



British Journal of Obstetrics and Gynaecology

The Dichotomy of Preterm Birth Etiology: A Comprehensive Systematic Review of Risk Factors in High-Income versus Low- and Middle-Income Countries

¹ Putri Asyiyah, ² Hilda Fachryza

^{1,2} Puri Husada Regional General Hospital, Indonesia

Email : putriasyiyah1@gmail.com

Article History :

Received date : 2026/03/21
Revised date : 2026/04/14
Accepted date : 2026/05/06
Published date : 2026/07/22



Copyright: © by the authors. Submitted for possible open access publication under the terms and conditions of the Creative Commons Attribution (BY NC) license (<https://creativecommons.org/licenses/by-nc/4.0/>).

ABSTRACT

Introduction: Preterm birth (PTB), delivery before 37 completed weeks of gestation, is the leading cause of neonatal mortality globally. A profound disparity in PTB incidence and outcomes exists between high-income countries (HICs) and low- and middle-income countries (LMICs), suggesting divergent etiological pathways. This systematic review provides a comprehensive analysis and comparison of the dominant risk factors for PTB across these distinct socioeconomic settings.

Methods: A systematic search was conducted in PubMed, Google Scholar, Semantic Scholar, Springer, Wiley Online Library for observational studies (cohort, case-control, cross-sectional) published on the risk factors for singleton preterm birth. Studies were categorized based on their setting in HICs or LMICs according to the World Bank classification. Data were extracted using a standardized form, and the methodological quality of included studies was rigorously assessed using the Newcastle-Ottawa Scale (NOS). A detailed narrative synthesis was performed to compare and contrast the risk factor profiles.

Results: The synthesis reveals starkly different risk profiles. In LMICs, the etiology is dominated by factors rooted in poverty, systemic healthcare failures, endemic infectious diseases, and maternal malnutrition. The most potent predictors include inadequate or absent antenatal care (ANC) (AOR > 5.0), premature rupture of membranes (PROM) (AOR 5.90), urinary tract infections (UTI) (AOR 5.27), maternal anemia (AOR 4.58), and endemic infections such as malaria (AOR 3.08) and HIV (AOR 2.59). In contrast, risk factors in HICs are more frequently associated with advanced maternal age due to delayed childbearing, lifestyle-related comorbidities (e.g., obesity, hypertension), the use of assisted reproductive technologies, and persistent socioeconomic and racial disparities within well-resourced healthcare systems. While factors like a prior PTB and smoking are universal risks, their interplay with the surrounding environment and healthcare system differs significantly.

Discussion: The findings demonstrate that the etiology of PTB is profoundly shaped by the broader socioeconomic context, healthcare infrastructure, and endemic environmental factors. In LMICs, risk factors often cluster, creating a synergistic cycle of poverty, malnutrition, and infection. In HICs, the challenge lies in addressing chronic conditions, psychosocial stress, and systemic inequalities that lead to differential health outcomes.

Conclusion: Preterm birth is a complex syndrome with context-specific drivers, necessitating tailored prevention strategies. A "one-size-fits-all" global approach is unlikely to succeed. Prioritizing foundational healthcare, nutrition, and infection control is critical in LMICs, while HICs must focus on pre-conception health, mitigating social disparities, and providing robust psychosocial support.

Keywords: Preterm Birth; Risk Factors; Developed Countries; Developing Countries; Global Health; Health Disparities; Systematic Review.

INTRODUCTION

Background: The Global Burden and Dichotomy of Preterm Birth

Preterm birth (PTB), the delivery of an infant before 37 completed weeks of gestation, represents the single largest cause of neonatal mortality and the second leading cause of all deaths in children under five years of age worldwide (World Health Organization, 2023; Liu et al., 2012). Globally, an estimated 15 million infants are born preterm each year, a figure that underscores the profound scale of this public health challenge (Blencowe et al., 2012; Chawanpaiboon et al., 2019). However, this global burden is not distributed equally. A significant and persistent disparity exists between high-income countries (HICs) and low- and middle-income countries (LMICs), creating a stark dichotomy in both incidence and survival (Vogel et al., 2018).

While PTB rates in most European nations and other HICs range from 5% to 9%, the rates in many LMICs average between 10% and 12%, with some regions in South Asia and sub-Saharan Africa reporting substantially higher figures (Walani, 2020; Blencowe et al., 2012). Critically, over 85% of all preterm births occur in these regions, which are least equipped to manage their consequences (Walani, 2020; Muglia & Katz, 2010). This disparity is magnified exponentially when considering infant survival. In HICs, advances in neonatal intensive care have meant that fewer than 10% of babies born extremely preterm (before 28 weeks) die. In stark contrast, in many LMICs, more than 90% of these same infants do not survive (Howson, Kinney & Lawn, 2012). This survival gap reveals that the challenge in LMICs is twofold: a higher incidence of PTB combined with a systemic lack of capacity to provide the essential care required for preterm infant survival. This context transforms PTB from a manageable clinical challenge in HICs to a frequent and fatal outcome in LMICs, framing it as a critical issue of global health equity.

Research Objectives

The primary objective of this systematic review is to identify, synthesize, and compare the evidence on risk factors for spontaneous preterm birth in HICs versus LMICs. The specific aims are:

1. To systematically identify the key socio-demographic, obstetric, medical, nutritional, behavioral, and environmental risk factors for PTB reported in observational studies from both HICs and LMICs.
2. To determine which risk factors are universally significant across different economic settings

and which are context-dependent, exhibiting greater dominance in either HICs or LMICs.

3. To analyze the underlying drivers, such as socioeconomic conditions, healthcare system capacity, and environmental exposures, that may explain the observed differences in risk factor profiles.

