Review Article

A Compounding Challenge: An Evidence-Based Case Report on the Association Between Obesity and Asthma Exacerbations in Pregnancy

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Abstract

Background: Asthma exacerbations during pregnancy have been associated with an increased risk of adverse perinatal outcomes. Asthma control through inflammatory mechanisms is hypothesized to worsen in the case of obesity during pregnancy. However, the scientific evidence regarding the association between the two variables remains contradictory. Therefore, this evidence-based case report aims to determine the association between early-pregnancy obesity and asthma exacerbation during pregnancy by synthesizing findings from various related studies.

Methods: A literature search was conducted using relevant keywords in the databases PubMed, ScienceDirect, Cochrane, and ClinicalTrials.gov. The Oxford Centre for Evidence-Based Medicine (CEBM) framework was used to appraise the studies that met the inclusion and exclusion criteria.

Results: This review identified five studies, comprising one systematic review and meta-analysis and four cohort studies. These studies were appraised as having acceptable validity, importance, and applicability. Four of the five studies reported a significantly increased risk of asthma exacerbation in pregnant women with early-pregnancy obesity. Stevens et al reported a decreased risk of exacerbation among pregnant women with obesity compared with the control group, attributing this to differences in perception thresholds between the groups and the possibility of study bias.

Conclusion: Pregnant women with obesity in early pregnancy have a higher risk of experiencing asthma exacerbations during pregnancy compared to non-obese groups. Consequently, these patients require intensified monitoring and optimized asthma management to prevent maternal and perinatal complications.

Keywords: 2HPMZ/2HPM, adverse effect, cutaneous adverse drug reaction, tuberculosis

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INTRODUCTION

Asthma is the most common chronic medical condition encountered during pregnancy, with a global prevalence of approximately 8-12%. This condition poses a significant clinical challenge, as up to 45% of pregnant individuals with asthma may experience exacerbations requiring medical intervention.[1] Asthma exacerbations during pregnancy have been associated with an increased risk of adverse perinatal outcomes, including low birth weight, preterm birth, and preeclampsia.[2,3] Concurrently, the prevalence of obesity among women of reproductive age is rising worldwide.[4] Obesity at the onset of pregnancy (body mass index [BMI] ≥30 kg/m^2) has garnered attention as a potential factor that may influence the clinical course of asthma.[5,6]

The relationship between obesity during pregnancy and asthma control throughout gestation is complex. Obesity induces a state of chronic systemic inflammation, characterized by elevated levels of pro-inflammatory adipokines such as IL-6, leptin, and TNF-α, alongside a reduction in protective adiponectin.[7,8] These obesity-driven alterations in systemic inflammatory responses have been reported to significantly influence asthma pathology.[9] This systemic inflammatory profile may exacerbate the underlying airway inflammation central to asthma pathogenesis, thereby potentially leading to poorer disease control and an increased susceptibility to exacerbations.[5,10]

Several observational studies provide evidence supporting this mechanism. For instance, a prospective study by Murphy et al reported that maternal obesity was associated with an increased risk of asthma exacerbation during pregnancy, which was partially mediated by macrophage activation.[11] Similar findings were reported by Stevens et al, who identified an association between a higher pregnancy BMI and worse asthma control.[12] However, the existing literature is not entirely consistent. Some studies, including a systematic review by Robijn et al, noted that while obesity is a significant risk factor, results across studies can be variable, and statistical significance sometimes diminishes after adjustment for specific confounding factors.[1]

These inconsistencies highlight a knowledge gap and underscore the need for a more comprehensive synthesis. A comprehensive evaluation of the existing epidemiology and evidence-based medicine is warranted to determine whether obesity in early pregnancy independently increases the risk of asthma exacerbation in pregnant individuals with asthma, after accounting for potential confounding factors.

This research was conducted as an Evidence-Based Case Report (EBCR) to clarify the relationship between obesity or high BMI status at the start of pregnancy and the incidence of asthma exacerbations during pregnancy by comparing this outcome against a population of pregnant individuals with asthma who have a normal or low BMI. The evidence synthesized from this report is expected to inform clinical practice by aiding in the identification of high-risk pregnant individuals with asthma, thereby enabling the implementation of targeted monitoring and preventive intervention strategies to improve maternal and fetal health outcomes.

