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Review Article

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Environmental factors and machine learning for Alzheimer's disease prediction

Shahriar Mohammadi[*], Soraya Zarei

Information Technology Group, Department of Industrial Engineering, K.N. Toosi University of Technology, Tehran, Iran

Abstract

Background: One of the brain anomalies that typically affects the elderly is Alzheimer's disease (AD) and its frequency has greatly grown during the previous few decades. AD is affected by many genetics and environmental circumstances. Environmental factors and the quantity of air pollutants are two of the most significant elements influencing the prevalence of AD.

Methods: In this study, information from articles on the effects of air and environmental pollutants on AD was utilized. Additionally, the role of machine learning in predicting diseases was examined.

Results: Several studies, approached from various perspectives, have delved into the factors influencing the onset of AD. The development of machine learning techniques has made it possible to record information about the environmental conditions and people's habitats to make possible the occurrence of dementia-related abnormalities. According to the reviewed studies, certain biological pollutants can significantly increase the likelihood of developing AD. Also, it indicated the use of this technique has been based on biological information recorded for various diseases. The results showed that unhealthy environmental conditions increase the odds ratio of AD several times. Therefore, using this information provides the possibility to prevent the occurrence of AD.

Conclusion: In general, reliable information on the living conditions of the elderly, together with other information about AD, allows for the accurate forecast needed to avert the loss of social and personal capital. The future contribution of this knowledge is something we can envision.

Keywords: Humans aged, Alzheimer's disease, Brain, Air pollution, Risk factors

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***Correspondence to:**
Shahriar Mohammadi,
Email: mohammadi@kntu.ac.ir

Introduction

Dementia is a pressing global health issue, with someone developing it every three seconds. The number of people affected is expected to surpass 55 million soon, reaching 78 million by 2030 and 139 million by 2050, with most of the increase occurring in developing countries. This highlights the urgent need for global action to address dementia (1). The fastest rises in their elder populations are happening in China, India, and its neighbors in South Asia and the western Pacific area. In 2015, it was anticipated that dementia would cost \$818 billion globally, or 1.09% of the world's gross domestic product. By 2030, the annual expense of dementia is projected to increase to US\$ 2.8 trillion from its current level of about US\$ 1.3 trillion (2) (Figure 1).

Alzheimer's disease (AD) is a brain disorder that slowly impairs a person's ability to think, recall things, and carry out even the most basic actions. The majority of patients with AD, 60%–70% of all cases worldwide, develop their first symptoms in their older years. It is a persistent, incapacitating, and developing disease (3).

Dementia, especially AD, significantly affects individuals aged 65 and older, with AD being the majority of cases. Life expectancy post-diagnosis varies but can be 4 to 8 years, with some living up to 20 years. By 2020, global dementia cases surpassed 50 million, highlighting concerns in public health and aging (4).

The situation is expected to worsen, with dementia cases projected to double every two decades, reaching 152 million by 2050. Developing nations, currently home to 60% of patients, will see this rise to 71%. This shift highlights the urgent need to strengthen healthcare systems, prioritize research on prevention and treatment, and ensure culturally sensitive care. Global initiatives are crucial to enhancing healthcare and providing adequate support for those affected by dementia. Key regions affected include Asia, Latin America, and Africa, where aging populations and limited healthcare infrastructure exacerbate the problem. Asia alone is expected to experience a dramatic increase, with over 81 million

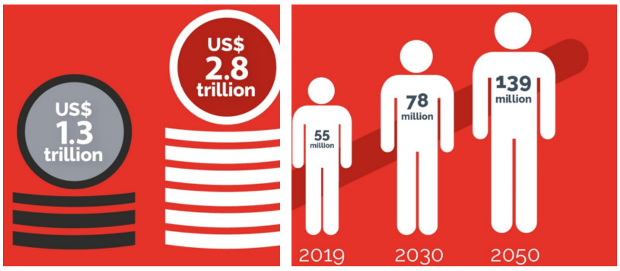

Figure 1. By 2030, it is anticipated that the expense of dementia will increase to US$ 2.8 trillion (left), with a projected increase in the number of dementia sufferers (right)

people living with dementia by 2050, especially in East, South, and Southeast Asia. Latin America and the Caribbean will also see substantial growth, with cases nearly quadrupling. Meanwhile, Sub-Saharan Africa and the Middle East are projected to face a surge in dementia cases as these regions age rapidly and face increased urbanization and lifestyle-related risk factors (2).

The World Alzheimer Reports conducted systematic investigations on global dementia prevalence until April 2017. Estimations of dementia cases were derived from regional incidence rates by age and sex, besides UN population projections from 2015 to 2050. Research on AD focuses on understanding risk factors to reduce its incidence, although only a small fraction of cases are associated with specific gene mutations. Empirical evidence regarding environmental risk or protective factors for AD has been inconsistent (1).

