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Maternal smoking during pregnancy and childhood seizure: a systematic review and meta-analysis

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Abstract

Background Maternal smoking during pregnancy is associated with adverse outcomes, but its relationship with childhood seizures remains unclear. Previous studies have produced inconsistent findings regarding the link between maternal smoking during pregnancy and seizure risk in offspring. We aim to investigate the association between maternal smoking during pregnancy and seizures in offspring through systematic review and meta-analysis.

Methods We conducted a search across multiple electronic databases such as PubMed, Embase, ScienceDirect, Scopus, and Web of Science. The search was performed on May 12, 2025. Papers reporting seizure frequency according to maternal smoking or odds ratios for seizure in offspring were selected. Dose-response analysis was performed based on restricted cubic spline analysis between the number of cigarettes per day and the effect estimate. The meta-analysis was performed using Review Manager version 5.4.1, and the dose-response analysis was conducted using STATA version 13 software.

Results Among the 1,128 articles initially identified, 14 studies involving 12,887,398 subjects were included. Offspring exposed to maternal smoking during pregnancy exhibited an increased association with seizures (odds ratio 1.49, 95% confidence interval 1.21–1.84) compared to those whose mothers did not smoke during pregnancy. Subgroup analysis revealed a significantly heightened association in febrile convulsion, epilepsy, and neonatal seizure. Dose-response analysis shows a linear increase in childhood epilepsy with maternal smoking, where each additional daily cigarette raises the odds ratio by 1.7%.

Conclusions Our study establishes a significant association between maternal smoking during pregnancy and seizures in offspring. These findings highlight the importance of public health efforts to reduce maternal smoking and highlight the potential impact on childhood health outcomes.

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Keywords Maternal smoking, Pregnancy, Seizure, Systematic review, Meta-analysis

Introduction

Smoking is one of the well-known preventable unhealthy factors that have pulmonary and extrapulmonary effects [1]. According to the 2023 World Health Organization (WHO) reports, more than 8 million people die each year related to smoking, which includes 1.3 million non-smokers exposed to second-hand smoke [2]. Although the overall global trend of tobacco use is declining, the estimated prevalence of smokers is around 15.2% [3]. According to a recent meta-analysis, a significant association has been observed between current smokers and epilepsy, highlighting smoking as a potential risk factor [4].

Globally, the prevalence of current smoking among women is estimated at 17%, with higher rates reported in specific subgroups, including pregnant women, where the prevalence reaches 21% [5]. Maternal smoking during pregnancy has been mentioned as a risk factor for various diseases in offspring such as fetal growth retardation, obesity, and attention deficit hyperactivity disorder [6–8]. In addition, the brain structure and volume of offspring can be affected by maternal smoking during pregnancy [9, 10].

Seizures represent a transient occurrence of abnormal excessive or synchronous neuronal activity in the brain, manifesting with a variety of clinical symptoms ranging from brief lapses in attention to convulsions [11]. In pediatric populations, seizures are broadly categorized based on age of onset and underlying etiology, with febrile seizures, childhood epilepsy, and neonatal seizures being the most commonly studied subtypes [12]. Febrile seizures predominantly occur in children aged 6 months to 5 years, with recovery usually without long-term issues. Their prevalence ranges from 3.2 to 5.5 per 1,000 in developed countries to 3.6–44 per 1,000 in developing countries [13]. Childhood epilepsy, affecting about 58 per 100,000 children aged 1 to 10, arises from diverse causes including genetic mutations, chromosomal abnormalities, and environmental factors such as infections [14]. Neonatal seizures show a prevalence of 0.02% to 0.12%, varying by gestational age [15].

There have been efforts to demonstrate the associations between maternal smoking during pregnancy and childhood seizure. Several studies indicate a higher occurrence of seizures in children whose mothers smoked during pregnancy [16–19], while other research reports no notable variation in seizure frequency related to maternal smoking during pregnancy [20–22]. Although there are discrepancies in the findings of these related investigations, to date, no comprehensive literature review or meta-analysis has been undertaken. We aim to investigate the potential association between maternal smoking during pregnancy and the seizures in offspring.

Methods

Search strategy and eligibility criteria

The study protocol was registered with PROSPERO (registration number: CRD42023416464), and the methodology adhered to the PRISMA guidelines [23, 24]. A systematic literature search was conducted on May 12, 2025. To find studies of maternal smoking during pregnancy and seizure in offspring, we performed online searches of published literature using PubMed, Embase, ScienceDirect, Scopus, and Web of Science using the following terms: *'smokers'*, *'smoking'*, *'tobacco'*, *'cigarette smoking'*, *'seizure'*, *'epilepsy'*, *'convulsion'*, *'pregnancy'*, *'maternal'*, *'mother'*, *'prenatal'*, *and 'antenatal'*. The specific search strategies were summarized in supplementary Table 1. The search was limited to titles and abstracts, and studies published in English and in any other language were considered eligible for inclusion. The language and publication year was not restricted. We manually searched the reference lists of the included studies.