CLINICAL SCENARIO

A 28-year-old pregnant woman at 4 weeks of gestation presented to the primary health care (PHC) for a routine antenatal examination. The patient has had a history of asthma since adolescence and currently reports intermittent mild shortness of breath, particularly at night. Her BMI is 31 kg/m², which is categorized as obese. The patient asked whether her obesity in early pregnancy could worsen her asthma symptoms throughout the gestation period. So, the physician sought to determine whether obesity in early pregnancy increases the risk of asthma exacerbations during pregnancy compared to pregnant asthma patients without obesity at the onset of pregnancy.

CLINICAL QUESTION

The clinical question “In pregnant women with asthma, does early-pregnancy obesity or a higher BMI increase the risk of asthma exacerbation during pregnancy compared to those with a normal BMI?” was structured using the PICO framework for evidence-based clinical research. The population (P) of interest is pregnant women with asthma. The intervention (I) or exposure is defined as overweight or obesity, indicated by an elevated BMI assessed before or during early pregnancy. This exposure is compared (C) to a normal BMI or the absence of obesity at the same pre-pregnancy or early-pregnancy time point. The primary outcome (O) is the incidence of asthma exacerbations during pregnancy.

METHODS

A systematic review was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guideline. A comprehensive search was conducted across four electronic databases: PubMed, ScienceDirect, the Cochrane Library, and ClinicalTrials.gov. The search was not limited by publication date to ensure maximum coverage of the available literature.

The search strategy was designed to identify relevant articles related to the association between BMI or obesity and the risk of asthma exacerbations during pregnancy. Keywords, and where applicable, controlled vocabulary (MeSH terms for PubMed and Cochrane) were searched in the title, abstract, and keyword fields. The core search query was: ((Body Mass Index) OR (Obesity)) AND (Asthma) AND

(exacerbations) AND ((pregnancy) OR (pregnant) OR (gestation)) AND ((prognosis) OR (Risk)).

The exposure variable was defined as overweight (25 to 29.9 kg/m^2), obesity (≥30 kg/m^2), or a numerical BMI score, assessed before or during early pregnancy, according to World Health Organization (WHO) criteria. The primary outcome of interest was the incidence of an asthma exacerbation, defined as any event requiring hospitalization, emergency department (ED)/unscheduled physician visit, or course of oral corticosteroids.

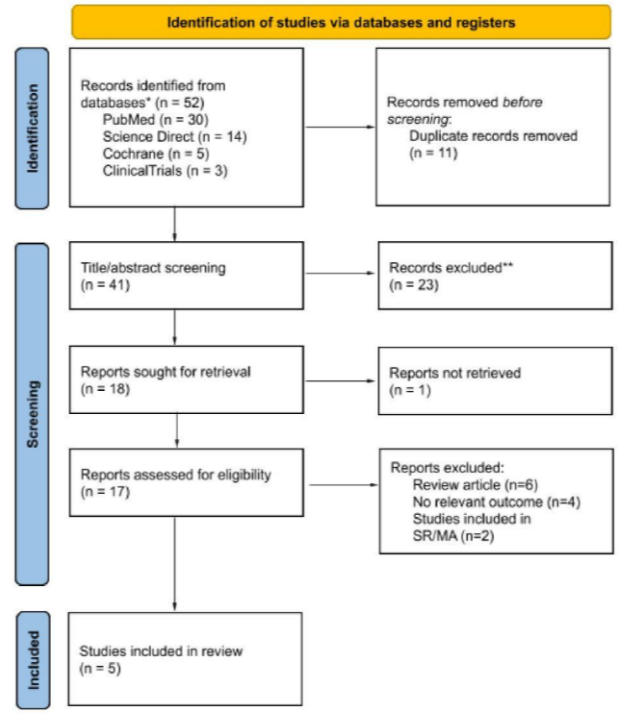

Figure 1. PRISMA Flow Diagram

Studies eligible for this review were systematic reviews/meta-analyses (SR/MA) or cohort studies published in either Indonesian or English. Two reviewers independently screened all identified studies. A third reviewer resolved any discrepancies. The population of interest was pregnant individuals with a physician-confirmed diagnosis of asthma prior to pregnancy.

