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Multi-omics of oxidative stress and particulate matter exposure: a systematic review

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Abstract

Background Exposure to particulate matter (PM) is a significant public health concern associated with respiratory, cardiovascular, and metabolic diseases. Oxidative stress is a key biological mechanism mediating the harmful effects of PM exposure. However, a comprehensive review of relating PM exposure to omics layers of oxidative stress has been lacking. We aimed to systematically review the current evidence on the associations between PM exposure and the multi-omics signatures of oxidative stress.

Methods We conducted a systematic review of studies published between January 2021 and March 2024 in PubMed and Web of Science, following a registered protocol (PROSPERO ID: CRD42024617742). Eligible studies assessed the impact of PM exposure on oxidative stress-related omics in adult human populations. Data on exposure assessment, study characteristics, and omics outcomes were extracted, and the risk of bias was evaluated using the Newcastle–Ottawa Scale and Cochrane's.

Results Seventy-seven studies were included. PM exposure was consistently associated with oxidative stress markers across multiple omics platforms. Studies on the analytes showed that PM was associated with an increase in oxidative markers. Metabolomics studies revealed alterations in pro-oxidant metabolites (e.g., eicosanoids, ceramides) and disruptions in antioxidant pathways (e.g., glutathione, vitamin C, and E metabolism). PM exposure was also linked to changes in energy metabolism, fatty acid oxidation, and detoxification pathways. Genomics studies reported differential methylation in genes involved in oxidative stress and inflammation. Microbiome studies suggest that PM exposure alters the composition of gut and nasal microbiota, favoring a pro-oxidative profile. However, some studies reported no significant associations, highlighting heterogeneity in findings.

Conclusion Our systematic review demonstrates that PM exposure affects multiple molecular pathways related to oxidative stress across diverse omics platforms. These findings highlight the complex responses to PM, underscoring the need for integrative multi-omics approaches to fully understand the health impacts of air pollution.

Keyword Particulate Matter; Oxidative Stress; Multi-Omics

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Background

Exposure to particulate matter (PM) has been associated with a range of adverse health effects, including respiratory, cardiovascular, and metabolic disorders [1]. Although global PM exposure slightly decreased between 2000 and 2019, many regions, such as the Middle East, sub-Saharan Africa, and South Asia, experienced worsening pollution [2]. These trends may raise concerns about the long-term health consequences for populations exposed to PM.

Research on the health impacts of PM suggests that oxidative stress is one of the key mechanisms in the harmful biological effects of PM [3]. Oxidative stress occurs due to an imbalance between the production of reactive oxygen species (ROS) and the body's ability to neutralize them, leading to cellular damage, inflammation, and disease development [4]. PM can induce oxidative stress through several pathways [5]. Upon inhalation, PM deposits in the respiratory tract and initiates local inflammatory responses, leading to the recruitment of immune cells such as macrophages and neutrophils, which generate ROS as part of the defense process [6]. PM can also disrupt mitochondrial function, further amplifying intracellular ROS generation [7]. These oxidative insults overwhelm cellular antioxidant systems, damage biomolecules such as lipids, proteins, and DNA, and activate redox-sensitive signaling pathways involved in inflammation, apoptosis, and tissue remodeling. Consequently, oxidative stress acts as a central mechanism linking PM exposure to a wide array of adverse health effects, including respiratory, cardiovascular, neurological, and metabolic disorders [8]. Oxidative stress can be measured by biomarkers such as superoxide dismutase (SOD) and malondialdehyde (MDA) in urine or plasma.

Multi-omics approaches have transformed the understanding of oxidative stress by enabling a comprehensive, systems-level investigation of biological responses. By integrating data across different molecular layers, including genomics, epigenomics, transcriptomics, proteomics, metabolomics, and microbiomics, multi-omics studies can capture the complex and interconnected pathways activated during oxidative stress [9–11].

To our knowledge, no systematic reviews have focused on the multi-omics of oxidative stress in relation to PM exposure. A previous meta-analysis focused only on short-term ambient PM and the biomarkers of oxidative stress; however, it did not include all PM exposures and other omics [12]. Our review will provide insights into how PM exposure affects oxidative response and provide a comprehensive overview of various biomarkers, metabolomics, genomics, and microbiome pathways related to oxidative stress. Unlike previous reviews that examined individual oxidative stress markers or short-term PM exposure effects, this review combines findings across multiple omics layers to capture broader molecular interactions.

Materials and methods

Search strategy and study selection

We conducted a comprehensive literature search to assess the impact of PM exposure on the multi-omics of oxidative stress. The search was conducted in PubMed and Web of Science (WoS), covering studies published from January 2021 to the present. Our systematic review protocol was registered on PROSPERO in November 2024 and can be accessed at Prospero ID CRD42024617742. There was no review protocol published. We followed the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) 2020 guidelines for the design, conduct, and reporting of this review. A completed PRISMA checklist is available in the Supplementary Table 1.

A comprehensive search was conducted in PubMed on (December 09, 2024) and in WoS on (December 15, 2024) using predefined search terms that included exposure-related keywords such as "PM", "ambient air pollution", "air pollution", "$PM_{2.5}$", and "PM_{10}", and omics-related terms such as "multi-omics", "genomics", "transcriptomics", "proteomics", "metabolomics", "epigenomics", "lipidomics", "microbiomics", and "metagenomics". For oxidative stress assessment, keywords included "oxidative stress", "ROS", "oxidants", and "oxidative damage".

[The full search strategy was structured as follows:

(("particulate matter" OR "air pollution" OR "ambient air pollution" OR "$PM_{2.5}$" OR "PM_{10}" OR "fine particulate matter" OR "coarse particulate matter") AND ("multi-omics" OR "omics" OR "genomics" OR "transcriptomics" OR "proteomics" OR "metabolomics" OR "epigenomics" OR "lipidomics" OR "microbiomics" OR "meta genomics" OR "oxidative stress" OR "reactive oxygen species" OR "ROS" OR "oxidants" OR "oxidative damage")) NOT ("review" OR "in vitro").]

Our search strategy included automatic database filters (full-text, human subjects, English language, publication from January 2021) and manual reference-list screening to identify relevant studies.

Study inclusion and exclusion criteria

Studies were included if they (1) were conducted on human participants, (2) included adults aged 18 years or older, (3) were written in English, (4) were published since January 2021, (5) examined the effects of PM exposure, (6) were available in peer-reviewed journals and (7) assessed at least one oxidative stress-related omics (biomarkers, metabolomics, genomics, and microbiome).

Studies were excluded if they (1) involved animal or in vitro models, (2) were case reports, case series, or translational research, (3) were focused on pregnant women

or the pediatric population, (4) were conference abstracts without a full peer-reviewed article, or (5) were non-English publications.

Screening and data extraction

Two independent reviewers screened the studies using Rayyan (https://www.rayyan.ai/) for title and abstract screening, followed by a full-text review. Any disagreements were resolved through consensus to ensure consistency and accuracy in study selection. After applying the eligibility criteria and removing the duplicates, two investigators extracted data by systematically recording relevant information, including author, year, country, study design, sample size, exposure, and outcome. This structured approach ensured accuracy and consistency in data collection.

Risk of bias and quality assessment

The risk of bias for the included studies was assessed using the Newcastle–Ottawa Scale (NOS), a widely used tool for evaluating the quality of non-randomized studies. The NOS evaluates studies based on three key domains: selection of study groups, comparability of groups, and outcome assessment (for cohort studies) or exposure assessment (for case–control studies). Each study was independently assessed by TM, and discrepancies were resolved through consensus. The total scores obtained from NOS were categorized as "good", "fair", or "poor" quality based on predefined criteria adapted from previous systematic reviews. Studies that lacked clear methodology had inadequate control for confounding factors or provided incomplete data were considered to have a higher risk of bias.

Risk of bias in randomized crossover and randomized controlled trials, was assessed using the Cochrane Risk of Bias 2.0 (RoB 2) [13]. This framework assesses bias across six domains: randomization process, deviations from intended interventions, missing outcome data, measurement of the outcome, selection of the reported result, and, specifically for crossover trials, carryover bias. Each domain was rated as low risk or some concerns, and an overall judgment was derived according to Cochrane guidance.

Results

Overview

We initially identified 1,621 and 2,942 studies through PubMed and WoS, respectively. After removing duplicates and applying the eligibility criteria, 77 studies were included in this systematic review ($n = 37$ in PubMed and $n = 40$ in WoS), Fig. 1. Thirteen additional studies initially appeared to meet the inclusion criteria based on title and abstract screening but were excluded after full-text review due to specific reasons, Supplementary Table 2.