Despite being the biggest risk factor for the disorder, age is not the main biological cause of AD. Furthermore, this disease affects people of all ages. Dementia affects young people in roughly 9% of instances up to age 65, according to research (5).

According to studies, factors such as physical activity, smoking, consuming alcohol, gaining weight, diet, blood pressure, cholesterol, and blood sugar all have a major impact on the development of AD. In addition, other factors affecting AD include depression, social isolation, education level, and air pollution (6).

Objective

The goal of this review study is to look into how different environmental factors influence the development of AD as well as how prediction and machine learning can help prevent it.

Criteria for selecting articles

In alignment with the research objectives, the selection criteria for the utilized articles were categorized into two distinctive groups: The first group focused on information sources exploring the impact of environmental factors at both the individual and cellular levels on the likelihood and probability of AD. This entailed investigating how exposure to air pollution may contribute to the development and progression of AD on a biological and molecular level. The second group centered on resources that delved into disease prediction algorithms. These sources were particularly valuable in understanding how algorithms designed for disease prediction, especially in the context of AD, could provide insights to mitigate early occurrences. The emphasis was on exploring the effectiveness of predictive models in identifying potential cases before symptomatic manifestation, thereby enabling preventive measures.

Materials and Methods

A comprehensive literature search was conducted to identify relevant studies on the role of environmental factors and machine learning techniques in predicting AD. The search spanned peer-reviewed journal articles, conference proceedings, and review papers published between 1990 and 2024. The databases used included PubMed, IEEE Xplore, Scopus, and Google Scholar. The following keywords and Boolean operators were employed in various combinations: Alzheimer's disease prediction, environmental factors, machine learning, neurodegenerative diseases, predictive modeling, data mining, and risk factors for AD.

Inclusion criteria

To ensure relevance and quality, specific inclusion and exclusion criteria were applied: Studies that focus on using machine learning algorithms for predicting AD. Research examining environmental risk factors (e.g., air pollution, diet, lifestyle) and their association with AD. Papers that discuss the integration of machine learning with environmental or clinical data to enhance predictive accuracy. Articles published in English and peer-reviewed. Also, studies did not directly address AD or prediction models. Papers that do not involve environmental factors. Non-peer-reviewed literature, such as editorials, commentaries, and unpublished theses. Studies focused solely on genetic or purely clinical biomarkers unless environmental factors were also considered.

Relevant data were extracted from the selected studies, including the type of machine learning algorithms used (e.g., support vector machines, neural networks, random forests), environmental factors considered (e.g., air quality, diet, lifestyle), and the performance metrics reported (e.g., accuracy, precision, recall). The methods used in each study were critically evaluated based on their robustness, reproducibility, and contribution to understanding the prediction of AD. The review also identified common challenges across studies, such as the quality and availability of environmental data, the complexity of integrating multifactorial data into predictive models, and the limitations of current machine-learning approaches in healthcare applications.

This section outlines a rigorous and systematic approach to reviewing the existing literature on the subject. By clearly specifying the search strategy, criteria, and methods of analysis, the review aims to provide a comprehensive and credible synthesis of the current state of research in predicting AD using environmental factors and machine learning.

Investigating cell damage and its role in Alzheimer's disease

According to Halliwell (7) and Migliore and Coppedè (8), reactive oxygen species (ROS), such as free radicals and their derivatives, lead to oxidative cell alterations. Although ROS are primarily produced by the mitochondrial electron transport chain, a variety of ROS are created throughout the body during normal metabolism at many cellular sites in healthy tissues (7,8). ROS are required for both the maintenance of tissue oxygen homeostasis and the removal of microbial intruders. They can, however, also affect the cell's oxidative processes and change the structure of lipids, proteins, and nucleic acids to bring on or exacerbate associated with age symptoms (9).

Air pollution, especially from fine particulate matter ($PM_{2.5}$) and nitrogen dioxide (NO_2), has been shown to increase ROS production in the body. When inhaled, these pollutants can enter the bloodstream and cross the blood-brain barrier, where they promote the production of ROS in brain cells. This leads to oxidative stress, which triggers inflammation and damages cellular structures, including lipids, proteins, and DNA (10).

A study by Block and Calderón-Garcidueñas demonstrated that exposure to high levels of air pollution, particularly from traffic emissions, significantly increases oxidative stress in the brain. The elevated ROS levels contribute to the accumulation of beta-amyloid plaques, a hallmark of AD. This study emphasizes how environmental factors like air pollution can accelerate the pathophysiological processes associated with AD (11).

