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Trend and Geographical Distribution of Diabetes Mellitus Mortality Attributed to Air Pollution in Iran from 1990 To 2021

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ABSTRACT

Introduction: The escalating incidence and mortality rates of diabetes, coupled with the growing threat of air pollution, pose a substantial threat to public health in Iran. This study seeks to examine the geographical distribution and temporal trends of diabetes-related deaths specifically linked to air pollution across the country.

Methods: Utilizing data from the Global Burden of Disease (GBD) study, we employed Joinpoint regression analysis to identify significant shifts in the mortality trends of type 2 diabetes mellitus (T2DM) linked to air pollution. Furthermore, spatial distribution patterns for the year 2021 were mapped and analyzed using ArcMap GIS v.10.

Results: The mortality rate of T2DM attributable to air pollution in Iran exhibited an upward trend between 1990 and 2019, after which a subsequent decline was observed from 2019 to 2021. The highest annual percentage change in females occurred between 2011 and 2016 (5.134, 95% UI: 4.704–5.563), whereas in males, it occurred between 2012 and 2015 (6.275, 95% UI: 4.867–6.934). The highest average annual percentage change in females was observed in Gilan (4.427, 95% UI: 4.305–4.535), and in males, it was observed in Bushehr (4.125, 95% UI: 3.873–4.320). Geographical analysis revealed that in 2021, Tehran and Khuzestan had the highest mortality rates, whereas the lowest rates were recorded in Zanjan, Kohgiluyeh, and Boyer-Ahmad for females and Kohgiluyeh, Boyer-Ahmad, and Hamadan for males.

Conclusion: These findings highlight the continued need for stronger environmental control measures, especially in high-risk areas, to further reduce the burden of air pollution-related diabetes mortality in Iran.

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Introduction

The global prevalence of type 2 diabetes is increasing, with projections indicating a significant increase in the number of affected individuals worldwide. Research suggests that in 2021, over 537 million cases of diabetes were reported globally, with estimates indicating that this figure could reach 783 million by 2045 [1, 2].

The burden of type 2 diabetes is rising, and the age-standardized incidence rate of this disease has steadily increased from 1990 to 2019, particularly in regions with high socioeconomic development

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indices (SDI), such as Central Asia, South Asia, as well as Sub-Saharan Africa [3]. Furthermore, the prevalence of type 2 diabetes is projected to continue increasing, reaching 7,079 per 100,000 by 2030, indicating a concerning trend in low-income countries [4]. Globally, there has been a significant rise in the age-standardized incidence rates and disability-adjusted life years (DALYs) associated with type 2 diabetes. This upward trend is particularly pronounced in Southeast Asia and within the middle SDI window, characterized by low-to-middle income levels [5].

Type 2 diabetes is recognized as a global health crisis, and multiple factors contribute to its incidence and mortality. In recent years, researchers have increasingly focused on the link between environmental factors and this chronic disease [6, 7]. Air pollution is one such environmental factor that has been extensively studied. Emerging evidence has underscored a profound association between air pollution exposure and an elevated risk of both type 2 diabetes onset and related mortality [1, 8, 9].

Systematic evidence indicates that increased exposure to ambient air pollutants is closely linked to diabetes risk; specifically, every 10-µg/m3 increment in PM2.5 and NO2 is associated with an 8–10% rise in T2DM risk [10]. Another meta-analysis reported similar findings, with PM2.5, PM10, NO2, and O3 significantly linked to increased diabetes-related mortality [11]. A large-scale cohort study conducted in the United States demonstrated that long-term exposure to PM2.5 and NO2 was associated with increased diabetes-related mortality [12].

In recent years, diabetes has experienced a concerning upward trend as one of the prevalent non-communicable diseases in Iran. According to the latest official statistics, 13.2% of the country's population is affected by this disease [13-17]. However, air pollution has become a serious environmental and public health concern in Iran, particularly in urban areas. Current trends show that many cities consistently exceed permissible levels of key air pollutants, including particulate matter (PM), sulfur dioxide (SO_2), and ozone [18]. Despite the growing burden of both diabetes and air pollution in Iran, no comprehensive national study has simultaneously examined long-term trends and provincial disparities in air pollution–attributable diabetes mortality. Therefore, this study aimed to address this gap by providing a temporal and geographical analysis at the national level.

