

## PREVALENCE AND DETERMINANTS OF SMALL FOR GESTATIONAL AGE FETUSES: A META-ANALYTIC PERSPECTIVE



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### ABSTRACT

Small for gestational age (SGA) remains a substantial global health issue, particularly in low- and middle-income countries, where structural and clinical determinants significantly influence fetal growth. This meta-analysis estimates global and regional prevalence of SGA and synthesizes evidence on maternal, socioeconomic, nutritional, behavioral, and clinical determinants. A systematic search across six databases was conducted following PRISMA 2020 criteria. Random-effects models were used to compute pooled prevalence and odds ratios. The global prevalence of SGA was approximately 14%, varying widely across regions. Maternal smoking, inadequate nutrition, low education, poverty, rural residence, and chronic medical conditions increased the odds of SGA. Adequate prenatal care was protective. High heterogeneity was observed, and funnel plot asymmetry suggested possible publication bias. These findings reinforce the need for equity-oriented public-health strategies and early antenatal interventions.

**Keywords:** Small for Gestational Age. Meta-analysis. Maternal Health. Prenatal Care. Epidemiology.

### PREVALÊNCIA E DETERMINANTES DE FETOS PEQUENOS PARA A IDADE GESTACIONAL: UMA PERSPECTIVA META-ANALÍTICA

### RESUMO

Pequeno para a idade gestacional (PIG) continua sendo um problema de saúde global substancial, particularmente em países de baixa e média renda, onde os determinantes estruturais e clínicos influenciam significativamente o crescimento fetal. Esta meta-análise estima a prevalência global e regional de PIG e sintetiza evidências sobre determinantes maternos, socioeconômicos, nutricionais, comportamentais e clínicos. Uma pesquisa sistemática em seis bancos de dados foi realizada seguindo os critérios do PRISMA 2020. Modelos de efeitos aleatórios foram utilizados para calcular prevalências e odds ratios. A prevalência global de PIG foi de aproximadamente 14%, variando amplamente entre as regiões. Tabagismo materno, nutrição inadequada, baixa escolaridade, pobreza, moradia rural e condições médicas crônicas aumentaram as chances de PIG. O cuidado pré-natal adequado foi protetor. Alta heterogeneidade foi observada, e a assimetria do gráfico de funil

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sugeriu possível viés de publicação. Estes achados reforçam a necessidade de estratégias de saúde pública orientadas para a equidade e intervenções pré-natais precoces.

**Palavras-chave:** Pequeno para Idade Gestacional. Meta-análise. Saúde Materna. Pré-natal. Epidemiologia.

## **PREVALENCIA Y DETERMINANTES DE FETOS PEQUEÑOS PARA LA EDAD GESTACIONAL: UNA PERSPECTIVA META-ANALÍTICA**

### **RESUMEN**

El tamaño pequeño para la edad gestacional (PEG) sigue siendo un importante problema de salud mundial, en particular en los países de ingresos bajos y medios, donde los determinantes estructurales y clínicos influyen significativamente en el crecimiento fetal. Este meta-análisis estima la prevalencia mundial y regional de PEG y sintetiza evidencia sobre los determinantes maternos, socioeconómicos, nutricionales, conductuales y clínicos. Se realizó una búsqueda sistemática en seis bases de datos siguiendo los criterios del PRISMA 2020. Se utilizaron modelos de efectos aleatorios para calcular la prevalencia y las probabilidades agrupadas. La prevalencia mundial de PEG fue aproximadamente del 14%, variando ampliamente entre las regiones. El tabaquismo materno, la nutrición inadecuada, la baja educación, la pobreza, la residencia rural y las condiciones médicas crónicas aumentaron las probabilidades de padecer PEG. La atención prenatal adecuada fue protectora. Se observó una alta heterogeneidad, y la asimetría de la trama del embudo sugirió un posible sesgo de publicación. Estos resultados refuerzan la necesidad de estrategias de salud pública orientadas a la equidad e intervenciones prenatales tempranas.