We included cohort or case–control studies that presented results as unadjusted odds ratios (ORs) for seizures in offspring with or without maternal smoking during pregnancy. Even if the OR was not presented, the studies were included if the frequency of seizures in offspring according to maternal smoking during pregnancy was provided. The term "smoking during pregnancy" also encompasses cases where smoking occurred only during a part of the pregnancy period but does not include smoking only postnatally or when the mother smoked only pre-pregnancy. Studies without enough data were excluded. Papers using duplicate databases or not meeting the inclusion criteria were excluded, along with reviews, abstracts, and editorial materials.

Study selection and data extraction

Two authors (SY and KK) independently conducted the records search and screened the titles and abstracts of each study. The same authors then reviewed and evaluated the full-text articles for eligibility. During the study selection process, duplicate records were manually identified and removed. Any discrepancies were resolved through discussions among all authors. The final results were reached through consensus without any disagreements. During the screening phase, we extracted the following data: title, abstract, journal, author name, and year of publication. Further information on the number of cases with or without maternal smoking during

pregnancy, the number of cases with or without seizures, the type of seizure, and the age of subjects was obtained through full-text evaluations.

Data analysis and synthesis

ORs and 95% confidence intervals (CIs) were extracted directly from papers. If the OR was not presented, it was calculated along with the 95% confidence intervals (CIs) based on the frequency of the 2 × 2 contingency Table [25]. We used the classification of I^2 statistics to evaluate heterogeneity [26]. If the I^2 value exceeded 50%, a random-effects model was applied, whereas for values below 50%, a fixed-effects model was applied [27]. The generic inverse variance method was used as a basic model for meta-analysis. Review Manager 5.4 software was used to synthesize the results. The exposure of interest was maternal smoking during pregnancy, which was defined as any smoking that occurred during any part of the pregnancy period. This definition excluded cases where smoking occurred only before pregnancy or only after delivery. The primary outcome of this study was the occurrence of seizures in offspring associated with maternal smoking during pregnancy, regardless of seizure subtype. Secondary outcomes included specific seizure subtypes—febrile convulsion, epilepsy/afebrile seizure, and neonatal seizure—as well as the dose-response relationship between the number of cigarettes smoked per day during pregnancy and seizure risk in offspring. To further explore potential sources of heterogeneity and assess the robustness of the findings, we conducted sensitivity analyses (including a leave-one-out method and exclusion of studies rated as 'poor' in quality) and stratified analyses by study design (cohort vs. case–control) and seizure subtype.

To conduct a dose-response examination of the relationship between smoking and the seizures in offspring, we employed restricted cubic spline analysis [28]. To construct a linear dose-response profile, relevant data on number of cigarettes per day, along with the number of cases and associated OR, were extracted from studies featuring a minimum of 3 quantitative exposure categories. A dose-response graph was generated using the STATA 13 software to visually represent the association.

Risk of bias assessment

The Newcastle-Ottawa Scale was utilized to assess the risk of bias [29]. Two authors (SY and KK) independently evaluated the included studies for the risk of bias, and any disagreements were resolved through discussion among all authors.

Publication bias

We created a funnel plot using Review Manager 5.4 software to visualize potential publication bias. Rank correlation and Egger's regression test were utilized to quantitatively assess publication bias.

Certainty assessment

In this study, the Grading of Recommendations, Assessment, Development, and Evaluations (GRADE) approach was applied to determine how maternal smoking during pregnancy affects the occurrence of seizures in their offspring [30]. The body of evidence was classified as high, moderate, low, or very low based on five essential domains and two additional domains.

Results

Study selection and characteristics of the included studies

The search yielded 1024 articles. We then obtained 461 candidate articles for title and abstract review after excluding 667 non-human studies or non-articles. Forty-four articles underwent full-text review after excluding 417 duplicated or non-eligible articles based on their title and abstract. We conducted a full-text review of 44 articles, of which 30 were excluded due to reasons such as lack of reporting on the exposure or outcome of interest, irrelevant study population, or unmatched study design (Supplementary Table 2). In total, 14 studies were included in the meta-analysis, comprising eight cohort studies and six case–control studies [16–22, 31–37]. Finally, we obtained unadjusted estimates from studies for febrile convulsion (n = 6), epilepsy/unprovoked seizure (n = 4), and neonatal seizure (n = 2). Two studies included various types of seizures (Fig. 1).

The included studies exhibited substantial variation in sample size, ranging from fewer than 200 participants in case–control studies to over 11 million individuals in large population-based cohorts. Maternal age was reported inconsistently, with some studies presenting categorical groups (< 20, 20–24, 25–29, 30–34, ≥ 35 years), while others reported mean values with standard deviations, typically between 25 and 29 years. Information on maternal comorbidities was also inconsistently reported. However, several studies provided data on conditions such as gestational diabetes, hypertension, preeclampsia, eclampsia, anticonvulsant use, and previous abortion. The characteristics of the included studies are summarized in Table 1.