Methods

Study Area

Iran is one of the Eastern Mediterranean regions in western Asia, and has 31 provinces. According to the last estimation, the population is approximately 84000000, of which is an almost equal percentage of men and women (50.5% men and 49.5% women) [19].

Data Source and Processing

This study utilized the latest Global Burden of Disease (GBD) dataset, characterized by its standardized methodology and broad-scale collaboration involving more than 10,000 experts from over 150 countries. The GBD metrics are derived from a robust array of sources, ranging from vital registration and censuses to clinical informatics and disease registries. Subnational estimates for Iran were specifically incorporated at the first administrative level [20]. The dataset provides annual updates, allowing for a longitudinal analysis spanning from 1990 to 2021. This dataset offers estimates for various measures, including mortality trends over time and across countries from 1990 to 2021. More details on GBD 2021 are provided elsewhere [20]. We used the GBD dataset to estimate the trend analysis of the T2D death rate attributable to air pollution according to sex and Iran provinces [21].

Statistical Analysis

In present study, Joinpoint regression was used to detect changes in the trend analysis of the T2D age-standardised death rate attributable to air pollution. Joinpoint regression was selected because it allows the identification of significant changes in trend over time and detects years (joinpoints) in which the slope of the trend significantly changes. This method is particularly

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suitable for long-term time-series analyses where non-linear patterns may occur. In this method, the annual death rate attributable to air pollution for T2D and its standard error (SE) are used as inputs to the model. To characterize temporal trends, Annual Percent Changes (APC) and Average Annual Percent Changes (AAPC) were estimated, along with their corresponding 95% Uncertainty Intervals (UIs), for each sex and province. In this model, if y_x shows the amount in year x, it will be $\log y_x = b_0 + b_1 x$, where b_0 represents the interceptand and b_1 denotes the slope coefficient. Based on this model, the APC from year x to year x+1 is calculated as:

$$APC = (e^{b_1} - 1) \times 100$$

Additionally, the AAPC was determined as the weighted mean of the APCs, as follows:

$$AAPC = (e^{\frac{\Sigma w_i APC_i}{\Sigma w_i}} - 1) \times 100$$

The years in which trend changes occurred were considered joinpoints, and the trend changes between these points were examined. The significance of the identified trends was assessed using the Monte Carlo permutation method. All statistical analyses were performed using Joinpoint software, developed by the US National Cancer Institute. Because the study was based on GBD 2021 estimates, rates were already age-standardized and derived from comparative risk assessment models that adjust for key demographic factors. Therefore, additional adjustment for confounders at the analytical stage was not performed.

Exposure Definition

In the GBD 2021 framework, air pollution–attributable mortality includes exposure to ambient particulate matter pollution (PM2.5) and indoor air pollution stemming from the combustion of solid fuels, as defined by the comparative risk assessment methodology. These exposures were not directly measured in this study but were obtained from GBD-modeled estimates.

Geographic Analysis

The geographic distribution of air pollution-related diabetes mortality in 2021, based on 100000 people and with a 95% UI, was visualized at the provincial level. Spatial analysis was performed using ArcMap GIS v.10 software to highlight the regional patterns.

Methodological Considerations

GBD estimates are derived from multiple data sources using statistical modeling techniques to address data gaps and inconsistencies in the data. While this approach enhances comparability across regions and years, the estimates remain subject to uncertainty related to data availability, model assumptions and potential misclassification.

