SSR Institute of International Journal of Life Sciences
ISSN (O): 2581-8740 | ISSN (P): 2581-8732
Tauseef *et al*., 2026
doi: 10.21276/SSR-IIJLS.2026.12.4.43

Review Article

open access

Dysregulation of the Pubertal Axis by Endocrine Disruptors: A Review of Mechanisms, Timing of Exposure, and Lifelong Consequences

Malik Tauseef[1]*, Shaikh Aquib[1], Arbaaz Khan[1], Shakib Shahab[1], Tahzeeb Fatima[1], Ansari Rehan[1], Waqas Alauddin[2]

[1]Third year MBBS Student, Naraina Medical College and Research Centre, Kanpur, India

[2]Associate Professor, Department of Physiology, Venkateshwara Institute of Medical Sciences, Amroha, India

***Address for Correspondence:** Dr. Malik Tauseef, Third year MBBS student, Naraina Medical College and Research Centre, Kanpur, India
E-mail: tauseefm825@gmail.com

Received: 21 Mar 2026/ Revised: 26 May 2026/ Accepted: 22 Jun 2026

ABSTRACT

Endocrine disruptors are increasingly recognized as important environmental determinants of pubertal dysregulation through their interference with the hypothalamic–pituitary–gonadal (HPG) axis. By mimicking, antagonizing, or altering endogenous hormone signaling, these exogenous agents can disrupt the timing and progression of puberty, with potential long-term consequences for reproductive and overall health. This narrative review synthesizes contemporary evidence on the role of endocrine disruptors in pubertal dysregulation. A literature search was conducted using PubMed, Scopus, and Google Scholar for studies published between 2020 and 2025, and evidence from human and experimental studies was narratively integrated to examine neuroendocrine, peripheral, and epigenetic mechanisms, critical developmental windows of exposure, and associated clinical outcomes. Endocrine disruptors exert estrogenic, anti-androgenic, thyroid-disrupting, and epigenetic effects that alter both central gonadotropin-releasing hormone (GnRH) signaling and peripheral gonadal steroidogenesis. Exposure during sensitive developmental periods, including prenatal life, minipuberty, and childhood, may induce persistent reprogramming of the HPG axis and disrupt pubertal timing. These alterations are associated with metabolic disorders, reproductive dysfunction, cardiovascular risk, hormone-dependent malignancies, and neurobehavioral disturbances. Puberty represents a critical window of vulnerability to endocrine disruption. Reducing early-life exposure to endocrine disruptors may help preserve normal pubertal development and decrease the risk of long-term metabolic, reproductive, and neurobehavioral complications. Further mechanistic and longitudinal studies are needed to strengthen causal evidence and guide effective public health strategies.

Key-words: Endocrine disruptors; Puberty; Hypothalamic–pituitary–gonadal axis; GnRH; Neuroendocrine regulation; Epigenetics

INTRODUCTION

Puberty is a tightly regulated neuroendocrine transition from childhood to sexual maturity, initiated by the reactivation of pulsatile gonadotropin-releasing hormone (GnRH) secretion from hypothalamic neurons.[1] This process is orchestrated through a complex interplay between central neuroendocrine networks and peripheral metabolic and hormonal signals.

How to cite this article
Tauseef M, Aquib S, Khan A, Shahab S, Fatima T, et al. Dysregulation of the Pubertal Axis by Endocrine Disruptors: A Review of Mechanisms, Timing of Exposure, and Lifelong Consequences. SSR Inst Int J Life Sci., 2026; 12(4): 10459-10464.

