Impact of Maternal Smoking During Pregnancy on Fetal and Neonatal Neurobehavioral Development: A Narrative Review

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ABSTRACT

BACKGROUND: Maternal smoking during pregnancy (MSDP) remains a common source of prenatal drug exposure worldwide. MSDP has been shown to increase fetal health risks and interfere with fetal development. Although newborns prenatally exposed to other substances (e.g., opiates, benzodiazepines) have been shown to have increased stress and withdrawal symptoms, few studies have explored the effect of MSDP on the fetal and neonatal periods.

METHODS: We performed a comprehensive search for empirical research articles investigating the effects of MSDP on fetal and neonatal neurobehavior and signs of abstinence in PubMed and PsycINFO databases. Our search yielded 11 fetal and 14 neonatal empirical articles published between 1980 and 2025.

RESULTS: In the fetal period, MSDP-exposed fetuses showed decreased fetal heart rate variability, and fetal movement and reactivity vs unexposed fetuses. In the early neonatal period (birth to five days), MSDP-exposed newborns showed increased excitability, irritability, need for handling, arousal, and alertness. In the late neonatal period (10 to 35 days), studies found MSDP to have an effect on neonatal self-regulation, attention, quality of movement, abnormalities in reflexes, lethargy, need for handling, and stress signs.

CONCLUSIONS: Our review of the literature revealed that MSDP has been associated with alterations in behavior suggestive of potential abstinence symptoms, especially found for excitability, irritability, hypertonicity, attention, reflex abnormalities, and stress/abstinence signs. Additional rigorous research needs to delineate the impact of MSDP on fetal and neonatal signs of abstinence to improve infant health.

KEYWORDS: pregnancy; smoking; infant; fetal; behavior; neurodevelopment; tobacco

INTRODUCTION

Although prevalence of cigarette use in pregnancy has declined in the US (approximately 5% of live births), rates are disproportionately higher in poor, young, Indigenous and Non-Hispanic White, and underserved populations, and in studies involving biochemical verification of tobacco use.[1] Further, rates of prenatal use of other nicotine and tobacco products (e.g., electronic cigarettes, hookah) continue to increase, and cigarette exposure remains a relevant behavioral health concern and common prenatal drug exposure worldwide.[2] In contrast to recreational use of other substances, cigarette use most commonly represents a repeated, daily habit that leads to consistent nicotine exposure to fetuses. Although rates of spontaneous quitting are increasing, a recent systematic review suggests that pregnant women who continue to smoke during pregnancy will do so into the last trimester.[2] This behavior continues to represent a major behavioral and public health problem, yet limited literature exists examining fetal and neonatal outcomes of maternal smoking during pregnancy (MSDP).

MSDP has the potential to interfere with fetal development in several ways, including intrauterine growth restriction, neuronal development, and epigenetic programming of placenta.[3-5] Neurobehavioral development can also be disrupted. Neurobehavior can be defined as the bidirectional relationship between biological impacts of the nervous system and behavioral output, such that infant neurobehavior is the one of the earliest observations of the integration of neurological, cognitive, emotional, and behavioral functioning.[6] Our recent paper used a novel, fetal, neurobehavioral-assessment system (FENS) to examine the relationship between MSDP and fetal neurobehavior.[7] We found fetuses exposed to MSDP had heightened fetal activity and increases in isolated head and limb movements. For infant outcomes, MSDP has been known to cause neonatal morbidity, mortality, and sudden infant death syndrome.[8-10] A meta-analysis investigated the impact of MSDP on pregnancy outcomes in 28 birth cohorts, with findings suggesting that MSDP is associated with small gestational size and preterm birth.[11] This relationship has been well-demonstrated in the literature, and therefore our review will solely focus on neurobehavior and not gestational growth or birthweight.[11,35]

A systematic review from Frogratt and colleagues reviewed 17 peer-reviewed articles investigating prenatal tobacco exposure on infant neurobehavior and temperament within the first year of life.[12] Within their review and meta-analysis, findings indicate that exposed infants had medium effect sizes for negative affect, attention, excitability, irrita-

bility, and orientation and small effect sizes for muscle tone, regulation, and difficult temperament.[12] Reporting on infant neurobehavior in the first year is an important developmental milestone, yet literature cites that there are observable differences in neurobehavior during fetal and neonatal development that can suggest the earliest signs of fetal/neonatal stress and possible signs of nicotine abstinence.

