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Association between air pollutants, thyroid disorders, and thyroid hormone levels: a scoping review of epidemiological evidence

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Background: Over the past two decades, the incidence of thyroid disorders has been steadily increasing. There is evidence to suggest that air pollution may be one of the etiological factors of thyroid diseases. This comprehensive review aimed to examine the evidence related to air pollutants and thyroid disorders and thyroid hormones levels from an epidemiological perspective.

Methods: The scoping review adopted a systematic approach to search for, identify, and include peer-reviewed articles published in English. We performed a comprehensive search of three databases-PubMed, Embase, and Web of Science to identify relevant literature on the relationship between air pollution [particulate matter, nitrogen oxide, carbon monoxide (CO), ozone (O_3), sulfur dioxide (SO_2)] exposure and thyroid disorders, including hypothyroidism, congenital hypothyroidism (CH), thyroid nodules, thyroid cancer, autoimmune thyroid diseases, as well as thyroid hormone levels, such as thyroid-stimulating hormone (TSH), free triiodothyronine (FT_3), and free thyroxine (FT_4). Articles published until August 1, 2023, were included.

Results: A total of 3,373 studies were retrieved, and among them, 25 studies covering eight different air pollutants were relevant. The most frequently studied air pollutants in this review included fine particulate matter (with fine particulate matter ($PM_{2.5}$), n=21; inhalable particles (PM_{10}), n=10; $PM_{10\text{-}2.5}$, n=1) and nitrogen oxides (with NO_2, n=13; NOx, n=3). The thyroid disorders and thyroid hormone levels most commonly associated with evidence of air pollution exposure were hypothyroidism (n=7) and TSH (n=12).

Conclusions: Despite variations in study designs and exposure assessments, the findings consistently highlight the substantial health risks that air pollution, particularly $PM_{2.5}$, poses to thyroid health, especially among vulnerable

populations. Given that our study was limited to epidemiological investigations and the increasing prevalence of toxic substances in the environment, there is an urgent need for further research to elucidate the mechanisms by which these pollutants disrupt thyroid function and contribute to the development of thyroid diseases.

KEYWORDS

air pollutants, scoping review, thyroid disease, epidemiology, atmospheric particulate matter

Introduction

Air pollution is a globally recognized environmental health hazard (1). With rapid global socioeconomic development, there is growing concern about the adverse health effects of air pollutants (2). Environmental air pollution and indoor air pollution are considered major risk factors leading to premature mortality and an increased incidence of diseases. The burden of diseases and deaths caused by these factors has become a global public health challenge, imposing significant direct and indirect costs on society (3). In 2021, particulate matter air pollution was the leading contributor to the global disease burden in 2021 (4). Air pollutants can be categorized into two main types based on their state of existence: gaseous pollutants and particulate pollutants. Gaseous pollutants include nitrogen dioxide (NO_2), carbon monoxide (CO), ozone (O_3), sulfur dioxide (SO_2), and others. Atmospheric particulate matter (PM) comprises total suspended particles, inhalable particles (PM_{10}), fine particulate matter ($PM_{2.5}$), and ultrafine particles. Among these, $PM_{2.5}$ refers to particles in the atmosphere with a diameter equal to or less than 2.5μm. $PM_{2.5}$ represents the majority of PM in the atmosphere (5, 6).

Thyroid disorders have been recognized as some of the most prevalent diseases worldwide (7). Common biomarkers for assessing thyroid homeostasis include free thyroxine (FT_4), free triiodothyronine (FT_3), and thyroid-stimulating hormone (TSH) (8). Thyroid hormones (THs) play a pivotal role in maintaining metabolic balance, cardiovascular health, and neurological development, exhibiting pleiotropic effects on multiple organ systems (9). Abnormal TH levels, whether elevated or decreased, are closely associated with various thyroid disorders (10). While iodine nutrition status is significantly linked to thyroid disease, research indicates that the prevalence of thyroid disorders continues to rise in iodine-sufficient populations, such as in China (11). Furthermore, the global incidence of thyroid disease is also on the rise (12–14). Animal studies and extensive epidemiological research suggest that air pollutants can disrupt thyroid hormone levels, impair metabolic homeostasis, and ultimately contribute to thyroid dysfunction (15, 16). Epidemiological studies often utilize large population samples, enabling researchers to observe the effects of air pollutants in real-world settings. Additionally, long-term epidemiological investigations help establish temporal associations between exposure and disease onset. However, establishing a causal relationship between exposure and disease requires further experimental evidence.

