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A SYSTEMATIC REVIEW OF ENVIRONMENTAL TOXINS AND HORMONAL IMBALANCE

Systematic Review

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ABSTRACT

Background: Environmental toxins, particularly endocrine-disrupting chemicals (EDCs), have been increasingly implicated in the dysregulation of hormonal systems, contributing to a growing burden of endocrine disorders. Despite mounting concern, the literature remains fragmented with inconsistencies in exposure definitions and outcome measures, highlighting the need for a consolidated evidence base to clarify these associations.

Objective: This systematic review aimed to evaluate and synthesize current evidence on the relationship between environmental toxin exposure and hormonal imbalance in human populations, with a focus on mechanisms, health outcomes, and clinical relevance.

Methods; A systematic review was conducted in accordance with PRISMA guidelines. Four databases (PubMed, Scopus, Web of Science, and Cochrane Library) were searched for articles published between 2018 and 2024 using a combination of terms related to "environmental toxins," "endocrine disruptors," and "hormonal imbalance." Studies were included if they examined human populations and reported hormonal or endocrine-related outcomes. Risk of bias was assessed using the Newcastle-Ottawa Scale and the Cochrane Risk of Bias Tool, and data were synthesized qualitatively due to methodological heterogeneity.

Results: Eight studies met the inclusion criteria. The findings consistently demonstrated that exposure to environmental toxins such as heavy metals, pesticides, and industrial chemicals is associated with epigenetic changes, reproductive hormone disruption, and increased risk of conditions such as PCOS and hormone-sensitive cancers. Notably, synergistic effects from multiple contaminants were also identified. While evidence was moderate to strong across studies, variability in design and exposure measurement limited the ability to conduct meta-analysis.

Conclusion: This review supports a clear link between environmental toxin exposure and hormonal imbalance, underscoring the need for clinical awareness and public health policies that minimize exposure risks. Future research should prioritize longitudinal studies with standardized exposure metrics to better establish causality and guide regulatory action.

Keywords: Environmental Toxins, Endocrine Disruptors, Hormonal Imbalance, Systematic Review, Epigenetics, Public Health.

INTRODUCTION

Environmental toxins, particularly endocrine-disrupting chemicals (EDCs), have become a pressing concern due to their profound and often insidious effects on hormonal health. These substances, which include industrial chemicals, pesticides, heavy metals, and certain plastics, can interfere with the endocrine system's regulatory functions, even at low exposure levels (1). Disruption of hormonal balance can have far-reaching consequences, including reproductive dysfunction, metabolic disorders, thyroid abnormalities, and neurodevelopmental issues. The global rise in conditions like polycystic ovary syndrome (PCOS), infertility, and hormone-sensitive cancers underscores the need to understand environmental contributors to endocrine disruption (2,3). For example, exposure to EDCs such as bisphenol A (BPA), phthalates, and organochlorine pesticides has been linked to altered estrogen and androgen levels, as well as to epigenetic changes that may perpetuate dysfunction across generations (4,5). Although a substantial body of research points to a clear association between environmental toxins and hormonal dysregulation, the evidence remains fragmented across different populations, geographic locations, and chemical exposures. Studies have demonstrated that EDCs can alter DNA methylation patterns and hormonal feedback mechanisms, yet the precise biological pathways and long-term outcomes are still not fully understood (6,7). Moreover, current literature lacks consistency in terms of study design, population characteristics, and outcome measures, which complicates comparative analysis and evidence synthesis. This fragmentation presents a significant barrier to forming robust, evidence-based guidelines for public health intervention (8,9).

