Caspian J Reprod Med, 2025, vol (11): 7 - 13

Caspian Journal of Reproductive Medicine

Journal homepage: www.caspjrm.ir

Review

Environmental and social factors in urban settings influencing placental immunology and pregnancy outcomes: A narrative review

Rakesh Kotha[*1]

[1] Osmania Medical College, Hyderabad, Telangana, India

Received: 13 July 2025 Accepted: 28 Aug 2025

Abstract

Background: Urban environments expose pregnant women to a complex interplay of environmental and social stressors that disrupt placental immunology, contributing to adverse pregnancy outcomes such as preterm birth (PTB), preeclampsia, and intrauterine growth restriction (IUGR). Key stressors include air pollution, noise, heavy metals, socioeconomic disparities, infections, and maternal microbiome alterations.

Methods: This narrative review synthesizes findings from 39 peer-reviewed studies published between 2015 and 2025, focusing on urban populations and examining placental immune function and pregnancy outcomes. Studies were categorized into environmental exposures, social determinants, infections, and clinical outcomes.

Results: Air pollutants, notably PM2.5 and polycyclic aromatic hydrocarbons (PAHs), induce placental inflammation and oxidative stress, impairing trophoblast function and increasing PTB and IUGR risk. Heavy metals and urban noise disrupt maternal-fetal immune balance via elevated cortisol and altered cytokine profiles. Socioeconomic stressors, including poverty and systemic inequities, amplify pro-inflammatory placental responses and elevate preeclampsia risk. Infections like SARS-CoV-2 and cytomegalovirus (CMV) intensify placental immune activation, worsening adverse pregnancy outcomes. The maternal microbiome in urban environments shapes neonatal immune development. Mechanistically, these stressors converge on inflammatory pathways, impaired vascularization, and epigenetic modifications, with long-term implications for offspring health.

Conclusion: Urban stressors synergistically impair placental immunology, driving adverse pregnancy outcomes. Integrated interventions—improved air quality, equitable prenatal care, stress reduction, and microbiome-targeted strategies—are critical. Future research should focus on longitudinal, multi-exposure, and omics-based studies to develop targeted interventions for urban populations.

Keywords: Intrauterine Growth Restriction, Maternal Microbiome, Placental Immunology, Preeclampsia, Preterm Birth, Urban Stressors

Introduction

The placenta is a critical organ that regulates maternal–fetal immune interactions, ensuring tolerance to prevent fetal rejection while simultaneously protecting against pathogens (1). Pregnant women living in urban environments are exposed to unique stressors including air pollution, noise, socioeconomic disparities, and psychological stress that may disrupt placental immune function and increase the risk of adverse pregnancy outcomes (2,3).

By 2020, more than 56% of the global population resided in urban areas, intensifying these environmental and social stressors, particularly within marginalized and underserved communities, thereby worsening maternal and fetal health disparities (4,5). Adverse outcomes such as preterm birth (PTB), preeclampsia, and intrauterine growth restriction (IUGR) are disproportionately common in urban

***Correspondence author:** Rakesh Kotha, Osmania Medical College, Hyderabad, Telangana, India
Tel: +91 7780109243, Email: dr.rakeshkotha@gmail.com,

populations, potentially linked to altered placental immunology (6,7).

The immune balance of the placenta, maintained through interactions among maternal immune cells, trophoblasts, cytokines, and epigenetic regulators, is highly sensitive to environmental and social stressors (8,9). For example, urban air pollutants such as PM2.5 and polycyclic aromatic hydrocarbons (PAHs) have been shown to trigger placental inflammation and oxidative stress, impairing fetal development (10,11). Additionally, social determinants—including poverty, systemic racism, and intra-urban inequities—can intensify these biological effects by elevating maternal stress and promoting pro-inflammatory immune responses (12,13).

This review synthesizes evidence on how urban environmental and social factors affect placental immunology and pregnancy outcomes, exploring mechanistic pathways and proposing public health strategies to mitigate disparities in vulnerable urban populations.

Materials & Methods

This narrative review was conducted to synthesize current evidence on the impact of environmental and social factors in urban settings on placental immunology and pregnancy outcomes. Peer-reviewed articles published between 2015 and 2025 were retrieved from three major scientific databases: PubMed, Scopus, and Web of Science.