Characteristics of included studies

Among the included studies, 42 evaluated analytes, 31 assessed metabolomics, 5 examined genomics, and 4 investigated the microbiome (some studies evaluated more than one omics), Table 1. Most studies were conducted in Asia ($n = 45$), Europe ($n = 12$), or North America ($n = 11$). The majority of studies assessed short-term PM exposure (< 1 month) ($n = 63$).

Risk of bias using NOS was assessed in cohort (n = 55), case–control (n = 3), randomized crossover trials (n = 8), cross-sectional studies (n = 10), and randomized controlled trials (n = 1), respectively, Supplementary Table 3A-E. Scores obtained from the NOS were adapted as in previously published studies to reflect the quality of each paper. Cutoff for each risk of bias assessment, depending on article type, can be found within the footnote of Supplemental Tables 3A-E. Among cohort studies, n = 49 articles were of good quality, n = 4 of fair quality, and n = 2 of poor quality. Among randomized crossover trials, n = 4 articles were of low risk, and n = 4 studies were categorized as some concerns. Among cross-sectional studies, n = 8 articles were of good quality and n = 2 of satisfactory quality. All case–control studies were of good quality. The randomized controlled trial was low risk. High-quality studies were marked in Supplementary Table 3 to assess whether findings differ across high- vs. lower-quality studies.

Analytes (biomarkers, enzymes, and proteins)

Across 42 studies, analytes reflecting oxidative stress showed heterogeneous but biologically consistent patterns (Supplementary Table 4). Lipid peroxidation markers, including MDA, thiobarbituric acid reactive substances (TBARS), and 8-isoprostane, were the most frequently elevated following $PM_{2.5}$ [14–22], PM_{10} [22, 23], and ultrafine particle (UFP) exposures [24, 25], indicating enhanced membrane lipid oxidation. Oxidized LDL (ox-LDL), lipoprotein-associated phospholipase A_2, and soluble lectin-like oxidized LDL receptor-1 were also positively associated with exposure [24–28], linking oxidative injury to vascular inflammation. In contrast, several studies reported null associations [29–43], reflecting variability in exposure timing, population susceptibility, and analytical sensitivity. When considering high-quality studies, the number of reports showing null associations was reduced.

Markers of oxidative DNA damage such as 8-hydroxy-2′-deoxyguanosine (8-OHdG) showed mixed associations, with increases observed in both short- and long-term PM exposures [16, 22, 33, 44–48], whereas some cohorts showed no significant relationship [20, 21, 29, 31, 32, 43, 49–51]. Antioxidant enzymes exhibited divergent trends: SOD was decreased in some studies [14, 17, 34], suggesting depletion of defense capacity,

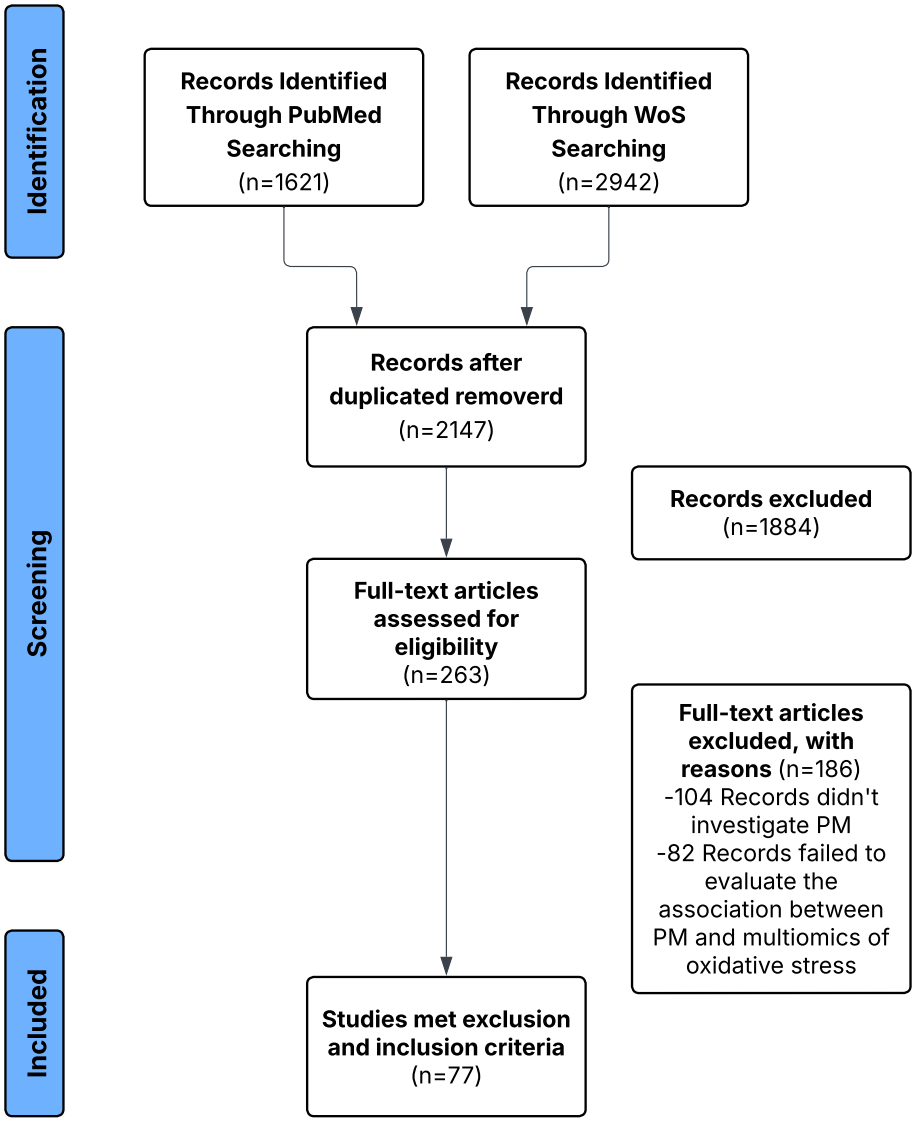

Fig. 1 Overview: studies identified and reviewed as per PRISMA

but increased in others [43, 52], possibly reflecting adaptive compensation. Total antioxidant capacity (TAC) and glutathione metabolism markers (GSH, GPx, GGT) were frequently reduced [17, 34, 36, 53] or showed no change [19, 32, 43, 50], supporting overall redox imbalance. Other inflammatory-oxidative markers such as myeloperoxidase (MPO), ceruloplasmin, haptoglobin, and ICAM-1 were consistently elevated [28, 36, 43, 50, 54], further implicating systemic oxidative and inflammatory activation. Most included studies were of high quality, and the exclusion of lower-quality studies did not affect the overall findings.

Metabolomics

Thirty-one studies investigated metabolomic perturbations associated with PM exposure. Pathway-level analysis revealed broad alterations in pro-oxidant, antioxidant, and energy-related metabolites (Supplementary Table 4). Pro-oxidant and inflammatory pathways were enriched for arachidonic acid-derived eicosanoids (e.g., leukotrienes, prostaglandins, HETEs, DHETs, thromboxanes), reflecting activation of lipoxygenase and cyclooxygenase cascades [24, 55–60]. Increases in ceramides, hydroxyoctadecadienoic acids (HODEs), and phenylalanine conjugates (e.g., hippuric acid) further supported lipid peroxidation and immune signaling [61–65]. Fatty acid–related metabolism showed consistent dysregulation across studies. PM exposure disrupted carnitine shuttle and peroxisomal β-oxidation, with increases in short- and long-term fatty acid oxidation and tricarboxylic acid (TCA) cycle intermediates [41, 60, 66, 67]. Alterations in arginine and proline metabolism suggested perturbed nitric oxide-related pathways [68], while alpha-linolenoyl carnitine and PGF1α were also changed

Table 1 Characteristics of included studies'