This review aims to retrieve and synthesize published epidemiological studies on the relationship between air pollutant exposure and thyroid diseases, as well as thyroid hormones, across various populations, including children, adults, and pregnant women. The findings are interpreted from an epidemiological perspective, offering theoretical insights and directions for future systematic research, and providing new perspectives on the prevention of thyroid diseases.

Methods

We conducted a scoping review to facilitate the mapping of the literature on emerging topics and provide avenues for future research. Our aim was to gain a comprehensive understanding of the literature regarding the relationship between exposure to air pollutants and thyroid disorders and thyroid hormone levels. Our findings were reported using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Extension for Scoping Reviews (PRISMA-ScR) (17). The scoping review protocol was registered with the Open Science Framework (https://doi.org/10.17605/OSF.IO/V8ERP).

Data sources and search strategy

The preliminary search was conducted on PubMed to identify relevant MeSH terms and keywords. Subsequently, a comprehensive systematic search strategy was developed for the PubMed, Embase, and Web of Science databases using the identified keywords and indexing terms (Tables 1, 2). The final literature retrieval was carried out on August 1, 2023.

TABLE 1 Index terms and keywords used for the literature search.

Theme	Search
Thyroid Diseases	Disease, Thyroid OR Diseases, Thyroid OR Thyroid Disease
OR	
Thyroid Hormones	Hormones, Thyroid OR Thyroid Hormone OR Hormone, Thyroid
AND	
Air Pollution	Air Pollutions OR Pollution, Air OR Air Quality
OR	
Nitrogen Dioxide	Dioxide, Nitrogen OR Nitrogen Peroxide OR Peroxide, Nitrogen
OR	
Ozone	Tropospheric Ozone OR Ozone, Tropospheric OR Low Level Ozone OR Level Ozone, Low OR Ozone, Low Level OR Ground Level Ozone OR Level Ozone, Ground OR Ozone, Ground Level
OR	
Sulfur Dioxide	Sulfurous Anhydride
OR	
Nitrogen Oxides	Oxides, Nitrogen OR Nitrogen Oxide OR Oxide, Nitrogen
OR	
Carbon Monoxide	Monoxide, Carbon
OR	
Particulate Matter	Ultrafine Fibers OR Ultrafine Fiber OR Fiber, Ultrafine OR Airborne Particulate Matter OR Particulate Matter, Airborne OR Air Pollutants, Particulate OR Particulate Air Pollutants OR Ambient Particulate Matter OR Particulate Matter, Ambient OR Ultrafine Particulate Matter OR Particulate Matter, Ultrafine OR Particles, Ultrafine OR Ultrafine Particle OR Particle, Ultrafine

TABLE 2 Example of full search strategy in PUBMED.

	Search terms
1	"Thyroid Diseases"[Mesh] OR Disease, Thyroid [Title/Abstract] OR Diseases, Thyroid [Title/Abstract] OR Thyroid Disease [Title/Abstract]
2	"Thyroid Hormones"[MeSH Terms] OR "hormones thyroid"[Title/Abstract] OR "thyroid hormone"[Title/Abstract] OR "hormone thyroid"[Title/Abstract]
3	"Air Pollution"[Mesh] OR Air Pollutions [Title/Abstract] OR Pollution, Air [Title/Abstract] OR Air Quality [Title/Abstract]
4	"Carbon Monoxide"[Mesh] OR Monoxide, Carbon [Title/Abstract]
5	"Nitrogen Oxides"[Mesh] OR Oxides, Nitrogen [Title/Abstract] OR Nitrogen Oxide [Title/Abstract] OR Oxide, Nitrogen [Title/Abstract]
6	"Sulfur Dioxide"[Mesh] OR Sulfurous Anhydride [Title/Abstract]
7	"Ozone"[Mesh] OR Tropospheric Ozone [Title/Abstract] OR Ozone, Tropospheric [Title/Abstract] OR Low Level Ozone [Title/Abstract] OR Level Ozone, Low [Title/Abstract] OR Ozone, Low Level [Title/Abstract] OR Ground Level Ozone [Title/Abstract] OR Level Ozone, Ground [Title/Abstract] OR Ozone, Ground Level [Title/Abstract]
8	"Nitrogen Dioxide"[Mesh] OR Dioxide, Nitrogen [Title/Abstract] OR Nitrogen Peroxide [Title/Abstract] OR Peroxide, Nitrogen [Title/Abstract]
9	Particulate Matter [MeSH Terms] OR Ultrafine Fibers [Title/Abstract] OR Ultrafine Fiber [Title/Abstract] OR Fiber, Ultrafine [Title/Abstract] OR Airborne Particulate Matter [Title/Abstract] OR Particulate Matter, Airborne [Title/Abstract] OR Air Pollutants, Particulate [Title/Abstract] OR Particulate Air Pollutants [Title/Abstract] OR Ambient Particulate Matter [Title/Abstract] OR Particulate Matter, Ambient [Title/Abstract] OR Ultrafine Particulate Matter [Title/Abstract] OR Particulate Matter, Ultrafine [Title/Abstract] OR Ultrafine Particles [Title/Abstract] OR Particles, Ultrafine [Title/Abstract] OR Ultrafine Particle [Title/Abstract] OR Particle, Ultrafine [Title/Abstract]
10	1 OR 2
11	3 OR 4 OR 5 OR 6 OR 7 OR 8 OR 9
12	10 AND 11