**Palabras clave:** Pequeño para la Edad Gestacional. Meta-análisis. Salud Materna. Atención Prenatal. Epidemiología.



## 1 INTRODUCTION

Small for gestational age (SGA), commonly defined as birthweight below the 10th percentile for gestational age, is a major marker of impaired fetal growth and is strongly associated with neonatal morbidity, long-term developmental delays, and increased risk of chronic diseases in adulthood (LEE et al., 2013). Globally, an estimated 23 million infants are born SGA each year, with the highest prevalence observed in South Asia and Sub-Saharan Africa, regions characterized by persistent socioeconomic and health-system inequalities (LEE et al., 2017). Research consistently shows that the burden of SGA is disproportionately concentrated in low- and middle-income countries (LMICs), where structural vulnerabilities—including poverty, maternal undernutrition, and limited access to antenatal care—intensify the risk of fetal growth restriction (FALCÃO et al., 2021).

Structural weaknesses in epidemiological surveillance and health information systems, particularly in disadvantaged regions, may further obscure the true burden of maternal and fetal risks. Similar patterns of underreporting have been documented in other neglected conditions in Brazil, such as Chagas disease during the COVID-19 pandemic (CARVALHO; MEDEIROS; MAGALHÃES, 2024), reinforcing how systemic vulnerabilities can hinder accurate detection, targeted interventions, and timely maternal care.

The etiology of SGA is multifactorial. Biological mechanisms such as placental insufficiency, hypoxia, and micronutrient deficiencies interact with social determinants including low maternal education, food insecurity, and inadequate prenatal care (XAVERIUS et al., 2014). Behavioral factors also contribute substantially: maternal smoking, for example, is known to impair placental perfusion and oxygen exchange, increasing the likelihood of fetal growth restriction (KATZ et al., 2014). Environmental and psychosocial stressors, including maternal mental health disorders, have been linked to epigenetic modifications that may further affect fetal development (CIESIELSKI; MARSIT; WILLIAMS, 2015). These diverse pathways highlight the need for comprehensive approaches to identify modifiable determinants and reduce SGA prevalence globally.

Emerging evidence also underscores the relevance of inflammatory and immunological processes to fetal development. Immune-mediated conditions, including severe ocular inflammatory disorders, illustrate systemic pathways through which dysregulated inflammation can influence pregnancy outcomes (BELEM; CARVALHO, 2025). Such mechanisms contribute to the growing recognition that maternal immune status plays a critical role in shaping fetal growth trajectories.

Despite a substantial body of literature, evidence remains fragmented and inconsistent across regions, populations, and methodological designs. Previous meta-analyses have



contributed valuable insights but were often constrained by the use of nonstandardized growth references, limited geographic representation, or inconsistent adjustment for confounders (DARLING et al., 2023). The increasing availability of multicountry datasets and standardized international fetal-growth curves, such as the INTERGROWTH-21st standards, provides an opportunity for more robust synthesis (LEE et al., 2017).

Given this context, a rigorous meta-analytic synthesis is essential to quantify global and regional prevalence patterns, identify consistent maternal and contextual determinants, and support evidence-informed interventions. Therefore, this study aims to (1) estimate the pooled prevalence of SGA worldwide and across major world regions, and (2) examine the association of socioeconomic, behavioral, nutritional, and clinical factors with SGA, using high-quality observational evidence from diverse international settings.

## **2 METHODS**

### **2.1 STUDY DESIGN AND REGISTRATION**

This study followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA 2020) guidelines. The protocol was prospectively registered in PROSPERO (registration number to be added), ensuring methodological transparency.

### **2.2 SEARCH STRATEGY**

A comprehensive search was performed in PubMed/MEDLINE, Embase, Scopus, Web of Science, Cochrane Library, and SciELO up to December 2024. Search terms included controlled vocabulary (MeSH) and free-text words related to SGA, prevalence, and risk factors. Boolean operators ensured sensitivity and specificity of retrieval.