ID	Author, Year (ref)	Omics Type	Outcome[a]	Study Design	Exposure					Country	Study Population	Sample Size	Sex Distribution %
					Type	Source	Concentration[b]	Assessment	Window				
1	Qi, 2024 [1]	Analyte	↑ • MDA • 8-OHdG ↓ • SOD • TAC	Observational	PM1, PM2.5, PM10	Personal & ambient	Personal $PM_{2.5}$≈30.9 Ambient $PM_{2.5}$≈52.8	Personal air monitor (PAM)	7 days	China	General population	251	F: 55.8/M: 44.2
2	Hsu, 2024 [2]	Analyte	↑ N7-meG (β = 0.13–0.18)	Cohort study	PM2.5	Ambient & personal	Personal: 26.9 Ambient: 24.7	Personal portable devices & monitoring station	24 h	Taiwan	Healthy participants	58	F: 60.3/M: 39.7
3	Tran, 2024 [3]	Analyte	↑ • 8-epi-$PGF_2\alpha$ • Δα1-antitrypsin (+42.16 μg/g) ΔITIH4 (+16.27 μg/g)	Cohort study	PM2.5	Personal occupational welding fumes in a shipyard	410	Personal portable devices	8 h	Taiwan	Shipyard workers	180	Male study
4	Kahe, 2024 [4]	Analyte	no association for MDA	Cross-sectional study	PM2.5	Ambient traffic and industrial	104.6	High-volume sampler positioned above ground	8 days	Iran	Healthy adults	89	F: 56.2/M: 43.8
5	Squillacioti, 2024 [5]	Analyte	↑ • 8-epi-$PGF_2\alpha$(+31–41%) • 8-OHdG (+20–23%)	Case–control	PM2.5, PM10	Ambient residential	$PM_{2.5}$: 25.2 PM_{10}: 39.2	Satellite observations elaborated by machine learning	3 years	Italy	Patients with airway disease and healthy controls	1,841	F: 49/M: 51
6	Kim, 2024 [6]	Analyte	↑ 8-OHdG (+4.9%, 95% CI 0.6–9.4)	Cross-sectional study	PM2.5, PM10	Ambient residential	$PM_{2.5}$ = 23.31	Community multi scale air quality model (CMAQ)	1–7 days	Korea	General population	2,199	F: 50/M: 50

Table 1 (continued)

ID	Author, Year (ref)	Omics Type	Outcome[a]	Study Design	Exposure					Country	Study Population	Sample Size	Sex Distribution %
					Type	Source	Concentration[b]	Assessment	Window				
7	Li X, 2024 [7]	Analyte	↑ • MDA ↓ • SOD	Panel study	PM2.5	Personal exposure	46.54	Time microenvironment activity pattern	7 days	China	Participants w/allergic rhinitis	49	F: 75.5/M: 24.5
8	Zeng, 2023 [8]	Analyte	↑ • LPCs ↓ • PCs	Panel study	PM2.5, PM10	Ambient residential	132.5[c]	Air monitoring stations	7 days	China	Healthy undergraduates	75	F: 71.4/M: 28.6
9	Song, 2022 [9]	Analyte	10 µg/m3 increase in $PM_{2.5}$ → ↑ 8-OHdG (+1.83%, 95% CI 0.59–3.08%)	Panel study	PM2.5	Ambient residential	150.6	Air monitoring station	24 h	China	Non-smoking college students	61	F: 78.6/M: 21.4
10	Xu, 2022 [10]	Analyte	10 µg/m3 ↑ $PM_{2.5}$ → ↑ MDA (+1.63%, 95% CI: 0.14–3.14%)	Panel study	PM2.5	Ambient city air	71.17	Air monitoring stations	24 h	China	Healthy adults	30	F:57/M: 43
11	Wang, Lin, 2022 [11]	Analyte	$PM_{2.5}$ exposure → ↑ • 9-HODE (+21.0%, 95% CI 5.8–38.5%) • 13(S)-HPODE (+18.8%, 95% CI 4.8–34.8%) • 12,13-DHOME (+21.8%, 95% CI 6.9–38.7%) ↓ • Melatonin(− 25.9%, 95% CI − 38.0 to − 11.5%) • ubiquinone-1(− 76.3%, 95% CI − 82.4 to − 68.2%)	Randomized crossover trial	PM2.5	Personal exposure	101.81	Air monitoring stations	24 h	China	Healthy college students	24	F: 54/M: 46
12	Zhang Q, 2022 [12]	Analyte	↑ • MDA (+0.78 nmol/mL), • 8-OHdG (+19.7 ng/mgCr)	Randomized crossover trial	PM2.5	Traffic	22.3	Real time monitoring	4 h	China	Non-smoking college students	56	F:55/M: 45

Table 1 (continued)

ID	Author, Year (ref)	Omics Type	Outcome[a]	Study Design	Exposure					Country	Study Population	Sample Size	Sex Distribution %
					Type	Source	Concentration[b]	Assessment	Window				
13	Sauvian, 2022 [13]	Analyte	↑ MDA	Pilot study	PM2.5, PM4, PM10	Occupational subway environment, personal sampling during work shifts	NR	Real time monitoring	Work shift	France	Subway workers	9	F: 33/M:67
14	Qui, 2022 [14]	Analyte	↓ 8-OHdG (−47.6%, 95% CI − 67.2 to − 16.5%)	Interventional study	PM2.5	Ambient residential	NR	Air monitoring stations	24 h	China	Healthy elders	214	F: 65/M: 35
15	Zhang L, 2022 [15]	Analyte	• 8-OHdG = 16.9 µg/g Cr (IQR 11.1–20.3) • 8-iso-$PGF_2\alpha$ = 0.1 µg/g Cr; CC16 = 20.6 ng/mL	Panel study	PM2.5	Personal exposure	106.8[c]	Air monitoring stations	24 h	China	Healthy young adults	45	F: 60/M: 40
16	Huang, 2022 [16]	Analyte	• MDA = 3.80 ± 1.49 nmol/mL; • SOD = 143.6 ± 36.8 U/mL; • GSH-Px = 442.3 ± 100.5 U/mL; • 8-OHdG = 6.87 ± 1.82 ng/m	Panel study	PM2.5	Household indoor air from cooking/heating w/ solid fuels	203.14[c]	Air samplers	24 h	China	Rural housewives	32	Female study
17	Sun, 2021 [17]	Analyte	• 8-epi-$PGF_2\alpha$ = 41.64 ± 20.94 µg/L	Panel study	PM2.5	Ambient residential	68.29	Air monitoring stations	24 h	China	Retired adults	32	F: 56.25/M: 43.75

Table 1 (continued)

ID	Author, Year (ref)	Omics Type	Outcome[a]	Study Design	Exposure					Country	Study Population	Sample Size	Sex Distribution %
					Type	Source	Concentration[b]	Assessment	Window				
18	Ni, 2021 [18]	Analyte	• sLOX-1 = 94.5 pg/mL; • nitrite = 24.7 µmol/L; • Each IQR ↑ in $PM_{2.5}$ → + 16.36% (95% CI: 0.1–35.3%) ↑ in sLOX-1 (continuous) • OR = 1.21 (95% CI: 1.01–1.44) for high vs. low sLOX-1	Cohort study	PM2.5	Ambient residential	NR	Air monitoring stations	24 h	United States	Asymptomatic elderly population	740	F: 48.8/M: 51.2
19	Zhu, 2021 [19]	Analyte	• CRP = 3.29 (0.86) ng/mL • TNF-α = 2.91 (0.94) ng/mL • 8-iso-$PGF_2α$ = 41.2 (15.3) µg/L • TAC = 1.12 (0.32) mmol/L	Panel study	PM2.5	Personal exposure	40.8	Personal portable monitor	48 h	China	Healthy adults	40	F: 75/M: 25
20	Lai, 2021 [20]	Analyte	↑ • 8-iso-$PGF_2α$: 15 ± 12 → 40 ± 30 pg/g (2nd visit) • 8-OHdG: 344 ± 397 → 529 ± 574 pg/g creatinine • IL-6: 0.24 ± 0.23 → 0.28 ± 0.21 pg/g creatinine	Repeat measurement study	PM2.5	Occupational welding fume exposure measured personally	716	Personal Environmental Monitor	8 h	Taiwan	Shipyard workers	69	F: 6/M: 94
21	Hu, 2021 [21]	Analyte	↑ • MDA • 8-OHdG ↓ • SOD	Cross-sectional study	PM2.5	Industrial emissions from a coking plant (coal)	216.30[c]	Air monitoring stations	8 h	China	High-level exposed population	210	F: 26.7/73.3
22	Liu, 2021 [22]	Analyte	↑ • MDA • 8-OHdG • SOD • TAC • Catalase • ox-LDL • MPO	Panel study	PM2.5	Ambient city air	91c	Air monitoring stations	24 h	China	Asthmatic adults	29	F: 55.2/M: 44.8

Table 1 (continued)