Research by Butterfield et al highlights that oxidative stress and ROS are among the earliest detectable changes in the brain associated with AD. This suggests that environmental factors, such as air pollution, which elevate ROS levels, may act as triggers or accelerators of the disease (12).

The level of stress caused by oxidation is determined by the balance between ROS creation and the antioxidant defense system. An oxidative stress state arises when the antioxidant defense mechanisms' capacity is surpassed, leading to oxidative damage to macromolecules, also mitochondria, and other cell compartments (13,14). Oxidative stress might show up as lipid peroxidation, oxidation of proteins, or DNA oxidation depending on the macromolecules that ROS are targeting. The decline in cognitive function and motor skills in aging brains is due to an increase in free radical oxidation of lipids, proteins, and DNA (15,16). It has been established that tangles of neurofibrillary cells contain enhanced macromolecule oxidation and its byproducts. Along with their brains, AD patients' peripheral tissues (such as blood cells) and biological fluids (like urine) have also been found to have markers of several types of oxidations (15).

The buildup of ROS is believed to encourage oncogenesis by altering redox-regulated signaling pathways. This suggests that the redox state is essential in processes such as signal transduction, cellular proliferation, differentiation, and apoptosis (17). Oxidative stress-induced damage has long been recognized as a factor in human diseases and a catalyst for tumor formation (18). For instance, long-term cigarette smoking creates an intracellular oxidative environment that triggers a series of inflammatory responses, which are believed to enhance the carcinogenic process (19). Genotoxic carcinogens linked to prolonged tobacco inhalation cause various effects, such as the oxidation of glutathione, elevated oxidative DNA damage, and reduced levels of circulating antioxidants. If left unrepaired, these carcinogens can induce mutations, including the activation of proto-oncogenes (like K-Ras) or the inactivation of tumor suppressor genes. Additionally, ROS are known to promote chromosomal aberrations, the formation of DNA and protein adducts, and epigenetic modifications (20). Conversely, numerous compounds in urban air, originating from both natural sources (such as volcanic eruptions and dust storms) and man-made sources (including combustion for heating, power generation, and vehicle emissions), have been associated with carcinogenesis through ROS-mediated cellular toxicity. Air pollutants can directly affect various signaling pathways through their non-cellular properties (such as shape, size, and solubility) and/or cellular mechanisms that lead to ROS production and subsequent toxicity. Additionally, polycyclic aromatic hydrocarbons and volatile organic compounds (like benzene) can become metabolically active, leading to oxidative DNA damage (21,22).

Air pollution and Alzheimer's disease

Air pollution, including ozone and particulate matter, poses significant health risks such as AD. Studies from 2015 to 2022 show a relationship between air pollutants, particularly rising particulate matter levels, and AD risk. Monitoring and reducing air pollution are vital for public health, as highlighted by the 2019 State of Global Air Report. Despite progress, air pollution caused nearly five million deaths worldwide in 2017, with developing nations most affected (23,24). Further research and preventive measures are essential to mitigate its impact. Air pollution is widely recognized across various disciplines as a significant threat to human health. Originating from various sources like industry, transportation, and the burning of coal, fossil fuels, and biomass, it contributes to respiratory and cardiovascular illnesses, as well as brain abnormalities. Pathological studies indicate that air pollutants such as PM, O_3, NO_2, SO_2, and CO can lead to neurodegeneration and brain damage. These effects are mediated by control functions linked to oxidative stress, inflammatory conditions, and mitochondrial damage, all associated with the progression of AD (25,26). A selection of the results related to pollutants affecting dementia is presented in Table 1. As shown, higher levels of air pollutants significantly increase the risk of dementia and AD.

Toxic heavy metals and Alzheimer's disease

Table 2 summarizes studies that associate toxic heavy metals with dementia risk. Increased rates of dementia were observed in areas with higher soil arsenic levels, though this country-level analysis is less indicative of individual risk factors (34). A case-control study involving 129 participants in each group found a higher incidence of Alzheimer's dementia among individuals born in regions with above-average lead concentrations (35). Aluminum has been the most extensively studied metal concerning dementia, with several studies involving nearly 22 000 dementia patients (36). A study revealed that consuming more than 0.1 mg of aluminum per day in drinking water doubled the risk of dementia and tripled the risk of Alzheimer's dementia. Conversely, another study found that higher aluminum levels in soil had a protective effect (37).

Two case-control studies examined the relationship between copper and iron and dementia. The results for copper were inconclusive. However, both studies found that higher soil levels of iron were linked to an increased risk of dementia (35,37). A cross-sectional study reported that a higher proportion of individuals with Alzheimer's dementia were born in areas with elevated levels of manganese (35). Conversely, another study found that higher zinc levels in the soil were associated with an increased risk of Alzheimer's dementia (37).