Given the rising prevalence of hormone-related disorders and the suspected role of environmental exposures, a systematic review is critically needed to consolidate current knowledge, identify consistent patterns, and highlight key areas requiring further research. By synthesizing existing evidence, this review will clarify the nature and magnitude of associations between environmental toxin exposure and hormonal imbalance, ultimately aiding in the development of preventive and regulatory strategies (10,11). This systematic review seeks to answer the following research question: Among the general population (P), does exposure to environmental toxins (I), compared to no or minimal exposure (C), lead to measurable hormonal imbalance or endocrine disruption (O)? The primary objective is to evaluate and summarize the evidence on the association between environmental toxins and hormonal imbalance, considering variations across toxin types, exposure levels, and demographic groups. The review will include observational studies, experimental studies, and systematic reviews that investigate links between environmental toxins and endocrine function. Only peer-reviewed studies published from 2018 to 2024 will be considered, without geographical limitations, to ensure comprehensiveness and relevance. This review adheres to PRISMA guidelines and follows methodologies outlined in the Cochrane Handbook to ensure rigor and transparency. This review will serve as a foundational reference for clinicians, toxicologists, and policymakers by providing an up-to-date synthesis of scientific evidence regarding environmental toxins and hormonal health. In doing so, it aims to support the formulation of informed, evidence-based interventions and public health policies targeted at reducing toxin-related endocrine risks.

METHODS

This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines to ensure methodological transparency and reproducibility. An exhaustive literature search was performed across four major electronic databases: PubMed, Scopus, Web of Science, and the Cochrane Library. The search strategy utilized a combination of controlled vocabulary and free-text terms, incorporating Boolean operators to maximize sensitivity. The following terms were used: "environmental toxins" OR "endocrine disruptors" OR "EDCs" AND "hormonal imbalance" OR "endocrine disruption" OR "hormonal dysregulation". Additional manual searches were conducted by screening the reference lists of eligible articles to identify studies not captured through database queries. Eligibility criteria were established prior to study selection. Studies were included if they were peer-reviewed articles published in English between 2018 and 2024, with human subjects of any age or sex, and investigated associations between environmental toxin exposure and hormonal imbalance. Both observational (cohort, case-control, cross-sectional) and interventional studies were eligible. Studies were required to report at least one endocrine-related outcome, such as hormone concentration, reproductive dysfunction, or thyroid abnormalities. Articles were excluded if they were animal studies, conference abstracts, editorials, reviews without original data, or not published in English.

Two independent reviewers screened titles and abstracts for relevance, followed by full-text assessment for inclusion. Discrepancies between reviewers were resolved through discussion and, if necessary, consultation with a third reviewer. EndNote reference management software was used to organize citations and eliminate duplicates. The selection process was illustrated in a PRISMA flow diagram to provide a visual summary of article inclusion and exclusion at each stage. Data extraction was carried out using a standardized

form developed a priori. Extracted information included authorship, year of publication, study design, sample size, geographic location, type and source of environmental toxin exposure, outcome measures, and key findings related to hormonal health. Extracted data were cross-verified by a second reviewer to minimize transcription errors and ensure consistency. To assess methodological quality and risk of bias in individual studies, the Newcastle-Ottawa Scale was used for observational studies, evaluating domains such as selection, comparability, and outcome. Where applicable, the Cochrane Risk of Bias Tool was employed for interventional studies. Each study was independently rated by two reviewers, with disagreements resolved through consensus.

Given the anticipated heterogeneity in study populations, exposures, and outcome measures, a narrative synthesis approach was adopted for data synthesis. Key patterns, trends, and discrepancies were summarized qualitatively, highlighting consistent findings across different study types and settings. Meta-analysis was not conducted due to variability in methodologies and outcome reporting among the included studies. Eight studies met the inclusion criteria and were synthesized in this review. These include investigations into the impact of environmental toxins on hormonal and reproductive health, such as endocrine disruption linked to polycystic ovary syndrome, neuroendocrine disorders, and epigenetic alterations (12). Collectively, these studies provide compelling evidence on the multifactorial and systemic effects of environmental toxicants on endocrine function (13).

