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# Secondhand smoke exposure and its role in the pathogenesis of preeclampsia: a narrative review of molecular and epidemiological perspectives

**Yenny Febriany[1], Irfannuddin[2]*, Mohammad Zulkarnain[3], Yusuf Effendi[4]**

[1]Doctoral Program in Biomedical Science, Faculty of Medicine, Universitas Sriwijaya, Palembang, South Sumatra, Indonesia, [2]Department of Physiology, Faculty of Medicine, Universitas Sriwijaya, Palembang, South Sumatra, Indonesia, [3]Department of Public Health and Community Medicine, Faculty of Medicine, Universitas Sriwijaya, Palembang, South Sumatra, Indonesia, [4]Department of Obstetrics and Gynecology, Faculty of Medicine, Universitas Sriwijaya, Palembang, South Sumatra, Indonesia

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## ABSTRACT

Preeclampsia (PE) is a pregnancy complication characterized by hypertension after 20 weeks of gestation, often accompanied by proteinuria or organ dysfunction. This condition is linked to genetic, environmental factors, and exposure to secondhand smoke (SHS). This review explores the relationship between SHS exposure and PE risk through a narrative literature review. Epidemiological and molecular data demonstrate that SHS exposure increases PE risk via oxidative stress, inflammation, and angiogenic disruptions. The analysis reveals that SHS exposure enhances reactive oxygen species (ROS) production, triggers systemic inflammation through the NF-κB pathway, and impairs angiogenic function by lowering the sFlt-1/PlGF ratio. The risk significantly increases with exposures ≥2 hours / day or frequencies ≥4 days/ week, particularly in poorly ventilated domestic and occupational settings. Biomarkers such as cotinine and carbon monoxide (CO) are employed to assess exposure levels, providing robust evidence that duration and intensity of exposure are pivotal in PE pathogenesis. These findings highlight the importance of preventive strategies, including smoking bans, public health education, and integration of biomarker-based assessments into prenatal care. Future research should aim to clarify the molecular and epigenetic mechanisms involved and explore therapeutic interventions to mitigate SHS-induced damage.

## ABSTRAK

Preeklampsia (PE) adalah komplikasi kehamilan yang ditandai oleh hipertensi setelah usia kehamilan 20 minggu, sering disertai proteinuria atau kerusakan organ. Kondisi ini terkait dengan faktor genetik, lingkungan, dan paparan asap rokok pasif (secondhand smoke/SHS). Tinjauan literatur ini mengeksplorasi hubungan antara paparan SHS dengan risiko PE melalui pendekatan tinjauan literatur naratif. Data dari studi epidemiologis dan molekuler menunjukkan bahwa paparan SHS meningkatkan risiko PE melalui mekanisme stres oksidatif, inflamasi, dan gangguan angiogenik. Analisis menunjukkan bahwa paparan SHS meningkatkan produksi reaktif oksigen spesies (ROS), memicu inflamasi sistemik melalui jalur nuklir NF-κB, dan menghambat fungsi angiogenik melalui penurunan rasio sFlt-1/PlGF. Risiko meningkat secara signifikan pada paparan ≥2 jam/hari atau ≥4 hari/minggu, terutama dalam lingkungan domestik dan kerja dengan ventilasi buruk. Biomarker seperti kotinin dan karbon monoksida digunakan untuk mengukur tingkat paparan, memberikan bukti kuat bahwa durasi dan intensitas paparan memainkan peran penting dalam patogenesis PE. Temuan ini menekankan pentingnya strategi pencegahan, termasuk larangan merokok, edukasi kesehatan masyarakat, dan integrasi penilaian berbasis biomarker ke dalam perawatan prenatal. Penelitian di masa depan sebaiknya difokuskan untuk memperjelas mekanisme molekuler dan epigenetik yang terlibat, serta mengeksplorasi intervensi terapeutik guna mengurangi kerusakan yang disebabkan oleh paparan asap rokok pasif.