Overall seizure risk

Based on the results of 12,887,398 children reported in 14 observational studies, offspring with maternal smoking during pregnancy were at an elevated occurrence of seizures, with an OR of 1.49 (95% CI: 1.21–1.84, $p < 0.001$, $I^2 = 91\%$, p for heterogeneity < 0.001), compared with offspring whose mother did not smoke during pregnancy (Fig. 2). This result exhibited high heterogeneity among the included studies.

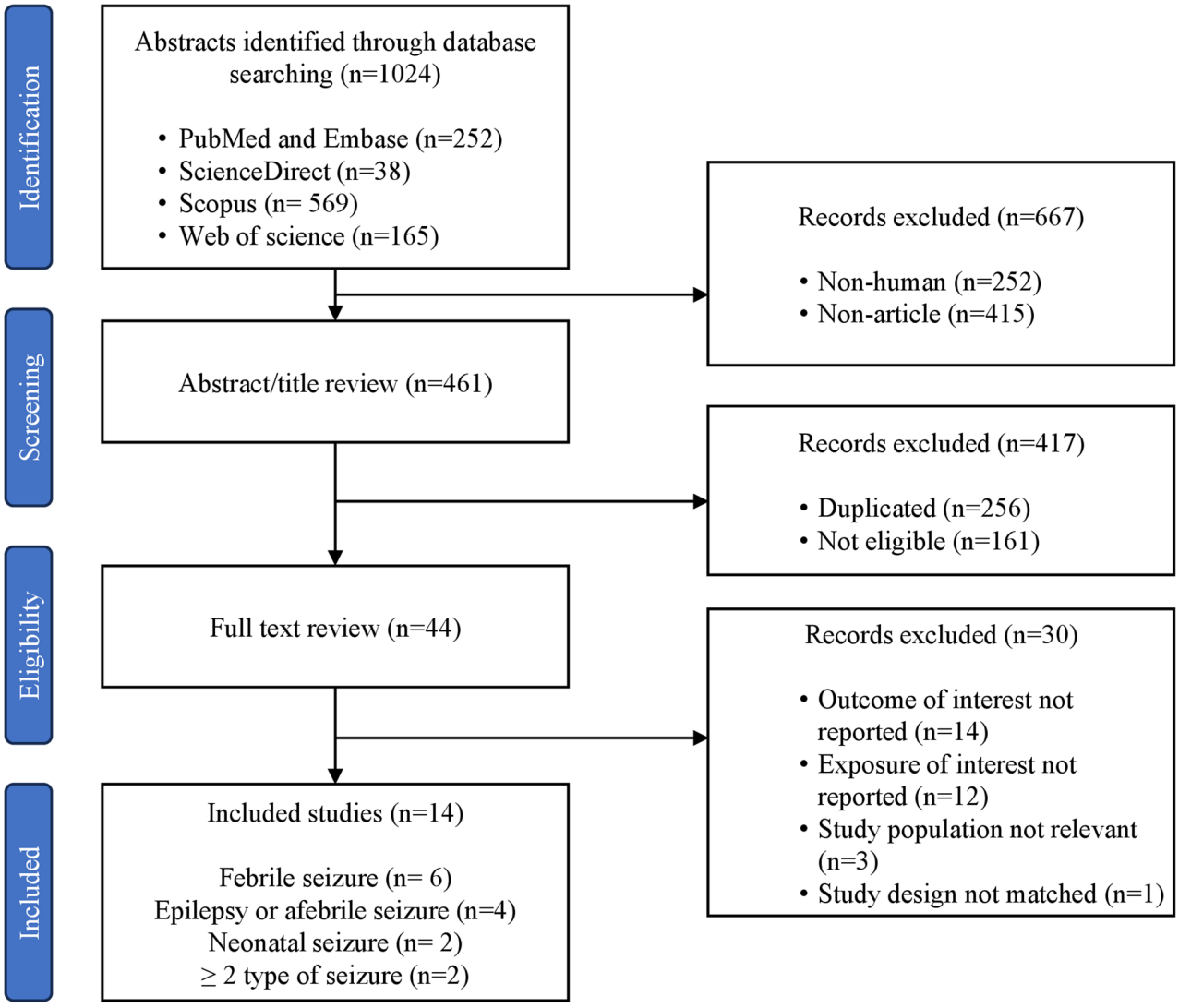

Fig. 1 Flow diagram illustrating the study selection process for the systematic review and meta-analysis

Subgroup analysis

In subgroup analyses by type of seizure, in febrile convulsion, offspring exposed to maternal smoking during pregnancy had a higher occurrence of seizures, with an OR of 1.36 (95% CI: 1.09–1.70, $p = 0.006$, $I^2 = 79\%$, p for heterogeneity < 0.001) based on 371,496 children from 8 studies, indicating high heterogeneity among the included studies (Supplementary Fig. 1). In epilepsy and afebrile seizure, this trend persisted with an OR of 1.30 (95% CI: 1.06–1.59, $p = 0.01$, $I^2 = 13\%$, p for heterogeneity = 0.33) based on 21,986 children from 6 studies (Supplementary Fig. 2). In neonatal seizure, newborns similarly exposed were at an even greater risk with an OR of 2.01 (95% CI: 1.50–2.70, $p < 0.001$, $I^2 = 74\%$, p for heterogeneity = 0.02) based on 12,510,908 children from 3 studies (Supplementary Fig. 3). Both case-control study (OR 1.84, 95% CI: 1.66–2.03, $p < 0.001$, $I^2 = 11\%$, p for heterogeneity = 0.34) and cohort study (OR 1.32 95% CI: 1.04–1.67, $p = 0.02$, $I^2 = 90\%$, p for heterogeneity < 0.001) showed a significant association in subjects with maternal smoking during pregnancy (Supplementary Fig. 4, and 5).