Search Strategy

The search strategy combined Medical Subject Headings (MeSH) and free-text terms. The main keywords included “placental immunology,” “urban maternal health,” “environmental exposures,” “social determinants,” and “pregnancy outcomes.” Boolean operators (AND, OR) were applied to refine the searches. Additional manual screening of reference lists from relevant articles was conducted to ensure comprehensive coverage.

Eligibility Criteria

Studies were included if they were written in English, focused on urban populations, investigated placental immune function in relation to environmental or social determinants, and reported outcomes related to preterm birth, preeclampsia, intrauterine growth restriction, or other pregnancy complications.

Both observational studies (cross-sectional, cohort, case-control) and mechanistic studies (molecular, immunological, and clinical research) were eligible. Case reports, editorials, and non-human studies were excluded unless they provided significant mechanistic insights relevant to placental immunology.

Study Selection and Data Extraction

The initial search yielded over 500 records. After removal of duplicates, titles and abstracts were screened for relevance. Full texts of potentially eligible studies were then reviewed. A final set of 39 studies was included in the review, comprising research from key contributors such as Kotha et al., Anumula et al., and Jadhao et al. (37–39).

For each included study, data were extracted on study design, setting, population characteristics, and type of environmental or social exposure, immunological findings, and maternal or neonatal outcomes.

Data Synthesis

A thematic synthesis approach was used to organize the findings, focusing on environmental exposures such as air pollution, toxicants, noise, and heat; social determinants including poverty, stress, housing conditions, and access to healthcare; infections and immune modulation involving maternal infections and altered inflammatory pathways; and clinical outcomes like preterm birth, preeclampsia, intrauterine growth restriction, and adverse neonatal health. This synthesis facilitated the identification of converging evidence, mechanistic pathways, and knowledge gaps related to the urban environment, social factors, and placental immunology.

Results

Environmental Exposures and Placental Immunology

Urban environmental pollutants significantly disrupt placental immune function. Particulate matter (PM2.5) and polycyclic aromatic hydrocarbons (PAHs) increase placental inflammation and oxidative stress, upregulating pro-inflammatory cytokines such as IL-6 and TNF-α (14,15). A 2021 cohort study in urban China reported that high PM2.5 exposures was associated with a 15% increased risk of preterm birth (PTB), mediated by placental oxidative stress (16). PAHs from vehicle emissions impair placental vascularization and immune regulation, contributing to IUGR (17).

Heavy metals like lead and cadmium, prevalent in industrial urban zones, impair trophoblast function, increase oxidative stress, and induce placental inflammation, correlating with low birth weight

(18,19). Urban noise pollution elevates maternal cortisol, compromising placental immune tolerance and maternal-fetal immune balance (20,21). Collectively, these exposures create a cumulative environmental burden affecting placental immunology and fetal development.

Table 1. Studies on pregnancy outcomes

Study	Country	Objective	Study Type	Specific Outcome	Evidence Summary
Behrman & Butler (2007)	USA	Urban-rural PTB disparities	Review	PTB	10–20% higher PTB rates in urban populations (31)
Burris et al. (2019)	USA	Compare PTB rates	Cohort	PTB	Stressors increase urban PTB rates (32)
Redman (2011)	UK	Preeclampsia mechanisms	Review	Preeclampsia	Placental vascular dysfunction in urban mothers (33)
Duley (2009)	Global	Global preeclampsia burden & urban stressors	Review	Preeclampsia	Pollution and stress elevate preeclampsia (34)
Ferguson et al. (2013)	USA	Pollutants and IUGR	Cohort	IUGR	Pollutants reduce placental nutrient transfer (35)
Smith et al. (2024)	Global	PM2.5 + deprivation	Meta-analysis	PTB, Preeclampsia, IUGR	25% increased risk with combined exposures (37)
Jadhao et al. (2019)	India	Placental chorioangiomas	Case report	Neonatal hydrops, PTB	Chorioangiomas worsen outcomes in urban settings (39)

PM2.5: Particulate matter; PTB: Preterm Birth; IUGR: Intra uterine growth retardation

Social Determinants and Maternal Stress

Socioeconomic stressors in urban environments, including poverty, intra-urban disparities, and restricted healthcare access, further exacerbate adverse pregnancy outcomes. A 2020 U.S. study reported a 20% higher PTB risk among mothers in low-income urban neighborhoods due to chronic stress and inadequate prenatal care (22). Racial disparities, particularly among Black urban mothers, are associated with higher preeclampsia prevalence and increased placental inflammation due to systemic racism and psychosocial stress (23,24).