The current narrative review expands on the work of Frogratt and colleagues to investigate the impact of MSDP on fetal and neonatal neurobehavioral development and to determine if we can observe any possible alterations in neurobehavioral development that could suggest stress/abstinence in utero or neonatal period.[12] Thus, the focus of the current narrative review expands the literature by characterizing associations between MSDP and fetal and neonatal neurobehavior, including stress/abstinence symptoms.

METHODS

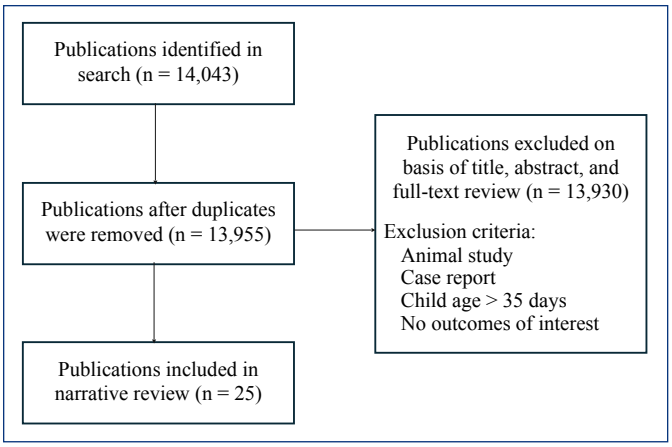
Eligibility Criteria and Search Strategy

A systematic review and meta-analysis on the impacts of maternal smoking during pregnancy and child neurobehavior within the first year of life was published in 2020. To extend findings to include the fetal and neonatal periods, the authors believed a narrative review with some systematic review methods would provide a thorough extension of the existing and niche literature.[12] Examining this specific window can provide insight into possible signs of neonatal abstinence to improve early detection and intervention. We performed a comprehensive literature search for empirical research articles investigating effects of MSDP on fetal and neonatal neurobehavior. We considered only peer-reviewed, original studies written in English published from 1980 to 2025. Two independent researchers screened studies for eligibility. PubMed and PsycINFO database searches used the search terms "pregnancy, maternal, and prenatal," "tobacco, cigarette, smoke, and smoking," and "neurobehavior, neurodevelopment, behavior, fetal, newborn, and neonatal," as well as backward searched of reference lists and forward searched of article citations. For the purposes of this narrative review, we define the early neonatal period as 0–5 days, and the late neonatal period as 10–35 days. Exclusion criteria included animal studies, case reports, infants over the age of five weeks, and studies that had intrauterine growth/birthweight as their only outcome. Our search yielded 25 empirical articles published between 1980 and 2025 for final analysis.

Selection and Data-Collection Process

Data collection was conducted by two independent researchers. The following information was extracted from each study: a) percentage of sample with MSDP exposure, b) average cotinine level for tobacco-exposed group (if reported), c) average cigarettes per day, d) number of neurobehavioral timepoints, e) type of tobacco, f) MSDP measurements, g) infant measurements, h) gestational or infant age, i) results, and j) study limitations.

Figure 1. Study Selection Diagram



Study Selection

The search resulted in 14,043 studies, and 13,955 were included after removal of duplicates. Broad terms were utilized to ensure research across disciplines, with varying terminology for pregnancy, smoking, and fetal/neonatal health, which resulted in a need to carefully review each study for relevance. After study titles and abstracts were reviewed, 13,930 studies were excluded for being animal studies, case reports, cohort studies about environmental or public health factors (e.g., pollution), examining outcomes outside of the fetal/neonatal window, examining fetal growth and birthweight as the sole outcome, and not being relevant to the goals of our review. Thus, 25 studies were given a full-text review [**Figure 1**].

Study Characteristics

The 25 studies included in the narrative review analyzed 2,850 infants and 419 fetuses with 1,408 of the infants/fetuses exposed to MSDP. Fourteen studies examined newborn neurobehavior outcomes and 11 studies examined fetal neurobehavioral outcomes. The neonatal studies were put into three categories: 1. Early Neonatal Outcomes (e.g., birth to five days postpartum), 2. Late Neonatal Outcomes (e.g., 10 to 35 days postpartum), and 3. Longitudinal Outcomes (e.g., any study with multiple measurement points between birth and 35 days postpartum). Fetal studies came from five countries and neonatal studies came from six countries.