Sensitivity analysis and Dose-response analysis

Leave-one-out sensitivity analysis confirmed the stability of the overall effect size, with no single study disproportionately influencing the results despite consistently high heterogeneity (Supplementary Fig. 6). Furthermore, we conducted an additional sensitivity analysis by excluding studies rated as 'poor' in quality. The pooled effect size remained significant, with an OR of 1.83 (95% CI: 1.36–2.43, $p < 0.001$; I^2=27%, p for heterogeneity = 0.24) (Supplementary Fig. 7).

We conducted a dose-response analysis utilizing data from four studies (two cohort and two case-control) that included per-day information on smoking [16, 17, 31, 32]. Employing a restricted cubic splines model, we

Table 1 Characteristics of the included studies ($n=14$)

Study design: Cohort study						
Author (year)	**No. of Total**	**Cohort data and study period**	**Age of subject**	**Smoking category**	**Type of seizure (*n*)**	**Diagnostic criteria of seizure**
Rantakallio et al. (1987) [21]	3,664	Live births in Northern Finland (1966)	O: NA, 0–14 yr[b] M: NA	Smokers / non-smokers	Epilepsy ($n=71$)	At least one episode of paroxymal disturbances of consciousness, sensation, or movement
Nelson et al. (1990) [31]	260,588[a]	Collaborative Perinatal Project of the National Institute of Neurological Disorders and Stroke. (1983–1985)	O: NA M: (No. of frequency(rate/10,000)) 10–14 year: (85) 15–19 year: (2,248) 20–24 year: (3,624) 25–29 year: (2,144) 30–34 year: (1,157) 35–49 year: (742)	0/day 1–10/day 11–20/day 21–40/day 41–61/day	FS ($n=9999$)	An event in infancy or childhood, usually occurring between three months and five years of age, associated with fever but without evidence of intracranial infection or defined cause
Greenwood et al. (1998) [32]	16,080	British national cohort study (1970)	O: NA, followed to age 10 yr M: (No. of frequency) < 20 year: (1579) 20–24 year: (5766) 25–29 year: (4973) 30–34 year: (2424) ≥ 35 year: (1322)	Never Stopped pre pregnancy Stopped in pregnancy < 5/day 5–14/day + 15/day	FS ($n=375$) AFS ($n=63$)	Associated with fever but without evidence of intracranial infection or defined cause Idiopathic afebrile seizure was defined as a paroxysmal disturbance of consciousness, sensation, or movement, primarily cerebral in origin
Vahidnia et al. (2008) [33]	10,108	Child Health and Development Studies in the San Francisco-East, Bay Area (1959–1966)	O: NA M: (mean age ± standard deviation) Non-smoker, non-alcohol drinker: 27 ± 6.1 yr Smoker, non-alcohol drinker: 25 ± 5.9 yr Non-smoker, alcohol drinker: 29 ± 5.6 yr Smoker, alcohol drinker: 28 ± 5.7 yr	Smokers / non-smokers	FS ($n=209$)	Convulsion occurred concurrently with a high fever and systemic infection
Nunes et al. (2011) [20]	542	Population based birth cohort study, Passo Fundo, Brazil	O: followed to age 12 mo Epilepsy: 23 ± 12 mo FS, NS, AFS: NA M: NA	Smokers / non-smokers	FS ($n=27$) NS ($n=10$) Epilepsy ($n=11$) AFS ($n=8$)	Epilepsy was defined as a condition characterized by recurrent unprovoked seizures A single unprovoked seizure or cluster of seizures occurring in a time interval below 24 h was considered a single seizure episode.
Mitsuda et al. (2019) [19]	81,969	Birth cohort study, Japan environmental and children's study, 2011–2014	O: NA, followed to age 12 mo M: (No. of frequency) < 20 year: (578) 20–35 year: (60586) ≥ 35 year: (22914)	Smokers / non-smokers	FS ($n=978$)	C-1y questionnaire - diagnosed in their children when 12 months of age or younger.
Doty et al. (2020) [34]	11,572,364	United States vital statistics data sets on period linked birth–infant death, 2013–2017	O: Term infant (37–41 weeks of gestation) M: (No. of frequency) < 20 year: (832,694) 20–34 year: (93,52,352) ≥ 35 year: (1,551,104)	Smokers / non-smokers	NS ($n=2834$)	Any of the following: 5-minute Apgar score less than 5, assisted ventilation longer than 6 h, and neonatal mortality
Specht et al. (2020) [22]	1,556	Danish Civil Registration System, 1994–2002	O: followed to age 5yr M: Cases 28.7 ± 5.0 year, controls: 29.4 ± 4.7yr	Smokers / non-smokers	Epilepsy ($n=403$)	Epilepsy diagnosis (ICD-10 G40.9) occurring between 1 and 4 years of age.