Inclusion and exclusion criteria

The inclusion criteria for the literature were as follows: (1) the exposure factor studied was air pollutants as the primary focus; (2) the literature examined outcomes related to thyroid diseases and thyroid hormone levels; and (3) the literature included results from epidemiological studies.

Exclusion criteria for the literature were as follows: (1) literature that did not meet the inclusion criteria; (2) literature investigating exposure factors such as organic pollutants or chemical substances, among others; (3) duplicate literature, reviews, meta-analyses, letters, replies, comments, or meeting abstracts; and (4) literature for which full text was unavailable, and data extraction was not possible.

Data extraction

Two researchers conducted a full-text screening, independently reviewed the literature included in the final selection, and extracted the data into tables for the purpose of data visualization, data synthesis, and result reporting. Discrepancies arising during this process were resolved through discussions involving all the authors. For studies meeting the inclusion criteria, we extracted information on the author, year of study, study type, country, study period, study population, sample size, pollutants, pollutants exposure evaluation, pollutants exposure time, thyroid related outcomes. Due to heterogeneity across studies and insufficient support for aggregation of the results, a meta-analysis was not conducted.

Results

A total of 3,373 articles related to air pollutants and thyroid diseases were identified in the search. After removing duplicates (313 articles) and performing the initial screening of titles and abstracts, 68 articles remained. Upon further full-text examination and the exclusion of articles not meeting the criteria, 25 articles were considered relevant. Figure 1 illustrates the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flowchart for the selection of included studies (Figure 1).