Access this article online
https://iijls.com/

Key upstream regulators, including kisspeptin, neurokinin B, and dynorphin, play essential roles in modulating GnRH pulsatility, whereas metabolic cues such as leptin and insulin integrate energy balance with reproductive function. GnRH stimulates the anterior pituitary to secrete luteinizing hormone (LH) and follicle-stimulating hormone (FSH), which subsequently promote gonadal steroidogenesis, gametogenesis, and the development of secondary sexual characteristics.[1] The precise timing and progression of puberty are fundamental for normal somatic growth, reproductive maturation, and psychosocial development.[1]

Over recent decades, a global trend toward earlier pubertal onset particularly among females has been increasingly recognized, suggesting that factors beyond

doi: 10.21276/SSR-IIJLS.2026.12.4.43

traditional determinants such as genetics and nutrition contribute to pubertal development.[2] Dysregulated pubertal timing has been associated with numerous adverse health outcomes, including obesity, insulin resistance, cardiovascular disease, reproductive disorders, and psychological disturbances. These observations have intensified interest in environmental factors that may influence endocrine function and pubertal maturation.[2]

Among these environmental influences, endocrine disruptors have emerged as significant and potentially modifiable contributors to pubertal dysregulation.[3] These exogenous agents can mimic, antagonize, or interfere with endogenous hormonal signaling, affecting both central components of the hypothalamic–pituitary–gonadal (HPG) axis and peripheral endocrine organs. Importantly, exposure during critical developmental windows including prenatal life, minipuberty, and childhood may induce persistent alterations in endocrine programming, thereby influencing pubertal timing, progression, and long-term health outcomes.[3]

The present narrative review aims to synthesize current evidence on the mechanisms by which endocrine disruptors dysregulate the pubertal axis, with particular emphasis on neuroendocrine pathways, critical windows of exposure, and their lifelong metabolic, reproductive, and neurobehavioral consequences.

This narrative review was conducted to synthesize contemporary evidence regarding the role of endocrine disruptors in the dysregulation of the pubertal axis. A comprehensive literature search was performed using the PubMed, Scopus, and Google Scholar databases to identify relevant studies published between January 2020 and December 2025.[2, 3]

The search strategy incorporated combinations of the following keywords: *"endocrine disruptors," "endocrine-disrupting chemicals," "puberty," "hypothalamic–pituitary–gonadal axis," "HPG axis," "pubertal timing," "neuroendocrine disruption," and "epigenetics."* Additional studies were identified through manual screening of the reference lists of eligible articles to ensure comprehensive literature coverage.[3]

Eligible studies included original research articles, systematic reviews, meta-analyses, and relevant experimental studies investigating the effects of endocrine disruptor exposure on pubertal development, neuroendocrine regulation, hormonal homeostasis, and long-term health outcomes.[4] Both human and animal studies were considered to provide complementary mechanistic and translational insights. The retrieved literature was narratively synthesized, with emphasis on mechanisms of action, critical windows of susceptibility, pubertal outcomes, and long-term clinical implications.

Mechanisms of Endocrine Disruptor Induced Pubertal Dysregulation- Endocrine disruptors influence pubertal development through multiple interconnected pathways involving central neuroendocrine regulation, peripheral endocrine function, and epigenetic modifications. Collectively, the available evidence supports a biologically plausible framework in which disruption of the hypothalamic–pituitary–gonadal (HPG) axis contributes to altered pubertal timing, progression, and long-term health outcomes.[3,4-8] The findings emphasize that endocrine disruptors act through diverse molecular mechanisms rather than a single pathway, underscoring the complexity of endocrine regulation during puberty.

Central Neuroendocrine Mechanisms- At the central level, interference with gonadotropin-releasing hormone (GnRH) neuronal activity and its upstream regulators, including kisspeptin and neurokinin B signaling, represents a major mechanism by which endocrine disruptors influence pubertal onset.[4] These neuroendocrine disturbances may result in either premature activation or delayed maturation of the pubertal axis depending on the timing, duration, and magnitude of exposure. Furthermore, the non-monotonic dose–response characteristics observed with several endocrine disruptors complicate traditional toxicological risk assessment and suggest that even low-dose exposures may have clinically relevant biological effects.[4]