***Keywords***:
preeclampsia;
secondhand smoke;
oxidative stress;
markers;
pregnancy

*corresponding author: Irfan.md.unsri@gmail.com

## INTRODUCTION

Preeclampsia (PE) is a significant and multifaceted complication of pregnancy, primarily characterized by hypertension emerging after 20 weeks of gestation, often accompanied by proteinuria or organ dysfunction. It is a multisystem disorder that profoundly affects maternal and fetal health, involving oxidative stress, endothelial dysfunction, and angiogenic imbalance.[1,2] Globally, PE is estimated to affect approximately 4.6% of pregnancies, contributing to up to 14% of maternal mortality, particularly in low- and middle-income countries.[3] According to the 2023 Indonesian Health Survey (SKI), 3.2% of childbirth cases in Indonesia had hypertension, a major risk factor for PE. These statistics highlight the pressing need for early detection and preventive strategies to mitigate its adverse outcomes.[4]

A broad spectrum of risk factors contributes to the development of PE, including pre-existing hypertension, obesity, gestational diabetes mellitus (GDM), advanced maternal age, a history of PE in previous pregnancies, and environmental exposures such as SHS.[5] The consequences of PE are severe and multifaceted, ranging from acute complications such as kidney failure, hemolysis, elevated liver enzymes, and low platelet (HELLP) syndrome, and eclampsia, to long-term health risks, including chronic hypertension and cardiovascular disease. Furthermore, PE-related placental insufficiency can lead to intrauterine growth restriction (IUGR), preterm birth, or neonatal mortality.[3,5] These significant complications underscore the necessity of targeted preventive measures and evidence-based interventions to reduce both maternal and neonatal morbidity and mortality.[6]

Among the various environmental risk factors, exposure to SHS has garnered increasing attention for its potential role in the pathogenesis of PE. Secondhand smoke contains numerous toxicants, including nicotine and CO, which interfere with key biological pathways such as placental angiogenesis and inflammatory responses.[7] These disruptions contribute to vascular complications in pregnant women, ultimately increasing the risk of PE. Epidemiological studies have reported a strong correlation between chronic SHS exposure and the development of PE.[8] A study by Liu *et al.*[2] found that SHS exposure disrupts placental perfusion and impairs spiral artery remodeling, leading to placental hypoxia. Furthermore, Matsumoto *et al.*,[9] reported that SHS exposure impacts the regulation of placental genes, including alterations in the expression of angiogenic genes, which exacerbate placental vascular instability.

Emerging biomarker-based studies have explored the utility of biochemical indicators such as the soluble Fms-like tyrosine kinase-1 (sFlt-1) to placental growth factor (PlGF) ratio to strengthen the link between SHS and PE.[10] These biomarkers have proven effective in predicting PE risk during early pregnancy. However, while advances in biomolecular research offer promising diagnostic tools, mitigating environmental risks, such as reducing SHS exposure, remains a crucial preventive measure.[9] Recent studies, such as Tanaka *et al.*,[1] have indicated a direct relationship between the duration of SHS exposure and an increased risk of gestational hypertension and PE. This evidence supports the need for public health policies, including stricter smoking bans in public areas, to reduce the prevalence of pregnancy complications.[1]

Despite accumulating evidence, the precise molecular mechanisms by which SHS contributes to PE development remain inadequately explored.[11] Therefore, this review aims to provide

a comprehensive narrative review examining the relationship between SHS exposure and PE pathogenesis. The review focuses on molecular pathways such as oxidative stress, inflammation, and angiogenic dysregulation, offering a scientific foundation for developing targeted, evidence-based health policies to protect pregnant women from harmful environmental exposures. The central research question guiding this study is: How does exposure to SHS influence the risk of PE through oxidative stress, inflammatory pathways, and angiogenic disruptions.

## MATERIAL AND METHODS

This study employs a narrative literature review (NLR) approach to synthesize data from various research types, including epidemiological, experimental, and molecular studies, aiming to provide a comprehensive understanding of the relationship between SHS exposure and the risk of PE. This method was chosen to elucidate the pathophysiological mechanisms of PE within the context of environmental exposures, focusing on oxidative stress, inflammation, and angiogenic dysregulation.