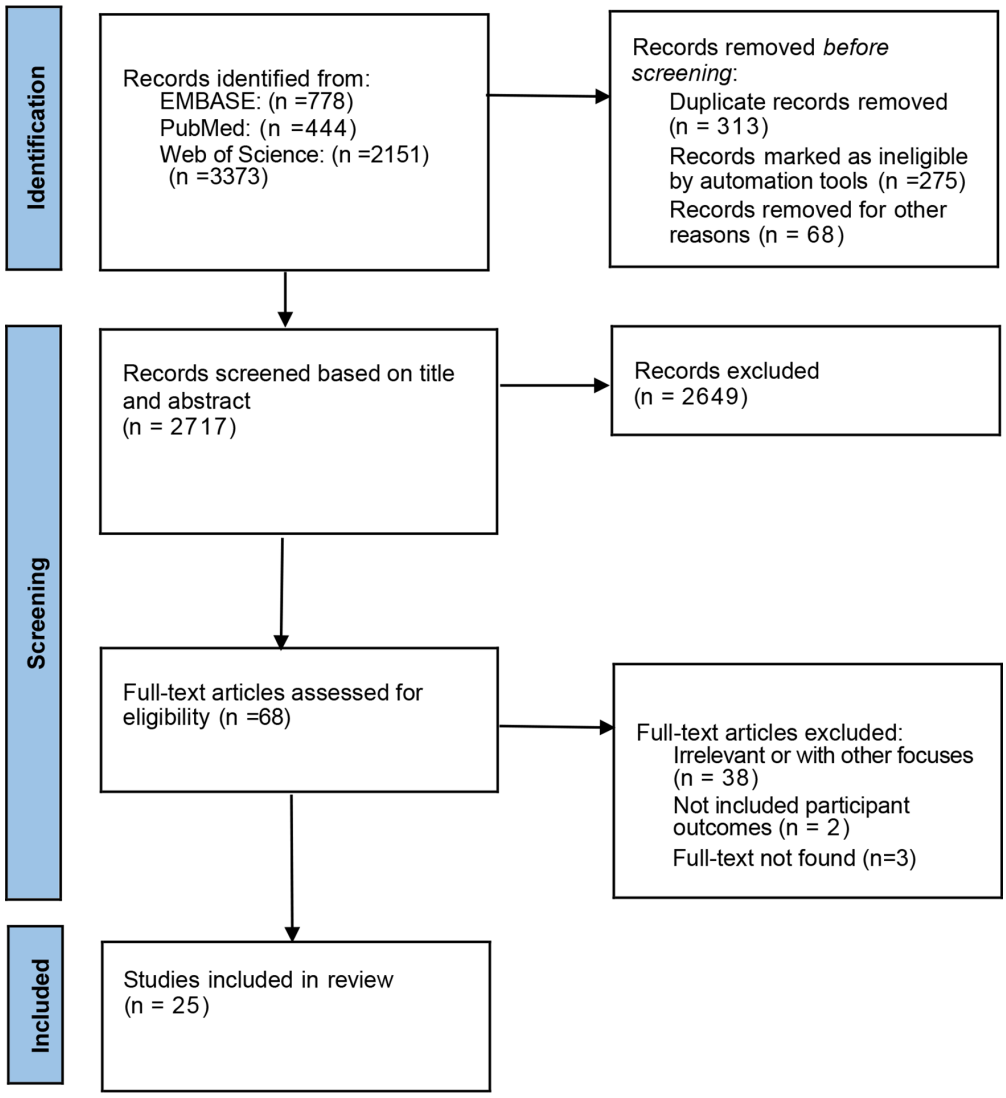

FIGURE 1
PRISMA flow diagram of study selection.

Study characteristics

The included literature consists of population-based epidemiological studies. Most studies employed a cohort study design (12 studies), followed by cross-sectional studies (8 studies), case–control studies (4 studies), and one Mendelian randomization study (Table 3). All the included articles were published within the past ten years, with nearly 70% published after 2020. Among the 25 studies, more than half were conducted in Asia, including 12 from China. This study examines eight different air pollutants ($PM_{2.5}$, PM_{10}, $PM_{10\text{-}2.5}$, O_3, NO_2, NOx, SO_2, CO) and twelve thyroid-related outcomes, including TSH (n=12), FT_4 (n=10), FT_3 (n=7), hypothyroidism [n=7, of which 3 are congenital hypothyroidism (CH)], and thyroid cancer (n=3), among others. The 25 studies primarily focus on pregnant women and newborns, with 10 studies involving pregnant women, 7 studies involving newborns, and 6 studies involving the general adult population.

Cohort studies

Out of the 25 studies included, 12 were cohort studies. Of these, 11 addressed thyroid hormone (THs) levels. Research found that, during late pregnancy, exposure to $PM_{2.5}$ was negatively correlated with both umbilical cord blood TSH levels and the FT_4/FT_3 ratio (18). Higher $PM_{2.5}$ exposure during pregnancy was associated with decreased maternal FT_4 levels (19) and a reduced FT_4/FT_3 ratio (20). However, some studies have found no statistically significant associations between maternal $PM_{2.5}$ exposure and neonatal TSH concentrations (19). Regarding thyroid disease, one large-scale cohort study spanning a decade among the Chinese population evaluated the relationship between O_3 and thyroid diseases (TNs). The study indicates that long-term exposure to high levels of O_3 in Hunan Province may be associated with an increased detection rate of TNs in general adults, potentially mediated by TSH (21). The other three studies focused on hypothyroidism, with one addressing full-term

TABLE 3 Association between air pollutants and thyroid disorders.