ID	Author, Year (ref)	Omics Type	Outcome[a]	Study Design	Exposure					Country	Study Population	Sample Size	Sex Distribution %
					Type	Source	Concentration[b]	Assessment	Window				
23	Lee, 2024 [23]	Analyte	• TAC = 1.98 ± 2.21 mM UA eq/mM • MDA = 4.60 ± 1.83 µg/g; • 8-OHdG = 6.91 ± 1.62 µg/g	Cross-sectional study	PM2.5	Personal exposure	16.9	Portable particulate matter sensor	24 h	Korea	Non-smokers	114	F: 71.1/M: 28.9
24	Maccarone, 2023 [24]	Analyte	• Total MDA ↑ + 6.96% per IQR indoor BC (95% CI 1.55–12.67) and ↑ + 9.24% per IQR BC of outdoor origin (95% CI 2.41–16.53) • 8-OHdG ↑ + 7.99% per IQR indoor BC (95% CI 1.77–14.59) and ↑ + 10.01% per IQR ambient BC (95% CI 3.66–16.74) • no change in free MDA or indoor $PM_{2.5}$ of indoor origin	Panel study	PM2.5	Ambient and Indoor residential	6.87[c]	In-home micro-environmental sampler	1 week	United states	COPD cohort	140	F: 2.9/M: 97.1
25	Wei, 2022 [25]	Analyte	↓ • CAT (β = − 0.039 U/mL, 95% CI − 0.060, − 0.017) • SOD (β = − 1.258 U/mL, 95% CI − 1.975, − 0.541) • T-AOC (β = − 0.076 mmol/L, 95% CI − 0.126, − 0.026)	Panel study	PM2.5	Indoor hospital environment	24.83	Laser inhalable dust measuring instrument	24 h	China	Schizophrenia cohort	24	Male study
26	Li J, 2024 [26]	Analyte	↑ • MDA ↓ • SOD	Panel study	PM2.5	Personal exposure	46.2	Air monitoring stations	24 h	China	Allergic rhinitis patients; Higher SRS (symptom severity score ↑), worsened quality of life	49	F: 75.5/M: 34.5
27	Sidebang, 2023 [27]	Analyte	Mean urinary GSH = 1.3 ± 0.5 µM; $PM_{2.5}$ ↑ → ↓ GSH (β = − 0.006, p = 0.026)	Cross-sectional study	PM2.5	Traffic	90.9	Air monitoring equipment	Long term (work years)	Indonesia	Microbus drivers	96	
28	Tong, 2022 [28]	Analyte	ox-LDL ↓ (− 12.3%)	Panel study	PM2.5	Ambient city air	10.26	Air monitoring stations	24 h	United states	Healthy adults	62	F: 62.9/M: 37.1

Table 1 (continued)

ID	Author, Year (ref)	Omics Type	Outcome[a]	Study Design	Exposure					Country	Study Population	Sample Size	Sex Distribution %
					Type	Source	Concentration[b]	Assessment	Window				
29	Wirsching, 2023 [29]	Analyte	↑ GGT by + 1.20% (95% CI 0.73–1.68) per 1.56 µg/m3 $PM_{2.5}$	Cohort study	PM2.5, PM10, PM coarse	Ambient residential	13.58	Air monitoring stations	14 days	Austria	General population	116,109	F: 55.9/M: 44.1
30	Mu, 2021 [30]	Analyte	8-iso-$PGF_2\alpha$ ↑ + 2.28% (95% CI 0.47–4.12)	Panel study	PM2.5	Personal exposure	142.57	Personal portable devices	7 days	China	General population	4,697	F: 64.2/M: 35.8
31	Qin, 2021 [31]	Analyte	ox-LDL ↑ 6.43% (95% CI 2.21–10.82)	Panel study	PM2.5	Personal exposure	183.16[c]	Personal portable devices	24 h	China	Healthy students	110	F: 54.5/M:45.5
32	Peng, 2022 [32]	Analyte	↑ SOD (+ 2.40 U/mL; 95% CI 0.37–4.42)	Panel study	PM2.5	Personal exposure	42.54	Personal portable devices	3 days	China	Healthy adults	35	F: 80/M:20
33	Azzouz, 2022 [33]	Analyte	↑ • ceruloplasmin (+ 15%) • orosomucoid (+ 23%) • C3 (+ 18%) • α_1-antitrypsin (+ 12%) • haptoglobin (+ 12%) • Lp-PLA_2 (+ 9%)	Cohort study	PM2.5, PM10	Ambient residential	10.5	Air monitoring stations	1 year	Sweden	General population	6,103	F: 57/M: 42
34	Eom, 2022 [34]	Analyte	↓ indoor $PM_{2.5}$ by 33.9% → • ↓ urinary 8-OHdG (− 15.6%, 95% CI: − 25.4 to − 4.5) • ↑ baroreflex sensitivity (xBRS + 14.4%)	Randomized Crossover Intervention Trial	PM2.5	Indoor residential	18.6	Indoor and outdoor air quality monitoring system	6 weeks	Korea	Coronary artery disease patients/ improved autonomic balance in CAD patients	38	F: 78.9/M: 21/1
35	Fawzy, 2024 [35]	Analyte	↑ • TBARS (UFP + 7.2%) • 8-isoprostane ($PM_{2.5}$ + 3.7%) • 11dTxB_2 (UFP)	Randomized clinical trial	Indoor PM10-2.5, PM2.5, UFP	Indoor home air	13.0	Partector devices	7 days	United States	Former smokers with COPD	116	F: 51.7/M: 48.3
36	Zhang Lei, 2023 [36]	Analyte	OX-LDL (no association)	Panel study	PM2.5	Personal exposure	53.5	Indoor and outdoor sampling sites	1–3 days	China	Healthy college students	45	F: 60/M: 40

Table 1 (continued)

ID	Author, Year (ref)	Omics Type	Outcome[a]	Study Design	Exposure					Country	Study Population	Sample Size	Sex Distribution %
					Type	Source	Concentration[b]	Assessment	Window				
37	Jiřík, 2024 [37]	Analyte	↑ • α−1-antitrypsin, • 8-isoprostane	Cohort study	PM2.5, PM10	Ambient residential	30.0	Air monitoring stations	Long term	Czech Republic	General population	201	F: 51/M: 49
38	Feng R, 2023 [38]	Analyte	↑ 8-OHdG	Cross-sectional study	Ambient PM2.5	Household solid fuel combustion	80.6	Air monitoring stations, indoor air quality sensors	24 h	China	General population	146	F: 56/M: 44
39	Zhu X, 2023 [39]	Analyte	↑ 8-isoprostane	Randomized crossover study	PM2.5, UFP	Traffic	22[c]	Portable device	4 h	China	Healthy, nonsmoking college students	56	F: 55.4/M: 44.6
40	Orach, 2024 [40]	Analyte	↓ CFI correlated with ↓FEV_1 ($r = 0.35$, $p = 0.02$) ↑nasal IL-1β ($r = -0.31$, $p = 0.04$) ↑IL-6 ($r = -0.32$, $p = 0.03$)	crossover study	PM2.5	Controlled diesel exhaust exposure	150	Air Pollution Exposure Laboratory	4 h	Canada	Healthy adults	15	F: 47/M: 53
41	Guo, 2021 [41]	Analyte	↓ • Fibrinogen (−15.1%), • MCP-1 (−17.7%), • MPO (−17.2%), • PAI-1 (−14.9%), • t-PA (−13.5%)	Randomized crossover study	PM1.0, PM2.5	Outdoor, traffic-generated PM infiltrating indoors	45.6	Environmental monitoring kit Air purifier	48 h	China	Elderly people	24	F: 50/M: 50
42	Cheng, Hedges, 2024 [42]	Metabolome	↑ • 8-OHdG • ox-LDL ↓ • TAC	Randomized crossover trial	PM2.5, PM10	Traffic	$PM_{2.5} = 20.5$	Personal portable devices	2 h	United Kingdom	Healthy or COPD/IHD diagnosed participants	50	F: 36/M: 64
43	Wang, 2024 [43]	Metabolome	↑ • Hippuric acid (+0.21 SMD) ↓ • DHA (−0.26 SMD)	Panel study	PM2.5	Ambient residential	73.3	Monitoring station	96 h	China	General population	110	F:57/M: 43

Table 1 (continued)