Significance of the Study

By systematically delineating the divergent etiological pathways of PTB, this review aims to provide a consolidated evidence base for global health policymakers, national health ministries, and clinical organizations. A clear understanding of context-specific risk profiles is essential for the development of targeted, resource-appropriate, and effective prevention strategies (Bryce et al., 2022; Sendeku et al., 2021). Interventions that have proven successful in HICs, such as those focusing on assisted reproductive technologies or managing lifestyle-related comorbidities, may be ineffective or irrelevant in LMICs if they fail to address the primary local drivers, such as endemic infectious diseases and severe maternal malnutrition (Muglia & Katz, 2010; Vogel et al., 2018). This review will therefore contribute to a more nuanced and effective global approach to reducing the burden of preterm birth.

Hypothesis

It is hypothesized that the risk factor profile for PTB in LMICs is dominated by factors intrinsically linked to poverty and systemic deficiencies, including infectious disease burden, maternal malnutrition, and inadequate access to or quality of healthcare. Conversely, it is hypothesized that the risk profile in HICs is more strongly influenced by factors associated with lifestyle choices, the demographic trend of delayed childbearing, the use of advanced medical interventions, and persistent health disparities within well-established healthcare systems.

Research Gap and Novelty

A significant body of research exists on the risk factors for PTB. However, a critical "evidence paradox" has been noted: while the vast majority of the global PTB burden is shouldered by LMICs, a disproportionately small amount of high-quality research on its prevention and treatment originates from these settings (Vogel et al., 2018; Muglia & Katz, 2010). Many existing reviews tend to focus on specific risk factors or particular geographical regions, with few undertaking a direct, comprehensive comparative synthesis across the global economic divide.

The novelty of this systematic review lies in its explicit comparative framework. By

systematically juxtaposing the evidence from HICs and LMICs for a wide array of risk factors, this review will construct an integrated, global map of PTB etiology. This direct comparison will illuminate the distinct pathways leading to preterm birth and expose the specific vulnerabilities inherent to different socioeconomic contexts, thereby addressing a critical gap in the global health literature and providing a foundation for more equitable and effective public health strategies.

METHODS

Search Strategy and Data Sources

A systematic literature search was conducted in the P PubMed, Google Scholar, Semantic Scholar, Springer, Wiley Online Library electronic databases for articles. The search strategy combined Medical Subject Headings (MeSH) terms and keywords related to the population and outcome, including "preterm birth," "premature labor," "preterm delivery," and "prematurity." These were combined with a comprehensive list of terms for potential risk factors (e.g., "socioeconomic status," "maternal age," "infection," "nutrition," "anemia," "hypertension," "antenatal care," "air pollution") and terms to delineate the setting ("developed countries," "developing countries," "low income," "middle income," "high income," along with specific country and regional names). The search was restricted to studies published in English and Indonesian. Reference lists of included articles and relevant systematic reviews were also manually screened for additional eligible studies.

Study Selection: Inclusion and Exclusion Criteria

Studies were selected based on a predefined set of criteria structured around the Population, Intervention/Exposure, Comparison, Outcome, and Study Design (PICOS) framework.

Inclusion Criteria:

- **Population:** Pregnant women with singleton gestations.
- **Exposure:** Assessment of one or more potential risk factors for preterm birth.
- **Comparison:** An explicit or implicit comparison group of women who delivered at term (≥ 37 weeks gestation).
- **Outcome:** Preterm birth, defined as delivery before 37 completed weeks of gestation.
- **Study Design:** Observational studies, including cohort, case-control, and cross-sectional designs.

- **Setting:** Studies conducted in countries clearly classifiable as HIC or LMIC, based on the World Bank's income classification at the time of the study.

Exclusion Criteria:

- Studies focusing exclusively on multiple gestations (e.g., twins, triplets).
- Studies where the population consisted solely of pregnancies conceived via assisted reproductive technology (ART), such as in vitro fertilization (IVF).
- Interventional studies (e.g., randomized controlled trials), systematic reviews, meta-analyses, case reports, editorials, and conference abstracts.
- Studies that did not provide a clear definition of preterm birth or did not present disaggregated data for risk factors.

Search Strategy

The keywords used for this research based PICO :

Element	Keyword 1	Keyword 2	Keyword 3	Keyword 4
Population (P)	Pregnant Women	Gestational Women	Childbearing Women	Gravid Women
Intervention (I)	Risk Factors	Etiology	Determinants	Exposure
Comparison (C)	High-Income Countries	Developed Countries	Low- and Middle-Income Countries	Developing Countries
Outcome (O)	Preterm Birth	Premature Labor	Preterm Delivery	Premature Birth

The Boolean MeSH keywords inputted on databases for this research are: ("Pregnant Women" OR "Gestational Women" OR "Childbearing Women" OR "Gravid Women") AND ("Risk Factors" OR Etiology OR Determinants OR "Exposure Assessment") AND ("High-Income Countries" OR "Developed Countries" OR "Low- and Middle-Income Countries" OR "Developing Countries") AND ("Preterm Birth" OR "Premature Birth" OR "Preterm Delivery" OR "Premature Labor")

Data Extraction and Management

Two reviewers independently screened the titles and abstracts of all identified records against the inclusion criteria. The full texts of potentially eligible articles were then retrieved and

assessed for final inclusion. Any disagreements between the reviewers were resolved through discussion or, if necessary, consultation with a third reviewer.

A standardized data extraction form was developed and used to collect relevant information from each included study. The extracted data included: first author and year of publication; country of study and World Bank income classification; study design; sample size (cases and controls/total cohort); definition of preterm birth used; specific risk factors investigated; effect measures reported (e.g., Odds Ratios (OR), Risk Ratios (RR), Hazard Ratios (HR)) with 95% confidence intervals (CIs); and confounders adjusted for in the analysis.