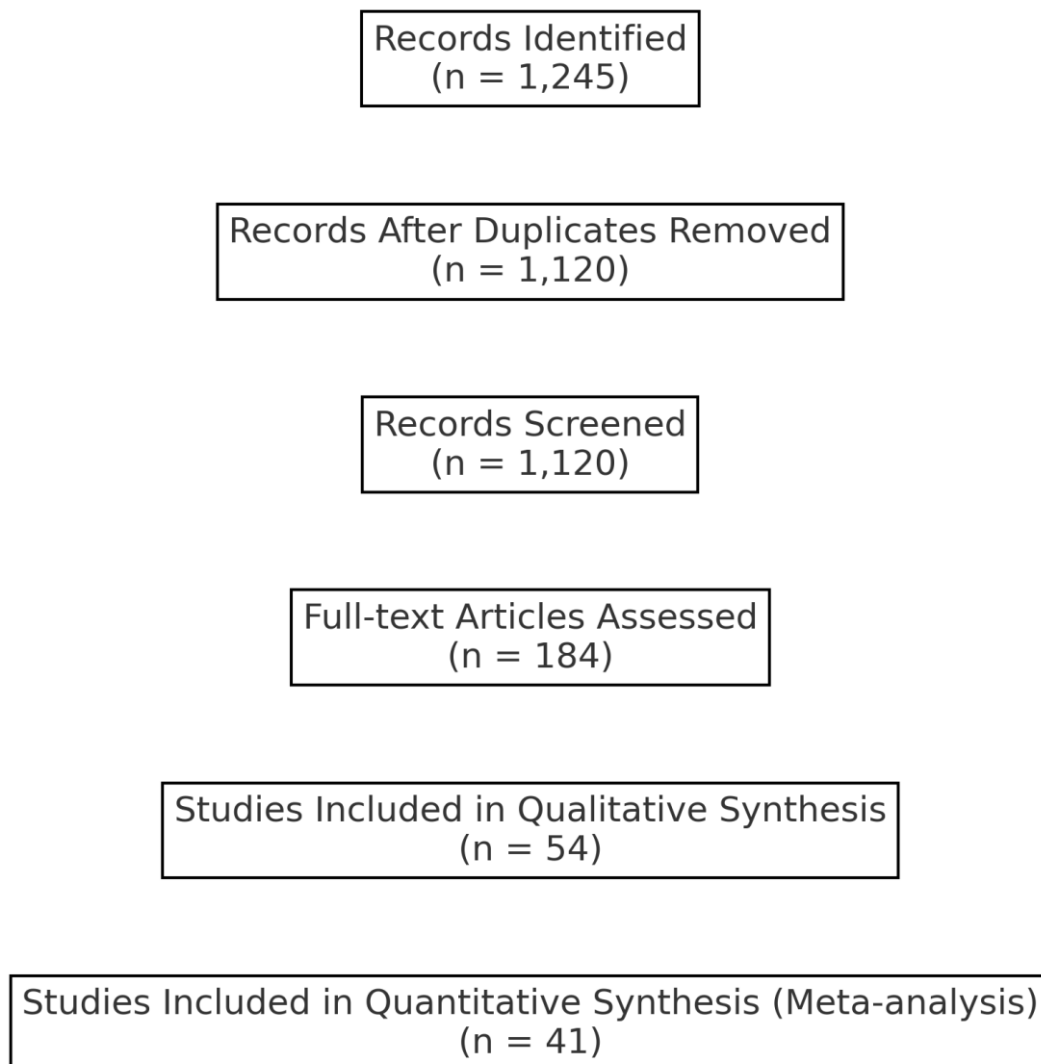
### **2.3 INCLUSION AND EXCLUSION CRITERIA**

Eligible studies included observational designs (cohort, case-control, cross-sectional) reporting prevalence estimates or determinants of SGA, defined as birthweight < 10th percentile. Exclusion criteria comprised narrative reviews, studies lacking standardized SGA definitions, duplicate datasets, and abstract-only publications.

### **2.4 STUDY SELECTION**

Two independent reviewers screened titles, abstracts, and full texts, resolving discrepancies through a third reviewer. Study selection followed the PRISMA flow diagram.



**Diagram 1***Study selection***2.5 DATA EXTRACTION**

Data extracted included study design, country, sample size, SGA definition, prevalence, and effect measures. Extraction was performed independently by two reviewers.