ID	Author, Year (ref)	Omics Type	Outcome[a]	Study Design	Exposure					Country	Study Population	Sample Size	Sex Distribution %
					Type	Source	Concentration[b]	Assessment	Window				
44	Yao, 2023 [44])	Metabolome	↓ • PCs • Arg • Trp ↑ • Gly • Met • Orn • Ser • Thr	Cohort study	PM2.5, PM coarse	Ambient residential	13.4	Fixed monitoring sites	2 days, 2 and 8 weeks	Germany	General population	2,583	_
45	Yu, 2023 [45]	Metabolome	↑ • Arginine • glycochenodeoxycholic acid ↓ • phosphatidylcholines • LPCs	Cohort study	PM2.5	Ambient city air	62.5	Air monitoring stations	1 month	China	Patients with COPD	38	F:36.8/M: 63.2
46	Zhao, 2022 [46]	Metabolome	↑ • Serum insulin (+1.64%, 95% CI 0.12–3.19) • HOMA-IR (+2.78%, 95% CI 0.94–4.66) • O-phosphoethanolamine (+2.15%) ↓ • IAI (−2.71%, 95% CI −4.45 to −0.93) per 10 μg/m3 increase in $PM_{2.5}$ • L-serine (−0.45%) • sphingosine (−2.04%) • ceramide (−0.82%)	Panel study	PM2.5	Personal exposure	57.11	Personal portable devices	3 days	China	Healthy seniors	76	F: 51.32/M: 48.68

Table 1 (continued)

ID	Author, Year (ref)	Omics Type	Outcome[a]	Study Design	Exposure					Country	Study Population	Sample Size	Sex Distribution %
					Type	Source	Concentration[b]	Assessment	Window				
47	Walker, 2021 [47]	Metabolome	↑ • lipid peroxidation products ↓ • antioxidants	Observational study	PM2.5	Occupational traffic-related/diesel exhaust at unionized US trucking terminals	work-week mean = 10.0	Stationary samplers	Work shift/workweek	United States	Participants from trucking terminals	73	Male study
48	Chu, 2021 [48]	Metabolome	↓ • LPCs • choline	Cohort study	PM2.5	Ambient city air	53	Air quality online monitoring	The day before physical examinations	China	Healthy college students	78	F: 54/M: 46
49	Li Z, 2022 [49]	Metabolome	↓ • Histamine • Tyrosine • Tryptophan • methionine ↑ • uracil	Cross-sectional study	PM2.5	Traffic	NR	Air monitoring stations	24 h	United states	University employees	180	F: 62.8/M: 37.2
50	Wang T, 2021 [50]	Metabolome	↑ • PUFAs • LOX/CYP oxylipins (pro-inflammatory & anti-inflammatory mediators) ↓ • COX prostaglandins	Panel study	PM2.5, UFP	Ambient residential	65.3	Monitoring station	1–3 days	China	General population	110	F: 57.3/M: 42.7
51	Nassan, Kelly, 2021 [51]	Metabolome	↓ • glutathione metabolites • purine antioxidants (inosine, guanosine) • TCA cycle intermediates ↑ • bilirubin, α-tocopherol	Cohort study	PM2.5	Ambient residential	10.1	Central site monitors	1 year	United states	Healthy men	456	Men study

Table 1 (continued)

ID	Author, Year (ref)	Omics Type	Outcome[a]	Study Design	Exposure					Country	Study Population	Sample Size	Sex Distribution %
					Type	Source	Concentration[b]	Assessment	Window				
52	Huan, 2021 [52]	Metabolome	↑ • GSH (+4.9%) • TRH (+2.95%) ↓ • bilirubin (−6.8%) • biliverdin (−5.9%) • melatonin (−5.3%) • acetylcysteine (−3.9%)	Panel study	PM2.5	Personal exposure	240	Personal portable devices	72 h	China	Healthy adults	63	F: 52.4/M: 47.6
53	Kalia, 2023 [53]	Metabolome	↓ • Cysteinylglycine disulfide • diglyceride • dicarboxylic acid lysophosphatidylethanolamine	Cohort study	PM2.5	Ambient residential	12.9	Air monitoring stations	1 year	United states	General population	107	F: 82/M: 18
54	Nassan, Wang, 2021 [54]	Metabolome	NR	Cohort study	UFP, PM2.5	Ambient city air	10.1	Air monitoring stations	24 h/7 days/30 days/365 days	United states	Healthy men	456	Male study
55	Zhuo, 2024 [55]	Metabolome	Per SD ↑ in $PM_{2.5}$ metabolomic signature → HR = 1.11 (95% CI: 1.09–1.14) for chronic respiratory disease risk	Cohort study	PM2.5, PM10	Ambient residential	10.64	Air monitoring stations	4 years	United Kingdom	Healthy adults/↑ CRD, COPD, and asthma risk; ↓ lung function	171,132	F: 50.50/M: 49.50
56	Feng, 2021 [56]	Metabolome	↑ • sICAM-1 ↓ • amino acids (Ala, Thr, Glu) • Ala and Thr mediated 46–83% of pollutant-related sICAM-1 elevation	Cohort study	PM2.5	Ambient residential	64.2	Air monitoring station	1–7 days	China	Healthy adults/↑ Vascular dysfunction and endothelial inflammation	73	F: 66/M: 34
57	Yuan Z, 2023 [57]	Metabolome	NR	Panel study	PM2.5	Ambient residential	30.21	Air monitoring station	1–5 days	China	Volunteer students/↑ blood pressure, anxiety, and depression risk	40	F: 75/M: 25

Table 1 (continued)

ID	Author, Year (ref)	Omics Type	Outcome[a]	Study Design	Exposure					Country	Study Population	Sample Size	Sex Distribution %
					Type	Source	Concentration[b]	Assessment	Window				
58	Li G, 2022 [58])	Metabolome	↑ • MDA ↓ • GSH • SOD	Panel study	PM2.5	Ambient outdoor air	NR	Air monitoring station	11 h	China	Healthy subjects	92	F: 47.8/M: 52.2
59	Zhu K, 2021 [59]	Metabolome	↑ • 12-HETE (+ 119%), • 13-HODE (+ 18%) • 12-HETE 16.1 ng/mL per 10 µg/m3 $PM_2.5$	Panel study	PM2.5	Ambient outdoor air	NR	Air monitoring station	Short term	China	The Beijing Olympics Air Pollution (BoaP) study	53	F: 60/M: 40
60	Wang T, 2021 [60]	Metabolome	↑ • 5,6-DHET (+ 28.8%) • 8,9-DHET (+ 9.7%) • 11,12-DHET (+ 8.3%) • 14,15-DHET (+ 7.4%) • 20-HETE (+ 8.9%) • TxB_2	Panel study	PM2.5	Ambient residential	74.6	Air monitoring station	1–4 days	China	Subjects with prediabetes	110	F: 57/M: 43
61	Ginos, 2024 [61]	Metabolome	↑ • MDA • 8-iso-$PGF_2\alpha$ ↓ • GSH • SOD	Cohort study	PM2.5	Ambient residential	22.8	Air monitoring station	1 year	The Netherlands	High-level exposed population	2,516	F: 56/M: 44
62	Yang L, 2024 [62]	Metabolome	↑ • Glycoprotein acetyl (inflammation) • MUFA/FA • SFA/FA • Pyruvate • Lactate • Phenylalanine • tyrosine ↓ • VLDL, LDL, cholesterol, • PUFA, DHA, LA, • omega-3, omega-6, • phosphatidylcholine, • sphingomyelin, • acetate	Cohort study	PM2.5, PM10	Ambient residential	9.93[c]	Air monitoring station	Average annual	United Kingdom	General population/↑ COPD risk	227,962	F: 53.97/M: 46.03

Table 1 (continued)

ID	Author, Year (ref)	Omics Type	Outcome[a]	Study Design	Exposure					Country	Study Population	Sample Size	Sex Distribution %
					Type	Source	Concentration[b]	Assessment	Window				
63	Hu X, 2021 [63]	Metabolome	↑ • Asparagine • Glutamine • methionine • citrulline ↓ • glutamate • taurine	Panel study	PM2.5	Personal exposure	29.5	Indoor and outdoor sampling sites	12 h/24 h/1 week/2 weeks	China	Healthy adults	43	F: 37.2/M: 62.8
64	Liao J, 2023 [64]	Metabolome	↑ free fatty acids, hydroxyl compounds, amino acids	Cross-sectional study	PM2.5, PM10	Ambient residential	12.3	Air monitoring stations	1 month/1 year	United states	Young adults	136	F: 44.1/M: 55.9
65	Raza, 2024 [65]	Metabolome	↓ • glucose (β = −1.22, p = 0.06) • lactate (β = −0.02, p = 0.7)	Cohort study	PM2.5	Ambient residential	6.75	Air monitoring stations	Short term/Long term	Brazil	Dementia and control subjects	321	F: 64/M: 36
66	Selley, 2021 [66]	Metabolome	↓ • Taurine • Dimethylamine • Pyroglutamate	prospective interventional study	UFP	Aviation-related ultrafine particles (airport emissions)	53,500 particles/cm3	Semi-controlled exposures to ambient air in a mobile lab	5 h	The Netherlands	Healthy adults	21	
67	Huang, 2024 [67]	Metabolome	↑ • Arachidonic acid • linoleic acid • EPA ↓ • Propionylcarnitine • 4-oxoproline	Cohort study	PM2.5	Air monitoring stations	2 weeks			China	Rural elderly	39,259	F: 41.5/M: 58.5