Table 1 (continued)

Study design: Case–control study						
Author (year)	**No. of Total**	**Hospital or area**	**Age**	**Smoking**	**Type of seizure (n)**	**Diagnostic criteria of seizure**
Cassano et al. (1990) [17]	944	Greater Seattle, Washington	O: 8 ~ 34 mo[b] M: cases 26.0 ± 5.0 year, controls 28.1 ± 4.6 yr	Nonsmoker Quit smoking during pregnancy Smoked throughout pregnancy 1–10/day 11–20/day > 21/day	FS (n = 472)	Febrile seizure was defined as complex if it lasted more than 15 min, had lateralized onset, or was followed by another febrile seizure within 24 h. Simple febrile seizures lacked all these characteristics.
Berg et al. (1995) [16]	168	Emergency departments of one of three hospitals in Bronx, New York. 1989–1992	O: cases 19.0 mo, control 19.3 mo M: NA	None < 1/day 1–5/day 6–10/day 11–20/day > 20/day	FS (n = 69)	Seizure with fever ≥ 101 °F and no history of previous febrile or unprovoked seizures
Sidenvall et al. (2001) [35]	166	Va¨sterbotten, northern Sweden in 1985	O: NA, 0–15 yr[b] M: Cases 28 year, controls: 27 yr	Smokers / non-smokers	AFS (n = 58)	Unprovoked seizure if they occurred without an identifiable causative metabolic or an acute structural abnormality or occurred after the first week subsequent to an acute neurologic insult
Heydarian et al. (2018) [36]	175	Ghaem Hospital, Iran	O: 23.0 ± 17.8 mo (6–60 mo) M: NA	Smokers / non-smokers	FS (n = 97)	Not specified
Habbal et al. (2021) [37]	334	Three medical centers in Damascus, Syria.	O: (No. of frequency) 28d–23 mo: (61) 2–11 year: (82) 12–18 year: (24) M: NA	Smokers / non-smokers	Epilepsy (n = 167)	Simple febrile seizures are seizures which last from a few seconds to 15 min and do not recur during the same day while complex seizures last more than 15 min and may recur during 24 h
McLaren et al. (2022) [18]	938,074	United States Natality database from the National Center for Health Statistics in 2016–2018	O: Late preterm births neonate M: Cases 29 (24–34) yr, controls: 29 (24–34) yr	Smokers / non-smokers	NS (n = 498)	United States Natality database

AFS Afebrile seizure, *FS* Febrile seizure, *M* Maternal age, *mo* Months, *NA* Not available, *NS* Neonatal seizure, *O* Offspring's age, *yr* Years

a. Total number of non-smoker and their seizure frequency were not directly described, so we indirectly calculated

b. If age of subject is not described, recruiting criteria of age was noted instead

Age was presented as mean ± standard deviation, median (interquartile range)

identified a linear increase between maternal smoking during pregnancy and the OR of offspring seizure (Fig. 3). The calculated regression coefficient was 1.017 (95% CI: 1.001–1.033, p = 0.04), suggesting that for each additional cigarette smoked per day, the OR increased by 1.7%. In practical terms, smoking 10 cigarettes per day during pregnancy was associated with an approximately 18% higher risk of seizures in offspring, while smoking 20 cigarettes per day was associated with about a 40% higher risk, compared with non-smokers.

Risk of bias within studies

The quality of the 14 included studies was found to be quite diverse (Supplementary Table 3). Out of these studies, four were rated as "good", one as "fair", and ten as "poor".

Publication bias

The funnel plot for Fig. 4 shows no evidence of publication bias. Rank correlation yielded a p-value of 0.747, indicating no evidence of publication bias. Egger's test for