The utilization of machine learning in forecasting dementia

Artificial intelligence (AI) has rapidly evolved from a theoretical concept to a transformative force, increasingly integrating into various fields and revolutionizing industries, with medicine standing out as a particularly promising domain for its applications and innovations (41).

John McCarthy coined the term "artificial intelligence" in 1956, envisioning machines replicating human behavior. Advancements in processing speed have integrated AI into daily life, notably in medicine, where it accelerates processes and enhances accuracy. Machine learning algorithms analyze medical data, aiding diagnosis and treatment. In the 1990s and early 2000s, automation improved specialized medical procedures, reducing errors and improving outcomes. These innovations mark a crucial moment in medical technology, augmenting healthcare professionals' capabilities and enhancing patient care (42).

Years of research into dementia, including the amyloid hypothesis, have provided valuable insights, yet a complete understanding remains elusive. Leveraging clinical data from electronic health records and conducting multi-omics research presents vast potential to explore AD biology (43). The wealth of data from thousands of AD patients exceeds the human capacity for full comprehension. Integrating clinical and biological data enables unprecedented insights into AD mechanisms, uncovering hidden patterns and associations. The rapid accumulation of data signifies significant progress in addressing AD. Cutting-edge techniques and vast data are pushing boundaries, potentially leading to breakthroughs

Table 1. Attributes chosen to investigate the connections between air pollution and Alzheimer's disease

Author	Year	Title	Output
Jung et al (27)	2015	Ozone, Particulate Matter, and Newly Diagnosed Alzheimer's Disease: A Population-Based Cohort Study in Taiwan	Increased HR of AD by 138% for every rise in $PM_{2.5}$ of 4.34 µg/m^3, and increased HR of AD by 10.91 ppb for every increase in O_3 over the follow-up period.
Li et al (28)	2012	Influence of $PM_{2.5}$ exposure level on the association between Alzheimer's disease and allergic rhinitis: A national population-based cohort study	The OR (2.656-5.604) of AD patients rose when the particulate matter 2.5 exposure level increased.
Wu et al (29)	2015	Association between air pollutants and dementia risk in the elderly	The highest (≥49.23 µg/m^3) vs. the lowest tertile of PM_{10}: OR = 4.17; the highest (≥21.56 ppb) vs. the lowest tertile of ozone: OR = 2.00.
Oudin et al (30)	2016	Traffic-related air pollution and dementia incidence in Northern Sweden: A longitudinal study	HR (1.43, CI: 0.998, 2.05) AD was elevated as a result of air pollution.
Cerza et al (31)	2019	Long-term exposure to air pollution and hospitalization for dementia in the Rome longitudinal study	Exposure to O_3, NOx, and $PM_{2.5}$ was adversely linked with AD, while exposure to NOx, NO_2, and PM_{10} was positively associated with dementia hospitalizations.
Carey et al (32)	2018	Are noise and air pollution related to the incidence of dementia? A cohort study in London	Increased dementia risk due to NO_2 > 41.5 µg/m^3 (HR = 1.40).
Kioumourtzoglou et al (1)	2016	Long-term $PM_{2.5}$ exposure and neurological hospital admissions in the northeastern United States	The HR of AD 1.15 increased with the amount of $PM_{2.5}$ in the city.
Yuchi et al (33)	2020	Road proximity, air pollution, noise, green space and neurologic disease incidence: A population-based cohort study	Road closeness was linked to outcomes in AD HR: 1.14

AD: Alzheimer's disease; PM: Particulate matter; HR: Hazard ratio; CI: Confidence interval; OR: Odds ratio.

Table 2. The relationship between exposure to toxic heavy metals and the development of dementia