Table 1 (continued)

ID	Author, Year (ref)	Omics Type	Outcome[a]	Study Design	Exposure					Country	Study Population	Sample Size	Sex Distribution %
					Type	Source	Concentration[b]	Assessment	Window				
68	Vlaanderen, 2022 [68]	Genomics	NR	Cohort study	PM2.5	Ambient residential	NR	Air monitoring stations	Annual	The Netherlands	The Netherlands Twin Register (NTR) and the Netherlands Study of Depression and Anxiety (NESDA)	4,005	F: 66/M: 34
69	Liang, 2021 [69]	Genomics	↓ overall DNAm of imprinted vs non-imprinted genes	Panel study	PM2.5	Personal exposure	78.38	Portable samplers	8 h	China	Healthy young adults	36	F: 47/M: 53
70	Liao J, 2022 [70]	Genomics	↓ amino acids	Cross-sectional study	PM2.5, PM10	Ambient regional/traffic	NR	Air monitoring stations	1 month/1 year	United states	Young adults with childhood asthma	102	F: 60/M: 40
71	Du, 2022 [71]	Genomics	NR	Randomized crossover study	PM2.5	Traffic	NR	MicroPEM Personal Exposure Monitors	4 h	China	Healthy college students	56	F: 48.5/M: 51.5
72	Yuan J, 2024 [72]	Microbiome	↓ • GSH-Px • SOD	Cross-sectional observational study	PM1, PM2.5, PM10	Indoor household air pollution–cooking/heating	PM 2.5: 181.22	Personal portable devices	16 h	China	General population	120	F: 67.5/M: 32.5
73	Zhang, 2024 [73]	Metabolome, Genomics	↑ • 8-OHdG (+5.2% per IQR increase)	Panel study	PM2.5	Personal	28.5	Personal portable devices	3 days	China	Young female participants	30	Female study

Table 1 (continued)

ID	Author, Year (ref)	Omics Type	Outcome[a]	Study Design	Exposure					Country	Study Population	Sample Size	Sex Distribution %
					Type	Source	Concentration[b]	Assessment	Window				
74	Jiang, 2024 [74]	Analytes, Metabolome	↑ • TNF-α, • IL-6, • MPO, • fibrinogen, • Ox-LDL, • MDA, ↓ • catalase	Longitudinal panel study	UFP	Location-adjusted individual exposure	12,000 particles/cm3	Fixed-site monitors	48 h	China	Healthy college students	32	F: 53/M: 47
75	Wang, 2024 [75]	Metabolome, Microbiome	↓ • L-proline, • rhamnose, • B. thetaiotaomicron, ↑ • R. gnavus, • CAH1	Cohort study	PM2.5	Ambient residential	35.40	Bilinear interpolation method	7 days	China	General population	3,267	F: 67.9/M: 32.1
76	Li H, 2024 [76]	Metabolome, Microbiome	↓ • α-diversity of gut flora (−2.16% per 10 µg/m3, 95% CI 1.8–2.5%)	Cohort study	PM2.5, PM10	Ambient city air	NR	Air quality monitoring stations	24 h	China	Patients with acute exacerbation of COPD	42	F: 69/M: 31
77	Li W, 2023 [77]	Metabolome, Microbiome	↓ • 8-epi-$PGF_2\alpha$ + 3.78% (−0.92 to 8.48%)	Panel study	PM2.5	Ambient city air	231.23[c]	Air monitoring stations	24 h	China	Healthy adults	68	F: 70.59/M: 29.01

Outcome quantification stated in table if available[a]

NR Not reported

[b]All reported values for concentration are Mean, and the unit is µg/m3 unless otherwise stated

[c]Median

↑ Increase

↓ Decrease

→ Association between exposure and biomarker

Abbreviations: *PM* particulate matter, *PM_1*, *$PM_{2.5}$*, *PM_{10}* particulate matter with aerodynamic diameter ≤ 1.0, ≤ 2.5, and ≤ 10 µm, *UFP* ultrafine particles, *BC* black carbon, *MDA* malondialdehyde, *8-OHdG* 8-hydroxy-2′-deoxyguanosine, *8-iso-$PGF_2\alpha$* 8-isoprostaglandin $F_2\alpha$, *TBARS* thiobarbituric acid reactive substances, *SOD* superoxide dismutase, *CAT* catalase, *GSH* glutathione, *GSH-Px* glutathione peroxidase, *TAC* total antioxidant capacity, *T-AOC* total antioxidant capacity, *ox-LDL* oxidized low-density lipoprotein, *sLOX-1* soluble lectin-like oxidized LDL receptor-1, *MPO* myeloperoxidase, *CC16* club cell secretory protein 16, *CRP* C-reactive protein, *TNF-α* tumor necrosis factor-α, *IL-6* interleukin-6, *IL-1β* interleukin-1β, *PAI-1* plasminogen activator inhibitor-1, *t-PA* tissue plasminogen activator, *MCP-1* monocyte chemoattractant protein-1, *CFI* complement factor I, *ICAM1* intercellular adhesion molecule 1, *ARG2* arginase 2, *HSPA5* heat shock protein family A (Hsp70) member 5, *LPC* lysophosphatidylcholine, *PC* phosphatidylcholine, *9-HODE* 9-hydroxyoctadecadienoic acid, *13(S)-HPODE* 13-hydroperoxyoctadecadienoic acid, *12,13-DHOME* 12,13-dihydroxyoctadecenoic acid, *PUFAs* polyunsaturated fatty acids, *MUFA* monounsaturated fatty acids, *SFA* saturated fatty acids, *DHA* docosahexaenoic acid, *LA* linoleic acid, *EPA* eicosapentaenoic acid, *HETE* hydroxyeicosatetraenoic acid, *DHET* dihydroxyeicosatrienoic acid, *HPODE* hydroperoxyoctadecadienoic acid, *TxB_2* thromboxane B_2, *LOX* lipoxygenase, *COX* cyclooxygenase, *CYP* cytochrome P450, *Trp* tryptophan, *Arg* arginine, *Gly* glycine, *Met* methionine, *Orn* ornithine, *Ser* serine, *Thr* threonine, *Ala* alanine, *Glu* glutamate, *B. thetaiotaomicron* Bacteroides thetaiotaomicron, *R. gnavus* Ruminococcus gnavus, *VLDL* very low-density lipoprotein, *LDL* low-density lipoprotein, *HDL* high-density lipoprotein, *HR* hazard ratio, *OR* odds ratio, *β* regression coefficient, *SMD* standardized mean difference, *CAD* coronary artery disease, *COPD* chronic obstructive pulmonary disease, *CRD* chronic respiratory disease

[69]. Several studies noted a decrease in oleic and linoleic acids (~3%), alongside reduced saturated fatty acids but higher total and ω−6 fatty acids, particularly after long-term exposure [24, 70, 71]. Collectively, these findings point to oxidative stress-linked remodeling of lipid metabolism and mitochondrial energy flux following PM exposure.

Antioxidant and protective metabolites, including vitamins C/E, tocopherols, and glutathione-related intermediates, showed both depletion and compensatory increases depending on exposure duration [24, 41, 67, 71–75]. PM exposure disrupted glutathione, methionine, and cysteine metabolism, as well as n-3 polyunsaturated fatty acid and melatonin pathways, highlighting redox-linked metabolic exhaustion [61, 64, 69, 76, 77].

Energy and detoxification metabolism were also affected: TCA intermediates (citrate, succinate), amino-acid pathways (glutamate, aspartate, taurine, methionine, arginine, and proline) were consistently altered, pointing to mitochondrial dysfunction [41, 54, 59, 67, 71, 72, 78–80], and purine, pyrimidine and xanthine metabolisms [41, 59, 71, 72, 76, 81]. Sphingolipid and glycerophospholipid metabolism exhibited alterations, particularly affecting sphinganine and phytosphingosine levels [59, 60, 69, 71, 74, 75, 81, 82] as well as decreases in sphingomyelin, ceramide, and phosphatidylcholine species, reflecting membrane remodeling under oxidative stress [70, 83].