### Search strategy

The literature search was conducted systematically using major scientific databases, including PubMed, Scopus, ScienceDirect, and Web of Science. The search employed relevant keywords such as “secondhand smoke (SHS)”, “preeclampsia”, “pregnancy complications”, “oxidative stress”, and “angiogenic imbalance.” Boolean operators (AND, OR, NOT) were applied to refine the search, for instance, “secondhand smoke” AND “preeclampsia” to capture relevant articles. In contrast, the Boolean Operator NOT was used, as in “preeclampsia” NOT “other pregnancy complications”, to exclude irrelevant studies.

### Article selection process

A rigorous screening process was applied to select articles for inclusion. Initially, all retrieved articles underwent a title and abstract review to assess their relevance to the research topic. Eligible articles were then subjected to a full-text review, where methodological quality, relevance, and adherence to the study criteria were evaluated. Two independent reviewers conducted this selection process, and discrepancies were resolved through discussion or consultation with a third reviewer.

### Inclusion and exclusion criteria

The inclusion criteria were strictly defined to ensure the reliability and relevance of the selected studies. Only peer-reviewed articles published between 2014 and 2025, indexed in scopus, and written in English were considered. Studies had to focus on the relationship between SHS exposure and PE, utilizing epidemiological, clinical, or molecular research methodologies. Preference was given to cohort, case-control, and cross-sectional studies with clearly defined methodologies and sample populations.

Studies such as conference abstracts, seminar reports, editorials, or non-peer-reviewed sources were excluded. Additionally, studies that did not specifically investigate SHS exposure with PE or lacked quantifiable exposure assessments were omitted to maintain methodological rigor.

### Risk of bias assessment

Established instruments were used to perform a risk-of-bias evaluation in order to appraise the validity and reliability of the included studies.

Cohort and case control studies were assessed using the Newcastle-Ottawa Scale (NOS), which examines selection bias, comparability, and outcome assessment.[12] For randomized controlled trials (RCTs), the Cochrane Risk of Bias Tool was applied, evaluating domains such as randomization, blinding, and completeness of outcome data. Cross-sectional studies were assessed using the Joanna Briggs Institute (JBI) Critical Appraisal Checklist to determine methodological soundness.[13] Studies with a high risk of bias were critically analyzed, and their limitations were considered in the overall discussion.

### Data extraction and analysis

Key information such as study design, sample size, exposure assessment techniques, primary outcomes, and statistical findings were taken from each chosen article after it was systematically reviewed. The extracted data were categorized based on thematic relevance, such as SHS impact on oxidative stress, inflammation, angiogenic imbalance, and potential interventions. Mendeley Desktop software was used to organize references and ensure consistency in citation formatting.

## RESULTS

### Preeclampsia

New-onset hypertension that appears after 20 weeks of gestation and is frequently accompanied by proteinuria or indications of organ damage, such as renal dysfunction or placental insufficiency, is the hallmark of PE, a dangerous pregnancy complication. This multisystem ailment has a major effect on the health of both the mother and the fetus, especially in underdeveloped nations where access to medical care is scarce.

Epidemiologically, PE is estimated to affect 2-8% of all pregnancies worldwide and is responsible for approximately 10-15% of global maternal mortality. In developing countries like Indonesia, the prevalence of PE is relatively high, with data indicating that it is the second leading cause of maternal death after postpartum hemorrhage. Nationally, PE accounts for up to 20% of total maternal deaths. These figures highlight the considerable challenges faced in early detection, management of high-risk pregnancies, and access to emergency medical care, especially in remote areas.

The pathogenesis of PE involves several complex mechanisms, including oxidative stress, endothelial dysfunction, and angiogenic imbalances. One factor exacerbating these mechanisms is exposure to SHS, which is known to increase the risk of pregnancy complications. Impaired trophoblast invasion of the uterine wall, leading to inadequate remodeling of spiral arteries, is one of the primary mechanisms underlying placental insufficiency. This condition directly affects oxygen and nutrient delivery to the fetus, potentially resulting in IUGR, preterm birth, or even neonatal death.