Peripheral Gonadal Mechanisms- Peripheral disruption of gonadal function also contributes substantially to pubertal dysregulation. Altered steroidogenic enzyme activity and impaired gonadal hormone production disrupt normal feedback regulation within the HPG axis, thereby amplifying endocrine imbalance.[6] In males, anti-androgenic effects have been associated with reduced testosterone synthesis, impaired spermatogenesis, and delayed or abnormal pubertal progression.[7]

doi: 10.21276/SSR-IIJLS.2026.12.4.43

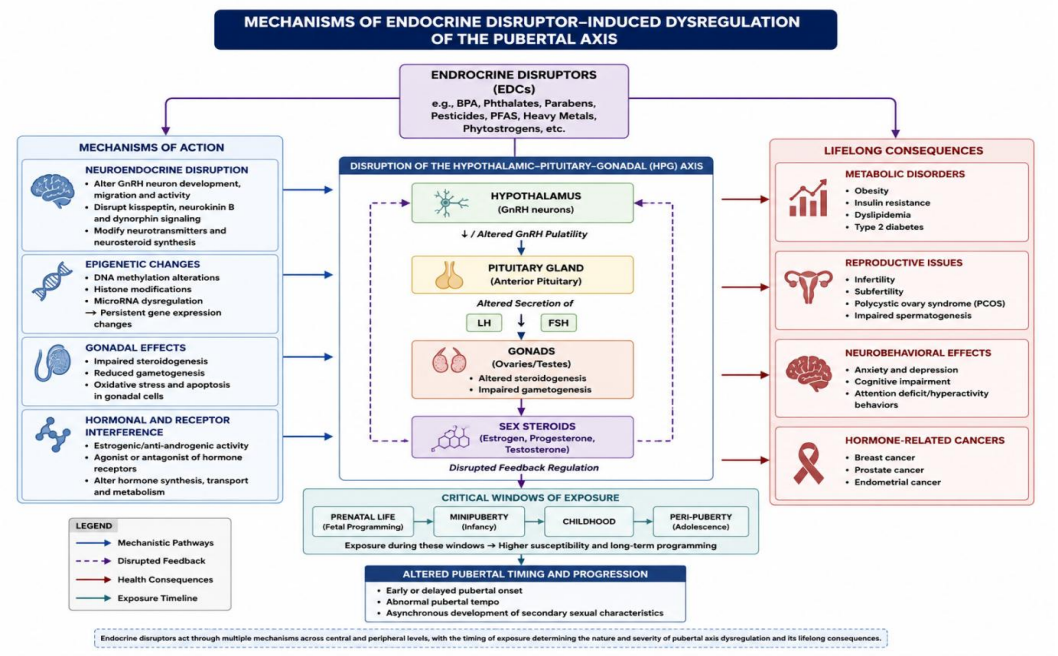

Fig. 1: Mechanisms of Endocrine Disruptor–Induced Dysregulation of the Pubertal Axis

Effects on Pubertal Timing and Hormonal Regulation

Alterations in Pubertal Timing- Literature consistently demonstrates that endocrine disruptors influence pubertal timing and progression through multiple interconnected pathways. Across studies, exposure has been associated with both advancement and delay in pubertal onset depending on the chemical class, timing, and dose of exposure.[3–6] Estrogenic compounds are more frequently associated with earlier pubertal onset, particularly in females,[7] whereas anti-androgenic compounds have been linked to delayed or abnormal pubertal progression in males.[3–6] Variability in pubertal tempo and asynchronous development of secondary sexual characteristics has also been reported.

Hormonal and HPG Axis Alterations- Several studies have demonstrated that endocrine disruptors alter central regulation of puberty by affecting GnRH pulsatility and hypothalamic signaling pathways.[6] Consistent changes in circulating LH, FSH, estrogen, and testosterone concentrations indicate disruption at both hypothalamic and gonadal levels. In addition, interference with normal feedback mechanisms within the HPG axis contributes to sustained hormonal imbalance and altered reproductive maturation.