Author	Year	Title	Output
Emard et al (35)	1994	Geographical distribution of Alzheimer's disease cases at birth and the geochemical profile of Saguenay-Lac-Saint-Jean/Québec, Canada (image project)	Among individuals with AD, 15 were born in regions with below-average lead concentrations, while 49 were born in areas with above-average lead concentrations.
Dani (34)	2010	Arsenic for the fool: An exponential connection	Small increases in soil arsenic concentration were associated with exponential rises in dementia rates at the national level.
McLachlan et al (38)	1996	Risk for neuropathologically confirmed Alzheimer's disease and residual aluminum in municipal drinking water employing weighted residential histories	Aluminum levels exceeding 100 µg/L, as opposed to levels below 100 µg/L, showed a higher likelihood of AD and dementia (OR, 1.7).
Vogt (39)	1986	Water quality and health: study of a possible relation between aluminum in drinking water and dementia (Pamphlet).	The zone with the highest aluminum concentration was linked to an elevated standardized dementia mortality rate compared to the zone with the lowest concentration (per 10 000 inhabitants per year: 48.3 vs 32.4). This difference was more pronounced in women (59.4 vs 38.5) than in men (36.9 vs 26.1).
Shen et al (37)	2014	Positive relationship between mortality from Alzheimer's disease and soil metal concentration in mainland China	After excluding three outlier provinces, there was a correlation between copper concentration and annual mortality from AD (correlation coefficient = 0.449, P = 0.021).
Shen et al (37)	2014	Positive relationship between mortality from Alzheimer's disease and soil metal concentration in mainland China	Elevated levels of iron in the soil were linked to higher mortality rates from AD (with a relative risk of 1.248 comparing the highest to the lowest group). Following the exclusion of three outlier provinces, there was a correlation between iron concentration and the annual mortality rate from AD (r = 0.537, P = 0.007).
Shen et al (37)	2014	Positive relationship between mortality from Alzheimer's disease and soil metal concentration in mainland China	Elevated zinc levels in the soil were linked to higher mortality rates from AD, with the highest group having a RR of 2.289 compared to the lowest group.
Gillette-Guyonnet et al (40)	2005	Cognitive impairment and composition of drinking water in women: findings of the EPIDOS study	Consuming low levels of silica in water (≤4 mg/d) was linked to a higher risk of dementia, with a multivariable-adjusted OR of 2.74.
Rondeau et al (36)	2009	Aluminum and silica in drinking water and the risk of Alzheimer's disease or cognitive decline: findings from 15-year follow-up of the PAQUID cohort	The highest quartile of silica concentration in drinking water compared to the lowest quartile was associated with an increased risk of dementia and AD.

AD: Alzheimer's disease; RR: relative risk; OR: Odds ratio.

in diagnosis, treatment, and prevention (44).

Advanced AI-based models can successfully mine big data for relevant information, but as their complexity increases, it gets tougher to understand how they produce their results. Making AI comprehensible is a significant obstacle to current AI technological advancement, but it is essential for healthcare applications since patients and doctors need to have faith in research methodology to make decisions about people's health (45).

The need for a precise individual diagnosis is reinforced by the AD pathology's extreme complexity and heterogeneity, the lack of etiological consistency, and the vast variety of treatments that can be helpful for certain people. To maximize the efficiency and enhance the outcomes of biological investigations, complex biological simulation, based on mathematical and statistical methods like Artificial Neural Networks, must be utilized to support and monitor these studies (46).

Combining structured knowledge from psychology, neuroscience, neurology, psychiatry, geriatric medicine, biology, and genetics offers a holistic approach to AD research. Innovative analytical methods, including bioinformatics and statistics, are applied to large datasets to gain comprehensive insights into disease progression, identify patient subgroups, and discover biomarker combinations through predictive models. This approach can lead to the development of effective treatment strategies and personalized medical care for individual AD patients (47).

Artificial intelligence has brought about a substantial transformation in the assessment and utilization of digital data. Currently, AI is deployed across various applications to perform basic functions like recognizing faces or speech, often surpassing human capabilities in these domains. This presents an extraordinary opportunity, particularly in the field of medical treatment, where AI's potential for swift, cost-effective, and precise automation, such as employing AI algorithms for the analysis of digital images, can be harnessed (48,49).

Machine learning enables computers to learn autonomously, making it valuable in disease detection and diagnosis with the vast amount of medical data available. It outperforms traditional statistical methods like logistic regression and Cox proportional hazard models, particularly with extensive datasets, overcoming challenges such as predictor independence assumptions and risks of overfitting and collinearity (50). This versatility allows varied data sources to be utilized in AD diagnosis, potentially leading to insightful results combined (51) (Figure 2).

Machine learning-based methods have been found in the last 10 years to be beneficial for AD diagnosis. Commonly used classification methods encompass support vector machines, artificial neural networks, gradient boosting techniques, random forest, K-nearest neighbor, and neural networks.