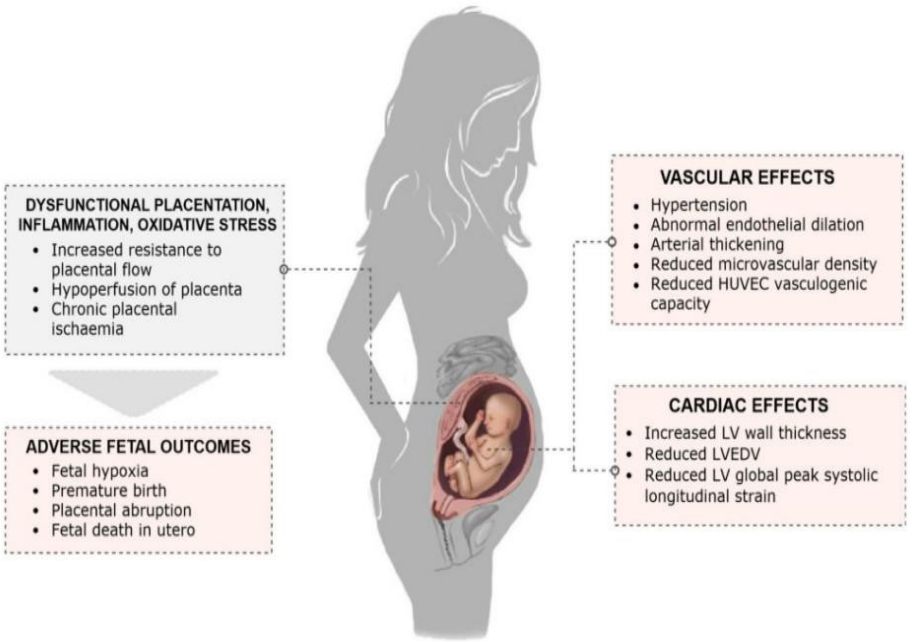


FIGURE 1. Impact of PE on the fetus and its offspring.

FIGURE 1, illustrates the impact of placental disruption in pregnant women, encompassing oxidative stress, inflammation, and placental blood flow dysfunction, which can lead to chronic placental ischemia. This condition increases the risk of complications such as fetal hypoxia, preterm birth, placental abruption, or even intrauterine fetal death. In mothers, this disruption can trigger vascular effects such as hypertension, arterial thickening, and reduced capacity of blood vessels to form new tissues. There are cardiovascular effects, including left ventricular wall thickening, decreased left ventricular end-diastolic volume (LVEDV), and impaired cardiac contractile function. These findings highlight the complex and interrelated health impacts on both mother and fetus due to placental disruption.[14]

Preeclampsia can be categorized according to the severity and timing of onset. Early-onset PE occurs before 34 weeks of gestation and is often associated with severe placental insufficiency and significant maternal complications. In contrast, late-onset PE develops after 34 weeks of gestation, typically triggered by maternal factors such as obesity or chronic hypertension. Based on severity, PE can also be categorized into mild PE, characterized by moderate hypertension and minimal proteinuria, and severe PE, which involves extremely high blood pressure and systemic organ damage such as acute kidney failure or pulmonary edema.[15]

The uniqueness of PE as a pregnancy complication lies in its long-term impact on the health of both mother and baby. Women with a history of PE have twice the risk of developing chronic hypertension, cardiovascular disease, and kidney failure.[16] On the other hand, babies born from pregnancies affected by PE often face risks of preterm birth, neurological developmental disorders, and future metabolic diseases.[17]

Raising public awareness and implementing evidence - based

interventions are crucial to reducing the prevalence of PE. One important approach is the utilization of biomarkers, such as the sFlt-1/PlGF ratio, which can predict PE risk early, enabling timely interventions to prevent further complications. The challenges in managing PE can be significantly minimized through comprehensive strategies, including policies to reduce exposure to SHS and improved access to healthcare services.