Studies were excluded if the full text was inaccessible or if participant follow-up was not conducted until the conclusion of pregnancy. The quality and level of evidence of all included studies were critically appraised using the Oxford Centre for Evidence-Based Medicine (CEBM) levels of evidence and corresponding critical appraisal tools.

RESULTS

Following the literature search, five studies involving 86,650 patients met the inclusion and exclusion criteria. The final analysis included one systematic review and meta-analysis, two retrospective cohort studies, and two prospective cohort studies. The primary outcome was asthma exacerbation, with exposures (risk factors) including overweight status, obesity, and/or increases in BMI. Table 1 lists the included studies and summarizes the relevant findings.

Based on Table 2, the four cohort studies demonstrated generally adequate methodological validity. Most validity criteria were fulfilled across studies. However, several items were rated as unclear. In Zhang et al, the follow-up criterion was judged unclear because 15.5% of participants had missing data that were excluded from the analysis, potentially undermining completeness and the representativeness of the final results.[13] In Murphy et al, baseline data were collected at 17 weeks' gestation, leading to the "representative subjects" criterion being rated as unclear.[11] Moreover, this study did not perform multivariable analyses to adjust for confounders, indicating an absence of confounding adjustment.

Findings from the four cohort studies were reported as odds ratios (ORs) or risk ratios (RRs) and were statistically significant. Three studies indicated that, among pregnant individuals with asthma, obesity was associated with up to a twofold higher risk of exacerbation compared with those with a healthy weight.

In contrast, Stevens et al reported a lower exacerbation risk with obesity (RR=0.41).[12] All studies had relatively narrow confidence intervals, suggesting good overall precision. Applicability was judged to be adequate across the cohort studies because most criteria were met. However, the "clinical importance" criterion was rated as unclear for Zhang et al and Stevens et al because the NHH could not be determined.[12,13]

Table 1. Summary of Study Findings

Author and Study Design	Outcome (Asthma Exacerbation)	Results	Key Findings
Lee et al (2025),[14] A retrospective cohort study involving 40,196 pregnant women in England with physician-diagnosed asthma. BMI was measured at early pregnancy (study baseline).	Oral corticosteroid use, ED visits, or hospitalization.	Overweight - aOR=1.09 (95% CI=1.00-1.19); ARR=0.01; *P*=0.045 Obese - aOR=1.24 (95% CI=1.14-1.35); aRR=0.04; *P*<0.001	Overweight and obesity independently increased the risk of exacerbation after adjustment for multiple confounders. The Asian race had a higher risk than White patients (OR=1.24; 95% CI=1.08–1.42), the highest among the racial groups analyzed.
Zhang et al (2025),[13] A retrospective cohort study including 10,985 pregnant women in the United States with pre-pregnancy asthma. BMI was measured within the six months preceding	Prescription of oral corticosteroids.	Adjusted BMI: aOR=1.01 (95% CI=1.00–1.02) per 1-kg/m^2 increase in multivariable analysis.	This study addresses the clinical question of the effect of obesity on asthma exacerbations. Its principal limitations are the high proportion of missing data (15.5%) and the single-center population, which may limit generalizability.
Robijn et al (2022),[1] A systematic review and meta-analysis including five studies and 35,002 pregnant individuals with asthma.	Hospitalization, ED visits, unscheduled physician visits, or use of oral corticosteroids.	Forest plot for obesity: pooled RR= 1.25; 95% CI=1.15–1.37; I^2 = 0.0%.	This systematic review and meta-analysis finding strengthens the evidence for an association between early-pregnancy obesity and asthma exacerbations, with the lowest heterogeneity among populations. Key limitations include variability in outcome definitions/assessments across the included studies.
Stevens et al (2022),[12] A prospective cohort study in the United States enrolling 299 pregnant women with pre-pregnancy asthma. Pre-pregnancy BMI was self-reported.	The ED visits, hospitalization, or unscheduled physician visits.	Asthma exacerbations - aRR overweight=0.18 (95% CI=0.06-0.53) - aRR obesity=0.47 (95% CI=0.28-0.79) Medical encounter - aRR overweight=0.41 (95% CI=0.21-0.82) - aRR obesity=0.75 (95% CI=0.48-1.18)	This article reported that overweight and obesity were associated with lower risks of asthma attacks and unscheduled physician visits. The authors suggested that poorer overall asthma control and more persistent symptoms might blunt the recognition or triggering of discrete exacerbation events, making patients less likely to seek acute medical care.
Murphy et al (2017),[11] A prospective cohort study in Australia enrolling 168 pregnant women with pre-pregnancy asthma, with BMI measured in early pregnancy.	Hospitalization, medical intervention, or use of oral corticosteroids.	Overweight - RR=2.04; aRR=0.26; *P*=0.014 Obese - RR=1.94; aRR=0.23; *P*=0.017	Overweight and obesity in early pregnancy were associated with a higher risk of asthma exacerbations during pregnancy, but this association remains subject to residual confounding. A proposed mechanism involves heightened systemic macrophage activation.