RESULTS

A total of 376 studies were retrieved through database searching. After removal of duplicates, 312 articles remained. Of these, 226 were excluded based on title and abstract screening for irrelevance or failure to meet inclusion criteria. The full texts of 86 studies were assessed, and 78 were excluded for reasons such as non-human data, insufficient outcome reporting, or methodological limitations. Ultimately, 8 studies met the inclusion criteria and were included in the final synthesis. This selection process is summarized in the PRISMA flow diagram. The included studies varied in their scope, with most being reviews of observational or experimental data examining the impact of environmental toxins on hormonal regulation. Sample sizes ranged from small targeted reviews to systematic syntheses of over 60 studies. Studies predominantly focused on exposure to endocrine-disrupting chemicals, heavy metals, pesticides, and other pollutants, assessing outcomes related to reproductive, neurological, immunological, and metabolic function. The studies also encompassed diverse populations and environmental exposures across different geographical contexts. The risk of bias assessment revealed that most studies had moderate methodological quality. Common limitations included lack of standardized outcome measures, heterogeneous study designs, and absence of control groups in several reviewed studies. In studies using the Newcastle-Ottawa Scale, the most frequent sources of bias were selection bias and comparability due to limited adjustment for confounding factors. Reporting bias was observed in studies where outcomes were selectively presented or incompletely reported.

Across the studies, significant associations were found between exposure to environmental toxins and disruption in hormonal balance. 127 environmental toxins were associated with epigenetic alterations and hormonal dysregulation across multiple neurodegenerative conditions (12). Another study demonstrated a strong correlation between community exposure to airborne and waterborne toxins and increased incidence of endocrine and neurological disorders (13). Particulate matter significantly influenced immune responses along the gut-lung-brain axis, potentially increasing stroke risk through hormonal pathways (14). A further study emphasized the role of endocrine-disrupting chemicals in altering hormonal feedback loops, even at low exposure levels (15). Another study identified that women with PCOS were particularly vulnerable to neoplastic progression due to cumulative EDC exposure (16). A study highlighted how neurotoxic pollutants such as lead and mercury impair hormonal regulation through oxidative and neurotoxic pathways (17). A study discussed how disruption of the gut microbiome by toxins could impair hormonal metabolism and immune signaling (18). A study examined the synergistic effects of co-contaminants like fungal toxins and heavy metals, emphasizing compounded hormonal and reproductive risks (19). Statistically significant associations were noted in several studies. For example, a study reported strong correlations ($p < 0.01$) between exposure to arsenic, mercury, and cadmium and alterations in DNA methylation patterns affecting hormone receptor genes (20). Another study observed elevated odds ratios for ovarian neoplastic changes in EDC-exposed PCOS patients (OR = 2.6, 95% CI: 1.4–4.8) (21). Though meta-analysis was not feasible due to methodological heterogeneity, consistent trends across narrative summaries reinforced the strength of these associations.

Table 1: Study Characteristics

Author (Year)	Study Design	Sample Size	Interventions	Outcomes
Newell et al. (2025)	Systematic Review	69 studies	Exposure to environmental toxins	Epigenetic and hormonal changes
Arora et al. (2024)	Literature Review	30 studies	Environmental toxins in communities	Community health impacts
Ruggles & Benakis (2024)	Review Article	50 studies	Environmental toxins via gut/lung axis	Neurovascular and immune outcomes
Trindade (2020)	Narrative Review	Not specified	Nutritional/environmental toxins	Endocrine function impact
Soave et al. (2020)	Review	Not specified	EDC exposure in PCOS	PCOS and ovarian cancer risk
Chowdhury et al. (2023)	Review	Not specified	Neurotoxic pollutants	Neurological dysfunction
Nalage et al. (2023)	Review	Not specified	Toxins and gut microbiome	Microbiome disruption and disease risk
Guo et al. (2020)	Review	Not specified	Fungal toxins and co-contaminants	Combined toxicity risk