## Cigarette Smoke Composition and Health Risks

Cigarettes are one of the significant risk factors that have a detrimental impact not only on active smokers but also on individuals exposed to its smoke passively (SHS). Secondhand smoke, often referred to as passive cigarette smoke, consists of a combination of mainstream smoke (the smoke directly inhaled by the smoker) and side stream smoke (the smoke released from the burning end of a cigarette). Additionally, there is third-hand smoke (THS), which refers to the chemical residue from cigarette smoke that clings to surfaces such as walls, clothing, or furniture. This residue can persist for a long time and pose toxic effects.[18]

The composition of cigarette smoke contains more than 7,000 harmful chemical compounds, with at least 250 of them known to be toxic, including nicotine, CO, tar, and formaldehyde. Nicotine is the primary component with addictive properties that affects the cardiovascular system by increasing blood pressure and constricting blood vessels. On the other hand, CO has a high affinity for hemoglobin, displacing oxygen in the blood and causing significant tissue hypoxia. Tar, a solid residue containing carcinogenic compounds such as polycyclic aromatic hydrocarbons (PAHs), contributes to DNA damage and systemic inflammation. Formaldehyde, another reactive compound, exacerbates oxidative stress, damaging the structure of DNA, proteins, and cell membranes.[19]

Exposure to these toxic components worsens pregnancy conditions by disrupting blood flow to the placenta, increasing oxidative stress, and triggering chronic inflammation. Research shows that SHS can cause placental insufficiency, leading to fetal hypoxia, preterm birth, and IUGR. Chronic exposure to cigarette smoke also directly affects the remodeling of placental spiral arteries, which is a key pathway in the pathogenesis of preeclampsia.

The frequency and duration of exposure to cigarette smoke are crucial factors in determining risk levels. Exposure for ≥2 hours/day or more than 4 days/week significantly increases biomarkers such as cotinine (a nicotine metabolite) and CO in the maternal body. Elevated cotinine levels are associated with an increased risk of gestational hypertension and early-onset preeclampsia.[20]

In addition to maternal risks, exposure to cigarette smoke also has long-term impacts on fetal health. The chemical compounds in cigarette smoke can alter gene expression through epigenetic mechanisms, such as changes in microRNA (miRNA) regulation, which are implicated in developmental disorders of metabolic and cardiovascular systems in offspring.

## SHS exposure and preeclampsia risk

Exposure to passive cigarette smoke, or SHS, has a significant impact on the risk of developing PE, a complex pregnancy complication with serious consequences for both mother and fetus. Studies have shown that SHS affects molecular mechanisms such as inflammation, placental hypoxia, oxidative stress, and vascular dysfunction, all of which

contribute to the progression of PE. This research highlights a strong correlation between the duration, intensity, and frequency of SHS exposure and an increased risk of PE, particularly in household and workplace settings with poor ventilation.[21]

Consistent findings from epidemiological studies confirm the link between SHS exposure and PE. A study by Tanaka *et al.*,[1] revealed that SHS exposure for more than 2 hours/day increases the relative risk of gestational hypertension, including PE, by 1.27 (95%CI: 0.96–1.67). This risk is significantly elevated with chronic exposure, commonly occurring in households or workplaces. Additionally, the study noted that SHS contributes to a fraction attributable risk of 3.8%, emphasizing the significant impact of environmental factors on maternal health.

The study by Huda *et al.*,[22] supports these findings, noting that exposure to SHS for more than 6 months increases the risk of PE by up to 1.75 times compared to women with no exposure. This research emphasizes the significance of exposure duration in raising the risk of pregnancy complications, particularly in developing countries with high domestic smoking prevalence. The primary source of this exposure is smoking by partners or family members, as reported by Tasnim *et al.*,[23] where 77.5% of women with PE had partners who were active smokers.

Furthermore, Noor *et al.*,[24] found that women living with smoking partners had a higher risk of developing gestational hypertension, which often progresses to late-onset PE. This study underscores the importance of controlling smoking habits within households as a preventive measure.

The association between SHS and PE is supported by the majority of the evidence, but some research produces inconsistent findings. Sari *et al.*,[25] reported that in certain populations, SHS exposure was not significantly associated with gestational hypertension, likely due to shorter exposure duration or differences in methodology. However, not all studies unequivocally support this association. Lewandowska *et al.*,[26] presented findings that challenge the prevailing consensus, suggesting that nicotine exposure during the first trimester might have paradoxical vasodilatory effects on the placenta, potentially reducing the risk of PE. This observation highlights the complexity of nicotine's physiological impact, which may vary depending on the timing, duration, and intensity of exposure. Nevertheless, the same study emphasized that this potential protective effect does not extend to other pregnancy complications, such as IUGR and preterm birth. These contradictory findings underscore the necessity of further investigation to elucidate the nuanced effects of SHS on maternal and fetal health.