Genomics

Five studies evaluated DNA methylation and transcriptomic alterations associated with PM exposure. Differential methylation was observed in genes regulating oxidative stress and inflammation, including TLR2 [62], ICAM-1 [62], IL-10 [62], and macrophage inflammatory protein loci [62]. Long-term $PM_{2.5}$ exposure was associated with epigenetic regulation of oxidative stress-related genes such as *DEK, ABAT*, *KDM1B*, and *EPM2AIP1* [84]. Increased methylation of ARG2 [62] and expression changes in *NMNAT3*, *RAC1,* and *CROT* suggested metabolic reprogramming of redox homeostasis [85]. Additionally, short-term PM exposure increased the expression of stress-response genes *HSPA5* and *MTHFD2* [80], while antioxidant genes (*COQ6, OMA1, FLVCR2, MDH2*) exhibited mixed up- and down-regulation patterns [85]. Conversely, two studies found no significant association between short-term $PM_{2.5}$ exposure [86] and long-term PM_{10} exposure [80] and the expression of oxidative-related genes. Collectively, these genomic findings indicate that PM may alter both oxidative defense and mitochondrial energy regulation through epigenetic and transcriptional mechanisms (Supplementary Table 4).

Microbiome

Four studies investigated the microbiome's response to PM exposure. Short- and long-term exposures were associated with compositional shifts in both gut and nasal microbiota, favoring a pro-oxidant and inflammatory microbial milieu (Supplementary Table 4). Protective, short-chain-fatty-acid–producing taxa such as *Roseburia, Akkermansia*, *Faecalibacterium*, and *Bifidobacterium longum* decreased following $PM_{2.5}$ and PM_{10} exposure [61, 87], whereas pro-inflammatory genera—including *Collinsella massiliensis, Bacteroides dorei, Clostridium sp., Enterococcus faecium*, and nasal Staphylococcaceae—were enriched [39, 61, 63, 87]. These compositional changes align with systemic oxidative stress, suggesting bidirectional crosstalk between PM-induced redox imbalance and microbiome dysbiosis.

Multi-omics integration

Integration of findings across omics platforms revealed consistent patterns linking oxidative biomarkers, metabolites, gene regulation, and microbial composition. Elevated lipid peroxidation markers (MDA, 8-epi-$PGF_2\alpha$, ox-LDL) paralleled metabolomic evidence of disrupted lipid and eicosanoid metabolism, including increased arachidonic-acid–derived HETEs, DHETs, and prostaglandins. These changes collectively indicate lipid oxidative injury and activation of pro-inflammatory pathways. Altered glutathione and energy-related metabolites further supported redox imbalance and mitochondrial dysfunction.

Genomic analyses demonstrated differential methylation and expression of oxidative and inflammatory genes (e.g., TLR2, ICAM1, IL10, ARG2, HSPA5), several of which are mechanistically linked to metabolic and mitochondrial pathways affected in the metabolome. Parallel shifts in the gut and nasal microbiome—characterized by depletion of short-chain fatty acid–producing taxa (e.g., *Roseburia*, *Faecalibacterium*) and enrichment of pro-oxidant species (*Collinsella*, Staphylococcaceae)—suggest microbiota-dependent modulation of host redox and immune responses. Together, these findings support a unified mechanistic model (Fig. 2) in which PM-induced oxidative stress propagates through interconnected metabolic, epigenetic, and microbial pathways. These cross-omics interactions reinforce a systemic oxidative–inflammatory feedback loop, ultimately contributing to epithelial injury, airway remodeling, and vascular dysfunction.

Discussion

This comprehensive systematic review focused on the effect of PM on multi-omics (biomarkers, methylomics, metabolomics, and microbiomics) of oxidative stress. Overall, findings suggest that PM exposure is frequently

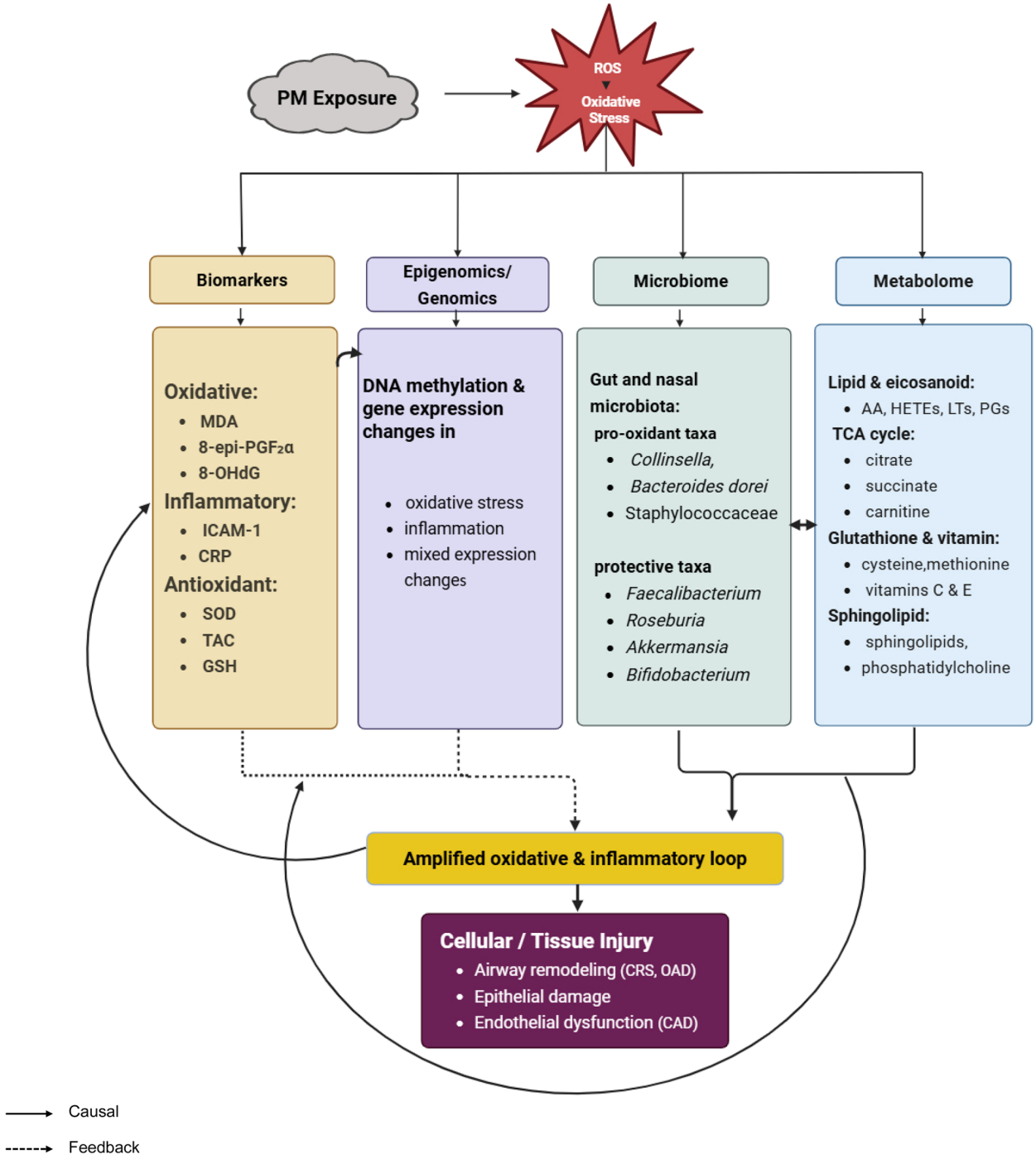

Fig. 2 Integrated multi-omics framework linking PM exposure to oxidative and inflammatory responses

associated with alterations in oxidative stress biomarkers, metabolic pathways involved in redox balance, epigenomics, and the microbiome, although results were not entirely consistent across studies. However, high variability observed across studies may be attributed to the exposure assessment methods and duration, specimen type, study location, and participants' demographics.

Our findings revealed associations between PM and oxidative stress biomarkers, primarily an increase in lipid peroxidation markers (8-epi-PGF2a/8-isoprostane), an increase in oxidative DNA damage markers (8-OHdG), and a decrease in antioxidant markers (TAC and SOD). However, the results were not entirely consistent, as some studies reported no significant associations between PM exposure and oxidative stress indicators, suggesting

that these oxidative responses may vary depending on study design, population characteristics, and exposure duration.