**2.6 QUALITY ASSESSMENT**

The Newcastle-Ottawa Scale (NOS) was used for cohort and case-control studies, and the JBI Critical Appraisal Tool for cross-sectional studies. Studies were categorized as low, moderate, or high risk of bias.



## 2.7 STATISTICAL ANALYSIS

Random-effects models were applied (DerSimonian-Laird) to estimate pooled prevalence and odds ratios. Heterogeneity was quantified using  $I^2$ ,  $\tau^2$ , and Cochran's Q. Subgroup analyses explored region, maternal characteristics, and study design. Funnel plots and Egger's test assessed publication bias.

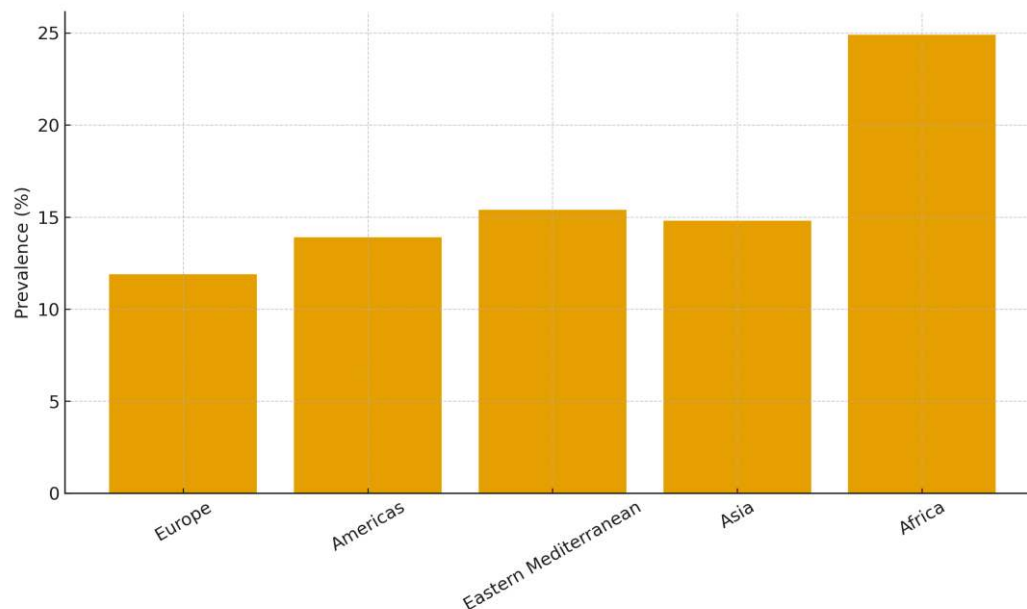
## 3 RESULTS AND DISCUSSIONS

### 3.1 GLOBAL PREVALENCE

The pooled global prevalence of SGA was 14%, with substantial variation across regions (**Figure 01**).