Biomarker measurements such as cotinine and CO provide objective evidence of SHS exposure levels. Munawaroh *et al.*,[27] reported that high cotinine levels in the blood of pregnant women correlate with an increased risk of gestational hypertension and early-onset PE. These biomarkers are more reliable compared to survey methods based on personal reporting, which are often biased or inaccurate. Furthermore, PAHs in SHS are known to trigger oxidative stress and systemic inflammation, increasing placental vascular resistance, as reported by Kannan *et al.*[28]

The results show that the duration and intensity of SHS exposure directly affect the risk of PE. The risk increases with exposure of ≥2 hours/day and ≥4 days/week, with an even more significant impact observed. Policy-based interventions, such as smoking bans in public spaces and public education, are necessary to reduce the prevalence of pregnancy complications.

The integration of biomarkers in early detection enables earlier intervention, which could potentially reduce the risk of PE significantly.

**Biomolecular mechanisms**

Exposure to passive smoke (SHS) during pregnancy triggers a series of biomolecular mechanisms involved in the pathogenesis of PE. These mechanisms include oxidative stress, chronic inflammation, angiogenic disturbances, and epigenetic effects, which directly impact placental function and maternal and fetal health.[29] Oxidative stress, as a key component, occurs due to exposure to more than 7,000 chemical compounds in cigarette smoke, which stimulate the production of ROS. The accumulation of ROS exceeds the body's antioxidant capacity, such as superoxide dismutase (SOD) and glutathione peroxidase (GPx), creating a pro-oxidant environment. This effect leads to lipid peroxidation, generating malondialdehyde (MDA), DNA damage in the placenta, and endothelial nitric oxide synthase (eNOS) dysfunction. Such damage reduces the bioavailability of nitric oxide (NO), which plays an essential role in blood vessel relaxation, leading to vasoconstriction, increased vascular resistance, and maternal hypertension.[30] Furthermore, oxidative stress activates the NF-κB inflammatory pathway, enhancing the release of pro-inflammatory cytokines like tumor necrosis factor-alpha (TNF-α) and interleukin-6 (IL-6), exacerbating vascular dysfunction.

Chronic inflammation is also an important pathophysiological pathway in PE. Compounds in cigarette smoke, such as nicotine and PAHs, trigger the release of pro-inflammatory cytokines and activate molecular pathways that damage the vascular endothelium. The activation of the NF-κB pathway enhances systemic inflammation, disrupts spiral artery remodeling, and impairs trophoblast invasion necessary for placental blood flow.[31] Furthermore, exposure to SHS disrupts the angiogenic balance by increasing levels of sFlt-1 and decreasing placental growth factor (PlGF), two key biomarkers that indicate placental dysfunction. This imbalance inhibits normal angiogenesis and affects placental perfusion, ultimately leading to placental insufficiency and gestational hypertension.

Epigenetic effects have also been found as a consequence of SHS exposure during pregnancy. Changes in miRNA expression and DNA methylation patterns due to tobacco smoke toxins not only affect the placenta but also have long-term effects on the fetus. These changes increase the risk of metabolic diseases and pregnancy complications in subsequent generations. The combination of oxidative stress, chronic inflammation, angiogenic disturbances, and these epigenetic effects forms a complex biomolecular pathway that exacerbates the risk of PE. Therefore, a deep understanding of these mechanisms is crucial for prevention strategies, such as reducing tobacco smoke exposure during pregnancy, to improve maternal and neonatal health.[32]

**Potential additional mechanisms**

Exposure to passive smoke (SHS) during pregnancy not only triggers oxidative stress and chronic inflammation but also opens the possibility of additional biomolecular mechanisms contributing to the pathogenesis of PE. Recent studies show that chemical components in SHS can affect epigenetic pathways, placenta exosomes, and mitochondrial dysfunction, all of which have direct impacts on maternal health and fetal development.[8]

Toxic compounds in SHS, such as PAHs and nicotine, are known to affect gene expression through epigenetic mechanisms. Research by Matsumoto *et*

*al.*[9] found that chronic exposure to SHS can cause dysregulation of miRNA in placental tissue, particularly miRNAs that regulate angiogenesis and trophoblast function. This dysregulation impairs trophoblast invasion into the spiral arteries, which is one of the main factors contributing to placental insufficiency. These findings suggest that epigenetic modifications may be a potential target for therapeutic intervention in pregnant women exposed to SHS.