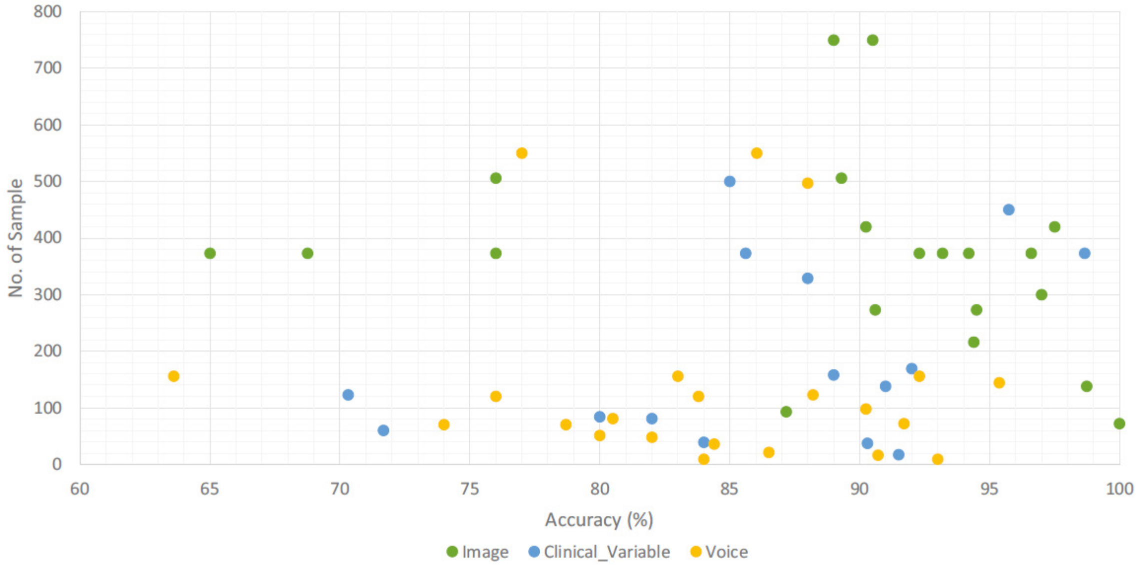

Figure 2. Assessing the accuracy of machine learning models concerning the dataset size, taking into account the data modality (23)

The economic advantages of early detection of Alzheimer's disease

The aging population presents challenges due to increased incidence of age-related illnesses, leading to rising healthcare and social support costs. Caring for the current 35 million dementia patients costs over $600 billion annually, exceeding 1% of global GDP. As people age, they become more vulnerable to conditions like dementia, imposing significant burdens on healthcare systems and societies. These challenges require innovative approaches to healthcare delivery and cost management (52). Early diagnosis and quality care for the elderly, especially those with dementia, are essential not only morally but also economically. Strategies must be developed to alleviate financial strain on healthcare systems while ensuring adequate support for the aging population. Also, demonstrated AD is ranked third on the list of costly diseases for the American economy, after cancer and cardiovascular disease. Between $50 billion and $100 billion is projected to be spent annually on treating AD. Formal or direct costs include things like long-term care and medical appointments. Long-term care and lost productivity from family carers are examples of informal or indirect costs (4). AD patients who reside in the community have two main costs: their direct medical costs and the indirect cost of caregivers' lost productivity. The predicted annual direct spending on healthcare might amount to $29.1 billion in 1998 currency. The annual cost per patient for lost productivity due to unpaid caregivers is estimated to be up to $47 000.

In 2010, global dementia costs were projected at around $604 billion, with Western Europe and North America bearing about 70% of these expenses (53). In high-income regions, direct social care and informal caregiving costs were nearly equal, while in low- and middle-income countries, informal caregiving dominated expenses. Dementia poses significant financial burdens globally, disproportionately impacting different regions. Concerns arise over rising costs as diagnosis-to-treatment time decreases (54). The shift from informal to formal social care spending in lower-income countries is expected to continue, affecting future expenditures and long-term care affordability. Investing in research and utilizing machine learning for early diagnosis and care is crucial to manage future societal costs effectively, ensuring sustainable and efficient healthcare systems (55).

Identifying individuals predisposed to AD before its onset can lead to cost savings at family, community, and societal levels. The economic impact of brain aging is well-documented, highlighting the need for proactive approaches (56). Artificial intelligence and machine learning offer promising avenues for disease prevention across medical fields. Predicting AD occurrence is feasible through comprehensive data collection on personal, social, environmental, and genetic factors, coupled with machine learning algorithms. Early detection of diseases offers significant economic benefits by reducing healthcare costs, improving quality of life, and alleviating the burden on caregivers. Identifying conditions at an early stage often allows for more effective and less expensive treatments, avoiding the higher costs associated with advanced disease management and emergency care. This proactive approach not only enhances patients' quality of life by enabling better disease management and maintaining their daily activities but also reduces the emotional and financial strain on caregivers. By minimizing the need for intensive care and prolonged support, early detection contributes to overall cost savings in the healthcare system and supports both patients and their families in managing their health more effectively (51).

Discussion

Air pollution, responsible for 7 million annual deaths, is a major global environmental health risk, linked to climate change. Improving air quality has benefits for the environment, the economy, and public health. Both versions clarify that improving air quality has multiple positive impacts. Notably, air pollution, a significant risk factor for dementia, including AD, increases with exposure to harmful compounds like $PM_{2.5}$. Research shows a clear correlation between $PM_{2.5}$ exposure and dementia risk, with implications for AD prediction (54).