Table 1: Endocrine Disruptors and Mechanisms of Pubertal Axis Dysregulation

EDC Class / Exposure	Primary mechanism	Level of action	Effect on Puberty	Reference
Bisphenols (BPA)	Estrogen receptor agonism	Hypothalamic	Early pubertal onset	[7]
Phthalates	Anti-androgenic activity	Gonadal	Delayed/abnormal male puberty	[9]
Mixed EDCs	Neuroendocrine disruption	HPG axis	Altered pubertal timing	[6]
Prenatal EDC exposure	Epigenetic modification	Central & peripheral	Long-term pubertal reprogramming	[10]
Childhood exposure	Cumulative hormonal imbalance	Systemic	Altered pubertal tempo	[7]

Legends: *Summary of major classes of endocrine disruptors (EDCs), their primary mechanisms of action, levels of interference within the hypothalamic–pituitary–gonadal (HPG) axis, and their effects on pubertal development.*

doi: 10.21276/SSR-IIJLS.2026.12.4.43

Critical Windows of Susceptibility

Prenatal Exposure- Prenatal exposure appears to exert the greatest influence because of active programming of the neuroendocrine and reproductive systems during fetal development.[9] Early exposure may permanently alter HPG axis function, resulting in long-term changes in pubertal timing and endocrine regulation.

Minipuberty and Childhood- Emerging evidence identifies minipuberty and childhood as additional periods of heightened susceptibility during which endocrine disruptors may induce persistent alterations in HPG axis function and pubertal progression.[9,10]

Peri-pubertal Exposure- Limited but growing evidence suggests that exposure during the peri-pubertal period may further modify pubertal outcomes, although additional longitudinal studies are needed to clarify this relationship.[11]

Table 2: Critical Windows of Endocrine Disruptor Exposure and Their Impact on Pubertal Development

Window of Exposure	Key Characteristics	Major Mechanisms	Pubertal Effects	Potential Long-Term Consequences
Prenatal life	HPG axis programming; placental EDC transfer	Epigenetic modification, altered steroidogenesis	Early or delayed puberty, abnormal sexual development	Metabolic disorders, infertility, neurobehavioral disorders
Minipuberty (0–6 months)	Transient HPG axis activation; reproductive programming	Altered GnRH/LH/FSH secretion, disrupted gonadal development	Hormonal imbalance, impaired germ cell maturation	Subfertility, endocrine dysfunction
Childhood	Ongoing HPG maturation; cumulative EDC exposure	Neuroendocrine disruption, hormone receptor interference	Altered pubertal timing and tempo	Obesity, insulin resistance, reproductive dysfunction
Peri-puberty / Adolescence	Increased hormonal sensitivity	Disrupted steroid hormone signaling, oxidative stress	Menstrual irregularities, delayed/abnormal pubertal progression	Cardiometabolic disease, mental health disorders, reduced fertility

Epigenetic Mechanisms and Developmental Programming

Epigenetic Alterations- Studies have identified persistent alterations in DNA methylation, histone modification, and gene expression involving HPG axis-related genes following endocrine disruptor exposure.[8,10]

Developmental Reprogramming- These molecular changes may remain clinically silent until activation of the HPG axis during adolescence, supporting the concept of developmental reprogramming as a plausible explanation for the delayed manifestation of endocrine disruptor-induced pubertal disorders.