Note: aOR=adjusted odds ratio; aRR=adjusted risk ratio; RR=risk ratio

Table 2. Critical Appraisal of Cohort Study

Author	Validity				Importance		Applicability			Level of evidence
	Representative subjects	Follow up	Objective outcome/ blinding	Confounding adjustment	Overweight	Obese	Patient characteristics	Clinical importance	NNH	
Lee et al (2025)[14]	+	+	+	+	RR=1.09 (95% CI= 1.00-1.19)	RR=1.24 (95% CI= 1.14-1.35)	+	+	25	2B
Zhang et Al (2025)[13]	+	N/A	+	+	aOR= 1.01 (1–1.02) for every 1 kg/m^2 increase		+	+	N/A	2B
Stevens et al (2022)[12]	+	+	+	+	RR=0.41 (95% CI= 0.21-0.82)	RR=0.75 (95% CI= 0.48-1.18)	+	+	N/A	1B
Murphy et al (2017)[11]	N/A	+	+	-	RR=2.04; *P*=0.0137	RR=1.94; *P*=0.0173	+	+	4	1B

Note: NNH=Number Needed to Harm**;** aOR=adjusted odds ratio; aRR=adjusted risk ratio

Table 3. Critical Appraisal of Systematic Review Study

Author	PICO	Appropriate searching	The relevant study included	Quality assessment of trials	Heterogeneity	Result	Level of Evidence
Robijn et al (2022)[1]	+	+	+	+	+	RR=1.25 (95% CI=1.15-1.37)	1A

Note: PICO refers to P=Population, I=Intervention, C=Compared, O=Outcome

Based on Table 3, the systematic review by Robijn et al met the critical appraisal criteria. This study demonstrated a 25% increased risk of exacerbations among pregnant individuals with obesity compared with those of healthy weight (pooled RR=1.25; 95% CI=1.15–1.37), with good precision.[1] Overall, all five articles exhibited satisfactory validity, importance, and applicability.

DISCUSSION

The primary clinical question addressed in this report is whether obesity in early pregnancy increases the risk of asthma exacerbations in pregnant women. Based on a critical appraisal of five relevant scientific articles, consisting of one SR/MA and four cohort studies, the overall findings indicate a significant association between obesity in early pregnancy and an increased risk of asthma exacerbations throughout pregnancy.