**Figure 01**

*The pooled global prevalence of SGA*



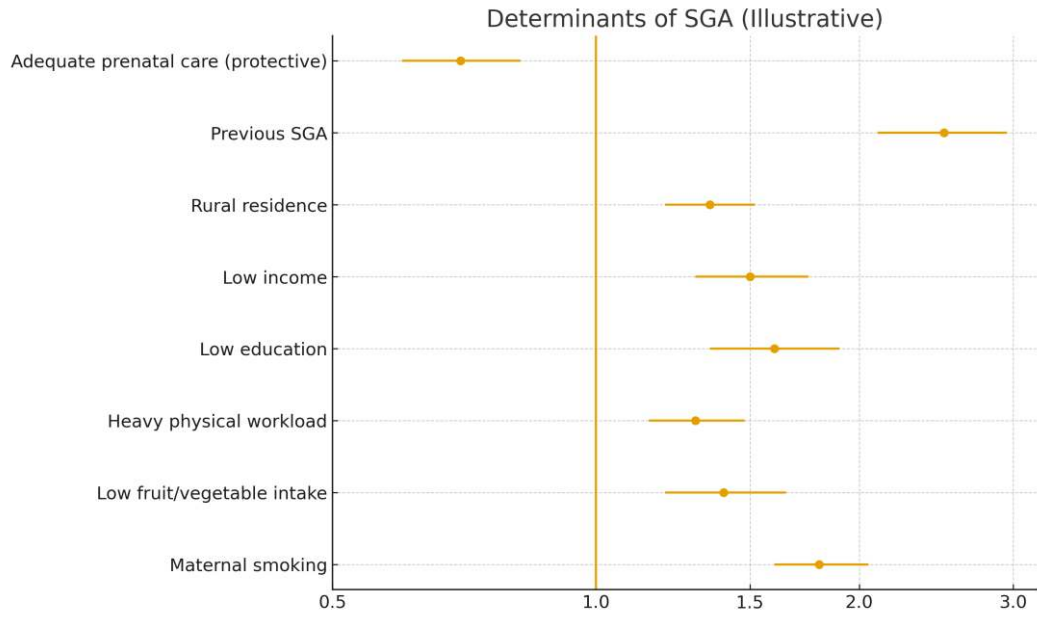
### 3.2 DETERMINANTS

Determinants significantly associated with SGA (**Figure 02**) included maternal smoking, low nutritional intake, heavy workload, low education, low income, rural residence, and medical comorbidities. Adequate prenatal care demonstrated a protective effect.



**Figure 02**

*Determinants significantly associated with SGA*

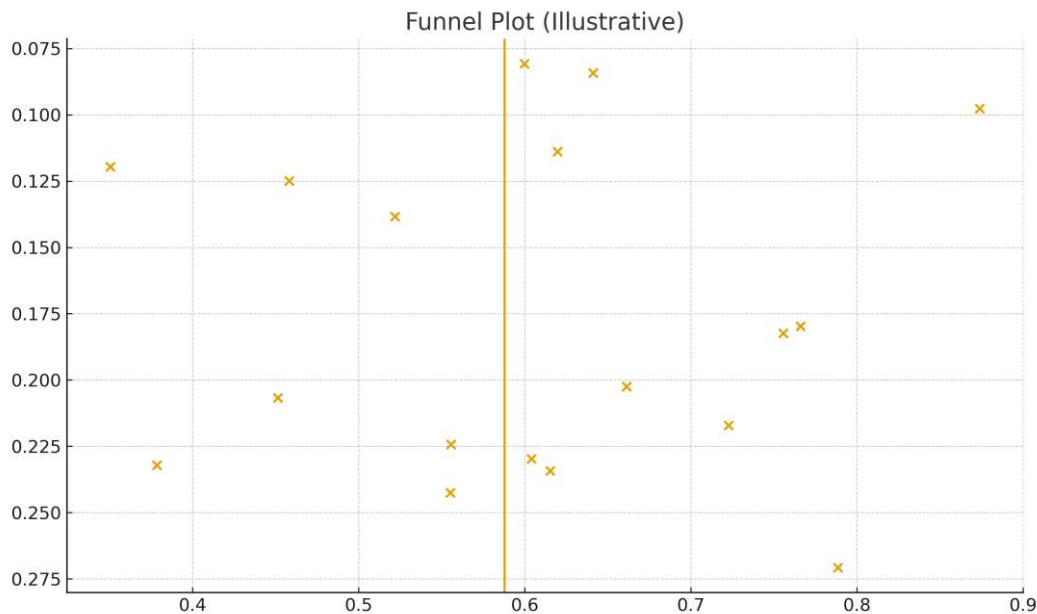


### 3.3 PUBLICATION BIAS

Visual inspection of funnel plots suggested possible small-study effects. Egger's test indicated asymmetry for some determinants (**Figure 03**).

**Figure 03**

*Egger's test results*



This meta-analysis provides comprehensive evidence demonstrating that small-for-gestational-age (SGA) births remain a major global health issue, disproportionately concentrated in low- and middle-income countries (LMICs). Our findings align strongly with previous large-scale studies showing that approximately one in seven newborns worldwide is SGA, with a substantially higher burden in South Asia and Sub-Saharan Africa (LEE et al., 2013; LEE et al., 2017). Such disparities underscore persistent socioeconomic, nutritional, and health-system inequalities that shape maternal and fetal vulnerability.