Research on the association between PM_{10} (particulate matter with a diameter of 10 µm or less) and AD yields varying and inconclusive results. PM_{10} concentrations in Rome and Taiwan during the assessment period were within the range of IT-2 (30 µg/m^3) and IT-3 (50 µg/m^3). Interestingly, AD risk increased in Taiwan but decreased in Rome (29). These divergent outcomes highlight the complexity of the PM_{10}-AD risk relationship, suggesting the influence of regional factors and individual characteristics. Further research is necessary for a comprehensive understanding of these dynamics. Decades ago, research identified the fundamental factors underlying PM-induced neurodegenerative diseases (31).

Emerging research suggests that environmental factors may significantly contribute to the risk and progression of AD. One important prediction is that prolonged exposure to air pollution, particularly fine particulate matter ($PM_{2.5}$), may increase the incidence of AD. Studies have shown that pollutants can induce oxidative stress and inflammation in the brain, which are critical pathways in developing neurodegenerative diseases. Populations living in highly polluted urban areas are especially at risk, with predictions indicating a potential rise in AD cases as air quality continues to decline due to increased industrial activities, vehicular emissions, and other pollutants (57,58).

The potential connection between heavy metal exposure and AD has been a subject of investigation for decades. Metals such as lead, mercury, and aluminum have drawn attention due to their known neurotoxic effects, but the evidence linking them to AD is complex and often inconsistent.

Lead exposure, particularly during early development, has been linked to cognitive decline later in life. Lead can accumulate in the brain and contribute to neurodegeneration by promoting oxidative stress and inflammation. A study by Cecil et al found that children with higher lead exposure had brain abnormalities linked to cognitive deficits, which could be precursors to dementia in adulthood (59). While some animal and human studies suggest a connection between lead exposure and AD, other studies have not found a significant association. The inconsistency arises due to variations in the timing and duration of exposure, differences in populations studied, and challenges in measuring long-term exposure accurately (60).

Mercury, particularly methylmercury, has been primarily introduced into the human body by consuming contaminated fish. Studies have shown that mercury can cross the blood-brain barrier and cause neurotoxicity, potentially contributing to Alzheimer's pathology. A study by Mutter et al suggested that mercury exposure could lead to beta-amyloid plaque formation, a hallmark of AD (61). Despite these findings, other research has not consistently supported the mercury-AD relationship. Some population studies have failed to show a significant increase in AD risk among individuals with higher mercury exposure, possibly due to variations in diet, mercury levels, and individual susceptibility.

Aluminum has been investigated for its potential role in AD for decades. It can accumulate in brain tissue and has been found in the plaques and tangles characteristic of AD. Some studies, such as those conducted by Exley, suggest that high aluminum levels in drinking water or from occupational exposure could be linked to an increased risk of AD. However, the aluminum hypothesis remains controversial. Large-scale studies have not consistently demonstrated a clear causal relationship between aluminum exposure and AD. The complexity of Alzheimer's etiology, involving multiple factors like genetics and lifestyle, makes it difficult to isolate aluminum as a significant contributor (62).

Machine learning is increasingly utilized to predict and understand the environmental factors contributing to AD. One significant prediction from ML models is the identification of complex interactions between air pollution and genetic predispositions that may increase AD risk. By analyzing vast datasets, including air quality indices and genetic information, ML algorithms can identify patterns and correlations that traditional statistical methods might miss. These models have predicted that individuals with certain genetic markers, such as the APOE ε4 allele, are more susceptible to the adverse effects of air pollution, particularly fine particulate matter ($PM_{2.5}$). This insight suggests a compounded risk factor where genetics and environment intersect, underscoring the need for targeted interventions in high-risk populations (63,64).

Another critical prediction made by machine learning involves the impact of lifestyle factors modulated by environmental conditions on AD progression. For example, ML models have shown that exposure to pesticides and heavy metals, combined with factors like diet and physical activity, can significantly influence the onset and severity of AD. By integrating data from various sources, such as environmental exposure records, healthcare databases, and personal health trackers, ML algorithms can forecast AD progression with higher accuracy. These predictions highlight the importance of holistic approaches to AD prevention, incorporating environmental regulations and personalized healthcare strategies to mitigate the risk factors identified through machine learning analyses (65,66).

Machine learning algorithms have revolutionized our ability to predict and comprehend complex diseases like AD. Their success in predicting AD occurrence marks a major advance in early diagnosis and intervention, potentially altering the disease's trajectory. These algorithms analyze extensive datasets containing genetic markers, neuroimaging, cognitive assessments, and environmental factors (67). Integrating diverse data points provides a comprehensive understanding, capturing subtle nuances beyond traditional diagnostic methods.