These findings are consistently supported by studies with large sample sizes. A retrospective cohort study by Lee et al involving more than 40,000 pregnant women demonstrated that both overweight (aOR=1.09) and obesity (aOR=1.24) independently increased the risk of asthma exacerbations after adjustment for potential confounders.[14] Similarly, Zhang et al reported a progressive increase in risk with each 1 kg/m^2 increase in BMI (aOR=1.01).[13] Furthermore, a prospective cohort study by Murphy et al also identified a significant elevation in relative risk among the overweight (RR=2.04) and obese (RR=1.94) groups.[11]

The highest level of evidence comes from the systematic review and meta-analysis conducted by Robijn et al. The pooled analysis of five studies yielded a precise risk estimate, demonstrating that obesity increased the risk of asthma exacerbations by 25% (RR=1.25; 95% CI=1.15–1.37), with very low heterogeneity between studies (I^2 = 0.0%). This strongly supports the validity of the conclusion that obesity is one of the important risk factors amongst pregnant women with asthma.[1]

From a pathophysiological perspective, this association can be explained through several mechanisms. Obesity is characterized by a state of low-grade, chronic systemic inflammation, or what is often referred to as “metabolic inflammation”. Many studies have shown a correlation between adipose tissue in obese individuals and pro-inflammatory cytokine production that contributes to a chronic systemic inflammation response.[15,16] Murphy et al specifically linked these findings to potential systemic macrophage activation, which may further impair asthma control.[11]

Although the findings described above suggest an effect of early-pregnancy obesity on the risk of asthma exacerbations, the study by Stevens et al reported contradictory results. This prospective cohort study found that overweight and obesity, in contrast, were associated with a lower risk of asthma attacks and medical visits. The authors hypothesized that this finding may be explained by the fact that women with higher BMIs already had poorer asthma control and symptoms at baseline, making them more “resistant” or having a different threshold for reporting exacerbations or seeking medical care.[12]

Nevertheless, pregnant women with obesity were found to experience night symptoms more frequently than non-obese women, particularly in the first trimester (RR=1.66; 95% CI=1.08–2.56). The discrepancy in results may be related to the reporting method used in Stevens et al, which relied on self-report, thereby introducing variability in patients' perceived and reported exacerbations (asthma attacks or hospital visits) or other symptoms.[12]

In the clinical scenario which are made, the available evidence is highly relevant to the case of a 28-year-old pregnant woman with a pre-pregnancy BMI of 31 kg/m^2. Overall, the evidence suggests that obesity places this patient at a higher risk of worsening asthma during pregnancy. This information is crucial for physicians to provide appropriate patient education and to plan more proactive management strategies, such as closer symptom monitoring and optimization of asthma therapy to prevent exacerbations. Moreover, the finding from Lee et al identifying Asian ethnicity as the group at highest risk of exacerbation should also be considered during patient counseling.[14]

LIMITATION

The strength of this analysis lies in the inclusion of evidence from diverse study designs, including a systematic review and meta-analysis, which represent the highest level of evidence (1A). However, several limitations must be acknowledged. Zhang et al was limited by a high proportion of missing data and was conducted at a single healthcare centre. The study by Stevens et al should be interpreted with caution due to the study's reliance on retrospective self-reported questionnaires for assessing asthma symptoms and pre-pregnancy weight. Such a methodology is inherently susceptible to recall or misclassification bias, as participants may not perfectly remember the exact frequency or intensity of symptoms during early stages of pregnancy. Furthermore, the studies analysed measured BMI at different time points (pre-pregnancy vs. early pregnancy) and adjusted for varying sets of confounders, which may have led to differences in baseline characteristics at study entry. In addition, most of the included studies were conducted in high-income countries, limiting the generalizability of the findings to low-income settings. In general, the research methods employed in the included studies may have been influenced by resource constraints.

CONCLUSION

Based on the analysis of this evidence-based case report, it can be concluded that pregnant women with asthma and early-pregnancy obesity have a higher risk of experiencing asthma exacerbations during their gestational period compared to those without obesity. This conclusion is supported by consistent evidence from several large cohort studies and is reinforced by a high-quality systematic review and meta-analysis, which demonstrated a significant increase in risk not only in the obese group but also in the overweight group and for each incremental increase in BMI.

In response to the clinical question, the patient's obesity in this scenario constitutes a critical risk factor that requires careful attention. These findings highlight the importance of risk identification and counselling patients accordingly, as well as the need for closer monitoring and optimal asthma management in pregnant women with obesity to prevent maternal and perinatal complications.

CONFLICT OF INTEREST

The authors have no relevant financial or non-financial interests to disclose.

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