Result

Trend Analysis Results

From 1990 to 2021, the death rate per 100,000 due to air pollution in Iranian T2DM patients exhibited a biphasic pattern marked by an initial rise until 2019 and a subsequent decline through 2021 for both sexes (Figure 1). The trend analysis of the death rate in T2DM females attributable to air pollution showed the highest APC between 2011 and 2016 (5.134, 95%UI; 4.704, 5.563) and the lowest between 1990 and 2002 (0.322, 95%UI; 0.173, 0.452) (Table 1). In males, the APC was highest between 2012 and 2015 (6.275, 95%UI; 4.867, 6.934) and lowest between 2006 and 2012 (1.293, 95% UI; 0.716, 1.753) (Table 2).

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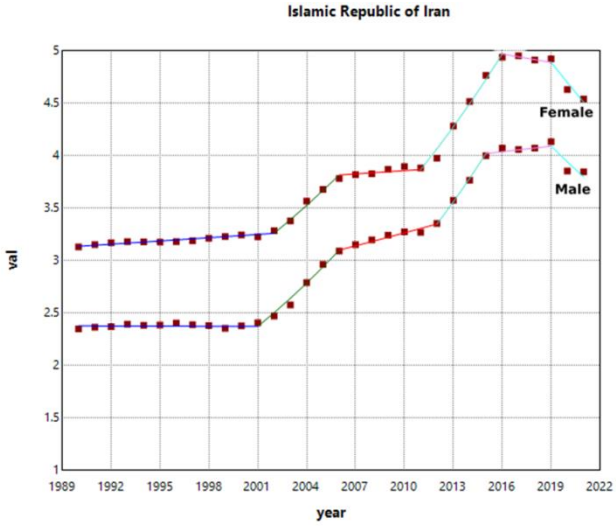


Figure 1: The annual percent change over 1990–2021 in mortality rate per 100,000 population in T2DM attributable to air pollution in Iran.

Table 1: The trends in the annual percent change in mortality rate per 100,000 population in T2DM attributable to air pollution in Iranian females over 1990–2021.

Segment (Year range)	Annual Percentage Change (95% UI)	P-Value
1990-2002	0.322 (0.173, 0.452)	0.004*
2002-2006	4.013 (3.203, 4.982)	0.003*
2006-2011	0.273 (-0.186, 0.793)	0.162
2011-2016	5.134 (4.704, 5.563)	0.004*
2016-2019	-0.536 (-1.151, 1.719)	0.150
2019-2021	-3.962 (-5.195, -2.735)	0.000*

Table 2: The trends in the annual percent change in mortality rate per 100,000 population in T2DM attributable to air pollution in Iranian males over 1990–2021.

Segment (Year range)	Annual Percentage Change (95% UI)	P-Value
1990-2001	-0.017 (-0.204, 0.164)	0.824
2001-2006	5.492 (4.893, 5.993)	0.002*
2006-2012	1.293 (0.716, 1.753)	0.003*
2012-2015	6.275 (4.867, 6.934)	0.000*
2015-2019	0.431 (-0.105, 1.144)	0.093
2019-2021	-3.655 (-5.025, -2.034)	0.000*

Table 3 presents the AAPC trends from 1990 to 2021 regarding the air pollution-attributable mortality rate per 100,000 population in T2DM across Iran and its provinces. Among females, Gilan province exhibited the highest AAPC (4.427; 95% UI: 4.305, 4.535), whereas Lorestan recorded the lowest (0.346; 95% UI: 0.253, 0.402). Similarly, in males, Bushehr province showed the most significant increase (AAPC: 4.125; 95% UI: 3.873, 4.320), while Qom province had the minimum AAPC (0.342; 95% UI: 0.210, 0.459).

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Table 3: The average annual percent change in mortality rate per 100,000 population in T2DM attributable to air pollution in Iran and its provinces over 1990–2021.