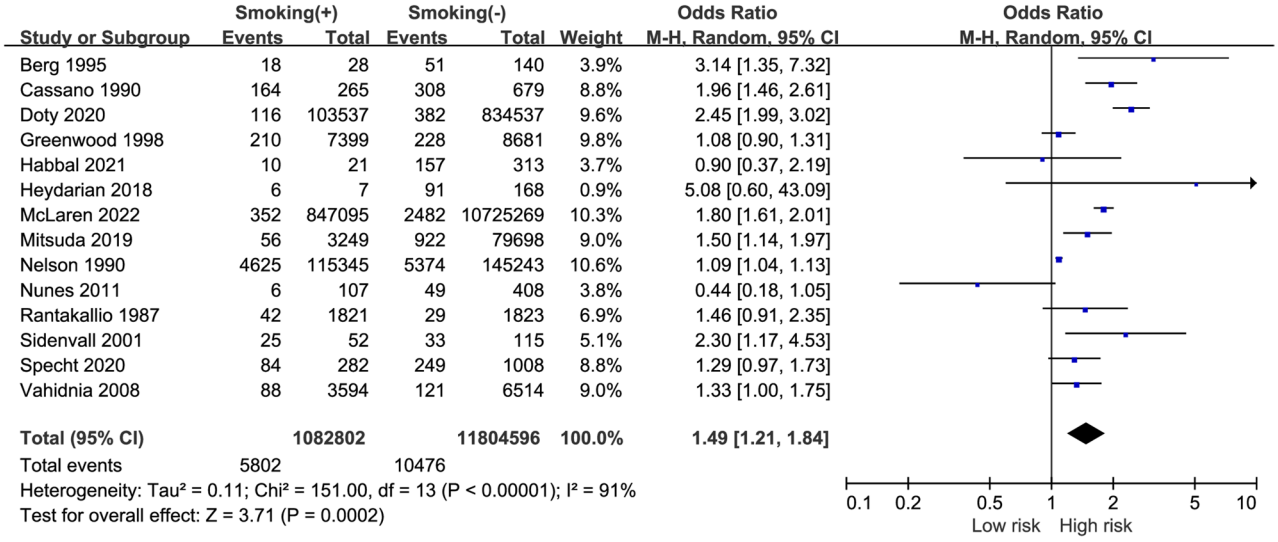

Fig. 2 Forest plot illustrating the association between maternal smoking during pregnancy and the risk of seizures in offspring

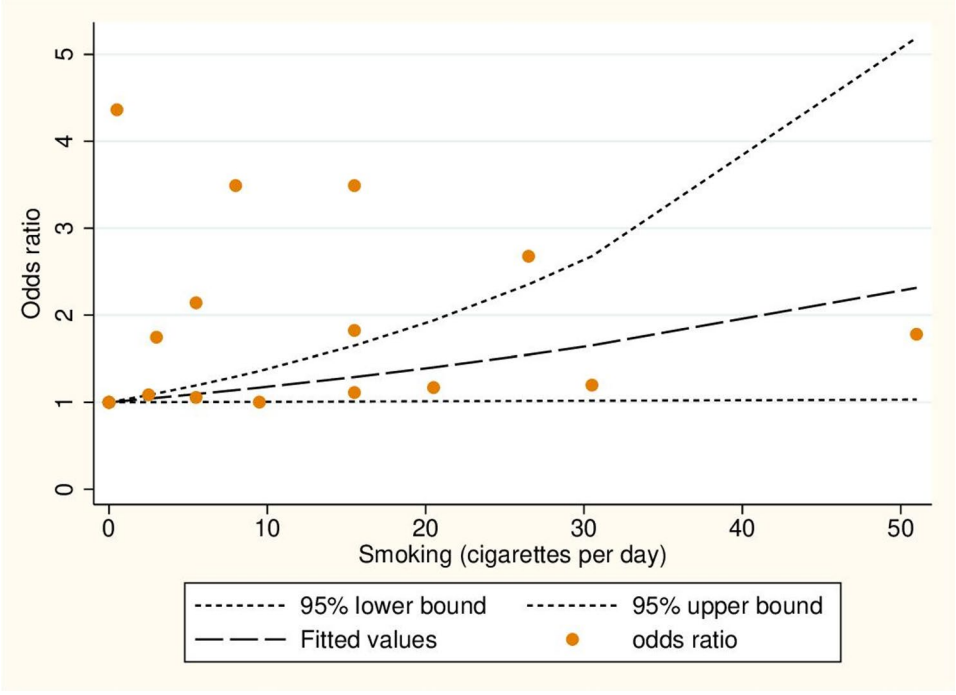

Fig. 3 Dose-response relationship between maternal smoking during pregnancy and the risk of childhood seizures, estimated using restricted cubic spline analysis (x-axis: maternal smoking per day; y-axis: odds ratio of childhood seizures)

a regression intercept yielded a *p*-value of 0.076, indicating no evidence of publication bias.

Certainty assessment

According to the GRADE approach, the certainty of the evidence for the primary outcome was rated as low. The assessment was performed on eight domains, and the results are summarized in Table 2.