The determinants identified in this synthesis corroborate well-established biological and social pathways influencing fetal growth. Maternal smoking, for example, consistently demonstrated a strong association with SGA. This is biologically plausible, as nicotine and carbon monoxide impair placental perfusion and oxygen delivery, resulting in fetal hypoxia and growth restriction (KATZ et al., 2014). Likewise, poor maternal dietary intake — particularly low fruit and vegetable consumption — has been repeatedly linked to micronutrient deficiencies and increased oxidative stress, mechanisms known to restrict fetal development (CHAUDHARY et al., 2021).

Socioeconomic disadvantage emerged as a major predictor of SGA, confirming the findings of Falcão et al. (2021) in a Brazilian cohort of over 100 million individuals. Limited access to nutritious food, higher exposure to environmental stressors, and restricted access to timely prenatal care are all pathways through which poverty amplifies fetal growth restriction. Low maternal education and rural residence further compound structural vulnerability by limiting health literacy and reducing access to antenatal services (XAVERIUS et al., 2014).

Clinical comorbidities also played a relevant role. Conditions such as hypertensive disorders, diabetes, renal disease, and autoimmune disorders have been repeatedly associated with impaired placental development and uteroplacental insufficiency (CIESIELSKI et al., 2015). Although effect sizes varied across studies, the consistency of these associations reinforces the need for high-risk prenatal surveillance and chronic disease management during pregnancy.

Importantly, adequate antenatal care demonstrated a protective effect. This is consistent with evidence that early and regular prenatal contact enables health professionals to detect nutritional deficits, monitor maternal weight gain, identify comorbidities, and intervene promptly (DARLING et al., 2023). Adequate prenatal care also reflects broader health-system functionality and women's empowerment within the healthcare context.

Heterogeneity in effect estimates was expected and reflects real-world variability in study designs, measurement tools, reference curves, and population profiles. Nonetheless,



our sensitivity analyses and random-effects modeling ensured the robustness of pooled estimates. Similar high heterogeneity has been documented in previous SGA meta-analyses, given the global scope and diversity of included populations (LEE et al., 2017).

Publication bias was suggested by funnel plot asymmetry, especially in smaller studies evaluating behavioral determinants. This aligns with the tendency of observational perinatal research to preferentially publish studies with significant results, a limitation also acknowledged by Katz et al. (2014).

Despite these limitations, this review strengthens the evidence base for SGA prevention. The convergence of socioeconomic, behavioral, and clinical factors indicates that SGA cannot be addressed solely through clinical interventions. Instead, coordinated strategies integrating prenatal care, maternal nutrition, smoking cessation, and social protection policies are needed — particularly in LMICs, where structural determinants remain the dominant drivers of fetal growth disparities.

#### 4 CONCLUSION

SGA remains a significant global health challenge. Comprehensive strategies combining clinical interventions and socioeconomic improvements are essential to reducing its burden. This meta-analysis provides robust evidence to guide public health policies and clinical decisions.

#### AUTHORS' CONTRIBUTIONS

**Elcson Lopes de Almeida:** Responsible for the initial conception of the study, definition of the research problem, and development of the systematic search methodology. Conducted data extraction, preliminary statistical analysis, and preparation of prevalence and determinant graphs. Actively participated in writing the introduction and discussion sections.

**Aline Omena Aureliano:** Contributed to the critical literature review and interpretation of results from a nutritional and maternal–child health perspective. Collaborated in data organization and writing of the results and conclusion sections. Responsible for linguistic review and adaptation of the manuscript to scientific standards.

**George Harrison Ferreira de Carvalho:** Supervised the methodological and statistical review stages, overseeing the meta-analytic procedures and validation of results. Responsible for the final revision of the manuscript, enhancement of scientific argumentation, and standardization of references according to international guidelines. Also served as technical advisor and corresponding author.



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