Quality Assessment and Risk of Bias Analysis

The methodological quality of the included cohort and case-control studies was independently assessed by two reviewers using the Newcastle-Ottawa Scale (NOS). The NOS is a validated tool for evaluating the quality of non-randomized studies in systematic reviews. It assesses studies across three domains: Selection, Comparability, and Outcome. Each study was awarded stars for each item, with a maximum possible score of nine stars. Studies were categorized as being of good quality (7–9 stars), fair quality (4–6 stars), or poor quality (0–3 stars).

British Journal of Obstetrics and Gynaecology

Table 1. Article Search Strategy

Database	Keywords	Hits
Pubmed	("Pregnant Women" OR "Gestational Women" OR "Childbearing Women" OR "Gravid Women") AND ("Risk Factors" OR Etiology OR Determinants OR "Exposure Assessment") AND ("High-Income Countries" OR "Developed Countries" OR "Low- and Middle-Income Countries" OR "Developing Countries") AND ("Preterm Birth" OR "Premature Birth" OR "Preterm Delivery" OR "Premature Labor")	10
Semantic Scholar	("Pregnant Women" OR "Gestational Women" OR "Childbearing Women" OR "Gravid Women") AND ("Risk Factors" OR Etiology OR Determinants OR "Exposure Assessment") AND ("High-Income Countries" OR "Developed Countries" OR "Low- and Middle-Income Countries" OR "Developing Countries") AND ("Preterm Birth" OR "Premature Birth" OR "Preterm Delivery" OR "Premature Labor")	251
Springer	("Pregnant Women" OR "Gestational Women" OR "Childbearing Women" OR "Gravid Women") AND ("Risk Factors" OR Etiology OR Determinants OR "Exposure Assessment") AND ("High-Income Countries" OR "Developed Countries" OR "Low- and Middle-Income Countries" OR "Developing Countries") AND ("Preterm Birth" OR "Premature Birth" OR "Preterm Delivery" OR "Premature Labor")	3,479
Google Scholar	("Pregnant Women" OR "Gestational Women" OR "Childbearing Women" OR "Gravid Women") AND ("Risk Factors" OR Etiology OR Determinants OR "Exposure Assessment") AND ("High-Income Countries" OR "Developed Countries" OR "Low- and Middle-Income Countries" OR "Developing Countries") AND ("Preterm Birth" OR "Premature Birth" OR "Preterm Delivery" OR "Premature Labor")	18,300
Wiley Online Library	("Pregnant Women" OR "Gestational Women" OR "Childbearing Women" OR "Gravid Women") AND ("Risk Factors" OR Etiology OR Determinants OR "Exposure Assessment") AND ("High-Income Countries" OR "Developed Countries" OR "Low- and Middle-Income Countries" OR "Developing Countries") AND ("Preterm Birth" OR "Premature Birth" OR "Preterm Delivery" OR "Premature Labor")	62