Discussion

This study presents the first systematic literature review and meta-analysis elucidating the correlation between maternal smoking during pregnancy and seizure occurrence in offspring. Previous studies have yielded inconsistent findings regarding this association, with some reporting an elevated risk while others observing no discernible relationship. Our findings indicate that offspring exposed to maternal smoking during pregnancy exhibit a 49% increased likelihood of developing seizures

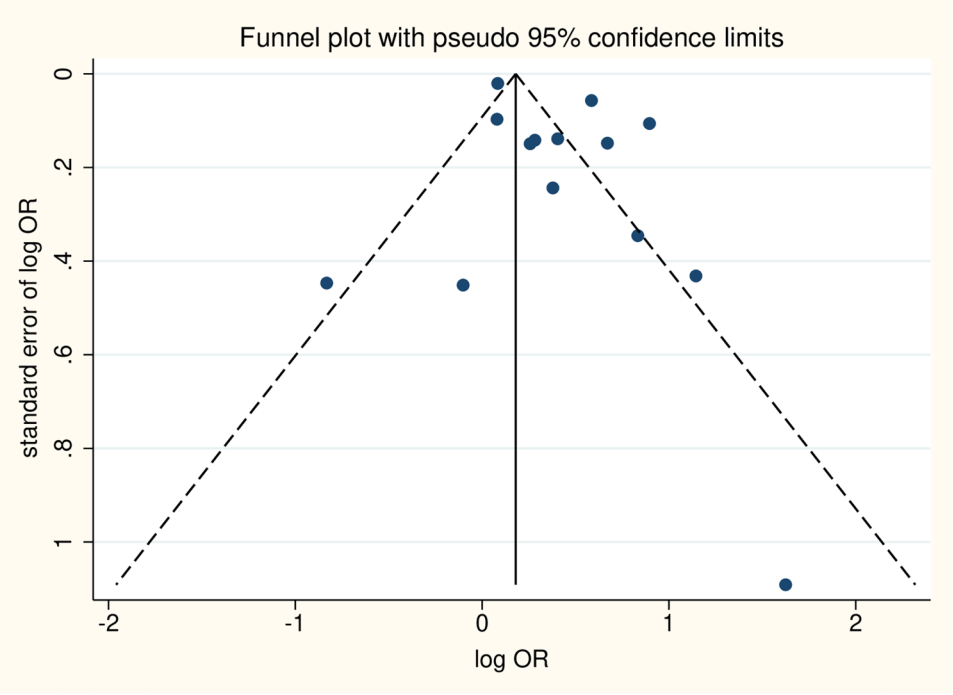

Fig. 4 Funnel plot assessing publication bias across 14 observational studies

Table 2 Grading of recommendations, assessment, development, and evaluations approach for the primary outcome

Outcomes	Certainty assessment									Effect	Certainty
	No. of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Dose-response association	Residual confounding	OR (95% CI)	
Maternal smoking - Pediatric seizure	14	Observational studies[a]	Serious[b]	Inconsistent[c]	Not serious[d]	Not serious[e]	Undetected[f]	Present	Present[g]	1.49 (1.21–1.84)	Low

CI Confidential interval, *OR* Odds ratio

[a]Study design: All included studies are observational design

[b]Risk of bias: Serious concerns due to the observational design of all included studies and the majority being rated as low quality using the Newcastle-Ottawa Scale

[c]Inconsistency: Serious inconsistency was observed with substantial heterogeneity ($I^2 = 91\%$) and a significant p-value

[d]Indirectness: No serious indirectness as the PICO elements were well aligned with the research question

[e]Imprecision: No serious imprecision as the pooled sample size was large and the confidence interval was narrow

[f]Publication bias: No strong evidence of publication bias according to Egger's test ($p = 0.076$)

[g]Residual confounding is likely given the observational design and variability in adjusted covariates across studies

compared to those unexposed. Subgroup analyses based on epilepsy type revealed significant correlations across febrile convulsion, epilepsy/afebrile seizure, and neonatal seizure. Furthermore, subgroup analyses based on study design consistently demonstrated significant associations in cohort and case-control studies. This study could fill a crucial gap in the literature by synthesizing epidemiological research on the association between maternal smoking during pregnancy and childhood epilepsy.

There is experimental evidence supporting the association between smoking, the central nervous system, and seizures. Tobacco smoke contains a complex mixture of over 5,000 toxic chemicals, including nicotine [38]. Recent studies have unveiled the negative impacts of smoking on the central nervous system, highlighting its effects on brain development, function, and volume; neurotransmitter activity; cognition; neurovascular diseases; and oxidative stress [9, 39]. Notably, maternal smoking during pregnancy has been shown to influence the gene expression critically involved in neurodevelopment and fetal brain programming of their child [40]. Moreover, research on nicotine-induced seizures in mice has demonstrated that nicotine triggers convulsive seizures by

activating neurons in the amygdala through nicotinic acetylcholine receptors [41].

In our study, substantial heterogeneity was observed, which may be attributed to differences in study design, population size, exposure definitions (e.g., timing and amount of maternal smoking), outcome classification (type of seizure), and inconsistent adjustment for confounders such as maternal age and family history of epilepsy. Despite these variations, our findings are consistent with previous studies indicating that maternal smoking during pregnancy is associated with adverse neurodevelopmental outcomes in offspring, including increased risks of attention deficit hyperactivity disorder (ADHD), cognitive impairment, and developmental coordination disorder [42–44]. In subgroup analysis, the ORs for neonatal seizure, febrile convulsion, and epilepsy/afebrile seizure were 2.01, 1.36, and 1.30, respectively. Although our study cannot explain why this difference in ORs exists according to seizure type, here are some speculative reasons for this difference. Firstly, the etiology of seizures differs among neonatal seizure, febrile convulsion, and epilepsy/afebrile [45, 46]. Second, the major causes of neonatal seizures, such as hypoxic-ischemic encephalopathy, ischemic stroke, and structural brain abnormalities, are among the factors associated with maternal smoking during pregnancy [9, 39, 45, 47, 48]. Third, epilepsy is a heterogeneous disorder with a wide range of age of onset, typically later than that of neonatal seizures and febrile convulsions [11]. The follow-up periods in the cohort studies may not be sufficient to confirm an association between epilepsy and maternal smoking during pregnancy.