RESULTS

Fetal Outcomes

Fetal neurobehavioral development was measured in 419 fetuses during 20- to 38-weeks' gestation. The primary constructs assessed were fetal heart rate variability and fetal

activity. Across 11 studies, 235 mothers engaged in smoking during pregnancy (56% of all pregnancies), and measured neurobehavioral outcomes using the Behavioral Reactivity Scale adapted from the Neonatal Behavioral Assessment Scale and Fetal Neurobehavioral Coding System. Fetal heart rate and motor activity was assessed using vibroacoustic stimuli, and maternal smoking during pregnancy was measured using salivary, carbon monoxide, and plasma samples, in addition to self-reporting cigarette use. Several studies reported decreased heart rate variability in fetuses with MSDP exposure, which can be a proxy for fetal distress.[13-15] Several studies also reported lower movement in fetuses with MSDP exposure, which included overall movements or solely trunk movements.[7,13,15,16] Some studies found differences in fetal activity such that fetuses with MSDP exposure had more small, isolated head and limb movements; whereas other studies found that fetuses were less reactive to stimuli or did not find any difference in fetal movements.[17-20] Cowperthwiate and colleagues found that fetuses exposed to MSDP had delayed recognition of maternal voice compared with non-exposed fetuses, and Thaler and colleagues (1980) reported increased breathing in MSDP-exposed fetuses.[21,16] Lastly, Gringas and colleagues did not report a significant difference in developmental or behavioral outcomes between exposed and non-exposed infants.[23]

Early Neonatal Outcomes

Early neonatal outcomes were measured from birth to five days postpartum in 1,868 infants. Across eight studies, 756 infants had MSDP exposure and their neurobehavioral outcomes were measured using NICU Network Neurobehavioral Scale, Finnegan scores, Graham-Rosenblith Behavioral Examination of the Neonate, Lipsitz score, Brazelton Neonatal Behavioral Assessment Scale, and Neonatal Temperament Assessment. Maternal smoking during pregnancy was measured using cotinine levels from saliva samples and maternal self-report. One of the key features noted across studies was increased excitability and irritability, and increased difficulty with regulation and consolability.[23-27] Several studies also document increased arousal as well as decreased alertness and attention.[23,7,27,28] Two studies reported the impact of withdrawal and abstinence on infants.[23,25] Interestingly, two studies had conflicting results related to muscle tone, such that Law and colleagues reported hypertonicity, and Godding and colleagues reported hypotonicity and decreased reflexes.[25,28] Lastly, there was a trend in the literature suggesting a dose-response relationship between cigarettes per day, cotinine levels, stress, and neurobehavioral functioning. Law and colleagues documented a dose-response relationship between more cigarettes per day/increased cotinine levels, and increased stress and signs of abstinence, such that as cigarette use and cotinine levels increased abstinence symptoms increased.[25] Godding and colleagues also observed a dose-response relationship between cotinine levels and reduced neurological functioning as measured by a neurological exam and Finnegan scores, such that increased cotinine levels have an inverse effect on neurological functioning in infants exposed to tobacco.[28]

Late Neonatal Outcomes

Late neonatal outcomes were measured from 10 to 35 days postpartum in 555 infants. Across four studies, 179 infants had MSDP exposure and their neurobehavioral outcomes were measured using NICU Network Neurobehavioral Scale and Neonatal Temperament Assessment. Maternal smoking during pregnancy was measured using cotinine levels from saliva samples and maternal self-report. Multiple studies both found decreased self-regulation.[29-31] Froggatt and colleagues also reported decreased motor quality and an increase in abnormal reflexes. Stroud and colleagues also reported that infants with MSDP exposure had an increased need for handling and increased arousal and excitability.[29,30] Yolton and colleagues reported both neurobehavioral and racial differences across infants with MSDP exposure.[31] MSDP-exposed infants demonstrated lower attention and quality of movement as well as increased stress and lethargy compared to infants without exposure.[31] Notably, racial differences between Black and White infants were observed across arousal, excitability, attention, and hypotonicity. Of particular significance, Wiebe and colleagues was the only study in the systematic review that reported there were not any differences between infants with and without exposure to tobacco across irritability, attention, and stress dysregulation.[32]

Longitudinal Neonatal Outcomes

Studies that included a longitudinal design for examining neonatal outcomes had multiple measurement points between birth and 35 days postpartum in 404 infants. These two studies included 196 infants with MSDP exposure, and their neurobehavioral outcomes were measured using Network Neurobehavioral Scale and Neonatal Temperament Assessment. Maternal smoking during pregnancy was measured using cotinine levels from saliva samples and maternal self-report. Only two studies have examined the longitudinal effects of MSDP with both assessing different neurobehavioral domains. Stroud and colleagues reported decreased attention and self-regulation across the first month of life, as well as increased lethargy and need for handling.[4] Epsy and colleagues found differences in attention at two days postpartum, yet those effects dissipate by four weeks postpartum. There also were not any significant differences in stress dysregulation and irritability across MSDP-exposed and non-exposed infants.[33]

DISCUSSION

This review aimed to synthesize the research on MSDP on fetal and neonatal neurobehavior to see if there could be early possible signs of stress or abstinence. Broadly, our review indicates that there are significant differences in fetal and neonatal neurobehavior as it relates to MSDP, which could suggest neonatal abstinence.