Long-Term Health Consequences

Metabolic and Cardiovascular Outcomes- Altered pubertal timing has been associated with increased risks of obesity, insulin resistance, cardiovascular disease, and adverse cardiometabolic outcomes, particularly among individuals with early pubertal onset.[12]

Reproductive Consequences- Delayed or abnormal puberty has been linked to impaired reproductive function, reduced fertility, hormonal imbalance, and hormone-dependent malignancies.[4–7]

Neurobehavioral Consequences- Accumulating evidence also indicates an increased risk of neurobehavioral disorders, including anxiety and depression, highlighting

doi: 10.21276/SSR-IIJLS.2026.12.4.43

the lifelong impact of endocrine disruptor-induced pubertal dysregulation.[12]

STRENGTHS

This review provides a contemporary synthesis of mechanistic and clinical evidence describing how endocrine disruptors influence pubertal development through central neuroendocrine, peripheral endocrine, and epigenetic pathways. By integrating findings from human and experimental studies, it highlights critical developmental windows of susceptibility and summarizes complex mechanisms using concise tables and a conceptual figure, thereby providing a comprehensive overview of current knowledge.

LIMITATIONS

As a narrative review, this article is based on qualitative synthesis rather than quantitative meta-analysis. Considerable heterogeneity exists among studies with respect to exposure assessment, outcome definitions, and study design, limiting direct comparisons. Most available studies also evaluate individual endocrine disruptors despite real-world exposure occurring as complex chemical mixtures. Additional longitudinal studies are required to clarify dose–response relationships, mixture effects, sex-specific susceptibility, and the impact of peri-pubertal exposure.

CONCLUSIONS

Recent evidence supports a biologically plausible and increasingly consistent role of endocrine disruptors in dysregulating the pubertal axis. Through disruption of central neuroendocrine signaling, peripheral gonadal function, and epigenetic programming, these environmental agents can alter the timing and progression of puberty, particularly when exposure occurs during critical developmental windows. The resulting disturbances have important implications for lifelong metabolic, reproductive, cardiovascular, and neurobehavioral health. Continued research aimed at elucidating dose–response relationships, combined chemical exposures, and underlying molecular mechanisms will further strengthen our understanding of endocrine disruptor-induced pubertal disorders. Reducing exposure to endocrine disruptors during early life should therefore be regarded as an important public health strategy to promote healthy pubertal development and improve long-term health outcomes.

ACKNOWLEDGMENTS

The authors gratefully acknowledge Naraina Medical College and Research Centre for providing academic support during the preparation of this review. They also thank all researchers whose published work contributed to the understanding of endocrine disruptors and pubertal development.

CONTRIBUTION OF AUTHORS

Research concept- Malik Tauseef, Shaikh Aquib, Arbaaz Khan, Shakib Shahab, Tahzeeb Fatima, Ansari Rehan, Waqas Alauddin

Research design- Malik Tauseef, Shaikh Aquib, Arbaaz Khan, Shakib Shahab, Tahzeeb Fatima, Ansari Rehan, Waqas Alauddin

Supervision- Malik Tauseef, Shaikh Aquib, Arbaaz Khan, Shakib Shahab, Tahzeeb Fatima, Ansari Rehan, Waqas Alauddin

Materials- Malik Tauseef, Shaikh Aquib, Arbaaz Khan, Shakib Shahab, Tahzeeb Fatima, Ansari Rehan, Waqas Alauddin

Data collection- Malik Tauseef, Shaikh Aquib, Arbaaz Khan, Shakib Shahab, Tahzeeb Fatima, Ansari Rehan, Waqas Alauddin

Data analysis and interpretation- Malik Tauseef, Shaikh Aquib, Arbaaz Khan, Shakib Shahab, Tahzeeb Fatima, Ansari Rehan, Waqas Alauddin

Literature search- Malik Tauseef, Shaikh Aquib, Arbaaz Khan, Shakib Shahab, Tahzeeb Fatima, Ansari Rehan, Waqas Alauddin

Writing article- Malik Tauseef, Shaikh Aquib, Arbaaz Khan, Shakib Shahab, Tahzeeb Fatima, Ansari Rehan, Waqas Alauddin

Critical review- Malik Tauseef, Shaikh Aquib, Arbaaz Khan, Shakib Shahab, Tahzeeb Fatima, Ansari Rehan, Waqas Alauddin