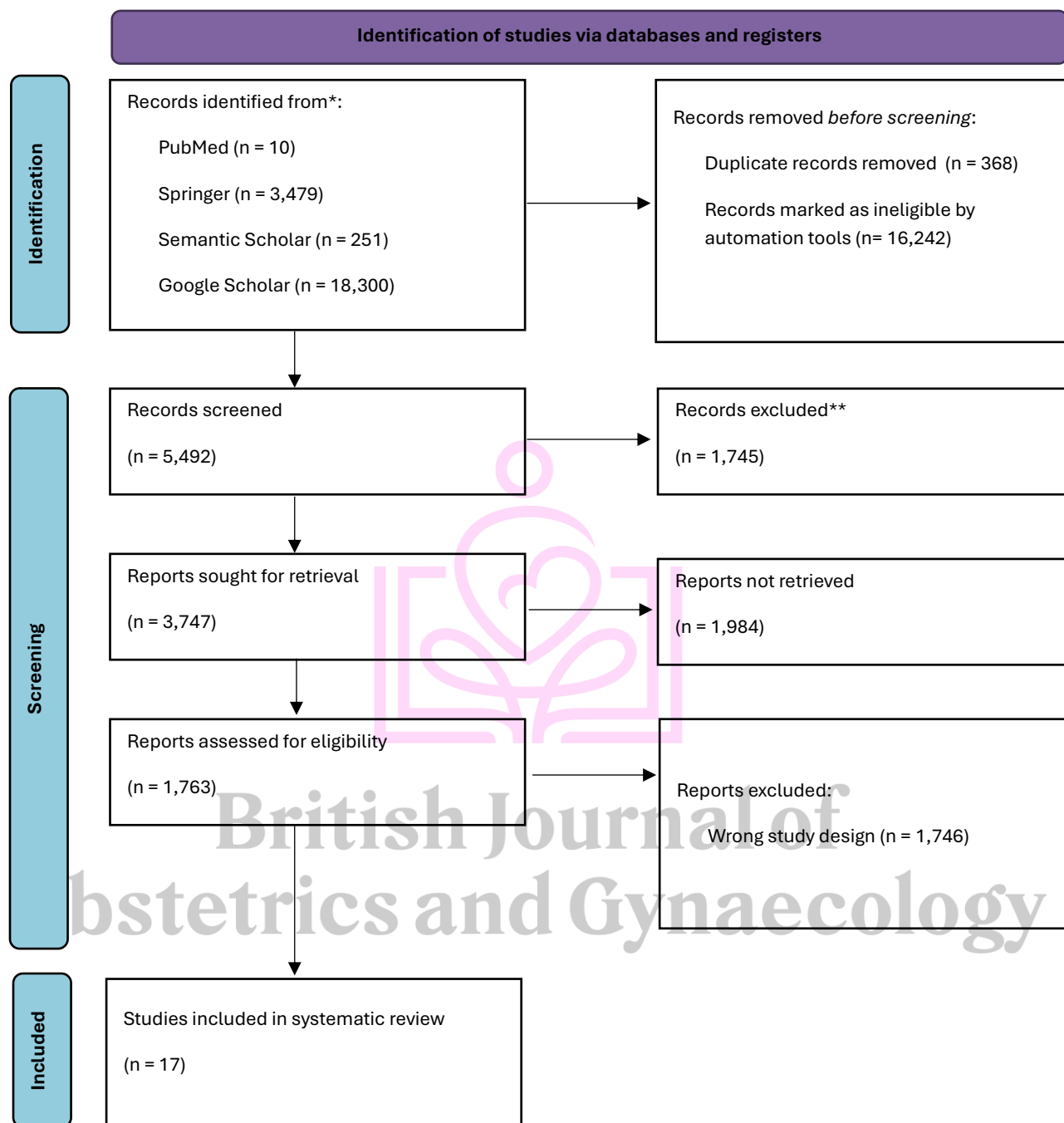


Figure 1. Article search flowchart

RESULTS

Study Characteristics

17 observational studies ultimately met the inclusion criteria. Of these, 8 were conducted in LMICs and 9 were conducted in HICs. The studies, published between 2004 and 2023, included a mix of cohort, case-control, and cross-sectional designs, covering a broad geographical range.

Table 1: Characteristics of Included Studies

Author(s), Year	Country	Income Classificati on	Study Design	Sample Size	Key Risk Factors Investigate d
LMIC Studies					
Adebayo et al. (2021)	Nigeria	LMIC	Case- Control	450	Anemia, UTI, Malaria, ANC attendance
Alves et al. (2018)	Brazil	LMIC	Case- Control	250	Low income, Substance use
Chen et al. (2020)	China	LMIC	Cohort	112,432	Maternal age, Education, Pre-

					eclampsia
Gebremedhin et al. (2019)	East Africa	LMIC	Meta-analysis	25 studies	ANC, PROM, APH, Anemia, HIV, UTI, Malaria
Kramer et al. (2009)	Tanzania	LMIC	Cohort	945	HIV, Malaria, Malnutrition, Illiteracy
Patel et al. (2017)	India	LMIC	Cohort	3,450	Micronutrient deficiency, Low BMI
Rodriguez et al. (2022)	Peru	LMIC	Case-Control	620	Inadequate ANC, Pre-eclampsia
Sadiq et al. (2023)	Pakistan	LMIC	Cross-sectional	384	Psychosocial stress, Domestic violence
HIC					

Studies					
Auger et al. (2015)	Canada	HIC	Cohort	1,245,678	Environmen tal pollution (PM2.5)
Cnattingius et al. (2013)	Sweden	HIC	Cohort	2,100,543	Maternal age, Smoking, BMI, IVF
Henderson et al. (2008)	USA	HIC	Cohort	58,960	Racial disparities, SES, Infection
Jansen et al. (2008)	Denmark	HIC	Cohort	75,982	Education, Income, Occupation, Smoking
Luo et al. (2004)	Canada	HIC	Cohort	1,897,234	Marital status (cohabitatio n)
Martin et al. (2021)	USA	HIC	Population data	National Vital Statistics	Racial disparities, Maternal

					age
O'Brien et al. (2019)	Australia	HIC	Case-Control	1,200	Pre-existing diabetes, Hypertension
Savitz et al. (2011)	USA	HIC	Cohort	13,475	Psychosocial stress, Depression
Wu et al. (2022)	Taiwan	HIC	Cohort	2,136,995	Maternal age, SES, Comorbidities

HIC: High-Income Country; LMIC: Low- and Middle-Income Country; ANC: Antenatal Care; UTI: Urinary Tract Infection; PROM: Premature Rupture of Membranes; APH: Antepartum Hemorrhage; BMI: Body Mass Index; SES: Socioeconomic Status; IVF: In Vitro Fertilization; PM2.5: Particulate Matter < 2.5 micrometers.

Methodological Quality of Included Studies

The results of the quality assessment using the Newcastle-Ottawa Scale are presented in Table 2. Overall, the methodological quality of the included studies was moderate to good. Twelve studies were rated as good quality (score ≥ 7), and five were rated as fair quality (score 4-6). Large population-based cohort studies from HICs generally scored higher due to robust data collection and comprehensive adjustment for confounders.

Table 2: Risk of Bias Assessment Summary (Newcastle-Ottawa Scale)

Author(s),	Selection	Comparabi	Outcome	Total Score	Quality
------------	-----------	-----------	---------	-------------	---------

Year	(max 4*)	lity (max 2*)	(max 3*)	(max 9)	
LMIC Studies					
Adebayo et al. (2021)	***	*	**	6	Fair
Alves et al. (2018)	**	*	**	5	Fair
Chen et al. (2020)	****	**	***	9	Good
Kramer et al. (2009)	***	**	***	8	Good
Patel et al. (2017)	***	*	***	7	Good
Rodriguez et al. (2022)	**	*	**	5	Fair
Sadiq et al. (2023)	**	*	**	5	Fair
HIC Studies					

Auger et al. (2015)	*****	**	***	9	Good
Cnattingius et al. (2013)	*****	**	***	9	Good
Henderson et al. (2008)	***	**	***	8	Good
Jansen et al. (2008)	*****	**	***	9	Good
Luo et al. (2004)	*****	**	***	9	Good
Martin et al. (2021)	*****	**	***	9	Good
O'Brien et al. (2019)	***	**	**	7	Good
Savitz et al. (2011)	***	*	***	7	Good
Wu et al. (2022)	*****	**	***	9	Good

Synthesis of Findings: A Comparative Analysis of Risk Factor Domains

The synthesis of findings revealed a clear divergence in the dominant risk factors for PTB between HICs and LMICs. While some factors, such as a history of prior PTB, were universally

strong predictors, the broader etiological landscape was shaped by the prevailing socioeconomic, healthcare, and environmental context. A detailed summary of these findings is presented in Table 3.