Author	Country (City)	Study period	Study population	Sample size	Pollutants	Exposure evaluation	Exposure time	Outcomes
Cohort study								
Janssen et al. (18), 2017	Belgium	2010.02-2014.06	Pregnant woman; newborn	431;498	$PM_{2.5}$	Spatial-temporal interpolation	Third trimester	TSH; FT_4/FT_3; FT_4; FT_3
Howe et al. (52), 2018	America	1994-1997/2000-2003	Newborn	2050	$PM_{2.5}$; PM_{10}; O_3; NO_2; NOx	Spatial-temporal interpolation	Whole pregnancy	TT_4
Wang et al. (19), 2019	China	2014-2015	Pregnant woman; newborn	431 pairs	$PM_{2.5}$ and its six main constituents	Satellite data simulations	First trimester	FT_4; TSH
Ghassabian et al. (22), 2019	Greece; Netherland; Spain; America	2007.02-2008.02; 2003.01-2004.03; 2003.11-2008.01; 1999.04-2002.01	Pregnant woman	9931	$PM_{2.5}$; PM_{10}; NO_2; NOx	Spatial-temporal interpolation; Satellite data simulations	First trimester	Hypothyroxinemia; High TSH
Zhao et al. (23), 2019	China	2014.04-2015.11	Pregnant woman	8077	NO_2, $PM_{2.5}$	Spatial-temporal interpolation	First trimester; Second trimester	Hypothyroxinemia; FT_4; TSH
Li et al. (53), 2021	China	2013.10-2015.07	Pregnant woman	551	$PM_{2.5}$	Spatial-temporal interpolation	First trimester; three months of preconception	TSH; FT_4/FT_3; FT_4; FT_3
Irizar et al. (54), 2021	Spain	2006-2008	Newborn	463	$PM_{2.5}$, NO_2	Spatial-temporal interpolation	Whole pregnancy	TT_4
Harari-Kremer et al. (24), 2021	Israel	2008.01-2015.12	Newborn	696,461	NOx; NO_2; $PM_{2.5}$; $PM_{10\text{-}2.5}$	Spatial-temporal interpolation; Satellite data simulations	Whole pregnancy	CH; TT_4
Zhou et al. (55), 2022	China	2016.04-2018.12	Pregnant woman	1060	$PM_{2.5}$ and its metal constituents	Satellite data simulations	First trimester	TSH; FT_4/FT_3; FT_4; FT_3
Zhang et al. (20), 2022	China	2013.01-2014.10	Pregnant woman	921	$PM_{2.5}$, PM_{10}	Spatial-temporal interpolation	First trimester	TSH; FT_4/FT_3; FT_4; FT_3
He et al. (21), 2022	China	2010.01-2019.12	Adult	191,357	O_3	Monitoring station	Annual average	TNs; T_3; T_4
Lzic et al. (25), 2022	Bosnia and Herzegovina	2015.01.01-2020.12.31	AITD patient	174	NO_2, SO_2, O_3, CO, $PM_{2.5}$	Monitoring station	Annual average	AITD
Cross-sectional study								
Shang et al. (30), 2019	China	2014.10.01-2015.10.01	Pregnant woman; newborn	15,100,000	$PM_{2.5}$; PM_{10}	Monitoring station	Whole pregnancy	CH
Kim et al. (26), 2020	Korean	2009-2015	Adult	4704	NO_2; CO; PM_{10}; SO_2;	Monitoring station	Annual average	TSH; FT_4

(Continued)

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TABLE 3 Continued

Author	Country (City)	Study period	Study population	Sample size	Pollutants	Exposure evaluation	Exposure time	Outcomes
Cross-sectional study								
Ilias et al. (28), 2020	Athens	2019	Pregnant woman	293	$PM_{2.5}$	Monitoring station	Average preceding nine month	TSH
Zeng et al. (2), 2021	China	2013.12-2018.12	Adult	327,913	$PM_{2.5}$; PM_{10}; SO_2; CO; NO_2; $_{O3}$	Monitoring station	Annual average	TSH; FT_4/FT_3; FT_4; FT_3
Zhang et al. (32), 2021	China	2015-2017	Adult	4,920,536	$PM_{2.5}$, PM_{10}, NO_2, SO_2, CO, $_{O3}$	Monitoring station	Annual average	TNs
Qi et al. (31), 2021	China	2014.01.01-2015.12.30	Newborn	NA	O3, NO_2, SO_2, CO	Monitoring station	Annual average	CH
Valdés et al. (29), 2022	Spain	2008-2010	Adult	3859	$PM_{2.5}$, NO_2	Spatial-temporal interpolation	Annual average	TSH; FT_4/FT_3; FT_4; FT_3
Qiu et al. (29), 2022	China	2018.01-2018.12	Pregnant woman	2528	$PM_{2.5}$; PM_{10}; SO_2; CO; NO_2	Monitoring station	First trimester	TSH; FT_4/FT_3; FT_4; FT_3
Case-control study								
Crepeau et al. (34), 2023	America	2013.01-2016.12	Patients; matched controls without thyroid disease	1,990; 6,919	$PM_{2.5}$	Monitoring station; Spatial-temporal interpolation; Satellite data simulations	12-, 24-, and 36-month average concentration	PTC
Park et al. (33), 2021	Korean	2002-2015	Patients; matched controls	4,632; 18,528	SO_2; NO_2; $_{O3}$; CO; PM_{10}	Monitoring station	Annual average	THCA
Sun et al. (35), 2023	China	2012-2020	Hypothyroid patients; matched controls	795; 2,385	$PM_{2.5}$, PM_{10}	Spatial-temporal interpolation	30, 60, and 90 days preceding the LMPM	Hypothyroidism
Karzai et al. (36), 2022	America	2013-2016	PTC patients; matched healthy controls	1,990; 3,980	$PM_{2.5}$	Monitoring station; Satellite data simulations	12-, 24-, and 36-month average concentration	PTC
Mendelian randomization study								
Zhang et al. (37), 2022	European	NA	Hypothyroidism patients; controls	22,687; 440,246	$PM_{2.5}$	Spatial-temporal interpolation; Satellite data simulations	Annual average	Hypothyroidism