Provinces	Average annual percent change (95% UI)	
	Female	Male
Iran	1.178 (1.104, 1.228)	1.520 (1.440, 1.585)
Alborz	1.986 (1.872, 2.069)	1.746 (1.627, 1.850)
Ardebil	1.296 (1.224, 1.363)	2.347 (2.23, 2.451)
Bushehr	3.945 (3.779, 4.103)	4.125 (3.873, 4.320)
Chahar Mahal and Bakhtiari	1.682 (1.543, 1.811)	2.479 (2.270, 2.678)
East Azarbayejan	2.906 (2.781, 3.021)	2.839 (2.650, 3.001)
Fars	3.062 (2.908, 3.200)	3.211 (3.042, 3.361)
Gilan	4.427 (4.305, 4.535)	3.697 (3.528, 3.829)
Golestan	3.544 (3.416, 3.653)	3.675 (3.543, 3.805)
Hamadan	2.043 (1.945, 2.128)	1.947 (1.829, 2.046)
Hormozgan	1.766 (1.659, 1.869)	1.850 (1.607, 2.057)
Ilam	3.575 (3.450, 3.690)	3.888 (3.731, 4.026)
Isfahan	2.847 (2.761, 2.927)	3.034 (2.904, 3.150)
Kerman	2.725 (2.604, 2.829)	2.212 (2.088, 2.328)
Kermanshah	2.342 (2.237, 2.431)	1.822 (1.734, 1.897)
Khorasan-e-Razavi	3.033 (2.936, 3.138)	3.059 (2.922, 3.179)
Khuzestan	1.839 (1.736, 1.920)	1.647 (1.532, 1.761)
Kohgiluyeh and Boyer-Ahmad	0.837 (0.765, 0.898)	0.971 (0.855, 1.064)
Kurdistan	2.356 (2.209, 2.478)	1.901 (1.727, 2.062)
Lorestan	0.346 (0.253, 0.402)	1.341 (1.259, 1.407)
Markazi	2.384 (2.233, 2.509)	2.085 (1.887, 2.249)
Mazandaran	2.046 (1.982, 2.095)	2.111 (2.037, 2.191)
North Khorasan	1.167 (1.080, 1.251)	0.686 (0.580, 0.761)
Qazvin	1.462 (1.375, 1.547)	2.481 (2.344, 2.609)
Qom	0.609 (0.493, 0.719)	0.342 (0.210, 0.459)
Semnan	2.545 (2.390, 2.682)	2.712 (2.545, 2.864)
Sistan and Baluchistan	3.478 (3.172, 3.679)	3.107 (2.918, 3.276)
South Khorasan	1.233 (1.128, 1.319)	0.789 (0.706, 0.866)
Tehran	-0.505 (-0.555, -0.466)	0.018 (-0.051, 0.095)
West Azarbayejan	3.431 (3.305, 3.543)	3.016 (2.896, 3.126)
Yazd	3.222 (3.032, 3.387)	2.999 (2.737, 3.204)
Zanjan	2.685 (2.541, 2.803)	3.313 (3.178, 3.437)

Geographic Analysis Results

The air pollution-related diabetes mortality rates in Iranian provinces in 2021 are shown in Figure 2. The highest rates in both sexes were observed in Golestan, Mazandaran, Tehran, Yazd, Isfahan, and Khuzestan. The lowest rates in both sexes were in Hamadan, Kohgiluyeh and Boyer-Ahmad, Kurdistan, South Khorasan, and Zanjan. The highest rates among women were observed in Tehran and Khuzestan (9.0 and 6.7 per 100,000, respectively), while the lowest rates were recorded in Zanjan and Kohgiluyeh and Boyer-Ahmad (1.1 and 1.3 per 100,000, respectively). Among men, the highest rates were found in Tehran and Khuzestan (7.9 and 5.1 per 100,000, respectively), and the lowest rates were in Kohgiluyeh and Boyer-Ahmad and Hamadan (1.1 and 1.2 per 100,000, respectively).