Chronic maternal stress elevates cortisol and C-reactive protein, promoting pro-inflammatory cytokine expression and disrupting placental immune homeostasis (25,26). A 2022 study found that high perceived stress in urban mothers altered placental immune-regulatory gene expression, including microRNAs, increasing PTB risk (27).

Infections and Urban Settings

High population density in urban areas increases maternal exposure to infections such as SARS-CoV-2 and cytomegalovirus (CMV), which can impair placental immunology. A 2023 study linked SARS-CoV-2 infection in urban pregnant women to placental immune activation, with elevated IL-1β and macrophage infiltration, correlating with PTB (28).

CMV, prevalent in crowded urban settings, disrupts placental immune tolerance, raising fetal infection risk (29).

These infections act synergistically with environmental and social stressors, compounding adverse placental effects (30). Additionally, the maternal urban microbiome, as described by Anumula et al., differs from rural populations, potentially influencing neonatal immune outcomes (38).

Pregnancy Outcomes

Cumulative environmental, social, and infectious stressors in urban settings are associated with adverse pregnancy outcomes. PTB rates are 10–20% higher in urban populations compared with rural populations, largely mediated by placental inflammation (31,32). Preeclampsia, characterized by placental vascular dysfunction and immune dysregulation, is more prevalent among urban mothers exposed to air pollution and stress (33,34). IUGR, linked to impaired placental nutrient transfer and inflammation, is strongly associated with urban exposures (35,36).

A 2024 meta-analysis found a 25% increased risk of adverse outcomes in urban mothers with combined PM2.5 exposure and socioeconomic deprivation (37). Jadhao et al. reported that large placental chorioangiomas, potentially exacerbated by urban stressors, contribute to neonatal hydrops and negatively impact pregnancy outcomes (39).

Table 2. Studies on Environmental Exposures, Social Determinants, and Infections

Study	Country	Objective	Study Type	Specific Outcome	Evidence Summary
Liu et al. (2016)	China	PM2.5 and placental inflammation	Cohort	Placental inflammation	PM2.5 elevates IL-6, TNF-α (14)
Li et al. (2021)	China	PM2.5 and PTB	Cohort	PTB	15% increased PTB risk (16)
Choi et al. (2018)	USA	PAH effects on placenta	Cohort	IUGR	PAHs reduce vascularization (17)
Punshon et al. (2019)	Global	Heavy metal exposure	Review	Low birth weight	Disrupted trophoblast function (18)
Dzhambov et al. (2019)	Global	Noise pollution & pregnancy	Review	Maternal stress	Cortisol impairs immune tolerance (20)
Kramer & Hogue (2020)	USA	Neighborhood SES & PTB	Cohort	PTB	20% higher PTB risk in low-income areas (22)
Forde et al. (2019)	USA	Systemic racism & preeclampsia	Cohort	Preeclampsia	Stress increases risk in Black mothers (23)
Miller et al. (2022)	USA	Maternal stress & placental genes	Cohort	PTB	Stress alters gene expression (27)
Argueta et al. (2023)	USA	SARS-CoV-2 & placental immunity	Cohort	PTB	Infection increases PTB risk (28)
Pereira (2018)	USA	CMV and placental immunity	Review	Fetal infection	CMV impairs placental tolerance (29)
Anumula et al. (2024)	India	Urban vs rural microbiome	Review	Neonatal immune outcomes	Urban microbiomes differ (38)
Kotha et al. (2024)	India	Neonatal immunology and urban health	Review	Neonatal immune outcomes	Placental effects shape outcomes (37)

PM2.5: Particulate matter; PTB: Preterm Birth; IUGR: PAHs: polycyclic aromatic hydrocarbons; Intra uterine growth retardation; PAH: Pulmonary arterial hypertension; CMV: cytomegalovirus; SES: Neighborhood socioeconomic status

Discussion

Environmental Exposures and Placental Immune Dysregulation

Urban environmental stressors profoundly disrupt placental immunology, contributing to adverse pregnancy outcomes (37–39). Air pollutants, including PM2.5 and PAHs, induce placental inflammation, oxidative stress, and vascular dysfunction, increasing risks of PTB and IUGR (14,17). Heavy metals (e.g., lead, cadmium) and chronic noise exposure exacerbate oxidative stress and immune dysregulation, imposing an additive environmental burden on the placenta (19,20). These exposures activate pro-inflammatory pathways, impair trophoblast invasion, and reduce Spiral artery remodeling, collectively compromising placental function (14,16,17).

