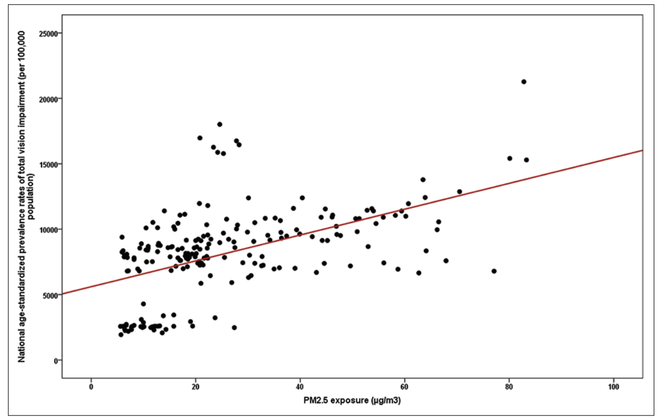

Figure 4: The positive correlation between age-standardized prevalence rate of total vision impairment and particulate matter 2.5 levels

in urban areas is 50% more than in rural areas, implying air pollutants are a probable risk factor for glaucoma.[33] Wang *et al*.[19] studied the association between glaucoma disability and national levels of PM2.5 and found a positive correlation between them; the higher the average levels of PM2.5, the more burden of glaucoma disability. Chua *et al*.[18] used data from the UK Biobank and identified an association between greater exposure to ambient PM2.5 and increased odds of glaucoma. They found that glaucoma-induced changes in inner retinal layers are greater in subjects with higher PM2.5 exposure levels.[18] However, the glaucoma detection was self-reported by patients, in their study. Similarly, Sun *et al*.[20] evaluated the Longitudinal Health Insurance Database of Taiwan from 3225 participants and identified that higher PM2.5 exposure levels were associated with increased risk of primary open-angle glaucoma in elderly patients.[20] We also observed that the glaucoma prevalence and DALY rates of countries with higher PM2.5 exposure levels are higher than countries with lower PM2.5 exposure.

The exact mechanism of air pollution-related glaucoma is unknown. One previous study reported the effect of long-term air pollution on elevating the IOP.[31] Li *et al*.[34] believed that PM2.5 exposure induces cell pyroptosis and inflammation in intraocular tissues such as trabecular meshwork which is responsible for controlling IOP, and consequently, it causes IOP rising. On the other hand, other studies found no clinically meaningful relationship between ambient PM2.5 with IOP.[4,18] In other words, although raised IOP is the cardinal risk factor for glaucoma, there may be other pressure-independent mechanisms including neuroinflammation or microvascular damages which have a prominent role in air-pollution-related glaucoma.[4,18]

AMD is a neurodegenerative condition which primarily affects the retina and choroid. Air pollution, especially PM2.5, has been proposed as a predisposing factor for AMD although the literature has discrepancies regarding the role of various air pollutants. A large community-based cohort study using UK Biobank data evaluated 115,954 people aged 40–69 years and found that greater exposure to PM2.5 was associated with self-reported AMD.[22] This study might even underestimate the risk because they used self-reported AMD as the sole determinant of AMD status.[22]

The development of AMD has been related to the interaction of several genetic and environmental risk factors.[35] As smoking is a known strong risk factor for AMD, it is plausible that ambient air pollution may also affect this disease.[35] Indeed, ambient air pollution can induce chronic oxidative stress and inflammation.[15] The retina has a favorable environment for oxidative stress owing to its high oxygen usage, high concentration of polyunsaturated fatty acids, and exposure to visible light.[36] Oxidative stress increases retinal pigment epithelium (RPE) lipofuscin, the main component of drusen.[37] Higher levels of PM2.5 lead to a thinner photoreceptor synaptic region, a thicker photoreceptor inner segment layer, and thinner RPE.[22] The thickening of photoreceptor outer segments may be secondary to RPE dysfunction as the RPE is involved in the turnover of photoreceptor outer segments. Chua *et al*.[4] also identified that higher levels of PM2.5 were associated with adverse changes in thicknesses of inner and outer retinal layers.