Further, fetal and neonatal neurobehaviors discussed in this review overlap with the clinical presentation of neonatal abstinence syndrome, including irritability, excessive crying, and difficulty soothing the baby.[34] Our review can expand on these findings by identifying early neurobehavioral patterns in utero and within the first month of life. With regards to fetal outcomes, the synthesis of our review yielded that fetuses with MSDP exposure had lower heart rate variability and, on the whole, lower fetal activity.[13-15,17-19] This finding comes with some nuance about the type and timing of fetal movement, such that MSDP may have increased isolated movements of their head and limbs (e.g., tremors) yet fewer trunk movements.[17] Taken together, these findings could suggest the presence of fetal distress as an immediate consequence of MSDP and, broadly, throughout gestation. However, further rigorous research is warranted as some studies did not find any significant differences across MSDP exposure.[20] For the early neonatal period, the literature suggests associations between MSDP exposure and hypertonicity, greater need for handling, more stress signs, and greater irritability within the first few days of life.[23-28] Two studies identified signs of stress, withdrawal, and abstinence.[23,25] In the late neonatal period, MSDP exposure was associated with worse self-regulation, increased need for handling, greater arousal and excitability, lower scores on attention, poor quality of movement, and increased stress signs.[29-31] For longitudinal studies, findings suggest that MSDP in the first month of life is associated with decreased attention and self-regulation, increased lethargy and need for handling, and no differences in irritability and stress dysregulation.[4,33] In sum, this review uniquely follows the trajectory of fetal and neonatal neurobehavioral development with alterations in behavior, suggestive of possible nicotine-abstinence symptoms. Decades of literature has documented the adult symptoms of nicotine withdrawal, including irritability, fatigue, and anxiety, and our review demonstrated a possible overlap with fetal and neonatal symptoms of withdrawal.[35]

From a clinical perspective, these findings can offer additional information about fetal and neonatal health to supplement smoking-cessation interventions. This information can be beneficial for both general smoking-cessation programs and prenatal smoking-cessation interventions to educate women on the immediate health impacts of prenatal smoking exposure. Similarly, our review can inform intergenerational behavioral-health interventions, as our findings could promote new postpartum and neonatal-care standards. For example, evidence-based protocols for neonatal abstinence syndrome, such as eat, sleep, console, could be useful for neonates with MSDP exposure.[36] Ultimately, our findings can further the scientific understanding of fetal and neonatal neurobehavioral development as it relates to nicotine abstinence and, in turn, inform behavioral-health i nterventions for mother and baby.

Although all of the studies in this review identify significant outcomes associated with MSDP, there are limitations. Many have a small sample size, low levels of smoking exposure, or used an unvalidated neurobehavior measure. Several studies did not include biochemical verification to measure nicotine exposure, which would have strengthened the ability to identify the impacts of MSDP. Furthermore, only two studies conducted assessments in the early neonatal period and repeated in the later neonatal period. Future research needs to delineate the impact of MSDP on fetal and newborn signs of abstinence to improve infant health.

CONCLUSIONS

MSDP is associated with poor infant outcomes, yet 5% of women continue to smoke during pregnancy.[1] Substantial research concludes that smoking during pregnancy has a causal effect on birthweight.[35,37] However, few studies have determined whether MSDP has an effect throughout gestation and into the neonatal period. MSDP exposure was associated with lower fetal heart rate variability, as well as hypertonicity, greater stress signs, and more need for handling in neonates. Neonatal studies, both in the first few days of life into the first month, suggest increased excitability, arousal, stress, and need for handling. These fetal and neonatal neurobehavioral alterations due to MSDP are suggestive of potential stress and abstinence symptoms. Given the known withdrawal effects of smoking cessation in adults and withdrawal symptoms caused by other drugs, we provide early evidence for possible fetal and neonatal abstinence from nicotine from observable differences in neurobehavioral development.

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Disclosures

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