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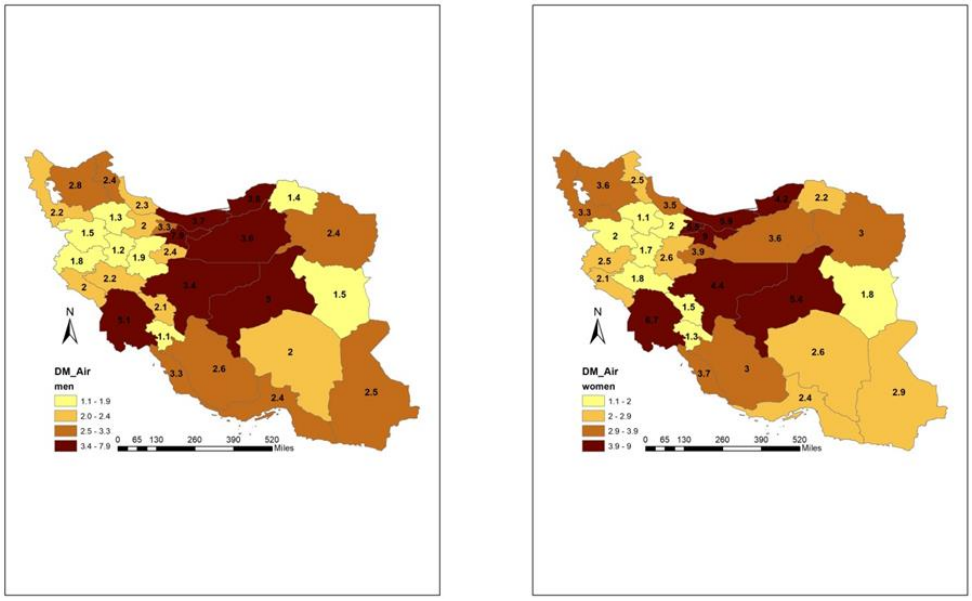


Figure 2: Geographic distribution of air pollution-related diabetes mortality rates by gender in Iran, 2021 (per 100,000 population).

Discussion

Overall trends and biological plausibility

This study, based on Global Burden of Disease (GBD) 2021 estimates, demonstrates a substantial three-decade increase (1990–2021) in age-standardized mortality rates attributable to air pollution among individuals with type 2 diabetes mellitus (T2DM) in Iran, followed by a noticeable decline between 2019 and 2021. Together with persistent sex differences and marked provincial variation, these findings highlight the significant contribution of ambient air pollution to diabetes-related mortality in a middle-income country undergoing rapid urbanization and industrial expansion. Our findings are consistent with previous epidemiological evidence. Cohort studies examining the relationship between diabetes mellitus and air pollution have demonstrated that exposure to air pollutants elevates the prevalence of diabetes mellitus [22]. The 2019 Burden of Disease Study indicated that approximately 20% of the global diabetes burden in 2019 was attributable to particulate matter 2.5 (PM2.5) air pollution [23]. Moreover, evidence from a 12-year longitudinal cohort study in China indicated that long-term exposure to ambient air pollution is significantly associated with an increased risk of diabetes onset and heightened mortality within this patient population. Specifically, PM10, SO_2, and NO_2 were associated with markedly higher diabetes incidence, while PM10 showed the strongest association with diabetes-related mortality, followed by NO_2 and SO_2. [24]. These findings provide context for the observed trends in Iran and set the stage for understanding the underlying biological mechanisms. Chronic exposure to air pollutants such as PM2.5, PM10, and gaseous pollutants contributes to T2DM development through mechanisms involving systemic inflammation, oxidative stress, and endoplasmic reticulum dysfunction [25]. Inhaled pollutants trigger pulmonary oxidative stress and the systemic release of pro-inflammatory cytokines [26, 27], activating pathways such as NF-κB that impair insulin signaling and promote insulin resistance[28]. Additional pathways include visceral adipose tissue inflammation, macrophage infiltration, and mitochondrial dysfunction following long-term PM2.5 exposure [29, 30], collectively disrupting glucose homeostasis and increasing cardiovascular and premature mortality risk in diabetes[1]. Experimental evidence indicates that PM2.5 penetrates deeply into the alveoli and generates reactive oxygen species more potently than larger particles [31], which may help explain rising pollution-attributable T2DM mortality in high-

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exposure settings such as Iran[32, 33].