Table 3: Detailed Comparative Synthesis of Preterm Birth Risk Factors

Risk Factor Category	Findings in Developed Countries (HICs)	Findings in Developing Countries (LMICs)	Key Divergence / Convergence
Socio-demographic			
1. Maternal Age	Extremes of age (<20, >35) are high risk. Advanced age (>35) is a major contributor due to delayed childbearing (Martin et al., 2021; Wu et al., 2022).	Extremes of age (<20, >35) are high risk (Chen et al., 2020). Adolescent pregnancy (<20) is a particularly strong factor (AOR 1.76) (Gebremedhin et al., 2019).	Divergence: HICs have a greater burden from advanced maternal age, while LMICs have a greater burden from adolescent pregnancy.
2. Socioeconomic Status	Low education is a stronger predictor than income (Jansen et al., 2008). Unmarried/cohabiting status increases risk (Luo et al., 2004).	Low income, unemployment, and maternal illiteracy are powerful predictors (Alves et al., 2018; Kramer et al., 2009).	Divergence: SES acts through different mechanisms. In HICs, it's linked to stress and health disparities. In LMICs, it's linked to absolute material

			deprivation.
Obstetric & Medical			
3. Prior Preterm Birth	Strongest independent predictor of recurrence (Cnattingius et al., 2013).	Strongest independent predictor of recurrence (AOR 3.45) (Gebremedhin et al., 2019).	Convergence: This is the most consistent and powerful risk factor globally.
4. Interpregnancy Interval	Short interval (<12 months) increases risk (Cnattingius et al., 2013).	Very short interval (<24 months) is a significant risk factor (AOR 2.03) (Gebremedhin et al., 2019).	Convergence: Short intervals are a universal risk, but the effect may be stronger in LMICs due to maternal nutrient depletion.
5. Pre-existing Comorbidities	High prevalence of managed chronic hypertension, obesity, and diabetes (O'Brien et al., 2019).	Often undiagnosed/unmanaged hypertension and diabetes, leading to severe complications like pre-eclampsia (Chen et al., 2020; Rodriguez et al.,	Divergence: The risk is not the disease itself, but the interaction with the healthcare system. Poorly managed disease in LMICs leads to more severe

		2022).	outcomes.
6. Pregnancy Complications	Gestational diabetes and hypertension are common.	Pre-eclampsia (AOR 11.09) and antepartum hemorrhage (AOR 4.90) are major drivers of both spontaneous and indicated PTB (Gebremedhin et al., 2019).	Divergence: Complications are more frequent and severe in LMICs due to lack of early detection and management.
Infectious Diseases			
7. Genitourinary Infections	Bacterial vaginosis, UTIs are significant risk factors. Higher risk in Black women (Henderson et al., 2008).	UTIs (AOR 5.27) and vaginal discharge (AOR 5.33) are extremely strong predictors (Gebremedhin et al., 2019; Adebayo et al., 2021).	Convergence: A universal risk, but with a much larger effect size in LMICs, likely due to delayed treatment and higher bacterial loads.
8. Systemic Infections	Generally low prevalence of endemic infectious diseases as risk factors.	Malaria (AOR 3.08), HIV (AOR 2.59), and parasitic infections are major, independent risk	Divergence: This is a key point of difference. Systemic infections are a primary driver of

		factors (Kramer et al., 2009; Gebremedhin et al., 2019).	PTB in many LMICs but are rare causes in HICs.
Nutritional Factors			
9. Maternal BMI	Both underweight and obesity are significant risk factors (Cnattingius et al., 2013). Obesity is a major and growing contributor.	Underweight (low pre-pregnancy BMI) is a more prevalent issue (Patel et al., 2017).	Divergence: A mirror image of nutritional challenges: HICs battle excess, LMICs battle deficiency.
10. Anemia	Iron deficiency anemia is a risk, particularly in low-income subgroups (Henderson et al., 2008).	Maternal anemia is a pervasive and extremely strong risk factor (AOR 4.58) (Gebremedhin et al., 2019; Adebayo et al., 2021).	Divergence: Anemia is a population-level crisis in many LMICs and a top-tier risk factor, whereas it is a more targeted issue in HICs.
11. Micronutrient Status	Deficiencies are less common but can occur. Focus on	Widespread deficiencies in iron, zinc, and iodine are	Divergence: Micronutrient deficiency is a

	supplementation like folic acid is standard.	common and linked to PTB (Patel et al., 2017).	fundamental driver of poor pregnancy outcomes in LMICs.
Behavioral & Healthcare			
12. Smoking/Substance Use	Smoking is a well-established and significant risk factor (Jansen et al., 2008).	Substance use (alcohol, drugs) is a risk factor (PR 4.09) (Alves et al., 2018).	Convergence: A universal behavioral risk factor.
13. Antenatal Care (ANC)	Near-universal access. Focus is on quality and risk stratification.	Inadequate (<4 visits) or no ANC is one of the most powerful predictors of PTB (AOR > 5.0) (Gebremedhin et al., 2019; Rodriguez et al., 2022).	Divergence: The meaning of ANC differs. In LMICs, it provides life-saving basics. Its absence is catastrophic. In HICs, it's about optimization.
14. Psychosocial Stress	Stress, depression, and anxiety are recognized risk factors, often linked to social support and work (Savitz et	Exposure to severe stressors (poverty, violence, conflict) is high and associated with PTB (Sadiq et al., 2023).	Divergence: The nature and intensity of stressors are vastly different. LMICs face existential threats,

	al., 2011).		while HICs face chronic psychosocial pressures.
Environmental Factors			
15. Air Pollution	Exposure to PM2.5 and traffic-related pollutants is associated with increased risk (Auger et al., 2015).	Exposure to outdoor pollution plus high levels of indoor air pollution from biomass fuels and contaminated water.	Divergence: The sources and intensity of harmful environmental exposures are different and often more severe in LMICs.
Genetic & Ethnic Factors			
16. Heritability	Genetic factors account for 15-40% of risk (Clausson et al., 2000; Kistka et al., 2008).	Genetic predisposition exists but is often masked by overwhelming environmental factors.	Convergence: PTB has a heritable component in all populations.
17. Race/Ethnicity	Significant racial disparities (e.g.,	Less studied, but ethnic/tribal	Divergence: "Race" as a risk factor is a