Long-term exposure to air pollutants may affect the incidence of cataracts. The pollutants can damage the membrane luminal and secretory proteins by initiating inflammatory cycles and producing reactive oxygen species.[38] West *et al*.[39] identified the role of household air pollution in cataract development. Shin *et al*.[21] evaluated data from the Korean National Insurance Service and identified exposure to PM10 associated with cataract development in Korean adults aged more than 50 years. They could not detect the role of PM2.5 in cataract formation because of no significant difference in regional distribution.[21]

The effect of air pollutants may be more evident in older people.[21] Indeed, the protective mechanisms against stress become weak by aging, and intraocular tissues are particularly susceptible to damage from air pollutants.[11,40] Moreover, there may be a cumulative effect of air pollution on the ocular disease. Therefore, it is important to standardize the countries based on age groups. It might explain why the national age-standardized prevalence and DALY rates correlated with PM2.5 exposure levels in the current study, whereas crude prevalence and DALY rates did not have a significant correlation with air pollution.

The HDI was used to assess the socioeconomic level across countries. It is a valuable indicator combining years of school education, expected years of school education, life expectancy, and gross national income.[25] However, the HDI has main shortcomings which may have influenced the study's findings. The first criticism is that the heterogeneity and divergence within countries are not considered by HDI.[41] Indeed, the HDI does not reflect the different degrees of development and inequalities across a country. Some countries, especially larger ones, have seen the computation of subnational HDIs precisely to gauge heterogeneity in development. On the other hand, new indicators such as Subnational HDI have been developed to overcome this problem.[42] The second criticism is that HDI uses long-term changes such as life expectancy which prevent this indicator to react to recent short-term changes. Gross national income does not necessarily increase economic welfare as it depends on how it is spent. These limitations of HDI may cause bias in the classification of countries based on socioeconomic level in the current study and thus, inhibit to show the real relationship between PM2.5 levels and VI in country subgroups.

Previous studies have demonstrated that some factors may enhance the effect of air pollutants on human health. There is a controversy regarding the sex. Although some studies showed that the female population is more susceptible to the influence of PM, others found the greater impact of air pollution on the male population or the lack of gender differences in terms of mortality, respiratory diseases, cardiovascular disease, etc.[43-46] Similarly, limited studies have reported the higher influence of air pollutants on females in terms of ocular diseases such as cataract and glaucoma.[19,21,39] Differences in hormonal levels, indoor exposure, and outdoor activities may be possible causes. However, Sun *et al*.[20] believed that the exposure level of PM2.5 is an independent risk for ocular disease after adjusting for sex. Similarly, the current study also showed that the correlation of PM2.5 levels with VI and three main ocular diseases (cataract, glaucoma, and AMD) remained significant in both the male and female populations which is in line with the independency of PM2.5 role on VI.

This study has some limitations. The main limitation of the study is related to the ecological fallacy that prevents reaching conclusions on individual risk from aggregate data. As a group of people (country) was the unit of analysis for the current study, the results may not be applicable for all individuals with high PM2.5 exposure who suffer from VI. Therefore, no causal relationship can be suggested. Although this study demonstrated a relationship between air pollution and VI, it is not clear whether PM2.5 is driving the primary pathologic processes in the common ocular disease or having an additive or synergistic effect on the pathophysiology of eye diseases. Moreover, this relationship may be affected by differences in race, exposure duration, lifestyle, which were not considered in the current study. Future studies may also be useful to investigate the correlation between PM2.5 levels and VI at a more local or regional level, to account for potential spatial variations in PM2.5 levels and VI prevalence. Indeed, an ecological study does not provide an opportunity to take into account or adjust other factors that may influence the outcome (i.e., confounding factors). Therefore, an apparent correlation or the lack of a correlation could be misleading. In addition, we did not evaluate the relationship of other less important air pollutants with VI. Another limitation of the current study is that the majority of air monitoring stations seem to be located in the most polluted cities that may not represent the exposure status of country's weighted average. Hence, raw data of national air pollution levels needs to be corrected for any changes in the number, location, and accuracy of monitoring stations. The current study also suffers from limitations and potential biases associated with the GBD database which may have influenced the study's findings. Despite these limitations, available data from GBD allow analysis of large amount of information from all over the world.

In conclusion, our findings support that the national prevalence rate of total VI as well as the national prevalence rates of glaucoma, AMD, and cataract correlates with national levels of fine PM2.5. More studies are needed to investigate the relationship between PM2.5 exposure and specific ocular outcomes, such as age-related eye disease, and the potential mechanisms underlying the relationship between PM2.5 exposure and ocular diseases. Assessment of trends in PM2.5 levels and VI by time at global and national levels can also be the aim of future studies. The national and international policies regarding the ocular health may focus on areas with higher PM2.5 levels. By defining the high-risk groups in future studies, these policies and interventions can be focused on target people.

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Conflicts of interest

There are no conflicts of interest.

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