Air pollution trends

Field studies indicate a dramatic global increase in air pollution, with the WHO reporting in 2019 that 99% of the global population is exposed to ambient air pollution that exceeds WHO guideline limits, with a disproportionate burden observed in low- and middle-income countries [34, 35]. In Iran, pollutant concentrations have intensified since the 1970s owing to industrialization, vehicular emissions, and dust storms, reaching critical levels in cities such as Tehran, Ahvaz, Mashhad, and Isfahan [18], where Ahvaz has ranked among the world's most polluted cities, with particulate concentrations sometimes threefold that of Beijing [36]. This severe pollution is consistent with the observed three-decade rise in attributable T2DM deaths in Iran.

Impact of COVID-19

Another key finding of the present study was the observed decline in mortality rates between 2019 and 2021, following three decades of increasing trends. This period coincided with global lockdowns and restrictions due to the COVID-19 pandemic, which also affected Iran [37]. Multiple studies have documented a notable improvement in air quality during this time. For example, the Air Quality Index (AQI) in Tehran decreased by 8% in the first four months of 2020 compared to the same period in 2016–2019 [38], and major pollutants, including PM10, CO, SO_2, and NO_2, showed significant reductions during March–April 2020 relative to 2019 [39]. Overall, the three-phase lockdown initiated in early 2020 led to a substantial drop in concentrations of PM10, SO_2, CO, and other pollutants, with improvements persisting into early 2021. However, as restrictions were gradually lifted and normal activities resumed, pollution levels began to rise again [40, 41].

Gender Differences

A consistent gender disparity was observed, with age-standardized mortality rates in female patients with diabetes significantly exceeding those of their male counterparts across the entire temporal range.

Research shows that women experience higher disability-adjusted life years (DALYs) and mortality rates attributable to air pollution, particularly from ambient particulate matter pollution (APMP) and household air pollution from solid fuels (HAP-SF), compared to men. This trend is observed globally and spans various age groups, with older adults being especially vulnerable [42]. This higher mortality rate due to air pollution in women in Iran could have various causes. The results of studies show that women, especially in low- and middle-income countries, spend more time at home and are usually responsible for cooking. Therefore, compared to men, they spend more hours of their lives exposed to indoor air pollution and suffer more damage [43]. Furthermore, women are more susceptible to air pollution because of certain biological factors. Research suggests that women have smaller lungs and narrower airways, which heighten their risk of lung diseases and damage caused by smoking and air pollution [44, 45]. Additionally, studies indicate that estrogen, particularly 17β-estradiol, plays a complex role in influencing the body's inflammatory response to environmental pollutants such as ozone, potentially amplifying the inflammatory reaction in women's lungs when exposed to ozone in polluted air [46]. These combined behavioral and biological factors may increase vulnerability to air pollution–related complications among women with diabetes in Iran.

Provincial Disparities and Environmental Contributors

This study shows substantial regional differences in air pollution-related T2DM mortality in Iran from 1990 to 2021. Provinces such as Gilan (for females) and Bushehr (for males) exhibited higher APC values, indicating faster increases in mortality, whereas Lorestan and Qom showed slower rises. These differences reflect a combination of industrialization, urban development, climatic conditions, and topography [47-50]. Bushehr, with major gas and petrochemical industries, has high PM2.5 levels that exacerbate health risks [48]. Gilan’s proximity to the Caspian