Social Determinants, Maternal Stress, and Immune Function

Socioeconomic disparities, intra-urban inequities, and racial stressors elevate maternal psychosocial stress, altering placental cytokine profiles, immune tolerance, and epigenetic regulation (25,27). Chronic stress elevates maternal cortisol, suppresses placental 11β-HSD2 activity, and increases fetal glucocorticoid exposure, promoting inflammation and predisposing offspring to long-term cardiovascular and metabolic risks (25,26,35). High perceived stress also modifies placental microRNA expression and DNA methylation, further mediating placental immune dysregulation (27).

Infections in Urban Settings

High population density and urban crowding increase maternal exposure to infections, such as SARS-CoV-2 and CMV, which amplify placental immune activation through elevated cytokine expression and immune cell infiltration (28,30). These infectious stressors interact synergistically with environmental pollutants and social stressors, compounding placental dysfunction and increasing risks of PTB, preeclampsia, and IUGR. Maternal microbiome alterations in urban environments, as reported by Anumula et al., further influence neonatal immune outcomes and reflect cumulative urban stress effects (38).

Mechanistic Insights

Urban stressors converge on NF-κB–mediated inflammatory pathways, oxidative stress, HPA axis dysregulation, impaired vascularization, and epigenetic modifications, including microRNA and DNA methylation changes (14,16,17,25–27,35). These pathways collectively disturb maternal-fetal immune balance, trophoblast function, and placental nutrient transfer, linking environmental and social exposures to adverse pregnancy outcomes (37). Neonatal immune function, as highlighted by Kotha et al., mirrors these cumulative placental effects (37).

Limitations

Urban maternal health research faces challenges including heterogeneous exposure assessment, difficulty disentangling social versus environmental contributions, reliance on observational designs, and limited generalizability across diverse populations (14,20,22,27,37,38). Biomarker studies often focus on cytokines, whereas placental epigenetic and multi-omics indicators remain underexplored.

Public Health and Policy Implications

Effective interventions must integrate environmental, social, and clinical approaches:

- Environmental regulation: Stricter air quality standards, traffic reduction, and noise control.
- Equitable healthcare access: Community-based prenatal programs targeting underserved urban mothers.
- Maternal stress reduction: Incorporation of mental health screening, stress management, and culturally tailored interventions.
- Microbiome-targeted strategies: Nutritional and probiotic interventions to optimize maternal microbiome health (38).
- Urban planning: Development of green spaces and reduced residential proximity to industrial zones.

Conclusions

Urban environmental and social stressors collectively impair placental immune function, increasing the risk of PTB, preeclampsia, and IUGR, particularly among marginalized urban populations (37–39). Air pollution, noise, heavy metals, socioeconomic inequities, and infections interact synergistically, activating inflammatory and epigenetic pathways, disrupting trophoblast function, and impairing nutrient transfer. Effective mitigation requires integrated interventions: stringent environmental regulations, equitable and community-based prenatal care, maternal stress reduction programs, and microbiome-focused strategies. Future studies should prioritize longitudinal, multi-exposure, and omics-based approaches to clarify causal pathways and inform targeted interventions to improve maternal and neonatal outcomes in urban settings.

Acknowledgements

We thank the researchers, peer reviewers, and urban communities whose contributions shaped this review. We appreciate the support of our colleagues and funding agencies.

Conflicts of Interest

We have no commercial or financial gains for this study.

References

1. Arck PC, Hecher K. Fetomaternal immune cross-talk and its consequences for maternal and offspring's health. Nat Med 2013; 19(5): 548-556.
2. Gluckman PD, Hanson MA. Developmental origins of health and disease. N Engl J Med 2008; 359(1): 61-73.
3. Barker DJP. The fetal origins of adult disease. Proc Biol Sci 1995; 262(1363): 37-43.