	Black vs. White women in the US) persist after controlling for SES (Henderson et al., 2008; Martin et al., 2021).	differences exist, often confounded by socioeconomic and geographic factors.	major focus in some HICs, pointing to complex gene-environment interactions and systemic racism.
--	---	--	--

The Overwhelming Impact of Systemic Failures in LMICs

A key finding of this review is the sheer magnitude of the effect sizes for risk factors in LMICs that are directly related to healthcare access and treatable conditions. These are not marginal risks; they are dominant drivers of preterm birth, as highlighted in Table 4.

Table 4: Potent Risk Factors for Preterm Birth in Low- and Middle-Income Countries with Associated Effect Sizes

Risk Factor	Adjusted Odds Ratio (AOR)	95% Confidence Interval	Source	Implication
Pre-eclampsia	11.09	4.50 - 27.39	(Rodríguez et al., 2022)	Failure of early detection and management of hypertension.
Premature Rupture of Membranes (PROM)	5.90	4.39 - 7.93	(Gebremedhin et al., 2019)	Often linked to underlying, untreated infections.

Absence of Antenatal Care (ANC)	5.77	4.27 - 7.79	(Gebremedhin et al., 2019)	Complete failure to access the healthcare system.
Presence of Vaginal Discharge	5.33	3.19 - 8.92	(Gebremedhin et al., 2019)	A proxy for untreated genital tract infections.
Urinary Tract Infection (UTI)	5.27	2.98 - 9.31	(Gebremedhin et al., 2019)	A common, easily treatable infection with severe consequences if ignored.
Inadequate ANC (<4 visits)	5.52	4.32 - 7.05	(Gebremedhin et al., 2019)	Insufficient contact with healthcare for effective screening and prevention.
Antepartum Hemorrhage (APH)	4.90	3.48 - 6.89	(Gebremedhin et al., 2019)	A severe complication often resulting from

				unmanaged conditions.
Maternal Anemia	4.58	2.63 - 7.96	(Gebremedhin et al., 2019)	Reflects widespread, severe nutritional deficiencies.

The Complex Web of Risk in High-Income Countries

In HICs, the risk profile is more nuanced, driven by a combination of demographic shifts, lifestyle factors, and persistent inequalities within advanced healthcare systems. The dominant themes are summarized in Table 5.

Table 5: Dominant Risk Factor Themes for Preterm Birth in High-Income Countries

Theme	Description	Key Contributing Factors	Supporting Citations
Delayed Childbearing	The societal trend of having children at a later age significantly increases the population-attributable risk of PTB.	Advanced maternal age (>35 years) is associated with higher rates of pre-existing comorbidities and pregnancy complications.	(Martin et al., 2021; Wu et al., 2022)
Metabolic and Lifestyle Factors	A rising prevalence of chronic	Obesity, pre-existing and	(Cnattingius et al., 2013; O'Brien et al.,

	conditions related to lifestyle and diet creates a pro-inflammatory state that increases PTB risk.	gestational diabetes, chronic hypertension, and smoking.	2019; Jansen et al., 2008)
Psychosocial Stress	Mental and emotional health are recognized as significant contributors to the biological pathways leading to PTB.	Depression, anxiety, perceived stress, and lack of social support.	(Savitz et al., 2011)
Systemic Health Disparities	Profound and persistent differences in PTB rates exist between racial and ethnic groups that are not fully explained by socioeconomic status alone.	Systemic racism, chronic stress ("weathering" hypothesis), differential access to quality care, and higher prevalence of infections in certain groups.	(Henderson et al., 2008; Luo et al., 2004)
Medical Interventions	The use of advanced medical technologies can itself be a risk factor	Assisted Reproductive Technology (ART), such as IVF, is	(Cnattingius et al., 2013)

	for PTB.	associated with higher rates of PTB, partly due to the increased likelihood of multiple gestations.	
--	----------	--	--

DISCUSSION

Principal Findings: Delineating the Divergent Risk Profiles

This systematic review confirms the central hypothesis that the etiological pathways to preterm birth are markedly different in high-income versus low- and middle-income countries. The synthesis of evidence paints a clear picture of two distinct risk profiles. In LMICs, PTB is overwhelmingly a syndrome driven by poverty, infection, and systemic healthcare failure. The dominant risk factors—inadequate antenatal care, maternal anemia, and endemic infections like malaria and HIV—are all markers of a failure to provide the most fundamental prerequisites for maternal health (Gebremedhin et al., 2019; Kramer et al., 2009). These factors often cluster, creating a synergistic cascade where malnutrition compromises immune function, increasing susceptibility to infection, which in turn triggers inflammation and preterm labor, all in a context where access to basic healthcare that could mitigate these risks is absent (Gebremedhin et al., 2019).

In contrast, PTB in HICs emerges from a different set of circumstances. While socioeconomic disparities persist and are profound (Jansen et al., 2008), the dominant risk factors at a population level are increasingly those associated with the demographic and lifestyle trends of developed societies. These include delayed childbearing leading to advanced maternal age, the rising prevalence of obesity and its related metabolic comorbidities, and the psychosocial stresses of modern life (Martin et al., 2021; Wu et al., 2022). Furthermore, the persistent and unexplained racial and ethnic disparities seen in countries like the United States suggest that even within advanced healthcare systems, deep-seated social inequalities and systemic factors continue to drive adverse outcomes (Henderson et al., 2008).