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Sea and humid climate may enhance pollutant retention, while Lorestan's mountains and Qom's arid climate facilitate dispersion or reduce particle retention [47, 49, 50]. In 2021, Tehran and Khuzestan had the highest air pollution-related T2DM mortality rates, whereas Zanjan, Kohgiluyeh and Boyer-Ahmad, and Hamadan recorded the lowest. These patterns correspond partly to baseline diabetes prevalence, climate, industrialization, urbanization, and lifestyle factors[13, 14, 51-54]. Khuzestan, characterized by oil refineries, petrochemical plants, and frequent dust storms, has one of the highest diabetes prevalence rates (~15.3%) and elevated exposure to pollutants [13, 14]. Yazd and Isfahan, both arid and industrial with natural dust exposure, also show high prevalence and mortality, where hot, dry climates and lower physical activity may amplify risk [14, 52-54]. In contrast, mountainous or rural provinces experience lower pollution exposure and reduced diabetes burden [49, 50]. Tehran, Iran's capital, frequently exceeds WHO limits for PM2.5 and NO2, particularly during colder months due to temperature inversions. High population density, vehicular emissions, and industrial activities worsen air quality, while urbanization further increases concentrations of PM2.5, PM10, NO2, and SO2 [55-59]. Khuzestan's industrial activities release VOCs, greenhouse gases, and particulate matter, compounded by dust storms, which contribute to respiratory, cardiovascular, and diabetes-related complications [1, 51, 60, 61]. Overall, these findings underscore the need for geographically tailored public health strategies. Targeted interventions in high-burden provinces, including pollution control, diabetes screening, and lifestyle modification programs, could mitigate the impact of environmental and industrial contributors on T2DM mortality.

Strengths and limitations

The primary strengths of this study lie in its novelty, as it represents the first analysis of sex-stratified and province-specific mortality trends in T2DM linked to air pollution within the Iranian context. Furthermore, the utilization of the GBD database ensures a high level of granularity and statistical power, providing critical insights that can assist in assessing the efficacy of the national healthcare system.

However, several limitations must be acknowledged. First, the study is primarily descriptive in nature, focusing on the characterization of temporal trends rather than identifying the causal determinants or biological mechanisms through explanatory variables or predictive modeling. Second, the reliance on GBD-sourced data introduces potential biases stemming from heterogeneous data collection methods and the use of statistical estimates in regions with limited primary data. In contexts such as Iran, where vital registration systems may be suboptimal, the risks of underreporting and measurement errors remain a significant concern [62]. Moreover, relying on estimated data for countries with limited information can influence the accuracy of national projections.

Conclusion

This study highlights the substantial impact of air pollution on type 2 diabetes mellitus (T2DM) mortality in Iran from 1990 to 2021. The key findings include a steady increase in age-standardized mortality rates until 2019, followed by a decline from 2019 to 2021 (likely due to COVID-19 lockdowns), alongside persistent sex disparities (higher in women) and marked provincial variations (highest in Tehran and Khuzestan, lowest in mountainous regions). These results indicate that air pollution remains a major preventable driver of diabetes-related mortality, exacerbating cardiovascular and metabolic burdens in high-exposure areas.

Policymakers should prioritize high-burden provinces with targeted interventions, such as stricter pollution controls (industrial/vehicular emissions and dust storm mitigation), enhanced diabetes screening and prevention, and promotion of lifestyle changes (especially physical activity). Geographically tailored national and provincial strategies are urgently needed to reduce this ongoing health burden in Iran.

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Data availability statement

The datasets are freely available in the Global Burden of Disease Study (GBD) repository, [https://vizhub.healthdata.org/gbd-results/].

Use of generative AI and AI-assisted technologies

During preparation, the authors used AI to assist with grammar checking and enhance the academic quality of the manuscript. After using this tool, the authors reviewed and edited the manuscript.

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The authors have no acknowledgements to declare.

Conflict of Interest

The authors declare that they have no competing interests.

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Ethical Considerations

This study used aggregated publicly available GBD data and did not require informed consent. All procedures were performed in accordance with relevant guidelines and regulations.

Code of Ethics

This study was approved by the Ethics Committee of Shahid Sadoughi University of Medical Sciences (Ethics Code: IR.SSU.REC.1403.134).

Authors' Contributions

S.H. and M.TS. conceived the idea. N.H. and S.H. contributed to designing the study. M.TS. collected the data. F.SS. and M.TS. analyzed the data. N.H., S.H., and F.SS. wrote the draft of the manuscript. Subsequently, all authors engaged in discussions regarding the results and provided feedback on the manuscript draft, and N.H. and F.SS. revised and finalized the draft of the manuscript based on the authors' comments.

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