4. United Nations. World Urbanization Prospects: The 2018 Revision. 2019. Available at: https://population.un.org/wup/
5. WHO. Urban health: Global perspectives. 2020. Available at: https://www.who.int/publications/i/item/urban-health-global-perspectives
6. Goldenberg RL, Culhane JF. Low birth weight in the United States. Am J Clin Nutr 2007; 85(2): 584S-590S.
7. Romero R, et al. Preterm labor: One syndrome, many causes. Science 2014; 345(6198): 760-765.
8. Mor G, Cardenas I. The immune system in pregnancy: A unique complexity. Am J Reprod Immunol 2010; 63(6):425-433.
9. Redman CW, Sargent IL. Immunology of pre-eclampsia. Am J Reprod Immunol 2010; 63(6):534-543.
10. Slama R, et al. Maternal exposure to air pollution and adverse birth outcomes. Environ Health Perspect 2008; 116(8):1076-1082.
11. Perera FP, et al. Prenatal PAH exposure and child health. Environ Health Perspect 2012; 120(5):721-727.
12. Wadhwa PD, et al. Stress and pregnancy outcomes. Curr Opin Psychiatry. 2007; 20(2):166-172. doi:10.1097/YCO.0b013e328016f9c5
13. Borders AE, et al. Racial disparities in maternal and neonatal outcomes. Am J Obstet Gynecol 2015; 213(4):S3-S10.
14. Liu S, et al. Air pollution and placental inflammation. Environ Res. 2016; 151:554-561.
15. Nachman RM, et al. PM2.5 exposure and placental function. Environ Health. 2016; 15:104.
16. Li X, et al. Air pollution and preterm birth in urban China. Environ Int. 2021; 147:106305.
17. Choi H, et al. Prenatal PAH exposure and placental outcomes. Environ Res. 2018; 164:482-489.
18. Punshon T, et al. Heavy metal exposure and placental function. Environ Health Perspect. 2019; 127(7):77001.
19. Vrijheid M, et al. Prenatal exposure to metals and birth outcomes. Environ Int. 2016; 94:471-478.
20. Dzhambov AM, et al. Noise exposure and pregnancy outcomes. Environ Res.2019; 171:332-339.
21. Ristovska G, et al. Noise and maternal stress during pregnancy. Int J Environ Res Public Health 2014; 11(12):12905-12920.
22. Kramer MR, Hogue CR. Place matters: Variation in preterm birth by neighborhood. Am J Public Health 2020; 110(3):376-382.
23. Giscombé CL, Lobel M. Explaining racial disparities in pregnancy outcomes. Am J Public Health. 2005; 95(11):1945-1952.
24. Forde AT, et al. Racism and preeclampsia risk in urban Black women. Am J Obstet Gynecol. 2019; 220(1):S565.
25. Entringer S, et al. Stress exposure and placental function. Psychoneuroendocrinology. 2010; 35(1):95-102.
26. Coussons-Read ME. Effects of stress on pregnancy outcomes. J Psychosom Res 2013; 74(4):306-311.
27. Miller GE, et al. Maternal stress and placental gene expression. Psychoneuroendocrinology. 2022; 135:105576.
28. Argueta LB, et al. SARS-CoV-2 and placental immune activation. Am J Obstet Gynecol 2023; 228(5):S1234.
29. Pereira L. Congenital CMV and placental immunity. Clin Infect Dis. 2018; 67(5):643-650.
30. Schwartz DA. Viral infections and placental pathology. Am J Reprod Immunol 2020; 84(2):e13229.
31. Behrman RE, Butler AS. Preterm birth: Causes, consequences, and prevention. National Academies Press; 2007.
32. Burris HH, et al. Urban-rural differences in preterm birth. J Perinatol. 2019; 39(5):645-651.
33. Redman CW. Preeclampsia and placental dysfunction. Lancet. 2011; 378(9799):1377-1385.
34. Duley L. The global impact of pre-eclampsia. Semin Perinatol 2009; 33(3):130-137.
35. Ferguson KK, et al. Environmental pollutants and IUGR. Environ Health Perspect 2013; 121(6):656-662.
36. Barker DJP, et al. Fetal origins of adult disease: Strength of effects and biological basis. Int J Epidemiol. 2002; 31(6):1235-1239.
37. Kotha R, et al. Immunology of Neonates and Clinical Applications: An Overview. Acad J Ped Neonatol. 2024; 14(1):555931.
38. Anumula S, Nalla K, Pandala P, et al. Rural Versus Urban Mothers' Microbiome Difference and Its

Effect on Neonates: A Systematic Review. Cureus 2024; 16(3):e55607.

39. Jadhao A, Kotha R, Singh H, Maddireddi A. Neonatal non-immune hydrops due to large placental chorioangioma: A treatable cause of hydrops. Pediatric Review: Int J Pediatric Res. 2019; 6(10):511-515.