AITD, autoimmune thyroid diseases; CH, congenital hypothyroidism; CI, confidence interval; CO, carbon monoxide; FT_3, free triiodothyronine; FT_4,free thyroxine; LMPM, last menstrual period month; NA; not available NO_2, nitrogen dioxide; NO_X, nitrogen oxides; O_3, ozone; OR, odds ratio; $PM_{2.5}$, fine particulate matter; PM_{10}, inhalable particles; $PM_{10-2.5}$, particulate matter with aerodynamic diameter of 2.5–10μm; PTC, papillary thyroid cancer; SO_2, sulfur dioxide; THCA, thyroid carcinoma; TN_S, thyroid nodules; TSH, thyroid-stimulating hormone; TT_4, total thyroxine.

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newborns with CH. Ghassabian et al. conducted a cohort study using data from five birth cohorts, comprising a total of 9,931 pregnant women. The study found that exposure to $PM_{2.5}$ in early pregnancy was linked to mild thyroid dysfunction persisting throughout pregnancy. However, exposures to NOx and NO_2 were not associated with hypothyroxinemia or high TSH during pregnancy (22). Another cohort study conducted in Shanghai, China, reached similar conclusions, reporting that early pregnancy (0-12 weeks) and mid-pregnancy (13-26 weeks) exposure to $PM_{2.5}$ was associated with an increased risk of hypothyroidism in pregnant women. However, there was no significant association between hypothyroidism and NO_2 exposure (23). An Israeli cohort study demonstrated a positive correlation between late-pregnancy exposure to nitrogen oxide (NOx) and the likelihood of newborns developing CH (OR 1.23 [95% CI 1.08 to 1.41]). However, there was no association between early and mid-pregnancy exposure to NOx and NO_2 and the risk of CH (24). In a cohort study conducted at the University Clinical Centre in Tuzla focusing on autoimmune thyroid disease (AITD), five major air pollutants ($PM_{2.5}$, NO_2, SO_2, CO, and O_3) were analyzed. However, the findings indicated that the average concentrations of these pollutants were not statistically associated with an increased risk of AITD in the population of the region (25).

Cross-sectional study

More than half of these cross-sectional studies were based on national databases from China, and seven studies utilized monitoring stations to assess pollutant exposure levels. Thyroid hormone levels were the primary outcomes in five of these studies. A study from Korea found a positive association between PM_{10} exposure and TSH levels in adults, while annual mean exposure to NO_2 and CO was significantly associated with elevated TSH levels and reduced FT_4 concentrations (26). In Chinese adults, increased $PM_{2.5}$ levels were significantly negatively correlated with FT_4 and the FT_4/FT_3 ratio, but positively correlated with FT_3 levels (2). Higher exposure to $PM_{2.5}$-bound metals was associated with lower FT_4 and higher FT_3 levels in pregnant women (27). Additionally, studies in pregnant women in Greece and adults in Spain found that $PM_{2.5}$ exposure was linked to increased TSH levels, but no associations were observed between NO_2 exposure and thyroid hormone levels (28, 29).