Moreover, Machine learning algorithms advance personalized medicine by tailoring predictions to individual risk profiles, incorporating genetic predispositions, lifestyle factors, and other variables (66). This nuanced approach fosters precise and targeted prediction models, marking a shift from one-size-fits-all healthcare strategies. Machine learning plays a pivotal role in transforming AD prediction towards personalized approaches. Machine learning in AD prediction faces challenges like ethical concerns, data privacy, and algorithm interpretability (68). Yet, the potential benefits, such as improved diagnostic accuracy and early intervention, drive ongoing research. Brain imaging modalities like MRI and PET scans offer valuable insights into brain alterations. Sophisticated algorithms analyze these images, revealing subtle indicators of Alzheimer's pathology, aiding early detection and understanding of disease mechanisms (69).

The research findings have significant implications for proactive and personalized healthcare. Accurate prediction of AD onset allows for timely intervention, potentially altering the disease's course. High accuracy and recall rates achieved by various algorithms demonstrate their effectiveness in detecting subtle patterns indicating AD risk (70). These studies also advance our understanding of AD complexities by integrating advanced algorithms with large-scale brain imaging datasets. This deeper comprehension is crucial for developing targeted therapeutic approaches and refining treatment methods. The study combined a genetic algorithm with a support vector machine to classify different types of AD (33). This integrated approach demonstrated impressive performance metrics: a precision of 93.01%, indicating accurate identification of AD cases; a recall rate of 89.13%, showing sensitivity in capturing positive instances; and a feature detection rate of 96.80%, highlighting effectiveness in identifying relevant disease characteristics (70).

Using machine algorithms to analyze air pollution data for predicting AD is highly valuable. While existing studies have used biological and MRI data for early detection, there's a lack of research on using environmental data. Heavy air particles are directly linked to AD risk, emphasizing the importance of incorporating such environmental factors into predictive models (71).

The data on COX-2 expression and Aβ42 buildup offer the potential for predicting AD before its onset, enabling tailored solutions, particularly by government bodies. Early diagnosis is crucial since AD cannot be cured, but early intervention may prevent its progression. Utilizing environmental data and predictive analytics beforehand could potentially prevent the disease, significantly enhancing its value (1,72).

Looking ahead, it is crucial to continue advancing research and investing in early detection technologies to realize their potential benefits fully. For instance, the development of advanced screening methods for diseases such as cancer or AD, such as liquid biopsies or digital biomarkers, could significantly enhance early detection capabilities. Future research should focus on improving the accuracy and accessibility of these technologies, exploring new biomarkers, and developing more sophisticated diagnostic tools that can detect diseases at their most treatable stages. Investment in these areas will enhance the effectiveness of early detection and ensure that these innovations are widely available, thereby reducing healthcare costs and improving patient outcomes. Additionally, integrating early detection technologies into routine medical practices and public health strategies will help maximize their impact. By prioritizing these efforts, we can further reduce the burden on healthcare systems and caregivers, ultimately leading to healthier populations and more efficient use of healthcare resources.

Conclusion

Incorporating environmental information into machine learning models is crucial for forecasting AD in its early stages. Early prediction and intervention can significantly alter the disease trajectory, providing opportunities for more effective management and improved quality of life. Environmental factors, such as exposure to air pollution, heavy metals, and pesticides, have been increasingly recognized as contributing factors to the risk and progression of AD. By integrating data on these environmental exposures with other health information, machine learning models can enhance the accuracy of early AD prediction.

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Authors' contributions

Conceptualization: Shahriar Mohammadi.
Data curation: Soraya Zarei.
Formal analysis: Shahriar Mohammadi.

Methodology: Shahriar Mohammadi, Soraya Zarei.
Project administration: Soraya Zarei.
Resources: Soraya Zarei.
Software: Soraya Zarei.
Supervision: Shahriar Mohammadi.
Validation: Shahriar Mohammadi.
Visualization: Soraya Zarei.
Writing–review & editing: Shahriar Mohammadi, Soraya Zarei.

Competing interests

The authors affirm that they do not have any known conflicting financial interests or personal relationships that could have influenced the findings presented in this paper.

Ethical issues

This research study adhered to the ethical guidelines and principles, ensuring the protection of human subjects, proper handling of hazardous materials, and scientific integrity. Informed consent was obtained, conflicts of interest were disclosed, and participant privacy and confidentiality were maintained. The authors are committed to upholding ethical standards in their research and reporting to contribute to knowledge advancement responsibly.

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