In addition to assessing the overall association, we explored the dose-response relationship between maternal smoking during pregnancy and the risk of seizures in offspring. Using a restricted cubic spline model, we identified a linear trend indicating that seizure risk increases with the number of cigarettes smoked per day. Specifically, the odds ratio increased by approximately 1.7% for each additional cigarette smoked daily. This finding suggests a potential biological gradient, where higher levels of prenatal tobacco exposure may lead to a greater disruption of neurodevelopmental processes in the fetus. Such a dose-dependent relationship supports the plausibility of a causal link, in line with Bradford Hill's criteria [49]. Previous studies have also reported dose-response associations between maternal smoking and adverse neurodevelopmental outcomes, including cognitive deficits, mood disorders, and attention disorders, which further corroborates our findings [50]. However, it is important to interpret these results with caution, as only a subset of included studies provided quantitative data on daily cigarette consumption. The limited number of studies and potential residual confounding factors, such as socioeconomic status and concurrent substance use, may influence the observed association. Despite these limitations, the dose-response analysis adds valuable evidence suggesting that even low levels of maternal smoking can contribute to seizure risk, emphasizing the importance of complete smoking cessation during pregnancy. Future large-scale prospective studies with detailed exposure assessment are warranted to further elucidate this relationship.

Our study has several limitations. Firstly, most of the included studies focused solely on maternal smoking during pregnancy, without considering exposure to passive environmental smoking or paternal smoking. Second, only three studies on neonatal seizures were included, which may be insufficient to conclusively determine that neonatal seizures are the most vulnerable to maternal smoking during pregnancy. Third, our results were not adjusted for potential confounding factors, such as family history of febrile seizures or epilepsy, and maternal age. Fourth, Substantial heterogeneity was observed, which may reflect differences in study design, population size, exposure definitions (timing and amount of maternal smoking), seizure classification, and adjustment for confounders. This heterogeneity suggests that the pooled estimate should be interpreted cautiously, as the true effect may vary across different settings. Despite these limitations, our study, complemented by prior observational and experimental studies, provides evidence that maternal smoking during pregnancy impacts seizure occurrence in offspring, as demonstrated through the first meta-analysis. Interestingly, while the extent of this impact varies, maternal smoking during pregnancy affects all three types of seizure disorders in offspring.

Conclusions

Based on a systematic review and meta-analysis of 14 observational studies, maternal smoking during pregnancy is associated with a 49% increased risk of seizures in offspring. According to the GRADE framework, the certainty of evidence for this association is rated as low, due to the observational design of included studies, serious risk of bias, and inconsistency among results. Accordingly, while our findings suggest a significant association, they should be interpreted with caution, and further high-quality prospective studies are needed to confirm this relationship. Nevertheless, considering the preventable nature of maternal smoking and its known adverse effects on fetal neurodevelopment, our findings support advising against smoking during pregnancy. These results should be communicated to healthcare providers and prospective parents to aid in smoking cessation efforts during pregnancy. In addition, healthcare providers may incorporate this evidence into prenatal

counseling and design targeted smoking cessation programs to reduce preventable risks to child health.

Abbreviations

GRADE	Grading of Recommendations, Assessment, Development, and Evaluations
OR	Odds ratio
WHO	World Health Organization

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12884-026-08850-7.

Supplementary Material 1.

Supplementary Material 2.

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None.

Authors' contributions
Author ContributionsSukdong Yoo: data curation, formal analysis, and writing – original draft preparation. Kihun Kim: data curation, formal analysis, and writing – original draft preparation. Eunjeong Son: methodology, software, supervision. Tae-Jin Song: validation, supervision Hyun-Woo Kim: validation, supervision. Kihyuk Shin: methodology, software, supervision. Dai Sik Ko: methodology, software, supervision. Su-Yeon Cho: methodology, software, supervision. Yujin Kwon: methodology, software, supervision. Won Kyu Kim: conceptualization, data curation, formal analysis, project administration, and writing – reviewing, and editing. Yun Hak Kim: conceptualization, data curation, formal analysis, funding acquisition, project administration, and writing – reviewing, and editing. All authors contributed to editing the manuscript. All authors have read and agreed to the published version of the manuscript.

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Data availability
Data sharing is not applicable to this article as no new data were created or analyzed in this study.

Declarations

Ethics approval and consent to participate
This systematic review and meta-analysis used previously published data and did not require ethical approval, as it did not involve new data collection involving humans or animals.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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