Article editing- Malik Tauseef, Shaikh Aquib, Arbaaz Khan, Shakib Shahab, Tahzeeb Fatima, Ansari Rehan, Waqas Alauddin

Final approval- Malik Tauseef, Shaikh Aquib, Arbaaz Khan, Shakib Shahab, Tahzeeb Fatima, Ansari Rehan, Waqas Alauddin

doi: 10.21276/SSR-IIJLS.2026.12.4.43

REFERENCES

[1] Lucaccioni L, Trevisani V, Marrozzini L, Bertoncelli N, Predieri B, et al. Endocrine-disrupting chemicals and their effects during female puberty: A review of current evidence. Int J Mol Sci., 2020; 21(6): 2078. doi: 10.3390/ijms21062078.

[2] Greenspan LC, Lee MM. Endocrine disrupters and pubertal timing. Curr Opin Endocrinol Diabetes Obes., 2018; 25(1): 49–54. doi: 10.1097/MED.0000000000000377.

[3] Uldbjerg CS, Koch T, Lim YH, Gregersen LS, Olesen CS, et al. Prenatal and postnatal exposures to endocrine-disrupting chemicals and timing of pubertal onset in girls and boys: A systematic review and meta-analysis. Hum Reprod Update, 2022; 28(5): 687–716. doi: 10.1093/humupd/dmac013.

[4] Lu X, Xie T, van Faassen M, Kema IP, van Beek AP, et al. Effects of endocrine-disrupting chemicals and their interactions with genetic risk scores on cardiometabolic traits. Sci Total Environ., 2024; 914: 169972. doi: 10.1016/j.scitotenv.2024.169972.

[5] Spaziani M, Tarantino C, Tahani N, Gianfrilli D, Sbardella E, et al. Hypothalamo-pituitary axis and puberty. Mol Cell Endocrinol., 2021; 520: 111094. doi: 10.1016/j.mce.2020.111094.

[6] Franssen D, Svingen T, Lopez Rodriguez D, Van Duursen M, Boberg J, et al. A putative adverse outcome pathway network for disrupted female pubertal onset to improve testing and regulation of endocrine-disrupting chemicals. Neuroendocrinol., 2022; 112(2): 101–14. doi: 10.1159/000515478.

[7] Rivera-Núñez Z, Kinkade CW, Zhang Y, Rockson A, Bandera EV, et al. Phenols, parabens, phthalates and puberty: A systematic review of synthetic chemicals commonly found in personal care products and girls' pubertal development. Curr Environ Health Rep., 2022; 9(4): 517–34. doi: 10.1007/s40572-022-00366-4.

[8] Walker C, Garza S, Papadopoulos V, Culty M. Impact of endocrine-disrupting chemicals on steroidogenesis and consequences on testicular function. Mol Cell Endocrinol., 2021; 527: 111215. doi: 10.1016/j.mce.2021.111215.

[9] Su PH, Huang JY, Wang SJ, Chang HP. Phthalates exposure and pubertal development in a 15-year follow-up birth cohort study in Taiwan. Front Endocrinol (Lausanne), 2023; 14: 1065918. doi: 10.3389/fendo.2023.1065918.

[10] Predieri B, Iughetti L, Bernasconi S, Street ME. Endocrine-disrupting chemicals' effects in children: What we know and what we need to learn? Int J Mol Sci., 2022; 23(19): 11899. doi: 10.3390/ijms231911899.

[11] Di Pietro G, Forcucci F, Chiarelli F. Endocrine disruptor chemicals and children's health. Int J Mol Sci., 2023; 24(3): 2671. doi: 10.3390/ijms24032671.

[12] Taylor KW, Joubert BR, Braun JM, Dilworth C, Gennings C, et al. Statistical approaches for assessing health effects of environmental chemical mixtures in epidemiology: Lessons from an innovative workshop. Environ Health Perspect., 2016; 124(12): A227–A29. doi: 10.1289/EHP547.