PM has been shown to trigger excessive production of ROS, leading to elevated oxidative stress levels [88]. Studies on both humans and animals provide strong evidence linking ambient PM exposure to oxidative stress biomarkers. A previous meta-analysis showed that ambient $PM_{2.5}$ exposure was significantly associated with an increase in MDA levels, while the associations with OHdG and SOD were not statistically significant [12]. Our current review expands upon this by incorporating multi-omics data, including metabolomics, epigenetics, and microbiome analyses, to provide a more comprehensive understanding of how PM impacts oxidative stress pathways at multiple biological levels. In vitro research has indicated that 8-OHdG levels in human lymphoblastoid and alveolar epithelial cells rise with higher $PM_{2.5}$ exposure [89]. In vivo studies have similarly reported reduced SOD activity and elevated MDA levels in Wistar rats [90, 91] and C57BL/6 J male mice [92]. Additionally, increased 8-OHdG levels have been observed in PM-exposed Sprague–Dawley rats [93].

Our findings support the involvement of oxidative stress-related metabolic pathways in response to PM exposure. This is in line with prior literature suggesting that air pollution elicits metabolomic alterations that contribute to oxidative stress. PM exposure was associated with elevated levels of arachidonic acid and its eicosanoids. These bioactive lipids are well-known mediators of inflammation and oxidative stress, implicating the activation of immune cells and lipid peroxidation processes [94]. The enrichment of leukotriene and prostaglandin pathways following PM exposure highlights the critical role of eicosanoid signaling in PM-induced pathophysiology. Additionally, increased levels of ceramides, hydroxy fatty acids (e.g., 9-HODE, 13-HPODE), and aromatic metabolites such as HPHPA and hippuric acid further implicate oxidative stress and lipid peroxidation in response to PM exposure [95]. PM-associated disruptions in arginine and proline metabolism also suggest enhanced nitric oxide production, a reactive species implicated in oxidative and nitrosative stress [96, 97]. Alterations in antioxidant pathways, including vitamin C, vitamin E, and glutathione metabolism, reflect either compensatory responses to increased ROS [98] or exhaustion of antioxidant reserves [99]. The magnitude of antioxidative response depends upon several factors, including duration of exposure, PM concentration and toxicity, and susceptibility of the subjects to air pollutants [3]. Alterations in the TCA cycle, including reduced citrate and succinate, reflect impaired mitochondrial metabolism, frequently observed in oxidative stress conditions [100].

Our findings demonstrated that environmental pollutants could influence genomic regulation, including changes in DNA methylation and gene expression in pathways linked to oxidative stress, inflammation, and cellular defense. Specifically, $PM_{2.5}$ exposure was linked to methylation changes in inflammatory genes [101], as well as in oxidative stress-related genes [102], reflecting immune activation and redox imbalance. Previous studies showed that 8-oxodG, a hallmark of oxidative stress, in lymphocyte DNA was correlated with personal exposure to $PM_{2.5}$ [103]. Additionally, gene expression shifts in *HSPA5* and *MTHFD2* suggest that PM may induce endoplasmic reticulum and mitochondrial stress responses. Altered expression of antioxidant defense genes, including *COQ6*, *FLVCR2*, and *OMA1*, further supports the role of PM in disrupting mitochondrial function and impairing cellular redox homeostasis.

Our findings are in line with a growing body of literature showing that PM may alter the composition of the gut and nasal microbiota, with implications for oxidative stress and inflammation. The microbial changes observed appear to follow distinct patterns, with both protective and harmful shifts in microbial communities depending on the duration and intensity of PM exposure. PM exposure can damage the host tissues and alter the immune response, which can change host-microbial interactions and alter host microbiomes [104]. Animal studies have also shown that PM can increase gut permeability, decrease colonic motility, and alter the gut microbial composition and metabolic function [105]. The gut microbiome can affect inflammation mainly in two ways: by regulating immune response and maintaining the gut lining, or by disrupting the gut barrier and launching an inflammatory response [106]. Moreover, the gut microbiome may impact oxidative stress by modulating the production of metabolites and antioxidant enzymes [107]. Multi-omics evidence delineates a unified system-level cascade linking PM exposure to oxidative stress and inflammation. At the molecular entry point, PM induces lipid peroxidation and mitochondrial dysfunction, generating oxidative intermediates that activate redox-sensitive transcription factors and inflammatory signaling. These metabolic disruptions are accompanied by epigenetic remodeling of oxidative-stress genes, reinforcing persistent changes in redox regulation and immune activation. Simultaneously, microbiome dysbiosis contributes additional oxidative load through microbial metabolite imbalance and impaired host-microbe signaling. The convergence of these domains, metabolome, methylome, and microbiome, illustrates that PM toxicity operates through an interconnected redox network rather than isolated molecular pathways.

This review has several limitations. First, there was considerable heterogeneity in how PM exposure was

assessed across studies, including differences in PM source attribution, measurement techniques, and duration of exposure. These variations limit the comparability of findings and may contribute to both positive and null results reported across studies, explaining the inconsistencies in reported outcomes. Additionally, due to heterogeneity in effect sizes and inconsistencies in reported metrics (with some studies reporting percentage changes and others beta coefficients), conducting a meta-analysis was not feasible. As an example we assessed studies of 8-OHdG as the outcome and the $PM_{2.5}$ as the exposure. We found that 1) exposure types were inherently different among studies, including ambient $PM_{2.5}$, indoor $PM_{2.5}$, or unspecified general $PM_{2.5}$ levels; 2) reported effect sizes were for different magnitudes of $PM_{2.5}$ changes, such as per IQR change (note different studies had different IQR values), per 10 unit increase, or per twofold change; and 3) models of percent change in the outcome depends on the reference outcome levels, which were unable to be extracted from the publications.

Second, the study populations were diverse, encompassing healthy individuals as well as those with underlying conditions such as COPD, which may influence baseline oxidative stress levels and biological responses to PM. Third, the scope of measured outcomes was broad, with included studies examining a wide range of metabolites, genes, and microbial taxa. While this diversity highlights the complexity of PM-induced biological effects, it also complicates the synthesis and generalization of results. Future studies with standardized exposure metrics, harmonized omics targets, and more homogeneous populations are needed to strengthen the evidence base.

Conclusion

This systematic review highlights the impact of PM exposure on oxidative stress through a multi-omics approach, including the biomarkers, metabolomics, genomics, and microbiomes. The evidence demonstrates that PM exposure disrupts redox homeostasis by altering oxidative stress biomarkers, metabolic pathways, epigenetics, and microbial communities. The convergence of findings across omics platforms supports a complex but coherent model in which PM triggers oxidative responses through interconnected molecular and microbial pathways. These insights may inform the development of novel biomarkers and targeted interventions to mitigate the health risks of air pollution.

Abbreviations

AA	Arachidonic acid
ARG2	Arginase 2
CAD	Coronary Artery Disease
COPD	Chronic obstructive pulmonary disease
CRP	C-reactive protein
CRS	Chronic rhinosinusitis
DNA	Deoxyribonucleic Acid
GSH	Glutathione
GPx	Glutathione Peroxidase
GGT	Gamma-Glutamyl Transferase
HETEs/DHETs	Hydroxyeicosatetraenoic Acids / Dihydroxyeicosatrienoic Acids
ICAM	Intercellular adhesion molecule
IL10	Interlukin-10
LDL	Low-Density Lipoprotein
LT	Leukotrienes
MPO	Myeloperoxidase
MDA	Malondialdehyde
NO	Nitric oxide
NOS	Newcastle-Ottawa Scale
OAD	Obstructive airway disease
Ox-LDL	Oxidized low-density lipoprotein
PGF1α	Prostaglandin F1α
PM	Particulate matter
PG	Prostaglandin
PGE2	Prostaglandin E_2
ROS	Reactive oxygen species
SOD	Superoxide dismutase
TAC	Total antioxidant capacity
TCA cycle	Tricarboxylic acid cycle
TBARS	Thiobarbituric Acid Reactive Substances
TLR2	Toll-Like Receptor 2
UFP	Ultrafine particle
HODE	Hydroxyoctadecadienoic acids
WoS	Web of Science
WTC	World Trade Center
8-OHdG	8-Hydroxy-2'-deoxyguanosine
8-epi-$PGF_2\alpha$	8-Epi-prostaglandin $F_2\alpha$

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12931-025-03487-0.

Supplementary Material 1.

Supplementary Material 2.

Supplementary Material 3.

Supplementary Material 4.

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Authors' contributions

AF and AN conceived and planned the systematic review. AF carried out the literature search. AF and TM performed the screening of articles. AF and TM carried out data extraction and analysis. ML provided statistical oversight and assessment. AF took the lead in writing the manuscript. SK provided a critical review. All authors helped write the manuscript and provided critical feedback, and helped shape the research, analysis, and manuscript.

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Data availability

No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate

Ethical approval was not required for this study as it is a systematic review of previously published literature and does not involve any new human or animal data.

Consent for publication

Consent for publication was not required for this study.

Competing interests

The authors declare no competing interests.

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