Placental exosomes play a crucial role in cellular communication between trophoblasts and maternal endothelial cells. Exposure to SHS alters the molecular composition of exosomes, including inflammatory proteins and pro-oxidant molecules, which subsequently trigger vascular dysfunction. The study by Kubo *et al.*[33] demonstrated that exosomes from trophoblasts exposed to SHS carry inflammatory mediators such as TNF-α, which exacerbate placental vascular resistance. This dysfunction also impacts fetal growth, increasing the risk of IUGR.

Toxic components such as CO and formaldehyde in SHS are known to damage mitochondrial function in the placenta and maternal tissues. Research shows that SHS exposure increases the production of ROS in mitochondria, which damages the electron transport chain and reduces energy production. This disruption exacerbates placental hypoxia and interferes with nutrient transfer from mother to fetus. Animal models by Bakrania *et al.*,[34] support these findings, showing increased apoptosis due to mitochondrial stress in the placenta of rats exposed to cigarette smoke.

The exposure to SHS increases the expression of anti-angiogenic factors such as sFlt-1 (soluble Fms-like tyrosine kinase-1) and decreases the levels of PlGF (placental growth factor). This imbalance worsens endothelial dysfunction and maternal hypertension, two key features of PE. Liu *et al.*,[2] highlighted that changes in the angiogenic pathway are more significant in women exposed to SHS with high duration and dose.

Secondhand smoke exposure also affects the maternal immune system. The decline in regulatory T cell (Tregs) function induced by toxic components in SHS enhances systemic inflammatory responses. This condition exacerbates the pre-existing pro-inflammatory environment caused by PE, creating a pathological cycle that reinforces itself.

A more balanced interpretation of these conflicting results is essential for a comprehensive understanding of SHS-related risks in pregnancy. While most evidence supports the detrimental effects of SHS on PE development, variations in study design, population demographics, and exposure assessment methods may contribute to discrepancies in findings. Future research should focus on refining exposure quantification and exploring genetic or environmental factors that might mediate individual susceptibility to SHS-related pregnancy complications. Addressing these gaps will enhance the reliability of public health recommendations and reinforce the need for stringent anti-smoking policies to protect maternal and fetal well-being.

## CONCLUSION

The findings of this review establish a strong association between secondhand smoke (SHS) exposure and an increased risk of preeclampsia (PE), driven by key molecular mechanisms including oxidative stress, activation of the NF-κB inflammatory pathway, and angiogenic imbalance marked by a reduced sFlt-1/PlGF ratio. SHS exposure intensifies the production of reactive oxygen species (ROS) and disrupts vascular homeostasis, especially with prolonged exposure exceeding two hours per day or four days per week, particularly in poorly ventilated environments. Biomarker-based assessments, such as cotinine and

carbon monoxide levels, offer reliable tools for early detection of SHS-related placental dysfunction. These insights not only advance our understanding of PE pathogenesis but also underscore the urgent need to integrate biomarker-based screening into antenatal care and strengthen public health interventions to reduce SHS exposure in pregnant women.

Future research should focus on identifying individual-level vulnerabilities—particularly genetic predispositions and epigenetic changes—that may modulate the maternal response to secondhand smoke (SHS). Exploring therapeutic approaches such as antioxidant and anti-inflammatory agents may help counteract SHS-induced placental injury and oxidative stress. Effective translation of scientific insights into preventive action requires strong interdisciplinary coordination among healthcare professionals, researchers, and policymakers. Emphasis should be placed on implementing biomarker-based screening protocols in prenatal care, strengthening enforcement of smoke-free regulations in both private and public settings, and raising public awareness to minimize environmental risks that threaten maternal and fetal health.

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