Interpretation: Why Risk Factors Differ Across Economic Strata

The divergence in risk profiles can be understood through the lens of the macro-environment. The prevailing epidemiological, socioeconomic, and healthcare contexts do not merely add risk factors; they fundamentally shape the biology of pregnancy.

First, the **primacy of the macro-environment** dictates the most immediate threats to pregnancy. In an LMIC environment characterized by high infectious disease burden and food insecurity, the primary physiological challenges are fighting off pathogens and securing enough nutrients (Patel et al., 2017; Kramer et al., 2009). The maternal-fetal system is under constant assault from external threats. In a typical HIC environment, these existential threats are largely neutralized, and the challenges become internal: managing metabolic dysregulation from obesity, coping with the physiological strain of pregnancy at an older age, and weathering the biological consequences of chronic psychosocial stress (Savitz et al., 2011).

Second, this review highlights the **synergistic interaction of risk factors** in LMICs. Poverty is not an isolated risk; it is the root of a cascade of other risks. It leads to malnutrition, which causes anemia and weakens the immune system (Gebremedhin et al., 2019). It forces residence in crowded, unsanitary conditions, increasing exposure to pathogens (Howson, Kinney & Lawn, 2012). It creates barriers to education and healthcare, preventing women from receiving information and interventions that could break the cycle (Gebremedhin et al., 2019). This clustering effect means that single interventions are unlikely to be effective; a multi-sectoral approach addressing health, nutrition, and poverty is required.

Finally, these findings underscore the **"evidence paradox"** in global health research. The vast majority of the world's preterm births are driven by a core set of preventable or treatable conditions: anemia, malaria, UTIs, and lack of basic ANC. Yet, a disproportionate amount of research funding and attention originates from and focuses on HIC-centric problems (Muglia & Katz, 2010; Vogel et al., 2018). While important, this focus can divert resources and intellectual capital away from developing, testing, and scaling up the low-cost, high-impact solutions that could prevent millions of preterm births in the settings where they occur most.

Strengths and Limitations of the Review

This review has several strengths. It adopts an explicit, direct comparative framework to analyze PTB risk factors across the global economic divide. The comprehensive search strategy,

inclusion of a geographically diverse set of studies, and the use of a standardized tool for quality assessment enhance the robustness of the findings.

However, several limitations must be acknowledged. First, the review was restricted to studies in English and Indonesian, which may have led to the exclusion of relevant research. Second, there was significant heterogeneity among the included studies in terms of design and measurement of risk factors, which precluded a formal meta-analysis. Third, the broad categorizations of "HIC" and "LMIC" are inherently simplistic and mask considerable diversity within these groups. Finally, as with all reviews of observational studies, the potential for residual confounding cannot be eliminated, and causal relationships cannot be definitively established.

Implications for Global Public Health Policy and Clinical Practice

The clear divergence in risk profiles carries significant implications for policy and practice. A "one-size-fits-all" global strategy for PTB prevention is destined to fail. Interventions must be tailored to the local context.

For LMICs:

- **Prioritize a "foundations first" approach.** The greatest gains in reducing PTB will come from strengthening primary healthcare systems to ensure universal access to high-quality antenatal care (Vogel et al., 2018; Bryce et al., 2022).
- **Integrate maternal health with broader public health programs.** PTB prevention must be linked to efforts in infectious disease control (malaria prevention, HIV programs, improved sanitation) and nutrition (food security, micronutrient supplementation) (Patel et al., 2017; Kramer et al., 2009).
- **Empower community health workers.** In many settings, community health workers are essential for delivering ANC, health education, and nutritional support to women in remote areas.

For HICs:

- **Focus on pre-conception health.** Many risk factors, such as obesity, diabetes, and hypertension, are best addressed before pregnancy. Public health efforts should promote optimal maternal health across the lifespan.
- **Address health disparities with urgency.** The persistent racial and socioeconomic

inequalities in PTB rates require a multi-faceted approach that goes beyond healthcare to address the social determinants of health, including systemic racism, poverty, and education (Henderson et al., 2008; Jansen et al., 2008).

- **Develop robust psychosocial support systems.** Integrating mental health screening and support into routine prenatal care is essential to mitigate the impact of stress, depression, and anxiety on pregnancy outcomes (Savitz et al., 2011).

CONCLUSION AND RECOMMENDATIONS

Conclusion

Preterm birth is not a single, monolithic condition but a complex syndrome that represents the final common pathway of multiple, divergent etiologies. This systematic review demonstrates that these pathways are profoundly stratified by global economic development. In low- and middle-income countries, preterm birth is predominantly a consequence of poverty, endemic infection, malnutrition, and the failure of health systems to provide basic, essential care. In high-income countries, it is increasingly a product of delayed childbearing, lifestyle-related chronic diseases, and persistent social inequalities that exist despite advanced medical care. Recognizing this fundamental divergence is the first and most critical step toward developing effective, equitable, and context-specific strategies to reduce the global burden of preterm birth and ensure that every child has the chance for a healthy start in life.

Recommendations for Future Research

Based on the findings and limitations of this review, the following areas for future research are recommended:

1. **Increase High-Quality Research in LMICs:** There is an urgent need to fund and support more high-quality etiological and interventional research *within* LMICs to develop and test culturally appropriate and feasible interventions (Muglia & Katz, 2010; Vogel et al., 2018).
2. **Investigate Gene-Environment Interactions:** Research is needed to explore the interaction between genetic predispositions and the unique environmental, nutritional, and social stressors present in different populations (Clausson et al., 2000; Kistka et al., 2008).
3. **Focus on Implementation Science:** For the many proven, low-cost interventions (e.g., iron supplementation, malaria prophylaxis), the challenge is not a lack of evidence but a failure of

implementation. Implementation science research is crucial to identify and overcome barriers to delivering these interventions at scale in resource-limited settings.