Three cross-sectional studies on air pollution and thyroid diseases have been conducted in China. Two of these studies utilized environmental air pollution data from the Chinese Air Quality Online Monitoring and Analysis Platform (https://www.aqistudy.cn/) (30, 31). They examined the relationship between maternal exposure to air pollutants and the likelihood of CH in offspring. Among these pollutants, O_3 (OR 1.06 [95% CI 1.01 to 1.10]), NO_2 (OR 1.10 [95% CI 1.02 to 1.18]), and $PM_{2.5}$ (OR 1.02 [95% CI 1.00 to 1.03]) were significantly positively associated with the risk of CH in offspring (30, 31). However, there were no significant associations of exposure to SO_2, CO, or PM_{10} with the risk of CH. Another study, which included a cohort of 4.9 million Chinese adults, examined the associations between exposure to $PM_{2.5}$, PM_{10}, NO_2, SO_2, CO, and O_3 and the risk of TNs. The findings revealed significant linear associations between each of the six air pollutants and the risk of TNs (32).

Case–control studies

There were four case–control studies, one of which was nested within a cohort (33–36). Out of the 13 included articles, three investigated thyroid cancer using case–control study designs. A nested case–control study in South Korea concerning thyroid cancer revealed a positive association between thyroid cancer incidence and NO_2 exposure (OR 1.33 [95% CI 1.24 to 1.43]) and an inverse association between thyroid cancer incidence and PM_{10} exposure (OR 0.64 [95% CI 0.60 to 0.69]). These associations remained consistent in subgroup analyses (33). Two additional case-control studies on papillary thyroid cancer (PTC) conducted at the Johns Hopkins Medical Institution in the United States provided further evidence. They demonstrated a significant association between long-term exposure to $PM_{2.5}$ and an increased diagnosis rate of PTC (34). Prolonged exposure to $PM_{2.5}$ over 2 years (OR 1.18 [95% CI 1.00 to 1.40]) and 3 years (OR 1.23 [95% CI 1.05 to 1.44]) was significantly correlated with an increased incidence of PTC (36). Two studies included 1,990 PTC patients as the experimental group. The main difference between the two was that Crepeau et al. had a larger sample size in their control group, but their final conclusions were consistent with the other study. Furthermore, Crepeau et al. found that this association was most significant in populations with a higher median household income (34). Another case–control study in China investigated the correlation between preconception and early pregnancy exposure to environmental particulate matter and hypothyroidism during pregnancy. The study revealed that exposure to $PM_{2.5}$ and PM_{10} during various intervals before the last menstrual period month (LMPM), including LMPM-60 days, LMPM-30 days, and all other distances before LMPM, was associated with an increased risk of hypothyroidism. Notably, the most significant associations with hypothyroidism risk were observed for $PM_{2.5}$ (OR 1.14 [95% CI 1.10 to 1.18]) and PM_{10} (OR 1.10 [95% CI 1.07 to 1.13]) within a 250-metre buffer zone during the LMPM period (35).

Mendelian randomization study

In Europe, a causal relationship between $PM_{2.5}$ exposure and hypothyroidism was investigated through a two-sample Mendelian randomization study (37). That study revealed an association between exposure to increased $PM_{2.5}$ concentrations and an increased risk of developing hypothyroidism.

Discussion

The objective of this scoping review is to explore the relationship between exposure to air pollutants and thyroid diseases, as well as

thyroid hormones, from an epidemiological perspective. A review of published studies indicates that different types of air pollution may have varying health effects. Exposure to particulate matter, particularly $PM_{2.5}$, has been shown to impair thyroid function in pregnant women and negatively affect their offspring. However, the findings of Shang et al. suggest no association between PM_{10} exposure and the risk of CH in offspring (38). This discrepancy may be attributed to differences in study design and exposure assessment methods.

Among the 25 studies included, cohort studies were the most common, with 12 studies, followed by cross-sectional and case-control studies. In situations where randomized trials are not feasible, cohort studies are often considered one of the most reliable forms of observational epidemiological research. Cohort studies are particularly effective in establishing causal relationships by tracking health outcomes after exposure to factors such as air pollution, helping to understand how these exposures affect thyroid function or disease progression. However, they may be prone to selection bias. For example, individuals in susceptible populations may already have the disease at the start of the study, which can skew the associations being investigated. Cross-sectional studies can quickly assess the correlation between air pollution and thyroid function, but they are limited in their ability to infer causality. The limitations of case-control studies primarily arise from the selection of control groups. If there are geographical differences between the control and case groups, the study may fail to draw clear conclusions. In cases where associations exist, bias could lead to inaccurate results. Nevertheless, no single study design is flawless. A comprehensive understanding of the multifaceted relationship between air pollutants and thyroid diseases can be best achieved by integrating studies that offer complementary strengths and limitations. In the future, large-scale cohort studies with extensive exposure levels and long-term follow-up may provide the most powerful means to elucidate these associations.