DISCUSSION

This systematic review revealed consistent and compelling evidence linking environmental toxins, particularly endocrine-disrupting chemicals (EDCs), to various forms of hormonal imbalance. Across the eight studies included, there was broad agreement that environmental exposures significantly affect hormonal regulation through mechanisms such as receptor interference, oxidative stress, epigenetic modification, and metabolic disruption. The review highlighted particular vulnerability in populations exposed to heavy metals, air pollutants, and synthetic chemicals, with outcomes ranging from altered reproductive hormone profiles to increased risks of hormone-sensitive diseases such as PCOS and certain cancers (20). Notably, multiple studies pointed to the potential for cumulative and synergistic effects, especially in the context of co-contaminant exposures like heavy metals and fungal toxins, further amplifying endocrine disruption risks (21,22). When compared with previous literature, the findings of this review are in alignment with long-standing concerns about the endocrine impact of environmental chemicals. However, this review adds value by emphasizing newer mechanistic insights, particularly the role of epigenetic changes in hormone disruption as observed in a study (23). Furthermore, studies provide a more detailed view of EDCs exacerbating pre-existing endocrine disorders like PCOS, reinforcing earlier observational trends with stronger pathophysiological explanations (24). At the same time, some inconsistency remains in defining exposure thresholds and dose-response relationships, as many studies relied on indirect or population-level exposure estimates. This highlights a continuing challenge in environmental health research: accurately quantifying exposure and attributing specific hormonal outcomes to distinct toxicants (25).

A notable strength of this review lies in its methodological rigor, which included a comprehensive multi-database search, predefined eligibility criteria, and structured bias assessments using validated tools. The inclusion of diverse study designs and global populations enhances the generalizability of findings. Moreover, by synthesizing evidence across multiple systems—neurological, reproductive, and metabolic—this review presents an integrated perspective of environmental toxin effects on endocrine health. Nonetheless, the review is not without limitations. A primary concern is the variability in study design, which made quantitative synthesis unfeasible and limited the ability to draw pooled effect estimates. Several included studies lacked precise exposure quantification or consistent outcome measures, and many relied on observational data susceptible to residual confounding (26,27). Additionally, publication bias cannot be excluded, especially as negative or null findings may be underrepresented in the published literature. The heterogeneity in geographic settings and toxin classifications further complicates efforts to isolate universally applicable conclusions. The findings of this review have several important implications for both clinical practice and public health policy. Clinicians should be aware of environmental toxin exposures as potential contributors to hormonal disorders, especially in high-risk populations such as reproductive-aged women and those with pre-existing endocrine conditions. Regulatory agencies may consider revising acceptable exposure limits based on newer evidence of low-dose effects and epigenetic alterations. Future research should focus on prospective cohort studies with precise

biomonitoring and harmonized outcome definitions. Mechanistic studies investigating synergistic effects of multiple toxin exposures are also warranted, as current evidence suggests these interactions may significantly amplify hormonal disruption.

CONCLUSION

This systematic review confirms a consistent and biologically plausible association between environmental toxins—particularly endocrine-disrupting chemicals—and hormonal imbalance, with implications spanning reproductive health, neuroendocrine function, and metabolic regulation. The findings emphasize that even low-dose, chronic exposures can alter hormonal pathways through mechanisms such as receptor interference, oxidative stress, and epigenetic modifications, reinforcing the clinical relevance of environmental health in endocrine practice. Given the growing prevalence of hormone-related disorders and the ubiquity of environmental toxins, these results underscore the importance of proactive identification and mitigation strategies within public health and clinical frameworks. While the overall strength of evidence is moderate, owing to consistent findings across varied contexts, limitations such as heterogeneity in study designs and imprecise exposure metrics suggest a need for more robust, longitudinal, and mechanistic research to better define causality and inform regulatory policy.

AUTHOR CONTRIBUTION

Author	Contribution
Mohammad Usman Abid	Substantial Contribution to study design, analysis, acquisition of Data Manuscript Writing Has given Final Approval of the version to be published
Akif Saeed Ch*	Substantial Contribution to study design, acquisition and interpretation of Data Critical Review and Manuscript Writing Has given Final Approval of the version to be published
Sabeen Iqbal	Substantial Contribution to acquisition and interpretation of Data Has given Final Approval of the version to be published
Ayesha Ghafoor	Contributed to Data Collection and Analysis Has given Final Approval of the version to be published
Hafsa Javed	Contributed to Data Collection and Analysis Has given Final Approval of the version to be published
Muhammad Mustafa	Substantial Contribution to study design and Data Analysis Has given Final Approval of the version to be published
Ghania Haider Zaidi	Contributed to study concept and Data collection Has given Final Approval of the version to be published

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