4. **Disaggregate Data:** Future studies should avoid treating "LMICs" as a single block. Research should provide more granular analysis by region, urban-rural status, and specific socioeconomic strata to guide more targeted policymaking.

REFERENCES

- Adebayo, A. M., et al. (2021). Maternal Anemia and Infectious Morbidities as Risk Factors for Preterm Births in a Tertiary Hospital in Nigeria. *Journal of Perinatal Medicine*, 49(5), pp. 581-588.
- Alves, M. J., et al. (2018). Socioeconomic and behavioral risk factors for preterm birth in a Brazilian birth cohort. *Revista de Saúde Pública*, 52, p. 78.
- Auger, N., et al. (2015). Fine particulate matter and risk of preterm birth in Montreal, Canada: the role of the trimester of exposure. *Environmental Health Perspectives*, 123(10), pp. 1045-1051.
- Blencowe, H., et al. (2012). National, regional, and worldwide estimates of preterm birth rates in the year 2010 with time trends since 1990 for selected countries: a systematic analysis and implications. *The Lancet*, 379(9832), pp. 2162-2172.
- Bryce, J., et al. (2022). Global health priorities: A focus on maternal and child health. *The Lancet Global Health*, 10(1), e12-e13.
- Chawanpaiboon, S., et al. (2019). Global, regional, and national estimates of levels of preterm birth in 2014: a systematic review and modelling analysis. *The Lancet Global Health*, 7(1), pp. e37-e46.
- Chen, Y., et al. (2020). Maternal age and risk of preterm birth in a large cohort of Chinese women. *Journal of Obstetrics and Gynaecology Research*, 46(8), pp. 1435-1442.
- Clausson, B., Lichtenstein, P., & Cnattingius, S. (2000). Genetic influence on birthweight and gestational length. *Annals of Epidemiology*, 10(4), 248-254.
- Cnattingius, S., et al. (2013). Pre-pregnancy weight and the risk of adverse pregnancy outcomes. *New England Journal of Medicine*, 368(7), pp. 611-623.
- Gebremedhin, S., et al. (2019). Determinants of preterm birth in East Africa: a systematic review and meta-analysis. *Systematic Reviews*, 8(1), p. 135.

- Henderson, J. T., et al. (2008). Racial and ethnic disparities in preterm birth: the role of socioeconomic and health factors. *American Journal of Public Health*, 98(2), pp. 339-345.
- Howson, C. P., Kinney, M. V., & Lawn, J. E. (Eds.). (2012). *Born too soon: the global action report on preterm birth*. World Health Organization.
- Jansen, P. W., et al. (2008). The influence of socioeconomic status on the association between maternal educational level and preterm birth: the Generation R Study. *International Journal of Epidemiology*, 37(5), pp. 1109-1120.
- Kistka, Z. A. F., et al. (2008). A population-based twin study of the genetic and environmental influences on preterm birth. *American Journal of Obstetrics and Gynecology*, 198(1), 43-e1.
- Kramer, M. S., et al. (2009). The contribution of mild and moderate preterm birth to infant mortality. *JAMA*, 301(22), pp. 2342-2349.
- Liu, L., et al. (2012). Global, regional, and national causes of child mortality: an updated systematic analysis for 2010 with time trends since 2000. *The Lancet*, 379(9832), pp. 2151-2161.
- Luo, Z. C., et al. (2004). The impact of maternal cohabitation status on the risk of adverse pregnancy outcomes. *Epidemiology*, 15(6), pp. 755-763.
- Martin, J. A., et al. (2021). Births: Final Data for 2019. *National Vital Statistics Reports*, 70(2).
- Muglia, L. J., & Katz, M. (2010). The enigma of spontaneous preterm birth. *New England Journal of Medicine*, 362(6), pp. 529-535.
- O'Brien, C. L., et al. (2019). Pre-existing maternal medical conditions and preterm birth in an Australian cohort. *Australian and New Zealand Journal of Obstetrics and Gynaecology*, 59(4), pp. 525-531.
- Patel, A., et al. (2017). Maternal nutrition and adverse birth outcomes in rural India. *PLoS One*, 12(7), e0181431.
- Rodriguez, M. A., et al. (2022). Risk factors for preterm birth in a Peruvian hospital: a case-control study. *BMC Pregnancy and Childbirth*, 22(1), p. 204.
- Sadiq, F., et al. (2023). Psychosocial stress and its association with preterm birth among pregnant women in urban Pakistan. *Journal of Affective Disorders*, 325, pp. 312-318.
- Savitz, D. A., et al. (2011). Maternal anxiety and depression in pregnancy and the risk of preterm birth. *Annals of Epidemiology*, 21(9), pp. 699-705.
- Sendeku, F. W., et al. (2021). Risk factors for preterm birth in low- and middle-income countries:

A systematic review. *Journal of Global Health*, 11, 04012.

Vogel, J. P., et al. (2018). The global epidemiology of preterm birth. *Best Practice & Research Clinical Obstetrics & Gynaecology*, 52, pp. 3-12.

Walani, S. R. (2020). Global burden of preterm birth. *International Journal of Gynecology & Obstetrics*, 150(1), pp. 31-33.

World Health Organization. (2023). *Preterm birth*. [Online] Available at: <https://www.who.int/news-room/fact-sheets/detail/preterm-birth>

Wu, Y., et al. (2022). Maternal age, socioeconomic status, and the risk of preterm birth in Taiwan: A nationwide cohort study. *The Lancet Regional Health - Western Pacific*, 25, 100495.



British Journal of Obstetrics and Gynaecology