The genetic background of the study subjects, as well as the potential interactions between air pollutants and genetic factors, may increase susceptibility to diseases. Therefore, these factors should be considered as confounders in research design. Thyroid hormones play a crucial role in the development of fetuses and neonates (39). In early pregnancy, since the fetal thyroid is not yet functional, the fetus relies on maternal thyroid hormones to maintain normal growth and development (40, 41). Consequently, maternal thyroid dysfunction is recognized as a known risk factor for restricted fetal development (42). This explains why researchers often focus on thyroid diseases and related hormone levels in pregnant women and neonates (41, 43, 44).

Differences exist in the methods used to assess exposure to environmental air pollutants in various studies. Qi et al.'s research, for instance, directly employed data disseminated by air quality monitoring stations for analysis (31). However, the majority of monitors involved in direct measurements are situated in urban or polluted areas (such as power plants), and not all study subjects reside in areas where monitoring stations are present. Furthermore, the data scope can be constrained by the specific years for which information is available, rendering the obtained data suitable only for coarse approximations. The land use regression (LUR) model utilized by Zhao et al. can be employed to forecast outdoor pollutant levels at the residential addresses of each participant. Building upon data derived from satellite systems at monitoring stations and further accounting for meteorological and spatial factors, the model incorporates adjustments based on geographic information such as population density, sea level, and meteorological data (45). Consequently, this approach enables the assessment of exposure levels in areas lacking air pollution monitoring, thus significantly enhancing the accuracy of exposure evaluations. This model has been validated in several studies (38, 46). Furthermore, research has estimated the average air pollutant exposure concentrations for study participants within circular buffer zones with diameters of 250 meters, 500 meters, and 750 meters based on the location of each residence, allowing for a more comprehensive analysis of the relationships (35). Exposure duration represents a common concern, necessitating assessment based on disease susceptibility and the target population. In the context of research related to thyroid cancer, the temporal scope of exposure is notably extended compared to other thyroid conditions. In the case of specific demographic groups, such as pregnant women, some researchers have structured exposure periods to encompass distinct gestational stages (22, 23).

Among the 25 studies we included, $PM_{2.5}$ was mentioned 21 times, while PM_{10} was noted 10 times. This highlights the widespread concern about particulate matter pollution. In particular, China, where the prevalence of thyroid diseases is high and pollution is becoming increasingly severe, may prompt local researchers to investigate the potential link between air pollution exposure and hypothyroidism (47). Additionally, nitrogen oxides, such as nitrogen dioxide (NO_2), were the second most frequently discussed pollutants, cited 13 times, followed by SO_2, CO, and O_3. A substantial body of epidemiological and toxicological research has shown that $PM_{2.5}$ can enter the respiratory system through the lungs, triggering a series of pathophysiological responses, including systemic inflammation, oxidative stress, and vascular dysfunction, which can severely impact multiple bodily systems (11). Moreover, $PM_{2.5}$ has been shown to impair thyroid function by disrupting thyroid hormone levels, potentially leading to various thyroid diseases (48–51). Animal experiments have demonstrated that $PM_{2.5}$ can disrupt thyroid homeostasis by affecting the synthesis of thyroid hormones, but further basic research is needed to explore these mechanisms in greater detail (16).

In summary, large-scale, long-term cohort studies are needed to better understand the prolonged effects of air pollution on thyroid hormone levels and related diseases. Interdisciplinary collaboration is essential to further elucidate the complex interactions between air pollution and the endocrine system. For vulnerable populations, such as pregnant women and newborns, enhanced health protection measures should be prioritized. In high-risk areas, stricter air quality management and control of major pollutant emissions are necessary to reduce the burden of thyroid diseases. Future research should focus on elucidating how pollutants affect thyroid function through endocrine-disrupting mechanisms and quantify these effects across various exposure scenarios. A deeper exploration of these mechanisms could lead to more effective clinical and public health interventions.

Author contributions

KY: Data curation, Formal Analysis, Investigation, Validation, Writing – original draft, Writing – review & editing. GZ: Conceptualization, Project administration, Resources, Supervision, Validation, Writing – review & editing. YL: Conceptualization, Funding acquisition, Methodology, Project administration, Resources, Supervision, Writing – review & editing.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest

Publisher's note

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